PT J
AU Pelletier, JP
Martel-Pelletier, J
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AF Pelletier, Jean-Pierre
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TI Efficacy and safety of oral NSAIDs and analgesics in the management of osteoarthritis: Evidence from real-life setting trials and surveys
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English
DT Review
DE Analgesics; Coxibs; Cyclo-oxygenase-2 (COX-2) inhibitors; Knee osteoarthritis; Oral non-steroidal anti-inflammatory drugs (NSAIDs); Tramadol
ID nonsteroidal antiinflammatory drugs; upper gastrointestinal complications; knee osteoarthritis; double-blind; cardiovascular risk; tramadol; celecoxib; recommendations; release; placebo
AB Non-steroidal anti-inflammatory drugs (NSAIDs) are at the cornerstone of treatment for osteoarthritis (OA). In recent years, the widespread use of oral NSAIDs has been called into question due to the appearance of significant upper gastrointestinal (GI) complications and cardiovascular (CV) adverse events (AEs). However, NSAIDs are non-homogeneous, and there are noticeable differences between them in AE risk for GI and CV events. Nevertheless, if properly prescribed oral NSAIDs can provide an effective and safe treatment for OA in real-life situations. The identification of patients with significant CV and/or GI risk is critical, and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) treatment algorithm provides guidance on appropriate treatments for OA patients with elevated risk. Among non-selective NSAIDs, ibuprofen and naproxen seem preferable to diclofenac, the latter being associated with higher CV risk. Recommendation has been made by some that naproxen may be the preferred agent in patients at high CV risk because of its lower risk of CV events. Low dose celecoxib (200 mg/day) is also associated with a lower risk of CV events compared with other coxibs. In addition, drugs with a demonstrated low GI risk profile may be of benefit, such as coxibs and nabumetone. Among patients who fail to respond adequately to sequential ESCEO algorithm Step 1 and Step 2 treatments, the short-term use of weak opioids, such as tramadol, for severely symptomatic OA patients is recommended. Although studies exploring the efficacy of tramadol in OA are limited, there is good evidence that tramadol works if prescribed properly. The sustained-release (SR) formulation of tramadol is preferred as it avoids the peak plasma concentrations reached with immediate-release tramadol, and is believed to reduce the incidence of AEs. Furthermore, slow upwards titration of tramadol SR is recommended to improve

tolerability and minimize treatment discontinuations. (C) 2015 The Authors. Published by Elsevier HS Journals, Inc.
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TI The controversial relationship between osteoarthritis and osteoporosis: an update on hand subtypes
SO INTERNATIONAL JOURNAL OF RHEUMATIC DISEASES
LA English
DT Article
DE bone mineral density; erosive hand osteoarthritis; osteoarthritis; osteoporosis; phalangeal radioabsorptiometry
ID bone-mineral density; postmenopausal women; erosive osteoarthritis; knee osteoarthritis; hip; fracture; risk; polymorphisms; association; metabolism
AB Aim: To compare hand osteoarthritis (HOA) subtypes and to examine possible links with local bone mineral density (BMD). Method: Fifty-five patients with erosive

hand osteoarthritis (EHOA) and 21 patients with nodal hand osteoarthritis (NOA) fulfilling American College of Rheumatology criteria for HOA were evaluated. Subjects showing at least two erosions of the interphalangeal joints were assigned to the EHOA group; the others were considered NOA. Disease duration, number of active joints and radiological scores were assessed. All patients and 174 controls underwent phalangeal radiographic absorptiometry (pRA) of the middle phalanges of the non-dominant hand to assess BMD, T- and Z-scores. Results: BMD was higher in EHOA with respect to NOA and controls (P = 0.05); T- and Z-scores were significantly higher in EHOA (P = 0.01 and P < 0.01). Values suggestive of osteopenia were found in 32% of EHOA and 22% of NOA patients, and in 44% of controls (P = 0.05 EHOA vs. NOA); a T- score < -2.5 standard deviations was present in 15% of EHOA and 28% of NOA patients, and in 21% of controls (P = 0.05 EHOA vs. NOA). Conclusion: Phalangeal BMD was higher in EHOA compared to NOA and controls. This characteristic could potentially be exploited to differentiate the two hand OA subtypes.
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PT J
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TI Mortality with musculoskeletal disorders as underlying cause in Sweden 1997-2013: a time trend aggregate level study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Mortality; Musculoskeletal disorders; Temporal trend; Sweden
ID systemic-lupus-erythematosus; rheumatoid-arthritis; death certificates; prevalence; france; burden; osteoarthritis; statistics; cancer; impact
AB Background: The aim was to assess time trend of mortality with musculoskeletal disorders (MSD) as underlying cause of death in Sweden from 1997 to 2013. Methods: We obtained data on MSD as underlying cause of death across age and sex groups from the National Board of Health and Welfare's Cause of Death Register. Age-standardized mortality rates per million population for all MSD, its six major subgroups, and all other ICD-10 (International Classification of Disease) chapters were calculated. We computed the average annual percent change (AAPC) in the mortality rates across age/sex groups using joinpoint regression analysis by fitting a regression line to the natural logarithm of the age-standardized mortality rates and calendar year as a predictor. Results: There were a total of 7 976 deaths (0.5 % of all causes deaths) with MSD as the underlying cause of death (32.5 % of these deaths caused by rheumatoid arthritis [RA]). The overall age-standardized mortality rates (95 % CI) were 16.0 (15.4 to 16.7) and 24.9 (24.1 to 25.7) per million among men and women, respectively (women/men rate ratio 1.55; 95% CI 1.47 to 1.63). On average, mortality rate declined by 2.3 % per year and only circulatory system mortality had a more favourable decline than mortality with MSD as underlying cause. Among MSD the highest decline was observed in RA (3.7 % per year) during study period. Across age groups, while there were generally stable or declining trends, spondylopathies and osteoporosis mortality among people >= 75 years increased by 2 and 1.5 % per year, respectively. Conclusion: In overall, mortality with MSD as underlying cause has declined in Sweden over last two

decades, with the highest decline for RA. However, there are variations across MSD subgroups which warrants further investigations.
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Delany, Anne M.
TI MicroRNA variants as genetic determinants of bone mass
SO BONE
LA English
DT Review
DE miRNA; SNP; Osteoporosis; Osteoarthritis; Osteoblast; Osteoclast
ID mesenchymal stem-cells; regulates osteogenic differentiation; promotes osteoblast differentiation; morphogenetic protein receptors; gastric-cancer susceptibility; prostate-cancer; chondrocyte apoptosis; rheumatoid-arthritis; down-regulation; messenger-rna
AB Single nucleotide polymorphisms (SNPs) are the most abundant genetic variants that contribute to the heritability of bone mass. MicroRNAs (miRNAs, miRs) are key post-transcriptional regulators that modulate the differentiation and function of skeletal cells by targeting multiple genes in the same or distinct signaling pathways. SNPs in miRNA genes and miRNA binding sites can alter miRNA abundance and mRNA targeting. This review describes the potential impact of miRNA-related SNPs on skeletal phenotype. Although many associations between SNPs and bone mass have been described, this review is limited to gene variants for which a function has been experimentally validated. SNPs in miRNA genes (miR-SNPs) that impair miRNA processing and alter the abundance of mature miRNA are discussed for miR-146a, miR-125a, miR-196a, miR-149 and miR-27a. SNPs in miRNA targeting sites (miR-TS-SNPs) that alter miRNA binding are described for the bone remodeling genes bone morphogenetic protein receptor 1 (Bmpr1), fibroblast growth factor 2 (Fgf2), osteonectin (Sparc) and histone deacetylase 5 (Hdac5). The review highlights two aspects of miRNA-associated SNPs: the mechanism for altering miRNA mediated gene regulation and the potential of miR-associated SNPs to alter osteoblast, osteoclast or chondrocyte differentiation and function. Given the polygenic nature of skeletal diseases like osteoporosis and osteoarthritis, validating the function of additional miRNA-associated SNPs has the potential to enhance our understanding of the

genetic determinants of bone mass and predisposition to selected skeletal diseases. (C) 2015 Elsevier Inc All rights reserved.
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TI Chondroprotective effects of the combination chondroitin sulfate-glucosamine in a model of osteoarthritis induced by anterior cruciate ligament transection in ovariectomised rats
SO BIOMEDICINE & PHARMACOTHERAPY
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DE Anterior cruciate ligament transection model; Osteoarthritis; Chondroitin sulfate-glucosamine; Ovariectomised rats
ID knee osteoarthritis; articular-cartilage; biological markers; identify patients; gene-expression; bone-resorption; will respond; high-risk; kappa-b; osteoporosis
AB Context: The efficacy of the combination chondroitin sulfate-glucosamine (CS-GlcN) in the treatment of knee osteoarthritis (OA) has been suggested in recent clinical studies. In vitro reports have also suggested anti-inflammatory and anti-resorptive effects of this combination. Objective: The aim of this study was to characterize the effects of CS-GlcN on joint degradation in vivo including the assessment of inflammation and bone metabolism in a model of OA. Materials and methods: We have used the OA model induced by anterior cruciate ligament transection (ACLT) in ovariectomised rats. CS-GlcN was administered daily (oral gavage) from week 0 until week 12 after ovariectomy at the dose of 140 (CS) + 175 (GlcN)(HCl) mg/kg. Histochemical analyses were performed, the levels of biomarkers and inflammatory mediators were measured by luminex or ELISA and bone microstructure was determined by mu CT. Results: CS-GlcN protected against cartilage degradation and reduced the levels of inflammatory mediators such as interleukin-1 beta and tumor necrosis factor-a in the affected knee. In addition, serum biomarkers of inflammation and cartilage and bone degradation including matrix metalloproteinase-3, C-telopeptide of type II collagen and the ratio receptor activator of nuclear factor kappa B ligand/osteoprotegerin were significantly decreased by CS-GlcN. This treatment also tended to improve some bone microstructural parameters without reaching statistical significance. Discussion and conclusions: These results demonstrate the chondroprotective effects of CS-GlcN in vivo, in the experimental model of ACLT in ovariectomised rats, and suggest that this combination may be useful to control the joint catabolic effects of inflammatory stress. These findings could have clinical relevance related to the prevention of joint degradation by CS-GlcN and support the potential development of OA treatments based on this combination. (C) 2016 Elsevier

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PT J
AU Brooks, AK
Udoji, MA
AF Brooks, Amber K.
Udoji, Mercy A.
TI Interventional Techniques for Management of Pain in Older Adults
SO CLINICS IN GERIATRIC MEDICINE
LA English
DT Article
DE Interventional pain management; Chronic pain; Osteoarthritis; Steroid injection; Osteoporosis; Vertebral compression fracture
ID platelet-rich plasma; sacroiliac joint pain; medicare population; growth-patterns; united-states; osteoarthritis; injections; viscosupplementation; diagnosis; epidemiology
AB Chronic pain in older patients is often treated with pain medications, physical rehabilitation, interventional pain management, and/or psychological interventions. The administration of pain medications is the most common form of chronic pain treatment. Physiologic changes in older adults make them more susceptible to the potential side effects of oral pain medications, especially opioids. Interventional pain management offers an alternative treatment option. This article reviews some of the interventional techniques used to treat the most common sites of pain in older adults: back, knee, and hip.
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PT J
AU Kucharz, EJ
Kovalenko, V
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AF Kucharz, Eugene J.
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Szanto, Sandor
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Cooper, Cyrus
Reginster, Jean-Yves
TI A review of glucosamine for knee osteoarthritis: why patented crystalline glucosamine sulfate should be differentiated from other glucosamines to maximize clinical outcomes
SO CURRENT MEDICAL RESEARCH AND OPINION
LA English

DT Review
DE Glucosamine; Osteoarthritis; Symptomatic slow-acting drugs for osteoarthritis
ID placebo-controlled trials; total joint replacement; chondroitin sulfate; cartilage explants; double-blind; task-force; management; recommendations; chondrocytes; progression
AB The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) treatment algorithm for knee osteoarthritis (OA) recommends symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) first line for the medium to long term management of OA, due to their ability to control pain, improve function, and delay joint structural changes. Among SYSADOAs, glucosamine is probably the most widely used intervention. In the present review of glucosamine for knee OA, we have investigated whether the evidence is greater for the patented crystalline glucosamine sulfate (pCGS) preparation (Rottapharm/Meda) than for other glucosamine formulations. Glucosamine is actually widely available in many forms, as the prescription-grade pCGS preparation, generic and over-the-counter formulations of glucosamine sulfate (GS) and food supplements containing glucosamine hydrochloride (GH), which vary substantially in molecular form, pharmaceutical formulation and dose regimens. Only pCGS is given as a highly bioavailable once daily dose (1500mg) with a proven pharmacological effect. pCGS consistently reaches the plasma levels of around 10 mu M required to inhibit interleukin-1 induced expression of genes involved in the pathophysiology of joint inflammation and tissue destruction, compared with sub-therapeutic levels achieved with GH. It is evident, from careful consideration of the evidence base, that only the pCGS formulation of glucosamine reliably provides an effect size on pain that is higher than that of paracetamol and equivalent to that provided by non-steroidal antiinflammatory drugs. In comparison, the effect size on pain of non-crystalline GS preparations and GH from randomized controlled trials is repeatedly demonstrated to be zero. In addition, there is evidence that chronic administration of pCGS has disease-modifying effects, with a reduction in the need for total joint replacement surgery lasting for at least 5 years after treatment cessation. Consequently, the pCGS preparation (Rottapharm/Meda) is the logical choice, with demonstrated medium-term control of pain and lasting impact on disease progression.
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Z9 51
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PT J
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Eisenhauer, PT
Maltenfort, MG
Parvizi, J
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Maltenfort, Mitchell G.
Parvizi, Javad
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TI Identifying Patient-Specific Pathology in Osteoarthritis Development Based on MicroCT Analysis of Subchondral Trabecular Bone
SO JOURNAL OF ARTHROPLASTY
LA English

DT Article
DE osteoarthritis; subchondral bone; microCT; osteoclasts; VEGF
ID osteochondral junction; articular-cartilage; growth-factor; knee; osteoporosis; model; pathogenesis; hip; angiogenesis; arthritis
AB The goal of this study was to identify alternative mechanisms of osteoarthritis pathology by analyzing subchondral bone. Femoral condyle samples were collected from post-menopausal female patients with knee osteoarthritis undegoing total knee arthroplasty. In the majority of patients, subchondral trabecular bone volume doubled under a region of the medial femoral condyle with full-thickness cartilage deterioration. However, in a subset of patients the bone volume in this region remained constant. This subset also had larger areas of vascular penetration in the calcified cartilage of the lateral condyle concurrent with increased vascular endothelial growth factor expression. Subtyping by subchondral bone characteristics identified a unique population, which lacked the sclerotic bone characteristic of late-stage osteoarthritis. Identification of subtypes within the osteoarthritis population allows investigation of alternate disease pathologies. (C) 2016 Elsevier Inc. All rights reserved.
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PT J
AU Dawson, A
Dennison, E
AF Dawson, Alice
Dennison, Elaine
TI Measuring the musculoskeletal aging phenotype
SO MATURITAS
LA English
DT Review
DE Sarcopenia; Osteoporosis; Osteoarthritis; Frailty; Aging
ID older-adults; sarcopenia; osteoarthritis; prevalence; definition; frailty; epidemiology; consensus; criteria
AB The world is aging. The population aged over sixty years worldwide is predicted

to rise from 841 million in 2013 to more than 2 billion by 2050. Musculoskeletal (MSK) disease is a significant burden on the aging population, contributing 7.5% of the disease burden in those aged over 60 years. MSK diseases have a pronounced effect on disability level and independence in old age, with a consequent significant public health burden and impact on quality of later life. As numbers of older individuals and their disease burden increase, it is important to examine MSK disease in older life in detail. The musculoskeletal aging phenotype comprises four often interwoven key elements osteoporosis, osteoarthritis, sarcopenia and frailty and this review will focus on these four themes. It is crucial that we are able to accurately measure each phenotype in order that we might identify those individuals at greatest risk of developing these conditions, and design trials of therapeutic agents that might impact their development. Accurate measurement of the musculoskeletal aging phenotype is necessary firstly to document the burden of each condition, and then to enable factors to be identified which may accelerate or retard their development or progression. In some areas of MSK disease, this work is more advanced (osteoporosis); in other areas (sarcopenia) the field is currently very rapidly evolving. We will explore the tools currently used to measure the musculoskeletal aging phenotype and how they compare, as well as highlight areas where more work is needed. (C) 2016 Elsevier Ireland Ltd. All rights reserved.
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Z9 67
U1 0
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WC Geriatrics & Gerontology; Obstetrics & Gynecology
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AU Zampetti, S
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AF Zampetti, Stefania
Mariotti, Valentina
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Belcastro, Maria Giovanna
TI Variation of Skeletal Degenerative Joint Disease Features in an Identified Italian Modern Skeletal Collection
SO AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY
LA English
DT Article
DE osteoarthritis; marginal lipping; osteophytes; eburnation; porosity
ID standardized scoring method; foot-preference; age estimation; tibiofibular syndesmosis; entheseal changes; pulp/tooth ratio; osteoarthritis; enthesopathy; epidemiology; arthritis
AB Objectives: The objective of this study was to investigate the relationship of degenerative joint disease (DJD) features (marginal lipping, porosity, surface osteophytes, eburnation, and loss of joint morphology) with sex, age, and occupation. Materials and Methods: We devised a recording method for scoring the single features in the shoulder, elbow, wrist, hip, knee, and ankle of an Italian skeletal sample of 332 individuals (males = 161, females = 171) of known sex, age, and occupation from the Frassetto collection (Sassari, Sardinia, 19th-20th century). Results: Our data revealed that: (1) the frequency of all features increases with age; (2) porosity is the first feature to appear, being in general the most frequent feature in young adults; (3) sex differences are especially found in the upper limbs of mature and elderly adults; (4) marginal lipping and surface osteophytes show a

lesser age correlation and, in general, higher frequencies in the left lower limb; (5) no differences were found among different occupations. Discussion: We explain these results in light of different metabolic and adaptive processes in relation to age and sex. Static (weight-bearing) rather than dynamic mechanical stress could play a pivotal role in the distribution of the features observed in the lower limbs. The considerable increase in marginal lipping and surface osteophytes in elderly adults may be an adaptation for sustaining mechanical loading, balancing the loss of bone tissue which is characteristic of ageing processes (osteopenia, osteoporosis). (C) 2016 Wiley Periodicals, Inc.
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Wang, Qingwen
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Wen, Shuzheng
TI The polymorphism of rs1799750 in matrix metallopeptidase 1 (MMP-1) gene contributes to osteoarthritis risk: a meta-analysis
SO INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE
LA English
DT Review
DE Osteoarthritis; MMP-1 rs1799750; SNP; meta-analysis

ID single nucleotide polymorphism; genome-wide association; knee osteoarthritis; clinical-trials; candidate genes; susceptibility; promoter; population; expression; osteoporosis
AB Since 2010, many studies have investigated the association between common single nucleotide polymorphism (SNP) rs1799750 located on matrix metallopeptidase 1 (MMP-1) and osteoarthritis (OA) risk; however, the results were inconclusive. To shed light on these contradictory results, we investigated the association between MMP-1 rs1799750 and OA risk by meta-analytic techniques, combining all published data up to December 2015. A total number of 783 knee or temporomandibular joint (TMJ) OA cases and 748 controls in 5 case-control studies were included in this study and the odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Finally, individuals in homozygote comparison (1G1G vs. 2G2G: OR = 0.528, 95% CI: 0.285-0.979), heterozygote comparison (1G2G vs. 2G2G: OR = 0.599, 95% CI: 0.387-0.927) and dominant model (1G2G/1G1G vs. 2G2G: OR = 0.562, 95% CI: 0.346-0.913) were associated with a significantly decreased risk of OA. Sub-group analysis revealed that the homozygote comparison (1G1G vs. 2G2G: OR = 0.432, 95% CI: 0.251-0.746), heterozygote comparison (1G2G vs. 2G2G: OR = 0.411, 95% CI: 0.276-0.612) and dominant model (1G2G/1G1G vs. 2G2G: OR = 0.415, 95% CI: 0.285-0.603) still showed a decreased risk of OA in TMJ. As for ethnicity, in European, there was a statistically decreased OA risk in homozygote (1G1G vs. 2G2G: OR = 0.609, 95% CI: 0.378-0.980) and dominant model (1G2G/1G1G vs. 2G2G: OR = 0.591, 95% CI: 0.357-0.979). Together with the reported functional studies, the results suggested that MMP-1 rs1799750 was associated with a significantly decreased risk of OA, especially the TMJ OA.
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PT J
AU Harkema, L
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AF Harkema, L.
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TI Pathology of Mouse Models of Accelerated Aging
SO VETERINARY PATHOLOGY
LA English
DT Review
DE aging; mice; mouse models of human disease; pathology; phenotype; progeria; review
ID cardiovascular-disease enterprises; age-related-changes; intervertebral disc degeneration; regenerative hair waves; causes early-onset; skeletal-muscle; mutant mice; macular degeneration; major shareholders; stem-cells
AB Progeroid mouse models display phenotypes in multiple organ systems that suggest premature aging and resemble features of natural aging of both mice and humans. The prospect of a significant increase in the global elderly population within the next decades has led to the emergence of geroscience, which aims at elucidating the molecular mechanisms involved in aging. Progeroid mouse models are frequently used in geroscience as they provide insight into the molecular mechanisms that are involved in the highly complex process of natural aging. This review provides an overview of the most commonly reported nonneoplastic macroscopic and microscopic pathologic findings in progeroid mouse models (eg, osteoporosis, osteoarthritis, degenerative joint disease, intervertebral disc degeneration, kyphosis, sarcopenia, cutaneous atrophy, wound healing, hair loss, alopecia, lymphoid atrophy, cataract, corneal endothelial dystrophy, retinal degenerative diseases, and vascular remodeling). Furthermore, several shortcomings in pathologic analysis and descriptions of these models are discussed. Progeroid mouse models are valuable models for aging, but thorough knowledge of both the mouse strain background and the progeria-related phenotype is required to guide interpretation and translation of the pathology

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TI S3-Guideline non-traumatic adult femoral head necrosis
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DT Article
DE Atraumatic avascular necrosis; AVN; Diagnosis; Ilomedin; Bisphosphonate; Core decompression; Bone grafting; Bone transplant; Total hip replacement; Total hip arthroplasty
ID bone-marrow-edema; total hip-arthroplasty; transtrochanteric rotational osteotomy; rapidly destructive arthropathy; systemic-lupus-erythematosus; porous tantalum implant; term-follow-up; avascular necrosis; core decompression; early osteonecrosis
AB The treatment of adult non-traumatic avascular necrosis of the femoral head (AVN; N-ANFH) within an estimated incidence of 5000-7000 cases per annum in Germany remains a challenge. Risk factors include steroids, alcohol abuse, chemotherapy and immunosuppressive medication, but a genetic predisposition has been suggested. Early diagnosis of this often bilateral disease process is essential for successful conservative or joint preserving surgical management. In this review, we present the update German consensus S3 guideline "diagnosis and management for N-ANFH" as a concise summary. This systematic review is based on the published literature from January 1, 1970 to April 31, 2013 (German and English language). Inclusion criteria were systematic reviews, meta-analyses and relevant peer review publications. We identified a total of 3715 related publications, of which 422 were suitable according to the SIGN criteria, but only 159 fulfilled our inclusion criteria. Clinical suspicion of N-ANFH mandates radiographic evaluation. If radiographs are normal MRI scans are recommended, which should be evaluated according to the ARCO-classification. Differential diagnoses include transient osteoporosis, bone bruise, insufficiency fracture and destructive arthropathy. Untreated, subchondral fractures commonly occur within 2

years, during which the risk for contralateral involvement is high-thereafter unlikely. Conservative management with Ilomedin and Alendronat can be tried, but other pharmacological or physical treatments are inappropriate. No specific joint preserving procedure can be recommended, but core decompression should be considered in early stages if necrosis is < 30 %. In ARCO stages IIIc or IV total hip arthroplasty (THA) should be contemplated, which offers similar outcome compared to osteoarthritis. Young age is the main risk factor for higher revision rates after THA for N-ANFH.
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Z9 70
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PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
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AU Chagin, AS
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TI Effectors of mTOR-autophagy pathway: targeting cancer, affecting the skeleton
SO CURRENT OPINION IN PHARMACOLOGY
LA English
DT Article
ID regulates autophagy; bone-resorption; cell-death; inhibition; tumorigenesis; suppression; cartilage; rapamycin; deletion; growth
AB Although some modulators of autophagy are emerging as drugs or supplements for anti-cancer therapy, the effects of these compounds on normal tissues must be examined carefully. Here, I review the role of autophagy in skeletal tissues in this context.First, I briefly review preclinical studies indicating the role of autophagy in cancer, as well as related on-going clinical trials. Thereafter, the role of autophagy in the physiology of skeletal tissues is discussed, with a focus on recent genetic preclinical studies. Specifically, I discuss the mTOR-autophagy pathway in relationship to epiphyseal chondrocytes, articular chondrocytes, osteoblasts, osteocytes and osteoclasts and potential side effects of targeting either mTOR pathway or autophagy in general in connection with anti-cancer therapy.Current preclinical findings indicate that inhibiting autophagy will not seriously reduce bone mass and enhance osteoporosis. However, inhibition of autophagy might damage articular cartilage and cause osteoarthritis, whereas treatment with rapalogs might result in relatively beneficial effects on articular cartilage. Modulation of the mTOR pathway or autophagy during childhood may have an undesirable influence on adult height, as well as acquisition of bone mass.
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Tarner, Ingo
Frommer, Klaus
Neumann, Elena
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Kuerten, Bernhard
TI The impact of serial radon and hyperthermia exposure in a therapeutic adit on pivotal cytokines of bone metabolism in rheumatoid arthritis and osteoarthritis
SO CLINICAL RHEUMATOLOGY
LA English
DT Article
DE Anti-CCP antibodies (ACPA); Osteoprotegerin; Receptor activator of NF kappa-B ligand; Rheumatoid arthritis; Serial radon (adit) therapy; TNF-alpha
ID low-dose radon; kappa-b ligand; ankylosing-spondylitis; receptor activator; serum-levels; osteoporosis; inflammation; destruction; disease
AB Secondary osteoporosis is a frequent complication of rheumatoid arthritis (RA) and the result of an imbalance of catabolic and anabolic mechanisms of bone metabolism. The effects of serial low-dose radon and hyperthermia (LDRnHT) exposure in a therapeutic adit (12 applications in 3 weeks) on the serum levels of the cytokines osteoprotegerin (OPG), receptor activator of NF kappa-B ligand (RANKL), tumor necrosis factor-alpha (TNF-alpha), and also on the RANKL/OPG ratio were investigated in 25 RA patients and an age-matched control of 24 patients with osteoarthritis (OA). Cytokine measurements were performed at baseline and after completion of LDRnHT. Anti-CCP antibodies (ACPA) were measured in RA patients in parallel. Medication in both groups was limited to non-steroidal anti-inflammatory drugs, and low-dose prednisolone (16 of 24 RA patients) as needed. RA and OA patients showed a significant decrease of TNF-alpha levels ($p < 0.001$). Both groups showed significantly decreased levels of RANKL (RA: $p < 0.001$, OA: $p < 0.01$). Only the RA patients presented a significant increase of OPG ($p < 0.01$) and decrease of the RANKL/OPG ratio ($p < 0.01$), and the ACPA levels ($p < 0.001$). LDRnHT results in a reduction of osteocatabolic and an

increase of osteoanabolic cytokines, which represents the molecular basis for inhibiting osteoclastic activity in secondary osteoporosis and explains in part the effect of LDRnHT this physical therapy modality in a key inflammatory disease. Although reduced ACPA levels were observed under the therapy and although this could potentially contribute to an osteoprotective effect, in this case, it is rather uncertain as the reduction was only minor in magnitude.
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U2 11
PU SPRINGER LONDON LTD
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J9 CLIN RHEUMATOL
JI Clin. Rheumatol.
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WC Rheumatology
SC Rheumatology
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PT J
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Xu, JK
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TI Implant-derived magnesium induces local neuronal production of CGRP to improve bone-fracture healing in rats
SO NATURE MEDICINE
LA English
DT Article
ID gene-related peptide; traumatic brain-injury; in-vitro; vivo; osteoporosis; alloys; differentiation; osteoarthritis; innervation; expression
AB Orthopedic implants containing biodegradable magnesium have been used for fracture repair with considerable efficacy; however, the underlying mechanisms by which these implants improve fracture healing remain elusive. Here we show the formation of abundant new bone at peripheral cortical sites after intramedullary implantation of a pin containing ultrapure magnesium into the intact distal femur in rats. This response was accompanied by substantial increases of neuronal calcitonin gene-related polypeptide-alpha (CGRP) in both the peripheral cortex of the femur and the ipsilateral dorsal root ganglia (DRG). Surgical removal of the periosteum, capsaicin denervation of sensory nerves or knockdown in vivo of the CGRP-receptor-encoding genes Cakrl or Ramp1 substantially reversed the magnesium-induced osteogenesis that we observed in this model. Overexpression of these genes, however, enhanced magnesium-induced osteogenesis. We further found that an elevation of extracellular magnesium induces magnesium transporter 1 (MAGT1)-dependent and transient receptor potential cation channel, subfamily M, member 7 (TRPM7)-dependent magnesium entry, as well as an increase in intracellular adenosine triphosphate (ATP) and the accumulation of terminal synaptic vesicles in isolated rat DRG neurons. In isolated rat periosteum-derived stem cells, CGRP induces CALCRL- and RAMP1-dependent activation of cAMP-responsive element binding protein 1 (CREB1) and SP7 (also known as osterix), and thus enhances osteogenic differentiation of these stem cells. Furthermore, we have developed an innovative, magnesium containing intramedullary nail that facilitates femur fracture repair in rats with ovariectomy-induced osteoporosis. Taken together, these findings reveal a previously undefined role of magnesium in promoting CGRP-mediated osteogenic differentiation, which suggests the therapeutic potential of this ion in orthopedics.
C1 [Zhang, Yifeng; Xu, Jiankun; O'Laughlin, Micheal; Tian, Li; Shi, Dufang; Wang,

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Z9 998
U1 58
U2 875
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PA 75 VARICK ST, 9TH FLR, NEW YORK, NY 10013-1917 USA
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JI Nat. Med.

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WC Biochemistry & Molecular Biology; Cell Biology; Medicine, Research & Experimental
SC Biochemistry & Molecular Biology; Cell Biology; Research & Experimental Medicine
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AU Dumitrescu, TP
Santos, LL
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Schmith, V. D.
TI A Novel Method for Studying the Pharmacokinetics of [14C]Umeclidinium After

Application to the Axilla or Palm of Healthy Male Subjects
SO CTS-CLINICAL AND TRANSLATIONAL SCIENCE
LA English
DT Article
ID obstructive pulmonary-disease; topical glycopyrrolate; percutaneous-absorption; double-blind; hyperhidrosis; skin; umeclidinium; safety
AB Umeclidinium (UMEC), a long-acting muscarinic antagonist approved for chronic obstructive pulmonary disease (COPD), was investigated for primary hyperhidrosis as topical therapy. This study evaluated the pharmacokinetics, safety, and tolerability of a single dose of [C-14]UMEC applied to either unoccluded axilla (UA), occluded axilla (OA), or occluded palm (OP) of healthy males. After 8 h the formulation was removed. [C-14]UMEC plasma concentrations (Cp) were quantified by accelerator mass spectrometry. Occlusion increased systemic exposure by 3.8-fold. Due to UMEC absorption-limited pharmacokinetics, Cp data from the OA were combined with intravenous data from a phase I study. The data were described by a two-compartment population model with sequential zero and first-order absorption and linear elimination. Simulated systemic exposure following q.d. doses to axilla was similar to the exposure from the inhaled therapy, suggesting that systemic safety following dermal administration can be bridged to the inhaled program, and offering the potential for a reduced number of studies and/or subjects.
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NR 22
TC 3
Z9 3
U1 0
U2 1
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PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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PT J
AU Cong, Y
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Bao, NR
Guo, T
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AF Cong, Yu
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TI A single nucleotide polymorphism in the TGF-β1 gene (rs1982073 C>T) may contribute to increased risks of bone fracture, osteoporosis, and osteoarthritis: a meta-analysis
SO CLINICAL RHEUMATOLOGY
LA English
DT Article
DE Bone fracture; Meta-analysis; Osteoarthritis; Osteoporosis; Single nucleotide polymorphism; Transforming growth factor-beta 1
ID growth-factor-beta; transforming growth-factor-beta-1; japanese women; osteoblast differentiation; knee osteoarthritis; mineral density; in-vivo; association; expression; susceptibility
AB Genetic factors have been shown to be of great importance for the pathogenesis of bone diseases, such as fracture, osteoporosis (OP), and osteoarthritis (OA). However, published studies on the correlations of transforming growth factor-beta 1 (TGF-beta 1) gene polymorphisms with bone diseases have been hampered by small sample sizes or inconclusive findings. We hence aimed at examining the relationships between a single nucleotide polymorphism in the TGF-beta 1 gene (rs1982073 C > T) with bone fracture, OP, and OA risks in this meta-analysis. A systematic electronic search of literature was conducted to identify all published studies in English or Chinese on the association between the TGF-beta 1 gene and fracture, OP, or OA risks. Data were abstracted independently by two reviewers. To investigate the strength of this relationship, crude odds ratios with 95 % confidence intervals were used. An updated meta-analysis based on nine independent case-control studies were chosen (patients with fracture, OP, or OA =

1569; healthy controls = 1638). Results identified a higher frequency of rs1982073 C > T in patients with fracture, OP, or OA than in healthy controls. Ethnicity and genotyping method-stratified analysis under both models implied that the rs1982073 C > T polymorphism was positively correlated with the risk of fracture, OP, and OA among Asians under detection via the non-PCR-RFLP method. Disease-stratified results yielded that rs1982073 C > T may increase the risk of fracture, OP, and OA under the allele model, but was only significantly related to OP under the dominant model. According to the sample size-stratified analysis, subjects with the rs1982073 C > T polymorphism in the allele model were more likely to develop the three bone diseases in both the small and large sample size groups, and only in the large sample size under the dominant model. Our findings show that TGF-beta 1 rs1982073 C > T has a modest effect in increasing susceptibility to bone fracture, OP, and OA.
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TI The relationships between bone mineral density and radiographic features of hand or knee osteoarthritis in older adults: data from the Dong-gu Study
SO RHEUMATOLOGY
LA English
DT Article
DE osteoarthritis; bone mineral density; radiography
ID osteoporotic fractures; degenerative disease; postmenopausal women; elderly men; hip; association; population; cartilage; mass; rotterdam
AB Objective. The relationship between OA and osteoporosis has exhibited contradictory features over the past four decades. The aim of this study was to determine using separate analysis of the radiographic features of OA whether various radiographic features of OA were associated differently with BMD in the Korean elderly. Methods. Data were derived from the Dong-gu cohort; 2354 subjects were enrolled in the present cross-sectional study. Baseline characteristics, the BMDs of the lumbar spine and femoral neck measured by DXA, and X-rays of knees and hands were collected. A semi-quantitative grading system was used to estimate the severities of individual radiographic features. We adjusted for confounders using multiple linear regression modelling to analyse the relationships. Results. After adjustment for confounders, hand and knee OA total scores were negatively associated with the BMDs of the lumbar spine and femoral neck, except for the total knee OA score and lumbar spine BMD. In detail, hand osteophytes and sclerosis exhibited positive relationships with the BMDs of the lumbar spine and femoral neck, except for hand osteophytes and femoral neck BMD. On the contrary, however, knee joint space narrowing (JSN), hand JSN, and hand subchondral cysts were negatively associated with the BMD of the lumbar spine and femoral neck. Knee JSN and hand subchondral cysts exerted the greatest effects on BMD. Conclusion. Separate analysis of the radiographic features of OA better reveals associations of OA with the BMD of the lumbar spine and femoral neck.
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AU Kodama, R
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TI Prevalence of hand osteoarthritis and its relationship to hand pain and grip strength in Japan: The third survey of the ROAD study
SO MODERN RHEUMATOLOGY
LA English
DT Article
DE Erosion; Hand; Osteoarthritis; Population-based; Prevalence

ID united-states; erosive osteoarthritis; beijing osteoarthritis; general-population; association; determinants; disability; progression; rotterdam; profile
AB Objectives: To examine the prevalence and pattern of hand osteoarthritis (HOA), and determine its relationship with grip strength and hand pain. Methods: Among the participants of the third survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study, 507 Japanese men and 1028 Japanese women were included. Radiographs of both hands were graded for osteoarthritis (OA) using the modified Kellgren-Lawrence (KL) scale. HOA was defined as the presence of at least one affected joint. The absence or presence of subchondral erosion was also scored. Results: The prevalence of HOA (KL grade >= 2) was 89.9% in men and 92.3% in women (p = 0.11), and it was significantly associated with age. OA in the distal interphalangeal (DIP) joint was the highest overall. After adjusting for age, sex, body mass index, and the residing area, both severity (KL grade >= 3) and erosion were significantly related to low grip strength and hand pain. With regard to the joint groups, severe OA in the DIP and first carpometacarpal joints were related to hand pain. Conclusion: This study showed a high prevalence of radiographic HOA and a significant relationship between hand pain and the severity of HOA, in addition to erosion.
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24659666, 26293329] Funding Source: KAKEN
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U2 3
PU TAYLOR & FRANCIS LTD
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PT J
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TI Merge of motion analysis, multibody dynamics and finite element method for the subject-specific analysis of cartilage loading patterns during gait: differences between rotation and moment-driven models of human knee joint
SO MULTIBODY SYSTEM DYNAMICS
LA English
DT Article
DE Menisci; Fibril-reinforced; Kinesiology; Computational model; Cartilage; Fibril-reinforced; Poroelastic
ID split-line pattern; anterior cruciate ligament; articular-cartilage; stance phase; in-vivo; unconfined compression; mechanical-behavior; collagen network; contact stresses; muscle forces
AB Understanding joint loading is important when evaluating sports training methods, sports equipment design, preventive training regimens, post-op recovery procedures, or in osteoarthritis' etiology research. A number of methods have been introduced to estimate joint loads but they have been limited by the lack of accuracy in the joint models, including primarily the lack of patient-specific motion inputs in the models with sophisticated, fibril-reinforced material models. The method reported here records and applies patient-specific human motion for in-depth cartilage stress estimation. First, the motion analysis of a subject was conducted. Due to skin motion, multibody simulation was used to correct motion capture. These data was used as an input in a finite element model. The model geometry was based on magnetic resonance imaging and cartilage was modeled as a fibril-reinforced poroviscoelastic material. Based on the experimental motion data (motion analysis and multibody simulation), two models were created: a rotation-controlled and a moment-controlled model. For comparison, a model with motion input from the literature was created. The rotation-controlled model showed the most even stress distribution between lateral and medial compartments and smallest stresses and strains in a depth-wise manner. The model based on the literature motion simulated very high stresses and uneven stress distribution between the joint compartments. Our new approach to determine dynamic knee cartilage loading enables estimations of stresses and strains for a specific subject over the entire motion cycle.
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TI The Mandibles of Castrated Male Rhesus Macaques (Macaca mulatta): The Effects of Orchidectomy on Bone and Teeth
SO AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY
LA English
DT Article
DE testosterone; osteoporosis; oral pathology; life span; Cayo Santiago
ID individual life-history; sex steroid-hormones; cayo-santiago; postmenopausal women; periodontal-disease; prostate-cancer; nonhuman-primates; dental pathology; controlled-trial; mineral density
AB Objectives: The objectives of this study were to evaluate the long-term effects of orchidectomy and low testosterone on the craniofaciodental development and maintenance of skeletal and oral health in rhesus macaques. Materials and Methods: Mandibles of four castrated and intact age-matched male rhesus monkeys (Macaca mulatta) from Cayo Santiago were compared for mandibular morphology and teeth, abnormalities, pathology, and cortical bone thickness and density using a digital sliding caliper and analysis of three-dimensional X-ray images. Results: Although all four castrates were generally comparable to intact males in overall mandible and teeth size, there were some significant differences. In the castrates, (1) the distance between the two rami was narrower than in intact males leading to a relatively narrower and longer face; (2) both the mandibular body and ramus had thinner cortical bone leading to less total bone mass; and (3) the canines and molar teeth were slender with lower and less robust tooth cusps. In addition, the alveolar bone of two geriatric castrates was greatly receded with signs of periodontitis more severe than in intact aged males. Old castrates also had severe temporomandibular joint osteoarthritis. Discussion: The findings suggest the importance of testosterone in craniofaciodental development, and maintenance of skeletal and oral health in male macaques. These results suggest that dental health professionals might want to include in their medical history questionnaires whether or not male patients have taken hormone (testosterone) replacement therapy. (c) 2015 Wiley Periodicals, Inc.
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TI Evolving Role of Molecular Imaging with 18F-Sodium Fluoride PET as a Biomarker for Calcium Metabolism
SO CURRENT OSTEOPOROSIS REPORTS
LA English
DT Review
DE 18F-sodiumfluoride; Metabolic bone disease; Positron emission tomography; Quantitative radionuclide imaging; Regional bone formation
ID positron-emission-tomography; regional bone metabolism; early-stage osteoarthritis; f-18-fluoride pet; parathyroid-hormone; ankylosing-spondylitis; postmenopausal women; risk-factors; vascular inflammation; plaque inflammation
AB F-18-sodium fluoride (NaF) as an imaging tracer portrays calcium metabolic activity either in the osseous structures or in soft tissue. Currently, clinical use of NaF-PET is confined to detecting metastasis to the bone, but this approach reveals indirect evidence for disease activity and will have limited use in the future in favor of more direct approaches that visualize cancer cells in the read marrow where they reside. This has proven to be the case with FDG-PET imaging in most cancers. However, a variety of studies support the application of NaF-PET to assess benign osseous diseases. In particular, bone turnover can be measured from NaF uptake to diagnose osteoporosis. Several studies have evaluated the efficacy of bisphosphonates and their lasting effects as treatment for osteoporosis using bone turnover measured by NaF-PET. Additionally, NaF uptake in vessels tracks calcification in the plaques at the molecular level, which is relevant to coronary artery disease. Also, NaF-PET imaging of diseased joints is able to project disease progression in osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Further studies suggest potential use of NaF-PET in domains such as back pain, osteosarcoma, stress-related fracture, and bisphosphonate-induced osteonecrosis of the jaw. The critical role of NaF-PET in disease detection and characterization of many musculoskeletal disorders has been clearly demonstrated in the literature, and these methods will become more widespread in the future. The data from PET imaging are quantitative in nature, and as such, it adds a major dimension to assessing disease activity.
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TI Balancing benefits and risks of glucocorticoids in rheumatic diseases and other inflammatory joint disorders: new insights from emerging data. An expert

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SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
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ID low-dose prednisone; modifying antirheumatic drugs; tight control strategy; to-target strategy; cardiovascular events; eular recommendations; myocardial-infarction; oral corticosteroids; diabetes-mellitus; serious infection
AB This consensus review article considers the question of whether glucocorticoid (GC) therapy is still relevant in the treatment of rheumatic diseases, with a particular focus on rheumatoid arthritis (RA), and whether its side effects can be adequately managed. Recent basic and clinical research on the molecular, cellular and clinical effects of GCs have considerably advanced our knowledge in this field. An overview of the subject seems appropriate. This review is the result of a multidisciplinary expert working group, organised by European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis. The recent literature was surveyed and the salient evidence synthetized. The pathophysiological basis of RA (and other inflammatory rheumatic diseases) now strongly implicates the adaptive immune system in addition to innate mechanisms. The molecular effect of GCs and differential GC sensitivity is better understood, although exploiting this knowledge is still in its infancy. The newer treatment strategies of early and aggressive control of RA have gr eatly improved clinical outcomes, but improvements are still possible. Newer targeted anti-inflammatory drugs have made an important impact, yet they too are associated with numerous side effects. Short durations of moderate doses of GCs are generally well tolerated and have a positive benefit/risk ratio. Patients should be assessed for fracture risk and bone preserving agents and be prescribed calcium and vitamin D supplementation. Within a strategy of a disease modifying approach to inflammatory disease, combination therapy including a GC is effective approach.
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NR 170
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PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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AU Ng, PY
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AF Ng, P. Y.
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Dass, C. R.
TI Treatment of bone disorders with parathyroid hormone: success and pitfalls
SO PHARMAZIE
LA English
DT Review
ID vertebral fracture risk; postmenopausal women; strontium ranelate; biochemical markers; osteoporosis; teriparatide; denosumab; metastases; disease; protein
AB Bone diseases such as osteoporosis, osteoarthritis, bone tumours and bone fractures are rather common and not just in the elderly. Parathyroid hormone (PTH) is responsible for maintaining calcium homeostasis, increasing bone mineral density (BMD), increasing cortical and trabecular bone thickness and thus increasing bone strength. Teriparatide (PTH 1-34) has the same effects as endogenous PTH and is pharmacologically used to treat bone diseases such as osteoporosis, osteoarthritis, bone fractures and bone tumours. This review discusses how PTH 1-34 plays a role in managing bone diseases. Clinical studies have shown that short or intermittent dosing of PTH 1-34 has minimal adverse effects, while long-term dosing (over two years) has been linked to de novo osteoarthritis and bone deformation. Currently PTH therapy is only approved in the treatment of post-menopausal osteoporosis, however it is also proven to have effects in treating osteoarthritis, bone tumours and bone fractures. If the patient undergoing therapy is closely monitored, the major pitfalls are very unlikely to take place, thus it is highly recommended that patients be closely monitored by a medical practitioner.
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NR 53
TC 9
Z9 10
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TI u Effects of Dairy Products Consumption on Health: Benefits and Beliefs-A Commentary from the Belgian Bone Club and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Review
DE Dairy products; Cardiovascular disease; Osteoporosis; Arthritis; Weight management; Lactose intolerance
ID randomized controlled-trials; nutrition examination survey; vitamin-d supplementation; placebo-controlled trial; dietary-protein intake; hip fracture; postmenopausal women; calcium supplementation; rheumatoid-arthritis; prospective cohort
AB Dairy products provide a package of essential nutrients that is difficult to obtain in low-dairy or dairy-free diets, and for many people it is not possible to achieve recommended daily calcium intakes with a dairy-free diet. Despite the established benefits for bone health, some people avoid dairy in their diet due to beliefs that dairy may be detrimental to health, especially in those with weight management issues, lactose intolerance, osteoarthritis, rheumatoid arthritis, or trying to avoid cardiovascular disease. This review provides information for health professionals to enable them to help their patients make informed decisions about consuming dairy products as part of a balanced diet. There may be a weak association between dairy consumption and a possible small weight reduction, with decreases in fat mass and waist circumference and increases in lean body mass. Lactose intolerant individuals may not need to completely eliminate dairy products from their diet, as both yogurt and hard cheese are well tolerated. Among people with arthritis, there is no evidence for a benefit to avoid dairy consumption. Dairy products do not increase the risk of cardiovascular disease, particularly if low fat. Intake of up to three servings of dairy products per day appears to be safe and may confer a favourable benefit with regard to bone health.
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TC 197
Z9 250
U1 4
U2 75
PU SPRINGER
PI NEW YORK
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AU Sadat-Ali, M
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TI High-Resolution Peripheral Quantitative Computed Tomography (HR-PQCT) and Dual Energy X-Ray Absorptiometry (DXA) Measurements of Proximal Tibia in Patients Undergoing Total Knee Arthroplasty
SO INTERNATIONAL SURGERY
LA English
DT Article
DE pQCT; Proximal tibia; Osteoporosis; Osteoarthritis
ID bone-mineral density; total hip-arthroplasty; trabecular bone; osteoarthritis; osteoporosis; women; microarchitecture; bmd
AB The aim of the study was to assess bone morphometric indices of the proximal tibia and compare it with bone mineral density (BMD) at hip and lumbar spine and compare with the pQCT. Fifty consecutive patients who underwent total knee arthroplasty (TKA) had a dual energy X-ray absorptiometry (DXA) scan of the upper femur and lumbar spine. Upper tibial cuts were harvested from the tibial condyles and a DXA of tibial cuts was done during TKA. Bone morphometry studies were carried out using HR-pQCT. The bone mineral density at the hip was 0.54 +/- 0.08 g/cm(2) and spine was 0.73 +/- 0.1 with a T score at the hip -2.23 +/- 0.44 and spine -2.61 +/- 0.45. The bone mineral density of the tibial cut was 0.356 +/- 0.03 g/cm(2) ($P < 0.001$) and Tscore was 6.58 +/- 2.87 ($P < 0.001$). The average bone volume (BV) was 115.27 +/- 40.45 mm(3), trabecular number (Tb.N) was 1.45 +/- 0.32 (1.009-2.37) and trabecular thickness (Tb.Th) was 0.181 +/- 0.03 mm (0.111-0.268). The mean bone mineral density measured was 206.24 +/- 50.58 mg HA/ccm. This study shows that there is highly significant difference between BMD measured by DXA and pQCT, and that bone morphometric analysis indicates that there is marked decrease in the mechanical properties of the bone in the proximal tibia due to knee Osteoarthritis and Osteoporosis indicating poor bone architecture

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TI A comprehensive fracture prevention strategy in older adults: The European Union Geriatric Medicine Society (EUGMS) statement
SO JOURNAL OF NUTRITION HEALTH & AGING
LA English
DT Article
DE Falls; fragility fracture; older people; prevention; position statement
ID bone-mineral density; fall prevention; hip-fracture; postmenopausal women; cost-effectiveness; zoledronic acid; risk-factors; pharmacological-treatments; strontium ranelate; liaison service
AB Prevention of fragility fractures in older people has become a public health priority, although the most appropriate and cost-effective strategy remains unclear. In the present statement, the Interest Group on Falls and Fracture Prevention of the European Union Geriatric Medicine Society (EUGMS), in collaboration with the International Association of Gerontology and Geriatrics for the European Region (IAGG-ER), the European Union of Medical Specialists (EUMS), the International Osteoporosis Foundation - European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, outlines its views on the main points in the current debate in relation to the primary and secondary prevention of falls, the diagnosis and treatment of bone fragility, and the place of combined falls and fracture liaison services for fracture prevention in older people.
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TI Are estrogen-related drugs new alternatives for the management of osteoarthritis?
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Review
DE Osteoarthritis; Estrogen; Selective estrogen receptor modulators; Joint; Bazedoxifene
ID radiographic knee osteoarthritis; receptor-alpha gene; bone-acting agents; middle-aged women; postmenopausal women; subchondral bone; human chondrocytes; ovariectomized rats; replacement-therapy; bazedoxifene/conjugated estrogens
AB Osteoarthritis (OA) is a chronic degenerative disease involving multiple physiopathological mechanisms. The increased prevalence of OA after menopause and the presence of estrogen receptors in joint tissues suggest that estrogen could help prevent development of OA. This review summarizes OA research with a focus on the effects of estrogen and selective estrogen receptor modulators (SERMs). Preclinical studies and clinical trials of estrogen therapy have reported inconsistent results. However, almost all studies assessing SERM treatment have obtained more consistent and favorable effects in OA with a relatively safety and tolerability

profiles. At present, some SERMs including raloxifene and bazedoxifene have been approved for the treatment of osteoporosis. In summary, estrogen-related agents may exert both a direct effect on subchondral bone and direct and/or indirect effects upon the surrounding tissues, including the articular cartilage, synovium, and muscle, to name a few. Estrogen and SERMs may be particularly favorable for postmenopausal patients with early-stage OA or osteoporotic OA, a phenotype defined by reduced bone mineral density related to high remodeling in subchondral bone. At present, no single drug exists that can prevent OA progression. Although estrogen-related drugs provide insight into the continued work in the field of OA drug administration, further research is required before SERMs can become therapeutic alternatives for OA treatment.
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TI Prevalence of radiographic hip osteoarthritis and its association with hip pain in Japanese men and women: the ROAD study
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Hip; Prevalence; Pain; Cross-sectional
ID acetabular dysplasia; physical-activity; united-states; population; community; knee; epidemiology; definitions; disability; britain
AB Objective: Although hip osteoarthritis (OA) is a major cause of hip pain and disability in elderly people, few epidemiologic studies have been performed. We investigated the prevalence of radiographic hip OA and its association with hip pain in Japanese men and women using a large-scale population of a nationwide cohort study, Research on Osteoarthritis/osteoporosis Against Disability (ROAD). Methods: From the baseline survey of the ROAD study, 2975 participants (1043 men and 1932 women), aged 23-94 years (mean 70.2 years), living in urban, mountainous, and coastal communities were analyzed. The radiographic severity at both hips was determined by the Kellgren/Lawrence (K/L) grading system. Radiographic hip OA was defined as K/L >= 2, and severe radiographic hip OA as K/L >= 3. Results: The crude prevalence of radiographic hip OA was 18.2% and 14.3% in men and women, respectively, that of severe radiographic hip OA was 1.34% and 2.54%, and that of symptomatic K/L >= 2 OA was 0.29% and 0.99%, respectively. The crude prevalence of hip OA, including severe OA, was not age-dependent in men or women. Male sex was a risk factor for radiographic hip OA, whereas female sex was a risk factor for severe radiographic hip OA and hip pain. Compared with K/L = 0/1, hip pain was significantly associated with K/L >= 3, but not with K/L = 2. Conclusion: The present cross-sectional study revealed the prevalence of radiographic hip OA and severe hip OA in Japanese men and women. Hip pain was strongly associated with K/L >= 3. (C) 2015 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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TI Sarcopenia in daily practice: assessment and management
SO BMC GERIATRICS

LA English
DT Article
DE Sarcopenia; Daily practice; Assessment; Management; Tools
ID anthropometric prediction equations; bioelectrical-impedance analysis; appendicular skeletal-muscle; x-ray absorptiometry; lean soft-tissue; physical performance; european-society; economic-aspects; protein-intake; vitamin-d
AB Background: Sarcopenia is increasingly recognized as a correlate of ageing and is associated with increased likelihood of adverse outcomes including falls, fractures, frailty and mortality. Several tools have been recommended to assess muscle mass, muscle strength and physical performance in clinical trials. Whilst these tools have proven to be accurate and reliable in investigational settings, many are not easily applied to daily practice. Methods: This paper is based on literature reviews performed by members of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) working group on frailty and sarcopenia. Face-to-face meetings were afterwards organized for the whole group to make amendments and discuss further recommendations. Results: This paper proposes some user-friendly and inexpensive methods that can be used to assess sarcopenia in real-life settings. Healthcare providers, particularly in primary care, should consider an assessment of sarcopenia in individuals at increased risk; suggested tools for assessing risk include the Red Flag Method, the SARC-F questionnaire, the SMI method or different prediction equations. Management of sarcopenia should primarily be patient centered and involve the combination of both resistance and endurance based activity programmes with or without dietary interventions. Development of a number of pharmacological interventions is also in progress. Conclusions: Assessment of sarcopenia in individuals with risk factors, symptoms and/or conditions exposing them to the risk of disability will become particularly important in the near future.
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TI Efficacy and safety of hyaluronic acid in the management of osteoarthritis: Evidence from real-life setting trials and surveys
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English
DT Review
DE Hyaluronic acid; Intra-articular injection; Knee osteoarthritis
ID randomized controlled-trial; knee osteoarthritis; molecular-weight; double-blind; hylan g-f-20; intraarticular hyaluronan; non-inferiority; metaanalysis; viscosupplementation; injections
AB The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) treatment algorithm recommends intra-articular (IA) hyaluronic acid (HA) for management of knee osteoarthritis (OA) as second-line treatment in patients who remain symptomatic despite use of non steroidal anti-inflammatory drugs (NSAIDs). This recommendation is based upon accumulating evidence that IA HA provides a significant benefit in knee OA. There is good evidence that IA HA injections reduce pain and increase function in knee OA, and the benefits are long-lasting as compared with IA corticosteroids. Evidence from real-life studies of repeat courses of IA HA demonstrates an improvement in pain or function lasting up to 40 months (12 months after the last injection cycle), a reduction in use of concomitant analgesia by up to 50%, and suggests that there may be a delay in the need for total knee replacement (TKR) of around 2 years. The

clinical benefit of IA HA on knee OA may be 2-fold: (i) mechanical viscosupplementation of the joint (allowing lubrication and shock absorption) and (ii) the re-establishment of joint homeostasis through induction of endogenous HA production, which continues long after the exogenous injection has left the joint. The magnitude of the clinical effect may be different for different HA products, but this has not been proven so far and requires further investigation. IA HA injections are generally considered to be safe, although a slightly higher number of cases of local reactions and post-injection non-septic arthritis has been reported with high molecular weight cross-linked HAs. The use of IA HA in knee OA patients with mild-moderate disease, and for more severe patients wishing to delay TKR surgery, is recommended by the ESCEO task force. Further investigation into the OA patient types most likely to benefit from IA HA is warranted. Viscosupplementation with IA HA is a safe and effective component of the multi-modal management of knee OA.
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TI Fructus Ligustri Lucidi ethanol extract inhibits osteoclastogenesis in RAW264.7 cells via the RANKL signaling pathway
SO MOLECULAR MEDICINE REPORTS
LA English
DT Article
DE Fructus ligustri Lucidi; oleanolic acid; ursolic acid; osteoclast; receptor activator of nuclear factor kappa B ligand
ID bone-mineral density; differentiation; osteoporosis; expression; identification; insights
AB Fructus ligustri Lucidi (FLL) is the fruit of Ligustrum lucidum Ait and a traditional Chinese medicine, primarily known for its role in osteoporosis prevention and treatment. The present study aimed to elucidate the effect and underlying mechanism of action of ethanol extract of FLL on osteoclast differentiation and bone resorption, and to identify the active compounds within it. RAW264.7 murine monocyte/macrophage cells were stimulated with the receptor activator of nuclear factor kappa B ligand (RANKL) to induce osteoclast differentiation in vitro. The present study demosntrated that FLL extract and its two primary components, oleanolic acid (OA) and ursolic acid (UA), significantly suppressed RANKL-induced tartrate resistant acid phosphatase (TRAP) activity and multinucleate osteoclast formation without inducing cytotoxicity; however, no effect was observed on the apoptosis of mature osteoclasts. Additionally, RANKL-induced mRNA expression levels of the key transcription factors, tumor necrosis factor receptor associated factor-6, nuclear factor of activated T cell-c1 and c-Fos, and the osteoclast markers, TRAP, cathepsin K and matrix metalloproteinase-9 were suppressed by FLL, OA and UA. However, no effect was observed on RANKL-induced mRNA expression levels of Src. These results demonstrated that FLL may inhibit osteoclastogenesis in RAW264.7 cells via RANKL signaling pathways. OA and UA are active compounds in inducing this effect; however, their specific roles remain to be elucidated.
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FU special fund for cultivation and development of Beijing Science and Technology Innovation Base [Z151100001615035]
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NR 44
TC 27
Z9 30
U1 0
U2 24
PU SPANDIDOS PUBL LTD
PI ATHENS
PA POB 18179, ATHENS, 116 10, GREECE
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J9 MOL MED REP
JI Mol. Med. Rep.
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BP 4767
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WC Oncology; Medicine, Research & Experimental
SC Oncology; Research & Experimental Medicine
GA EB3DD
UT WOS:000387241600097
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AF Cinar, Y.
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TI A comparison of the femur heads histomorphometrically regarding trabecular bone properties in the patients with osteoporosis and osteoarthritis
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Osteoarthritis; Osteoporosis; Bone densitometry; Bone Turnover Marker
ID hip osteoarthritis; structural basis; fracture; fragility; density; disease
AB The purpose was to compare the bone samples histomorphometrically regarding trabecular bone properties in the patients with osteoarthritis (OA) and osteoporosis (OP). Femoral head specimens were obtained from 18 patients with OA and 17 patients with femoral neck fracture due to OP during hip arthroplasty. Histomorphometric analyses were performed by soft ware program (Carl Zeiss) to measure trabecular area (Tb.a, mm(3)), trabecular thickness (Tb.th, A mu m) and trabecular separation (Tb.s, A mu m). In the results, Tb.a and Tb.th values were significantly lower ($p < 0.05$), Tb.s was higher in the patients with OP ($p < 0.05$). Bone metabolism parameters were different between the groups ($p < 0.05$). All histomorphometric parameters were highly correlated with the BMDs ($p < 0.01$). This study showed inverse relation between OA and OP regarding trabecular bone properties, BMD and bone turnover metabolism markers. The strong relations between results suggest that either BMDs or bone turnover markers can be used for prescience of the fractures.
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NR 12
TC 3
Z9 4
U1 1
U2 25
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 1594-0667
EI 1720-8319
J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
PD OCT 15
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VL 28
IS 5
BP 997
EP 1001
DI 10.1007/s40520-015-0491-4
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA DV4FP
UT WOS:000382881100025
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PT J

AU Zhao, HW
Luo, W
Maly, RC
Liu, J
Lee, JY
Cui, YN
AF Zhao, Huiwen
Luo, Wen
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Cui, Yaning
TI Validation of the Chinese version 10-item Perceived Efficacy in Patient-Physician Interactions scale in patients with osteoarthritis
SO PATIENT PREFERENCE AND ADHERENCE
LA English
DT Article
DE assessment of osteoarthritis; patient-physician communication; self-efficacy; instrument validation
ID self-efficacy; communication; pain; hip
AB Objectives: This study aimed to assess the reliability and validity of the Chinese version of the 10-item Perceived Efficacy in Patient-Physician Interaction (PEPPI-10) scale in hospitalized patients with severe knee osteoarthritis in the People's Republic of China. Methods: Between January and March 2015, the Chinese versions of PEPPI, self-efficacy for exercise scale, osteoporosis self-efficacy scale, and modified fall efficacy scale were applied to assess 110 severe knee osteoarthritis patients who were hospitalized in the second ward of the department of arthroplasty surgery of Tianjin Hospital. Results: The Chinese version of the PEPPI-10 scale had a high coefficient of internal consistency (Cronbach's alpha coefficient, 0.907). The score of the Chinese version of PEPPI was weakly correlated with the scores of the Chinese versions of self-efficacy for exercise scale, osteoporosis self-efficacy scale, and modified fall efficacy scale. Conclusion: The Chinese version of the PEPPI-10 scale exhibits sufficient internal consistency and convergent validity in hospitalized patients with severe knee osteoarthritis in the People's Republic of China.
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NR 26
TC 15
Z9 17
U1 1
U2 24
PU DOVE MEDICAL PRESS LTD

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J9 PATIENT PREFER ADHER
JI Patient Prefer. Adherence
PD JUN 15
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IS
BP 2189
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DI 10.2147/PPA.S110883
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WC Medicine, General & Internal
SC General & Internal Medicine
GA EA9XJ
UT WOS:000386997700001
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PT J
AU Wang, BL
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AF Wang, Bailiang
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Chemnitz, John
Ding, Ming
TI Cancellous and Cortical Bone Microarchitectures of Femoral Neck in Rheumatoid Arthritis and Osteoarthritis Compared with Donor Controls
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE 3D microarchitecture; Rheumatoid arthritis; Osteoarthritis; Femoral neck; Cancellous/cortical bones
ID age-related-changes; hip fracture; ultradistal radius; microstructure; osteoporosis; head; quantification; connectivity; thickness; women
AB This study investigated the 3D microarchitecture of cancellous and cortical bones of the femoral neck in rheumatoid arthritis (RA), osteoarthritis (OA) and donor controls. 26 femoral necks (including heads) were harvested during total hip replacement surgeries in 11 patients with RA (mean age 66.7 +/- 12.8 years) and 15

patients with OA (67.3 +/- 8.4 years). Femoral heads/necks were also harvested from 8 donors (74.9 +/- 10.2 years). Bone samples of 10 mm thickness were prepared from each femoral neck and scanned with micro-CT to evaluate microarchitectural parameters. The RA and OA samples showed no significant differences in microarchitectural parameters in cancellous or cortical bone. Compared with the donor controls, bone volume fraction in RA and OA cancellous bone was significantly greater, the structure model index in OA was significantly lower, and the surface density in RA was significantly greater. The RA bone tissues showed erosion and marked osteophyte formation. This study demonstrated that RA and OA have similar trends of overall microarchitectural degeneration in the femoral neck, despite marked erosion in RA bone and osteophyte formation in OA bone. However, we could not eliminate the possibility of local differences between RA and OA bone. The age-related bone loss in RA and OA was less severe than those of normal ageing and osteoporosis, suggesting a compensatory effect of the diseases to increase bone density.
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NR 36
TC 7
Z9 7
U1 0
U2 10
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 0171-967X
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J9 CALCIFIED TISSUE INT
JI Calcif. Tissue Int.
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA DK5NN
UT WOS:000374966700005
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PT J
AU Henriksen, K
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Alexandersen, Peter
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Qvist, Per
Lau, Edith
Riis, Bente J.
Christiansen, Claus
Karsdal, Morten A.
TI A randomized, double-blind, multicenter, placebo-controlled study to evaluate the efficacy and safety of oral salmon calcitonin in the treatment of osteoporosis in postmenopausal women taking calcium and vitamin D
SO BONE

LA English
DT Article
DE Osteoporosis; Calcitonin; Fractures; Efficacy; Safety
ID cancer-risk; nasal spray; fractures; osteoarthritis; trials
AB This randomized, double-blind, placebo-controlled phase III study was conducted to assess the efficacy and safety of oral calcitonin (SMC021) for the treatment of postmenopausal osteoporosis. A total of 4665 postmenopausal women with osteoporosis were randomized 1:1 to receive calcium and vitamin D plus either SMC021 tablets (0.8 mg/d) or placebo for 36 months. The primary endpoint was the proportion of patients with a new vertebral fracture. The two groups were well balanced at baseline with regards to demographic and clinical data. No effect of SMC021 on preventing new vertebral fractures was observed, nor was any effect seen on new hip or non vertebral fractures. Women receiving SMC021 had a mean 1.02% (+/- 0.12%) increase in lumbar spine bone mineral density (BMD) compared with a mean 0.18% (+/- 0.12%) increase in the placebo group by the end of the study ($p < 0.0001$). Similarly, small increases in BMD were observed at the femoral neck and hip in both groups. Levels of the biomarkers of bone turnover, urinary CTX-I and CTX-II, were 15% lower in the SMC021 group than in the placebo arm at 12 and 24 months, but not at 36 months. No change in quality of life between groups, assessed by the Qualeffo-14 questionnaire, was observed in either group between baseline and month 36. Pharmacokinetics analysis confirmed exposure to SMC021, but the drug levels were markedly lower than expected. Approximately 92% of subjects in each treatment group experienced an adverse event (AE), the majority of which were mild or moderate in intensity. AEs associated with SMC021 were primarily of gastrointestinal origin and included nausea, vomiting and abdominal pain, as well as hot flushes which were the reason for the slightly higher drop-out rate in the active treatment arm compared to placebo. The number of severe AEs was low in both groups. Thirty-five deaths were reported but none were considered treatment-related. Due to the lack of efficacy in preventing fractures, the development of the orally formulated calcitonin was terminated despite the promising results in earlier studies. (C) 2016 Elsevier Inc. All rights reserved.
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TI Epidemiology of Fracture Nonunion in 18 Human Bones
SO JAMA SURGERY
LA English
DT Article
ID tibial shaft fractures; midshaft clavicular fractures; external fixation; nonoperative treatment; risk-factors; open reduction; plate osteosynthesis; intramedullary nail; internal-fixation; complications
AB IMPORTANCE Failure of bone fracture healing occurs in 5% to 10% of all patients. Nonunion risk is associated with the severity of injury and with the surgical treatment technique, yet progression to nonunion is not fully explained by these risk factors. OBJECTIVE To test a hypothesis that fracture characteristics and patient-related risk factors assessable by the clinician at patient presentation can indicate the probability of fracture nonunion. DESIGN, SETTING, AND PARTICIPANTS An inception cohort study in a large payer database of patients with fracture in the United States was conducted using patient-level health claims for medical and drug expenses compiled for approximately 90.1 million patients in calendar year 2011. The final database collated demographic descriptors, treatment procedures as per Current Procedural Terminology codes; comorbidities as per International Classification of Diseases, Ninth Revision codes; and drug prescriptions as per National Drug Code Directory codes. Logistic regression was used to calculate odds ratios (ORs) for variables associated with nonunion. Data analysis was performed from January 1, 2011, to December 31, 2012, EXPOSURES Continuous enrollment in the database was required for 12 months after fracture to allow sufficient time to capture a nonunion diagnosis. RESULTS The final analysis of 309 330 fractures in 18 bones included 178 952 women (57.9%); mean (SD) age was 44.48 (13.68) years. The nonunion rate was 4.9%. Elevated nonunion risk was associated with severe fracture (eg, open fracture, multiple fractures), high body mass index, smoking, and alcoholism. Women experienced more fractures, but men were more prone to nonunion. The nonunion rate also varied with fracture location: scaphoid, tibia plus fibula, and femur were most likely to be nonunion. The ORs for nonunion fractures were significantly increased for risk factors, including number of fractures (OR, 2.65; 95% CI, 2.34-2.99), use of nonsteroidal anti-inflammatory drugs plus opioids (OR, 1.84; 95% CI, 1.73-1.95), operative treatment (OR, 1.78; 95% CI, 1.69-1.86), open fracture (OR, 1.66; 95% CI, 1.55-1.77), anticoagulant use (OR, 1.58; 95% CI, 1.51-1.66), osteoarthritis with rheumatoid arthritis (OR, 1.58; 95% CI, 1.38-1.82), anticonvulsant use with benzodiazepines (OR, 1.49; 95% CI, 1.36-1.62), opioid use (OR, 1.43; 95% CI, 1.34-1.52), diabetes (OR, 1.40;

95% CI, 1.21-1.61), high-energy injury (OR, 1.38; 95% CI, 1.27-1.49), anticonvulsant use (OR, 1.37; 95% CI, 1.31-1.43), osteoporosis (OR, 1.24; 95% CI, 1.14-1.34), male gender (OR, 1.21; 95% CI, 1.16-1.25), insulin use (OR, 1.21; 95% CI, 1.10-1.31), smoking (OR, 1.20; 95% CI, 1.14-1.26), benzodiazepine use (OR, 1.20; 95% CI, 1.10-1.31), obesity (OR, 1.19; 95% CI, 1.12-1.25), antibiotic use (OR, 1.17; 95% CI, 1.13-1.21), osteoporosis medication use (OR, 1.17; 95% CI, 1.08-1.26), vitamin D deficiency (OR, 1.14; 95% CI, 1.05-1.22), diuretic use (OR, 1.13; 95% CI, 1.07-1.18), and renal insufficiency (OR, 1.11; 95% CI, 1.04-1.17) (multivariate P < .001 for all). CONCLUSIONS AND RELEVANCE The probability of fracture nonunion can be based on patient-specific risk factors at presentation. Risk of nonunion is a function of fracture severity, fracture location, disease comorbidity, and medication use.
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TI Characterization of nano-structural and nano-mechanical properties of osteoarthritic subchondral bone
SO BMC MUSCULOSKELETAL DISORDERS
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DT Article
DE Osteoarthritis; Subchondral bone; Nano-structure; Crystallinity; Ca/P; Bone hierarchical structure
ID articular-cartilage; trabecular bone; elastic-modulus; sclerotic bone; femoral-head; crystallinity; spectroscopy; nanoindentation; osteoporosis; associations
AB Background: Although articular cartilage is the primary tissues affected by osteoarthritis (OA), the underlying subchondral bone also undergoes noticeable changes. Despite the growing body of research into the biophysical and mechanical properties of OA bone there are few studies that have analysed the structure of the subchondral sclerosis at the nanoscale. In this study, the composition and nano-structural changes of human osteoarthritis (OA) subchondral bone were investigated to better understand the site-specific changes. Methods: OA bone samples were collected from patients undergoing total knee replacement surgery and graded according to disease severity (grade I: mild OA; grade IV: severe OA). Transmission electron microscopy (TEM), Electron Diffraction, and Elemental Analysis techniques were used to explore the cross-banding pattern, nature of mineral phase and orientation of the crystal lattice. Subchondral bone nano-hydroxyapatite powders were prepared and characterised using high resolution transmission electron microscopy (HR-TEM) and fourier transform

infrared spectroscopy (FTIR). Subchondal bone mechanical properties were investigated using a nano-indentation method. Results: In grade I subchondral bone samples, a regular periodic fibril banding pattern was observed and the c-axis orientation of the apatite crystals was parallel to the long axis of the fibrils. By contrast, in grade IV OA bone samples, the bulk of fibrils formed a random and undulated arrangement accompanied by a circular oriented pattern of apatite crystals. Fibrils in grade IV bone showed non-hierarchical intra-fibrillar mineralization and higher calcium (Ca) to phosphorous (P) (Ca/P) ratios. Grade IV OA bone showed higher crystallinity of the mineral content, increased modulus and hardness compared with grade I OA bone. Conclusions: The findings from this study suggest that OA subchondral sclerotic bone has an altered mineralization process which results in nano-structural changes of apatite crystals that is likely to account for the compromised mechanical properties of OA subchondral bones.
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NR 47
TC 37
Z9 45
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PU BMC
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 BMC MUSCULOSKEL DIS
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AU Desando, G
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TI Autologous Bone Marrow Concentrate in a Sheep Model of Osteoarthritis: New Perspectives for Cartilage and Meniscus Repair
SO TISSUE ENGINEERING PART C-METHODS
LA English
DT Article
ID mesenchymal stem-cells; articular-cartilage; knee osteoarthritis; mononuclear-cells; in-vitro; scaffold; transplantation; microfracture; rationale; mechanics
AB Introduction: Cell-based therapies are becoming a valuable tool to treat osteoarthritis (OA). This study investigated and compared the regenerative potential of bone marrow concentrate (BMC) and mesenchymal stem cells (MSC), both engineered with Hyaff (R)-11 (HA) for OA treatment in a sheep model. Methods: OA was induced via unilateral medial meniscectomy. Bone marrow was aspirated from the iliac crest, followed by concentration processes or cell isolation and expansion to obtain BMC and MSC, respectively. Treatments consisted of autologous BMC and MSC seeded onto HA. The regenerative potential of bone, cartilage, menisci, and synovia was monitored using macroscopy, histology, immunohistochemistry, and micro-computed tomography at 12 weeks post-op. Data were analyzed using the general linear model with adjusted Sidak's multiple comparison and Spearman's tests. Results: BMC-HA treatment showed a greater repair ability in inhibiting OA progression compared to MSC-HA, leading to a reduction of inflammation in cartilage, meniscus, and synovium. Indeed, the decrease of inflammation positively contributed to counteract the progression of fibrotic and hypertrophic processes, known to be involved in tissue failure. Moreover, the treatment with BMC-HA showed the best results in allowing meniscus regeneration. Minor healing effects were noticed at bone level for both cell strategies; however, a downregulation of subchondral bone thickness (Cs.Th) was found in both cell treatments compared to the OA group in the femur. Conclusion: The transplantation of BMC-HA provided the best effects in supporting regenerative processes in cartilage, meniscus, and synovium and at less extent in

bone. On the whole, both MSC and BMC combined with HA reduced inflammation and contributed to switch off fibrotic and hypertrophic processes. The observed regenerative potential by BMC-HA on meniscus could open new perspectives, suggesting its use not only for OA care but also for the treatment of meniscal lesions, even if further analyses are necessary to confirm its healing potential at long-term follow-up.
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NR 55
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J9 TISSUE ENG PART C-ME
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WC Cell & Tissue Engineering; Cell Biology; Engineering, Biomedical; Materials Science, Biomaterials
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TI Increased trabecular bone and improved biomechanics in an osteocalcin-null rat model created by CRISPR/Cas9 technology
SO DISEASE MODELS & MECHANISMS
LA English
DT Article
DE Osteocalcin; Bone strength; Bone structure; Genetic animal models; Osteocalcin knockout
ID cleidocranial dysplasia; gene; inhibition; expression; differentiation; osteoporosis; adiponectin; promoter; protein; system
AB Osteocalcin, also known as bone gamma-carboxyglutamate protein (Bglap), is expressed by osteoblasts and is commonly used as a clinical marker of bone turnover. A mouse model of osteocalcin deficiency has implicated osteocalcin as a mediator of changes to the skeleton, endocrine system, reproductive organs and central nervous system. However, differences between mouse and human osteocalcin at both the genome and protein levels have challenged the validity of extrapolating findings from the osteocalcin-deficient mouse model to human disease. The rat osteocalcin (Bglap) gene locus shares greater synteny with that of humans. To further examine the role of osteocalcin in disease, we created a rat model with complete loss of osteocalcin using the CRISPR/Cas9 system. Rat osteocalcin was modified by injection of CRISPR/Cas9 mRNA into the pronuclei of fertilized single cell Sprague-Dawley embryos, and animals were bred to

homozygosity and compound heterozygosity for the mutant alleles. Dual-energy X-ray absorptiometry (DXA), glucose tolerance testing (GTT), insulin tolerance testing (ITT), microcomputed tomography (mu CT), and a three-point break biomechanical assay were performed on the excised femurs at 5 months of age. Complete loss of osteocalcin resulted in bones with significantly increased trabecular thickness, density and volume. Cortical bone volume and density were not increased in null animals. The bones had improved functional quality as evidenced by an increase in failure load during the biomechanical stress assay. Differences in glucose homeostasis were observed between groups, but there were no differences in body weight or composition. This rat model of complete loss of osteocalcin provides a platform for further understanding the role of osteocalcin in disease, and it is a novel model of increased bone formation with potential utility in osteoporosis and osteoarthritis research.
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SC Cell Biology; Research & Experimental Medicine; Pathology
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TI Determinants of Serum 25-Hydroxyvitamin D Concentrations and a Screening Test for Moderate-to-Severe Hypovitaminosis D in Chinese Patients Undergoing Total Joint Arthroplasty
SO JOURNAL OF ARTHROPLASTY
LA English

DT Article
DE vitamin D; sunlight; determinants; total joint arthroplasty; screening test
ID vitamin-d-status; d insufficiency; d deficiency; hong-kong; adults; osteoporosis; prevalence; exposure; women; supplementation
AB Background: Hypovitaminosis D is associated with adverse surgical outcomes. We quantified the environmental, demographic, and modifiable determinants of serum 25-hydroxyvitamin D (25-OHD) concentration and assessed the potential impact of a preoperative screening questionnaire for moderate-to-severe hypovitaminosis D (25-OHD < 30 nmol/L). Methods: In a retrospective cohort study of 227 Chinese patients (69 males and 158 females) undergoing 261 joint arthroplasty, we collected information on recent sun exposure, dietary vitamin D intake, vitamin D supplementation, and Western Ontario and McMaster Universities osteoarthritis index using a questionnaire and measured a fasting 25-OHD concentration using a liquid chromatographyetandem mass spectrometry before surgery. Results: The multiple regression model on the determinants of 25-OHD concentration described 14% of the total variance, with the greatest relative contribution from ambient ultraviolet radiation (42%). A 4-item screening test for moderate-to-severe hypovitaminosis D had acceptable discrimination (area under receiver operating characteristic curve = 0.76, 95% CI, 0.65-0.87), good calibration (HosmereLemeshow goodness-of-fit; P = .93). Decision curve analysis showed that the screening test can potentially reduce unnecessary 25-OHD testing by 390 per 1000 patients at a threshold probability of 10%. Conclusion: The screening test appears moderately useful in avoiding a substantial number of unnecessary 25-OHD testing in a setting where the prevalence of moderate-to-severe hypovitaminosis D is less than 10%. (C) 2016 Elsevier Inc. All rights reserved.
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TI Orthopedic tissue regeneration: cells, scaffolds, and small molecules
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DE Osteoporosis; Osteoarthritis; Bone; Cartilage; Stemcells; Scaffolds; Small molecules
ID mesenchymal stem-cells; osteoarthritic subchondral bone; articular-cartilage defect; in-vitro chondrogenesis; platelet-rich plasma; strontium ranelate; osteogenic differentiation; knee osteoarthritis; adipose-tissue; cathepsin-k
AB Orthopedic tissue regeneration would benefit the aging population or patients with degenerative bone and cartilage diseases, especially osteoporosis and osteoarthritis. Despite progress in surgical and pharmacological interventions, new regenerative approaches are needed to meet the challenge of creating bone and articular cartilage tissues that are not only structurally sound but also functional, primarily to maintain mechanical integrity in their high load-bearing environments. In this review, we discuss new advances made in exploiting the three classes of materials in bone and cartilage regenerative medicine-cells, biomaterial-based scaffolds, and small molecules-and their successes and challenges reported in the

clinic. In particular, the focus will be on the development of tissue-engineered bone and cartilage ex vivo by combining stem cells with biomaterials, providing appropriate structural, compositional, and mechanical cues to restore damaged tissue function. In addition, using small molecules to locally promote regeneration will be discussed, with potential approaches that combine bone and cartilage targeted therapeutics for the orthopedic-related disease, especially osteoporosis and osteoarthritis.
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DE Vacuum extraction; Operative delivery; Occipito-posterior position; Adverse outcome; Delivery
ID occiput posterior position; instrumental vaginal delivery; operative delivery; risk-factors; intrapartum sonography; 2nd-stage; labor; cohort; laceration; duration
AB Objective To estimate the association of fetal head position prior to vacuum extraction (VE) and pregnancy outcome. Study design A retrospective cohort study of singleton pregnancies who underwent VE. Pregnancy outcome of occipito-anterior (OA) position of the fetal head was compared to those with occipito-posterior (OP) position. Results Amongst overall 12,063 women undergoing trial of labor, there were 1118 (9.2 %) VE deliveries. Of them, 871 (77.9 %) had OA and 247 (22.1 %) had OP position of the fetal head. Except for a higher rate of nulliparity in the OA group, no significant differences between the groups regarding pregnancy complications and birthweight were noted. In the OP group, there were higher rates of prolonged 2nd-stage of labor as an indication for VE (49.8 vs. 36.5 %, p< 0.001) and single detachment of vacuum cup (11.3 vs. 6.7 %, p = 0.02) without any increased risk of failed extraction. Higher risks for sub-galeal hematoma (aOR = 4.36, p = 0.03) and low 5-min Apgar score (aOR = 4.63, p = 0.02) were observed in the OP group with otherwise similar rates of adverse maternal and neonatal outcomes. Conclusion Among women undergoing VE, OP position is associated with higher rate of vacuum cup detachment, low 5-min Apgar score and increased risk for sub-galeal hematoma with otherwise similar rates of adverse maternal and neonatal outcomes.
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NR 35
TC 14
Z9 15
U1 0
U2 2
PU SPRINGER HEIDELBERG
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JI Arch. Gynecol. Obstet.
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SC Obstetrics & Gynecology
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ER

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TI The role of sarcopenia with and without fracture
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE Sarcopenia; Osteoporosis; Osteoarthritis; Hip fracture; Aging; Risk of falling; Muscle fibre atrophy; Satellite cells; BMP2; Myostatin
ID bone-mineral density; femoral-neck; tgf-beta; muscle; osteoporosis; exercise; dysfunction; diseases; obesity; cells
AB Introduction: Bone and muscle tissues are in a close relationship. They are linked from a biological and functional point of view and both are related to an increased fracture risk in the elderly. The aging process is involved in the loss of functionality of both bones and muscles. In particular, aging-induced decline in muscle size and quality accompanies catabolic alterations in bone tissue; furthermore, age-related changes in bone alter its response to muscle-derived stimulation. The increased fracture risk in individuals with sarcopenia and osteoporosis is due to the decline of muscle mass and strength, the decrease in bone mineral density (BMD) and limited mobility. In this study, we investigated the role of sarcopenia and the main age-related bone diseases, osteoporosis (OP) and osteoarthritis (OA). Methods: Muscular performance status was evaluated using the

Physical Activity Scale for the Elderly (PASE) test in 27 female patients with OP who underwent total hip arthroplasty for hip fracture, and in 27 age-matched female patients with OA who underwent total hip arthroplasty. Dual-energy X-ray absorptiometry (DEXA) was performed and the T-score values were used to discriminate between OP and OA patients. Body Mass Index (BMI) was calculated. As part of a multiparametric model of evaluation, biopsies of vastus lateralis muscle were analysed by immunohistochemical reaction to find a correlation with the above mentioned functional index. Results: The PASE test showed that the OP patients had a low or moderate level of physical activity before fracture occurred, whereas the OA patients had more intensive pre-fracture physical performances. Histological analysis showed that osteoporosis is characterised by a preferential type II fibre atrophy; in particular, data correlation showed that lower PASE test scores were related to lower diameter of type II fibres. No correlation was found between bone mineral density (BMD) and PASE test results. Discussion and conclusion: Osteoporosis is closely related to sarcopenia before and after fracture. Bone remodelling is influenced by muscle morphological and functional impairment and sarcopenia is considered one of the major factors for functional limitation and motor dependency in elderly osteoporotic individuals. Therefore, physical activity should be strongly recommended for OP patients at diagnosis. (C) 2016 Elsevier Ltd. All rights reserved.
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NR 46
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Z9 37
U1 1
U2 15
PU ELSEVIER SCI LTD
PI London
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JI Injury-Int. J. Care Inj.
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WC Critical Care Medicine; Emergency Medicine; Orthopedics; Surgery
SC General & Internal Medicine; Emergency Medicine; Orthopedics; Surgery
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PT J
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Pelletier, JP
Martel-Pelletier, J
AF Rannou, Francois
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Martel-Pelletier, Johanne
TI Efficacy and safety of topical NSAIDs in the management of osteoarthritis: Evidence from real-life setting trials and surveys
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English

DT Review
DE Hand osteoarthritis; Knee osteoarthritis; Topical non-steroidal anti-inflammatory drugs (NSAIDs); Personalized medicine
ID diclofenac solution; knee pain; double-blind; gel; recommendations; metaanalysis; ketoprofen; therapy; hand
AB Topical non-steroidal anti-inflammatory drugs (NSAIDs) are recommended in international and national guidelines as an early treatment option for the symptomatic management of knee and hand osteoarthritis (OA), and may be used ahead of oral NSAIDs due to their superior safety profile. The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) treatment algorithm recommends topical NSAIDs for knee OA in addition to the pharmacological background of symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) and rescue analgesia with paracetamol and non-pharmacological treatment, if the patient is still symptomatic. Topical NSAIDs have a moderate effect on pain relief, with efficacy similar to that of oral NSAIDs, with the advantage of a better risk: benefit ratio. In real-life studies, topical and oral NSAIDs demonstrate an equivalent effect on knee pain over 1 year of treatment, with fewer adverse events due to lower systemic absorption of topical NSAIDs compared with oral NSAIDs. As a result, topical NSAIDs may be the preferred treatment option, especially in OA patients aged >= 75 years, and those with co-morbidities or at an increased risk of cardiovascular, gastrointestinal, or renal side effects. Furthermore, using topical NSAIDs in inflammatory rheumatic diseases leads to a 40% reduction in the need for concomitant oral NSAIDs. When selecting a topical NSAID, absorption and bioavailability are important because of heterogeneity among topical drug formulations. Molecules like etofenamate have a bioavailability of >20% and evidence for accumulation in synovial tissues, with efficacy demonstrated as improvement in pain and function in real-life studies of OA patients. Diclofenac also shows good efficacy alongside evidence that diclofenac accumulates in the synovium. (C) 2015 The Authors. Published by Elsevier HS Journals, Inc.
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Z9 210
U1 1
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JI Semin. Arthritis Rheum.
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WC Rheumatology
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PT J
AU Anderson, MJ
Diko, S
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AF Anderson, Matthew J.
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TI Contribution of mechanical unloading to trabecular bone loss following non-invasive knee injury in mice
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE post-traumatic osteoarthritis; hindlimb unloading; trabecular bone; knee injury; mechanical loading
ID anterior cruciate ligament; posttraumatic osteoarthritis; computed tomography;

disuse osteoporosis; hindlimb suspension; skeletal-muscle; bed rest; model; rat; atrophy
AB Development of osteoarthritis commonly involves degeneration of epiphyseal trabecular bone. In previous studies, we observed 30-44% loss of epiphyseal trabecular bone (BV/TV) from the distal femur within 1 week following non-invasive knee injury in mice. Mechanical unloading (disuse) may contribute to this bone loss; however, it is unclear to what extent the injured limb is unloaded following injury, and whether disuse can fully account for the observed magnitude of bone loss. In this study, we investigated the contribution of mechanical unloading to trabecular bone changes observed following non-invasive knee injury in mice (female C57BL/6N). We investigated changes in gait during treadmill walking, and changes in voluntary activity level using Open Field analysis at 4, 14, 28, and 42 days post-injury. We also quantified epiphyseal trabecular bone using CT and weighed lower-limb muscles to quantify atrophy following knee injury in both ground control and hindlimb unloaded (HLU) mice. Gait analysis revealed a slightly altered stride pattern in the injured limb, with a decreased stance phase and increased swing phase. However, Open Field analysis revealed no differences in voluntary movement between injured and sham mice at any time point. Both knee injury and HLU resulted in comparable magnitudes of trabecular bone loss; however, HLU resulted in considerably more muscle loss than knee injury, suggesting another mechanism contributing to bone loss following injury. Altogether, these data suggest that mechanical unloading likely contributes to trabecular bone loss following non-invasive knee injury, but the magnitude of this bone loss cannot be fully explained by disuse. (c) 2016 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 34:1680-1687, 2016.
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NR 31
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U1 0
U2 11
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PI HOBOKEN
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AU Hutt, JRB
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AF Hutt, J. R. B.
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Masse, V.
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TI Kinematic TKA using navigation: Surgical technique and initial results
SO ORTHOPAEDICS & TRAUMATOLOGY-SURGERY & RESEARCH
LA English
DT Article
DE Knee Arthroplasty; Navigation; TKA; Technique; Outcomes; Kinematic
ID total knee arthroplasty; mechanical axis alignment; lower-extremity; follow-up; replacements; thickness; survival
AB Background: Kinematic alignment for total knee arthroplasty (TKA) may be one way of improving outcomes. Previous studies have either used patient-specific instrumentation, which adds cost, or standard instrumentation, which provides no intraoperative feedback on resection alignment. Hypothesis: To determine if computer navigation could reproduce native patient anatomy and simplify ligament balance during TKA whilst giving satisfactory improvements in functional scores at early follow-up. Materials and methods: Computer navigation was used for kinematic distal femoral and proximal tibial cuts in 100 consecutive and unselected TKAs. Resections were modified only if measured angles fell outside a

pre-defined safe range of combined coronal orientation within +/- 3 degrees of neutral and/or independent femoral or tibial cuts within +/- 5 degrees. Pre- and postoperative measurements of the hip-knee-ankle (HKA) angle, the lateral distal femoral angle (LDFA) and the medial proximal tibial angle (MPTA) were taken using long-leg standing radiographs. Clinical evaluation was with the WOMAC and KOOS scales. Results: Mean follow-up was 2.4 years (range 1.0-3.7, SD 0.8). The mean pre-op LDFA was 2.1 degrees valgus (9.2 valgus to 3.7 varus, SD 2.5) and 1.8 degrees valgus post-op (5.7 valgus to 4.2 varus, SD 2.0) (P=0.41). The mean pre-op MPTA was 3.0 degrees varus (10.6 valgus to 10.2 varus, SD 3.2) and 2.4 degrees varus post-op (4.0 valgus to 6.8 varus, SD 2.2) (P=0.03). The mean WOMAC score improved from 49.4 (29-85, SD 12.8) to 24.7 (0-73, SD 16.5) (P<0.001) and the mean KOOS score from 37.1 (7.2-77.2, SD 13.0) to 65.1 (26.8-100, SD 16) (P<0.001). Five knees (5%) required additional ligament release, four with valgus OA and one with varus OA. Two knees (2%) required lateral retinacular release for patellar tracking. Discussion: Computer navigation for kinematic TKA provides the operating surgeon with full control and feedback at each step, whilst also allowing partial correction of more extreme anatomy that might be unsuitable for recreation during TKA. This technique helps to preserve ligament isometry and produces satisfactory improvements in functional scores. (C) 2015 Elsevier Masson SAS. All rights reserved.
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Chen, X.
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TI Integrative analysis of genome-wide association studies and gene expression profiles identified candidate genes for osteoporosis in Kashin-Beck disease patients
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Gene expression profile; Genome-wide association study; Kashin-Beck disease; Osteoporosis; Pleiotropy
ID inflammatory markers; articular-cartilage; hip fracture; apoptosis; osteopontin; growth; osteoarthritis; chondrocytes; osteoclasts; activate
AB A Summary The molecular mechanism of osteoporosis (OP) in Kashin-Beck disease (KBD) patients was unclear. Our results suggest that KBD and OP shared some common causal genes, functionally involved in skeletal growth and development and chronic inflammation. Our results provide novel clues for clarifying the molecular mechanism of OP in KBD patients. Introduction KBD is a chronic skeletal disorder with osteopenia and OP. The pathogenesis of OP in KBD patients remains elusive. Methods A total of 1717 subjects participated in this study. KBD was diagnosed according to the clinical diagnosis criteria of China (GB16395-1996). The bone mineral density (BMD) and bone areas of the ulna and radius, hip, and lumbar (L1-L4) were measured with a Hologic 4500 W dual-energy X-ray absorptiometry scanner. Genotyping was conducted using Affymetrix SNP Array 6.0. Gene expression profiling of peripheral blood mononuclear cells of KBD and OP patients were compared using Affymetrix HG-U133 plus 2.0 arrays and Agilent Human 1A arrays, respectively. Genome-wide association studies (GWAS) were conducted by PLINK. SCEA and DAVID were applied for pleiotropy and functional enrichment analysis, respectively. Results SCEA analysis observed significant pleiotropic effects between KBD and the ulna and radius BMD (P value(-) 5.99 x 10(-3)). GWAS meta-analysis identified six candidate genes with pleiotropic effects, including PDGFD, SOX5, DPYD, CTR9, SPP1, and COL4A1. GO analysis identified 16 significant GO shared by KBD and the ulna and radius BMD, involved in cell morphogenesis and apoptosis. Pathway enrichment analysis detected two common pathways for KBD and the ulna and radius BMD, including calcium signaling pathway and vascular smooth muscle contraction pathway. Gene expression analysis detected three up-regulated inflammation-related genes for KBD and OP, including IL1B, IL8, and CCL1. Conclusion This study reported several candidate genes involved in the development of OP in KBD patients.
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AU Schiller, J
Korallus, C

Bethge, M
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Fink, MG
AF Schiller, Joerg
Korallus, Christoph
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Karst, Matthias
Schmalhofer, Marie-Lena
Gutenbrunner, Christoph
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TI Effects of acupuncture on quality of life and pain in patients with osteoporosis-a pilot randomized controlled trial
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Osteoporosis; Acupuncture; Pain; Quality of life; QUALEFFO-41
ID low-back-pain; postmenopausal women; vertebral fractures; auricular acupuncture; hip-arthroplasty; risk; multicenter; bone; osteoarthritis; questionnaire
AB A Summary In this sham-controlled study, 53 patients received 10 sessions of acupuncture treatment over 5 weeks to investigate the effects of acupuncture on the pain and quality of life of patients with osteoporosis. The results showed significant favorable effects of verumacupuncture on quality of life. Both interventions showed sustained and clinically relevant effects on pain. Purpose Standard analgesic treatment is associated with adverse events in patients with osteoporosis, especially elderly and/or comorbid patients. As acupuncture has gained widespread acceptance as a complementary treatment modality with few side effects, the aim of this study was to evaluate the effects of acupuncture on the pain and quality of life of patients with osteoporosis. Methods In total, 53 patients with vertebral compression fractures, osteoporosis-associated spinal deformities, and resultant pain were randomly allocated to the verum acupuncture with deep needling of specific points following the principles of traditional Chinese medicine (n = 29) or control acupuncture group with superficial needling of non-acupuncture points (n = 24). All patients received 10 sessions of standardized verum or control acupuncture treatment over 5 weeks. Pain (VAS score 1-100) and quality of life (QUALEFFO-41) were measured at the start of treatment (T0), before each acupuncture session (T1), and at 1 (T2) and 3 months (T3) post-treatment. Results Both acupuncture treatments significantly reduced activity-related pain and pain at rest over time. The verum acupuncture group experienced a significantly greater reduction in mean pain intensity at rest than the control group. In the control group, quality of life improved only temporarily post-treatment (T2) and slightly declined at the end of the follow-up period (T3). In contrast, patients in the verum acupuncture group experienced continuous and significant improvements in

quality of life up to 3 months after treatment (T3). Conclusions Both types of acupuncture were equally effective in producing sustained, clinically relevant pain relief in patients with osteoporosis. Verum acupuncture had stronger and longer-lasting effects on quality of life and pain at rest. The possible reasons for these findings include the specificity of acupuncture point selection and the performance of needle stimulation.
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Z9 27
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AU Pavelka, K
Bruyère, O
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TI Diacerein: Benefits, Risks and Place in the Management of Osteoarthritis. An Opinion-Based Report from the ESCEO
SO DRUGS & AGING
LA English
DT Article
ID nonsteroidal antiinflammatory drugs; human articular chondrocytes; acute liver-failure; factor-kappa-b; knee osteoarthritis; rhein reduce; double-blind; task-force; diacerhein; efficacy
AB Diacerein is a symptomatic slow-acting drug in osteoarthritis (SYSADOA) with anti-inflammatory, anti-catabolic and pro-anabolic properties on cartilage and synovial membrane. It has also recently been shown to have protective effects against subchondral bone remodelling. Following the end of the revision procedure by the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency, the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) constituted a panel of 11 experts to better define the real place of diacerein in the armamentarium for treating OA. Based on a literature review of clinical trials and meta-analyses, the ESCEO confirms that the efficacy of diacerein is similar to that of non-steroidal anti-inflammatory drugs (NSAIDs) after the first month of treatment, and superior to that of paracetamol. Additionally, diacerein has shown a prolonged effect on symptoms of several months once treatment was stopped. The use of diacerein is associated with common gastrointestinal disorders such as soft stools and diarrhoea, common mild skin reactions, and, uncommonly, hepatobiliary disorders. However, NSAIDs and paracetamol are known to cause potentially severe hepatic, gastrointestinal, renal, cutaneous and cardiovascular reactions. Therefore, the ESCEO concludes that the benefit-risk balance of diacerein remains positive in the symptomatic treatment of hip and knee osteoarthritis. Furthermore, similarly to other SYSADOAs, the ESCEO positions diacerein as a first-line pharmacological background treatment of osteoarthritis, particularly for patients in whom NSAIDs or paracetamol are contraindicated.
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FU Glynn Brothers Chemicals; IBSA; Merck Sharp Dohme; Novartis; Nutraveris; Pfizer; Rottapharm; Servier; SMB; Theramex; Bayer; Genevrier; Alliance for Better Bone Health; Amgen; Eli Lilly; GlaxoSmithKline; Medtronic; Merck; Roche; Takeda; UCB; TRB Chemedica; Negma; Lilly; Wyeth; Merckle; Nycomed-Takeda; NPS; IBSA-Genevrier; Asahi Kasei; Endocyte; Teijin; Teva; Analis; Nycomed; NovoNordisk; Ebewee Pharma; Zodiac; Danone; Will-Pharma; Bristol Myers Squibb; Organon; Therabel; Boehringer; Chiltern and Galapagos; Medical Research Council [MC_U147585827, MC_UP_A620_1014, MC_UU_12011/1, U1475000001, MC_U147585819] Funding Source: researchfish; National Institute for Health Research [NF-SI-0513-10085, NF-SI-0508-10082] Funding Source: researchfish; MRC [MC_U147585827, MC_U147585819] Funding Source: UKRI
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NR 91
TC 117
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U1 0
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PA 5 THE WAREHOUSE WAY, NORTHCOTE 0627, AUCKLAND, NEW ZEALAND
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AF Rehman, Haroon
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TI Imaging of occult hip fractures: CT or MRI?
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE CT; MRI; Occult hip fractures
ID proximal femur; osteoporosis; osteoarthritis; diagnosis; mortality
AB Objectives: Patients presenting with hip pain but normal plain radiographs may ultimately be shown on further investigation to have suffered an occult hip fracture (OHF). This diagnosis can be made with CT or MRI. Traditionally MRI has been considered a superior modality. We performed a retrospective review of all patients presenting to our service with a suspected OHF over a four-year period, investigated with either CT or MRI. Design: Retrospective review. Setting: Urban trauma centre. Patients: Patients with suspected hip fractures and negative radiographs. Intervention: CT or MRI. Main outcome measures: Detection rate; delay in request for further imaging; delay to theatre; representations with missed fractures. Results: A total of 179 patients were investigated, with a mean age of 82 +/- 13 years. The ultimate diagnosis was of an OHF in 71 cases and pelvic or acetabular fracture in 34. The average time from presentation plain radiograph to further imaging was 2.0 +/- 2.7 days, but was significantly shorter for CT. No patient re-presented with unidentified fractures or other localised hip pathology within a 12-month period. Conclusions: Modern imaging technology does not appear to miss clinically significant fractures. As CT is usually more accessible than MRI, the results of our study should encourage surgeons to consider CT as a first line investigation for occult hip fractures. We advocate a high index of suspicion and early imaging referral for elderly patients presenting with non-specific hip pain

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TI Evidence for Altered Canonical Wnt Signaling in the Trabecular Bone of Elderly Postmenopausal Women with Fragility Femoral Fracture
SO BIOMED RESEARCH INTERNATIONAL
LA English
DT Article
ID mesenchymal stem-cells; gene-expression; differentiation; osteoarthritis; osteoporosis; osteoblasts; marrow; repair; runx2
AB Wnt signaling, a major regulator of bone formation and homeostasis, might be involved in the bone loss of osteoporotic patients and the consequent impaired response to fracture. Therefore we analyzed Wnt-related, osteogenic, and adipogenic genes in bone tissue of elderly postmenopausal women undergoing hip replacement for either femoral fracture or osteoarthritis. Bone specimens derived from the intertrochanteric region of the femurs of 25 women with fracture (F) and 29 with osteoarthritis without fracture (OA) were analyzed. Specific miRNAs were analyzed in bone and in matched blood samples. RUNX2, BGP, and OPG showed lower expression in F than in OA samples, while OSX, OPN, BSP, and RANKL were not different. Inhibitory genes of Wnt pathway were lower in F versus OA. beta-Catenin protein levels were higher in F versus OA, whereas its cotranscriptional regulator (Lef1) was lower in F group. miR-204, which targets RUNX2, and miR-130a, which inhibits PPAR gamma, were lower and higher, respectively, in F versus OA serum samples. The present study showed an inefficient Wnt signal transduction in F group despite higher beta-catenin protein levels, consistent with the expected overall postfracture systemic activation towards osteogenesis. This transcriptional inefficiency could contribute to the osteoporotic bone fragility.
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TC 9
Z9 9
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PU HINDAWI LTD
PI LONDON
PA ADAM HOUSE, 3RD FLR, 1 FITZROY SQ, LONDON, W1T 5HF, ENGLAND
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J9 BIOMED RES INT
JI Biomed Res. Int.
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WC Biotechnology & Applied Microbiology; Medicine, Research & Experimental
SC Biotechnology & Applied Microbiology; Research & Experimental Medicine
GA EE2LG
UT WOS:000389415000001
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PT J
AU Eftekhar-Sadat, B
Ghavami, M
Toopchizadeh, V
Akbari, MG
AF Eftekhar-Sadat, Bina
Ghavami, Mostafa
Toopchizadeh, Vahideh
Akbari, Masood Ghahvechi
TI Wrist bone mineral density utility in diagnosing hip osteoporosis in postmenopausal women
SO THERAPEUTIC ADVANCES IN ENDOCRINOLOGY AND METABOLISM
LA English
DT Article
DE dual-energy X-ray absorptiometry; menopause; osteoporosis; wrist joint
ID lumbar spine; dxa; classification; osteoarthritis; degeneration; discordance;

fracture; risk; men
AB Background: Osteoporosis is a common bone disease that increases with age. Wrist bone mineral density (BMD) has significant correlation with other skeletal sites and it could be used as a diagnostic method for osteoporosis. The purpose of this study was to evaluate the role of wrist BMD in diagnosing osteoporosis in postmenopausal women. Methods: In this cross-sectional study, 99 postmenopausal women with mean age of 57 +/- 6.9 (range 50-76) years were evaluated. BMD of nondominant wrist, lumbar spine (L2-L4) and femur bone using a dual-energy X-ray absorptiometry (DXA) device as well as lateral lumbosacral X-ray for degenerative joint disease (DJD) evaluation were measured. Mean T-score of wrist was lower than hip and lumbar area. Results: Osteopenia and osteoporosis were observed in 40.4% and 59.6% in the wrist, 38.4% and 24.2% in the hip and 36.4% and 49.5% in lumbar-spine BMD measurements, respectively. There was positive correlation between wrist BMD with hip BMD ($r = 0.468$, $p < 0.001$) and lumbar BMD ($r = 0.322$, $p = 0.001$). DJD due to lumbosacral X-ray was reported in 84 cases (84.8%) including mild DJD in 45 (53.5%), moderate DJD in 33 (39.3%) and severe DJD in 6 (7.2%). Conclusions: Our results showed that wrist BMD has better accuracy than lumbar BMD in diagnosing osteoporosis in postmenopausal women.
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TC 27
Z9 29
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U2 7
PU SAGE PUBLICATIONS LTD
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PA 1 OLIVERS YARD, 55 CITY ROAD, LONDON EC1Y 1SP, ENGLAND
SN 2042-0188
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J9 THER ADV ENDOCRINOL
JI Ther. Adv. Endocrinol. Metab.
PD DEC 15
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EP 211
DI 10.1177/2042018816658164
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA EG9JB
UT WOS:000391373800001
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PT J
AU Dong, CH

Wang, ZM
Zhao, XL
Wang, AM
AF Dong, C. -H.
Wang, Z. -M.
Zhao, X. -L.
Wang, A. -M.
TI The use of damage control orthopaedics to minimize negative sequelae of surgery delay in elderly comorbid patients with hip fracture
SO EUROPEAN REVIEW FOR MEDICAL AND PHARMACOLOGICAL SCIENCES
LA English
DT Article
DE Hip fracture; Elderly; Older patient; Frail; Damage control orthopaedics; Surgery; ASA; P-POSSUM; Comorbidity; Algorithm
ID fall-related fractures; rheumatoid-arthritis; parkinsons-disease; increased risk; older women; united-states; osteoarthritis; osteoporosis; mortality; association
AB Hip surgeries count to the most frequent orthopaedic operations in older patients. Nonelective surgeries for hip fractures cause substantial economic burden because of high costs of medical treatment and high associated mortality. Surgery for hip fracture in the elderly comorbid patient still presents a challenge to orthopaedic surgeons. It is recommended that this surgery is performed within 48 hours after sustaining the hip fracture to decrease mortality. Yet the recommended early surgery (i.e. 48 hours after the incident) is not always feasible due to the frequent overall frailty of the patients or conditions of concomitant disease. The care of patients unfit for early surgery has been not adequately addressed in the literature. We have previously introduced an algorithm based on ASA-PS and P-POSSUM scores to stratify elderly comorbid patients for early vs delayed hip surgery, and used principles of Damage Control Orthopaedics to minimized negative sequelae of surgery delay (Dong C et al., PLoS One 2016). In this paper, we elaborate on Damage Control Orthopaedics and the proposed approach in the context of frequent comorbidities in the elderly orthopaedic patients. Further studies on this subject are urgently needed to establish international consensus on hip fracture surgery delayed due to overall patient frailty or extensive comorbidities.
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NR 74
TC 10
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U1 0
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PI ROME
PA VIA GREGORIO VII, ROME, 186-00165, ITALY
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J9 EUR REV MED PHARMACO
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WC Pharmacology & Pharmacy
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AU Shim, J

Lee, K
Kim, H
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Kang, CN
AF Shim, Jihoon
Lee, Kwanghyun
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Kang, Byungjik
Jeong, Haewon
Kang, Chang-Nam
TI Outcome of balloon kyphoplasty for the treatment of osteoporotic vertebral compression fracture in patients with rheumatoid arthritis
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Rheumatoid osteoarthritis; Osteoporotic vertebral compression fracture; Kyphoplasty
ID bone-mineral density; vertebroplasty; risk; cement; women
AB Background: Osteoporosis and osteoporotic fractures are widely known as complications of rheumatoid arthritis. Kyphoplasty (KP) is known as an effective treatment modality for reducing pain and correcting kyphotic deformity in osteoporotic vertebral compression fracture (OVCF). However, cutcomes of KP in rheumatoid patients are not well known. The purpose of the study was to investigate the clinical and radiological outcomes of balloon KP on OVCF in patients with rheumatoid arthritis. Methods: A total of 23 patients (31 vertebral bodies) with rheumatoid arthritis who received KP for OVCF and could be followed up for at least 1 year were examined. For clinical outcomes, visual analogue scale (VAS) and the Korean version of the Oswestry disability index (KODI) were evaluated. For radiological outcomes, changes in anterior vertebral height and local kyphotic angle were measured, alongside cement leakage, adjacent fracture, and the recollapse of cemented vertebra. Results: The anterior vertebral height was significantly restored after surgery compared with prior to surgery ($p < 0.001$). Cement leakage was found in 14 cases (45.1 %), and disc space leakage was prevalent (50 %), while vascular cement leakage was found in one case. Adjacent fracture was found in 3 patients (11.5 %). VAS for lumbago showed a significant decrease ($p < 0.001$) after surgery (VAS = 2.4) compared with that before (VAS = 8.1); it was somewhat increased after the 1-year follow-up (VAS = 2.8; $p = 0.223$). KODI also decreased (48.8 %) after surgery compared with before (84.6 %). However, it increased somewhat (49.9 %) after the 1-year follow-up. Conclusion: KP on rheumatoid arthritis patients for OVCF was effective for reducing pain in the early stage and restoring vertebral body height. Recollapse of the treated vertebral body was found relatively frequently alongside the correction loss of local kyphotic angle.

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NR 28
TC 8

Z9 12
U1 0
U2 2
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AU Shi, SP
Man, ZT
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TI Silencing of Wnt5a prevents interleukin-1β-induced collagen type II degradation in rat chondrocytes
SO EXPERIMENTAL AND THERAPEUTIC MEDICINE
LA English
DT Article
DE osteoarthritis; Wnt5a signaling pathway; small interfering RNA; gene silencing; collagen type II

ID cartilage degeneration; osteoarthritis; expression; osteoporosis; arthritis; therapy; culture; wnt-5a; cells; model
AB Osteoarthritis (OA) is a joint disease, and few treatments to date have been able to delay OA progression. The degradation of collagen type II (COL2) in the cartilage matrix is an important initiating factor for OA progression; the upregulation of Wnt5a protein activates COL2 degradation. In the present study, small interfering RNA of Wnt-5a was delivered by a lentiviral vector (LV-Wnt5a-RNAi) to silence Wnt-5a mRNA and prevent COL2 degradation. To determine the function of LV-Wnt5a-RNAi, the OA chondrocyte model (OA-like chondrocytes) were constructed using interleukin (IL)-1 beta. Detected using reverse transcription-quantitative polymerase chain reaction (RT-qPCR), Wnt-5a mRNA in the OA-like chondrocytes were upregulated in a time-dependent manner, indicating that OA-like chondrocytes were successfully constructed. The bioactivity of OA-like chondrocytes was determined using Live-Dead staining, and the result illustrated that the OA-like chondrocytes stimulated with IL-1 beta for 6 h remained viable, and these were used in Wnt5a silencing. The OA-like chondrocytes were divided into three groups: Group I, cultivated with common medium; group II, cultivated with common medium supplemented with empty lentiviral vector; group III, cultivated with common medium supplemented with LV-Wnt5a-RNAi. The efficiency of LV-Wnt5a-RNAi transfection was determined using fluorescence microscopy, the result of which indicated that LV-Wnt5a-RNAi could efficiently be transfected into the OA-like chondrocytes. The LV-Wnt5a-RNAi efficiency for the Wnt5a mRNA silencing was determined using RT-qPCR. The result illustrated that the mRNA of Wnt5a in group III was significantly lower in group I compared with that in group II ($P<0.05$), indicating that the LV-Wnt5a-RNAi could successfully silence Wnt5a mRNA. To further verify whether the silencing of Wnt5a mRNA could prevent COL2 degradation, western blotting and immunohistochemical analyses were performed. The results demonstrated that COL2 in group III was significantly higher compared with that in groups I and II ($P<0.05$), which illustrated that the silencing of Wnt5a mRNA could prevent COL2 degradation. In conclusion, LV-Wnt5a-RNAi was formed successfully and could efficiently silence Wnt5a mRNA expressed by OA-like chondrocytes. In addition, the silencing of Wnt5a mRNA could prevent the degradation of COL2 in OA-like chondrocytes, confirming that LV-Wnt5a-RNAi may be used as a novel tool for OA treatment.
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SC Research & Experimental Medicine
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PT J
AU Chung, SM
Hyun, MH
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AF Chung, S. M.
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TI Novel effects of sarcopenic osteoarthritis on metabolic syndrome, insulin resistance, osteoporosis, and bone fracture: the national survey
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Insulin resistance; Metabolic syndrome; Osteoarthritis; Sarcopenia
ID skeletal-muscle mass; knee osteoarthritis; mineral density; prospective cohort; body-composition; korean adults; visceral fat; obesity; association; prevalence
AB This study compared the effects sarcopenic osteoarthritis on metabolic syndrome, insulin resistance, osteoporosis, and bone fracture. By using national survey data, we suggest that the relationship between sarcopenia and metabolic syndrome or insulin resistance is potentiated by the severity of osteoarthritis and is independent of body weight. Sarcopenia and osteoarthritis are known risk factors for metabolic syndrome. However, their combined effects on metabolic syndrome, insulin resistance and osteoporosis remain uncertain. We used data from the fifth Korean National Health and Nutrition Examination Survey using a total of 3158 adults (age > 50 years). Sarcopenia was defined as a skeletal muscle index score (appendicular skeletal muscle mass/body weight) within the fifth percentile of

sex-matched younger reference participants. Radiographic knee osteoarthritis was defined as a Kellgren-Lawrence (K-L) grade of 2 or greater. Metabolic syndrome was diagnosed using the National Cholesterol Education Program criteria. Insulin resistance was evaluated using the homeostasis model assessment-estimated insulin resistance index (HOMA-IR). Osteoporosis was defined using the World Health Organization T-score criteria. In multivariable logistic regression analysis, the sarcopenic osteoarthritis group had a higher odds ratio (OR) for metabolic syndrome (OR = 11.00, 95 % confidential interval (CI) = 2.12-56.99, p = 0.013) than the non-sarcopenic osteoarthritis (OR = 1.02, 95 % CI = 0.65-1.62, p = 0.972) and sarcopenic non-osteoarthritis groups (OR = 7.15, 95 % CI = 1.57-32.53, p = 0.027). Similarly, sarcopenic osteoarthritis had a greater OR of highest HOMA-IR quartiles (OR = 8.19, 95 % CI = 2.03-33.05, p = 0.003) than the other groups. Overall, the association between the K-L grade and body mass index was significant; however, this significance was lower in individuals with sarcopenia and was lost in those with sarcopenic osteoarthritis. Additionally, osteoporosis and bone fracture were not associated to sarcopenic osteoarthritis (p > 0.05). These results suggest that the relationship between sarcopenia and metabolic syndrome or insulin resistance is potentiated by the severity of osteoarthritis and is independent of body weight.
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TI Osteoarthritis guidelines: Barriers to implementation and solutions
SO ANNALS OF PHYSICAL AND REHABILITATION MEDICINE
LA English
DT Review
DE Osteoarthritis; Clinical practice guidelines; Implementation
ID nonpharmacological core management; knee osteoarthritis; eular recommendations; european-society; economic-aspects; hip; care; osteoporosis; epidemiology
AB Osteoarthritis (OA) is a leading cause of disability worldwide. Clinical practice guidelines (CPGs) have been developed to facilitate improved OA management. Scientific communities worldwide have proposed CPGs for OA treatment. Despite the number of highly prominent guidelines available and their remarkable consistency, their uptake has been suboptimal. Possibly because of the multitude of barriers related to the implementation of CPGs. For example, different guidelines show contradictions, some lack evidence, and they lack a hierarchy or tools to facilitate their translation and application. Also, the guidelines do not acknowledge the effect of comorbidities on choosing the treatments. Finally, poor integration of multidisciplinary services within and across healthcare settings is a major barrier to the effective implementation of management guidelines. Here we describe the main problems related to the OA guidelines and some solutions so as to offer some guidance on the elaboration of future CPGs and their implementation in primary care. (C) 2016 Elsevier Masson SAS. All rights reserved.
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Hsieh, Shih-Peng
Lee, Hsin-Pai
Lin, Sung-Chun
Chen, Wu-Fu
Jean, Yen-Hsuan
TI Calcitonin attenuates cartilage degeneration and nociception in an experimental rat model of osteoarthritis: role of TGF-β in chondrocytes
SO SCIENTIFIC REPORTS
LA English
DT Article
ID canine experimental osteoarthritis; growth-factor-beta; articular-cartilage; salmon-calcitonin; postmenopausal women; osteophyte formation; ovariectomized rats; ii degradation; bone changes; pain
AB We investigated the role of the calcitonin (Miacalcin) in the progression of osteoarthritis (OA) and in nociceptive behavior in an experimental rat model of OA and osteoporosis. OA was induced by anterior cruciate ligament transection (ACLT)

of the right knee and by bilateral ovariectomy (OVX) in Wistar rats. Nociceptive behaviors (secondary mechanical allodynia and weight-bearing distribution of the hind paws) were analyzed prior to surgery and every week, beginning at 12 weeks after surgery, up to 20 weeks. At 20 weeks, histopathological studies were performed on the cartilage of the knee joints. Immunohistochemical analysis was performed to examine the effect of calcitonin on transforming growth factor (TGF)-beta 1 expression in articular cartilage chondrocytes. Rats subjected to ACLT + OVX surgery showed obvious OA changes in the joints. Animals subjected to ACLT + OVX and treated with calcitonin showed significantly less cartilage degeneration and improved nociceptive tests compared with animals subjected to ACLT + OVX surgeries alone. Moreover, calcitonin increased TGF-beta 1 expression in chondrocytes in ACLT + OVX-affected cartilage. Subcutaneous injection of calcitonin (1) attenuated the development of OA, (2) concomitantly reduced nociception, and (3) modulated chondrocyte metabolism, possibly by increasing cellular TGF-beta 1 expression.
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AU Xiao, J
Yu, WF
Wang, XR
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AF Xiao, Jie
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Wang, Bo
Chen, Jianwei
Liu, Yue
Li, Zhanchun
TI Correlation between neuropeptide distribution, cancellous bone microstructure and joint pain in postmenopausal women with osteoarthritis and osteoporosis
SO NEUROPEPTIDES
LA English
DT Article
DE Osteoarthritis; Osteoporosis; Neuropeptide; Microstructure; Pain
ID gene-related peptide; vasoactive-intestinal-peptide; necrosis-factor-alpha;

spinal-cord-injury; substance-p; in-vitro; biomechanical property; rheumatoid-arthritis; subchondral bone; rat model
AB Objectives: To explore the relationship between the distribution of neuropeptides, cancellous bone microstructure and joint pain in postmenopausal women with osteoarthritis (OA) and osteoporosis (OP). Methods: Cancellous bone of the femoral head was obtained at the time of hip arthroplasty from 20 postmenopausal women, 10 with OA and 10 with OP. Pain intensity was evaluated using the visual analog scale (VAS) before the operation. The microstructural parameters were measured with micro-CT and the neuropeptides of the cancellous bone were stained by an immunohistochemical method. Results: We observed that BV/TV, Tb.Th and Th.N values in the OP were significantly decreased compared to those in the OA. Immunohistochemical analysis revealed that the mean optical density (MOD) values for SP, CGRP, and VIP in the OA group were significantly higher than those in the OP, and the MOD value for NPY in the OA was significantly lower than that in the OP. We also observed that the MOD values for SP were positively correlated with AD, BV/TV, Tb.Th, Tb.N and Conn.D and negatively with MD, Tb.Sp and SMI in all patients. The MOD values for CGRP were positively correlated with AD, BV/TV and Tb.Th. MOD values for VIP were positively correlated with BV/TV and Tb.Th and negatively with SMI. The VAS score was correlated positively with the MOD values for SP, CGRP, VIP and negatively with NPY in all patients. Conclusions: Neuropeptides play an important role in the pathogenesis of OA and OP, which may cause pain and influence the bone microstructure. (C) 2015 Elsevier Ltd. All rights reserved.
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Z9 30
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U2 24
PU CHURCHILL LIVINGSTONE
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WC Endocrinology & Metabolism; Neurosciences
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TI Association Between Physical Therapy and Risk of Coronary Artery Disease and Dyslipidemia Among Osteoarthritis Patients: A Nationwide Database Study
SO ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION
LA English
DT Article
DE Comorbidity; Dyslipidemias; Osteoarthritis; Physical therapy modalities; Rehabilitation
ID cross-sectional analysis; whole-body vibration; bone-density; older-adults; exercise; population; knee; interventions; health; individuals
AB Objective: To provide empirical evidence on the effect of early physical therapy (PT) within the first year of osteoarthritis (OA) diagnosis on reduction in OA-related comorbidities in patients with OA. Design: Retrospective cohort study. Setting: The study was conducted using a nationally representative sample of 1 million National Health Insurance enrollees. Participants: Newly diagnosed patients with OA (N=13,545). One-to-one propensity score matching was used to match patients who received PT within the first year of OA diagnosis (PT group; n=3403) with an equal number of patients with OA who did not receive PT (non-PT group). Interventions: Not applicable. Main Outcome Measures: The 4-year cumulative risk of comorbidities including coronary artery disease (CAD), diabetes mellitus, dyslipidemia, osteoporosis, gastrointestinal tract ulcer, and renal failure was estimated. A Cox proportional hazards regression analysis was performed to identify the dose-response relation between the PT dosage and the risk of OA-related comorbidities. Results: A total of 3403 patients (25.1%) received PT within the first year of OA diagnosis. The PT group had a significantly lower 4-year cumulative risk of dyslipidemia (P=.05) and a potentially lower 4-year cumulative risk of CAD (P=.09). After adjusting for other potential confounders, the Cox proportional hazards regression analysis showed that patients with OA who received a high PT dosage had a low risk of CAD and dyslipidemia. Conclusions: Patients with OA who received PT had a lower risk of OA-related comorbidities such as dyslipidemia or CAD. (C) 2016 by the American Congress of Rehabilitation Medicine
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PT J
AU Broome, DT
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AF Broome, David T.
Datta, Nabanita S.
TI Mitogen-activated protein kinase phosphatase-1: function and regulation in bone and related tissues
SO CONNECTIVE TISSUE RESEARCH
LA English
DT Review
DE Bone; fat; MAPK phosphatase-1; muscle; pathophysiology; signaling
ID cyclooxygenase-2 messenger-rna; innate immune-responses; hormone-related protein; skeletal-muscle differentiation; distinct signaling pathways; osteoblast gene-expression; focal adhesion kinase; map kinase; parathyroid-hormone; adipocyte differentiation
AB In this review, we have highlighted work that has clearly demonstrated that mitogen-activated protein kinase (MAPK) phosphatase-1 (MKP-1), a negative regulator of MAPKs, is an important signaling mediator in bone, muscle, and fat tissue homeostasis and differentiation. Further, we examined recent studies with particular focus on MKP-1 overexpression or deletion and its impact on tissues connected to bone. We also summarized regulation of MKP-1 by known skeletal regulators like parathyroid hormone (PTH)/PTH-related peptide (PTHrP) and bone morphogenic proteins. MKP-1's integration into the pathophysiological state of osteoporosis, osteoarthritis, rheumatoid arthritis, obesity, and muscular dystrophy are examined to emphasize possible involvement of MKP-1 both at the molecular level and in disease complications such as sarcopenia- or diabetes-related osteoporosis. We predict that understanding the mechanism of MKP-1-mediated signaling in bone-muscle-fat crosstalk will be a key in coordinating their activities and developing therapeutics to improve clinical outcomes for diseases associated with advanced age.
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AF Seeliger, Claudine
Balmayor, Elizabeth R.
van Griensven, Martijn
TI miRNAs Related to Skeletal Diseases
SO STEM CELLS AND DEVELOPMENT
LA English

DT Review
ID mesenchymal stem-cells; fatty-acid synthase; article. see april; suppresses osteogenic differentiation; regulates chondrogenic differentiation; pre-osteoblast differentiation; osteosarcoma tumor-growth; down-regulation; microrna expression; circulating micrornas
AB miRNAs as non-coding, short, double-stranded RNA segments are important for cellular biological functions, such as proliferation, differentiation, and apoptosis. miRNAs mainly contribute to the inhibition of important protein translations through their cleavage or direct repression of target messenger RNAs expressions. In the last decade, miRNAs got in the focus of interest with new publications on miRNAs in the context of different diseases. For many types of cancer or myocardial damage, typical signatures of local or systemically circulating miRNAs have already been described. However, little is known about miRNA expressions and their molecular effect in skeletal diseases. An overview of published studies reporting miRNAs detection linked with skeletal diseases was conducted. All regulated miRNAs were summarized and their molecular interactions were illustrated. This review summarizes the involvement and interaction of miRNAs in different skeletal diseases. Thereby, 59 miRNAs were described to be deregulated in tissue, cells, or in the circulation of osteoarthritis (OA), 23 miRNAs deregulated in osteoporosis, and 107 miRNAs deregulated in osteosarcoma (OS). The molecular influences of miRNAs regarding OA, osteoporosis, and OS were illustrated. Specific miRNA signatures for skeletal diseases are described in the literature. Some overlapped, but also unique ones for each disease exist. These miRNAs may present useful targets for the development of new therapeutic approaches and are candidates for diagnostic evaluations.
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TI Efficacy and safety of glucosamine sulfate in the management of osteoarthritis: Evidence from real-life setting trials and surveys
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DE Chondroitin; Glucosamine; Knee osteoarthritis; Symptomatic slow-acting drugs for osteoarthritis (SYSADOAs)
ID placebo-controlled trials; controlled clinical-trial; total joint replacement; knee osteoarthritis; chondroitin sulfate; double-blind; cartilage explants; metaanalysis; progression; recommendations
AB The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) treatment algorithm recommends chronic symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) including glucosamine sulfate (GS) and chondroitin sulfate (CS) as first-line therapy for knee osteoarthritis (OA). Numerous studies are published on the use of SYSADOAs in OA; however, the efficacy of this class is still called into question largely due to the regulatory status, labeling and availability of these medications which differ substantially across the world. Examination of the evidence for the prescription patented crystalline GS (pCGS) formulation at a dose of 1500 mg once-daily demonstrates superiority over other GS and glucosamine hydrochloride (GH) formulations and dosage regimens.

Thus, the ESCEO task force advocates differentiation of prescription pCGS over other glucosamine preparations. Long-term clinical trials and real-life studies show that pCGS may delay joint structural changes, suggesting potential benefit beyond symptom control when used early in the management of knee OA. Real-life pharmacoeconomic studies demonstrate a long-term reduction in the need for additional pain analgesia and non-steroidal anti-inflammatory drugs (NSAIDs) with pCGS, with a significant reduction of over 50% in costs associated with medications, healthcare consultations and examinations over 12 months. Furthermore, treatment with pCGS for at least 12 months leads to a reduction in the need for total joint replacement for at least 5 years following treatment cessation. Thus, pCGS (1500 mg od) is a logical choice to maximize clinical benefit in OA patients, with demonstrated medium-term control of pain and lasting impact on disease progression. (C) 2015 The Authors. Published by Elsevier HS Journals, Inc.

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NR 45
TC 73
Z9 99
U1 0
U2 40
PU W B SAUNDERS CO-ELSEVIER INC
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SN 0049-0172
EI 1532-866X
J9 SEMIN ARTHRITIS RHEU
JI Semin. Arthritis Rheum.
PD FEB 15
PY 2016
VL 45
IS 4
BP S12
EP S17
DI 10.1016/j.semarthrit.2015.11.011
PG 6
WC Rheumatology
SC Rheumatology
GA DF9AK
UT WOS:000371652400003
PM 26806187
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AU El-Haj, M
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Cohen-Kfir, E
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Safran, O.
Dresner-Pollak, R.
TI Reduced Sirtuin1 expression at the femoral neck in women who sustained an osteoporotic hip fracture
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE d Femoral neck; Osteoarthritis; Osteoporotic hip fracture; Sclerostin; Sirtuin1
ID bone-formation; beta-catenin; sirt1; osteoarthritis; sclerostin; regulator; mass
AB To investigate the role of Sirtuin1 in osteoporosis, Sirtuin1 was determined at the femoral neck in female patients undergoing hip operation for fractured hip or osteoarthritis. Reduced Sirtuin1 was found in osteoporotic patients. Pharmacologic activation of Sirtuin1 reduced sclerostin, an inhibitor of bone formation. Activation of Sirtuin1 may be a new direction to generate therapies for osteoporosis. The aim of the study are to investigate the role of Sirtuin1 (Sirt1), an anti-aging factor and a player in age-associated diseases, in osteoporotic hip fractures, and test the hypothesis that Sirt1 is a negative regulator of sclerostin, a bone formation inhibitor, in human femoral bone marrow mesenchymal cells (BM-MSCs). Sirt1 and sclerostin were determined by western blot in bone samples obtained intra-operatively from the inferior medial cortex of the femoral neck (calcar region) in female patients undergoing partial hip replacement for fractured neck of femur (N = 10) or hip replacement for osteoarthritis (N = 8) (mean +/- SD age 81 +/- 8.1 vs. 68 +/- 9.3 years; BMI 26.2 +/- 3.6 vs. 25.9 +/- 7.1 kg/m(2) in osteoporotic and osteoarthritis patients). Calcar thickness and femoral bone mineral density (BMD) were determined preoperatively by X-ray using a digital TraumaCad((TM)) software and DEXA. Femoral BM-MSCs were collected intra-operatively and treated with SRT3025, a Sirt1 activator. Sclerostin and dentin matrix acidic phosphoprotein (DMP1) were determined by western blot and messenger RNA (mRNA) expression of Lef1 and DMP1 was evaluated by quantitative real-time PCR. Osteoporotic (OP) patients had reduced cortical thickness, femoral neck, and total hip BMD compared

to osteoarthritis (OA) patients. Calcar Sirt1 expression was significantly reduced, while sclerostin was markedly increased in OP compared to OA patients. Sirt1 and sclersotin expressions were inversely correlated (r = -0.49, P = 0.047). SRT3025 administration down-regulated sclerostin and up-regulated DMP1 protein level and increased LEF1 and DMP1 mRNA expressions in OP patient-derived BM-MSCs. Reduced femoral neck Sirt1 may play a role in osteoporotic hip fractures in part via influencing local sclerostin expression. The therapeutic potential of Sirt1 activation in osteoporosis warrants further investigation.
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TC 27
Z9 30
U1 0
U2 10
PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 0937-941X
EI 1433-2965
J9 OSTEOPOROSIS INT
JI Osteoporosis Int.
PD JUL 15
PY 2016
VL 27
IS 7
BP 2373
EP 2378
DI 10.1007/s00198-016-3536-4
PG 6
WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA DO8AQ
UT WOS:000378004800024
PM 26902093
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Adachi, JD
Binkley, N
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Meisner, P. D.
Libanati, C.
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TI Romosozumab Treatment in Postmenopausal Women with Osteoporosis
SO NEW ENGLAND JOURNAL OF MEDICINE
LA English
DT Article
ID bone-formation; fracture; sclerostin; sost; wnt; teriparatide; density; protein; product; costs
AB BACKGROUND Romosozumab, a monoclonal antibody that binds sclerostin, increases bone formation and decreases bone resorption. METHODS We enrolled 7180 postmenopausal women who had a T score of -2.5 to -3.5 at the total hip or femoral neck. Patients were randomly assigned to receive subcutaneous injections of romosozumab (at a dose of 210 mg) or placebo monthly for 12 months; thereafter, patients in each group received denosumab for 12 months, at a dose of 60 mg, administered subcutaneously every 6 months. The coprimary end points were the cumulative incidences of new vertebral fractures at 12 months and 24 months. Secondary end points included clinical (a composite of nonvertebral and symptomatic vertebral) and nonvertebral fractures. RESULTS At 12 months, new vertebral fractures had occurred in 16 of 3321 patients (0.5%) in the romosozumab group, as compared with 59 of 3322 (1.8%) in the placebo group (representing a 73% lower risk with romosozumab; P<0.001). Clinical fractures had occurred in 58 of 3589 patients (1.6%) in the romosozumab group, as compared with 90 of 3591 (2.5%) in the placebo group (a 36% lower risk with romosozumab; P = 0.008). Nonvertebral fractures had occurred in 56 of 3589 patients (1.6%) in the romosozumab group and in 75 of 3591 (2.1%) in the placebo group (P = 0.10). At 24 months, the rates of vertebral fractures were significantly lower in the romosozumab group than in the placebo group after each group made the transition to denosumab (0.6% [21 of 3325 patients] in the romosozumab group

vs. 2.5% [84 of 3327] in the placebo group, a 75% lower risk with romosozumab; P<0.001). Adverse events, including instances of hyperostosis, cardiovascular events, osteoarthritis, and cancer, appeared to be balanced between the groups. One atypical femoral fracture and two cases of osteonecrosis of the jaw were observed in the romosozumab group. CONCLUSIONS In postmenopausal women with osteoporosis, romosozumab was associated with a lower risk of vertebral fracture than placebo at 12 months and, after the transition to denosumab, at 24 months. The lower risk of clinical fracture that was seen with romosozumab was evident at 1 year.
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NR 24
TC 1276
Z9 1490
U1 7
U2 182
PU MASSACHUSETTS MEDICAL SOC
PI WALTHAM
PA WALTHAM WOODS CENTER, 860 WINTER ST,, WALTHAM, MA 02451-1413 USA
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EI 1533-4406
J9 NEW ENGL J MED
JI N. Engl. J. Med.
PD OCT 20
PY 2016
VL 375
IS 16
BP 1532
EP 1543
DI 10.1056/NEJMoa1607948
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WC Medicine, General & Internal
SC General & Internal Medicine
GA EJ3HF
UT WOS:000393102500006
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AU Kim, BJ
Shin, KO
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TI The effect of sphingosine-1-phosphate on bone metabolism in humans depends on its plasma/bone marrow gradient
SO JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION
LA English
DT Article
DE Plasma S1P; Bone marrow S1P; Gradient; Hip fracture; Osteoporosis
ID sphingosine 1-phosphate levels; postmenopausal women; osteoblastic cells; osteoclast differentiation; mineral density; osteoporosis; fracture; homeostasis; prevention; receptors
AB Background Although recent studies provide clinical evidence that sphingosine-1-phosphate (S1P) may primarily affect bone resorption in humans, rather than bone formation or the osteoclast-osteoblast coupling phenomenon, those studies could not determine which bone resorption mechanism is more important, i.e., chemorepulsion of osteoclast precursors via the blood to bone marrow S1P gradient or receptor activator of NF-kappa B ligand (RANKL) elevation in osteoblasts via local S1P. Aim To investigate how S1P mainly contributes to increased bone resorption in humans, we performed this case-control study at a clinical unit in Korea. Methods Blood and bone marrow samples were contemporaneously collected from 70 patients who underwent hip surgery due to either osteoporotic hip fracture (HF) (n = 10) or other causes such as osteoarthritis (n = 60). Results After adjusting for sex, age, BMI, smoking, alcohol, previous

fracture, diabetes, and stroke, subjects with osteoporotic HF demonstrated a 3.2-fold higher plasma/bone marrow S1P ratio than those without HF, whereas plasma and bone marrow S1P levels were not significantly different between these groups. Consistently, the risk of osteoporotic HF increased 1.38-fold per increment in the plasma/bone marrow S1P ratio in a multivariate adjustment model. However, the odds ratios for prevalent HF according to the increment in the plasma and bone marrow S1P level were not statistically significant. Conclusion Our current results using simultaneously collected blood and bone marrow samples suggest that the detrimental effects of S1P on bone metabolism in humans may depend on the S1P gradient between the peripheral blood and bone marrow cavity.
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FU Korea Health Technology RD Project; National Research Foundation (NRF) - Korean government [KRF-2010-0025271]; Ministry of Health & Welfare, Republic of Korea [HI13C1432, HI14C2185]
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NR 28
TC 15
Z9 18
U1 0
U2 8
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 1720-8386
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J9 J ENDOCRINOL INVEST
JI J. Endocrinol. Invest.
PD MAR 15
PY 2016
VL 39
IS 3
BP 297
EP 303
DI 10.1007/s40618-015-0364-x
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA DE7UQ
UT WOS:000370842600007
PM 26219613
DA 2026-02-10
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PT J

AU Mays, S
AF Mays, Simon
TI Bone-formers and bone-losers in an archaeological population
SO AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY
LA English
DT Article
DE DISH; osteoporosis; enthesophyte; anterior longitudinal ligament; cortical thickness
ID idiopathic skeletal hyperostosis; mineral density; cortical bone; radiographic absorptiometry; postmenopausal women; logistic-regression; spinal involvement; osteoarthritis; prevalence; dish
AB ObjectivesRecent biomedical research suggests that, in modern human populations, individuals may vary in their inherent tendency toward bone formation at skeletal and extra-skeletal locations. However, the nature of this phenomenon is incompletely understood, and the extent to which it might apply to past populations is unclear. It is hypothesized that if there is inter-individual variation in some overall tendency toward bone formation in skeletal and extra-skeletal sites then there should be a positive relationship between ligamentous ossification and thickness of cortical bone. This work is a test of this hypothesis in an archaeological population. Materials and MethodsThe study material comprises adult skeletons (N=137 individuals) of documented age at death from 18th to 19th century London. It examines the relationship between bone deposition in the anterior longitudinal ligament (ALL) in the thoracic spine and cortical index (CI) at the metacarpal measured by radiogrammetry. ResultsControlling for the potential confounders age, sex, skeletal completeness, occupation (males) and parity (females), there was a positive association between ossification into the ALL and CI. This reflects lesser medullary cavity width in those showing ALL ossification. DiscussionLigamentous ossification in the axial skeleton and peripheral cortical bone status are linked, individuals with ALL ossification showing lesser resorption of cortical bone at the endosteal surface. This is consistent with the idea of inter-individual variation in some general bone-forming/bone-losing tendency in this 200 year old study population, but there was no evidence of a link between ALL ossification and increased skeletal subperiosteal bone deposition. Am J Phys Anthropol 159:577-584, 2016. (c) 2015 The Authors American Journal of Physical Anthropology Published by Wiley Periodicals, Inc.
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TI Solid-state NMR study of discrete environments of bone mineral nanoparticles using phosphorus-31 relaxation
SO JOURNAL OF APPLIED BIOMEDICINE
LA English
DT Article
DE Apatite; Bone; Nanomaterial; Osteoarthritis; Osteoporosis; Nuclear magnetic resonance
ID nuclear-magnetic-resonance; cortical bone; mas nmr; mechanical-property; postmenopausal women; reference intervals; cationic sites; femoral-head; bound water; in-vivo
AB Bone mineral nanoparticles, residing between collagenous fibres, contain a crystalline apatite core (CAC) covered by an amorphous hydrated surface layer (AHSL). The main objectives of this work were to characterize the nanoparticles of human bone mineral and their discrete CAC and AHSL regions and relate this

information to bone diseases. This pilot study involved 18 postmenopausal women suffering from osteoarthritis together with osteoporosis or osteopenia. Trabecular tissue specimens were acquired from the femoral intertrochanteric region during total hip arthroplasty. The specimens of whole bone were examined by P-31 solid-state NMR (ssNMR) to measure the concentration ratio of phosphorus in the AHSL and CAC locations, together with their P-31 linewidths and spin-lattice relaxation times. It was found that the AHSL region of the studied specimens contained 13-24% apatite phosphorus. The magnitude, hydration and structural order of AHSL and CAC were dependent on the progress of the pertinent diseases. Thus, the P-31 ssNMR spectroscopy can be used ex vivo to selectively analyse the discrete nanoapatite environments in whole bone specimens and possibly assist in postoperative medical diagnostics. (C) 2016 Faculty of Health and Social Sciences, University of South Bohemia in Ceske Budejovice. Published by Elsevier Sp. z o. o. All rights reserved.
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TI Segmentation of joint and musculoskeletal tissue in the study of arthritis
SO MAGNETIC RESONANCE MATERIALS IN PHYSICS BIOLOGY AND MEDICINE
LA English
DT Review
DE MRI; Image segmentation; Osteoarthritis; Rheumatoid arthritis; Knee; Hip; Wrist
ID anterior cruciate ligament; early rheumatoid-arthritis; magnetic-resonance images; marrow edema pattern; of-the-art; mr-images; articular-cartilage; quantitative assessment; hip-joint; bone edema
AB As the most frequent cause of physical disability, musculoskeletal diseases such as arthritis and osteoporosis have a great social and economical impact. Quantitative magnetic resonance imaging (MRI) biomarkers are important tools that allow clinicians to better characterize, monitor, and even predict musculoskeletal disease progression. Post-processing pipelines often include image segmentation. Manually identifying the border of the region of interest (ROI) is a difficult and time-consuming task. Manual segmentation is also affected by inter- and intrauser variability, thus limiting standardization. Fully automatic or semi-automatic methods that minimize the user interaction are highly desirable. Unfortunately, an ultimate, highly reliable and extensively evaluated solution for joint and musculoskeletal tissue segmentation has not yet been proposed, and many clinical studies still adopt fully manual procedures. Moreover, the clinical translation of several promising quantitative MRI techniques is highly affected by the lack of an established, fast, and accurate segmentation method. The goal of this review is to present some of the techniques proposed in recent literature that have been adopted in clinical studies for joint and musculoskeletal tissue analyses in arthritis patients. The most widely used MRI sequences and image processing algorithms employed to accomplish segmentation challenges will be discussed in this paper.
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TI Non-Communicable Disease Clinical Practice Guidelines in Brazil: A Systematic Assessment of Methodological Quality and Transparency
SO PLOS ONE
LA English
DT Article
ID agree ii; primary-care; multimorbidity; management; appraisal; china; instrument
AB Background Annually, non-communicable diseases (NCDs) kill 38 million people worldwide, with low and middle-income countries accounting for three-quarters of these deaths. High-quality clinical practice guidelines (CPGs) are fundamental to improving NCD management. The present study evaluated the methodological rigor and transparency of Brazilian CPGs that recommend pharmacological treatment for the most prevalent NCDs. Methods We conducted a systematic search for CPGs of the following NCDs: asthma, atrial fibrillation, benign prostatic hyperplasia, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease and/or stable angina, dementia, depression, diabetes, gastroesophageal reflux disease, hypercholesterolemia, hypertension, osteoarthritis, and osteoporosis. CPGs comprising pharmacological treatment recommendations were included. No language or year restrictions were applied. CPGs were excluded if they were merely for local use and referred to NCDs not listed above. CPG quality was independently assessed by two reviewers using the Appraisal of Guidelines Research and Evaluation instrument, version II (AGREE II).

Main Findings "Scope and purpose" and "clarity and presentation" domains received the highest scores. Sixteen of 26 CPGs were classified as low quality, and none were classified as high overall quality. No CPG was recommended without modification (77% were not recommended at all). After 2009, 2 domain scores ("rigor of development" and "clarity and presentation") increased (61% and 73%, respectively). However, "rigor of development" was still rated <30%. Conclusion Brazilian healthcare professionals should be concerned with CPG quality for the treatment of selected NCDs. Features that undermined AGREE II scores included the lack of a multidisciplinary team for the development group, no consideration of patients' preferences, insufficient information regarding literature searches, lack of selection criteria, formulating recommendations, authors' conflict of interest disclosures, and funding body influence.
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AU Thomasius, F

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TI Phase IV randomized preference study in patients eligible for calcium and vitamin D supplementation
SO CURRENT MEDICAL RESEARCH AND OPINION
LA English
DT Article
DE Acceptability; Calcium; Osteoporosis; Preference; Supplement; Vitamin D
ID cost-effectiveness; european-society; economic-aspects; dairy-products; osteoporotic fractures; postmenopausal women; plus vitamin-d-3; prevention; health; osteoarthritis
AB Introduction/objectives: Preference for supplement formulation helps determine an individual's adherence to long-term medication and can improve clinical benefit for chronic illnesses such as osteoporosis. This study compared the preference, acceptability and tolerability of a reformulation of Calcichew D3(1) 500mg/400IU and Calcichew D3 500mg/800IU (Takeda UK Ltd, Wobrun Green, UK) with Adcal-D3(2) 500mg/400IU (ProStrakan Ltd, Galashiels, UK) and Kalcipos-D 500mg/800IU (Meda Pharmaceuticals Ltd, Bishop's Stortford, UK), respectively.Method: This phase IV, randomized, open-label, two-period, cross-over study was conducted at nine sites in the UK and Germany. Eligible subjects (65 years requiring calcium/vitamin D supplementation for prevention/treatment of deficiencies, or 18 years requiring supplementation as an adjunct to osteoporosis treatment) were randomly assigned to one of two 2 week treatment sequences - Group 1: Calcichew D3 500/400 then Adcal-D3 500/400 (or vice versa), or Group 2: Calcichew D3 500/800 then Kalcipos-D 500/800 (or vice versa). After each treatment period, patients rated the treatment for acceptability using 100mm visual analogue scales. After the second treatment period, patients indicated their treatment preference. The primary endpoint, the percentage of patients with a preference for each treatment, was analyzed with a logistic regression model.Results: Two hundred and seventy-six patients were randomly assigned by treatment sequence, 138 to each group. Preference questionnaires among patients who preferred Calcichew or comparator revealed the odds for patients preferring Calcichew 500/400 (77.6%) over Adcal-D3 was 3.46 ([95% CI 2.24, 5.36], $p<0.001$) in Group 1, and Calcichew D3 500/800 (63.2%) over Kalcipos-D was 1.72 ([1.19, 2.47], $p=0.004$) in Group 2. Adverse events were mostly gastrointestinal and were comparable between groups. The new formulation of Calcichew D3 is acceptable and consistent with its known tolerability profile.Conclusions: In this short-term 30day study, patients preferred Calcichew D3 500/400 and Calcichew D3 500/800 over respective comparators. A trend towards better compliance with Calcichew D3 preference observed in Group 1 warrants a longer term study to identify treatment compliance.Trial registration: Clinicaltrials.gov: NCT02457247.

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TI Novel heterocyclic ring-fused oleanolic acid derivatives as osteoclast inhibitors for osteoporosis
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DT Article
ID nitric-oxide production; ursane triterpenoids; synthetic oleanane; nfat; differentiation; molecules; pyrazole; targets; design; roles
AB Osteoporosis is a major public health problem in our aging society. In the present study, a series of novel oleanolic acid (OA) derivatives were synthesized via modifications in the A-ring and C-28 position of OA, and their anti-bone resorption activities were evaluated. Screening results revealed that most of the derivatives inhibited RANKL-induced osteoclast formation from RAW264.7 cells. Among the derivatives, 6g exhibited a potent inhibitory activity with an IC50 of 24 nM. Furthermore, 6g prevented ovariectomy-induced bone loss in rats. The preliminary mechanism investigation demonstrated that 6g suppressed the protein and mRNA expressions of c-Fos and NFATc1, and downregulated the mRNA of other osteoclastogenic markers. The results suggested that the OA derivatives might serve as potential leads for the development of novel agents for the treatment of osteoporosis.
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NR 38
TC 10
Z9 12
U1 0
U2 23
PU ROYAL SOC CHEMISTRY
PI CAMBRIDGE
PA THOMAS GRAHAM HOUSE, SCIENCE PARK, MILTON RD, CAMBRIDGE CB4 0WF, CAMBS, ENGLAND
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J9 MEDCHEMCOMM
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PD JUN 15
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VL 7
IS 2
BP 371
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DI 10.1039/c5md00482a
PG 7
WC Biochemistry & Molecular Biology; Chemistry, Medicinal
SC Biochemistry & Molecular Biology; Pharmacology & Pharmacy
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ER

PT J
AU Seo, BK
Ryu, HK
Park, YC
Huh, JE
Baek, YH

AF Seo, Byung-Kwan
Ryu, Hee-Kyoung
Park, Yeon-Cheol
Huh, Jeong-Eun
Baek, Yong-Hyeon
TI Dual effect of WIN-34B on osteogenesis and osteoclastogenesis in cytokine-induced mesenchymal stem cells and bone marrow cells
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE WIN-34B; Osteogenesis; Osteoclastogenesis; Mesenchymal stem cells; Bone marrow cells; Osteoporosis
ID in-vitro; osteoporosis; differentiation; phosphorylation; osteoarthritis; mineralization; activation; pathways; therapy; runx2
AB Ethnopharmacological relevance: As an n-butanol fractionated extracted mixture of Lonicera japonica Thunb, dried flowers and Anemarrhena asphodeloides Bunge, root, WIN-34B has been reported the analgesic, anti-inflammatory, cartilage-repairing and protective effects in previous studies. Aim of the study: To investigate the effect of WIN-34B on osteogenesis and osteoclastogenesis in cytokine-induced mesenchymal stem cells and bone marrow cells. Materials and methods: To examine the effect of WIN-34B on osteogenic differentiation, human mesenchymal stem cells (hMSCs) were treated with WIN-34B (1 mu g/mL and 10 mu g/mL). Alkaline phosphatase (ALP) activity was evaluated and Von Kossa staining was conducted. Mice bone marrow macrophages (BMMs) were obtained and treated with receptor activator of nuclear factor-kappa B ligand (RANKL) and macrophage colony stimulating factor (m-CSF) to induce osteoclastogenesis. To investigate osteoclast differentiation, tartrate-resistant acid phosphatase (TRAP) staining was conducted after treatment with WIN-34B. Osteoclastogenic conditions were induced by stimulating the cells with interleukin (IL)-1 alpha, IL-17, and tumor necrosis factor (TNF-alpha) in hMSCs and BMMs co-culture systems. The expression levels of osteoprotegerin (OPG), RANKL, runt-related transcription factor 2 (RUNX2), IL-17, c-Fos, TNF-alpha, and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) were measured by reverse transcription polymerase chain reaction (RT-PCR). The expression levels of nuclear factor-kappaB (NF-KB), inhibitory kappa B-alpha (I kappa B alpha), phospho-NF-kappa B, phospho-I kappa B alpha, beta-actin, p38 MAPK, phospho-c-Jun N-terminal kinase UNK), phospho-extracellular-signal regulated kinase (ERK), phospho-p38 mitogen-activated protein kinase (MAPK), phospho-JNK, and phospho-ERK were measured by western blot analysis. Results: WIN-34B promoted ALP activity and mineralization of hMSCs. In TRAP-stained BMMs, the number of multinucleated cells decreased after WIN-34B treatment. WIN-34B increased the OPG/RAN-KL ratio and the expression of RUNX2, and suppressed the expression of IL-17, c-Fos, and TNF-alpha. It also suppressed the activation of NF-kappa B, I kappa B alpha, p38 MAPK, and JNK in a dose-dependent manner. Conclusions: These results

demonstrated that WIN-34B increased osteogenesis and decreased osteoclastogenesis in cytokine-induced mesenchymal stem cells and bone marrow cells via inhibition of the NF-kappa B, JNK, and p38 MAPK pathways. (C) 2016 Elsevier Ireland Ltd. All rights reserved.
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NR 31
TC 12
Z9 12
U1 0
U2 35
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
SN 0378-8741
EI
J9 J ETHNOPHARMACOL
JI J. Ethnopharmacol.
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IS
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PG 10
WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
SC Plant Sciences; Pharmacology & Pharmacy; Integrative & Complementary Medicine
GA ED7ZF
UT WOS:000389090600024
PM 27401292
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PT J
AU Chen, Y
Zeng, GS
Liu, WY
AF Chen, Yi
Zeng, Guangsheng
Liu, Wenyong
TI Robust and stimuli-responsive POSS hybrid PDMAEMA hydrogels for controlled drug release
SO JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A
LA English
DT Article
DE POSS; double stimulus responsiveness; nanocomposite hydrogels; drug release
ID polyhedral oligomeric silsesquioxane; delivery; poly(n-isopropylacrylamide); nanocomposites; nanoparticles; polymers; carriers
AB A new polyhedral oligomeric silsesquioxane (POSS) hybrid hydrogels were desinged and fabricated by introducing cationic octa-ammonium (Oa)-POSS) into chemically cross-linked cationic PDMAEMA hydrogels via in situ radical freezing polymerization. The prepared gels (shorten as OP-PD gels) show considerably improved properties through the effective incorporation and dispersion of Oa-POSS particles in gels. Comparing to the Oa-POSS-free gels, the hybrid gels own better mechanical properties with higher tensile and compressive strength. Meantime, except the decreased swelling ratio in acid condition, the OP-PD gels still keep excellent swelling ability with obvious pH and temperature double responsiveness, which is affected by the content of Oa-POSS slightly. All OP-PD gels exhibit an ultrarapid deswelling rate due to the interconnected micropores structure caused by freezing and the formation of microhydrophobic region around POSS particles. Moreover, the application potential of OP-PD gels in drug release was exploited by using flutamide as target drug, the result showed that the increased Oa-POSS could improve the drug loading ability, and OP-PD gels showed well controlled-release effect in simulated human stomachic condition. (c) 2016 Wiley Periodicals, Inc. J Biomed Mater Res Part A: 104A: 2345-2355, 2016.
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TC 12
Z9 13
U1 0
U2 76
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 J BIOMED MATER RES A
JI J. Biomed. Mater. Res. Part A
PD SEP 15
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VL 104
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BP 2345
EP 2355
DI 10.1002/jbm.a.35771
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WC Engineering, Biomedical; Materials Science, Biomaterials
SC Engineering; Materials Science
GA DS4CL
UT WOS:000380728900023
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PT J
AU Tomanik, M
Nikodem, A
Filipiak, J
AF Tomanik, Magdalena
Nikodem, Anna
Filipiak, Jaroslaw
TI Microhardness of human cancellous bone tissue in progressive hip osteoarthritis
SO JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS
LA English
DT Article
DE Microhardness; Osteoarthritis; Hip; Cancellous bone; Mineralization
ID mechanical-property; trabecular bone; femoral-head; hardness; osteoporosis; microindentation
AB Bone tissue is a biological system in which the dynamic processes of, among others, bone formation or internal reconstruction will determine the spatial structure of the tissue and its mechanical properties. The appearance of a factor disturbing the balance between biological processes, e.g. a disease, will cause changes in the spatial structure of bones, thus affecting its mechanical properties. One of the bone diseases most common in an increasingly ageing population is osteoarthritis, also referred to as degenerative joint disease. It is estimated that in 2050 about 1300 million people will show symptoms of OA. The appearance of a

pathological stimulus disturbs the balance of the processes of degradation and synthesis of articular cartilage, chondrocytes and the extracellular matrix, and the subchondral bone layer. As osteoarthritis progresses, study of the epiphysis reveals increasingly widespread changes of the articular surface and the internal structure of bone tissue. In this paper, the authors point out the differences in the mechanical properties of cancellous bone tissue forming the proximal epiphysis of the femoral bone during the progressive stages of OA. In order to determine microproperties of bone trabeculae, specimens from different stages of the disease (N=9) were subjected to microindentation testing, which made it possible to determine the material properties of bone tissue, such as microhardness HV and Young's modulus E. In addition, mechanical tests were supplemented with Raman spectroscopy, which determine the degree of bone mineralization, and measurements of structural properties based on analysis using microCT. The conducted tests were used to establish both quantitative and quantitative description of changes in the structural and mechanical properties connected with reorganization of trabeculae making up the bone in the various stages of osteoarthritis. The proposed description will supplement existing knowledge in the literature about identification of the processes occurring during the development of this disease. (C) 2016 Elsevier Ltd. All rights reserved.
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NR 31
TC 21
Z9 24
U1 0
U2 47
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 1751-6161
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J9 J MECH BEHAV BIOMED
JI J. Mech. Behav. Biomed. Mater.
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WC Engineering, Biomedical; Materials Science, Biomaterials
SC Engineering; Materials Science

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PT J
AU Liu, XD
Cai, F
Zhang, Y
Yang, AL
Liu, L
AF Liu, Xiaodong
Cai, Feng
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Yang, Anli
Liu, Liang
TI Celastrol, an NF-κB inhibitor, ameliorates hypercalciuria and articular cartilage lesions in a mouse model of secondary osteoporosis
SO JOURNAL OF PHARMACOLOGICAL SCIENCES
LA English
DT Article
DE Celastrol; NF-kappa B inhibitor; Secondary osteoporosis; Cartilage lesions
ID antiinflammatory activity; subchondral bone; i collagen; osteoarthritis; inflammation; degradation; suppression; activation; expression; turnover
AB Notwithstanding compelling contribution of NF-kappa B to the progression of osteoporosis has been reported, little is known regarding direct inhibition of NF-kappa B benefiting osteoporosis. In this study, therefore, we evaluated the role of celastrol, an NF-kappa B inhibitor, in a mouse model of secondary osteoporosis. Animals were divided into three groups as Sham (control), SO (secondary osteoporosis) and SO + CA (secondary osteoporosis treated with celastrol). Significant decreases in body weight and body fat were observed following celastrol treatment in SO group, but leptin levels were much higher. Celastrol also exhibited a significant decrease in urinary calcium excretion. Moreover, other important events were observed after celastrol treatment, covering substantial decrements in serum concentrations of PTH, TRAP-5b, CTX and DPD, improved structure of articular cartilage and cancellous bone (revealed by H&E and safranin-O staining), and significant decline in levels of NF-kappa B (P65), MMP-1, and MMP-9. These findings demonstrated that celastrol treatment not only improved abnormal lipid metabolism and hypercalciuria in mice subjected to secondary osteoporosis, but also ameliorated articular cartilage lesions. Our results provided evidence of targeted therapy for NF-kappa B in the clinical treatment of secondary osteoporosis. (C) 2016 The Authors. Production and hosting by Elsevier B.V. on behalf of Japanese Pharmacological Society. This is an open access article

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FU National Natural Science Foundation of China [81372015]; Shanghai Municipal Health Bureau Project [2013214]
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AB Recently, we have begun to realize that the billions of microorganisms living in symbiosis with us have an influence on disease. Evidence is mounting that the alimentary tract microbiome, in particular, influences both host metabolic potential and its innate and adaptive immune system. Inflammatory states characterize many bone and joint diseases of aging. This prompts the hypothesis that the gut microbiome could alter the inflammatory state of the individual and directly influence the development of these common and burdensome clinical problems. Because the microbiome is easily modifiable, this could have major therapeutic impact. This perspective discusses evidence to date on the role of the microbiome and the highly prevalent age-related disorders of osteoporosis, osteoarthritis, gout, rheumatoid arthritis, sarcopenia, and frailty. It also reviews data on the effects of probiotics and prebiotic interventions in animal and human models. Despite suggestive findings, research to date is not conclusive, and we identify priorities for research to substantiate and translate findings. (c) 2015 American Society for Bone and Mineral Research.

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ID magnetic-resonance-spectroscopy; mesenchymal stem-cells; l-carnitine fumarate; induced osteoporosis; knee osteoarthritis; hplc-ms; taurine; osteoblast; differentiation; cartilage
AB Osteoarthritis (OA), one of the most widespread musculoskeletal joint diseases among the aged, is characterized by the progressive loss of articular cartilage and

continuous changes in subchondral bone. The exact pathogenesis of osteoarthritis is not completely clear. In this work, ultra-performance liquid chromatography coupled with quadrupole time-of-flight tandem mass spectrometry (UPLC/Q-TOF-MS) in combination with multivariate statistical analysis was applied to analyze the metabolic profiling of subchondral bone from 42 primary osteoarthritis patients. This paper described a modified two-step method for extracting the metabolites of subchondral bone from primary osteoarthritis patients. Finally, 68 metabolites were identified to be significantly changed in the sclerotic subchondral bone compared with the non-sclerotic subchondral bone. Taurine and hypotaurine metabolism and beta-alanine metabolism were probably relevant to the sclerosis of subchondral bone. Taurine, l-carnitine, and glycerophospholipids played a vital regulation role in the pathological process of sclerotic subchondral bone. In the sclerotic process, beta-alanine and l-carnitine might be related to the increase of energy consumption. In addition, our findings suggested that the intra-cellular environment of sclerotic subchondral bone might be more acidotic and hypoxic compared with the non-sclerotic subchondral bone. In conclusion, this study provided a new insight into the pathogenesis of subchondral bone sclerosis. Our results indicated that metabolomics could serve as a promising approach for elucidating the pathogenesis of subchondral bone sclerosis in primary osteoarthritis.
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TI Potential of PET-MRI for imaging of non-oncologic musculoskeletal disease
SO QUANTITATIVE IMAGING IN MEDICINE AND SURGERY
LA English
DT Review
DE Positron emission tomography-magnetic resonance imaging (PET-MRI); musculoskeletal imaging; nuclear medicine; arthritis; osteoporosis
ID positron-emission-tomography; early-stage osteoarthritis; contrast-enhanced mri; magnetic-resonance; in-vivo; rheumatoid-arthritis; attenuation correction; cartilage composition; f-18-fdg pet/mri; skeletal-muscle
AB Early detection of musculoskeletal disease leads to improved therapies and patient outcomes, and would benefit greatly from imaging at the cellular and molecular level. As it becomes clear that assessment of multiple tissues and functional processes are often necessary to study the complex pathogenesis of musculoskeletal disorders, the role of multi-modality molecular imaging becomes increasingly important. New positron emission tomography-magnetic resonance imaging (PET-MRI) systems offer to combine high-resolution MRI with simultaneous molecular information from PET to study the multifaceted processes involved in numerous musculoskeletal disorders. In this article, we aim to outline the potential clinical utility of hybrid PET-MRI to these non-oncologic musculoskeletal diseases. We summarize current applications of PET molecular imaging in osteoarthritis (OA), rheumatoid arthritis (RA), metabolic bone diseases and neuropathic peripheral pain. Advanced MRI approaches that reveal

biochemical and functional information offer complementary assessment in soft tissues. Additionally, we discuss technical considerations for hybrid PET-MR imaging including MR attenuation correction, workflow, radiation dose, and quantification.
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PT J
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TI Health benefits of tai chi What is the evidence?
SO CANADIAN FAMILY PHYSICIAN
LA English
DT Review
ID quality-of-life; practitioner-based complementary; obstructive pulmonary-disease; cognitive-behavioral therapy; randomized controlled-trial; improving aerobic capacity; coronary-heart-disease; older-adults; risk-factors; parkinsons-disease
AB Objective To summarize the evidence on the health benefits of tai chi. Sources of information A literature review was conducted on the benefits of tai chi for 25 specific conditions, as well as for general health and fitness, to update a 2014 review of systematic reviews. Systematic reviews and recent clinical trials were assessed and organized into 5 different groups: evidence of benefit as excellent, good, fair, or preliminary, or evidence of no direct benefit. Main message During the past 45 years more than 500 trials and 120 systematic reviews have been published on the health benefits of tai chi. Systematic reviews of tai chi for specific conditions indicate excellent evidence of benefit for preventing falls, osteoarthritis, Parkinson disease, rehabilitation for chronic obstructive pulmonary disease, and improving cognitive capacity in older adults. There is good evidence of benefit for depression, cardiac and stroke rehabilitation, and dementia. There is fair evidence of benefit for improving quality of life for cancer patients, fibromyalgia,

hypertension, and osteoporosis. Current evidence indicates no direct benefit for diabetes, rheumatoid arthritis, or chronic heart failure. Systematic reviews of general health and fitness benefits show excellent evidence of benefit for improving balance and aerobic capacity in those with poor fitness. There is good evidence for increased strength in the lower limbs. There is fair evidence for increased well-being and improved sleep. There were no studies that found tai chi worsened a condition. A recent systematic review on the safety of tai chi found adverse events were typically minor and primarily musculoskeletal; no intervention-related serious adverse events have been reported. Conclusion There is abundant evidence on the health and fitness effects of tai chi. Based on this, physicians can now offer evidence-based recommendations to their patients, noting that tai chi is still an area of active research, and patients should continue to receive medical follow-up for any clinical conditions.
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TI De novo degenerative lumbar scoliosis: a systematic review of prognostic factors for curve progression
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DT Review
DE De novo degenerative lumbar scoliosis; Adult's scoliosis; Prognostic factors;

Curve progression; Systematic review
ID low-back; nonoperative treatment; health; adults; pain; osteoarthritis; prevalence; quality; burden; impact
AB To identify prognostic factors for curve progression in de novo degenerative lumbar scoliosis (DNDLS) by performing a systematic review of the literature. Studies were selected for inclusion following a systematic search in the bibliographic databases PubMed and EMBASE prior to September 2015 and hand searches of the reference lists of retrieved articles. Two authors independently assessed methodological quality. Data were extracted and presented according to a best evidence synthesis. The literature search generated a total of 2696 references. After removing duplicates and articles that did not meet inclusion criteria, 12 studies were included. Due to the lack of statistical analyses, pooling of data was not possible. Strong evidence indicates that increasing intervertebral disk degeneration, lateral vertebral translation a parts per thousand yen6 mm, and an intercrest line through L5 (rather than L4) are associated with DNDLS curve progression. Moderate evidence suggests that apical vertebral rotation Grade II or III is associated with curve progression. For the majority of other prognostic factors, we found limited, conflicting, or inconclusive evidence. Osteoporosis, a coronal Cobb angle < 30A degrees, lumbar lordosis, lateral osteophytes difference of a parts per thousand yen5 mm, and degenerative spondylolisthesis have not been shown to be risk factors. Clinical risk factors for progression were not identified. This review shows strong evidence that increased intervertebral disk degeneration, an intercrest line through L5, and apical lateral vertebral translation a parts per thousand yen6 mm are associated with DNDLS curve progression. Moderate evidence was found for apical vertebral rotation (Grade II/III) as a risk factor for curve progression. These results, however, may not be directly applicable to the individual patient.
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NR 52
TC 53
Z9 65
U1 1
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PU SPRINGER
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PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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WC Clinical Neurology; Orthopedics
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PT J
AU Takahashi, M

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TI Analgesic Effects of 1st Generation Anti-histamines in Mice
SO BIOLOGICAL & PHARMACEUTICAL BULLETIN
LA English
DT Article
DE anti-histamine; analgesic effect; non-steroidal anti-inflammatory drug; cyproheptadine; pain; histamine-H1-receptor
ID pain perception; histamine; receptor; roles; muscle; diphenhydramine; hyperalgesia; pharmacology; antagonists; mechanisms
AB Pain is sensed, transmitted, and modified by a variety of mediators and receptors. Histamine is a well-known mediator of pain. In addition to their anti-histaminic effects, the classical, or 1st generation, anti-histamines (1st AHs) possess, to various degrees, anti-muscarinic, anti-serotonergic, anti-adrenergic, and other pharmacologic effects. Although there have been attempts to use 1st Ails as analgesics and/or analgesic adjuvants, the advent of non-steroidal anti-inflammatory drugs (NSAIDs) discouraged such trials. We previously reported that in patients with temporomandibular disorders, osteoporosis, and/or osteoarthritis, the analgesic effects of certain 1st AHs (chlorpheniramine and diphenhydramine) are superior to those of the NSAIDs flurbiprofen and indomethacin. Here, we compared analgesic effects among 1st AHs and NSAIDs against responses shown by mice to intraperitoneally injected 0.7% acetic acid. Since 1st Ails are water soluble, we selected water-soluble NSAIDs. For direct

comparison, drugs were intravenously injected 30min before the above tests. Histamine-H1-receptor-deficient (H1R-KO) mice were used for evaluating 111-receptor-independent effects. The tested 1st Ails (especially cyproheptadine) displayed or tended to display analgesic effects comparable to those of NSAIDs in normal and H1R-KO mice. Our data suggest that the anti-serotonergic and/or anti-adrenergic effects of 1st Ails make important contributions to their analgesic effects. Moreover, combination of a 1st AH with an NSAID (cyclooxygenase-1 inhibitor) produced remarkably potent analgesic effects. We propose that a 1st Ail, by itself or in combination with a cyclooxygenase-1 inhibitor, should undergo testing to evaluate its usefulness in analgesia.
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NR 31
TC 6
Z9 6
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PT J
AU Jiang, ZS
Hao, ZH
AF Jiang, Zhen-Song
Hao, Zhen-Hai
TI An insertion/deletion polymorphism within the 3′-untranslated region of COL1A2 confers susceptibility to osteoporosis
SO MOLECULAR MEDICINE REPORTS
LA English
DT Article
DE polymorphism; COL1A2; 3 '-untranslated region; osteoporosis
ID bone-mineral density; hepatocellular-carcinoma; genetic-determinants; microrna function; chinese; heritability; targets; women; mass; osteoarthritis
AB Polymorphisms located in microRNA (miRNA) binding sites may interfere with the interaction between miRNAs and mRNAs, and thereby alter the expression of genes. The current study aimed to investigate the association between an insertion/deletion (INS/DEL) polymorphism in the 3'-untranslated region (3'-UTR) of COL1A2 and the risk of developing osteoporosis. In the present study, COL1A2 was identified as a target gene of let-7g in osteoblast cells obtained from patients, using a luciferase reporter system. This was further confirmed by the observation that exogenous overexpression of let-7g in the osteoblast cells downregulated the expression of COL1A2 in the cells in the INS/INS group, however not in the DEL/DEL group. In addition, a total of 487 subjects were enrolled in the present study and their bone mineral density (BMD) was measured. The BMD at the four tested sites, the femoral neck, total left hip, L1-L4 and intertrochanteric areas, were significantly reduced in the INS/DEL or DEL/DEL group compared with the INS/INS group. Furthermore, the levels of COL1A2 and let-7g were measured in the primary osteoblasts obtained from 48 patients with osteoporosis. While the let-7g levels were comparable between each genotype group, the expression level of COL1A2 in the DEL/DEL and INS/DEL group was significantly greater compared with the

INS/INS group. In conclusion, the present study demonstrated that the INS/DEL polymorphism in the 3'-UTR of COL1A2 is able to interfere with the interaction between miRNA and mRNA. In addition, it is the first study, to the best of our knowledge, to indicate that the minor allele (Del) is associated with a reduced risk of developing osteoporosis.
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PA POB 18179, ATHENS, 116 10, GREECE
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WC Oncology; Medicine, Research & Experimental
SC Oncology; Research & Experimental Medicine
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TI The phenolic acids of Agen prunes (dried plums) or Agen prune juice concentrates do not account for the protective action on bone in a rat model of postmenopausal osteoporosis
SO NUTRITION RESEARCH
LA English
DT Article
DE Osteoporosis; Agen prunes; Chlorogenic acid; Fiber osteoblast; Rat
ID alkaline-phosphatase; host metabolism; dietary boron; ii collagen; vitamin-d; calcium; health; supplementation; women; osteoarthritis
AB Dietary supplementation with dried plum (DP) has been shown to protect against and reverse established osteopenia in ovariectomized rodents. Based on in vitro studies, we hypothesized that DP polyphenols may be responsible for that bone-sparing effect. This study was designed to (1) analyze whether the main phenolic acids of DP control preosteoblast proliferation and activity in vitro; (2) determine if the polyphenolic content of DP or DP juice concentrate is the main component improving bone health in vivo; and (3) analyze whether DP metabolites directly modulate preosteoblast physiology ex vivo. In vitro, we found that neochlorogenic, chlorogenic, and caffeic acids induce the proliferation and repress the alkaline phosphatase activity of primary preosteoblasts in a dose-dependent manner. In vivo, low-chlorogenic acid Agen prunes (AP) enriched with a high-fiber diet and low-chlorogenic acid AP juice concentrate prevented the decrease of total femoral bone mineral density induced by estrogen deficiency in 5-month-old female rats and positively restored the variations of the bone markers osteocalcin and deoxypyridinoline. Ex vivo, we demonstrated that serum from rats fed with low-chlorogenic acid AP enriched with a high-fiber diet showed repressed

proliferation and stimulated alkaline phosphatase activity of primary preosteoblasts. Overall, the beneficial action of AP on bone health was not dependent on its polyphenolic content. (C) 2016 Elsevier Inc. All rights reserved.
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NR 54
TC 13

Z9 18
U1 0
U2 43
PU PERGAMON-ELSEVIER SCIENCE LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND
SN 0271-5317
EI
J9 NUTR RES
JI Nutr. Res.
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WC Nutrition & Dietetics
SC Nutrition & Dietetics
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ER

PT J
AU Zhang, LY
Li, SL
Hao, S
Yuan, Z
AF Zhang, Lingyan
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Yuan, Zhen
TI Quantification of fat deposition in bone marrow in the lumbar vertebra by proton MRS and in-phase and out-of-phase MRI for the diagnosis of osteoporosis
SO JOURNAL OF X-RAY SCIENCE AND TECHNOLOGY
LA English
DT Article
DE 1H-MRS; in-phase and out-of-phase MRI; bones; osteoporosis; dual-energy x-ray absorptiometry
ID photoacoustic tomography; mineral density; adipose-tissue; spectroscopy;

osteoarthritis; disease; adults; fnirs; women; spine
AB The goal for this study was to investigate if proton MRS(1H-MRS) and out-of-phase and in-phase MRI can quantify the fat deposition in bone marrow within the lumbar vertebra that can be used to distinguish well between osteoporosis patients and healthy control subjects. Sixty-eight subjects participated in this study. The diagnostic results from dual-energy x-ray absorptiometry served as the gold standard, which was able to separate the subjects into osteoporosis (38 subjects) and non-osteoporosis group (30 subjects). Then the 68 subjects were further scanned by 1H-MRS and in-phase and out-of-phase MRI and the findings from the imaging methods were also compared and analyzed. It was found that the measured signal intensity ratio (SIR), lipid-water ratio (LWR) and fat fraction (FF) in L2 vertebra from the two imaging methods were able to identify the fat deposition in bone marrow, which could be used to diagnose osteoporosis. Diagnostic accuracy for osteoporosis based on identified SIR, LRW and FF was analyzed by using ROC curves. Our findings suggested that statistically significant differences were identified between osteoporosis patients and healthy subjects. The sensitivity and specificity equal to 78.9% and 75.9% for SIR, 79.2% and 66.7% for LRW, 71.4% and 72.4% for FF, can be achieved when fat deposition-related parameters in bone marrow from the lumbar vertebra are used as classifiers. Our results showed that fat deposition-related parameters including fat content in bone marrow and water content in the lumbar vertebra are clearly different between the osteoporosis and non-osteoporosis group, suggesting that both 1H-MRS and in-phase and out-of-phase MRI can be used for diagnosing osteoporosis and monitoring its progression.
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NR 32
TC 9
Z9 10
U1 0
U2 13
PU IOS PRESS
PI AMSTERDAM
PA NIEUWE HEMWEG 6B, 1013 BG AMSTERDAM, NETHERLANDS
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J9 J X-RAY SCI TECHNOL
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SC Instruments & Instrumentation; Optics; Physics
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PT J
AU Levy, JC
Ashukem, MT
Formaini, NT
AF Levy, Jonathan C.
Ashukem, Moses T.
Formaini, Nathan T.
TI Factors predicting postoperative range of motion for anatomic total shoulder arthroplasty
SO JOURNAL OF SHOULDER AND ELBOW SURGERY
LA English
DT Article
DE Total shoulder arthroplasty; TSA; range of motion; comorbidities
ID lesser tuberosity osteotomy; degenerative joint disease; total knee arthroplasty; quality-of-life; glenohumeral osteoarthritis; subscapularis tenotomy; functional improvement; replacement; hemiarthroplasty; multicenter
AB Background: Total shoulder arthroplasty (TSA) has repeatedly been shown to be an effective and durable treatment option for end-stage arthritis with good long-term survivorship. Whereas pain relief is typically the primary goal, improvements in range of motion are typically expected as well. The factors that influence postoperative motion have not been well characterized. The purpose of the study was to examine the factors that influence ultimate postoperative motion after TSA. Methods: A retrospective review was conducted of prospectively collected data of 230 patients with minimum 1-year follow-up after TSA for end-stage arthropathy with an intact rotator cuff. Analysis was focused on factors that may correlate with postoperative measured forward flexion, abduction, external rotation, and internal rotation. Included in this analysis was perception of motion, age, body mass index (BMI), comorbidities (smoking, diabetes, osteoporosis, hypercholesterolemia, inflammatory arthritis, and thyroid disease), and number of comorbidities. Results: Preoperative motion in all directions was predictive of postoperative motion for forward flexion ($R = 0.235$; $P < .001$), abduction ($R = 0.363$; $P < .001$), external rotation ($R = 0.325$; $P < .001$), and internal

rotation (R = 0.213; P = .002). BMI and diabetes both negatively correlated with internal rotation (R = -0.134, P = .40 and R = -0.196, P = .003, respectively). Individual and total number of comorbidities were not predictive of postoperative motion. The patient's perception of preoperative motion also did not correlate with postoperative motion. Conclusions: Preoperative range of motion before TSA is most predictive of final motion achieved. Individual and total number of comorbidities are not predictive of postoperative motion. Patients with high diabetes and increased BMI have limited postoperative internal rotation. (C) 2016 Journal of Shoulder and Elbow Surgery Board of Trustees.
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NR 24
TC 32
Z9 43
U1 0
U2 5
PU MOSBY-ELSEVIER
PI NEW YORK
PA 360 PARK AVENUE SOUTH, NEW YORK, NY 10010-1710 USA
SN 1058-2746
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J9 J SHOULDER ELB SURG
JI J. Shoulder Elbow Surg.
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WC Orthopedics; Sport Sciences; Surgery
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ER

PT J
AU Kitaoka, M

Mitoma, J
Asakura, H
Anyenda, OE
Nguyen, TTT
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Hibino, Yuri
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Hitomi, Yoshiaki
Shikura, Naoto
Hiroyuki, Nakamura
TI The relationship between hypertension and health-related quality of life: adjusted by chronic pain, chronic diseases, and life habits in the general middle-aged population in Japan
SO ENVIRONMENTAL HEALTH AND PREVENTIVE MEDICINE
LA English
DT Article
DE Health-related quality of life; Hypertension; Chronic pain; Sex difference
ID body-mass index; blood-pressure; impact; sf-36; association; obesity; prevalence; mortality; insomnia; validity
AB Objectives The aim of this study was to examine the relationship between hypertension and health-related quality of life (HRQoL) adjusted by chronic pain, other chronic diseases, and life habits in the general middle-aged population in Japan. Methods This study is a population-based cross-sectional study. In this

study, 1117 participants aged 40-65 years and living in Shika Town completed a self-administered questionnaire including Short Form-36 (SF-36). The scores of SF-36 among hypertensives were compared with those of normotensives. The independent association of hypertension with each SF-36 subscale was analyzed using a multiple linear regression model adjusted by age, BMI, chronic pain, chronic diseases, sleep, exercise, and occupational status. We analyzed two groups; Group 1 which contained 846 participants completed the questionnaire without coronary heart disease and cerebral vascular disease, Group 2 which contained 686 participants without coronary heart disease, cerebral vascular disease, or diseases accompanied by chronic pain (gastroduodenal ulcer, fracture, osteoarthritis, osteoporosis, rheumatoid arthritis, and disc herniation). Results In Group 2, hypertensive women had a lower general health perception than normotensive women [unstandardized coefficients; B = -8.84, 95 % confidence interval (95 % CI) = -13.3 to -4.34, standardized coefficients; beta = -0.200, p < 0.001], whereas hypertensive men had higher social functioning than normotensive men (B = 5.66, 95 % CI = 1.30-10.0, beta = 0.149, p < 0.05) after adjusting by chronic pain and life habits. Conclusions These results may be due to the sex difference in the light of the perception for health.
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NR 55
TC 20
Z9 25
U1 1
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PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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PT J
AU Konrad, M
Bohlken, J
Rapp, MA
Kostev, K
AF Konrad, Marcel
Bohlken, Jens
Rapp, Michael A.
Kostev, Karel
TI Depression risk in patients with heart failure in primary care practices in Germany
SO INTERNATIONAL PSYCHOGERIATRICS
LA English
DT Article
DE depression; primary care; risk factors; antidepressants
ID disease; prevention; prevalence; prognosis; symptoms; anxiety; history
AB Background: The goal of this study was to estimate the prevalence of and risk factors for diagnosed depression in heart failure (HF) patients in German primary care practices. Methods: This study was a retrospective database analysis in Germany utilizing the Disease Analyzer (R) Database (IMS Health, Germany). The study population included 132,994 patients between 40 and 90 years of age from 1,072 primary care practices. The observation period was between 2004 and 2013. Follow-up lasted up to five years and ended in April 2015. A total of 66,497 HF patients were selected after applying exclusion criteria. The same number of 66,497 controls were chosen and were matched (1:1) to HF patients on the basis of age, sex, health insurance, depression diagnosis in the past, and follow-up duration after index date. Results: HF was a strong risk factor for diagnosed depression ($p < 0.0001$). A total of 10.5% of HF patients and 6.3% of matched controls developed depression after one year of follow-up ($p < 0.001$). Depression was documented in 28.9% of the HF group and 18.2% of the control group after the five-year follow-up ($p < 0.001$). Cancer, dementia, osteoporosis, stroke, and osteoarthritis were associated with a higher risk of developing depression. Male gender and private health insurance were associated with lower risk of depression. Conclusions: The risk of diagnosed depression is significantly increased in patients with HF compared to patients without HF in primary care practices in Germany.
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AF Zhou, Wu
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Liu, Xian-Zhe
TI Increased serum fibroblast growth factor-23 (FGF-23) and bone turnover in patients with osteoarthritis of knee
SO INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE
LA English
DT Article
DE Fibroblast growth factor-23; osteoarthritis; osteoporosis; bone turnover
ID mineral density; kidney-disease; osteoporosis; chondrocytes; arthritis; apoptosis; damage; fgf23; mice; hip
AB Objective: This study aimed to investigate the serum fibroblast growth factor-23 (FGF-23) of patients with knee osteoarthritis (OA) and to elaborate its correlation with radiographic and symptomatic severity of OA. Methods: Sixty-three subjects were divided into three groups, including healthy controls group (n = 15), patients

with rheumatoid arthritis (RA, n = 23) and OA (n = 25). Serum FGF-23 levels were examined by ELISA, and other clinical biochemical parameters were tested based on standard methods. Results: First, we found a significant increase in FGF-23 level in the serum of patients with knee OA compared to healthy controls. Next, an increased trabecular bone formation in subchondral bone was confirmed in the patients with knee OA. In addition, FGF-23 levels were positively correlated with radiographic grading and symptomatic severity of knee OA, and this observation indicated a significant elevation in the systemic levels of FGF-23 correlation with WOMAC scores in patients with knee OA. Furthermore, the results showed that the mRNA and protein expression of FGF-23 were significantly increased in synovial fluid from OA patients as compared to those in healthy control, and the upregulation of FGF-23 could inhibit the apoptosis of mononuclear cell in synovial fluid from OA patients. Conclusions: Serum FGF-23 level was significantly higher and was a significant determinant of increased bone turnover in knee OA patients. FGF-23 might be a potential biomarker for diagnosing and evaluating the onset and development of knee OA.
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TI A comprehensive fracture prevention strategy in older adults: the European Union Geriatric Medicine Society (EUGMS) statement
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Falls; Fragility fracture; Older people; Prevention; Position statement
ID bone-mineral density; fall prevention; hip-fracture; postmenopausal women;

cost-effectiveness; zoledronic acid; risk-factors; pharmacological-treatments; strontium ranelate; liaison service
AB Prevention of fragility fractures in older people has become a public health priority, although the most appropriate and cost-effective strategy remains unclear. In the present statement, the Interest Group on Falls and Fracture Prevention of the European Union Geriatric Medicine Society, in collaboration with the International Association of Gerontology and Geriatrics for the European Region, the European Union of Medical Specialists, and the International Osteoporosis Foundation-European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, outlines its views on the main points in the current debate in relation to the primary and secondary prevention of falls, the diagnosis and treatment of bone fragility, and the place of combined falls and fracture liaison services for fracture prevention in older people.
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AF Brown, Victoria Tzortziou
Underwood, Martin
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Westwood, Olwyn
Morrissey, Dylan
TI Professional interventions for general practitioners on the management of musculoskeletal conditions
SO COCHRANE DATABASE OF SYSTEMATIC REVIEWS

LA English
DT Review
ID randomized controlled-trial; primary-care physicians; shoulder acute pain; primary-health-care; osteoporosis management; multifaceted intervention; educational intervention; reminder messages; improve; guidelines
AB Background Musculoskeletal conditions require particular management skills. Identification of interventions which are effective in equipping general practitioners (GPs) with such necessary skills could translate to improved health outcomes for patients and reduced healthcare and societal costs. Objectives To determine the effectiveness of professional interventions for GPs that aim to improve the management of musculoskeletal conditions in primary care. Search methods We searched the Cochrane Central Register of Controlled Trials (CENTRAL), 2010, Issue 2; MEDLINE, Ovid (1950 - October 2013); EMBASE, Ovid (1980 - Ocotber 2013); CINAHL, EbscoHost (1980 - November 2013), and the EPOC Specialised Register. We conducted cited reference searches using ISI Web of Knowledge and Google Scholar; and handsearched selected issues of Arthritis and Rheumatism and Primary Care-Clinics in Office Practice. The latest search was conducted in November 2013. Selection criteria We included randomised controlled trials (RCTs), non-randomised controlled trials (NRCTs), controlled before-and-after studies (CBAs) and interrupted time series (ITS) studies of professional interventions for GPs, taking place in a community setting, aiming to improve themanagement (including diagnosis and treatment) of musculoskeletal conditions and reporting any objective measure of GP behaviour, patient or economic outcomes. We considered professional interventions of any length, duration, intensity and complexity compared with active or inactive controls. Data collection and analysis Two review authors independently abstracted all data. We calculated the risk difference (RD) and risk ratio (RR) of compliance with desired practice for dichotomous outcomes, and the mean difference (MD) and standardised mean difference (SMD) for continuous outcomes. We investigated whether the direction of the targeted behavioural change affects the effectiveness of interventions. Main results Thirty studies met our inclusion criteria. From 11 studies on osteoporosis, meta-analysis of five studies (high-certainty evidence) showed that a combination of a GP alerting system on a patient's increased risk of osteoporosis and a patient-directed intervention (including patient education and a reminder to see their GP) improves GP behaviour with regard to diagnostic bone mineral density (BMD) testing and osteoporosis medication prescribing (RR 4.44; (95% confidence interval (CI) 3.54 to 5.55; 3 studies; 3,386 participants)) for BMD and RR 1.71 (95% CI 1.50 to 1.94; 5 studies; 4,223 participants) for osteoporosis medication. Meta-analysis of two studies showed that GP alerting on its own also probably improves osteoporosis guideline-consistent GP behaviour (RR 4.75 (95% CI 3.62 to 6.24; 3,047 participants)) for BMD and RR 1.52 (95% CI 1.26 to 1.84; 3.047 participants) for osteoporosis medication) and that adding the patient-directed component probably does not lead to a greater effect (RR 0.94 (95% CI 0.81 to 1.09; 2,995 participants)) for BMD and RR 0.93 (95% CI 0.79 to 1.10; 2,995

participants) for osteoporosis medication. Of the 10 studies on low back pain, seven showed that guideline dissemination and educational opportunities for GPs may lead to little or no improvement with regard to guideline-consistent GP behaviour. Two studies showed that the combination of guidelines and GP feedback on the total number of investigations requested may have an effect on GP behaviour and result in a slight reduction in the number of tests, while one of these studies showed that the combination of guidelines and GP reminders attached to radiology reports may result in a small but sustained reduction in the number of investigation requests. Of the four studies on osteoarthritis, one study showed that using educationally influential physicians may result in improvement in guideline-consistent GP behaviour. Another study showed slight improvements in patient outcomes (pain control) after training GPs on pain management. Of three studies on shoulder pain, one study reported that there may be little or no improvement in patient outcomes (functional capacity) after GP education on shoulder pain and injection training. Of two studies on other musculoskeletal conditions, one study on pain management showed that there may be worse patient outcomes (pain control) after GP training on the use of validated assessment scales. The 12 remaining studies across all musculoskeletal conditions showed little or no improvement in GP behaviour and patient outcomes. The direction of the targeted behaviour (i.e. increasing or decreasing a behaviour) does not seem to affect the effectiveness of an intervention. The majority of the studies did not investigate the potential adverse effects of the interventions and only three studies included a cost-effectiveness analysis. Overall, there were important methodological limitations in the body of evidence, with just a third of the studies reporting adequate allocation concealment and blinded outcome assessments. While our confidence in the pooled effect estimate of interventions for improving diagnostic testing and medication prescribing in osteoporosis is high, our confidence in the reported effect estimates in the remaining studies is low. Authors' conclusions There is good-quality evidence that a GP alerting system with or without patient-directed education on osteoporosis improves guideline-consistent GP behaviour, resulting in better diagnosis and treatment rates. Interventions such as GP reminder messages and GP feedback on performance combined with guideline dissemination may lead to small improvements in guideline-consistent GP behaviour with regard to low back pain, while GP education on osteoarthritis pain and the use of educationally influential physicians may lead to slight improvement in patient outcomes and guideline-consistent behaviour respectively. However, further studies are needed to ascertain the effectiveness of such interventions in improving GP behaviour and patient outcomes.

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TI Relation between the stand-up test and gait speed, knee osteoarthritis, and osteoporosis using calcaneal quantitative ultrasound - Cross-sectional study
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English

DT Article
ID sarcopenia; people; health
AB Objective: The aim of the present study was to clarify the relationship between the stand-up test and gait speed, knee osteoarthritis (OA), and osteoporosis using calcaneal quantitative ultrasound. Study design: Cross-sectional study. Methods: A total of 185 subjects (55 men, 130 women) aged >= 40 years (mean age, 63.7 years; range, 40 79 years) were evaluated using the stand-up test to screen for locomotive syndrome. We also assessed OA of the knee using X-rays and a subjective questionnaire, physical characteristics, 6-m gait speed (m/s), and bone density. If results on the stand-up test were worse than benchmarks by age group (i.e., the height at which 50% of each age group could stand-up), the subject was defined as having a risk for locomotive syndrome (L group). We analyzed the relationship between the stand-up test and other variables. Results: Of 185 subjects, 50 (27.0%) were classified into the L group. In univariate analysis, there were significant differences between the L group and non-L group in bone density ($p < 0.001$), gait speed ($p < 0.001$), osteoporosis ($p < 0.001$), slow gait speed group (SGSG) (cut off 1 m/s), and Japanese knee osteoarthritis measure score. Multivariate logistic regression analysis adjusted for age, height, weight, and gender showed a significant association between the stand-up test and bone density (OR 0.960, 95% confidence interval (95% CI) 0.927-0.994), gait speed (m/s) (OR 0.073, 95% CI 0.016-0.342), osteoporosis (OR 3.710, 95% CI 1.410-9.764), and SGSG (OR 7.849, 95% CI 1.628-37.845). Conclusions: The stand-up test to screen for the risk for locomotive syndrome was associated with bone density, gait speed, osteoporosis, SGSG. The stand-up test is an easy test to use to screen for possible disability among the elderly. (C) 2015 The Japanese Orthopaedic Association. Published by Elsevier B.V. All rights reserved.
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TI A Mechatronic Loading Device to Stimulate Bone Growth via a Human Knee
SO SENSORS
LA English
DT Article
DE knee-loading; modality; electro-mechanical device; loading force; bone healing; knee rehabilitation; slider crank mechanism; Arduino; Megunolink
ID modality
AB This paper presents the design of an innovative device that applies dynamic mechanical load to human knee joints. Dynamic loading is employed by applying cyclic and periodic force on a target area. The repeated force loading was considered to be an effective modality for repair and rehabilitation of long bones that are subject to ailments like fractures, osteoporosis, osteoarthritis, etc. The proposed device design builds on the knowledge gained in previous animal and mechanical studies. It employs a modified slider-crank linkage mechanism actuated by a brushless Direct Current (DC) motor and provides uniform and cyclic force. The functionality of the device was simulated in a software environment and the structural integrity was analyzed using a finite element method for the prototype construction. The device is controlled by a microcontroller that is programmed to provide the desired loading force at a predetermined frequency and for a specific duration. The device was successfully tested in various experiments for its usability and full functionality. The results reveal that the device works according to the requirements of force magnitude and operational frequency. This device is considered ready to be used for a clinical study to examine whether controlled knee-loading could be an effective regimen for treating the stated bone-related ailments.
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TI Influence of high glucose and advanced glycation end-products (ages) levels in human osteoblast-like cells gene expression
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
ID type-2 diabetes-mellitus; osteogenic differentiation; messenger-rna; fracture risk; in-vitro; bone; rankl; apoptosis; receptor; osteoprotegerin
AB Background: Type 2 diabetes mellitus (T2DM) is associated with an increased risk of osteoporotic fracture. Several factors have been identified as being potentially responsible for this risk, such as alterations in bone remodelling that may have been induced by changes in circulating glucose or/and by the presence of non-oxidative end products of glycosylation (AGEs). The aim of this study is to assess whether such variations generate a change in the gene expression related to the differentiation and osteoblast activity (OPG, RANKL, RUNX2, OSTERIX, and AGE receptor) in primary cultures of human osteoblast-like cells (hOB). Methods: We recruited 32 patients; 10 patients had osteoporotic hip fractures (OP group), 12 patients had osteoporotic hip fractures with T2DM (T2DM group), and 10 patients had hip osteoarthritis (OA group) with no osteoporotic fractures and no T2DM. The gene expression was analyzed in hOB cultures treated with physiological glucose concentration (4.5 mM) as control, high glucose (25 mM), and high glucose plus AGEs (2 mu g/ml) for 24 h. Results: The hOB cultures from patients with hip fractures presented slower proliferation. Additionally, the hOB cultures from the T2DM group were the most negatively affected with respect to RUNX2 and OSX gene expression when treated solely with high glucose or with high glucose plus AGEs. Moreover, high levels of glucose induced a major decrease in the RANKL/OPG ratio when comparing the OP and the T2DM groups to the OA group. Conclusions: Our data indicates an altered bone remodelling rate in the T2DM group, which may, at least partially, explain the reduced bone strength and increased incidence of non-traumatic fractures in diabetic patients.
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TI Mesenchymal stem cells (MSCs) as skeletal therapeutics-an update
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DT Review
DE MSCs; Autologous; Osteogenic imperfecta; Infantile Hypo-phosphatasia; Craniofacial; Vertebral disc; Cartilage repair; Bone fracture; Osteoporosis; Osteo-arthritis
ID marrow stromal cells; human bone-marrow; intervertebral disc repair; adipose-tissue; autologous chondrocyte; osteogenesis imperfecta; cartilage defects; knee osteoarthritis; transplantation; differentiation
AB Mesenchymal stem cells hold the promise to treat not only several congenital and acquired bone degenerative diseases but also to repair and regenerate morbid bone tissues. Utilizing MSCs, several lines of evidences advocate promising clinical outcomes in skeletal diseases and skeletal tissue repair/regeneration. In this context, both, autologous and allogeneic cell transfer options have been utilized. Studies suggest that MSCs are transplanted either alone by mixing with autogenous plasma/serum or by loading onto repair/induction supportive resorb-able scaffolds. Thus, this review is aimed at highlighting a wide range of pertinent clinical therapeutic options of MSCs in the treatment of skeletal diseases and skeletal tissue regeneration. Additionally, in skeletal disease and regenerative sections, only the early and more recent preclinical evidences are discussed followed by all the pertinent clinical studies. Moreover, germane post transplant therapeutic mechanisms afforded by MSCs have also been conversed. Nonetheless, assertive use of MSCs in the clinic for skeletal disorders and repair is far from a mature therapeutic option, therefore, posed challenges and future directions are also discussed. Importantly, for uniformity at all instances, term MSCs is used throughout the review.
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ID growth-factor receptor; trabecular bone mass; group box-1 protein; fatigue in-vivo; articular-cartilage; cyclin d1; parathyroid-hormone; indian-hedgehog; nitric-oxide; human osteoarthritis
AB Cell death in skeletal component cells, including chondrocytes, osteoblasts, and osteocytes, plays roles in skeletal development, maintenance, and repair as well as in the pathogenesis of osteoarthritis and osteoporosis. Chondrocyte proliferation, differentiation, and apoptosis are important steps for endochondral ossification. Although the inactivation of P53 and RB is involved in the pathogenesis of osteosarcomas, the deletion of p53 and inactivation of Rb are insufficient to enhance chondrocyte proliferation, indicating the presence of multiple inhibitory mechanisms against sarcomagenesis in chondrocytes. The inflammatory processes induced by mechanical injury and chondrocyte death through the release of danger-associated molecular patterns (DAMPs) are involved in the pathogenesis of posttraumatic osteoarthritis. The overexpression of BCLXL increases bone volume with a normal structure and maintains bone during aging by inhibiting osteoblast apoptosis. p53 inhibits osteoblast proliferation and enhances osteoblast apoptosis, thereby reducing bone formation, but also exerts positive effects on osteoblast differentiation through the Akt-FoxOs pathway. Apoptotic osteocytes release ATP, which induces the receptor activator of nuclear factor kappa-B ligand (Rankl) expression and osteoclastogenesis, from pannexin 1 channels. Osteocyte death ultimately results in necrosis; DAMPs are released to the bone surface and promote the production of proinflammatory cytokines, which induce Rankl expression, and osteoclastogenesis is further enhanced.
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TI Recommendations for the conduct of clinical trials for drugs to treat or prevent sarcopenia
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Clinical trials; Sarcopenia; Public health; Preventative health care; Frailty
ID quality-of-life; lower-extremity function; muscle strength; older-adults; skeletal-muscle; gait-speed; physical performance; body-composition; functional impairment; age-discrimination
AB Sarcopenia is an age-related muscle condition which is frequently a precursor of frailty, mobility disability and premature death. It has a high prevalence in older populations and presents a considerable social and economic burden. Potential treatments are under development but, as yet, no guidelines support regulatory studies for new drugs to manage sarcopenia. The objective of this position paper is therefore to suggest a set of potential endpoints and target population definitions to stimulate debate and progress within the medico-scientific and regulatory communities. A multidisciplinary expert working group was hosted by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, which reviewed and discussed the recent literature from a perspective of clinical experience and guideline development. Relevant parallels were drawn from the development of definition of osteoporosis as a disease and clinical assessment of pharmaceutical treatments for that indication. A case-finding decision tree is briefly reviewed with a discussion of recent prevalence estimations of different relevant threshold values. The selection criteria for patients in regulatory studies are discussed according to the aims of the investigation (sarcopenia prevention or treatment) and the stage of project development. The possible endpoints of such studies are reviewed and a plea is made for the establishment of a core outcome set to be used in all clinical trials of sarcopenia. The current lack of guidelines for the assessment of new therapeutic treatments for sarcopenia could potentially hinder the delivery of effective medicines to patients at risk.
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TI Simvastatin Effect on Calcium and Silicon Plasma Levels in Postmenopausal Women with Osteoarthritis
SO BIOLOGICAL TRACE ELEMENT RESEARCH
LA English
DT Article
DE Osteoarthritis; Postmenopausal women; Simvastatin; Plasma bioelements; HPLC
ID bone-mineral density; osteoporosis; progression; statins; health
AB Postmenopausal women more often suffered from knee osteoarthritis and its pathogenesis still remains unclear. Calcium and silicon are significant elements involved in bone and joint metabolism, especially in older people. Cardiovascular diseases are common worldwide and simvastatin is the most prescribed drug in such population of patients. The purpose of this study was to evaluate the effect of simvastatin administration on calcium and silicon concentration in the plasma of postmenopausal women with osteoarthritis. Sixty postmenopausal mild hypercholesterolemic women (mean age 61.4 years, range 54-68) were enrolled. Thirty patients received simvastatin (20 or 40 mg/day) for at least 1 year before being enrolled (simvastatin "+" group). Control group consists of remaining 30 women (simvastatin "-aEuroegroup). Silicon and calcium concentrations were measured spectrophotometrically. Plasma simvastatin level was determined 3 h after the drug administration using HPLC-UV-Vis. Calcium but not silicon level was significantly lower in patients receiving simvastatin in comparison with non-statin group (1.91 +/- A 0.32 vs. 2.33 +/- A 0.19 mmol/l, $p < 0.05$). A weak but significant positive correlation between plasma silicon and simvastatin levels ($r = 0.3$, $p < 0.05$) was observed; this may be due to the fact that simvastatin contains silicon dioxide as an inactive ingredient. The mean simvastatin concentration was 9.02 ng/ml. All hypotheses were verified at the significance level of $p < 0.05$. A statistically significant decrease in the plasma calcium concentration of postmenopausal women, treated with simvastatin suggests that simvastatin may play a role in calcium metabolism in postmenopausal women with osteoarthritis. Positive correlation of simvastatin concentration with silicon level in the plasma suggests that both might prompt the positive effect of osteoarthritis treatment.
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TI Resistance Training as a Tool for Preventing and Treating Musculoskeletal Disorders
SO SPORTS MEDICINE
LA English
DT Review
ID low-back-pain; bone-mineral density; aging skeletal-muscle;

rheumatoid-arthritis; knee osteoarthritis; physical-activity; body-composition; older-adults; postmenopausal women; risk-factors
AB The aging process is characterized by several physiological, morphological, and psychological alterations that result in a decreased functional and health status throughout the life span. Among these alterations, the loss of muscle mass and strength (sarcopenia) is receiving increased attention because of its association with innumerous age-related disorders, including (but not limited to) osteoporosis, osteoarthritis, low back pain, risk of fall, and disability. Regular participation in resistance training programs can minimize the musculoskeletal alterations that occur during aging, and may contribute to the health and well-being of the older population. Compelling evidence suggest that regular practice of resistance exercise may prevent and control the development of several musculoskeletal chronic diseases. Moreover, resistance training may also improve physical fitness, function, and independence in older people with musculoskeletal disorders, which may result in improved quality of the years lived. In summary, regular participation in resistance training programs plays an important role in aging and may be a preventive and therapeutic tool for several musculoskeletal disorders.
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TC 71
Z9 82
U1 3
U2 48
PU ADIS INT LTD
PI NORTHCOTE
PA 5 THE WAREHOUSE WAY, NORTHCOTE 0627, AUCKLAND, NEW ZEALAND
SN 0112-1642
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J9 SPORTS MED
JI Sports Med.
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WC Sport Sciences
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PT J
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TI Weekly injection of teriparatide for bone ingrowth after cementless total knee arthroplasty
SO JOURNAL OF ORTHOPAEDIC SURGERY
LA English
DT Article
DE arthroplasty, replacement, knee; bone density; teriparatide
ID x-ray absorptiometry; mineral density; proximal tibia; trabecular bone; follow-up; microstructural analysis; primary osteoporosis; computed-tomography; fracture; hydroxyapatite
AB Purpose. To compare bone mineral density (BMD) in patients with or without weekly injection of teriparatide to promote bone ingrowth after cementless total knee arthroplasty (TKA). Methods. Records of 8 men and 32 women (mean age, 75.6 years) who underwent cementless TKA for medial knee osteoarthritis with (n=20) or without (n=20) once-weekly subcutaneous/hypodermic injection of teriparatide for 48 weeks were reviewed. BMD and bone volume/total volume (BV/TV) of the bone-prosthesis interface of the proximal tibia in 6 regions of interest (ROI) were assessed at 3, 6, 9, and 12 months using multi-detector computed tomography. Results. Patients with or without weekly injection of teriparatide after cementless TKA were comparable in terms of baseline characteristics and pre- and post-operative knee range of motion and Knee Society knee and function scores. In ROI 1 (medial), ROI 3 (anteromedial), and ROI 4 (posteromedial), the BV/TV increased throughout the postoperative period in patients with weekly injection of teriparatide and declined after 6 months in patients without weekly injection of teriparatide. These 3 ROIs of the 2 groups differed significantly only in BMD at 6, 9, and 12 months. In ROI 2 (lateral), ROI 5 (anterolateral), and ROI 6 (posterolateral), both BV/TV and BMD showed a

decreasing trend, and these 3 ROIs of the 2 groups did not differ significantly. Conclusion. Weekly injection of, teriparatide after cementless TKA promoted bone ingrowth mostly in the medial aspect of the bone-prosthesis interface.
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Z9 16
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PA 9/F/, ROOM 901, 99 WONG CHUK HANG RD, ABERDEEN, HONG KONG, 00000, PEOPLES R CHINA
SN 1022-5536
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J9 J ORTHOP SURG-HONG K
JI J. Orthop. Surg.
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WC Orthopedics; Surgery
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TI How Hand Osteoarthritis, Comorbidity, and Pain Interact to Determine Functional Limitation in Older People: Observations From the European Project on OSteoArthritis Study
SO ARTHRITIS & RHEUMATOLOGY
LA English
DT Article
ID physical function; burden; instruments; depression; prevalence; anxiety; impact; index
AB ObjectiveTo examine the role of comorbidity and pain in the associations of hand osteoarthritis (OA) with self-reported and performance-based physical function in a general population of elderly persons. MethodsWe studied data from 2,942 participants ages 65-85 years in the European Project on OSteoArthritis, a collaborative observational study of 6 European cohorts (from Germany, Italy, The Netherlands, Spain, Sweden, and the UK). Outcome measures included self-reported physical function of the hands measured by the AUStralian/CANadian Osteoarthritis Hand Index (AUSCAN) for hand OA physical function subscale and performance-based grip strength measured using a strain gauge dynamometer. ResultsComorbidity was not a confounder in the association of hand OA with self-reported and performance-based functional limitations, while the role of pain as a mediator was confirmed. Anxiety, depression, stroke, and osteoporosis were associated with AUSCAN scores reflecting more impairment. Depression and osteoporosis were associated with less grip strength. ConclusionAlthough comorbidity was decidedly and independently associated with hand functional limitation, it had no effect on the relationship of hand OA with physical function.

Hand OA was found to be associated with both self-reported and performance-based physical function impairment; the association was found to be partially mediated by pain, which reduced its impact.
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NR 24
TC 27
Z9 32
U1 0
U2 11
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 2326-5191
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J9 ARTHRITIS RHEUMATOL
JI Arthritis Rheumatol.
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IS 11
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WC Rheumatology
SC Rheumatology

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PT J
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Zeng, C
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Lei, Guang-hua
TI Relation between phalangeal bone mineral density and radiographic knee osteoarthritis: a cross-sectional study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Osteoarthritis; Knee; Phalangeal; Bone mineral density; Kellgren-Lawrence grade
ID body-mass index; total hip; postmenopausal women; risk-factors; follow-up; osteoporosis; absorptiometry; epidemiology; association; hand
AB Background: Major reports have suggested that bone mineral density (BMD) is higher in patients with osteoarthritis (OA), while other studies do not agree. Our aim was to examine the cross-sectional association between phalangeal BMD and radiographic knee OA. Methods: A total of 2855 participants were included in this study. Radiographic knee OA was defined as Kellgren-Lawrence (K-L) Grade >= 2 in at least one leg. BMD scans of the middle phalanges of the second, third and fourth digits of the nondominant hand were performed with a compact radiographic absorptiometry system (Alara MetriScan (R)). A multivariable logistic analysis model was applied to test the relation between phalangeal BMD with radiographic knee OA, the presence of knee osteophytes (OSTs), and knee joint space narrowing (JSN) after adjusting for a number of potential confounding factors. Results: The multivariable-adjusted odds ratios with 95 % confidence intervals [ORs (95 % CI)] of radiographic knee OA across phalangeal BMDs were 1.08 (95 % CI 0.89-1.32) and 0.62 (95 % CI 0.45-0.86), respectively. The P for trend was 0.09. For the female population, the multivariable-adjusted ORs (95 % CI) of

radiographic knee OA across phalangeal BMD were 1.01 (95 % CI 0.73-1.37) and 0.58 (95 % CI 0.38 - 0.87), respectively. The P for trend was 0.02. This positive finding, however, did not exist in the male subgroup. There was a significantly lower prevalence of OST in the osteoporosis (OP) group than in the normal group (OR = 0.59, 95 % CI 0.40-0.88; P for trend was 0.01). In contrast, the prevalence of JSN was significantly higher in the osteopenia group (OR = 1.22, 95 % CI 1.00-1.48) and the OP group (OR = 1.35, 95 % CI 1.00-1.84) than in the normal group. The P for trend was 0.02. Conclusions: This study observed lower odds for the presence of radiographic knee OA and OST in OP patients than in normal subjects. The prevalence of JSN was higher in the osteopenia and OP groups than in normal subjects.
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PU BMC
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EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD FEB 11
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DI 10.1186/s12891-016-0918-x
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
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AF Geusens, Piet P.
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TI Osteoporosis and osteoarthritis: shared mechanisms and epidemiology
SO CURRENT OPINION IN RHEUMATOLOGY
LA English
DT Review
DE bone; osteoarthritis; osteoporosis
ID high bone mass; population-based cohort; knee osteoarthritis; mineral density; trabecular bone; hand osteoarthritis; fracture risk; all-cause; association; women
AB Purpose of reviewOsteoporosis and osteoarthritis are different diseases, with differences in risk factors, bone mineral density (BMD), BMI, phenotype, morbidity and mortality. We review new data on the role of bone metabolism in osteoporosis and osteoarthritis.Recent findingsThe insights in the common convergent and divergent risk factors between osteoarthritis and osteoporosis have resulted in new findings on the role of BMD, BMI, falls, genetics and epigenetics in the pathophysiology of both diseases and on the increased fracture risk in osteoporosis and osteoarthritis. The relation between BMD, BMI and fracture risk in osteoarthritis is dependent on the stage, definition and location of the osteoarthritis and method of BMD measurement. It has been suggested that osteoarthritis should be further specified in terms of bone involvement.SummaryThese new findings open the way to better understand the bone subtypes of osteoarthritis (osteoporotic, bone forming and erosive) and the common and different ways bone is involved in osteoporosis and osteoarthritis. Much can be expected from further prospective studies, when taking into account the heterogeneous nature of both osteoporosis and osteoarthritis.
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TI Integrative Analysis of Genomics and Transcriptome Data to Identify Potential Functional Genes of BMDs in Females
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE OSTEOPOROSIS; BMD; SYSTEM GENETICS; HOMER1
ID coexpression network analysis; wide association data; missing heritability; susceptibility genes; glutamate receptors; bone-resorption; chinese women; osteoporosis; osteoarthritis; identification
AB Osteoporosis is known to be highly heritable. However, to date, the findings from more than 20 genorne wide association studies (GWASs) have explained less than 6% of genetic risks. Studies suggest that the missing heritability data may be because of joint effects among genes. To identify novel heritability for osteoporosis, we performed a system-level study on bone mineral density (BMD) by weighted gene coexpression network analysis (WGCNA), using the largest

GWAS data set for BMD in the field, Genetic Factors for Osteoporosis Consortium (GEFOS-2), and a transcriptomic gene expression data set generated from transiliac bone biopsies in women. A weighted gene coexpression network was generated for 1574 genes with GWAS nominal evidence of association (p <= 0.05) based on dissimilarity measurement on the expression data. Twelve distinct gene modules were identified, and four modules showed nominally significant associations with BMD (p 0.05), but only one module, the yellow module, demonstrated a good correlation between module membership (MM) and gene significance (GS), suggesting that the yellow module serves any important biological role in bone regulation. Interestingly, through characterization of module content and topology, the yellow module was found to be significantly enriched with contractile fiber part (GO:044449), which is widely ecognized as having a close relationship between muscle and bone. Furthermore, detailed subrnodule analyses of important candidate genes (HOMER1, SPTBN1) by all edges within the yellow module implied significant enrichment of functional connections between bone and cytoskeletal protein binding. Our study yielded novel information from system genetics analyses of GWAS data jointly with transcriptomic data. The findings highlighted a module and several genes in the model as playing important roles in the regulation of bone mass in females, which may yield novel insights into the;genetic;basis of osteoporosis. (C) 2016 American Society or Bone and Mineral Research.
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TC 36
Z9 39
U1 0
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PU WILEY
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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TI Patterns of Non-adherence to Supplementation with Calcium and Vitamin D in Persistent Postmenopausal Women Are Similar at Start and 1Year Later: A Qualitative Longitudinal Study
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE medication adherence; patient adherence; longitudinal studies; medication event monitoring system (MEMS); drug holidays; osteoporosis; calcium supplementation; electronic monitoring
ID self-reported adherence; antiretroviral therapy; drug-therapy; osteoporosis; medication; metaanalysis; time; questionnaires; combination; rates
AB Background: Osteoporosis is a chronic disease and adherence can fluctuate over time. Therefore, longer observation is necessary to investigate the stability of patients' adherence. The study aim was to compare the overall adherence (OA) to supplementation with the fixed combination of calcium and vitamin D (Ca/D) in postmenopausal women at baseline and after 1 year, and to evaluate the fluctuation of the OA in individual months. Furthermore, we studied whether adherence is influenced by signing of informed consent and routine medical check-up. Methods: This was a longitudinal, observational study. The data were obtained from the Osteocenter of University Hospital in Hradec Kralove, Czech Republic. Adherence was measured using electronic bottles type Medication Events Monitoring System (MEMS). The study was carried out in two 3-month periods; the baseline in 2013 (signing of informed consent while medical check-up) and the follow-up (medical check-up) in 2014. The adherence and adherence-related outcomes were studied in patients who had initiated osteoporosis treatment and were persistent. Results: 21 (49%) out of 43 patients who avoided drug dispenser and were persistent both at baseline and at follow-up, completed the study and were included. Median age was 76. Evaluating the whole 3-month periods, the OA did not differ significantly at baseline and at follow-up, the OA was 71 and 68%, respectively. However, the adherence in month 1 at baseline was significantly higher than the adherence in month 2 at baseline ($p < 0.001$) and also than the adherence in month 1 at follow-up ($p = 0.010$). Analysing the study period without

month 1, a stable adherence was observed in 48% of patients. About 33% of doses were omitted at baseline and 34% at follow-up. As many as 71% of the patients took drug holidays at baseline, and 76% at follow-up. Conclusion: The OA was insufficient, around 70% both at baseline and at follow-up. One half of the patients showed a stable adherence. The patterns of non-adherence were very similar at follow-up. Signing of the informed consent seems to act as bias more than regular medical check-up.
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AU Stamm, TA
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TI Impairment in the activities of daily living in older adults with and without osteoporosis, osteoarthritis and chronic back pain: a secondary analysis of population-based health survey data
SO BMC MUSCULOSKELETAL DISORDERS
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DT Article
DE Activities of daily living; Population-based study; Occupational therapy
ID depressive symptoms; arthritis; people; disability
AB Background: Independence in performing activities of daily living (ADLs) is a central aspect of functioning. Older adults frequently experience impairments and limitations in functioning in various life areas. The aim of this survey was to explore the limitations in the ADLs in older adults in a population-based survey in Austria. Method: A population-based cross-sectional study in 3097 subjects aged >= 65 years who were included in the Austrian health interview survey was performed. Descriptive statistics were used to calculate frequencies of problems in the ADLs. A principal component analysis was applied to analyze the main dimensions of 19 ADL items. Binary logistic regression models were used with the ADL dimensions as the dependent variables and osteoarthritis, chronic back pain, osteoporosis, sex, education level, anxiety or depression, age and pain intensity as independent variables. Results: People with musculoskeletal conditions were significantly more often affected by ADL problems than people without these diseases. The ADL domain which caused problems in the highest proportion of people was "doing heavy housework" (43.9 %). It was followed by the ADL domains "bending or kneeling down" (39.3 %), "climbing stairs up and down without walking aids" (23.1 %), and "walking 500 m without walking aids" (22.8 %). The principal components analysis revealed four dimensions of ADLs: (1) intense "heavy burden" ADLs, (2) basic instrumental ADLs, (3) basic ADLs and (3) hand-focused ADLs. The proportion of subjects who had problems with the respective dimensions was 58.2, 29.2, 23.0, and 9.2 %. Anxiety/depression (greatest effect), followed by the chronic musculoskeletal disease itself, female sex, higher age and pain intensity were significant predictors of ADL problems. Conclusion: This population-based survey indicates that older people have considerable ADL problems. More attention should be paid to the high impact of pain intensity, anxiety and depression on ADLs.
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NR 24
TC 83

Z9 101
U1 0
U2 21
PU BMC
PI LONDON
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J9 BMC MUSCULOSKEL DIS
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WC Orthopedics; Rheumatology
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GA DI0IB
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AF Bhutia, Sonam Choden
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TI Correlation of cartilage metabolic markers & antioxidants with the severity of knee osteoarthritis
SO INDIAN JOURNAL OF MEDICAL RESEARCH
LA English
DT Article
DE Antioxidants; cartilage metabolic markers; osteoarthritis; osteogenic protein-1
ID osteogenic protein-1; arthritis
AB Osteoarthritis is characterized by the degeneration of articular cartilage. Cartilage metabolic markers have been explored as possible markers for

osteoarthritis, and osteogenic protein-1 (OP-1) has emerged out to play a major role in cartilage repair. Oxidative stress has been implicated as a mediator of cartilage damage in patients with osteoarthritis. The aim of this study was to correlate the cartilage metabolic markers and antioxidants with the severity of knee osteoarthritis.
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NR 19
TC 7
Z9 9
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WC Immunology; Medicine, General & Internal; Medicine, Research & Experimental
SC Immunology; General & Internal Medicine; Research & Experimental Medicine
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PT J
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AF Cosman, Felicia
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TI Effect of Teriparatide on Bone Formation in the Human Femoral Neck
SO JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM
LA English
DT Article

ID randomized controlled-trial; parathyroid-hormone 1-34; postmenopausal osteoporosis; hip fracture; vertebral fractures; zoledronic acid; cancellous bone; women; alendronate; histomorphometry
AB Purpose: Teriparatide (TPTD) improves bone mass and microstructure resulting in reduced risk of vertebral and nonvertebral fractures. However, hip bone mineral density improvements are modest and there are no data confirming that TPTD reduces hip fracture risk. To study the effects of TPTD on the proximal femur, we performed a double-blind trial of TPTD vs placebo (PBO) in patients with osteoarthritis from whom femoral neck (FN) samples were obtained at total hip replacement (THR) surgery. Methods: Participants were randomly assigned to receive TPTD or PBO for an average of 40 days before THR. Double tetracycline labeling was initiated 21 days prior to THR to allow histomorphometric assessment of bone formation. During the THR, an intact sample of the FN was procured, fixed, and sectioned transversely. Serum levels of bone turnover markers were measured at baseline and during the THR. Standard histomorphometric parameters were measured and calculated on four bone envelopes (cancellous, endocortical, intracortical, and periosteal). The primary outcome measure was bone formation rate/bone surface (BFR/BS). Results: Forty individuals were enrolled (25 women, mean age, 71.5 +/- 8.0 y and 15 men, mean age, 68.9 +/- 7.7 y). In cancellous and endocortical envelopes, BFR/BS was 100% higher in the TPTD vs PBO group ($P < .05$). Bone turnover markers measured at the time of THR correlated with BFR/BS. Conclusion: TPTD stimulates bone formation rapidly in cancellous and endocortical envelopes of the FN. Our findings provide a mechanistic basis for TPTD-mediated improvement in FN bone mass and ultimately hip strength. This study is the first demonstration of the effect of any osteoporosis medication on osteoblast activity in the human proximal femur.
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NR 34
TC 27
Z9 33
U1 0
U2 2
PU ENDOCRINE SOC
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JI J. Clin. Endocrinol. Metab.
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WC Endocrinology & Metabolism
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PT J
AU Smolen, JS
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Boers, M
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TI Clinical trials of new drugs for the treatment of rheumatoid arthritis: focus on early disease
SO ANNALS OF THE RHEUMATIC DISEASES
LA English
DT Article
ID american-college; double-blind; rheumatology/european league; receptor inhibition; remission; tocilizumab; criteria; multicenter; monotherapy; definition
AB The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases convened a task force of experts in rheumatoid arthritis (RA) and clinical trial methodology to comment on the new draft 'Guideline on clinical investigation of medicinal products for the treatment of RA' released by the European Medicines Agency (EMA). Special emphasis was placed by the group on the development of new drugs for the treatment of early RA. In the absence of a clear definition of early RA, it was suggested that clinical investigations in this condition were conducted in disease-modifying antirheumatic drugs naive patients with no more than 1 year disease duration. The expert group recommended using an appropriate improvement in disease activity (American College of Rheumatology (ACR) or Simplified/Clinical Disease Activity Index (SDAI/CDAI) response criteria) or low disease activity (by any score) as primary endpoints, with ACR/European League Against Rheumatism remission as a secondary endpoint. Finally, as compelling evidence showed that the Disease Acrivity Score using 28-joint counts (DAS28) might not provide a reliable definition of remission, or sometimes even low disease activity, the group suggested replacing DAS28 as a measurement instrument to evaluate disease activity in RA clinical trials. Proposed alternatives included SDAI, CDAI and Boolean criteria.

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AU Acar, N
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AF Acar, Nuray
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TI The determination of apoptosis rates on articular cartilages of ovariectomized rats with and without alendronate treatment
SO HISTOLOGY AND HISTOPATHOLOGY
LA English
DT Article
DE Alendronate; Apoptosis; Articular cartilage; Osteoarthritis; Rat
ID subchondral bone loss; chondrocyte apoptosis; intraarticular injection; cell-death; osteoarthritis; model; degeneration; expression; fractures; osteoporosis
AB Osteoporosis (OP) is a major health problem characterized by compromised bone strength. Osteoarthritis (OA) is a joint disease that progresses slowly and is characterized by breakdown of the cartilage matrix. Alendronate (ALN), a nitrogen-containing bisphosphonate (BIS), inhibits bone loss and increases bone mineralization, and has been used clinically for the treatment of OP. It is still controversial whether BIS is effective in inhibiting the progression of OA. Chondrocyte apoptosis has been described in both human and experimentally induced OA models. In our study we aimed to detect whether ALN could protect articular cartilage from degeneration and reduce apoptosis rates in experimentally OA induced rats. For this rats were ovariectomized (ovex), nine weeks after operation rats were injected 30 mu g/kg/week ALN subcutaneously for six weeks. After six weeks articular cartilages were obtained. We did Safranin O staining and Mankin and Pritzker scorings to evaluate degeneration and investigated the expressions of p53, cleaved caspase 3, Poly ADP-ribose (PAR), Poly ADP-ribose polymerase 1 (PARP 1), and applied TUNEL technique to determine apoptotis rates. We found a significant decrease in glycosaminoglycan (GAG) amount and increased apoptosis which indicates damage on articular cartilages of ovex rats. GAG amount was higher and apoptosis rate was lower on articular cartilages of

ALN treated ovex rats compared to the ovex group. In contrary to studies showing that early ALN treatment has a protective effect, our study shows late ALN treatment has a chondroprotective effect on articular cartilage since we treated rats nine weeks after ovariectomy.
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AU Liu, Y
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TI Osteoprotegerin deficiency leads to deformation of the articular cartilage in femoral head
SO JOURNAL OF MOLECULAR HISTOLOGY
LA English
DT Article
DE OPG; Osteoarthritis; Degenerative joint disease; Femoral head; Articular cartilage
ID endochondral ossification; osteoarthritis; bone; disease; mice; opg; calcification;

osteoporosis; chondrocytes; targets
AB Osteoarthritis (OA) was a degenerative joint disease characterized by articular cartilage degradation and extensive remodeling of the subchondral bone. Multiple lines of evidence indicated that Osteoprotegerin (OPG), a member of TNF receptor superfamily that was expressed in the chondrocytes of articular cartilage and adjacent locations in the physiological setting, was involved in maintaining integrity of articular cartilage. OPG could prevent subchondral bone from resorption, and also protect cartilage from degradation. In this study, we used Osteoprotegerin-knockout mice (Opg-KO mice) to find out the role of OPG in articular cartilage. We examined articular cartilage in the femoral head of Opg-KO mice began in early adulthood using modern molecular and imaging methods. We found cartilage changes starting from adulthood and progressively with age, reminiscent of pathological changes in OA. Deficiency of OPG caused thinned articular cartilage and extensive remodeling of the subchondral bone in femoral head in comparison with wild-type mice (WT mice). Also, the articular cartilage of femoral head expressed significantly less of Aggrecan, Col-II and Col-X, but more Col-I and Matrix Metalloproteinases-13 (Mmp-13) than WT mice both at gene and protein level. Moreover, increased chondrocyte apoptosis and decreased chondrocyte proliferation were observed in femoral head of Opg-KO mice compared to WT mice. These data suggested that OPG played an important role in maintaining the homeostasis of articular cartilage of femoral head.
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AU Chiba, D
Tsuda, E
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TI Lumbar spondylosis, lumbar spinal stenosis, knee pain, back muscle strength are associated with the locomotive syndrome: Rural population study in Japan
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English
DT Article
ID quality-of-life; facet joint osteoarthritis; diagnostic support tool; postmenopausal osteoporosis; height loss; vertebral fractures; paraspinal muscles;

disc degeneration; mobility; deformity
AB Objectives: To comprehensively investigate the clinical and physical factors associating with locomotive syndrome (Loc-S); the locomotorium-disability for daily life. Methods: 647 volunteers participated (247 males, 400 females, Age: 58.4 +/- 11.0, BMI: 22.5 +/- 3.3). Three self-assessment questionnaires were administered: 1) "25-question Geriatric Locomotive Function Scale" (GELS-25) for evaluating Loc-S (GLFS-25 >= 16 defined as Loc-S); 2) "diagnostic support tool for LSS" (LSS-DST) for evaluating the prevalence of lumbar spinal stenosis (LSS); 3) Knee injury and Osteoarthritis Outcome Score (KOOS). Plain radiographs of the bilateral knees and lumbar spine were evaluated, and the severity of lumbar spondylosis (LS) and knee osteoarthritis (KOA) defined by Kellgren-Lawrence grade. Bone status was evaluated by using the osteo-sono assessment index (OSI) at the calcaneus. Isometric muscle strength of trunk and leg (Nm/kg, both extension and flexion) were evaluated. Linear regression analysis was performed to elucidate the factors concerned with GFLS-25 including age, sex, and BMI. Results: Thirty-nine subjects (6.0%, 13 males, 26 females) were defined as having Loc-S. Single regression model showed that age, height, BMI, skeletal muscle mass, OSI, LSS, KOOS, the severity of LS and KOA, and trunk- and leg-muscle strength were correlated with the degree of GLFS-25. Stepwise multiple regression model showed that sex, height, LSS, KOOS, the severity of LS, and back muscle strength were significantly correlated with that of GLFS-25. Conclusion: In this cross-sectional study, pain status associated with LSS and knee joint, structural severity for LS, and back muscle strength primarily affected the degree of GFLS-25. For managing Loc-S, we must pay more intensive attention to these factors. (C) 2016 The Japanese Orthopaedic Association. Published by Elsevier B.V. All rights reserved.
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PT J
AU Shen, JL
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AF Shen, Jianlin
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TI The potential role of sclerostin in the development of osteoarthritis
SO INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE
LA English
DT Review
DE Sclerostin; Wnt/beta-catenin signalling; osteoarthritis
ID bone morphogenetic protein; knee osteoarthritis; serum sclerostin; subchondral bone; cartilage degradation; postmenopausal osteoporosis; therapeutic target; signaling pathway; physical-activity; rabbit model
AB Osteoarthritis (OA), a debilitating degenerative joint disease which is greatly influenced by alterations in the local mechanical loading environment in the joint. The exact aetiology of OA remains unknown, but loss of articular cartilage, subchondral sclerosis, and bone remodeling has been known to play important roles in OA development. Wnt/beta-catenin signaling has a substantial role in bone

and cartilage homeostasis in the adult skeleton, and has been implicated in the process of cartilage degradation and subchondral remodeling in OA. Sclerostin (SOST), secreted mainly by osteocytes and downregulated by mechanical loading, is a potent inhibitor of Wnt signaling and a regulator of bone metabolism. Thus, by studying the expression of sclerostin and the Wnt pathway, it is possible to investigate the role of the osteocyte in bone remodeling in human musculoskeletal disease, such as OA. However few of literatures have reported about the relation between Sclerostin and OA. In this review we have tried to summarize the current knowledge on the effect of Sclerostin and to explore the potential role of Sclerostin during the process of OA. A better understanding of the relationship between Sclerostin and cartilage/subchondral in both physiological and pathological conditions may lead to development of more effective strategies for treating OA patients.

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TI A Comparative Study to Determine Functional and Clinical Outcome Differences Between Patients Receiving Outpatient Direct Physical Therapy Versus Home Physical Therapy Followed by Outpatient Physical Therapy After Total Knee Arthroplasty
SO ORTHOPAEDIC NURSING
LA English
DT Article
ID total hip; joint replacement; rehabilitation; osteoarthritis; performance; population; exercise; obesity; motion; range
AB BACKGROUND: Rehabilitation outcomes for patients with total knee arthroplasty (TKA) after hospital discharge are not well understood. PURPOSE: The purpose of this retrospective cohort study was to describe outpatient physical therapy (PT) after TKA and compare short-term (2 months) functional and clinical outcomes of patients following TKA who were discharged from the hospital to home and received (a) outpatient PT immediately (OP) or (b) home health PT before outpatient PT (HH). METHODS: The medical records of 109 men and women postoperative TKA discharged home were abstracted for the 6-minute walk test (6MWT), Knee Osteoarthritis and Outcome Score (KOOS), and knee range of motion (ROM) preoperatively and after discharge from all postoperative PT. Patients received outpatient clinic-based PT immediately after discharge from the hospital (OP) (n = 87) or home health PT before continued rehabilitation in an outpatient setting (HH) (n = 22). RESULTS: Despite demographic differences between OP and HH preoperatively, adjusted models revealed no signifi cant differences among KOOS, 6MWT, or knee ROM between OP and HH upon completion of postoperative PT. Patients in OP completed PT on average 20 days sooner (p = .0007), although the amount of time in outpatient PT (p = .55) and the number of outpatient PT visits (p = .68) were similar between groups. CONCLUSION: Gains in function were achieved by patients in OP and HH independent of the postoperative PT setting, although OP achieved gains sooner.
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AF Simmons, H. A.
TI Age-Associated Pathology in Rhesus Macaques (Macaca mulatta)
SO VETERINARY PATHOLOGY
LA English
DT Article
DE Macaca mulatta; rhesus macaque; neoplasia; aging; diabetes; endometriosis; amyloid; diverticulosis; cross-sectional studies; disease prevalence
ID nonhuman-primates; calorie restriction; pulmonary acariasis; monkeys; lesions; endometriosis; atherosclerosis; neoplasia; prostate; system
AB The rhesus macaque (Macaca mulatta) is one of the most extensively used nonhuman primate models for human diseases. This article presents a literature review focusing on major organ systems and age-associated conditions in humans and primates, combined with information from the Wisconsin National Primate Research Center Electronic Health Record database to highlight and contrast age-associated lesions in geriatric rhesus macaques with younger cohorts. Rhesus macaques are excellent models for age-associated conditions, including diabetes, osteoarthritis, endometriosis, visual accommodation, hypertension, osteoporosis, and amyloidosis. Adenocarcinoma of the large intestine (ileocecocolic junction, cecum, and colon) is the most common spontaneous neoplasm in the rhesus macaque. A combination of cross-sectional and longitudinal studies is required to truly define mechanisms of maturation, aging, and the pathology of age-associated conditions in macaques and thus humans. The rhesus macaque is and will continue to be an appropriate and valuable model for investigation of the mechanisms and treatment of age-associated diseases.
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AU Luo, S
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Guo, H
AF Luo, S.
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Ke, J.
Guo, H.
TI Association of COL1A1 polymorphism with subchondral bone degeneration of the temporomandibular joint
SO INTERNATIONAL JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY
LA English
DT Article
DE temporomandibular joint; osteoarthritis; subchondral bone; COL1A1; polymorphism; susceptibility
ID upstream regulatory region; mineral density; diagnostic-criteria; osteoarthritis; osteoporosis; collagens; disorders; severity; genetics; promoter
AB The G/T polymorphism of the COL1A1 gene exhibits a clinically significant influence on bone remodelling, leading to a predisposition to degenerative diseases. The enhancement of bone turnover and further loss of bone mass are thought to be the primary pathological changes in the early degenerative course of temporomandibular joint osteoarthritis (TMJ OA), with the appearance of low density lesions. Thus, it was hypothesized that this polymorphism may also affect this type of bone lesion in TMJ OA. A total of 130 TMJ OA patients with low density lesions (cortical bone erosion, condylar head resorption, cyst-like lesion) and 186 healthy individuals were recruited. DNA samples were extracted from buccal mucosa swabs; genotyping was performed by high-resolution melting assay. The distribution of genotypes in these groups was compared using a multivariate logistic regression model. No significant differences in the distributions of TT and TG genotypes were observed between the groups ($P > 0.05$). Significance was detected for GG homozygous carriers ($P = 0.043$); this genotype might be a risk factor for this type of low-density lesion (odds ratio 1.643, 95% confidence interval 1.016-2.658). This study indicates that the GG genotype might be a risk factor for

low-density lesions in the TMJ.
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NR 31
TC 7
Z9 10
U1 0
U2 15
PU CHURCHILL LIVINGSTONE
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PA JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND
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AU Huang, CC
Jiang, CC
Hsieh, CH
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TI Local bone quality affects the outcome of prosthetic total knee arthroplasty
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE micro-computed tomography; bone mineral density; osteoarthritis; osteoporosis; implants
ID posterior tibial slope; marrow edema pattern; mineral density; total hip; strength; flexion; microstructure; fractures; migration; failure
AB Osteoporosis and osteoarthritis commonly coexist in the elderly. In patients undergoing prosthetic total knee arthroplasty (TKA), the bone quality around the knee joint may affect the safety of prosthetic implantation and consequently satisfaction with the surgical outcome. We recruited 50 postmenopausal women undergoing TKA for primary osteoarthritis; 43 completed the study protocol. The bone quality parameters of the operated knee, including bone mineral density assessed using dual-energy X-ray absorptiometry and microarchitecture variables assessed using micro-computed tomography, were determined. Surgical outcomes were assessed according to immediate (<1week) postoperative pain quantified using the visual analog scale and knee function quantified using the Knee Injury and Osteoarthritis Outcome Score (KOOS) at 2 and 6months postoperatively. The influence of bone quality parameters on surgical outcomes was analyzed using simple and multiple regression analyses. Volumetric bone mineral density (R-2=0.187-0.234, p<0.01), the structural model index (R-2=0.103-0.181, p<0.05), and trabecular separation (R-2=0.289-0.424, p<0.05) were significantly associated with postoperative pain and improvement according to the KOOS. In conclusion, local bone quality, including mineral content and microarchitecture, affects the surgical outcome of TKA. (c) 2015 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 34:240-248, 2016.
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NR 38
TC 28
Z9 36
U1 0
U2 7
PU WILEY-BLACKWELL
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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PT J
AU Bassett, JHD
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AF Bassett, J. H. Duncan
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TI Role of Thyroid Hormones in Skeletal Development and Bone Maintenance
SO ENDOCRINE REVIEWS
LA English
DT Review
ID type-2 iodothyronine deiodinase; growth-factor-i; stimulated osteocalcin synthesis; alkaline-phosphatase activity; dominant-negative mutation; activated protein-kinase; osteoblastic cell-line; l-thyroxine treatment; receptor-beta gene; thyrotropin-suppressive therapy
AB The skeleton is an exquisitely sensitive and archetypal T-3-target tissue that demonstrates the critical role for thyroid hormones during development, linear growth, and adult bone turnover and maintenance. Thyrotoxicosis is an established cause of secondary osteoporosis, and abnormal thyroid hormone signaling has recently been identified as a novel risk factor for osteoarthritis. Skeletal phenotypes in genetically modified mice have faithfully reproduced genetic disorders in humans, revealing the complex physiological relationship between centrally regulated thyroid status and the peripheral actions of thyroid hormones. Studies in mutant mice also established the paradigm that T-3 exerts anabolic actions during growth and catabolic effects on adult bone. Thus, the skeleton represents an ideal physiological system in which to characterize thyroid hormone transport, metabolism, and action during development and adulthood and in response to injury. Future analysis of T-3 action in individual skeletal cell lineages will provide new insights into cell-specific molecular mechanisms and may ultimately identify novel therapeutic targets for chronic degenerative diseases such as osteoporosis and osteoarthritis. This review provides a comprehensive analysis of the current state of the art.
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TI A consensus statement on the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) algorithm for the management of knee osteoarthritis-From evidence-based medicine to the real-life setting
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English
DT Review
DE Glucosamine; Chondroitin; Hyaluronic acid; Knee osteoarthritis; Non-steroidal anti-inflammatory drugs; Symptomatic slow-acting drugs for osteoarthritis (SYSADOAs); Tramadol
ID nonsteroidal antiinflammatory drugs; upper gastrointestinal complications; randomized controlled-trial; double-blind; hyaluronic-acid; glucosamine sulfate; molecular-weight; chondroitin sulfate; analgesic use; hylan g-f-20
AB The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) published a treatment algorithm for the management of knee osteoarthritis (OA) in 2014, which provides practical guidance for the

prioritization of interventions. Further analysis of real-world data for OA provides additional evidence in support of pharmacological interventions, in terms of management of OA pain and function, avoidance of adverse events, disease-modifying effects and long-term outcomes, e.g., delay of total joint replacement surgery, and pharmacoeconomic factors such as reduction in healthcare resource utilization. This article provides an updated assessment of the literature for selected interventions in OA, focusing on real-life data, with the aim of providing easy-to-follow advice on how to establish a treatment flow in patients with knee OA in primary care clinical practice, in support of the clinicians' individualized assessment of the patient. In step 1, background maintenance therapy with symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) is recommended, for which high-quality evidence is provided only for the prescription formulations of patented crystalline glucosamine sulfate and chondroitin sulfate. Paracetamol may be added for rescue analgesia only, due to limited efficacy and increasing safety signals. Topical non-steroidal anti-inflammatory drugs (NSAIDs) may provide additional symptomatic treatment with the same degree of efficacy as oral NSAIDs without the systemic safety concerns. Oral NSAIDs maintain a central role in step 2 advanced management of persistent symptoms. However, oral NSAIDs are highly heterogeneous in terms of gastrointestinal and cardiovascular safety profile, and patient stratification with careful treatment selection is advocated to maximize the risk: benefit ratio. Intra-articular hyaluronic acid as a next step provides sustained clinical benefit with effects lasting up to 6 months after a short-course of weekly injections. As a last step before surgery, the slow titration of sustained-release tramadol, a weak opioid, affords sustained analgesia with improved tolerability. (C) 2015 The Authors. Published by Elsevier HS Journals, Inc.
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TI Serum and bone pentosidine in patients with low impact hip fractures and in patients with advanced osteoarthritis
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DT Article
DE Biomarkers; Osteoarthritis; Osteoporosis; Pentosidine; Proximal femoral fracture
ID glycation end-product; collagen cross-links; rheumatoid-arthritis; femoral-neck; biomechanical property; postmenopausal women; synovial-fluid; bisphosphonate treatment; nonenzymatic glycation; inflammatory markers
AB Background: Femoral neck fractures are a common occurrence in patients suffering from osteoporosis, while intracapsular hip fracture is rare in cases of osteoarthritis of the hip. Previous histomorphometric studies have emphasized the association between bone microarchitecture and the risk of low-impact fractures in osteoarthritis and osteoporosis patients. However, the strength of bone material is also a function of composition of organic bone matrix. In order to compare tissue material properties in these two clinical conditions, serum and bone pentosidine, a non-enzymatic collagen crosslinking element, was measured in patients who suffered a low-impact fracture, and in patients with advanced osteoarthritis. Methods: The patient population consisted of 70 patients who underwent hemiarthroplasty surgery for a femoral neck fracture, and 41 patients with advanced hip joint osteoarthritis without a history of low-impact fracture, who were indicated for total hip joint replacement. Pentosidine content was analyzed in bone samples and in serum obtained from fracture and osteoarthritis patients using high performance liquid chromatography. Results: Serum and bone concentrations of pentosidine were higher in subjects with hip fractures compared with osteoarthritis

after adjustment for age, sex, weight, serum creatinine, and diabetes. A significant positive correlation was found between bone and serum pentosidine in fractured cases. A comparable relationship was also demonstrated for pentosidine levels in serum and bone relative to differentiation of fracture and osteoarthritis cases. Conclusions: Serum pentosidine can be considered a potential biomarker for identification of subjects with impaired bone quality and bone strength.
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TI Key components and potential benefits of a comprehensive approach to women's musculoskeletal health
SO PHYSICIAN AND SPORTSMEDICINE
LA English
DT Review
DE Women's musculoskeletal health; sports medicine; Female Athlete Triad; ACL tears; orthopedic injuries
ID anterior cruciate ligament; bone-mineral density; female athlete triad; menstrual-cycle; risk-factors; injury risk; knee injury; acl reconstruction; primary

immunolocalization; neuromuscular control
AB Over the last 40years there has been a significant increase in the number of female athletes, as well as a rise in musculoskeletal injuries observed in women. There is sufficient evidence from past medical research identifying various musculoskeletal injuries and conditions that more commonly affect women, such as osteoarthritis, osteoporosis, stress fractures, and anterior cruciate ligament tears. Several women's sports medicine and musculoskeletal health programs have been developed throughout the United States in an attempt to provide more tailored care to the female athlete. The goal of a comprehensive approach to women's musculoskeletal health is to create an interdisciplinary team to facilitate treatment for a variety of injuries and related conditions. This manuscript outlines the musculoskeletal conditions that commonly affect women and highlights the various etiologies of these sex disparities. We discuss the role of interdisciplinary women's musculoskeletal health and sports medicine programs, and define the potential benefits of such an approach. Future studies should focus on assessing the outcomes of multidisciplinary women's sports medicine programs as current literature in this area is lacking.
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PA 2-4 PARK SQUARE, MILTON PARK, ABINGDON OR14 4RN, OXON, ENGLAND
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TI Tai Chi for Chronic Pain Conditions: A Systematic Review and Meta-analysis of Randomized Controlled Trials
SO SCIENTIFIC REPORTS
LA English
DT Article
ID quality-of-life; knee osteoarthritis; physical function; older-adults; balance; pilot; women; exercise; health; gait
AB Several studies reported that Tai Chi showed potential effects for chronic pain, but its role remains controversial. This review assessed the evidence regarding the effects of Tai Chi for chronic pain conditions. 18 randomized controlled trials were included in our review. The aggregated results have indicated that Tai Chi showed positive evidence on immediate relief of chronic pain from osteoarthritis (standardized mean difference [SMD], -0.54; 95% confidence intervals [CI], -0.77 to -0.30; P < 0.05). The valid duration of Tai Chi practice for osteoarthritis may be more than 5 weeks. And there were some beneficial evidences regarding the effects of Tai Chi on immediate relief of chronic pain from low back pain (SMD, -0.81; 95% CI, -1.11 to -0.52; P < 0.05) and osteoporosis (SMD, -0.83; 95% CI, -1.37 to -0.28; P = 0.003). Therefore, clinicians may consider Tai Chi as a viable complementary and alternative medicine for chronic pain conditions.
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TI Pharmacodynamics and pharmacokinetics of oral salmon calcitonin in the treatment of osteoporosis
SO EXPERT OPINION ON DRUG METABOLISM & TOXICOLOGY
LA English
DT Review
DE 5-CNAC; bone mineral density; calcitonin; Eudragit; fracture; osteoporosis; treatment
ID painful diabetic-neuropathy; alpha-amino-acids; postmenopausal women; nasal spray; bone mass; recombinant calcitonin; knee osteoarthritis; parathyroid-hormone; controlled-trial; hip fracture
AB Introduction: Salmon calcitonin (sCT) has been used for the treatment of postmenopausal osteoporosis for over 30 years. It is available in injectable and intranasal formulations. Two oral formulations have recently been developed. Areas covered: The basis for oral sCT's bioavailability rests with a carrier molecule (8-(N-2-hydroxy-5-chloro-benzoyl)-amino-caprylic acid) or an acid-resistant enteric coating (Eudragit (R) polymer containing citric acid). With these formulations, sCT is resistant to gastric acid, and thus becomes available for absorption at the higher pH of the small intestine. Even though the changes in bone mineral density and bone turnover markers are greater with oral compared to nasal sCT, it shows only minor effects on these surrogate markers. Expert opinion: Oral sCT is attractive in concept as it is would be more convenient to patients than other routes of administration. While there may be other advantages to the oral formulation such as improving bone mineral density to a greater extent than nasal CT, anti-fracture efficacy has not been shown in a recent major clinical trial. Together with the possibility of an association between the drug and cancer and the availability of antiresorptive drug classes that are clearly more efficacious than sCT, successful development of oral sCT as a treatment for postmenopausal osteoporosis is uncertain.
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TI A comprehensive fracture prevention strategy in older adults: The European union geriatric medicine society (EUGMS) statement
SO EUROPEAN GERIATRIC MEDICINE
LA English
DT Article
DE Falls; Fragility fracture; Older people; Prevention; Position statement
ID bone-mineral density; fall prevention; hip-fracture; postmenopausal women; cost-effectiveness; zoledronic acid; risk-factors; pharmacological-treatments; strontium ranelate; liaison service
AB Prevention of fragility fractures in older people has become a public health priority, although the most appropriate and cost-effective strategy remains unclear. In the present statement, the Interest group on falls and fracture prevention of the European union geriatric medicine society (EUGMS), in collaboration with the International association of gerontology and geriatrics for the European region (IAGG-ER), the European union of medical specialists (EUMS), the Fragility fracture network (FFN), the International osteoporosis foundation (IOF) - European society for clinical and economic aspects of osteoporosis and osteoarthritis (ECCEO), outlines its views on the main points in the current debate in relation to the

primary and secondary prevention of falls, the diagnosis and treatment of bone fragility, and the place of combined falls and fracture liaison services for fracture prevention in older people. (C) 2016 Published by Elsevier Masson SAS.
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TI Unmet needs and current and future approaches for osteoporotic patients at high risk of hip fracture
SO ARCHIVES OF OSTEOPOROSIS
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DE Fracture; Osteoporosis; Treatment; BMD; Bone strength; Surgical treatment
ID finite-element-analysis; bone-mineral density; postmenopausal women; femoral-neck; zoledronic acid; proximal femur; fragility fracture; cortical bone; nonvertebral fractures; practice framework
AB A Summary This review provides a critical analysis of currently available approaches to increase bone mass, structure and strength through drug therapy and of possible direct intra-osseous interventions for the management of patients at imminent risk of hip fracture. Purpose Osteoporotic hip fractures represent a particularly high burden in morbidity-, mortality- and health care-related costs. There are challenges and unmet needs in the early prevention of hip fractures, opening the perspective of new developments for the management of osteoporotic patients at imminent and/or at very high risk of hip fracture. Amongst them, preventive surgical intervention needs to be considered. Methods A European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)/International Osteoporosis Foundation (IOF) working group reviewed the presently available intervention modalities including preventive surgical options for hip fragility. This paper represents a summary of the discussions. Results Prevention of hip fracture is currently based on regular physical activity; prevention of falls; correction of nutritional deficiencies, including vitamin D repletion; and pharmacological intervention. However, efficacy of these various measures to reduce hip fractures is at most 50% and may need months or years before becoming effective. To face the challenges of early prevention of hip fractures for osteoporotic patients at imminent and/or at very high risk of hip fracture, preventive surgical intervention needs further investigation. Conclusion Preventive surgical intervention needs to be appraised for osteoporotic patients at imminent and/or at very high risk of hip fracture.

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TI Falls in older adults with cancer: a systematic review of prevalence, injurious falls, and impact on cancer treatment
SO SUPPORTIVE CARE IN CANCER
LA English
DT Review
DE Falls; Systematic review; Geriatric oncology; Cancer treatment
ID risk-factors; prostate-cancer; cognitive impairment; geriatric syndrm; community; people; predictors; hospitals; care; osteoporosis

AB The purpose of this systematic review was to update and expand the existing systematic review with the aim to answer the following questions: (1) How often do older adults (OA)s with cancer fall? (2) What are the predictors of falls in OA with cancer? (3) What is the rate of injurious falls and predictors of injurious falls in OA with cancer? (4) What are the circumstances and outcomes of falls in this population? (5) How do falls in cancer patients affect subsequent cancer treatment? Medline, Pubmed, Embase, and CINAHL were searched. Eligible studies included clinical trials, cross-sectional, cohort, case-control, and qualitative studies in which the entire sample or a sub-group of the sample were OA aged 60 and above, had cancer, in which falls were examined as a primary or secondary outcome and published in English. Twenty-seven studies met our inclusion criteria with most involving the outpatient setting. Fall rates and injurious fall rates varied widely. Consistent predictors of falls were prior falls among outpatients and cognitive impairment among inpatients. There were no data on impact of falls on cancer treatment. Data on circumstances of falls were limited. Falls and fall-related injuries are common in older cancer patients. However, little is known about circumstances of falls and impact of falls on cancer treatment. Many known fall predictors in community-dwelling OA have not been explored in oncology. More research is needed to address gaps in these areas.
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NR 76
TC 54
Z9 59
U1 0
U2 4
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 SUPPORT CARE CANCER
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WC Oncology; Health Care Sciences & Services; Rehabilitation
SC Oncology; Health Care Sciences & Services; Rehabilitation
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PT J
AU Föger-Samwald, U
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TI Molecular mechanisms of osteoporotic hip fractures in elderly women
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Article
DE Osteoporosis; Hip fracture; Gene expression; Bone formation; Oxidative stress
ID mesenchymal stem-cells; postmenopausal women; bone loss; serum sclerostin; messenger-rna; osteoblast differentiation; osteoclast differentiation; antioxidant enzymes; gene-expression; trabecular bone
AB A common manifestation of age-related bone loss and resultant osteoporosis are fractures of the hip. Age-related osteoporosis is thought to be determined by a number of intrinsic factors including genetics, hormonal changes, changes in levels of oxidative stress, or an inflammatory status associated with the aging process. The aim of this study was to investigate gene expression and bone architecture in bone samples derived from elderly osteoporotic women with hip fractures (OP) in comparison to bone samples from age matched women with osteoarthritis of the hip (OA). Femoral heads and adjacent neck tissue were collected from 10 women with low-trauma hip fractures (mean age 83 +/- 6) and consecutive surgical hip replacement. Ten bone samples from patients undergoing hip replacement due to osteoarthritis (mean age 80 +/- 5) served as controls. One half of each bone sample was subjected to gene expression analysis. The second half of each bone sample was analyzed by microcomputed tomography. From each half, samples from four different regions, the central and subcortical region of the femoral head and neck, were analyzed. We could show a significantly decreased expression of the osteoblast related genes RUNX2, Osterix, Sclerostin, WNT10B, and Osteocalcin, a significantly increased ratio of RANKL to Osteoprotegerin, and a significantly increased expression of the enzymes superoxide dismutase 2 (SOD2) and glutathione peroxidase GPX3, and of the inflammatory cytokine IL6 in bone samples from hip fracture patients compared to controls. Major microstructural changes in OP bone were seen in the neck and were characterized by a significant decrease of bone volume, trabecular number, and connectivity density and a significant increase of trabecular separation. In conclusion, our data give evidence for a decreased expression of osteoblast related genes and increased expression of osteoclast related genes. Furthermore, increased expression of SOD2 and GPX3 suggest increased antioxidative activity in bone samples from elderly osteoporotic women with hip fractures. (C) 2015 Elsevier Inc. All rights reserved.
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FU Austrian Society of Bone and Mineral Research [AP00604OFF]; Ludwig Boltzmann Institut fur Altersforschung [FA648A0607]; Austrian Society of Geriatrics and Gerontology [AP00570OFF]; Novartis Pharma [FA648A0606]
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NR 68
TC 21
Z9 23
U1 1
U2 13
PU PERGAMON-ELSEVIER SCIENCE LTD
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WC Geriatrics & Gerontology
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PT J
AU Lu, J
Fan, YJ
Gong, XY
Zhou, X
Yi, CX
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AF Lu, Juan
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Gong, Xiaoyuan
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Zhang, Yinxing
Pan, Jun
TI The Lineage Specification of Mesenchymal Stem Cells Is Directed by the Rate of Fluid Shear Stress
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Article
ID marrow stromal cells; chondrogenic differentiation; matrix elasticity; gene-expression; mc3t3-e1 cells; nitric-oxide; bone-cells; ca2+; substrate; pressure
AB The effective regulation of fluid shear stress (FSS) on the lineage specification of mesenchymal stem cells (MSCs) remains to be addressed. We hypothesized that when MSCs are recruited to musculoskeletal system following stimulation, their differentiation into osteogenic or chondrogenic cells is directed by the rate of FSS (SS) through modulation of the mechanosensitive, cation-selective channels (MSCCs), intracellular calcium levels, and F-actin. To this end, MSCs were exposed to laminar FSS linearly increased from 0 to 10dyn/cm(2) in 0, 2, or 20min and maintained at 10dyn/cm(2) for a total of 20min (termed as SS 0-0, 0-2, and 0-20, respectively, representing more physiological (0-0) and non-physiological (0-2 and 0-20) SS treatments). Our results showed 0-0 facilitated MSC differentiation towards chondrogenic and not osteogenic phenotype, by promoting moderate intracellular calcium concentration ([Ca2+](i)) increase from the calcium channels with the exception of MSCCs or intracellular calcium stores, and F-actin organization. In contrast, 0-2 promoted MSCs towards osteogenic and not chondrogenic phenotype, by inducing significant [Ca2+](i) increase mainly from the MSCCs, and F-actin assembly. However, 0-20 elicited the modest osteogenic and chondrogenic phenotypes, as it induced the lowest [Ca2+](i) increase mainly from MSCCs, and F-actin assembly. Our results suggest that compared to the more physiological SS, the non-physiological SS favors [Ca2+](i) influx from MSCCs. An appropriate non-physiological SS (0-2) even elicits a large [Ca2+](i) influx from the

MSCCs that reverses the lineage specification of MSCs, providing validation for the high mechanosensitivity of MSCs and guidance for training osteoporosis and osteoarthritis patients. J. Cell. Physiol. 231: 1752-1760, 2016. (c) 2015 Wiley Periodicals, Inc.
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NR 39
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Z9 46
U1 1
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PT J
AU Brodt, S
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TI Cementless Total Hip Arthroplasty in Primary Myelofibrosis - a Case Report
SO ACTA CHIRURGIAE ORTHOPAEDICAE ET TRAUMATOLOGIAE CECHOSLOVACA
LA English
DT Article
DE hip; primary myelofibrosis; cementless; THA; total hip replacement
AB There is a great deal of data available, in part contradictory, on the best fixation technique to use for total hip arthroplasty (THA) in hip osteoarthritis. Both the cementless and the cemented versions offer excellent long-term outcomes if the respective technique is applied correctly. However, as far as we know, no recommendation has been made regarding cemented vs. cementless THA in primary myelofibrosis. The case described here concerns a very active 76-year-old patient with primary myelofibrosis. This is a rare hematological disease. It develops from clonal hematopoiesis with impaired blood formation and progressive bone marrow fibrosis. An MRI scan of the patients pelvis showed a marked spotted change over all of the imaged bone. Ultimately, in preoperative planning we decided in favor of a proven cementless implant (Allofit Alloclassic cup and the CLS Spotorno stem from Zimmer). Complication-free osseous integration of the cementless implants was observed. Histologic analysis of the bone showed a focally sclerotically altered bone structure. Neither osteoporosis nor osteopenia were found. In our opinion, taking into account all other indication criteria, there is no reason not to perform a cementless THA implantation in the presence of primary myelofibrosis.
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Tefferi A, 2014, AM J HEMATOL, V89, P916, DOI 10.1002/ajh.23703
NR 9
TC 1
Z9 1
U1 0
U2 0
PU GALEN SRO
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PA NA BELIDLE 34, PRAGUE 5, 150 00, CZECH REPUBLIC
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JI Acta Chir. Orthop. Traumatol. Cechoslov.
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WC Orthopedics
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AU Reppe, S
Datta, HK
Gautvik, KM
AF Reppe, Sjur
Datta, Harish K.
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TI Omics analysis of human bone to identify genes and molecular networks regulating skeletal remodeling in health and disease
SO BONE
LA English
DT Review
DE Omics; Osteoporosis; Osteoarthritis; Review; Bone biopsy; Transcriptomics; Epigenetics
ID endogenous cushings-syndrome; peripheral-blood leukocytes; messenger-rna; dna methylation; osteoporotic fractures; subchondral bone; trabecular bone; expression; tissue; osteoarthritis
AB The skeleton is a metabolically active organ throughout life where specific bone cell activity and paracrine/endocrine factors regulate its morphogenesis and remodeling. In recent years, an increasing number of reports have used multi-omics technologies to characterize subsets of bone biological molecular networks. The skeleton is affected by primary and secondary disease, lifestyle and many drugs. Therefore, to obtain relevant and reliable data from well characterized patient and control cohorts are vital. Here we provide a brief overview of omics studies performed on human bone, of which our own studies performed on trans-iliacal bone biopsies from postmenopausal women with osteoporosis (OP) and healthy controls are among the first and largest. Most other studies have been performed on smaller groups of patients, undergoing hip replacement for osteoarthritis (OA) or fracture, and without healthy controls. The major findings emerging from the combined studies are: 1. Unstressed and stressed bone show profoundly different gene expression reflecting differences in bone turnover and remodeling and 2. Omics analyses comparing healthy/OP and control/OA cohorts reveal characteristic changes in transcriptomics, epigenomics (DNA methylation), proteomics and metabolomics. These studies, together with genome-wide association studies, in vitro observations and transgenic animal models have identified a number of genes and gene products that act via Wnt and other signaling systems and are highly associated to bone density and fracture. Future challenge is to understand the functional interactions between bone-related molecular networks and their significance in OP and OA pathogenesis, and also how the genomic architecture is affected in health and disease. (C) 2017 Elsevier Inc. All rights reserved.
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TI Heavy metals accumulation affects bone microarchitecture in osteoporotic patients
SO ENVIRONMENTAL TOXICOLOGY
LA English
DT Article
DE heavy metals; osteoporosis; osteoarthrosis; bone health; environmental pollution
ID mineral density; environmental exposure; cadmium exposure; ros 17/2.8; lead; population; resorption; health; copper; women
AB Bone metabolism is affected by mechanical, genetic, and environmental factors and plays a major role in osteoporosis. Nevertheless, the influence of environmental pollution on the occurrence of osteoporosis is still unclear and controversial. In this context, heavy metals are the most important pollutants capable to affect bone mass. The aim of this study was to investigate whether heavy metals accumulation in bone tissues could be related to the altered bone metabolism and architecture of osteoporotic patients. To this end, we analyzed 25 bone head biopsies osteoporotic patients and 25 bone head biopsies of osteoarthritic patients. Moreover we enrolled 15 patients underwent hip arthroplasty for high-energy hip fracture or osteonecrosis of the femoral head as a control group. Bone head biopsies were studied by BioQuant-osteo software, scanning electron microscopy and Energy Dispersive X-ray microanalysis. We found a prevalence of lead, cadmium and chromium accumulation in osteoporotic patients. Noteworthy, high levels of sclerostin, detected by immunohistochemistry, correlate with the accumulation of heavy metal found in the bone of osteoporotic patients, suggesting a molecular link between heavy metal accumulation and bone metabolism impairment. In conclusion, the presence of heavy metals into bone shed new light on the comprehension of the pathogenesis of osteoporosis since these elements could play a non redundant role in the development of osteoporosis at cellular/molecular and epigenetic level. Nevertheless, in vivo and in vitro studies need to better elucidate the molecular mechanism in which heavy metals can participate to osteoporosis. (c) 2016 Wiley Periodicals, Inc. Environ Toxicol 32: 1333-1342, 2017.
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TI The roles and perspectives of microRNAs as biomarkers for intervertebral disc degeneration
SO JOURNAL OF TISSUE ENGINEERING AND REGENERATIVE MEDICINE
LA English
DT Review
DE intervertebral disc degeneration; microRNA; biomarker; NP cell apoptosis; NP cell proliferation; ECM metabolism
ID nucleus pulposus cells; fas-mediated apoptosis; circulating micrornas; rheumatoid-arthritis; up-regulation; tnf-alpha; expression; cancer; mir-21; degradation
AB MicroRNAs (miRNAs) are highly conserved molecules that regulate protein levels post-transcriptionally. Aberrant miRNA expression presents in various musculoskeletal disorders, such as osteoporosis, osteoarthritis and rheumatoid arthritis. The expression levels of miRNAs are characterized by endogenous properties and tissue specificity. This raises the possibility that miRNAs could serve as useful clinical biomarkers in the diagnosis of certain diseases. Intervertebral disc

degeneration (IDD) is one of the major causes of back pain, and a process characterized by a cascade of molecular, cellular, biochemical and structural changes. The presence of dysregulated miRNA expression in patients with disc degeneration diseases indicates that miRNAs may play a vital role in the pathogenesis of IDD. Here, we provide an introduction of the roles of miRNAs in the process of IDD, and the prospective application of miRNAs as biomarkers for IDD. Copyright (c) 2017 John Wiley & Sons, Ltd.
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TI The contribution of musculoskeletal disorders in multimorbidity: Implications for practice and policy
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DE Multimorbidity; Co-morbidity; Musculoskeletal; Arthritis; Osteoarthritis; Osteoporosis; Back pain; Management; Prevalence; Policy
ID health-care utilization; quality-of-life; knee osteoarthritis; risk-factors; rheumatoid-arthritis; physical-activity; back-pain; work-loss; prevalence; impact
AB People frequently live for many years with multiple chronic conditions (multimorbidity) that impair health outcomes and are expensive to manage. Multimorbidity has been shown to reduce quality of life and increase mortality. People with multimorbidity also rely more heavily on health and care services and have poorer work outcomes. Musculoskeletal disorders (MSDs) are ubiquitous in multimorbidity because of their high prevalence, shared risk factors, and shared pathogenic processes amongst other long-term conditions. Additionally, these conditions significantly contribute to the total impact of multimorbidity, having been shown to reduce quality of life, increase work disability, and increase treatment burden and healthcare costs. For people living with multimorbidity, MSDs could impair the ability to cope and maintain health and independence, leading to precipitous physical and social decline. Recognition, by health professionals, policymakers, non-profit organisations, and research funders, of the impact of musculoskeletal health in multimorbidity is essential when planning support for people living with multimorbidity. (C) 2017 The Authors. Published by Elsevier Ltd.
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AB The skeletal system, comprising bones, ligaments, cartilage and their connective tissues, is critical for the structure and support of the body. Diseases that affect the skeletal system can be difficult to treat, mainly because of the avascular cartilage region. Targeting drugs to the site of action can not only increase efficacy but also reduce toxicity. Bone-targeting drugs are designed with either of two general targeting moieties, aimed at the entire skeletal system or a specific cell type. Most bone-targeting drugs utilize an affinity to hydroxyapatite, a major component of the bone matrix that includes a high concentration of positively-charged Ca2+. The strategies for designing such targeting moieties can involve synthetic and/or biological components including negatively-charged amino acid peptides or bisphosphonates. Efficient delivery of bone-specific drugs provides significant impact in the treatment of skeletal related disorders including infectious diseases (osteoarthritis, osteomyelitis, etc.), osteoporosis, and metabolic skeletal dysplasia. Despite recent advances, however, both delivering the drug to its target without losing activity and avoiding adverse local effects remain a challenge. In this review, we investigate the current development of bone-targeting moieties, their efficacy and limitations, and discuss future directions for the development of these specific targeted treatments.
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NR 71
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Z9 111
U1 1
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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PT J
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TI Quantitative regional and sub-regional analysis of femoral and tibial subchondral bone mineral density (sBMD) using computed tomography (CT): comparison of non-osteoarthritic (OA) and severe OA knees
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis (OA); Subchondral bone; Computed tomography (CT); Quantitative; Bone mineral density
ID cartilage thickness; radiographic osteoarthritis; disease progression; joint; alignment; osteoporosis; compartment; adduction; walking; loads
AB Objective: This study aimed to compare subchondral bone mineral density (sBMD) between non-radiographic osteoarthritic (OA) and medial femorotibial OA knees, using computed tomography (CT). Design: CT exams from 16 non-radiographic OA (KL grade < 2) and 16 severe medial OA (KL grade >= 3) knees (average age of 61.7 +/- 3 and 62.2 +/- 5 years old respectively, 50% male in each group), were retrospectively analyzed. CT exams were segmented and 3D maps of sBMD based on the CT number in the most superficial 3 mm of femoral and tibial subchondral bone were computed. Average sBMD and medial-to-lateral sBMD ratios were calculated for total load-bearing regions and for sub-regions of interest in the femur and tibia. Results: The analysis of total load-bearing regions did not reveal any significant difference between groups, except for the lateral tibia, where OA knees had lower sBMD. Sub-regional analysis unveiled differences with some sub-regions of the femur and tibia presenting significantly lower (in the lateral compartment) or higher (in the medial compartment) sBMD in OA knees compared to non-OA knees. The M/L sBMD ratios were significantly higher for OA knees compared to non-OA knees for all regions and sub-regions, except for the internal sub-regions. Conclusions: sBMD locally differs between non-OA and OA knees, in agreement with prior knowledge on biomechanics. CT proved to be a valuable tool for 3D analysis of femoral and tibial sBMD, which can be used in future studies to describe the chronology of sBMD alterations and improve our understanding of the role of subchondral bone in knee OA. (C) 2017 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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NR 50
TC 23
Z9 27
U1 0
U2 10
PU ELSEVIER SCI LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON,

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AU Fu, SH
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Yang, RS
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AF Fu, Shau-Huai
Wang, Chen-Yu
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Hsiao, Fei-Yuan
TI Bisphosphonate Use and the Risk of Undergoing Total Knee Arthroplasty in Osteoporotic Patients with Osteoarthritis A Nationwide Cohort Study in Taiwan
SO JOURNAL OF BONE AND JOINT SURGERY-AMERICAN VOLUME
LA English
DT Article
ID oral bisphosphonates; randomized-trial; fracture risk; bone; alendronate; adherence; risedronate; progression; symptoms; survival
AB Background: The use of bisphosphonates has been reported to have potential beneficial effects on knee osteoarthritis, but existing studies have limitations. The purpose of this study was to examine the association of bisphosphonate use with the risk of undergoing total knee arthroplasty and with the consumption of pain medication among osteoporotic patients with knee osteoarthritis. Methods: We

identified patients who were newly diagnosed with knee osteoarthritis among a cohort of patients with osteoporosis from 2009 to 2012 in the National Health Insurance Research Database in Taiwan. We further categorized these patients into 2 groups: those who were treated with bisphosphonates (bisphosphonate users) and those who were not treated with any antiosteoporosis drug (nonusers). Bisphosphonate treatment adherence was calculated by the medication possession ratio (MPR) as the proportion of days of bisphosphonate treatment within a fixed duration; an MPR of >= 80% was considered high adherence. The primary and secondary outcomes of interest were undergoing total knee arthroplasty and the use of pain medication, respectively. Analyses using Cox proportional hazard models with propensity-score adjustment were performed to estimate the association between bisphosphonate use and the risk of undergoing total knee arthroplasty. The incremental change in the mean accumulated defined daily doses of pain medications among both bisphosphonate users and nonusers was calculated. Results: We identified 16,276 bisphosphonate users and 123,791 nonusers of any anti-osteoporosis drug among the patients with osteoporosis who were newly diagnosed with osteoarthritis. Bisphosphonate use was significantly associated with a decreased risk of total knee arthroplasty (adjusted hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.69 to 0.83; p < 0.001). In patients with a follow-up period of >= 24 months and an MPR of >= 80%, the effect size was significantly greater (adjusted HR, 0.66; p = 0.048). Over the 5 years of follow-up, we found a significantly greater decrease in the use of pain medication among bisphosphonate users than among nonusers (p < 0.001; Chow test). Conclusions: Among patients with osteoporosis and osteoarthritis, bisphosphonate use was associated with a significantly lower risk of total knee arthroplasty, especially in patients with high adherence and longer treatment duration. A lower consumption of pain medication was also found for bisphosphonate users among the patients with osteoporosis and osteoarthritis.

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NR 31
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PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
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TI Development of nanomaterials for bone-targeted drug delivery
SO DRUG DISCOVERY TODAY
LA English
DT Review
ID mesoporous silica nanoparticles; endoplasmic-reticulum stress; bioactive glass nanoparticles; nonviral gene delivery; of-the-art; gold nanoparticles; in-vitro; osteoclast differentiation; multifunctional nanoparticles; morphogenetic protein-2
AB Bone is one of the major organs of the human body; it supports and protects other organs, produces blood cells, stores minerals, and regulates hormones. Therefore, disorders in bone can cause serious morbidity, complications, or mortality of patients. However, despite the significant occurrence of bone diseases, such as osteoarthritis (OA), osteoporosis (OP), non-union bone defects, bone cancer, and myeloma-related bone disease, their effective treatments remain a challenge. In this review, we highlight recent progress in the development of nanotechnology-based drug delivery for bone treatment, based on its improved delivery efficiency and safety. We summarize the most commonly used nanomaterials for bone drug delivery. We then discuss the targeting strategies of these nanomaterials to the diseased sites of bone tissue. We also highlight nanotechnology-based drug delivery to bone cells and subcellular organelles. We envision that nanotechnology-based drug delivery will serve as a powerful tool for developing treatments for currently incurable bone diseases.
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ID facet joint osteoarthritis; low-back-pain; bone-density; osteoporotic fractures; osteo-arthrosis; lumbar spine; population; association; deformity; evos

AB Objectives. To assess the prevalences across Europe of radiological indices of degenerative inter-vertebral disc disease (DDD); and to quantify their associations with, age, sex, physical anthropometry, areal BMD (aBMD) and change in aBMD with time. Methods. In the population-based European Prospective Osteoporosis Study, 27 age-stratified samples of men and women from across the continent aged 50+ years had standardized lateral radiographs of the lumbar and thoracic spine to evaluate the severity of DDD, using the Kellgren-Lawrence (KL) scale. Measurements of anterior, mid-body and posterior vertebral heights on all assessed vertebrae from T4 to L4 were used to generate indices of end-plate curvature. Results. Images from 10 132 participants (56% female, mean age 63.9 years) passed quality checks. Overall, 47% of men and women had DDD grade 3 or more in the lumbar spine and 36% in both thoracic and lumbar spine. Risk ratios for DDD grades 3 and 4, adjusted for age and anthropometric determinants, varied across a three-fold range between centres, yet prevalences were highly correlated in men and women. DDD was associated with flattened, non-ovoid inter-vertebral disc spaces. KL grade 4 and loss of inter-vertebral disc space were associated with higher spine aBMD. Conclusion. KL grades 3 and 4 are often used clinically to categorize radiological DDD. Highly variable European prevalences of radiologically defined DDD grades 3+ along with the large effects of age may have growing and geographically unequal health and economic impacts as the population ages. These data encourage further studies of potential genetic and environmental causes.
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Aghazadeh-Habashi, A
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Wu, YC
Bhandari, KH
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AF Yang, Yang
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TI Bone-targeting parathyroid hormone conjugates outperform unmodified PTH in the anabolic treatment of osteoporosis in rats
SO DRUG DELIVERY AND TRANSLATIONAL RESEARCH
LA English
DT Article
DE PTH; Bone drug delivery; Anabolic therapy; Osteoporosis; Micro-CT
ID postmenopausal women; ovariectomized rats; mineral crystals; strontium; mass;

receptors; model; osteoarthritis; teriparatide; alendronate
AB Synthetic parathyroid hoinione (PTH) is clinically indicated for the treatment of osteoporosis, through its anabolic effects on parathyroid hormone receptors (PTHRs), located on osteoblast cells. However, the bioavailability of PTH for hone cells is restricted by the short half-life of PTH and the widespread distribution of PTHRs in non-skeletal tissues. To impart affinity for mineralized hone surfaces, bisphosphonate (BP)-mediated PTH analogues were synthesized, characterized, and evaluated in vitro and in vivo. The successful synthesis of PTH-PEG-BP was identified on MALDI-ToF mass spectra; bone-targeting potential was evaluated by hydroxyapatite binding test; and receptor bioactivity was assessed in UMR-106 (rat osteosarcoma) cells that constitutively express PTHRs. Therapeutic efficacy was evaluated using ovariectomized rats that remained untreated for 8 weeks to allow development of osteopenia. Those rats then received daily subcutaneous injections of PTH-PEG-BP, thiol-BP vehicle, or unmodified PTH, and compared to sham-operated healthy rats at 0, 4, 8, 12, and 16 weeks. In vivo micro-CT was conducted on the proximal tibial metaphysis to measure microstnictural hone parameters, and new bone formation was detected using dynamic labeling. Bone strength was assessed using three-point bending mechanical testing. Our study determined that PTH-PEG-BP conjugates significantly enhanced PTH targeting to the hone matrix while retaining full PTH bioactivity. Moreover, PTH-PEG-BP conjugates significantly increased trabecular bone quality, anabolic bone forma lion, and improved bone strength over systemically administered PTH alone. We highlight the promise of a novel class of bone-targeting anabolic compound for the treatment of osteoporosis and related bone disorders.
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FU Mimes Elevate Strategic Fellowship Program (SFP); Osteoarthritis Alberta Team Grant from Alberta Innovates-Health Solutions (AIHS); Canadian Institutes for Health Research (CIHR)
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NR 52
TC 10
Z9 11
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PU SPRINGER HEIDELBERG
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WC Instruments & Instrumentation; Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Instruments & Instrumentation; Research & Experimental Medicine; Pharmacology & Pharmacy
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PT J
AU Jaul, E

Barron, J
AF Jaul, Efraim
Barron, Jeremy
TI Age-Related Diseases and Clinical and Public Health implications for the 85 Years Old and Over Population
SO FRONTIERS IN PUBLIC HEALTH
LA English
DT Review
DE oldest-old; medical decision-making; public policy; aging; longevity
ID all-cause mortality; physical function; womens health; hearing-loss; young-old; adults; prevalence; services; disability; atherosclerosis
AB By 2050, the American 85 years old and over population will triple. Clinicians and the public health community need to develop a culture of sensitivity to the needs of this population and its subgroups. Sensory changes, cognitive changes, and weakness may be subtle or may be severe in the heterogeneous population of people over age 85. Falls, cardiovascular disease, and difficulty with activities of daily living are common but not universal. This paper reviews relevant changes of normal aging, diseases, and syndromes common in people over age 85, cognitive and psychological changes, social and environmental changes, and then reviews common discussions which clinicians routinely have with these patients and their families. Some hearing and vision loss are a part of normal aging as is decline in immune function. Cardiovascular disease and osteoporosis and dementia are common chronic conditions at age 85. Osteoarthritis, diabetes, and related mobility disability will increase in prevalence as the population ages and becomes more overweight. These population changes have considerable public health importance. Caregiver support, services in the home, assistive technologies, and promotion of home exercise programs as well as consideration of transportation and housing policies are recommended. For clinicians, judicious prescribing and ordering of tests includes a consideration of life expectancy, lag time to benefit, and patient goals. Furthermore, healthy behaviors starting in early childhood can optimize quality of life among the oldest-old.
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TI The impact of musculoskeletal diseases on mortality-comparison with internal diseases: A 15-year longitudinal study
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English
DT Article
ID follow-up; obesity; hypertension; smoking; risk; osteoarthritis; prevalence; health; cohort; death
AB Background: Aging is associated with an increased incidence of diabetes (DM), hypertension (HT), hyperlipidemia (HL), as well as musculoskeletal disorders, such as osteoarthritis (OA) and osteoporosis (OP). However, the impact of musculoskeletal disorders on mortality remains unclear. This study investigated the risk of mortality if having knee OA or OP. Methods: 601 participants (mean age 67.8 +/- 5.3 years) who underwent musculoskeletal check-ups in Yakumo town were enrolled in this study, 248 were males and 353 were females. The following parameters were assessed: age, sex, body mass index, smoking habit, alcohol drinking habit, physical exercise habit, knee OA, OP, HT, DM and HL. Kaplan-Meier survival curves for smoking, drinking and physical exercise habits, knee OA, OP, HT, DM and HL were prepared, and the log-rank test was performed. Furthermore, the Cox hazard model was used for multivariate analysis of all variables. Results: Knee OA, OP, HT, and DM were associated with a significantly higher mortality rate. Cox regression analysis results showed a hazard ratio of 1.972 for OA (95% CI: 1.356-2.867), 1.965 for DM (1.146-3.368), 1.706 for smoking habits (1.141-2.552), and 1.614 for OP (1.126-2.313). Cardiovascular diseases were the most common causes of death. Conclusions: Smoking, knee OA, OP and DM were all associated with increased risk of mortality. Knee OA had a high hazard ratio, comparable to that of DM. These findings suggest that interventions against smoking, knee OA, OP and DM may reduce the risk of mortality. (C) 2017 The Japanese Orthopaedic Association. Published by Elsevier B.V. All rights reserved.
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NR 28
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AF Osterberga, Anja
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TI Subchondral bone sclerosis and cancellous bone loss following OA induction depend on the underlying bone phenotype
SO JOINT BONE SPINE
LA English
DT Article

DE Osteoarthritis; Osteoporosis; Subchondral bone sclerosis; Cancellous bone loss
ID articular-cartilage; str/ort mice; alendronate treatment; knee osteoarthritis; mouse; osteoporosis; resorption; turnover; plate; model
AB Objectives: Osteoarthritis (OA) is increasingly considered a disease of the whole joint, yet the interplay between the articular cartilage and the subchondral bone remains obscure. We here set out to investigate the impact of bone mass on the progression of surgically induced knee OA in the mouse. Methods: OA was induced in the right knees of female C57BL/6 (low bone mass) and STR/ort (high bone mass) mice via anterior cruciate ligament transection and destabilization of the medial meniscus. At 36 weeks of age, left and right knee joints were histologically compared for cartilage degeneration and via microCT analysis for subchondral bone plate thickness. In addition, femora were analyzed for bone mass at diaphysis and distal meta-and epiphysis. Results: The severity of cartilage deterioration did not differ under high and low bone mass conditions. However, the extent of bone sclerosis differed and was proportional to the baseline subchondral bone plate thickness. Moreover, the cancellous bone loss following OA progression was inversely related to the bone mass: high bone mass restricted the loss to the epiphysis, whereas low bone mass allowed for a more widespread loss extending into the metaphysis. Conclusions: Our results suggest that cartilage degeneration is independent of the underlying bone mass. In contrast, subchondral bone remodeling associated with OA progression seem to correlate with the initial bone mass and suggest an enhanced crosstalk between the deteriorating cartilage and the subchondral bone under low bone mass conditions. (C) 2016 Societe francaise de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.
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AU Gao, CZ
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TI Efficacy of acupuncture in pain management of chronic diseases of bone and joint: a review of literature
SO INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE
LA English
DT Review
DE Acupuncture; osteoarthritis; rheumatoid arthritis; osteoporosis; pain; anti-inflammatory agents
ID randomized controlled-trial; severe knee osteoarthritis; carpal-tunnel-syndrome; low-back-pain; rheumatoid-arthritis; hyaluronic-acid; pharmacological-treatment; supervised exercise; convergent neurons; adjunctive therapy
AB Acupuncture is in use in China for several millennia as a procedure believed to restore altered energy balance of the body due to any disease through insertion of needles at specific points called energy channels. The use of acupuncture in various types of musculoskeletal pain is on the rise. The analgesic action of acupuncture is mediated by local production of endogenous opioid peptides (EOP) and modulation of nociceptor function. Several high quality randomized clinical trials (RCT) have generally concluded that acupuncture is effective in relieving back pain compared with no treatment and comparable to usual care for back pain. Several high quality studies found significant pain reduction in patients with osteoarthritis of knee although lack of analgesic effect of acupuncture in this disease setting has also been reported. High quality studies on the effect of acupuncture in

rheumatoid arthritis (RA) are lacking. When two well-designed (double-blind, randomized and placebo-controlled) studies with RA patients were considered, one found significantly improved tender joint and pain by traditional acupuncture but the other failed to find any effect of acupuncture over placebo. In case of gouty arthritis, a systematic meta-analysis found significant efficacy of acupuncture treatment in decreasing blood uric acid and improving the overall quality of life. Effect of acupuncture on post-menopausal osteoporosis remains understudied. Results from preclinical studies in gonadectomised rats suggests bone conserving effect of acupuncture; however, efficacy trials in postmenopausal osteoporotic patients are not yet available. The goal of the review was to comprehensively discuss the scientific basis of acupuncture in alleviating chronic pain arising from bone and joint diseases.
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TI Aliskiren has chondroprotective efficacy in a rat model of osteoarthritis through suppression of the local renin-angiotensin system
SO MOLECULAR MEDICINE REPORTS
LA English
DT Article
DE aliskiren; osteoarthritis; renin-angiotensin system; chondroprotective efficacy
ID articular-cartilage; gene-expression; knee osteoarthritis; bone-resorption; joint injury; inhibition; differentiation; osteoporosis; chondrocytes; cells
AB The local renin-angiotensin system (RAS) has been reported to have an important role in the pathogenesis and progression of metabolic bone diseases, including osteoarthritis (OA). Aliskiren is the first in a new class of orally effective direct renin inhibitors and is approved for the treatment of hypertension in humans. However, its efficacy in patients with OA is unknown. A rat model of OA was induced to investigate the potential efficacy of aliskiren. Effects of aliskiren on the cartilage structure were detected by safranin O staining and its effects on the widths of the proliferation zone and hypertrophic zone (HZ) of chondrocytes were analyzed by Masson's staining. Tartate-resistant acid phosphatase staining was used to evaluate the effects of aliskiren on osteoclasts in the chondrocytes. Relative histological analyses were performed. Additionally, the expression levels of factors associated with osteoclast differentiation (receptor activator of nuclear factor.B ligand and osteoprotegerin), articular cartilage destruction [tumor necrosis factor-alpha (TNF-alpha) and matrix metalloproteinase 9] and osteoblast differentiation [runt related transcription factor 2 (Runx2)], along with RAS components (renin, renin-receptor, angiotensin type 1 receptor (AT1R), AT2R, angiotensin converting enzyme (ACE) and angiotensin II (Ang II)] were detected in samples from the proximal tibias. Aliskiren did not fully suppress the inflammatory

reaction in OA model animals and had marginal regulatory effects on biochemical bone markers induced by OA. However, aliskiren attenuated cartilage destruction, abnormal cartilage cellularity and the expansion of the HZ of chondrocytes, and significantly attenuated the expression of interleukin-1, TNF-alpha, Runx2 and procollagen type I N-terminal propeptide. These chondroprotective properties were accompanied by reductions in the levels of RAS components (renin, Ang II, ACE and AT1R), indicating that aliskiren exerts multiple effects of on bone formation, osteoblast differentiation and articular cartilage protection via the RAS. OA activates the local bone RAS, inhibits bone formation and stimulates bone resorption. Aliskiren, a renin inhibitor, demonstrated chondroprotective efficacy in a rat model of OA through suppression of the local RAS.
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Z9 18
U1 0
U2 3
PU SPANDIDOS PUBL LTD
PI ATHENS
PA POB 18179, ATHENS, 116 10, GREECE
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PT J
AU Vadalia, J
Vekariya, S
Raval, M
Sheth, N
AF Vadalia, Jigna
Vekariya, Shruti
Raval, Mihir
Sheth, Navin
TI In vitro cystein protease inhibitory activity of selected Indian antimalarial plants
SO INDIAN JOURNAL OF TRADITIONAL KNOWLEDGE
LA English
DT Article
DE Nyctanthes arbor- tristis; Falcipain; Cysteine protease inhibitor; Papain inhibition; Malaria
AB In this study few plants having antimalarial activity (leaves of Nyctanthes arbor-tristis L., Caesalpinia crista L., Ailanthus excelsa Roxb., Bauhinia variegate L., seed of Balanites aegyptiaca Delile, entire plant of Enicostema littorale Blume, fruits of Momordica charantia L.) were screened for cystein protease inhibitory activity. Cysteine protease inhibitory activity was done by papain inhibition assay. Water and methanol extracts of all selected plants were screened for in vitro enzyme inhibition assay. Percentage inhibition of papain was measured and IC50 for all the extracts were calculated. Comparative study of above selected medicinal plants methanolic and water extract showed the maximum inhibition in leaves of N. arbor-tristis, 87.8051 %, IC50 - 13.03 mu g/ml and 85.6189 %, IC50 - 16.54 mu g/ml, respectively. The present study has provided scientific validity to leaves of N. arbor-tristis against cysteine protease inhibition activity and it is concluded that protease inhibitor of N. arbor-tristis-leaves are an indicator of wide range of pharmacological activities such as anticancer, antimalarial, osteoarthritis,

osteoporosis, etc., isolation of cysteine protease inhibitors may provide a lead compound for development of novel therapeutic agents in the above areas.
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AU Westerik, JAM
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AF Westerik, Janine A. M.
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TI Associations between chronic comorbidity and exacerbation risk in primary care patients with COPD
SO RESPIRATORY RESEARCH
LA English
DT Article
ID obstructive pulmonary-disease; health-status; retrospective cohort; prevalence; index; management; mortality; outcm
AB Background: COPD often coexists with chronic conditions that may influence disease prognosis. We investigated associations between chronic (co) morbidities and exacerbations in primary care COPD patients. Method: Retrospective cohort study based on 2012-2013 electronic health records from 179 Dutch general

practices. Comorbidities from patients with physician-diagnosed COPD were categorized according to International Classification of Primary Care (ICPC) codes. Chi-squared tests, uni-and multivariable logistic, and Cox regression analyses were used to study associations with exacerbations, defined as oral corticosteroid prescriptions. Results: Fourteen thousand six hundred three patients with COPD could be studied (mean age 67 (SD 12) years, 53% male) for two years. At baseline 12,826 (88%) suffered from >= 1 comorbidities, 3263 (22%) from >= 5. The most prevalent comorbidities were hypertension (35%), coronary heart disease (19%), and osteoarthritis (18%). Several comorbidities showed statistically significant associations with frequent (i.e., >= 2/year) exacerbations: heart failure (odds ratio [OR], 95% confidence interval: 1.72; 1.38-2.14), blindness & low vision (OR 1.46; 1.21-1.75), pulmonary cancer (OR 1.85; 1.28-2.67), depression 1.48; 1.14-1.91), prostate disorders (OR 1.50; 1.13-1.98), asthma (OR 1.36; 1.11-1.70), osteoporosis (OR 1.41; 1.11-1.80), diabetes (OR 0.80; 0.66-0.97), dyspepsia (OR 1.25; 1.03-1.50), and peripheral vascular disease (OR 1.20; 1.00-1.45). From all comorbidity categories, having another chronic respiratory disease beside COPD showed the highest risk for developing a new exacerbation (Cox hazard ratio 1.26; 1.17-1.36). Conclusion: Chronic comorbidities are highly prevalent in primary care COPD patients. Several chronic comorbidities were associated with having frequent exacerbations and increased exacerbation risk.
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PU BIOMED CENTRAL LTD
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PA 236 GRAYS INN RD, FLOOR 6, LONDON WC1X 8HL, ENGLAND
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AU Beck, BR
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AF Beck, Belinda R.
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TI Exercise and Sports Science Australia (ESSA) position statement on exercise prescription for the prevention and management of osteoporosis
SO JOURNAL OF SCIENCE AND MEDICINE IN SPORT
LA English
DT Review
DE Ageing; Balance; Bone; Exercise guidelines; Falls; Fracture prevention; Muscle; Osteopenia; Physical activity
ID bone-mineral density; randomized controlled-trial; provides lifelong benefits; high-impact exercise; postmenopausal women; physical-activity; older-adults; resistance exercise; falls prevention; vitamin-d
AB Objectives: Osteoporotic fractures are associated with substantial morbidity and mortality. Although exercise has long been recommended for the prevention and management of osteoporosis, existing guidelines are often non-specific and do not account for individual differences in bone health, fracture risk and functional

capacity. The aim of the current position statement is to provide health practitioners with specific, evidence-based guidelines for safe and effective exercise prescription for the prevention or management of osteoporosis, accommodating a range of potential comorbidities. Design: Position statement. Methods: Interpretation and application of research reports describing the effects of exercise interventions for the prevention and management of low bone mass, osteoporosis and osteoporotic fracture. Results: Evidence from animal and human trials indicates that bone responds positively to impact activities and high intensity progressive resistance training. Furthermore, the optimisation of muscle strength, balance and mobility minimises the risk of falls (and thereby fracture), which is particularly relevant for individuals with limited functional capacity and/or a very high risk of osteoporotic fracture. It is important that all exercise programs be accompanied by sufficient calcium and vitamin D, and address issues of comorbidity and safety. For example, loaded spine flexion is not recommended, and impact activities may require modification in the presence of osteoarthritis or frailty. Conclusions: Specific guidelines for safe and effective exercise for bone health are presented. Individual exercise prescription must take into account existing bone health status, co-morbidities, and functional or clinical risk factors for falls and fracture. (C) 2016 Sports Medicine Australia. Published by Elsevier Ltd. All rights reserved.
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AU Chen, JY
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Guo, WS
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AF Chen, Ji-ying
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TI Chinese Guideline for the Diagnosis and Treatment of Osteonecrosis of the Femoral Head in Adults
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE Diagnosis; Guideline; Osteonecrosis of the femoral head (ONFH); Treatment
ID untreated asymptomatic osteonecrosis; avascular necrosis; nontraumatic osteonecrosis; bone-marrow; core-decompression; natural-history; risk-factors; follow-up; hip; collapse
AB The treatment of adult osteonecrosis of the femoral head (ONFH), with 8.12 million patients in China, remains a challenge to surgeons. To standardize and improve the efficacy of the treatment of ONFH, Chinese specialists updated the experts' suggestions in March 2015, and an experts' consensus was given to provide a current basis for the diagnosis, treatment and evaluation of ONFH. The current guideline provides recommendations for ONFH with respect to epidemiology, etiology, diagnostic criteria, differential diagnosis, staging, treatment, as well as rehabilitation. Risk factors of non-traumatic ONFH include corticosteroid use, alcohol abuse, dysbarism, sickle cell disease and autoimmune disease and others, but the etiology remains unclear. The Association Research Circulation Osseous (ARCO) staging system, including plain radiograph, magnetic

resonance imaging, radionuclide examination, and histological findings, is frequently used in staging ONFH. A staging and classification system was proposed by Chinese scholars in recent years. The major differential diagnoses include mid-late term osteoarthritis, transient osteoporosis, and subchondral insufficiency fracture. Management alternatives for ONFH consist of non-operative treatment and operative treatment. Core decompression is currently the most common procedure used in the early stages of ONFH. Vascularized bone grafting is the recommended treatment for ARCO early stage III ONFH. This guideline gives a brief account of principles for selection of treatment for ONFH, and stage, classification, volume of necrosis, joint function, age of the patient, patient occupation, and other factors should be taken into consideration.
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Z9 95
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JI Orthop. Surg.
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AF Back, Karin
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TI Relation between osteoporosis and radiographic and clinical signs of osteoarthritis/arthrosis in the temporomandibular joint: a population-based, cross-sectional study in an older Swedish population
SO GERODONTOLOGY
LA English
DT Article
DE epidemiology; osteoarthritis; osteoporosis; temporomandibular joint
ID research diagnostic-criteria; disorders rdc/tmd; reliability; gothenburg
AB Objective: The aim was to elucidate the relation between osteoporosis and osteoarthritis/arthrosis (OA) in the temporomandibular joint (TMJ). Background: General epidemiological data support the hypothesis that osteoporosis and OA are inversely correlated but is not conclusively investigated in the TMJ. Materials and methods: A group of 114 representative elderly women and men, randomised from a comprehensive population study in Gothenburg, Sweden, had bone mineral density established with whole-body, dual-energy X-ray absorptiometry (DXA) as part of a health survey. In addition, dental examinations were performed, including panoramic radiographs exposed as an overview of the TMJ's and jaws. In 88 of the 80-year-old participants (48 women and 40 men), a clinical orofacial examination according to the RDC/TMD system was performed. Results: A diagnosis of osteopenia/osteoporosis was found in 36% of the 114, with a statistically different greater proportion of women. Condylar alterations evaluated from panoramic radiographs were observed in 34%, with no significant gender difference. No significant differences were found in the proportion of individuals with osteopenia/osteoporosis and any condylar radiographic alteration or not. Forty-one of the clinically examined subjects, 47%, fulfilled the criteria for an RDC/TMD diagnosis with no gender difference. All participants graded the orofacial pain as low chronic pain. An opening capacity of <40 mm denoted a higher risk of having pain in the temporomandibular system. No association was found between clinical diagnosis of RDC/TMD and osteopenia/osteoporosis. Conclusion: The

prevalence of osteopenia/osteoporosis appears not to be of importance for radiological or clinical findings of OA in the TMJ.
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NR 34
TC 17
Z9 20
U1 0
U2 6
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0734-0664
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J9 GERODONTOLOGY
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WC Dentistry, Oral Surgery & Medicine; Geriatrics & Gerontology
SC Dentistry, Oral Surgery & Medicine; Geriatrics & Gerontology
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PT J
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TI Influence of sinomenine upon mesenchymal stem cells in osteoclastogenesis
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Sinomenine; Mesenchymal stem cells; Osteoclastogenesis; RANKL; OPG; PGE2
ID rheumatoid-arthritis; bone-resorption; joint damage; osteoarthritis; targets
AB With the advent of aging, the morbidity rates of such diseases as osteoarthritis, rheumatoid arthritis, and osteoporosis has witnessed a significant increase. As a common rattan drug, sinomenine (SIN) has been widely applied for the treatment of various arthritic diseases in traditional Chinese medicine (TCM) clinics. Given that SIN has been reported to inhibit the expression of Prostaglandin E2 (PGE2) in several types of cells, in this study, the influence of SIN treatment on PGE2 expression in mesenchymal stem cells (MSCs), thereby changing the osteoprotegerin (OPG) receptor/activator for the nuclear factor-kappa B ligand (RANKL) ratio, was investigated. Our results showed that, when compared with the untreated cells, treatment with 0.25 mM SIN can down-regulate the mRNA and protein expression levels of the Prostaglandin E synthase 3 (PTGES3) or PGE2 and RANKL, while the OPG was up-regulated. After being cultured with SIN treated MSC-conditioned medium (stMSC-CM), the amount of TRAP-positive multinucleated osteoclasts differentiated from RAW264.7 cells was reduced. Also, the expression levels of specific markers for active osteoclasts were decreased when incubated with stMSC-CM. Moreover, these changes were able to be recovered when the exogenous RANKL was added to the MSC-CM culture. This indicates that the increased OPG/RANKL ratio can reduce the osteoclastogenesis of RAW264.7 cells. Our results demonstrated that SIN has an inhibitory effect on osteoclast differentiation through mechanisms involving the inhibition of the

PGE2-induced OPG/RANKL ratio. SIN can also serve as a proinflammatory mediator to regulate the MSC immunosuppressive effects. Our findings suggest that SIN can be useful for the treatment of bone diseases associated with over-activity of osteoclasts. (C) 2017 Elsevier Masson SAS. All rights reserved.
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NR 34
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Z9 30
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PU ELSEVIER FRANCE-EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER
PI ISSY-LES-MOULINEAUX
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TI Rottinger approach with dual-mobility cup to improve functional recovery in hip osteoarthritis patients: biomechanical and clinical follow-up
SO INTERNATIONAL ORTHOPAEDICS
LA English
DT Article
DE Arthroplasty; Gait analysis; Hip; Osteoarthritis; Minimal invasive surgery; Postural balance
ID prevent dislocation; arthroplasty; replacement; gait; anterior; surgery; score
AB Purpose We assumed that the combination of dual-mobility total hip arthroplasty (THA) using the minimally-invasive Rottinger anterolateral approach could guarantee hip stability with faster functional recovery. We objectively analyzed functional improvement after dual-mobility THA by quantitative gait analysis. Methods We compared the results achieved following two different surgical approaches: Rottinger's versus Moore's approach (posterolateral approach). We included 70 patients in an open prospective single-centre study: 38 by Rottinger's approach (age = 67yo) and 32 by Moores's approach (age = 68yo). Clinical and biomechanical analysis (kinematic and kinetic parameters of the hip) were conducted at the pre-operative period and at six months post-op Results We found a significant improvement in all clinical scores and all biomechanical parameters but no difference was found between the two approaches. However, the study showed marked clinical, biomechanical and functional improvements for patients treated with dual-mobility THA for osteoarthritis without complete hip recovery compared with a control group. Conclusions The combination of the Rottinger approach with a dual-mobility cup remains a valid choice for primary THA without functional advantage at midterm.
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NR 25
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U1 0
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TI Hyperuricemia, Cardiovascular Profile, and Comorbidity in Older Men and Women: The Pro. VA Study
SO REJUVENATION RESEARCH
LA English
DT Article
DE cardiovascular disease; comorbidity; elderly; epidemiology; hyperuricemia; uric acid
ID serum uric-acid; us general-population; metabolic syndrome; risk-factor; gout; prevalence; management; disease; recommendations; hypertension
AB Hyperuricemia (HU) is growing worldwide and associates with several medical conditions in the elderly. However, data about older people and possible gender differences are sparse. The aim of this study was to compare HU prevalence rates and association with relevant medical disorders in elderly subjects of both sexes. Pro. V.A. is a survey of 3099 individuals aged 65+, focusing on chronic diseases and disability. Uric acid (UA) levels were dichotomized using 6.0 mg/dL (females) and 7.0 mg/dL (males), and multivariate logistic regression models were used to estimate odds ratios (ORs) between HU and single comorbidity. HU prevalence was 21.5% in females and 15.8% in males. HU was associated with most anthropometric and laboratory variables in women, but not in men. After adjustment for age, body mass index, and renal function, HU was independently associated with the presence of cardiovascular diseases in both sexes. In women, HU was associated with hand osteoarthritis (OR = 1.52; 95% CI: 1.12-2.08) and edentulism (OR = 1.31; 95% CI: 1.01-1.71), while resulted protective for osteoporosis (OR = 0.69; 95% CI: 0.53-0.91). In men, HU was significantly related with knee osteoarthritis (OR = 1.72; 95% CI: 1.06-2.79) and chronic obstructive pulmonary disease (OR = 1.60; 95% CI: 1.04-2.45). The presence of >= 4 comorbidities was a stronger determinant of HU in men (OR = 2.54; 95% CI: 1.21-5.37) than in women (ns). Patterns of age-dependent UA increase are markedly different in men and women. HU

prevalence is substantial and its association with other diseases is gender specific, connoting a peculiar clinical profile.
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TI Effect of progressive high-impact exercise on femoral neck structural strength in postmenopausal women with mild knee osteoarthritis: a 12-month RCT
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Cartilage; Exercise; Menopause; RCT
ID bone-mineral density; physical performance; articular-cartilage; hip; fracture; therapy; risk; intensity; mass; mri
AB It is uncertain whether subjects with mild knee osteoarthritis, and who may be at risk of osteoporosis, can exercise safely with the aim of improving hip bone strength. This RCT showed that participating in a high-impact exercise program improved femoral neck strength without any detrimental effects on knee cartilage composition. No previous studies have examined whether high-impact exercise can improve bone strength and articular cartilage quality in subjects with mild knee osteoarthritis. In this 12-month RCT, we assessed the effects of progressive high-impact exercise on femoral neck structural strength and biochemical composition of knee cartilage in postmenopausal women. Eighty postmenopausal women with mild knee radiographic osteoarthritis were randomly assigned into the exercise (n = 40) or control (n = 40) group. Femoral neck structural strength was assessed with dual-energy X-ray absorptiometry. The knee cartilage region exposed to exercise loading was measured by the quantitative MRI techniques of T2 mapping and delayed gadolinium-enhanced MRI of cartilage (dGEMRIC). Also, an accelerometer-based body movement monitor was used to evaluate the total physical activity loading on the changes of femoral neck strength in all participants. Training effects on the outcome variables were estimated by the bootstrap analysis of covariance. A significant between-group difference in femoral neck bending strength in favor of the trainees was observed after the 12-month intervention (4.4%, $p < 0.01$). The change in femoral neck bending strength remained significant after adjusting for baseline value, age, height, and body mass (4.0%, $p = 0.020$). In all participants, the change in bending strength was associated with the total physical activity loading ($r = 0.29$, $p = 0.012$). The exercise participation had no effect on knee cartilage composition. The high-impact training increased femoral neck strength without having any harmful effect on knee cartilage in women with mild knee osteoarthritis. These findings imply that progressive high-impact exercise is a feasible method in seeking to prevent hip fractures in postmenopausal women whose articular cartilage may also be frail.

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PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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JI Osteoporosis Int.
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PT J
AU Jain, RK
   Vokes, T
AF Jain, Rajesh K.
   Vokes, Tamara
TI Dual-energy X-ray Absorptiometry
SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE DXA; ethnicity; fracture; osteoporosis
ID bone-mineral density; prevalent vertebral fractures; iscd official positions; hip axis length; older us adults; osteoporotic fractures; white women; t-score; proximal femur; task-force
AB Bone mineral density (BMD) measurement by dual-energy X-ray absorptiometry (DXA) is the most commonly used method to assess fracture risk. DXA utilizes two different energy X-rays to calculate BMD and, by comparison to a young normative

database, the T-score. In 1994, the World Health Organization defined osteoporosis based on T-score, changing the paradigm of the field and forever placing DXA measurements in the center of osteoporosis diagnosis. Since then, many large studies have demonstrated the predictive value of BMD by DXA-for every standard deviation decline in BMD, there is a relative risk of 1.5-2.5 for fracture. This predictive ability is similar to how blood pressure can predict myocardial infarction. Limitations of DXA are also important to consider. While BMD by DXA can identify those at risk, there is a significant overlap in the BMD of patients who will and will not fracture. Special considerations are also needed in men and ethnic minority groups. These groups may have different bone size, thus affecting the normative range of BMD, and/or distinct bone structure that affect the association between BMD and fractures. Finally, BMD can be affected by positioning errors or artifacts, including osteoarthritis, fracture, and jewelry. Of course, DXA has tremendous strengths as well-namely its wide availability, its low radiation exposure, and a large body of evidence that relate DXA measurements to fracture risk. For these reasons, DXA remains the cornerstone of fracture assessment now and for the foreseeable future.

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NR 92
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U1 1
U2 13
PU ELSEVIER SCIENCE INC
PI NEW YORK
PA 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA
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J9 J CLIN DENSITOM
JI J. Clin. Densitom.
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WC Endocrinology & Metabolism
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PT J
AU Jiang, LT
Shen, X
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AF Jiang, Liting
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Wei, Li
Zhou, Qi
Gao, Yiming
TI Effects of bisphosphonates on mandibular condyle of ovariectomized osteoporotic rats using micro-ct and histomorphometric analysis
SO JOURNAL OF ORAL PATHOLOGY & MEDICINE
LA English
DT Article
DE bisphosphonate-induced osteonecrosis of the jaws; collagen; mandibular condyle; osteoporosis; ovariectomy
ID subchondral bone; cartilage; estrogen; osteoarthritis; alendronate; growth; joint; beta; degeneration; turnover
AB ObjectiveTo evaluate microarchitectural changes in condylar cartilage and associated subchondral bone after bisphosphonates treatment using an ovariectomized (OVX) osteoporosis rat model. MethodsThirty six-month-old female Sprague-Dawley rats were randomly divided into sham, OVX, and risedronate (RIS)-treated groups. Both OVX and RIS groups received bilateral ovariectomy. OVX group was treated subcutaneously with saline, whereas RIS group received risedronate treatment (2.4 g/kg) subcutaneously for 3 months. At the end of 3 months, animals were sacrificed and the entire condyles were harvested for micro-CT and histological analyses. Immunohistochemistry (IHC) was performed to assess the expression of type I/II collagen protein by semiquantitative imaging analysis. ResultsMicro-CT analysis showed OVX group had significant condylar subchondral bone loss compared to sham as shown by significant decrease in bone volume fraction ($P = 0.028$), trabecular thickness ($P = 0.041$), and significant increase in trabecular spacing ($P = 0.003$). In RIS group, partial inhibition of OVX-induced bone loss was detected. HE staining showed proliferative layer of condylar cartilage reduced, while hypertrophic chondrocyte layer increased significantly in RIS group compared to sham and OVX groups. IHC showed reduced expression of Col I in both the OVX and RIS groups, whereas expression of Col II was reduced in the OVX group but increased in the RIS group. ConclusionOur findings suggest that systemic bisphosphonate treatment influences the structure and ossification of condylar cartilage and it has a dual action on condyle in a postmenopausal osteoporosis rat model which raises the concerns for the potential side effects of BPs on condyle to elder patients.
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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PT J
AU Dionello, CF
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TI Do whole body vibration exercises affect lower limbs neuromuscular activity in populations with a medical condition? A systematic review
SO RESTORATIVE NEUROLOGY AND NEUROSCIENCE
LA English
DT Review
DE Electromyography; muscle; whole body vibration; rehabilitation
ID quality-of-life; muscle strength; blood-flow; knee osteoarthritis; skeletal-muscle; motor function; chronic stroke; elderly-women; intervention; osteoporosis
AB Background: The use of surface electromyography (sEMG) to evaluate muscle activation when executing whole body vibration exercises (WBVE) in studies provide neuromuscular findings, in healthy and diseased populations. Objectives: Perform a systematic review of the effects of WBVE by sEMG of lower limbs in non-healthy populations. Methods: The search using the defined keywords was performed in PubMed, PEDRo and EMBASE databases by three independent researchers. Applying the PRISMA statement several studies were selected according to eligibility criteria and organized for the review. Full papers were included if they described effects of WBVE for the treatment of illnesses, evaluated by sEMG of lower limbs independently on the year of the publication; in comparison or associated with other treatment and evaluation techniques. Results: Seven publications were selected; two in spinal cord injury patients, one in Friedreich's ataxia patients, three in stroke patients and one study in breast cancer survivors. Reported effects of WBV in were muscle activation by sEMG and also on strength, blood flow and exercise resistance; even in paretic limbs. Conclusion: By the use of sEMG it was verified that WBVE elicits muscle activation in diseased population. These results may lead to the definition of exercise protocols to maintain or increase muscular activation. However, due to the heterogeneity of methods among studies, there is currently no consensus on the sEMG signal processing. These strategies might also induce effects on muscle strength, balance and flexibility in these and other illnesses.
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TI Osteoarthritis of the hip joint in elderly patients is most commonly atrophic, with low parameters of acetabular dysplasia and possible involvement of osteoporosis
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Osteoarthritis; Osteoporosis; Acetabular dysplasia; Aging
ID subchondral bone; alendronate treatment; knee osteoarthritis; increased risk; white women; cartilage; patterns; microarchitecture; pathogenesis; damage
AB A Summary As elderly patients with hip osteoarthritis aged, acetabular dysplasia

parameters decreased (Sharp's angle, acetabular roof obliquity angle, and acetabular head index) and the incidence of the atrophic type increased. Vertebral body fracture was more frequent in the atrophic type, suggesting the involvement of osteoporosis at the onset of hip osteoarthritis. Introduction Osteoarthritis (OA) is associated with increased bone formation at a local site. However, excessive bone resorption has also been found to occur in the early stages of OA. Osteoporosis may be involved in the onset of OA in elderly patients. We conducted a cross-sectional radiographic study of patients with hip OA and examined the association between age and factors of acetabular dysplasia (Sharp's angle, acetabular roof obliquity angle, and acetabular head index) as well as the osteoblastic response to determine the potential involvement of osteoporosis. Methods This study included 366 patients (58 men, 308 women) who had undergone total hip arthroplasty for the diagnosis of hip OA. We measured the parameters of acetabular dysplasia using preoperative frontal X-ray images and evaluated each patient according to Bombelli classification of OA (hypertrophic, normotrophic, or atrophic type). Results As the patients aged, the parameters of acetabular dysplasia decreased. The incidence of the atrophic type of OA was significantly higher in older patients. Vertebral body fractures were more frequent in the atrophic type than in the other types. Additionally, the index of acetabular dysplasia was lower in the atrophic type. By contrast, the hypertrophic type was present in relatively younger patients and was associated with an increased index of acetabular dysplasia. Conclusion In elderly patients with hip OA, the parameters of acetabular dysplasia decreased and the incidence of the atrophic type increased as the patients aged. The frequency of vertebral body fracture was high in patients with the atrophic type, suggesting the involvement of osteoporosis in the onset of hip OA.
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NR 39
TC 10
Z9 14
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WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
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TI Overweight in patients with chronic obstructive pulmonary disease needs more attention: a cross-sectional study in general practice
SO NPJ PRIMARY CARE RESPIRATORY MEDICINE
LA English
DT Article
ID body-mass index; prognostic value; copd; obesity; prevalence
AB Guidelines for management of chronic obstructive pulmonary disease (COPD) primarily focus on the prevention of weight loss, while overweight and obesity are highly prevalent in patients with milder stages of COPD. This cross-sectional study examines the association of overweight and obesity with the prevalence of comorbid disorders and prescribed medication for obstructive airway disease, in patients with mild to moderate COPD. Data were used from electronic health records of 380 Dutch general practices in 2014. In total, we identified 4938 patients with mild or moderate COPD based on spirometry data, and a recorded body mass index (BMI) of >= 21 kg/m(2). Outcomes in overweight (BMI >= 25 and < 30 kg/m(2)) and obese (BMI >= 30 kg/m(2)) patients with COPD were compared to those with a normal weight (BMI >= 21 and < 25 kg/m(2)), by logistic multilevel analyses. Compared to COPD patients with a normal weight, positive associations were found for diabetes, osteoarthritis, and hypertension, for both overweight (OR: 1.4-1.7) and obese (OR: 2.4-3.8) patients, and for heart failure in obese patients (OR: 2.3). Osteoporosis was less prevalent in overweight (OR: 0.7) and obese (OR: 0.5) patients, and anxiety disorders in obese patients (OR: 0.5). No associations were found for coronary heart disease, stroke, sleep disturbance, depression, and pneumonia. Furthermore, obese patients were in general more often prescribed medication for obstructive airway disease compared to patients with a normal weight. The findings of this study underline the need to increase awareness in general practitioners for excess weight in patients with mild to moderate COPD.
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U1 0
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AU Chan, PMB
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AF Chan, Pok Man Boris
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TI Is subchondral bone cyst formation in non-load-bearing region of osteoarthritic knee a vascular problem?
SO MEDICAL HYPOTHESES
LA English
DT Article
ID osteoporosis; angiogenesis
AB Subchondral bone cyst is common in the progressive knee osteoarthritis yet its underlying mechanism remains unclear. In addition to the existing theories such as synovial fluid influx and mechanical contusion, we identified the potential link between vascular pathology and osteoarthritic bone pathologies including cystic lesion formation, particularly in the non-load-bearing region. This new hypothesis for SBC formation in non-load-bearing region for knee, which cannot be explained by the existing theories, will provide us a new angle to understand the pathomechanism and pathophysiology of subchondral bone disturbance in osteoarthritis in addition to the classical biomechanical overloading theories. It might guide us to develop a novel diagnostic and therapeutic approach to treat progressive osteoarthritis via targeting vascular pathology.
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NR 22
TC 14
Z9 18
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U2 3
PU CHURCHILL LIVINGSTONE
PI EDINBURGH
PA JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND
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PT J
AU Wildberger, L
Boyadzhieva, V
Hans, D
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AF Wildberger, Laura
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TI Impact of lumbar syndesmophyte on bone health as assessed by bone density (BMD) and bone texture (TBS) in men with axial spondyloarthritis
SO JOINT BONE SPINE
LA English
DT Article
DE Spondyloarthritis; Syndesmophytes; TBS; Spine BMD
ID ankylosing-spondylitis; mineral density; vertebral fractures; score tbs; osteoporotic fractures; radiographic damage; caucasian women; spine; microarchitecture; progression
AB Introduction: Patients with spondyloarthritis (SpA) have an elevated incidence of osteoporosis and are at increased risk of pathological vertebral fracture. Evaluation of bone density by dual energy X-ray absorptiometry (DXA) has its limits in fracture prediction, already known in this population. One hypothesis is that the presence of lumbar syndesmophyte could overestimate the spine bone mineral density

(BMD). Trabecular bone score (TBS) is a new texture measurement correlated with bone microarchitecture. Previous studies have shown that TBS is mildly impacted by osteoarthritis and thus could be a predictor of fracture better than spine BMD. We aimed to evaluate a male population of SpA with BMD and TBS measurement and see the impact of lumbar syndesmophytes. Method: Two cohorts of SpA male patients (Lausanne, Sofia) with SpA disease, clinical and bone parameters (femoral neck and total spine BMD + spine TBS) were merged. We compared BMD and TBS results regarding to the presence/absence of syndesmophytes. Results: Our study concerned 51 men [29 with lumbar syndesmophytes (L1 to L4,>= 1), 22 without], fulfilling the European Spondyloarthropathy Study Group (ESSG) and the Assessment of SpondyloArthritis international Society (ASAS) criteria. Mean age was 52.18 years old (no difference between the 2 groups) and mean body mass index (BMI) 27.47 kg/m(2) (29.12 +/- 0.67 with and 25.30 +/- 0.81 without, A=0.0006). For the overall population mean BMD T-score at the spine was 0.55 +/- 1.54, mean BMD T-score at the femoral neck 1.20 +/- 0.95 and mean lumbar spine TBS was 1.26 +/- 0.13. Regarding to the presence or the absence of syndesmophytes, mean spine BMD T-score was 0.07 +/- 1.63 and 1.18 +/- 1.16 (A=0.009 and 0.250 before and after adjustment for BMI), mean femoral neck BMD T-score was 1.37 +/- 0.93 and 0.97 +/- 0.94 (A=0.14 and 0.03 before and after adjustment for BMI) and mean TBS was 1.21 +/- 0.12 and 1.33 +/- 0.11 (A=0.001 and 0.06 before and after adjustment for BMI) respectively for SpA men with and without syndesmophytes. Conclusion: Our results showed that SpA men with and without syndesmophytes have lower results compared to the normal population regarding hip BMD, spine TBS and spine BMD except for men with syndesmophytes who have a normal BMD spine T-score. These results suggest that TBS is not influenced by the syndesmophytes in opposite to spine BMD and could be measured in this population in addition to the neck BMD to assess the bone fragility. (C) 2016 Societe francaise de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.
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AU Kruse, C
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AF Kruse, C.
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TI Clinical fracture risk evaluated by hierarchical agglomerative clustering
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Clustering; Densitometry; Machine learning; Osteoporosis; Risk factors
ID bone-mineral density; world-health-organization; postmenopausal osteoporosis; antiepileptic drugs; hip osteoarthritis; comorbidity index; lumbar spine; women; men; hyponatremia
AB Clustering analysis can identify subgroups of patients based on similarities of traits. From data on 10,775 subjects, we document nine patient clusters of different fracture risks. Differences emerged after age 60 and treatment compliance differed by hip and lumbar spine bone mineral density profiles. The purposes of this study were to establish and quantify patient clusters of high, average and low fracture risk using an unsupervised machine learning algorithm. Regional and national Danish patient data on dual-energy X-ray absorptiometry (DXA) scans, medication reimbursement, primary healthcare sector use and comorbidity of female subjects

were combined. Standardized variable means, Euclidean distances and Ward's D2 method of hierarchical agglomerative clustering (HAC), were used to form the clustering object. K number of clusters was selected with the lowest cluster containing less than 250 subjects. Clusters were identified as high, average or low fracture risk based on bone mineral density (BMD) characteristics. Cluster-based descriptive statistics and relative Z-scores for variable means were computed. Ten thousand seven hundred seventy-five women were included in this study. Nine (k = 9) clusters were identified. Four clusters (n = 2886) were identified based on low to very low BMD with differences in comorbidity, anthropometrics and future bisphosphonate compliance. Two clusters of younger subjects (n = 1058, mean ages 30 and 51 years) were identified as low fracture risk with high to very high BMD. A mean age of 60 years was the earliest that allowed for separation of high-risk clusters. DXA scan results could identify high-risk subjects with different antiresorptive treatment compliance levels based on similarities and differences in lumbar spine and hip region BMD. Unsupervised HAC presents a novel technology to improve patient characteristics in bone disease beyond traditional T-score-based diagnosis. Technological and validation limitations need to be overcome to improve its use in internal medicine. Current DXA scan indication guidelines could be further improved by clustering algorithms.
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NR 44

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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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AU McCann, MR
Veras, MA
Yeung, C
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AF McCann, Matthew R.
Veras, Matthew A.
Yeung, Cynthia
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Leitch, Kristyn M.
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Dixon, S. Jeffrey
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TI Whole-body vibration of mice induces progressive degeneration of intervertebral discs associated with increased expression of Il-1β and multiple matrix degrading enzymes
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Whole-body vibration; Intervertebral disc; Disc degeneration; Bone; Inflammation; Spine
ID low-back-pain; randomized controlled-trial; magnitude mechanical signals; placebo-controlled trial; high-frequency; bone-density; in-vivo; postmenopausal women; lumbar spine; rat
AB Objective: Whole-body vibration (WBV) is a popular fitness trend based on claims of increased muscle mass, weight loss and reduced joint pain. Following its original implementation as a treatment to increase bone mass in patients with osteoporosis, WBV has been incorporated into clinical practice for musculoskeletal disorders, including back pain. However, our recent studies revealed damaging effects of WBV on joint health in a murine model. In this report, we examined potential mechanisms underlying disc degeneration following exposure of mice to WBV. Methods: Ten-week-old male mice were exposed to WBV (45 Hz, 0.3 g peak acceleration, 30 min/day, 5 days/week) for 4 weeks, 8 weeks, or 4 weeks WBV followed by 4 weeks recovery. Micro-computed tomography (micro-CT), histological, and gene expression analyses were used to assess the effects of WBV on spinal tissues. Results: Exposure of mice to 4 or 8 weeks of WBV did not alter total body composition or induce significant changes in vertebral bone density. On the other hand, WBV-induced intervertebral disc (IVD) degeneration, associated with decreased disc height and degenerative changes in the annulus fibrosus (AF) that did not recover within 4 weeks after cessation of WBV. Gene expression analysis showed that WBV for 8 weeks induced expression of Mmp3, Mmp13, and Adamts5 in IVD tissues, changes preceded by increased expression of Il-1 beta. Conclusions: Progressive IVD degeneration induced by WBV was associated with increased expression of Il-1 beta within the IVD that preceded Mmp and Adamts gene induction. Moreover, WBV-induced IVD degeneration is not reversed following cessation of vibration. (C) 2017 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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AU Ganguly, P
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TI Age-related Changes in Bone Marrow Mesenchymal Stromal Cells: A Potential

Impact on Osteoporosis and Osteoarthritis Development
SO CELL TRANSPLANTATION
LA English
DT Article
DE aging; bone marrow (BM); mesenchymal stromal cells (MSCs); in vitro; in vivo
ID stem-cells; progenitor cells; osteogenic differentiation; adipocyte differentiation; postmenopausal women; subchondral bone; aging mechanisms; life-span; senescence; osteoblast
AB Aging at the cellular level is a complex process resulting from accumulation of various damages leading to functional impairment and a reduced quality of life at the level of the organism. With a rise in the elderly population, the worldwide incidence of osteoporosis (OP) and osteoarthritis (OA) has increased in the past few decades. A decline in the number and "fitness" of mesenchymal stromal cells (MSCs) in the bone marrow (BM) niche has been suggested as one of the factors contributing to bone abnormalities in OP and OA. It is well recognized that MSCs in vitro acquire culture-induced aging features such as gradual telomere shortening, increased numbers of senescent cells, and reduced resistance to oxidative stress as a result of serial population doublings. In contrast, there is only limited evidence that human BM-MSCs "age" similarly in vivo. This review compares the various aspects of in vitro and in vivo MSC aging and suggests how our current knowledge on rejuvenating cultured MSCs could be applied to develop future strategies to target altered bone formation processes in OP and OA.
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AU Reginster, JY
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AF Reginster, Jean-Yves
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Pavelka, Karel
TI Pharmaceutical-grade Chondroitin sulfate is as effective as celecoxib and superior to placebo in symptomatic knee osteoarthritis: the ChONdroitin versus CElecoxib versus Placebo Trial (CONCEPT)
SO ANNALS OF THE RHEUMATIC DISEASES
LA English
DT Article
ID patient reported outcm; european-society; economic-aspects; double-blind; hip osteoarthritis; clinical-trial; task-force; recommendations; osteoporosis; management
AB Objectives Chondroitin sulfate 800 mg/day (CS) pharmaceutical-grade in the management of symptomatic knee osteoarthritis consistent with the European Medicines Agency guideline. Methods A prospective, randomised, 6-month, 3-arm, double-blind, double-dummy, placebo and celecoxib (200 mg/day)-controlled trial assessing changes in pain on a Visual Analogue Scale (VAS) and in the Lequesne Index (LI) as coprimary endpoints. Minimal-Clinically Important Improvement (MCII), Patient-Acceptable Symptoms State (PASS) were used as secondary endpoints. Results 604 patients (knee osteoarthritis) diagnosed according to American College of Rheumalogy (ACR) criteria, recruited in five European countries and followed for 182 days. CS and celecoxib showed a greater significant reduction in pain and LI than placebo. In the intention-to-treat (ITT) population, pain reduction in VAS at day 182 in the CS group (-42.6 mm) and in celecoxib group (-39.5 mm) was significantly greater than the placebo group (-33.3 mm) (p=0.001 for CS and p=0.009 for celecoxib), while no difference observed between CS and celecoxib. Similar trend for the LI, as reduction in this metric in the CS group (-4.7) and celecoxib group (-4.6) was significantly greater than the placebo group (-3.7) (p=0.023 for CS and p=0.015 for celecoxib), no difference was observed between CS and celecoxib. Both secondary endpoints (MCII and PASS) at day 182 improved significantly in the CS and celecoxib groups. All treatments demonstrated excellent safety profiles. Conclusion A 800 mg/day

pharmaceutical-grade CS is superior to placebo and similar to celecoxib in reducing pain and improving function over 6 months in symptomatic knee osteoarthritis (OA) patients. This formulation of CS should be considered a first-line treatment in the medical management of knee OA.
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TI A highly sensitive electrochemical biosensor based on AuNP-modified gold electrodes for selective determination of serum levels of crosslaps
SO 3 BIOTECH
LA English
DT Article
DE CTX; Biosensor; Bone turnover marker; Electrochemistry; Crosslaps
ID antibody-based sensors; i collagen; degradation-products; c-telopeptide; nanoparticles; osteoporosis; markers; urine; ctx; osteoarthritis
AB This article explains a step-wise protocol to develop an electrochemical sensor to quantify serum levels of C-telopeptide (CTX) crosslinks also known as crosslaps in a matter of minutes and with high level of accuracy. The technique needs only one-step (incubation) and can thus be used for point of care screening. Due to the

excellent electrical properties of the as-prepared immunosensor, CTX levels were successfully measured from 1 to 1000 pg/mL. This is while the normal reference of the marker is 50-450 pg/mL, suggesting that the sensor can acceptably detect CTX. The results also showed a good correlation with ECLIA in measuring serum levels of CTX.
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PU SPRINGER HEIDELBERG
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AF Fein, Paul M.
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TI Is bone density associated with intervertebral disc pressure in healthy and degenerated discs?
SO JOURNAL OF BIOMECHANICS

LA English
DT Article
DE Disc degeneration; Vertebra; Endplate; Intervertebral disc; Nucleus pulposus; Annulus fibrosus; Glycosaminoglycan; Disc space narrowing; Computed tomography
ID vertebral body; lumbar disc; postmenopausal women; proteoglycan content; spine; age; fracture; osteoarthritis; osteoporosis; architecture
AB The coupling of the intervertebral disc (IVD) and vertebra as a biomechanical unit suggests that changes in the distribution of pressure within the 1VD (intradiscal pressure, IDP) as a result of disc degeneration can influence the distribution of bone density within the vertebra, and vice versa. The goal of this study was to assess the correspondence between IDP and bone density in the adjacent vertebrae, with emphasis on how this correspondence differs between healthy and degenerated IVDs. Bone density of the endplates and subchondral bone in regions adjacent to the anterior and posterior annulus fibrosus (aAF and pAF, respectively) and nucleus pulposus (NP) was measured via quantitative computed tomography (QCT) in 61 spine segments (T7-9,19-11,110-12: 71 +/- 14 years). IDP was measured in the aAF, NP, and pAF regions in 26 of the spine segments (68 16 years) while they were tested in flexed (5) or erect postures. Disc degeneration was assessed by multiple grading schemes. No correlation was found between bone density and IDP in either posture ($p > 0.104$). Regional variations in 1DP and, to a greater extent bone density, were found to change with advancing degeneration: both IDP ($p = 0.045$) and bone density ($p = 0.024$) decreased in the NP region relative to the aAF region. The finding of only a modest correspondence between degeneration-associated changes in IDP and bone density may arise from complexity in how IDP relates to mechanical force transmission through the endplate and from limitations of the available IVD grading schemes in estimating the mechanical behavior of the IVD. (C) 2017 Elsevier Ltd. All rights reserved.
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PT J
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TI Assessment of the trabecular structure of mandibular condyles in patients with temporomandibular disorders using fractal analysis
SO ORAL SURGERY ORAL MEDICINE ORAL PATHOLOGY ORAL RADIOLOGY
LA English
DT Article
ID research diagnostic-criteria; internal derangement; bone changes; dimension; joint; radiographs; osteoarthrosis; osteoporosis; reliability; morphology
AB Objectives. The aim of this study was to evaluate changes in the trabecular structure of the mandibular condyle in patients with temporomandibular disorders (TMDs) using fractal analysis. Study Design. A total of 100 patients ages 18 to 73 years were clinically assessed using the Diagnostic Criteria for Temporomandibular Disorders. The control group was age-and sex-matched with the patient group. Panoramic radiographs were obtained using a Kodak 8000 digital device with 73 kVp and 5 mA fixed parameters. The degree of degeneration in the mandibular condyles was calculated. Regions of interest (84 X 84 pixels) were selected within the cortical boundary of the mandibular condyle, and the fractal dimension (FD) was calculated using ImageJ version 1.48. Results. Radiographic degenerative changes were more frequently present and more severe in the patient group ($P < .001$). The mean value of FD was 1.22 +/- 0.06 in the patient group and 1.25 +/- 0.06 in the control group ($P = .001$). A significant decrease in FD was observed ($P = .001$) in the left temporomandibular joints of the patient group, whereas a nonsignificant decrease in FD was observed in the right temporomandibular joints ($P = .073$) as degenerative changes increased. Conclusions. Lower FD values were associated with more severe degenerative changes in the patient group. The trabecular structure of condyles in patients with TMD exhibited decreased complexity when erosive and sclerotic changes were evident. As a result, fractal analysis enhanced the use of panoramic radiography in detecting degenerative changes in patients with TMD. (Oral Surg Oral Med Oral Pathol Oral Radiol 2017;123: 382-391)
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TI Radiographic measurements of the hip joint and their associations with hip pain in Japanese men and women: the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Acetabular dysplasia; Prevalence; Pain; Cross-sectional
ID acetabular dysplasia; progression; prevalence; osteoarthrosis; arthroplasty; definitions; rotterdam; space; knee
AB Objective: To investigate radiographic measurements of the hip joint and their associations with hip pain, and the prevalence of acetabular dysplasia defined by radiographic measurements of the hip joint in Japanese men and women using the large-scale population-based cohort of the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study. Methods: From the

baseline survey of the ROAD study (cross-sectional study), 2963 participants (1040 men, 1923 women; mean age, 70.2 years) were analyzed. All participants underwent radiographic examinations of both hips using an anteroposterior view under weight-bearing. Minimum joint space width (mJSW), central-edge (CE) angle, acetabular depth-to-width ratio (ADR), and acetabular head index (AHI) were measured. Associations between these radiographic measurements and hip pain were assessed by calculating odds ratios (ORs) using multivariable logistic-regression analysis. Acetabular dysplasia was defined as a CE angle < 20 degrees. Results: Mean radiographic measurements of the hip joint for men were: mJSW, 3.8 mm; CE angle, 30.6 degrees; ADR, 262.1 per 1000; and AHI, 81.4%. For women, these values were: mJSW, 3.4 mm; CE angle, 29.9 degrees; ADR, 262.7 per 1000; and AHI, 81.2%. Associations were seen between hip pain and each of mJSW, CE angle, ADR, and AHI (OR 4.52, 95% confidence interval 3.45-5.97; 1.14, 1.11-1.18; 1.31, 1.24-1.40; and 1.15, 1.12-1.18, respectively). Acetabular dysplasia showed an overall prevalence of 13.9%, and was significantly more prevalent in women than in men (P = 0.012). C onclusion: The present study of radiographic measurements of the hip joint showed that mJSW, CE angle, ADR, and AHI were associated with hip pain. (C) 2017 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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AB Introduction Optimal vitamin D status promotes skeletal health and is recommended with specific treatment in individuals at high risk for fragility fractures. A growing body of literature has provided indirect and some direct evidence for possible extraskeletal vitamin D-related effects. Purpose and Methods Members of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis have reviewed the main evidence for possible proven benefits of vitamin D supplementation in adults at risk of or with overt chronic extra-skeletal diseases, providing recommendations and guidelines for future studies in this field. Results and conclusions Robust mechanistic evidence is available from in vitro studies and in vivo animal studies, usually employing cholecalciferol, calcidiol or calcitriol in pharmacologic rather than physiologic doses. Although many cross-sectional and prospective association studies in humans have shown that low 25-hydroxyvitamin D levels (i.e., < 50 nmol/L) are consistently associated with chronic diseases, further strengthened by a dose-response relationship, several meta-analyses of clinical trials have shown contradictory results. Overall, large randomized controlled trials with sufficient doses of vitamin D are missing, and available small to moderate-size trials often included people with baseline levels of serum 25-hydroxyvitamin D levels > 50 nmol/L, did not simultaneously assess multiple outcomes, and did not report overall safety (e.g., falls). Thus, no recommendations can be made to date for the use of vitamin D supplementation in general, parental compounds, or non-hypercalcemic vitamin D analogs in the prevention and treatment of extra-skeletal chronic diseases. Moreover, attainment of serum 25-hydroxyvitamin D levels well above the threshold desired for bone health cannot be recommended based on current evidence, since safety has yet to be confirmed. Finally, the promising findings from mechanistic studies, large cohort studies, and small clinical trials obtained for autoimmune diseases (including type 1 diabetes, multiple sclerosis, and systemic lupus erythematosus), cardiovascular disorders, and overall reduction in mortality require further confirmation.

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TI How clinical practitioners assess frailty in their daily practice: an international survey
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Frailty; Survey; Clinical practice; Standardisation
ID screening tool; health; definition; phenotype; consensus; questionnaire; population; sarcopenia; indicator
AB Introduction Various operational definitions have been proposed to assess the frailty condition among older individuals. Our objective was to assess how practitioners measure the geriatric syndrome of frailty in their daily routine. Methods An online survey was sent to national geriatric societies affiliated to the European Union Geriatric Medicine Society (EUGMS) and to members of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Results A total of 388 clinicians from 44 countries answered to the survey. Most of them were medical doctors (93%), and their primary field of practice was geriatrics (83%). Two hundred and five clinicians (52.8%) always assessed frailty in their daily practice, 38.1% reported to "sometimes" measure it, and 9.1% never assess it. A substantial proportion of clinicians (64.9%) diagnose frailty using more than one instrument. The most widely used tool was the gait speed test, adopted by 43.8% of the clinicians, followed by clinical frailty scale (34.3%), the SPPB test (30.2%), the frailty phenotype (26.8%) and the frailty index (16.8%). Conclusion A variety of tools is used to assess frailty of older patients in clinical practice highlighting the need for standardisation and guidelines.
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AF Knowles, Helen J.
TI Multiple Roles of Angiopoietin-Like 4 in Osteolytic Disease
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE angiopoietin-like 4; bone resorption; cartilage degradation; angiogenesis; inflammation; rheumatoid arthritis
ID hypoxia-inducible factor; giant-cell tumor; gene-expression; vascular-permeability; bone-resorption; osteoclast differentiation; articular-cartilage; lipoprotein-lipase; protein; angiogenesis
AB Hypoxia and the hypoxia-inducible factor (HIF) transcription factor drive pathological bone loss in conditions including rheumatoid arthritis (RA), osteoarthritis, osteoporosis, primary bone tumours, and bone metastatic cancer. There is therefore considerable interest in determining the function(s) of HIF-induced genes in these pathologies. Angiopoietin-like 4 (ANGPTL4) is an adipose-derived, HIF-1 alpha- and PPAR gamma-induced gene that was originally discovered as an endocrine and autocrine/paracrine regulator of lipid metabolism. Given the inverse relationship between bone adiposity and fracture risk, ANGPTL4 might be considered a good candidate for mediating the downstream effects of HIF-1 alpha relevant to osteolytic disease. This review will consider the possible roles of ANGPTL4 in regulation of osteoclast-mediated bone resorption, cartilage degradation, angiogenesis, and inflammation, focusing on results obtained in the study of RA. Possible roles in other musculoskeletal pathologies will also be

discussed. This will highlight ANGPTL4 as a regulator of multiple disease processes, which could represent a novel therapeutic target in osteolytic musculoskeletal disease.
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TI PTH [1-34] induced differentiation and mineralization of mandibular condylar cartilage
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DT Article
ID parathyroid-hormone; subchondral bone; articular-cartilage; i collagen; osteoarthritis; intermittent; cells; chondrocytes; phosphatase; progression
AB Intermittent Parathyroid Hormone (I-PTH) is the only FDA approved anabolic drug therapy available for the treatment of osteoporosis in males and

postmenopausal females. The effects of I-PTH on the chondrogenic lineage of the mandibular condylar cartilage (MCC) are not well understood. To investigate the role of I-PTH on the MCC and subchondral bone, we carried out our studies using 4 to 5 week old triple transgenic mice (Col1a1XCol2a1XCol10a1). The experimental group was injected with PTH (80 mu g/kg) daily for 2 weeks, while control group was injected with saline. Our histology showed that the I-PTH treatment led to an increased number of cells expressing Col1a1, Col2a1 and Col10a1. Additionally, there was an increase in cellular proliferation, increased proteoglycan distribution, increased cartilage thickness, increased TRAP activity, and mineralization. Immunohistochemical staining showed increased expression of pSMAD158 and VEGF in the MCC and subchondral bone. Furthermore our microCT data showed that I-PTH treatment led to an increased bone volume fraction, tissue density and trabecular thickness, with a decrease in trabecular spacing. Morphometric measurements showed increased mandibular length and condyle head length following I-PTH treatment. In conclusion, our study suggests that I-PTH plays a critical role in cellular proliferation, proteoglycan distribution, and mineralization of the MCC.
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U2 4
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PT J
AU Zrubka, Z
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TI EQ-5D studies in musculoskeletal and connective tissue diseases in eight Central and Eastern European countries: a systematic literature review and meta-analysis
SO RHEUMATOLOGY INTERNATIONAL
LA English
DT Review
DE EQ-5D; Musculoskeletal diseases; Central and Eastern Europe; Patient reported outcomes; Health-related quality of life; Meta-analysis
ID quality-of-life; low-back-pain; rheumatoid-arthritis; ankylosing-spondylitis; health-status; single-blind; osteoporotic fractures; psoriatic-arthritis; utility; osteoarthritis
AB EQ-5D is becoming the preferred instrument to measure health-state utilities involved in health technology assessment. The objective of this study is to assess the state of EQ-5D research in musculoskeletal disorders in 8 Central and Eastern European countries and to provide a meta-analysis of EQ-5D index scores. Original research articles published in any language between Jan 2000 and Sept 2016 were included, if they reported any EQ-5D outcome from at least two musculoskeletal patients from Austria, Bulgaria, the Czech Republic, Hungary, Poland, Romania, Slovakia, or Slovenia. Risk of bias was assessed with the Cochrane Collaboration's tool. Twenty-nine articles (5992 patients) were included on rheumatoid arthritis (n = 7), osteoporosis (n = 5), chronic pain (n = 5), osteoarthritis (n = 4), ankylosing spondylitis (n = 2), psoriatic arthritis (n = 2), total hip replacement (n = 2), and scleroderma (n = 2). Low back pain was under-represented, while studies in neck pain, systemic lupus erythematosus, gout, and childhood disorders were lacking. EQ-5D index scores were reported in 24 studies, while the version of the instrument and the value-set was not specified in 41% and 46% of the articles, respectively. Meta-analysis was performed on 24 disease states involving 6876 observation points. Intervention effect was reported in 22 subgroups, out of which risk of bias was low in 41%. This review provides recommendations to improve reporting standards of EQ-5D results and highlights potential areas for future research. Coordinated research in conditions with greatest public health impact as well as a development of a regional value-set could provide locally relevant health-state utilities that are transferable among countries within the region.
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TC 10
Z9 11
U1 0
U2 18
PU SPRINGER HEIDELBERG
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PA TIERGARTENSTRASSE 17, D-69121 HEIDELBERG, GERMANY
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J9 RHEUMATOL INT
JI Rheumatol. Int.
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BP 1957
EP 1977
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WC Rheumatology
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PT J
AU Veronese, N
Stubbs, B
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AF Veronese, Nicola
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TI Dietary magnesium intake and fracture risk: data from a large prospective study
SO BRITISH JOURNAL OF NUTRITION
LA English
DT Article
DE Magnesium; Fractures; Osteoporosis; Epidemiology
ID bone; metaanalysis; women; inflammation; performance; patterns; calcium; disease; people; cohort
AB Research considering the relationship between dietary Mg and osteoporosis as well as fractures are sparse and conflicting. We therefore aimed to investigate Mg intake and the onset of fractures in a large cohort of American men and women involved in the Osteoarthritis Initiative over a follow-up period of 8 years. Dietary Mg intake (including that derived from supplementation) was evaluated through a FFQ at baseline and categorised using sex-specific quintiles (Q); osteoporotic fractures were evaluated through self-reported history. Overall, 3765 participants (1577 men; 2071 women) with a mean age of 60.6 (sd 9.1) years were included. During follow-up, 560 individuals (198 men and 368 women) developed a new fracture. After adjusting for fourteen potential confounders at baseline and taking those with lower Mg intake as reference (Q1). men (hazard ratio (HR) 0.47; 95 % CI 0.21, 1.00, P = 0.05) and women (HR 0.38; 95 % CI 0.17, 0.82, P = 0.01) in the highest quintile reported a significantly lower risk for fracture. Women meeting the recommended Mg intake were at a 27 % decreased risk for future fractures. In conclusion, higher dietary Mg intake has a protective effect on future osteoporotic fractures, especially in women with a high risk for knee osteoarthritis. Those women meeting the recommended Mg intake appear to be at a lower risk for fractures.
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Z9 58
U1 0
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PU CAMBRIDGE UNIV PRESS
PI CAMBRIDGE
PA EDINBURGH BLDG, SHAFTESBURY RD, CB2 8RU CAMBRIDGE, ENGLAND
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JI Br. J. Nutr.
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WC Nutrition & Dietetics
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PT J
AU Alkan, G
Akgol, G
AF Alkan, Gokhan
Akgol, Gurkan
TI Do vitamin D levels affect the clinical prognoses of patients with knee osteoarthritis?
SO JOURNAL OF BACK AND MUSCULOSKELETAL REHABILITATION
LA English
DT Article
DE Knee osteoarthritis; vitamin D deficiency; quality of life
ID serum-levels; d deficiency; cartilage
AB OBJECTIVE: Although vitamin D deficiency has been associated with

osteoporosis, as well as fractures, in elderly men and women, the role of vitamin D deficiency in the pathogenesis of osteoarthritis (OA) remains controversial. In this study, we aimed to investigate the effects of vitamin D deficiency on the functional status and disease prognosis of patients with knee osteoarthritis. PATIENTS AND METHODS: Our study comprised 100 patients that met the American College of Rheumatology criteria for a diagnosis of knee osteoarthritis. Each patient underwent knee radiography, the results of which were graded according to Kellgren and Lawrence radiographic grading scale; those that met the diagnostic criteria were included in the study. The visual analog scale (VAS), Nottingham Health Profile (NHP), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Lequesne Knee Osteoarthritis Index were used to assess patients' pain, function and quality of life. Complete blood counts, sedimentation rates and serum C-reactive protein, rheumatoid factor, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, sodium, potassium, calcium, phosphorus, parathyroid and thyroid hormone levels were routinely recorded for each patient. Vitamin D levels were analyzed in winter (between November and February) using high performance liquid chromatography. RESULTS: Patients were divided into two groups, Group 1 and Group 2, according to the presence or absence of vitamin D deficiency. The groups did not differ significantly in terms of age, disease duration, sex distribution, presence of osteoporosis or radiographic stage of knee osteoarthritis ($p = 0.793$, 0.092, 0.250, 0.835 and 0.257, respectively). However, the NHP pain, physical activity, fatigue, social isolation, and emotional reactions subsets, WOMAC pain and physical function subsets and total score, Lequesne knee osteoarthritis index, and patient/physician VAS scores were significantly higher in Group 1 than in Group 2 ($p < 0.05$). CONCLUSIONS: Our study therefore suggests that vitamin D deficiency exacerbates pain, dysfunction and a poorer quality of life in patients with knee osteoarthritis. Further longer-term studies are needed to investigate the effects of vitamin D deficiency on OA-related symptoms.
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U2 12
PU IOS PRESS
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EP 901
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PG 5
WC Orthopedics; Rehabilitation
SC Orthopedics; Rehabilitation

GA FD7ZU
UT WOS:000407745600033
PM 28372319
DA 2026-02-10
ER

PT J
AU Kutzner, KP
Donner, S
Schneider, M
Pfeil, J
Rehbein, P
AF Kutzner, K. P.
Donner, S.
Schneider, M.
Pfeil, J.
Rehbein, P.
TI One-stage bilateral implantation of a calcar-guided short-stem in total hip arthroplasty Minimally invasive modified anterolateral approach in supine position
SO OPERATIVE ORTHOPADIE UND TRAUMATOLOGIE
LA English
DT Article
DE Arthroplasty, replacement, hip; Prostheses and implants; Minimally invasive surgical procedures; Round-the-corner; Optimys
ID replacement; mortality
AB One-stage bilateral, muscle-preserving, calcar-guided implantation technique through the modified minimally invasive anterolateral approach in supine position. Bilateral primary/secondary osteoarthritis of the hip; bilateral femoral head necrosis; ASA I-III. ASA IV; severe osteoporosis, other factors jeopardizing stable anchorage of cementless, calcar-guided short-stem; infection. Supine position. Skin incision. Opening of fascia; blunt dissection, pushing gluteal muscles dorsally with the index finger. Capsulectomy. Individual osteotomy according to preoperative plan to determine short-stem position. Remove femoral head. Prepare acetabulum. Position cup. Femoral preparation with the curved opening awl. Spare greater trochanter and gluteal muscles. Insert trial rasps in ascending sizes with "round-the-corner" technique. Select offset version, then trial reposition with intraoperative radiograph and implantation of the definitive implant. Wound closure. Consultation with the anesthesiologist to confirm a stable patient. Same procedure on contralateral hip. Mobilization on day 1 with immediate full weight bearing. Remove wound drains and urinary catheter (only female patients) on day 2. Intensive protocol of physiotherapy and rehabilitation. Thrombosis prophylaxis. Rehabilitation from day 7. Almost 500 patients have undergone surgery since 2010. First consecutive 54 patients (108 hips) prospectively evaluated. After 2 years, Harris Hip Score was 98.8; satisfaction on visual analogue scale was 9.9. Low peri- and

postoperative complication rates; no implant revisions. The muscle-sparing approach and the special "round-the-corner" technique in one-stage bilateral procedure leads to rapid mobilization and rehabilitation with excellent early clinical results and high satisfaction rates.
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Wohlrab D, 2004, Z ORTHOP GRENZGEB, V142, P685, DOI 10.1055/s-2004-832447
NR 22
TC 19
Z9 23
U1 0
U2 4
PU URBAN & VOGEL

PI MUNICH
PA NEUMARKTER STRASSE 43, D-81673 MUNICH, GERMANY
SN 0934-6694
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J9 OPER ORTHOP TRAUMATO
JI Oper. Orthopade Traumatol.
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WC Orthopedics
SC Orthopedics
GA ER9ND
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PT J
AU Edwards, MH
Paccou, J
Ward, KA
Jameson, KA
Moss, C
Woolston, J
Javaid, MK
Cooper, C
Dennison, EM
AF Edwards, M. H.
Paccou, J.
Ward, K. A.
Jameson, K. A.
Moss, C.
Woolston, J.
Javaid, M. K.
Cooper, C.
Dennison, E. M.
TI The relationship of bone properties using high resolution peripheral quantitative computed tomography to radiographic components of hip osteoarthritis
SO OSTEOARTHRITIS AND CARTILAGE

LA English
DT Article
DE Osteoarthritis; Bone microarchitecture; Epidemiology; Osteoporosis; Cortical; Trabecular
ID mineral density; fractures; risk; mass; men
AB Objective: Positive associations between radiographic osteoarthritis (OA) and areal bone mineral density (BMD) have been demonstrated and appear strongest when bony features of OA are considered. To date, these associations have not been assessed using HRpQCT. Design: A total of 318 participants (170 men and 148 women), aged 72.1-81.4 years from a non-selected cohort, underwent HRpQCT of the distal radius and tibia along with hip radiography. Differences in bone microarchitecture were assessed between those with and without osteophytes, sclerosis or joint space narrowing (JSN) in either hip. Results: Men with osteophytes alone had significantly higher radial trabecular volumetric BMD (Tb.vBMD) and radial and tibial trabecular thickness (Tb.Th). Men with both sclerosis and osteophytes had significantly higher cortical volumetric BMD (Ct.vBMD) and cortical thickness (Ct.Th) at the distal tibia than those with osteophytes alone ($P < 0.05$). These relationships were maintained after adjustment for age and Body Mass Index (BMI), and were not replicated in women. Bone microarchitecture did not differ significantly in those with JSN from those without it in men or women. Conclusions: Our findings suggest higher Tb.vBMD and Tb.Th in men with osteophytosis but higher tibial Ct.vBMD and Ct.Th in men with hip joint sclerosis. These results do however require replication in other cohorts. (C) 2017 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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FU International Osteoporosis Foundation; SERVIER; Arthritis Research UK; MRC Programme [U105960371]; Medical Research Council (MRC) of Great Britain; Arthritis Research UK [19583]; NIHR Nutrition BRC, University of Southampton; NIHR Musculoskeletal BRU, University of Oxford; MRC [MC_U147585819, G0400491, MC_U105960371, MC_U147585827] Funding Source: UKRI; Medical Research Council [G0400491, MC_U147585827, MC_UP_A620_1014, MC_UU_12011/1, MC_U147585819, U1475000001, MC_U105960371, MC_U147585824] Funding Source: researchfish; National Institute for Health Research [NF-SI-0508-10082, NF-SI-0513-10085] Funding Source: researchfish; Versus Arthritis [19583] Funding Source: researchfish
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NR 16
TC 6
Z9 7
U1 0
U2 3

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PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
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EP 1483
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA FE0UA
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ER

PT J
AU Olaosebikan, BH
Adelowo, OO
Animashaun, BA
Akintayo, RO
AF Olaosebikan, Babatunde Hakeem
Adelowo, Olufemi Oladipo
Animashaun, Barakat Adeola
Akintayo, Richard Oluyinka
TI Spectrum of paediatric rheumatic diseases in Nigeria
SO PEDIATRIC RHEUMATOLOGY
LA English
DT Article
DE Paediatric rheumatic disease; Nigeria; Juvenile idiopathic arthritis; Juvenile systemic lupus erythematosus
ID systemic-lupus-erythematosus; united-states; east-africa; populations; prevalence
AB Background: Paediatric rheumatology service in Sub-Sahara African is virtually not available as there is a shortage of paediatric rheumatologists and other rheumatology health professionals. We aim to describe the clinical spectrum and

the frequencies of paediatric rheumatic diseases (PRDs) in Lagos State University Teaching Hospital (LASUTH), Lagos, Nigeria. Methods: This is a retrospective review of patients with PRDs seen over a five year period (March 2010 to February 2016) at the rheumatology clinic and children ward of LASUTH. We reviewed the folders of 57 patients from our records. The demographics, baseline laboratory features, clinical diagnosis, treatment patterns and patient outcomes were extracted and analyzed. Clinical and laboratory characteristics between patients with Juvenile idiopathic arthritis (JIA) and patients with juvenile connective tissue diseases (JCTD) were compared using Fisher's exact test. Results: Fifty seven patients were studied with a female to male ratio of 3 to 1 (Female: 43; M: 14). The mean age at presentation in years was 14 +/- 4.4 years (range: 1.5-22 years). The mean duration of symptoms before diagnosis was 18.4 +/- .9 months (range: 2-60 months). The diagnostic types of PRDs included 28(49.1%) cases of JIA. These were made up of 14 cases of polyarticular JIA, nine cases of oligoarticular JIA and 5 cases of systemic onset JIA. Others were 18 (24.6%) cases of juvenile systemic lupus erythematosus (JSLE), 3 (5.3%) cases of joint hypermobility syndrome, 2 (3.5%) cases of juvenile systemic sclerosis, 2 (3.5%) cases of fibromyalgia, 2 (3.5%) cases of plantar fasciitis, 1 (1.6%) case of juvenile dermatomyositis (JDM), 1 (1.6%) case of juvenile polymyositis-systemic lupus erythematosus (PM-SLE) overlap, 1 (1.6%) case of secondary bilateral knee osteoarthritis from Blount disease, 1 (1.6%) case of secondary osteoporosis from childhood leukemia and 1 (1.6%) case of Osgood-Schlatter's disease. Constitutional symptoms and extra-articular diseases were significantly more frequent among JCTD cases than among the JIA cases (Constitutional symptoms: 100% vs 83.3%, p = 0.003; extra-articular disease: 100% vs 10.7%, p = 0.001). The percentage mortality in this study was 10.5% while 20 (35.1%) of the patients were lost to clinic follow up. Conclusion: The pattern of PRDs observed in this study is similar to that described in South African and North American series but it differs from patterns reported in Asian series. Although hitherto largely unrecognized, PRDs may constitute a substantial cause of morbidity and mortality in black Africans.
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NR 22
TC 17
Z9 23
U1 0
U2 4
PU BIOMED CENTRAL LTD
PI LONDON
PA 236 GRAYS INN RD, FLOOR 6, LONDON WC1X 8HL, ENGLAND
SN 1546-0096
EI
J9 PEDIATR RHEUMATOL
JI Pediatr. Rheumatol.
PD JAN 31
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WC Pediatrics; Rheumatology
SC Pediatrics; Rheumatology

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UT WOS:000392993600001
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PT J
AU Wang, YXJ
AF Wang, Yi Xiang J.
TI Menopause as a potential cause for higher prevalence of low back pain in women than in age-matched men
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Article
DE epidemiology; intervertebral disc degeneration; low back pain; oestrogen; physiological sex difference
ID estrogen-replacement therapy; lumbar disc degeneration; elderly chinese men; hormone-therapy; risk-factors; general-population; sex-differences; association; osteoarthritis; fractures
AB Female sex hormones play an important role in the aetiology and pathophysiology of a variety of musculoskeletal degenerative diseases. Postmenopausal women show accelerated disc degeneration due to relative oestrogen deficiency, resulting in narrower intervertebral disc space in women than age-matched men, increased prevalence of spondylolisthesis, and increased prevalence of facet joint osteoarthritis. Postmenopausal women also show higher osteoporosis related spine fracture rate, particularly at the thoracic-lumbar junction site. I propose the concept that low back pain (LBP) is more prevalent in postmenopausal women than age-matched men and is associated with the physiological changes caused by the relatively lower level of sex hormones after menopause in women. Considering hormone replacement treatment (HRT)'s consistent efficacy reported with menopause-associated osteoarthritis, an in-depth understanding of the role of the gonadal hormones in LBP modulation warrants further study. HRT initiated at early postmenopausal phase may be protective for recurring LBP. If this is the case, further cost-benefit analysis should be performed for optimal HRT regimen in cases of women with high risk of recurring severe LBP.
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NR 48
TC 46
Z9 54
U1 2
U2 29
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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J9 J ORTHOP TRANSL
JI J. Orthop. Transl.
PD JAN 15
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IS
BP 1
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WC Orthopedics
SC Orthopedics
GA EG5LY
UT WOS:000391086500001

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PT J
AU Lee, YK
Kim, SW
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AF Lee, Yeon Kyung
Kim, Sang-Woo
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TI Suppression of human arthritis synovial fibroblasts inflammation using dexamethasone-carbon nanotubes via increasing caveolin-dependent endocytosis and recovering mitochondrial membrane potential
SO INTERNATIONAL JOURNAL OF NANOMEDICINE
LA English
DT Article
DE carbon nanotubes; polyethylene-glycol; dexamethasone; arthritis; fibroblast-like synoviocytes; caveolin-dependent endocytosis
ID rheumatoid-arthritis; oxidative stress; delivery; tnf; synoviocytes; nanoparticle; pathogenesis; cytokines; micelles; hypoxia
AB Dexamethasone (DEX), a non-particulate glucocorticoid (GC) to inhibit anti-inflammatory response, has been widely used for the treatment of various diseases such as arthritis, cancer, asthma, chronic obstructive pulmonary disease, cerebral edema, and multiple sclerosis. However, prolonged and/or high-dose GC therapy can cause various serious adverse effects (adrenal insufficiency, hyperglycemia, Cushing's syndrome, osteoporosis, Charcot arthropathy, etc). In this study, developed DEX-carbon nanotube (CNT) conjugates improved intracellular drug delivery via increased caveolin-dependent endocytosis and ultimately suppressed the expression of major pro-inflammatory cytokines in tumor necrosis factor-alpha (TNF-alpha)stimulated human fibroblast-like synoviocytes (FLS) at low drug concentrations. Specifically, DEX on polyethylene-glycol (PEG)-coated CNTs induced caveolin uptake, recovered mitochondrial disruption, and inhibited reactive oxygen species production by targeting mitochondria that was released from the early endosome in TNF-alpha-stimulated FLS. The obtained results clearly demonstrated that DEX-PEG-coated CNTs significantly inhibited the inflammation by FLS in rheumatoid arthritis (RA) by achieving greater drug uptake and efficient intracellular drug release from the endosome, thus suggesting a mechanism of

effective low-dose GC therapy to treat inflammatory diseases, including RA and osteoarthritis.
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TI Relationships between fish and otolith size of nine deep-sea fishes from the Andaman and Nicobar waters, North Indian Ocean
SO JOURNAL OF APPLIED ICHTHYOLOGY
LA English
DT Article
ID weight-length relationships; eastern arabian sea; age-determination; stock discrimination; primary productivity; growth increments; back-calculation; predator-prey; persian-gulf; western bay
AB The study presents for the first time the otolith morphology of nine species of deep-sea fishes. This study was based on sampling carried out on-board FORV Sagar Sampada (Cruise No 349) during March-April 2016, along the continental margin of the Andaman and Nicobar Islands in the Bay of Bengal using high speed demersal trawl. Unbroken (complete) otoliths from Polymixia fusca Kotthaus, 1970, Neoepinnula orientalis (Gilchrist & von Bonde 1924), Chlorophthalmus nigromarginatus (Kamohara, 1953), Cubiceps baxteri (McCulloch, 1923), Bembrops caudimacula (Steindachner, 1876), Neoscopelus microchir (Matsubara, 1943), Ostracoberyx dorygenis Fowler, 1934, Synagrops japonicus (Doderlein, 1883), and Bathyclupea hoskynii Alcock 1891) were used for this study. Length-weight

relationships (LWR) and the regression between otolith size (width, weight, area and perimeter) and fish length (TL) of nine deep-sea Fishes were considered. Numerical relationships derived from the relationship between otolith size and the fish can be used as predictors to estimate the prey size as well as to understand trophic relations and food web dynamics of these hitherto unexamined deep-sea ichthyofauna. LWR showed negative allometric otolith growth in five species; four species showed positive allometric growth. Otolith size to fish size (TL) relation is explained by a simple linear regression considering otolith width (OW), otolith weight (OWe), otolith area (OA) and otolith perimeter (OP). Stronger r(2) values (>.76) indicate robustness, except for Cubiceps baxteri (r(2)=.65), and give better estimates for the TL of the fish.
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U1 0
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TI OSTEOPOROSIS IN BRAZILIAN PATIENTS AWAITING KNEE ARTHROPLASTY
SO ACTA ORTOPEDICA BRASILEIRA
LA English
DT Article
DE Osteoporosis; Climacteric; Arthroplasty
ID total hip-arthroplasty; risk-factors; osteoarthritis; validation; women
AB Objective: The primary objective of this study was to determine the prevalence of osteoporosis and osteopenia prior to total knee arthroplasty (TKA) in female patients. As a secondary objective, we evaluated the incidence of hip fractures, types of drugs to treat osteoporosis and serum vitamin D levels. Method: This is a transversal, descriptive and observational study which evaluated 60 women above age 55 prior to total knee replacement. Results: Mean patient age was 71.4 years. Osteoporosis was present in 16.7% of the sample and osteopenia in 15%. In the patients with osteoporosis, femur fracture (20%) was most frequent. Most of the group with osteopenia did not take any medication to treat this condition (55.6%), while most patients with osteoporosis took alendronate (30%) and 30% did not take any medication. Conclusion: The female population awaiting total knee replacement should be considered at risk for osteoporosis, confirming recent findings in the literature.
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TI Effect of strontium ranelate on pain behavior in an experimental model of osteoarthritis
SO BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH
LA English
DT Article
DE Osteoarthritis; Strontium ranelate; Pain; Treatment; Prophylaxis
ID postmenopausal women; vertebral fracture; risk; mechanism; bone; knee
AB Strontium ranelate (SrRan) is a drug usually prescribed to treat osteoporosis, with proven effects of decreasing the risk of fractures and an indication of reducing the progression of osteoarthritis (OA). This study aimed to investigate the effects of SrRan as either a prophylactic or a treatment drug, using an OA rat model to assess pain behavior. A monoiodoacetate (MIA)-induced knee joint OA model in Wistar rats was used. Thirty Wistar rats (both sexes, 60 days old) were distributed in five groups of 6 rats each: the control group, that received no intervention; a prophylactic group, that received oral administration of 25 mg . kg(-1) . day(-1) of SrRan for 28 days before induction of OA; a group treated with 25 mg . kg(-1) . day(-1) of SrRan for 28 days after OA induction; a group treated with 50 mg . kg(-1) . day(-1) during 28 days after OA induction; and a group that received oral saline for 28 days after induction. The assessment of pain behavior was performed considering articular incapacitation (weight-bearing test), mechanical hyperalgesia (Randall Selitto test) and motor activity (rotarod test), on days 0, 7, 14, 21, and 28. This experiment did not yield a significant difference when comparing the group that received SrRan prophylactically with the groups treated with 25 or 50 mg . kg(-1) . day(-1) and the group that received oral saline. Thus, SrRan did not provide analgesia in either treated rats or as a prophylactic drug with the tested doses. Higher doses should be tested further to achieve possible significant results.
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TI Mass spectrometry imaging: a novel technology in rheumatology
SO NATURE REVIEWS RHEUMATOLOGY
LA English
DT Review
ID ablation electrospray-ionization; paraffin-embedded tissue; maldi-ms; proteomic analysis; mouse-brain; tof-sims; in-vivo; atmospheric-pressure; bone mineralization; spatial-resolution
AB Mass spectrometry imaging (MSI) is used to determine the relative abundance and spatial distribution of biomolecules such as peptides, proteins, lipids and other organic compounds in tissue sections by their molecular masses. This technique provides a sensitive and label-free approach for high-resolution imaging, and is currently used in an increasing number of biomedical applications such as biomarker discovery, tissue classification and drug monitoring. Owing to technological advances in the past 5 years in diverse MSI strategies, this technology is expected to become a standard tool in clinical practice and provides information complementary to that obtained using existing methods. Given that MSI is able to extract mass-spectral signatures from pathological tissue samples, this technique provides a novel platform to study joint-related tissues affected by rheumatic diseases. In rheumatology, MSI has been performed on articular cartilage, synovium and bone to increase the understanding of articular destruction and to characterize diagnostic and prognostic biomarkers for osteoarthritis, rheumatoid arthritis and osteoporosis. In this Review, we provide an overview of MSI technology and of the studies in which joint tissues have been analysed by use of this methodology. This approach might increase knowledge of rheumatic pathologies and ultimately prompt the development of targeted strategies for their management.
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TI Identification and management of patients at increased risk of osteoporotic fracture: outcomes of an ESCEO expert consensus meeting
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Review
DE Fracture risk; Healthcare burden; Management; Osteoporosis; Secondary prevention; Treatment gap
ID postmenopausal women; hip fracture; vertebral fractures; nonvertebral fractures; strontium ranelate; united-kingdom; abaloparatide; teriparatide; probability; health
AB Osteoporosis represents a significant and increasing healthcare burden in Europe, but most patients at increased risk of fracture do not receive medication, resulting in a large treatment gap. Identification of patients who are at particularly high risk will help clinicians target appropriate treatment more precisely and cost-effectively, and should be the focus of future research. The purpose of the study was to review data on the identification and treatment of patients with osteoporosis at increased risk of fracture. A working group convened by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis met to review current data on the epidemiology and burden of osteoporosis and the patterns of medical management throughout Europe. In Europe in 2010, the cost of managing osteoporosis was estimated at a,notsign37 billion and notably the costs of treatment and long-term care of patients with fractures were considerably higher than the costs for pharmacological prevention. Despite the availability of effective treatments, the uptake of osteoporosis therapy is low and declining, in particular for secondary fracture prevention where the risk of a subsequent fracture following a first fracture is high. Consequently, there is a significant treatment gap between those who would benefit from treatment and those who receive it, which urgently needs to be addressed so that the burden of disease can be reduced. Implementation of global fracture prevention strategies is a critical need. Future research should focus on identifying specific risk factors for imminent fractures, periods of high fracture risk, patients who are at increased risk of fracture and therapies that are most suited to such high-risk patients and optimal implementation strategies in primary, secondary and tertiary care.
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AU Tarquini, C
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TI Comparison of tissue transglutaminase 2 and bone biological markers osteocalcin, osteopontin and sclerostin expression in human osteoporosis and osteoarthritis
SO AMINO ACIDS
LA English
DT Article
DE Osteoporosis; Osteoarthritis; Transglutaminase 2; Cartilage; Bone remodeling
ID femoral-neck fracture; articular-cartilage; extracellular-matrix; knee osteoarthritis; subchondral bone; cross-linking; endochondral ossification; messenger-rna; hip; cells
AB Osteoporosis (OP) and osteoarthritis (OA) are the most common joint diseases, with a high incidence in the elderly population. OP is characterized by trabecular bone remodeling and reabsorption, whereas articular cartilage and subchondral bone remodeling are major features of OA. Although classically considered as independent or even conflicting processes, clinical coexistence of OP and OA was recently described. Transglutaminase 2 (TG2) expression is considered a biomarker of OA, but its role in osteoporotic bone remodeling is still uncertain. We investigated TG2 and bone biological markers (Osteocalcin, Osteopontin, and Sclerostin) in osteoporotic and osteoarthritic osteocartilagineous tissue (n = 54) and human chondrocyte cultures in vitro by immunohistochemistry, immunofluorescence and RT-PCR. Histomorphometric evaluation of bone trabecular remodeling was also performed. In cartilage, TG2 expression was faint in control and OP and significantly less than in OA and OP + OA chondrocytes; the opposite was found for Osteocalcin, whereas Osteopontin and Sclerostin expression was similar. In the subchondral trabecular bone, osteocytes/osteoblasts TG2 expression was slight and similar comparing control, OP, OA, and OP + OA group, whereas Osteocalcin and Osteopontin expression was lower in OP compared to control, OA and OP + OA. Increased TG2 and reduced Osteocalcin expression were maintained in human osteoarthritic chondrocytes in vitro. Histomorphometric analysis confirmed reduced trabecular bone mass in OP and OP + OA compared with OA patients. TG2 represented a suitable biomarker of osteoarthritic chondrocyte activation, whereas osteocalcin and osteopontin characterized osteoporotic osteocyte/osteoblast changes; differences were lost in OP + OA patients, suggesting careful consideration when coexistence of the two diseases occurs.
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NR 74
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AU Kapucu, S
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TI PAIN AND FRAILTY IN ELDERLY FEMALES WITH OSTEOPOROSIS
SO TURKISH JOURNAL OF GERIATRICS-TURK GERIATRI DERGISI
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DT Article
DE Aged; Female; Frail Elderly; Geriatrics; Osteoporosis; Pain
ID quality-of-life; older-adults; rheumatoid-arthritis; back-pain; osteoarthritis; prevalence; population; fracture; knee
AB Introduction: Most adults who live to an advanced age become frail. Although not a disease, frailty is a combination of age-related changes and associated medical problems. This descriptive study aimed to determine the pain level and frailty status of elderly females with osteoporosis. Materials and Method: The present study sample consisted of 105 elderly females with osteoporosis who were admitted to the geriatric outpatient units of two university hospitals. Data were collected using the questionnaire prepared by the author on the basis of a literature review, the Geriatric Pain Scale and the Edmonton Frail Scale. Data were analysed using descriptive statistics, the Mann-Whitney U test, the Kruskal-Wallis H test and correlation analysis. Results: In total, 6.7% of the elderly females with osteoporosis reported a slight level of pain, 67.3% reported mild pain and 26% reported severe pain. Edmonton Frail Scale mean scores indicated that 16.3% of the subjects had moderate frailty and that 44.2% had severe frailty. Elderly females with osteoporosis who were sad and depressed during the past seven days due to pain were found to be more fragile ($p<0.05$). In addition, weight loss, depressive symptoms and urinary incontinence were related to frailty ($p<0.05$). A poor positive significant relationship was found between the mean scores of the Geriatric Pain Scale and the Edmonton Frail Scale. Conclusion: Nurses and people involved in health care should assess the frailty status of elderly females with osteoporosis, particularly those reporting pain, and be aware of the characteristics, possible symptoms and affecting factors.
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U1 0
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TI Radiologic and Clinical Features of Misdiagnosed Idiopathic Osteonecrosis of the Femoral Head

SO ORTHOPEDICS
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DT Article
ID distinguishing transient osteoporosis; advanced hip osteoarthritis; bone-marrow edema; avascular necrosis; nontraumatic osteonecrosis; mri findings; osteotomy; histopathology; fracture; cells
AB Idiopathic osteonecrosis of the femoral head (ONFH) can be correctly diagnosed in accordance with the established criteria. However, some general orthopedic physicians have misdiagnosed patients as having ONFH. The goal of this study was to clarify the radiologic and clinical features of misdiagnosed patients. This study included 50 patients who were referred to the authors' hospital by general physicians with a diagnosis of ONFH. The correct diagnosis was made based on the Japanese Investigation Committee diagnostic criteria for ONFH. Demographic data were compared between patients with and without ONFH. Of the 50 patients, 24 were diagnosed with other diseases: 10 with osteoarthritis, 7 with transient osteoporosis of the femoral head, 4 with rapidly destructive coxopathy, and 3 with subchondral insufficiency fracture. Seventeen patients who did not have ONFH had magnetic resonance imaging findings that showed a bone marrow edema pattern at the femoral head. The mean age of 62.9 years among patients without ONFH was significantly higher than that of 45.2 years among patients with ONFH. There were 18 female patients in the non-ONFH group and 5 female patients in the ONFH group. Bilateral disease was found in 1 patient in the non-ONFH group and 17 patients in the ONFH group. No patients in the non-ONFH group had a history of systemic steroid administration compared with 11 patients in the ONFH group. Clinical features associated with the non-ONFH group were female sex, older age, unilateral disease, and no history of systemic steroid administration. For patients with these features, the diagnosis of ONFH should be made carefully.
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NR 34
TC 7
Z9 9
U1 1
U2 16
PU SLACK INC
PI THOROFARE
PA 6900 GROVE RD, THOROFARE, NJ 08086 USA
SN 0147-7447
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J9 ORTHOPEDICS
JI Orthopedics
PD JAN-FEB 15
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BP E117
EP E123
DI 10.3928/01477447-20161013-03
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WC Orthopedics
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GA EP0MW
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PM 27755641
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ER

PT J
AU Yukizawa, Y
Inaba, Y
Kobayashi, N
Choe, H
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Saito, T
AF Yukizawa, Yohei
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Kubota, So
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TI Efficacy of Alendronate for the Prevention of Bone Loss in Calcar Region Following Total Hip Arthroplasty

SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE alendronate; alfacalcidol; total hip arthroplasty; stress shielding; bone mineral density
ID mineral density; femoral components; proximal femur; stem; dimensions; implant; dxa
AB Background: Bone mineral density (BMD) loss around femoral implants, particularly in the proximal femur, is a common outcome after total hip arthroplasty. Previous studies reported the prevention of postsurgical decrease in BMD with the use of osteoporosis drug therapy. This randomized study evaluated the efficacy of alendronate and alfacalcidol for preserving BMD over a long-term follow-up. Methods: Sixty consecutive patients with hip osteoarthritis who had undergone primary cementless total hip arthroplasty were randomly assigned to an alendronate (n = 20), alfacalcidol (n = 18), or control (n = 22) group. Periprosthetic BMD was measured using dual-energy X-ray absorptiometry at 1 week, 1 year, and the current follow-up (minimum 9 years after surgery). Changes in BMD are reported as mean percentages relative to the values at 1 week (baseline reference). Results: All groups showed a significant decrease in the BMD of the calcar at the current follow-up compared to the values at both 1 week and 1 year postoperatively (P < .001). The BMD values were significantly higher in the alendronate group than in the alfacalcidol and control groups (P < .05). The BMD values at the current follow-up were 76% +/- 30% (alendronate group), 64% +/- 22% (alfacalcidol group), and 59% +/- 22% (control group) of the baseline values. Conclusion: Our findings demonstrate the efficacy of early administration of alendronate for the prevention of bone loss in the calcar region. (C) 2017 Elsevier Inc. All rights reserved.
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NR 20
TC 22
Z9 27
U1 0
U2 5
PU CHURCHILL LIVINGSTONE INC MEDICAL PUBLISHERS
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JI J. Arthroplast.
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WC Orthopedics
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ER

PT J
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TI Influences of osteoarthritis and osteoporosis on the electrical properties of human bones as in vivo electrets produced due to Wolff's law
SO BIO-MEDICAL MATERIALS AND ENGINEERING
LA English
DT Article
DE Electrical property; human bone; electrical polarization; osteoarthritis; osteoporosis; proximal femur
ID hydroxyapatite; polarization
AB We characterized the electrical properties of living bone obtained from patients who had undergone total hip arthroplasty (THA) or hemiarthroplasty by means of analysis of the electrically polarized and nonpolarized bone specimens, and we discussed the role of an organic and inorganic matrix of human bone in bone piezoelectricity. We used human femoral neck bone that was harvested during THA for advanced osteoarthritis of the hip joint (OA group) and hemiarthroplasty for femoral neck fracture (FNF group). The specimens were scanned to evaluate the cancellous bone structures using micro-computed tomography, and we quantified the carbonic acid by attenuated total reflection (ATR) spectra to estimate carbonate apatite. The stored electrical charge in the electrically polarized and nonpolarized bone specimens were calculated using thermally stimulated depolarized current (TSDC) measurements. Each TSDC curve in the groups had peaks at 100 degrees C, 300 degrees C and 500 degrees C, which may be attributed to collagen, carbonate apatite and hydroxyapatite, respectively. It is suggested that organic substances are more effectively electrically polarized than apatite minerals by the polarization at room temperature and that the stored charge in living bone may be affected not only by total bone mass but also by bone quality, including 3-dimensional structure and structural component.
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FU Grants-in-Aid for Scientific Research [16H05531] Funding Source: KAKEN
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NR 14
TC 3
Z9 5
U1 0
U2 12
PU IOS PRESS
PI AMSTERDAM
PA NIEUWE HEMWEG 6B, 1013 BG AMSTERDAM, NETHERLANDS
SN 0959-2989
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J9 BIO-MED MATER ENG
JI Bio-Med. Mater. Eng.
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WC Engineering, Biomedical; Materials Science, Biomaterials
SC Engineering; Materials Science

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UT WOS:000396026000009
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ER

PT J
AU Liu, C
Sun, J
Zhang, HS
Li, LJ
AF Liu, Chang
Sun, Jian
Zhang, Haisen
Li, Longjie
TI TGF β1 gene polymorphisms correlate with the susceptibility of osteoarthritis
SO INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL PATHOLOGY
LA English
DT Article
DE Transforming growth factor beta 1; polymorphism; osteoarthritis
ID risk-factors; tgf-beta; disease; association; bone; hip; age; osteoporosis; arthritis; impact
AB Purpose: We investigated the potential role of transforming growth factor beta 1 (TGF beta 1) gene polymorphisms (rs1800470 and rs1800469) in the occurrence of osteoarthritis (OA). Methods: Genotypes of TGF beta 1 gene polymorphisms (rs1800470 and 1800469) were genotyped by TaqMan method in 111 OA patients and 129 healthy controls. The representativeness of case and control was inspected by Hardy-Weinberg equilibrium (HWE). Genotype and allele distribution differences between case and control groups were calculated by Chi-square test. Odds ratios (ORs) and their corresponding 95% confidence intervals (95% CIs) were utilized to emerge the relative risk of OA. Results: Genotype distributions of the two TGF beta 1 gene polymorphisms were according to HWE examination. TT genotype of rs1800470 was significantly associated with the occurrence of OA (P=0.046, OR=2.093, 95% CI=1.009-4.340). For rs1800469, both TT genotype and T allele had significant association with the susceptibility of OA (P=0.000, OR=3.650, 95% CI=1.759-7.575; P=0.000, OR=1.957, 95% CI=1.360-2.817). Conclusion: TT genotype of rs1800470, TT genotype and T allele of rs1800469 were increased the risk of OA. We conjectured that the polymorphisms of TGF beta 1 gene might increase the individual susceptible of OA.
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FU Natural Science Foundation of Shandong Province [ZR2016HP39]
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JI Int. J. Clin. Exp. Pathol.
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WC Oncology; Pathology
SC Oncology; Pathology
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DA 2026-02-10
ER

PT J
AU Ali, MA
Rehman, M
Saeed, M
AF Ali, Muhammad Armughan
Rehman, Marium
Saeed, Mohammad

TI Rheumatoid Arthritis Masquerading as Fibromyalgia
SO JCPSP-JOURNAL OF THE COLLEGE OF PHYSICIANS AND SURGEONS PAKISTAN
LA English
DT Article
DE Musculoskeletal ultrasound; Rheumatoid arthritis; Fibromyalgia
AB Symptoms of inflammatory arthritis such as rheumatoid arthritis (RA) can overlap with fibromyalgia syndrome (FMS). Moreover, FMS and RA can coexist. Hence, the diagnosis of low intensity, antibody-negative RA may present a challenge. Here, we present the case of a middle-aged woman thought to have FMS, osteoarthritis and osteoporosis for 4 years prior to being diagnosed as seronegative RA on musculoskeletal ultrasound (MSKUS). Targeted therapy with etanercept led to a complete clinical response and normalization of previously elevated C-reactive protein. We conclude that MSKUS is a sensitive tool for distinguishing low-intensity inflammatory arthritis from FMS with important clinical consequences.
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NR 7
TC 1
Z9 2
U1 0
U2 3
PU COLL PHYSICIANS & SURGEONS PAKISTAN
PI KARACHI
PA SEVENTH CENTRAL ST, DEFENCE HOUSING AUTHORITY, KARACHI, 75500, PAKISTAN
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J9 JCPSP-J COLL PHYSICI
JI JCPSP-J. Coll. Physicians Surg.
PD SEP 15

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WC Medicine, General & Internal
SC General & Internal Medicine
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PT J
AU Hiligsmann, M
Neuprez, A
Buckinx, F
Locquet, M
Reginster, JY
AF Hiligsmann, Mickael
Neuprez, Audrey
Buckinx, Fanny
Locquet, Medea
Reginster, Jean-Yves
TI A scoping review of the public health impact of vitamin D-fortified dairy products for fracture prevention
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Review
DE Cost-effectiveness; Dairy products; Fractures; Nutrition; Osteoporosis; Public health
ID cost-effectiveness; european-society; economic-aspects; intervention thresholds; calcium supplementation; postmenopausal women; osteoporosis; osteoarthritis; management; consensus
AB Purpose Dairy products are rich in nutrients that positively influence bone health and hence fracture risk, and have therefore been recommended and used for fracture prevention. To help decision makers to efficiently allocate scare resources, it is further important to assess the public health and economic impact of any health intervention. In recent years, several studies have been conducted to estimate the public health and/or economic impact of dairy products but no overview is currently available. This article aims therefore to summarize evidence and review articles that estimated the public health and/or economic impact of

vitamin D-fortified dairy products for fracture prevention. Methods A literature review was conducted using PubMed to identify original studies that assessed the public health and/or economic impact of dairy products (or of calcium/vitamin D supplementation) for fracture prevention up to January 15, 2017. Results Seven articles were identified. Different strategies were used by the authors to model the economic/public health impact of dairy products. The four studies assessing the public health impact of dairy products revealed a substantial benefit in terms of fracture prevented, life years, disability-adjusted life years and/or quality-adjusted life years gained. Studies assessing the cost-effectiveness revealed that the use of dairy products is generally cost-effective in the general population aged above 70 years, and from the age of 60 years in populations at high risk of fractures. Conclusion This systematic review suggests that the use of dairy products could substantially reduce the burden of osteoporotic fractures and seem to be an economically beneficial strategy.
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NR 26
TC 13
Z9 20
U1 0
U2 10
PU SPRINGER LONDON LTD
PI LONDON
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J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
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WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
GA EY9OP
UT WOS:000404328200001
PM 28634891
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ER

PT J
AU Lin, RC
Lue, KH
Lu, KH
AF Lin, Renn-Chia
Lue, Ko-Huang
Lu, Ko-Hsiu
TI Arthroscopic Lateral Retinacular Release and Modified Elmslie-Trillat Operation Improve Severe Isolated Lateral Patello-Femoral Osteoarthritis
SO JOURNAL OF KNEE SURGERY
LA English
DT Article
DE arthroscopy; patello-femoral OA; Elmslie-Trillat operation
ID tibial tubercle osteotomy; recurrent patellar instability; subchondral bone; articular-cartilage; contact pressure; proximal tibia; in-vitro; osteoporosis; malalignment; progression
AB To evaluate whether arthroscopic lateral retinacular release and the modified Elmslie-Trillat operation improve osteoarthritis (OA) progression and clinical outcomes in patients with severe isolated lateral patello-femoral OA. Nine women (11 knees) and one man (one knee) with isolated late-stage lateral patello-femoral OA underwent surgery. The severity of patello-femoral OA was recorded using the Merchant method, while the level of pain and anterior knee function were scored using the visual analogue scale (VAS) and Kujala knee scores, respectively. The articular cartilage was graded under arthroscopy using the Outerbridge classification. All of the patients underwent the modified Elmslie-Trillat operation after arthroscopic surgery, including lateral retinacular release. Ten patients (12 knees) had a mean 6.45 +/- 0.80 mm of medial transfer, 6.02 +/- 0.80 mm of anterior transfer of the tibial tubercle, and follow-up of 67.0 months. The mean VAS and Kujala knee scores improved from 8 +/- 0.17 preoperatively to 2.33 +/- 0.33 on the last follow-up and from 43.08 +/- 2.09 to 68.83 +/- 2.59, respectively (both $p < 0.001$). Postoperatively, all had improved subchondral bone remodeling, including cyst resolution, density and trabeculae normalization, and subchondral smoothing in the patello-femoral compartment. The patello-femoral joint space and patellar thickness increased from 0.39 +/- 0.16 mm to 1.77 +/- 0.18 mm and from 18.28 +/- 0.67 mm to 19.60 +/- 0.69 mm, respectively ($p < 0.001$ and $p = 0.005$). Treatment of severe isolated lateral patello-femoral OA using arthroscopic

lateral retinacular release and the modified Elmslie-Trillat operation can improve pain relief, functional outcomes, and subchondral bone remodeling, and also restore the patello-femoral joint space and patellar thickness. Prompt transfer of the tibial tubercle seems to reverse the progress of OA radiographically.
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NR 37
TC 6
Z9 7
U1 0
U2 2
PU GEORG THIEME VERLAG KG
PI STUTTGART
PA RUDIGERSTR 14, D-70469 STUTTGART, GERMANY
SN 1538-8506
EI 1938-2480
J9 J KNEE SURG
JI J. Knee Surg.
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WC Orthopedics
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PT J
AU Pan, F
Tian, J
Aitken, D
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AF Pan, Feng
Tian, Jing
Aitken, Dawn
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TI The association of knee structural pathology with pain at the knee is modified by pain at other sites in those with knee osteoarthritis
SO CLINICAL RHEUMATOLOGY
LA English
DT Article
DE Generalized pain; Knee pain; Knee structures; MRI
ID musculoskeletal pain; neuropathic pain; sensitization; impact; epidemiology; mechanisms; people; mri; comorbidity; diagnosis
AB The objective of this study was to investigate the associations of knee structural abnormalities with different patterns of pain. A total of 891 participants (average age 63 years; range 50 to 80 years) participated in this study. Presence of pain at the neck, back, hands, shoulders, hips, knees, and feet was assessed by questionnaire. Participants were categorized as having no pain at any site (no pain), pain only at the knee (KP), pain at other sites but not the knee (OP), and pain at the knee and other sites (KOP). T1-weighted or T2-weighted MRI of the right knee was performed to measure cartilage defects, bone marrow lesions (BMLs), and effusion-synovitis. Osteophytes and joint space narrowing were assessed by X-ray. KP, KOP, and OP were, respectively, present in 3, 43, and 42% of the participants. In multivariable analyses, KOP was associated with the presence of cartilage defects, BMLs, and osteophytes (OR 3.57 (95% CI 1.78 to 7.14), 2.37 (1.27 to 4.43), and 2.87

(1.10 to 7.51), respectively) in those with radiographic knee OA. KP was also associated with presence of these structural abnormalities as well as effusion-synovitis, and these associations were much stronger. The associations between structural abnormalities and KOP were weaker than those with KP in those with radiographic knee OA. This suggests that mechanisms mediating the association between structural pathology, localized, and generalized pain may be different, and central sensitization is possibly involved in generalized pain. Pain at other sites needs to be considered in the management and treatment of OA-related pain.
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 0770-3198
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J9 CLIN RHEUMATOL
JI Clin. Rheumatol.
PD NOV 15
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IS 11
BP 2549
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WC Rheumatology
SC Rheumatology
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PT J
AU Weivoda, MM
Youssef, SJ
Oursler, MJ
AF Weivoda, Megan M.
Youssef, Stephanie J.
Oursler, Merry Jo
TI Sclerostin expression and functions beyond the osteocyte
SO BONE
LA English
DT Article
DE Sclerostin; Wnt; Osteoarthritis; Ankylosing spondylitis; Rheumatoid arthritis
ID van-buchem-disease; bone-formation; serum sclerostin; prostate-cancer; ankylosing-spondylitis; postmenopausal women; cell proliferation; multiple-myeloma; sost expression; bmp antagonist
AB Sclerostin, the product of the SOSTgene, is a secreted inhibitor of Wnt signaling that is produced by osteocytes to regulate bone formation. While it is often considered an osteocyte-specific protein, SOST expression has been reported in numerous other cell types, including hypertrophic chondrocytes and cementocytes. Of interest, SOST/sclerostin expression is altered in certain pathogenic conditions, including osteoarthritis and rheumatic joint disease, and it is unclear whether sclerostin plays a protective role or whether sclerostin may mediate disease pathogenesis. Therefore, as anti-sclerostin antibodies are being developed for the treatment of osteoporosis, it is important to understand the functions of sclerostin beyond the regulation of bone formation. (C) 2016 Elsevier Inc. All rights reserved.
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PT J
AU Wang, CY
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Chiang, Shih-Wei
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Lin, Ming-Huang
Huang, Guo-Shu
TI Knee subchondral bone perfusion and its relationship to marrow fat and trabeculation on multi-parametric MRI and micro-CT in experimental CKD
SO SCIENTIFIC REPORTS
LA English
DT Article
ID chronic kidney-disease; quantitative-analysis; vascular axis; osteoarthritis; model; osteoporosis; images; quantification; progression; lesions
AB The pathogenesis of chronic kidney disease (CKD) is multifactorial. In the

progression of CKD arthropathy, arteriosclerosis may alter the knee subchondral bone marrow by altering blood flow through the bone vasculature. Herein, multi-parametric MRI assessment, including dynamic contrast enhanced magnetic resonance imaging (DCE-MRI), magnetic resonance spectroscopy (MRS), MRIT2*, contrast enhanced MR angiography (CE-MRA), and micro-CT were applied in a rodent nephrectomy model to: 1) investigate the blood perfusion of subchondral bone marrow and its relationship to fat water content and trabeculation pattern in CKD and 2) demonstrate the feasibility of using multi-parametric MRI parameters as imaging biomarkers to evaluate the disease's progression. Two groups of rats in our study underwent either 1) no intervention or 2) 5/6 nephrectomy. We found that in the CKD group, perfusion amplitude A and elimination constant k(ei) values were significantly decreased, and vascular permeability k(ep) was significantly increased. MRS showed that fat fraction (FF) was significantly lower, water fraction (WF) was significantly higher in the CKD group. Micro-CT showed a significant loss of trabecular bone. Knee subchondral bone marrow perfusion deficiency in experimental CKD may be associated with decreased fat content, increased water content, and sparse trabeculation.
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WC Multidisciplinary Sciences
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TI Differential analysis of genome-wide methylation and gene expression in mesenchymal stem cells of patients with fractures and osteoarthritis
SO EPIGENETICS
LA English
DT Article
DE Epigenetics; osteoarthritis; osteoporosis; stem cells; transcription factors
ID dna methylation; subchondral bone; osteoporosis; bmp-2; stimulation; mechanisms; cartilage; skeletal; regions; lineage
AB Insufficient activity of the bone-forming osteoblasts leads to low bone mass and predisposes to fragility fractures. The functional capacity of human mesenchymal stem cells (hMSCs), the precursors of osteoblasts, may be compromised in elderly individuals, in relation with the epigenetic changes associated with aging. However, the role of hMSCs in the pathogenesis of osteoporosis is still unclear. Therefore, we aimed to characterize the genome-wide methylation and gene expression signatures and the differentiation capacity of hMSCs from patients with hip fractures. We obtained hMSCs from the femoral heads of women undergoing hip replacement due to hip fractures and controls with hip osteoarthritis. DNA methylation was explored with the Infinium 450K bead array. Transcriptome analysis was done by RNA sequencing. The genomic analyses revealed that most differentially methylated loci were situated in genomic regions with enhancer activity, distant from gene bodies and promoters. These regions were associated with differentially expressed genes enriched in pathways related to hMSC growth and osteoblast differentiation. hMSCs from patients with fractures showed enhanced proliferation and upregulation of the osteogenic drivers RUNX2/OSX. Also, they showed some signs of accelerated methylation aging. When cultured in osteogenic medium, hMSCs from patients with fractures showed an impaired differentiation capacity, with reduced alkaline phosphatase activity and poor accumulation of a mineralized matrix. Our results point to 2 areas of potential interest for discovering new therapeutic targets for low bone mass disorders and bone regeneration: the mechanisms stimulating MSCs proliferation after fracture and those impairing their terminal differentiation.
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NR 34
TC 57
Z9 63
U1 0
U2 20
PU TAYLOR & FRANCIS INC
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J9 EPIGENETICS-US
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WC Biochemistry & Molecular Biology; Genetics & Heredity
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AU Park, KR
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AF Park, Kyung-Ran
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Hong, Jin Tae
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TI A novel organosulfur compound, thiacremonone, regulates RANKL-induced osteoclast differentiation
SO RSC ADVANCES
LA English
DT Article
ID osteoblastic differentiation; bone-resorption; mc3t3-e1 cells; c-fos; osteoporosis; activation; mineralization; pathways; receptor; system
AB The medicinal properties of functionally active organosulfur compounds have received great attention for applications in treating various diseases. Thiacremonone (2,4-dihydroxy-2,5-dimethyl-thiophene-3-one, THIA) is a novel organosulfur compound generated from high-temperature-high-pressure-treated garlic and has been reported to display pharmacological effects against various diseases. However, the role of THIA in bone resorbing cells was not reported. Herein, we have examined the pharmacological properties of THIA on osteoclast differentiation in primary cultured bone marrow macrophages (BMMs). Our results showed that THIA suppressed receptor activator of NF-kappa B ligand (RANKL)-induced gene expression (c-Fos and NF-ATc1) for osteoclast differentiation under no cytotoxicity condition. In addition, THIA significantly inhibited TRAP positive multinucleated osteoclasts and F-actin ring formation during RANKL-mediated osteoclastogenesis. However, in primary cultured calvarial pre-osteoblasts, THIA did not influence the cytotoxicity and osteoblast differentiation, as assessed from the alkaline phosphatase (ALP) activity and mineralized nodule formation. Our findings have suggested that THIA can be considered as a potential agent for the therapeutics of bone diseases such as osteoporosis, alveolar bone resorption, and osteoarthritis.
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AU Park, KR
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AF Park, Kyung-Ran
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TI RANKL-induced osteoclastogenesis is suppressed by 4-O-methylhonokiol in bone marrow-derived macrophages
SO ARCHIVES OF PHARMACAL RESEARCH
LA English
DT Article
DE Magnolia officinalis; 4-O-methylhonokiol; Osteoblast; Osteoclast; RANKL
ID osteoblastic differentiation; mc3t3-e1 cells; c-fos; osteoporosis; activation; receptor; mineralization; resorption; pathways; system
AB Magnolol, honokiol, and obovatol are well known bioactive constituents of the bark of Magnolia officinalis and have been reported to have beneficial effects in various diseases. We recently isolated a novel active compound,

4-O-methylhonokiol (4-O-MH) from the ethanol extract of M. officinalis, which was previously reported to have pharmacological effects including anti-inflammatory, anti-oxidative, and anti-aging activities. Here, we examined the pharmacological properties of 4-O-MH on osteoblast (bone-forming cells) and osteoclast (bone-resorbing cells) differentiation, and its underlying signaling pathways in primary cultured pre-osteoblasts and bone marrow macrophages. Our results showed that 4-O-MH did not affect cell viability in pre-osteoblasts and did not influence osteoblast differentiation and mineralized nodule formation, as assessed by alkaline phosphatase activity and Alizarin red staining. However, 4-O-MH significantly inhibited TRAP-positive multinuclear osteoclasts and F-actin ring formation during Receptor activator of NF-kappa B ligand (RANKL)-mediated osteoclastogenesis without cytotoxicity. In addition, 4-O-MH suppressed RANKL-induced critical factors (c-Fos, NF-ATc1, TRAP, and ITB3) for osteoclast differentiation and function. Furthermore, RANKL-mediated signaling, including ERK1/2, AKT, and NF-kB pathways was attenuated by 4-O-MH. Taken together, 4-O-MH has an inhibitory role in RANKL-mediated osteoclastogenesis but not osteoblast differentiation, and our findings also suggest that 4-O-MH is a potential therapeutic agent for bone-destructive diseases such as osteoporosis, alveolar bone resorption, and osteoarthritis.

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AU Sadat-Ali, M
Almomen, AW
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AF Sadat-Ali, Mir
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TI THE CURRENT ISSUES ON OSTEOPOROSIS AMONG MALE SAUDI ARABIANS
SO JOURNAL OF MENS HEALTH
LA English
DT Article
ID bone-mineral density; glucocorticoid-induced osteoporosis; hip fracture; vertebral fractures; older men; prevalence; prevention; women; risk; population
AB Background and Objectives Osteoporosis was reported to be common among the Saudi Arabian population. In the last decade there have been no reports related to the male osteoporosis in Saudi Arabian citizens. The objective of this study was to find the hospital-based prevalence of male osteoporosis and the associated diseases. Methodology This is a retrospective study between January 2014 and December 2016 in which all patients who were referred for DEXA (Dual Energy X-ray Absorptiometry) scan to the radiology department of the King Fahd Hospital of the University, AlKhobar were included. Patient's demographic data were collected from the medical records. Patients who were younger than 50 and those

who had a fragility fracture were excluded from the analysis. From the Picture Archiving and Communication System (PACS, Siemens AG, Erlangen, Germany) the readings of the DEXA were collected. Associated diseases of the patients were also extracted from the QuadruMed Data Base. The data was entered in the database and analyzed using SPSS Inc. version 19 and p value of <0.05 was considered significant. Results Four hundred and fifty-five patients had a DEXA scan during the study period. Three hundred and seventy-one (81.5%) were >= 50 years. The average was 65.33 +/- 9.85 years (range 50-97). On the basis of Spinal T score, 222 (59.8%) were osteoporotic with the Spinal T score of <-3.58 +/- 0.88, while, with Hip T score 120 (32.3%) were osteoporotic with T score of <-3.24 +/- 0.59. Thirty-six (9.7%) had a normal DEXA of spine and 74(19.9%) of patients had normal DEXA when the Hip T score was taken into consideration. Patients could be divided into 4 groups based on their diseases; they were on treatment for cardiac disease 106 (28.5%), Diabetes mellitus 95 (25.7%), osteoarthritis 141 (38%) and respiratory disease 29 (7.8%). Based on the Spinal T score osteoporosis was observed in 61/106 (57.5%) patients with cardiac disease, 62/95 (65.3%) in diabetics, in osteoarthritis 83/141 (58.9%) and 16/29 (55.1%) in patients with respiratory system diseases. Majority of the patients had vitamin D3 analysis and were most of the patients were in the deficiency range. From 222 (59.83%) patients who were diagnosed to have osteoporosis only 108 (48.64%) were on appropriate treatment for osteoporosis. Conclusion This study finds that the prevalence of osteoporosis in Saudi Arabian males is higher than in the western world and has increased in the last decade. The authors believe a more determined effort is needed to lower the screening age for osteoporosis and report the observations. This will allow a consensus to be reached regarding the frequency of osteoporosis in Saudi Arabian males and implement appropriate measures to limit its growth.
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AU Hernandez, CJ
AF Hernandez, Christopher J.
TI The Microbiome and Bone and Joint Disease
SO CURRENT RHEUMATOLOGY REPORTS
LA English
DT Article
DE Microbiome; Osteoarthritis; Osteoporosis; Bone; Inflammation
ID gut microbiota; inflammation; mice; osteoarthritis; arthritis; increases; intestine; severity; obesity; growth
AB Purpose of Review Changes in the constituents and activity of the microbiome have been associated with a number of conditions linked to bone and joint disease.

This review concentrates on ways in which the microbiome is known to influence osteoarthritis and osteoporosis. Recent Findings Animal studies have demonstrated that changes in the microbiome can mediate the effects of obesity on cartilage degeneration. Additionally, the microbiome influences the amount of the bone (bone quantity), as well as bone tissue material properties (bone quality). Early clinical findings support the effects of the microbiome on osteoporosis and osteoarthritis. Summary Although animal studies implicate the microbiome in the development of bone and joint disease, available results are limited and can be conflicting. Further investigation of the mechanisms linking from changes in the microbiome to alterations in the bones and joints are necessary.
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AU Zhang, YQ
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TI MicroRNA-221 is involved in the regulation of osteoporosis through regulates RUNX2 protein expression and osteoblast differentiation
SO AMERICAN JOURNAL OF TRANSLATIONAL RESEARCH
LA English
DT Article
DE Osteoporosis; osteoblast; osteogenic differentiation; microRNA-221; RUNX2
ID mesenchymal stem-cells; osteogenic differentiation; bone-development; pathway; cancer; pathogenesis; chondrocyte; activation; mir-221; mirnas
AB Introduction: MicroRNAs (miRNAs) has emerged as important factors in osteogenesis and chondrogenesis. This study aimed to determine whether miR-221 is involved in the regulation of osteoporosis and its underlying mechanism.

Methods: Total RNA was extracted from fresh femoral neck trabecular bone from women undergoing hip replacement due to either osteoporotic fracture (OP group, n = 12) or osteoarthritis in the absence of osteoporosis (Control group, n = 12). Gene expression was quantified using TaqMan quantitative RT-PCR assays and protein production was determined by western blot analysis. The role of miR-221 in osteoblast differentiation was identified by gain or loss function experiment. MiRNA targets were identified using bioinformatics and luciferase reporter assay. Results: MiR-221 was down-regulated in the osteoporotic samples compared with non-osteoporotic controls, and decreased in a C2C12 cell model of osteogenic differentiation. Overexpression of miR-221 resulted in a decrease in the osteogenic potential, as indicated by the reduced expression levels of key osteoblast markers, including osteocalcin (OC), alkaline phosphatase (ALP) and collagen, type I, a 1 (COL1A1), whereas inhibition of miR-221 promoted the activity of OC, ALP and COL1A1. Then bioinformatic analysis identified potential target sites of the miR-221 located in the 3' untranslated regions of RUNX2. Western blot analysis demonstrated that miR-221 inhibited RUNX2 gene expression. Furthermore, dual-luciferase reporter assays confirmed that RUNX2 was a direct target of miR-221. Rescue experiments showed that overexpression of RUNX2 significantly attenuated the effect of miR-221 on osteoblast markers providing strong evidence that miR-221 mediated the osteoblast differentiation by targeting RUNX2. Conclusions: Taken together, these data implied that miR-221 played an important part in osteoporosis through regulating RUNX2 expression and osteoblast differentiation.
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TI Non-guideline-recommended prescribing of proton pump inhibitors in the general population
SO CURRENT MEDICAL RESEARCH AND OPINION
LA English
DT Article
DE Guideline adherence; health services; prescriptions; proton pump inhibitors
ID inappropriate prescription; hospitalized-patients; predictors; patterns; overuse
AB Objectives: To determine the magnitude of non-guideline-recommended prescribing (NGRP) of proton pump inhibitors (PPIs) in the general population, its associated factors and expense. Methods: We undertook a cross-sectional observational study in three community pharmacies in a Spanish region in 2013 involving a total of 302 patients with a prescription for PPIs. The main variable was the NGRP of PPIs. Secondary variables were: gender, age, antidepressants, osteoporosis, osteoarthritis, prescription cost per month and total number of chronic diseases. The cost associated with NGRP was calculated. To evaluate the associated factors, a multivariate binary logistic regression model was constructed and the adjusted odds ratios (OR) were obtained. Results: NGRP was observed in 192 cases (63.6%). The average cost associated with NGRP per prescription was 3.24 euros per month. The factors significantly associated with NGRP (p<. 05) were: antidepressants (OR = 2.66, p =.001), osteoporosis (OR = 3.53, p =.001), osteoarthritis (OR = 3.57, p<. 001) and number of chronic diseases (OR = 0.73, p =.003). Conclusion: A novel approach was used to quantify the NGRP of PPIs in a

Spanish community, as well as the associated economic costs. Qualitative studies are needed to better understand the causes of NGRP of PPIs. This analysis will aid in designing interventions to minimize this problem. Limitations: Qualitative studies are needed to better understand the attitude of health professionals when prescribing PPIs.
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TI The role of calcium supplementation in healthy musculoskeletal ageing
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Review
DE Calcium supplementation; Fracture reduction; Myocardial infarction; Vitamin D supplementation
ID vitamin-d supplementation; bone-mineral density; calcium/vitamin-d supplementation; coronary-artery calcification; placebo-controlled trial; cardiovascular-disease; postmenopausal women; serum-calcium; older women; myocardial-infarction
AB The place of calcium supplementation, with or without concomitant vitamin D supplementation, has been much debated in terms of both efficacy and safety. There have been numerous trials and meta-analyses of supplementation for

fracture reduction, and associations with risk of myocardial infarction have been suggested in recent years. In this report, the product of an expert consensus meeting of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Foundation for Osteoporosis (IOF), we review the evidence for the value of calcium supplementation, with or without vitamin D supplementation, for healthy musculoskeletal ageing. We conclude that (1) calcium and vitamin D supplementation leads to a modest reduction in fracture risk, although population-level intervention has not been shown to be an effective public health strategy; (2) supplementation with calcium alone for fracture reduction is not supported by the literature; (3) side effects of calcium supplementation include renal stones and gastrointestinal symptoms; (4) vitamin D supplementation, rather than calcium supplementation, may reduce falls risk; and (5) assertions of increased cardiovascular risk consequent to calcium supplementation are not convincingly supported by current evidence. In conclusion, we recommend, on the basis of the current evidence, that calcium supplementation, with concomitant vitamin D supplementation, is supported for patients at high risk of calcium and vitamin D insufficiency, and in those who are receiving treatment for osteoporosis.
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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PT J
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AF More, Namdev
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TI Piezoelectric material - A promising approach for bone and cartilage regeneration
SO MEDICAL HYPOTHESES
LA English
DT Article
DE Piezoelectricity; Bone regeneration; Cartilage regeneration; Tissue engineering
ID mesenchymal stem-cells; articular-cartilage; growth-factors; morphogenetic proteins; calcium; microfracture; defects; matrix; repair; differentiation
AB Bone and cartilage are major weight-bearing connective tissues in human and possesses utmost vulnerability for degeneration. The potential causes are mechanical trauma, cancer and disease condition like osteoarthritis and osteoporosis, etc. The regeneration/repair is a challenging, since their complex structures and activities. Current treatment options comprise of auto graft, allograft, artificial bone sub-stituent, autologous chondrocyte implantation, mosaicplasty, marrow stimulation and tissue engineering. Were incompetent to overcome the problem like abandoned growth factor degradation, indistinct growth factor dose and lack of integrity and mechanical properties in regenerated tissues. Present, paper focuses on the novel hypothesis for regeneration of bone and cartilage by using piezoelectric smart property of scaffold material. (c) 2017 Elsevier Ltd. All rights reserved.
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TI Bone Mineral Density is Lower in Patients with Severe Knee Osteoarthritis and Attrition
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Osteoarthritis; Bone mineral density; Biomarkers; Attrition; Knee arthroplasty; Bone turnover markers
ID total hip-arthroplasty; vitamin-d status; biochemical markers; general-population; 2-year rsa; osteoporosis; epidemiology; prevalence; women; replacement
AB Bone quality is probably important for the survival of knee arthroplasty (KA), but little is known about systemic bone mineral density and bone turnover in patients prior to KA surgery. The aim of this study was to explore the prevalence of osteoporosis and bone turnover in relation to knee osteoarthritis (OA) grade in patients scheduled for KA surgery. Prospective preoperative evaluation of 450 patients (259 females) prior to KA between 2014 and 2016 with standing knee radiography, Dual-energy X-ray absorptiometry (DXA), biomarkers for bone turnover (CTX, P1NP), and vitamin D. Grading of knee OA was done with the Altman Atlas and Kellgren Lawrence (KL). Adjustments for age and BMI were made. The mean age was 67.9 years (range 39-94), and mean BMI was 28.8 (SD 4.8). The prevalence of osteoporosis was 9.6% (CI 95% 7.2; 12.7), while the proportion of patients with osteopenia was 36.0%. T score was similar between KL OA grade 3 and 4 ($p = 0.06$); however, T score was lower ($p = 0.02$) with the worst knee OA grade (attrition). The median serum Vitamin D level was 78.5 nmol/L (range 10-196), and there was no association between serum vitamin D and the grade of OA ($p > 0.88$). P1NP was significantly higher in KL grade 4 compared to KL grade 3 ($p = 0.03$), but there was no association between KL grade and CTX ($p = 0.21$). 10% had osteoporosis, which is similar to the age-matched background population. Bone mineral density was lower with severe knee osteoarthritis (attrition), and P1NP was higher with worse osteoarthritis grading.
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PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
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Lee, Joon Woo
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Kang, Heung Sik
TI Metal Artifact Reduction for Orthopedic Implants (O-MAR): Usefulness in CT Evaluation of Reverse Total Shoulder Arthroplasty
SO AMERICAN JOURNAL OF ROENTGENOLOGY
LA English
DT Article
DE arthroplasty; CT; metal artifact; prosthesis; shoulder
ID density; osteoarthritis; osteoporosis; strength; tool
AB OBJECTIVE. The objective of this study is to evaluate the effect of the metal artifact reduction algorithm for orthopedic implants (O-MAR) on CT image quality for patients with reverse total shoulder arthroplasty (RTSA), with emphasis placed on the evaluation of bone in the vicinity of prostheses. MATERIALS AND METHODS. Sixty-five patients who underwent CT scanning after RTSA were enrolled in the study. Two radiologists analyzed the images reconstructed with filtered back projection (FBP) with or without O-MAR processing. Images were evaluated to determine the degree of streaking artifacts, the confidence in depicting various structures around the prosthesis, and the presence of pseudolesions. The mean CT number and SD of the selected ROIs placed in the greater tuberosity, glenoid bone, and deltoid muscle were recorded. For measurements from the greater tuberosity and glenoid bone, the frequency with which the measurement met the typical CT number of bone was calculated. RESULTS. O-MAR images showed less metal streak artifact and noise and provided better visualization of the axillary neurovascular bundle compared with FBP images, with a statistically significant difference ($p < 0.001$ for all). FBP images were found to be statistically significantly better than O-MAR images, offering better visualization of bone cortex, bone trabeculae, and the bone-prosthesis interface ($p < 0.001$ for all). Scapular pseudonotching was observed on 4.6% of FBP images and 36.9% of O-MAR images. The pseudocemented appearance was noted on 47.7% of O-MAR images but was not seen on FBP images. CONCLUSION. The use of O-MAR improved CT image quality for patients with RTSA in the aspect of metal artifact reduction and soft-tissue profile. However, O-MAR tends to degrade depiction of the bone trabeculae and

bone cortex and generate new artifacts, including a pseudocemented appearance and scapular pseudonotching.
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PU AMER ROENTGEN RAY SOC
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PA 1891 PRESTON WHITE DR, SUBSCRIPTION FULFILLMENT, RESTON, VA 22091 USA
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J9 AM J ROENTGENOL
JI Am. J. Roentgenol.
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BP 860
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DI 10.2214/AJR.16.17684
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WC Radiology, Nuclear Medicine & Medical Imaging
SC Radiology, Nuclear Medicine & Medical Imaging
GA FH8JM
UT WOS:000411440600031
PM 28796543
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PT J
AU Chen, FR
Chen, RS
Liu, HY
Sun, RP
Huang, JM
Huang, ZY
Jian, GJ
AF Chen, Fengrong
Chen, Ruisong
Liu, Haoyuan
Sun, Rupeng
Huang, Jianming
Huang, Zheyuan
Jian, Guojian
TI BMP-7 ameliorates cobalt alloy particle-induced inflammation by suppressing Th17 responses

SO APMIS
LA English
DT Article
DE OP-1; Th17; total joint arthroplasty
ID periprosthetic osteolysis; autoimmune arthritis; cells; macrophages; wear; hip; metal; replacements; activate
AB Metal wear debris has been shown to activate an aseptic osteolytic process that causes failure in total joint arthroplasty (TJA). This osteolysis is characterized by a proinflammatory, self-propagating immune response involving primarily macrophages, dendritic cells, and activated osteoclasts, as well as T cells and B cells. The human bone morphogenic protein (BMP)-7, on the other hand, was shown to promote osteoblast survival, and reversed the downregulation of anabolic Smad proteins and Runx2 following cobalt injury. Therefore, we investigated the effect and mechanism of BMP-7 on the proinflammatory immune responses in osteoarthritis patients with previous TJA. Cobalt-treated monocytes/macrophages presented significantly elevated levels of interleukin 6 (IL-6) and tumor necrosis factor (TNF), both of which were suppressed by the addition of exogenous BMP-7. In patients with TJA, the serum BMP-7 level was inversely associated with the level of IL-6 and TNF secreted by monocytes/macrophages. Cobalt-treated monocytes/macrophages effectively supported Th17 inflammation, by an IL-6-dependent but not TNF-dependent mechanism. BMP-7, however, significantly suppressed cobalt-induced Th17 inflammation. In patients with TJA, the risk of osteolysis development was positively associated with the frequency of Th17 cells and negatively associated with the level of BMP-7. Together, these results demonstrated that BMP-7 could serve as a therapeutic agent in treating patients with metal wear debris-induced inflammation.
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NR 28
TC 6
Z9 6
U1 0
U2 3
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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EI 1600-0463
J9 APMIS
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WC Immunology; Microbiology; Pathology
SC Immunology; Microbiology; Pathology
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ER

PT J
AU Xu, J
Xiao, J
Shi, ZJ
AF Xu, Jie
Xiao, Jun
Shi, Zhan Jun
TI Correlation between age-related serum follicle stimulating hormone levels and osteoarthritis in postmenopausal women
SO BIOMEDICAL RESEARCH-INDIA
LA English
DT Article
DE FSH; Osteoarthritis; Menopause
ID bone turnover; fsh; osteoporosis; association; markers; risk; men
AB Objective: To study the changes of age-related serum Follicle Stimulating Hormone (FSH) level and Xray of knee joint and the relationship between FSH and postmenopausal knee osteoarthritis in postmenopausal women. Methods: 248 postmenopausal women aged over 50 y were randomly selected from Shandong Provincial Hospital affiliated with Shandong University after excluding patients with related diseases and medication history that affected bone metabolism and the that long-term used bone metabolism drugs. The levels of serum FSH, Luteinizing Hormone (LH) and Estradiol (E2) were measured by radioimmunoassay, and knee joint by X-ray. The changes of serum FSH, LH, E2 with age were analysed. The difference of FSH level between patients with postmenopausal osteoarthritis and control group was compared. Results: The serum FSH and LH levels increased with age, reaching a peak around 60 y old, and then decreased with age. Serum E2 levels decreased with age after menopause. Serum FSH and LH levels in patients with knee osteoarthritis were significantly higher than those in the control group ($P<0.05$), while E2 was significantly lower ($P<0.05$). Conclusion: This work shows the changes of FSH, LH and E2 in the postmenopausal women and indicates that FSH level may have an effect on the development of osteoarthritis.
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NR 18
TC 1
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U2 4
PU ALLIED ACAD
PI LONDON
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WC Engineering, Biomedical; Medicine, Research & Experimental
SC Engineering; Research & Experimental Medicine
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ER

PT J
AU Melcer, T
Walker, J
Bhatnagar, V
Richard, E
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AF Melcer, Ted
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TI A Comparison of Four-Year Health Outcomes following Combat Amputation and Limb Salvage
SO PLOS ONE
LA English
DT Article
ID injury severity score; military; iraq; afghanistan; trauma; prevalence; veterans
AB Little research has described the long-term health outcomes of patients who had combatrelated amputations or leg-threatening injuries. We conducted retrospective analysis of Department of Defense and Department of Veterans Affairs health data for lower extremity combat-injured patients with (1) unilateral amputation within 90 days postinjury (early amputation, n = 440), (2) unilateral amputation more than 90 days postinjury (late amputation, n = 78), or (3) leg-threatening injuries without amputation (limb salvage, n = 107). Patient medical records were analyzed for four years postinjury. After adjusting for group differences, early amputation was generally associated with a lower or similar prevalence for adverse physical and psychological diagnoses (e. g., pain, osteoarthritis, posttraumatic stress disorder) versus late amputation and/or limb salvage. By contrast, early amputation was associated with an increased likelihood of osteoporosis during the first year postinjury. The prevalence of posttraumatic stress disorder increased for all patient groups over four years postinjury,

particularly in the second year. The different clinical outcomes among combat extremity injured patients treated with early amputation, late amputation, or limb salvage highlight their different healthcare requirements. These findings can inform and optimize the specific treatment pathways that address the physical and psychological healthcare needs of such patients over time.
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NR 43
TC 32
Z9 37
U1 0
U2 4
PU PUBLIC LIBRARY SCIENCE
PI SAN FRANCISCO

PA 1160 BATTERY STREET, STE 100, SAN FRANCISCO, CA 94111 USA
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J9 PLOS ONE
JI PLoS One
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
GA EN7FK
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PT J
AU Roddy, E
Muller, S
Paskins, Z
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AF Roddy, Edward
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TI Incident acute pseudogout and prior bisphosphonate use: Matched case-control study in the UK-Clinical Practice Research Datalink
SO MEDICINE
LA English
DT Article
DE acute pseudogout; bisphosphonates; calcium pyrophosphate crystal deposition; case-control study; primary care
ID practice research database; american-society; vascular events; task-force; bone; chondrocalcinosis; risk; gout; osteoarthritis; epidemiology
AB Oral bisphosphonates are the most commonly used drugs to treat

postmenopausal osteoporosis. Acute pseudogout is anecdotally reported to occur following bisphosphonate initiation but empirical data are lacking. We investigated whether treatment with oral bisphosphonates is a risk factor for incident acute pseudogout. A matched case-control study was undertaken using data from the UK-Clinical Practice Research Datalink. Adults who consulted for incident acute pseudogout between 1987 and 2012 were each matched for gender, age at pseudogout diagnosis, and general practice to up to 4 control subjects without pseudogout. The exposure of interest was a prescription for an oral bisphosphonate issued within the 60-day period prior to the date of incident acute pseudogout. Associations between incident acute pseudogout and prior bisphosphonate prescription were examined using conditional logistic regression, adjusting for hyperparathyroidism, osteoarthritis, rheumatoid arthritis, hemochromatosis, hypophosphatasia, and prescriptions for diuretics and oral corticosteroids. Two thousand eleven acute pseudogout cases were compared with 8013 matched controls without acute pseudogout (mean age [standard deviation] 72 years [14]; 52% male). One hundred twenty-three cases (6.1%) had received an oral bisphosphonate prescription in the 60-day exposure period compared with 305 controls (3.8%) (adjusted incidence rate ratio [IRR] 1.33; 95% confidence interval [CI] 1.05-1.69). This association was stronger in females (adjusted IRR 1.49; 95% CI 1.15-1.94) and was nonsignificant in males (0.83; 0.48-1.44). Incident acute pseudogout was associated with prescription of an oral bisphosphonate in the preceding 60 days. Prescribers should be aware of acute pseudogout as a possible side effect of bisphosphonate treatment. Further research is needed to explore the risks conferred by different bisphosphonates and the mechanism underlying this association.
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FU National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands; NIHR School for Primary Care Research; NIHR Research Professorship; NIHR; National Institute for Health Research [RP_2014-04-026, SPCR-023, SPCR-004] Funding Source: researchfish
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NR 37

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Z9 19
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PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0025-7974
EI 1536-5964
J9 MEDICINE
JI Medicine (Baltimore)
PD MAR 15
PY 2017
VL 96
IS 12
BP
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DI 10.1097/MD.0000000000006177
PG 6
WC Medicine, General & Internal
SC General & Internal Medicine
GA EP8IT
UT WOS:000397619800006
PM 28328803
DA 2026-02-10
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PT J
AU Jenkins, T
Katsamenis, OL
Andriotis, OG
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Dunlop, D. G.

Oreffo, R. O. C.
Cooper, C.
Harvey, N. C.
Thurner, P. J.
TI The inferomedial femoral neck is compromised by age but not disease: Fracture toughness and the multifactorial mechanisms comprising reference point microindentation
SO JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS
LA English
DT Article
DE Bone quality; Femoral Neck; Fracture Toughness; Reference point indentation; Osteoporosis; Osteoarthritis
ID human cortical bone; in-vivo; indentation fracture; subchondral bone; mineral density; hard tissue; osteoarthritis; nanoindentation; osteoporosis; damage
AB The influence of ageing on the fracture mechanics of cortical bone tissue is well documented, though little is known about if and how related material properties are further affected in two of the most prominent musculoskeletal diseases, osteoporosis and osteoarthritis (OA). The femoral neck, in close proximity to the most pertinent osteoporotic fracture site and near the hip joint affected by osteoarthritis, is a site of particular interest for investigation. We have recently shown that Reference Point micro-Indentation (RPI) detects differences between cortical bone from the femoral neck of healthy, osteoporotic fractured and osteoarthritic hip replacement patients. RPI is a new technique with potential for in vivo bone quality assessment. However, interpretation of RPI results is limited because the specific changes in bone properties with pathology are not well understood and, further, because it is not conclusive what properties are being assessed by RPI. Here, we investigate whether the differences previously detected between healthy and diseased cortical bone from the femoral neck might reflect changes in fracture toughness. Together with this, we investigate which additional properties are reflected in RPI measures. RPI (using the Biodent device) and fracture toughness tests were conducted on samples from the inferomedial neck of bone resected from donors with: OA (41 samples from 15 donors), osteoporosis (48 samples from 14 donors) and non age-matched cadaveric controls (37 samples from 10 donoros) with no history of bone disease. Further, a subset of indented samples were imaged using micro-computed tomography (3 osteoporotic and 4 control samples each from different donors) as well as fluorescence microscopy in combination with serial sectioning after basic fuchsin staining (7 osteoporotic and 5 control samples from 5 osteoporotic and 5 control donors). In this study, the bulk indentation and fracture resistance properties of the inferomedial femoral neck in osteoporotic fracture, severe OA and control bone were comparable ($p > 0.05$ for fracture properties and < 10% difference for indentation) but fracture toughness reduced with advancing age (7.0% per decade, $r = 0.36$, $p = 0.029$). Further, RPI properties (in particular, the indentation distance increase, IDI) showed partial correlation with fracture toughness ($r = -0.40$, $p = 0.023$) or derived elastic modulus

(r = -0.40, p = 0.023). Multimodal indent imaging revealed evidence of toughening mechanisms (i.e. crack deflection, bridging and microcracking), elastoplastic response (in terms of the non-conical imprint shape and presence of pile-up) and correlation of RPI with damage extent (up to r = 0.79, p = 0.034) and indent size (up to r = 0.82, p < 0.001). Therefore, crack resistance, deformation resistance and, additionally, micro-structure (porosity: r = 0.93, p = 0.002 as well as pore proximity: r = -0.55, p = 0.027 for correlation with IDI) are all contributory to RPI. Consequently, it becomes clear that RPI measures represent a multitude of properties, various aspects of bone quality, but are not necessarily strongly correlated to a single mechanical property. In addition, osteoporosis or osteoarthritis do not seem to further influence fracture toughness of the inferomedial femoral neck beyond natural ageing. Since bone is highly heterogeneous, whether this finding can be extended to the whole femoral neck or whether it also holds true for other femoral neck quadrants or other material properties remains to be shown.
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TI To assess differential features of marrow adiposity between postmenopausal women with osteoarthritis and osteoporosis using water/fat MRI
SO MENOPAUSE-THE JOURNAL OF THE NORTH AMERICAN MENOPAUSE SOCIETY
LA English
DT Article
DE Marrow fat; Osteoarthritis; Osteoporosis; Water/fat MRI
ID bone-mineral density; mesenchymal stem-cells; trabecular bone; fat-content; stromal cells; hip; quantification; spectroscopy; leptin; fracture
AB Objective: To assess the differential features of marrow adiposity between osteoarthritis (OA) and osteoporosis (OP) in postmenopausal women using water/fat MRI. Methods: This cross-sectional study included 97 postmenopausal women (OA [n = 25], OA + osteopenia [n = 27], OA + OP [n = 23], and OP groups [n = 22]). Water/fat MRI, dual-energy x-ray absorptiometry and biochemical analysis were performed to assess vertebral marrow fat fraction, bone mineral density, and bone biomarkers, respectively. Harris Hip Score was recorded to evaluate hip function. Results: There were significant differences in marrow fat content among the OA, OA + osteopenia, and OA + OP groups, between OP and OA participants with normal bone mass or osteopenia (all $P < 0.05$); no significant difference was observed between OA + OP and OP groups. Serum levels of leptin and beta-Crosslaps in OA with normal bone mass and osteopenic OA groups were higher than in OP group. Marrow fat fraction was inversely correlated with Harris Hip Score ($r = -0.371$, $P = 0.013$), bone mineral density ($r = -0.554$, $P = 0.009$) and leptin levels ($r = -0.610$, $P < 0.001$). In multivariate regression analysis, marrow fat fraction was found to have a consistent and unchanged inverse association with leptin levels (S beta = -0.311, $P = 0.002$) and bone mineral density (S beta = -0.265, $P = 0.006$) after adjusting for age, years since menopause, and body mass index. Conclusions: Postmenopausal OA with OP have a phenotype with higher marrow adiposity. OA and OP could coexist, for the presence of a specific subgroup of OA with increased marrow fat accumulation and high risk of developing OP.
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TI Bone Morphogenetic Proteins and myostatin pathways: key mediator of human sarcopenia
SO JOURNAL OF TRANSLATIONAL MEDICINE
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DT Article
ID fragility fractures; italy extension; osteoporosis; regulator
AB Background: Sarcopenia, osteoporosis and osteoarthritis are the most frequent musculoskeletal disorders affecting older people. The main aim of this study was to test the hypothesis that the balance between BMPs and myostatin pathways regulates the age-related muscle degeneration in OP and OA patients. To this end, we investigated the relationship among the expression of BMP-2/4-7, myostatin and phosphorylated Smads1-5-8 and the muscle quality, evaluated in term of fibers atrophy and satellite cells activity. Methods: In this retrospective study, we collected 123 biopsies of vastus lateralis: 48 biopsies from patients who underwent hip arthroplasty for subcapital fractures of the femur (OP), 55 biopsies from patients who underwent hip arthroplasty for osteoarthritis (OA) and 20 biopsies from patients who underwent hip arthroplasty for high-energy hip fractures (CTRL). Muscle biopsies were fixed in 4% paraformaldehyde and paraffin embedded. Serial sections were used for morphometrical and immunohistochemical analysis (BMP/2/4-7, myostatin, Smads1-5-8, Pax7 and myogenin). In addition, 1 mm(3) of muscle tissue of each patient was embedded in epon for ultrastructural study. Results: Morphometric data indicated an increase of the number of atrophic fibers in OP patients compare to OA. In line with these data, we found an high regenerative potential in muscle tissues of OA patients due to the significant amount of both Pax7 and myogenin positive satellite cells detected in OA group. In addition, our data showed the decrease of BMP2/4 and -7 expression in OP patients compared to both OA group and CTRL. Conversely, OP patients were characterized by high levels of myostatin expression. A different expression profile

was also found for phosphorylated Smad1-5-8 between OP and OA patients. In particular, OP patients showed a low number of positive phosphorylated Smad1-5-8 nuclei. Conclusion: The identification of molecular pathways involved in the pathogenesis of sarcopenia open new prospective for the development of drugs able to prevent/treat the muscle impairment that occur in elderly. Results here reported, highlighting the role of BMPs and myostatin pathways in physio-pathogenesis of human sarcopenia, allow us to propose human recombinant BMP-2/7 and anti-myostatin antibodies as a possible therapeutic option for the sarcopenia.
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NR 27
TC 34
Z9 45
U1 0
U2 13
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 J TRANSL MED
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WC Medicine, Research & Experimental
SC Research & Experimental Medicine
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AU McGuigan, FE
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AF McGuigan, Fiona E.
Bartosch, Patrik
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TI Musculoskeletal health and frailty
SO BEST PRACTICE & RESEARCH IN CLINICAL RHEUMATOLOGY
LA English
DT Article
DE Frailty; Index; Fracture; Osteoarthritis; Elderly
ID quality-of-life; older-adults; vitamin-d; hip fracture; pre-frail; physical frailty; heart-failure; elderly-women; risk-factors; mortality
AB Frailty is a consequence of advanced aging, where the frailty phenotype tries to capture overall decline in health. Frailty involves multiple physiological systems that are intrinsically interrelated and with highly complex interactions. Frailty is closely linked to musculoskeletal health; musculoskeletal functioning is a key component in quantifying frailty, while at the same time, frailty is associated with the most common age-related musculoskeletal conditions: osteoporosis, fractures, falls, osteoarthritis, and spinal conditions. Beyond that, frailty includes additional physical domains such as nutrition and energy, psychological, and social factors. Despite its recognized role in aging health, there is still a lack of consensus on a core set of variables and how to best define clinically relevant thresholds. This would be of utmost importance for additional use to evaluate many aspects associated with musculoskeletal health, progression and personalized interventions, and rehabilitation. (C) 2017 Elsevier Ltd. All rights reserved.
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Z9 42
U1 0
U2 18
PU ELSEVIER SCI LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
SN 1521-6942
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J9 BEST PRACT RES CL RH
JI Best Pract. Res. Clin. Rheumatol.
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BP 145
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WC Rheumatology
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PT J
AU Schwab, P
Dhamane, AD
Hopson, SD
Moretz, C
Annavarapu, S
Burslem, K
Renda, A
Kaila, S
AF Schwab, Phil
Dhamane, Amol D.
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Moretz, Chad
Annavarapu, Srinivas
Burslem, Kate
Renda, Andrew
Kaila, Shuchita
TI Impact of comorbid conditions in COPD patients on health care resource utilization and costs in a predominantly Medicare population
SO INTERNATIONAL JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE
LA English
DT Article
DE COPD; comorbidities; utilization; cost; database; Medicare
ID obstructive pulmonary-disease; economic burden; united-states; depression; prevalence; anxiety
AB Background: Patients with chronic obstructive pulmonary disease (COPD) often have multiple underlying comorbidities, which may lead to increased health care resource utilization (HCRU) and costs. Objective: To describe the comorbidity profiles of COPD patients and examine the associations between the presence of comorbidities and HCRU or health care costs. Methods: A retrospective cohort study utilizing data from a large US national health plan with a predominantly Medicare population was conducted. COPD patients aged 40-89 years and continuously enrolled for 12 months prior to and 24 months after the first COPD diagnosis during the period of January 01, 2009, through December 31, 2010, were selected. Eleven comorbidities of interest were identified 12 months prior through 12 months after COPD diagnosis. All-cause and COPD-related hospitalizations and costs were assessed 24 months after diagnosis, and the associations with comorbidities were determined using multivariate statistical models. Results: Ninety-two percent of 52,643 COPD patients identified had at least one of the 11 comorbidities. Congestive heart failure (CHF), coronary artery disease, and cerebrovascular disease (CVA) had the strongest associations with all-cause

hospitalizations (mean ratio: 1.56, 1.32, and 1.30, respectively; P<0.0001); other comorbidities examined had moderate associations. CHF, anxiety, and sleep apnea had the strongest associations with COPD-related hospitalizations (mean ratio: 2.01, 1.32, and 1.21, respectively; P<0.0001); other comorbidities examined (except chronic kidney disease [CKD], obesity, and osteoarthritis) had moderate associations. All comorbidities assessed (except obesity and CKD) were associated with higher all-cause costs (mean ratio range: 1.07-1.54, P<0.0001). CHF, sleep apnea, anxiety, and osteoporosis were associated with higher COPD-related costs (mean ratio range: 1.08-1.67, P<0.0001), while CVA, CKD, obesity, osteoarthritis, and type 2 diabetes were associated with lower COPD-related costs. Conclusion: This study confirms that specific comorbidities among COPD patients add significant burden with higher HCRU and costs compared to patients without these comorbidities. Payers may use this information to develop tailored therapeutic interventions for improved management of patients with specific comorbidities.
C1 [Schwab, Phil; Hopson, Sari D.; Moretz, Chad; Annavarapu, Srinivas] Comprehens Hlth Insights Inc, 515 West Market St, Louisville, KY 40202 USA.
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FU Humana Inc.; Boehringer Ingelheim Pharmaceuticals Inc.
CR 26Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2015, GLOB STRAT DIAGN MAN, V0, P0
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NR 31
TC 55
Z9 66
U1 0
U2 11
PU DOVE MEDICAL PRESS LTD
PI ALBANY
PA PO BOX 300-008, ALBANY, AUCKLAND 0752, NEW ZEALAND
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J9 INT J CHRONIC OBSTR
JI Int. J. Chronic Obstr. Pulm. Dis.
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IS
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WC Respiratory System
SC Respiratory System
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PT J
AU Karagülle, M
Kardes, S
Karagülle, MZ
AF Karagulle, Mine
Kardes, Sinan
Karagulle, Mufit Zeki
TI Real-life effectiveness of spa therapy in rheumatic and musculoskeletal diseases: a retrospective study of 819 patients
SO INTERNATIONAL JOURNAL OF BIOMETEOROLOGY
LA English
DT Article
DE Spa therapy; Balneotherapy; Rheumatic diseases; Musculoskeletal disorders
ID low-back-pain; randomized controlled-trial; quality-of-life; fibromyalgia impact questionnaire; shoulder disability questionnaire; health-assessment questionnaire; 4-week rehabilitation program; chronic neck pain; mud-bath therapy; knee osteoarthritis
AB The objective of this study is to determine the use and efficacy of spa therapy in patients with a wide spectrum of rheumatic and musculoskeletal diseases under real-life clinical practice circumstances. In this retrospective observational study at the Medical Ecology and Hydroclimatology Department of Istanbul Faculty of Medicine, the records of all adult patients with rheumatic and musculoskeletal diseases who were prescribed a spa therapy in various health resorts in Turkey between 2002 and 2012 were analyzed. Patients sojourned to and stayed at a health resort and followed a usual 2-week course of spa therapy. The patients were examined within a week before and after the spa therapy at the department by the physicians and outcome measures were pain intensity (visual analog scale, VAS), patient's general evaluation (VAS), physician's general evaluation (VAS), Health Assessment Questionnaire (HAQ), Lequesne's Functional Index (LFI), Western Ontario and McMaster Universities Index (WOMAC), Waddell Index (WI), Neck Pain and Disability Scale (NPDS), Shoulder Disability Questionnaire (SDQ), Fibromyalgia Impact Questionnaire (FIQ), and Beck's Depression Inventory (BDI). In total, 819 patients were included in the analysis. The diagnoses were 536 osteoarthritis; 115 fibromyalgia; 50 lumbar disc herniation; 34 cervical disc herniation; 23 nonspecific low back pain; 22 ankylosing spondylitis; 16 rheumatoid arthritis; 9 rotator cuff tendinitis; and 14 other conditions/diseases including scoliosis, stenosing flexor tenosynovitis, congenital hip dislocation in adult, Beh double dagger et's disease, de Quervain tendinopathy, psoriatic arthritis, osteoporosis, fracture rehabilitation, and diffuse idiopathic skeletal hyperostosis. Statistically significant decrease in pain scores was found in all patients except hip osteoarthritis ($p = 0.063$) and rheumatoid arthritis ($p = 0.134$) subgroups; and statistically significant

improvement in function in all patients except hip osteoarthritis (p = 0.068), rheumatoid arthritis (p = 0.111), and rotator cuff tendinitis (p = 0.078) subgroups. In daily clinical practice, spa therapy is prescribed and practiced mainly for osteoarthritis, then fibromyalgia, lumbar/cervical disc herniation, and nonspecific low back pain; and less for ankylosing spondylitis, rheumatoid arthritis, and rotator cuff tendinitis. The study results suggest that real-life spa therapy may be effective in a variety of rheumatic and musculoskeletal diseases by improving pain and function.
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TI Beneficial Effects and Toxicity Studies of Xian-ling-gu-bao on Bone Metabolism in Ovariectomized Rats
SO FRONTIERS IN PHARMACOLOGY
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DT Article
DE XLGB; ovariectomized rats; osteoporosis; toxicity test; OPG/RANKL
ID osteoporosis; zebrafish; mice; mass
AB Xian-ling-gu-bao (XLGB) is a well-known patented traditional Chinese prescription widely used to treat osteoporosis, osteoarthritis, aseptic bone necrosis, or climacteric syndrome. However, recent reports have suggested that XLGB may cause liver injury in humans. In the present study, we aimed to evaluate the efficacy of XLGB in the prevention of osteoporosis in the zebrafish and ovariectomized (OVX) rats, both of which have been used as osteoporosis models. The safety of XLGB after long-term administration to OVX rats was also assessed. OVX rats were administered by oral gavage 270 mg/kg (recommended daily dose), 1350 mg/kg, and 1800 mg/kg of XLGB for 26 weeks. Bone mineral density, relative bone surface to bone volume, relative bone volume to total volume, trabecular number, mean trabecular thickness, and mean trabecular spacing in OVX rats were examined at the end of the 26-week dosing period. Additionally, OPG and RANKL expression in the femur were determined by western blot and immunohistochemical staining. To evaluate the safety of XLGB, body weight, hematology, serum biochemistry markers related to toxicology, and organ histopathology were determined in each group of OVX rats. Conversely, the zebrafish was treated with prednisolone to induce osteoporosis in the embryo. Disodium etidronate was used as a treatment control. XLGB was shown to be effective in preventing osteoporosis in both the OVX rats and the prednisolone-treated zebrafish. Similarly, XLGB increased OPG protein and decreased RANKL protein in OVX rats. Interestingly, no obvious toxicity was observed in the heart, liver, kidney, small intestine, or stomach at dosages of up to

1800 mg/kg after treating the OVX rats for 26 weeks. XLGB was shown to be very effective in treating osteoporosis in OVX rats. No obvious toxicity or adverse effects developed in OVX rats at dosages up to 1800 mg/kg, which is equivalent to six times the daily-recommended dose. Therefore, XLGB should be considered a good option for the treatment of post-menopausal osteoporosis.
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TI Multimorbidity in Middle-Aged Adults with Cerebral Palsy
SO AMERICAN JOURNAL OF MEDICINE
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DT Article
DE Cerebral palsy; Diabetes; Hypertension; Multimorbidity; Obesity; Osteoporosis
ID older-adults; musculoskeletal; mobility; health; risk; sex
AB OBJECTIVE: Individuals with cerebral palsy have less lean body mass, greater relative adiposity, and lower fitness and physical activity participation, and yet the prevalence of age-related multimorbidity in this population has yet to be established. The study objective was to examine the prevalence of lifestyle-related chronic conditions and multimorbidity in a sample of middle-aged adults with cerebral palsy. METHODS: A clinic-based sample of middle-aged adults with cerebral palsy was examined using Electronic Medical Records Search Engine software. Our cohort included 435 individuals aged 40 to 60 years, with an International Classification of Diseases, Clinical Modification, 9th and 10th Revisions Diagnosis Code for cerebral palsy. Prevalence of 12 chronic conditions was evaluated, including existing diagnoses or historical record of osteopenia/osteoporosis, myocardial infarction, stroke, coronary artery disease, impaired glucose tolerance/type 2 diabetes, other cardiovascular conditions, rheumatoid arthritis, osteoarthritis, asthma, emphysema, prehypertension/hypertension, and hyperlipidemia. Multivariate logistic models were used to estimate multimorbidity (ie, >= 2 chronic conditions), adjusting for age, sex, smoking status, obesity, and Gross Motor Function Classification System (GMFCS). RESULTS: There were 137 unique multimorbidity combinations. Multimorbidity was significantly more prevalent among obese versus nonobese individuals for both GMFCS I-III (75.8% vs 53.6%) and GMFCS IV-V (79.0% vs 64.2%), but was also significantly higher in nonobese individuals with GMFCS IV-V (64.2%) compared with nonobese individuals with GMFCS I-III (53.6%). Both the obesity status (odds ratio, 2.20; 95% confidence interval, 1.32-2.79) and the GMFCS IV-V category (odds ratio, 1.81; 95% confidence interval, 1.32-3.68) were independently associated with multimorbidity. CONCLUSIONS: Middle-aged adults with cerebral palsy have high estimates of multimorbidity; both obesity and higher GMFCS levels are independently associated with greater risk. (C) 2017 Elsevier Inc. All rights reserved.

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PT J
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TI Vitamin D status correction in Saudi Arabia: an experts' consensus under the auspices of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases (ESCEO)
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Vitamin D; Saudi Arabia; ESCEO; Recommendations; Consensus
ID 25-hydroxyvitamin d concentrations; d deficiency; d supplementation; middle-east; recommendations; population; management; women; risk; prevention
AB Background Vitamin D deficiency is common in the Middle East and in Saudi Arabia, in particular. While several international recommendations on the management of vitamin D deficiency have been documented and practiced globally, these recommendations should be adapted to the conditions of the Middle Eastern region. To address this challenge, the Prince Mutaib Chair for Biomarkers of Osteoporosis (PMCO) in King Saud University (KSU), Riyadh, KSA,

together with local experts and in cooperation with the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO), organized a panel that formulated unified recommendations in the diagnosis and treatment of vitamin D deficiency in the region. Methods The selection of local and international experts commenced during the 2nd International Vitamin D Symposium conducted in Riyadh, Saudi Arabia, last January 20-21, 2016. Reviews of the most recent literature were done, and face-to-face meetings were conducted for revisions and final recommendations. Results: Vitamin D sufficiency is defined as circulating serum 25(OH) D >= 50 nmol (>= 20 ng/ml) for the general population and vitamin D adequacy as serum 25(OH) D >75 nmol/L l (>30 ng/ml) for the frail and osteoporotic elderly. Despite overwhelming prevalence of vitamin D deficiency, universal screening is not recommended. Recommendations for the general population, children, pregnant/lactating women, postmenopausal women, the elderly, and those with subsequent metabolic diseases were provided. Results Vitamin D sufficiency is defined as circulating serum 25(OH) D >= 50 nmol (>= 20 ng/ml) for the general population and vitamin D adequacy as serum 25(OH) D > 75 nmol/L l (>30 ng/ml) for the frail and osteoporotic elderly. Despite overwhelming prevalence of vitamin D deficiency, universal screening is not recommended. Recommendations for the general population, children, pregnant/lactating women, post-menopausal women, the elderly, and those with subsequent metabolic diseases were provided. Conclusion Vitamin D supplementation/correction is advised in all persons whose serum 25(OH) D falls below 50 nmol/l (20 ng/ml), and achieving a target of 75 nmol/l (30 ng/ml) is particularly suited for frail, osteoporotic, and older patients. Conducting well-designed clinical trials in the region that will address economic implications and investigations on the treatment persistence and compliance to vitamin D treatment in the region are encouraged.
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AU Kleiber Balderrama, C
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AF Kleiber Balderrama, Crystal
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TI Calcium Pyrophosphate Deposition Disease and Associated Medical Comorbidities: A National Cross-Sectional Study of US Veterans
SO ARTHRITIS CARE & RESEARCH
LA English
DT Article
ID dihydrate crystal deposition; monosodium urate crystals; proton pump inhibitors; rheumatoid-arthritis; synovial-fluid; articular chondrocalcinosis;

prevalence; osteoarthritis; hypomagnesemia; calcification
AB ObjectiveCalcium pyrophosphate deposition disease (CPDD) is a common cause of acute and chronic arthritis, yet there are few large epidemiologic studies of CPDD. We sought to characterize CPDD in the national Veterans Affairs (VA) population. MethodsUsing data from the Department of VA Corporate Data Warehouse, patients with International Classification of Diseases, Ninth Revision, codes for CPDD seen at any VA medical center from 2010 through 2014 were matched by age and sex with control patients without CPDD. We used multivariate analysis to compare the prevalence and odds ratios (ORs) of various comorbidities, substance use, medication exposures, and arthroplasties among patients with and without CPDD. ResultsWe identified 25,157 patients with CPDD, yielding a point prevalence of 5.2 per 1,000. The meanSD age was 68.1 +/- 12.3 years, and 95% were male. The strongest positive associations with CPDD were hyperparathyroidism (OR 3.35 [95% confidence interval (95% CI) 2.96-3.79]), gout (OR 2.82 [95% CI 2.69-2.95]), osteoarthritis (OR 2.26 [95% CI 2.15-2.37]), rheumatoid arthritis (OR 1.88 [95% CI 1.74-2.03]), and hemochromatosis (OR 1.87 [95% CI 1.57-2.24]). Positive associations were also seen with higher odds for osteoporosis (OR 1.26 [95% CI 1.16-1.36]), hypomagnesemia (OR 1.23 [95% CI 1.16-1.30]), chronic kidney disease (OR 1.12 [95% CI 1.07-1.18]), and calcium supplementation (OR 1.15 [95% CI 1.06-1.24). Negative associations were seen with proton-pump inhibitors (OR 0.58 [95% CI 0.55-0.60]) and loop diuretics (OR 0.80 [95% CI 0.76-0.84]). ConclusionUsing a large national data set, we confirmed known associations with CPDD, provided support for positive associations with rheumatoid arthritis, hypomagnesemia, and osteoporosis, and suggested potential novel negative associations with commonly used medications.
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TI The role of mineral elements and other chemical compounds used in balneology: data from double-blind randomized clinical trials
SO INTERNATIONAL JOURNAL OF BIOMETEOROLOGY
LA English
DT Review
DE Spa therapy; Balneotherapy; Peloid therapy; Mud therapy; Double blind trial; Review

ID mud-bath therapy; low-back-pain; bilateral knee osteoarthritis; radon spa therapy; follow-up; rheumatoid-arthritis; single-blind; thermal water; pack therapy; hand osteoarthritis
AB The aims of this study were to conduct a systematic literature review on balneotherapy about the specific therapeutic role of mineral elements and other chemical compounds of mineral waters and derivate peloids/muds and to discuss the study methods used to evaluate it (in musculoskeletal conditions). We searched Medline by PubMed using the following key words: "spa therapy" "balneotherapy" "mud" "peloid" "mud pack Therapy" in combination with "randomized controlled trial" "double blind trial." We also reviewed the reference list of articles retrieved by the Medline search. We selected the double-blind randomized clinical trials that assessed the effects of mineral water or mud treatments compared to tap water, attenuated peloid/mud therapy or similar treatments without the specific minerals or chemical compounds of the treatment group ("non-mineral"). We evaluated the internal validity and the quality of the statistical analysis of these trials. The final selection comprised 27 double-blind randomized clinical trials, 20 related to rheumatology. A total of 1118 patients with rheumatological and other musculoskeletal diseases were evaluated in these studies: 552 of knee osteoarthritis, 47 of hand osteoarthritis, 147 chronic low back pain, 308 of reumathoid arthritis, and 64 of osteoporosis; 293 of these participants were assigned to the experimental groups of knee osteoarthritis, 24 in hand osteoarthritis, 82 of low back pain, 152 with reumathoid arthritis, and 32 with osteoporosis. They were treated with mineral water baths and/or mud/peloid (with or without other forms of treatment, like physical therapy, exerciseaEuro broken vertical bar). The rest were allocated to the control groups; they received mainly tap water and/or "non-mineral" mud/peloid treatments. Mineral water or mud treatments had better and longer improvements in pain, function, quality of life, clinical parameters, and others in some rheumatologic diseases (knee and hand osteoarthritis, chronic low back pain, rheumatoid arthritis, and osteoporosis) compared to baseline and non-mineral similar treatments. Internal validity and other limitations of the study's methodology impede causal relation of spa therapy on these improvements. Randomized clinical trials are very heterogeneous. Double-blind randomized clinical trials seem to be the key for studying the role of mineral elements and other chemical compounds, observing enough consistency to demonstrate better and longer improvements for mineral waters or derivate compared to tap water; but due to heterogeneity and gaps on study protocol and methodology, existing research is not sufficiently strong to draw firm conclusions. Well-designed studies in larger patients' population are needed to establish the role of minerals and other chemical compounds in spa therapy.
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NR 92
TC 79
Z9 90
U1 0
U2 37
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 0020-7128
EI 1432-1254
J9 INT J BIOMETEOROL
JI Int. J. Biometeorol.
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WC Biophysics; Environmental Sciences; Meteorology & Atmospheric Sciences; Physiology
SC Biophysics; Environmental Sciences & Ecology; Meteorology & Atmospheric Sciences; Physiology
GA FQ6DE
UT WOS:000418453200013
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ER

PT J
AU Assiotis, A
Giannakakis, N
Hacker, A
AF Assiotis, Angelos
Giannakakis, Nikos
Hacker, Andrew
TI Trapeziumectomy and Mini Tightrope stabilization of the first metacarpal for thumb carpometacarpal osteoarthritis : a prospective case series
SO ACTA ORTHOPAEDICA BELGICA
LA English
DT Article
DE First carpometacarpal joint; Mini Tightrope; Trapezium; Osteoarthritis; Trapeziumectomy
ID suture-button suspensionplasty; trapeziometacarpal joint osteoarthritis; ligament reconstruction; tendon interposition; implant arthroplasty; follow-up; arthritis; trapeziectomy; allograft; excision
AB Our purpose was to investigate the short-term results of trapeziumectomy and stabilization of the first metacarpal by using the TightRope (c) device, at a maximum follow-up of 1 year post-op. This is a novel method in treating first carpometacarpal joint osteoarthritis and an alternative to the variety of other methods that have been previously reported. We recruited 21 patients and assessed them at regular intervals, comparing pre-operative and postoperative variables. We recorded all complications during the study period. There was a statistically significant improvement in pain, hand grip and tip pinch power and functional outcome scores. Patients were very satisfied at 12 months after surgery. No significant change in thumb opposition was noted. There was subsidence of the first metacarpal at 1 year after surgery. Despite the existence of a significant number of alternative procedures, we feel that the procedure described in this paper has promising short-term results and is safe.
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NR 30
TC 6
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U1 0
U2 1

PU ACTA MEDICA BELGICA
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EI
J9 ACTA ORTHOP BELG
JI Acta Orthop. Belg.
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PT J
AU Gromov, K
Bersang, A
Nielsen, CS
Kallemose, T
Husted, H
Troelsen, A
AF Gromov, K.
Bersang, A.
Nielsen, C. S.
Kallemose, T.
Husted, H.
Troelsen, A.
TI Risk factors for post-operative periprosthetic fractures following primary total hip arthroplasty with a proximally coated double-tapered cementless femoral component
SO BONE & JOINT JOURNAL
LA English
DT Article
ID femur fracture; joint registry; stem design; replacement; knee; epidemiology;

osteoporosis; mortality; revision; index
AB Aims The aim of this study was to identify patient-and surgery-related risk factors for sustaining an early periprosthetic fracture following primary total hip arthroplasty (THA) performed using a double-tapered cementless femoral component (Bi-Metric femoral stem; Biomet Inc., Warsaw, Indiana). Patients and Methods A total of 1598 consecutive hips, in 1441 patients receiving primary THA between January 2010 and June 2015, were retrospectively identified. Level of pre-operative osteoarthritis, femoral Dorr type and cortical index were recorded. Varus/valgus placement of the stem and canal fill ratio were recorded post-operatively. Periprosthetic fractures were identified and classified according to the Vancouver classification. Regression analysis was performed to identify risk factors for early periprosthetic fracture. Results The mean follow-up was 713 days (1 to 2058). A total of 48 periprosthetic fractures (3.0%) were identified during the follow-up and median time until fracture was 16 days, (interquartile range 10 to 31.5). Patients with femoral Dorr type C had a 5.2 times increased risk of post-operative periprosthetic fracture compared with type B, while female patients had a near significant two times increased risk over time for post-operative fracture. Conclusion Dorr type C is an independent risk factor for early periprosthetic fracture, following THA using a double tapered cementless stem such as the Bi-Metric. Surgeons should take bone morphology into consideration when planning for primary THA and consider using cemented femoral components in female patients with poor bone quality.
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NR 51
TC 82
Z9 94
U1 0
U2 5
PU BRITISH EDITORIAL SOC BONE JOINT SURGERY
PI LONDON
PA 22 BUCKINGHAM STREET, LONDON WC2N 6ET, ENGLAND
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EI
J9 BONE JOINT J
JI Bone Joint J.
PD APR 15
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IS 4
BP 451
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WC Orthopedics; Surgery
SC Orthopedics; Surgery
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PT J
AU Zura, R
Braid-Forbes, MJ
Jeray, K
Mehta, S
Einhorn, TA
Watson, JT
Della Rocca, GJ
Forbes, K
Steen, RG
AF Zura, Robert
Braid-Forbes, Mary Jo
Jeray, Kyle
Mehta, Samir
Einhorn, Thomas A.
Watson, J. Tracy
Della Rocca, Gregory J.
Forbes, Kevin
Steen, R. Grant
TI Bone fracture nonunion rate decreases with increasing age: A prospective inception cohort study
SO BONE
LA English
DT Article
DE Geriatric fracture; Fragility fracture; Smoking; Osteoporosis; Arthritis; Hypertension
ID older-adults; hip fracture; osteoporotic fracture; risk prediction; pelvic ring; bed rest; mortality; metaanalysis; disability; prevention
AB Background: Fracture nonunion risk is related to severity of injury and type of treatment, yet fracture healing is not fully explained by these factors alone. We hypothesize that patient demographic factors assessable by the clinician at fracture presentation can predict nonunion. Methods: A prospective cohort study design was used to examine similar to 2.5 million Medicare patients nationwide. Patients making fracture claims in the 5% Medicare Standard Analytic Files in 2011 were analyzed; continuous enrollment for 12 months after fracture was required to capture the ICD-9-CM nonunion diagnosis code (733.82) or any procedure codes for nonunion repair. A stepwise regression analysis was used which dropped variables from analysis if they did not contribute sufficient explanatory power. In-sample predictive accuracy was assessed using a receiver operating characteristic (ROC) curve approach, and an out-of-sample comparison was drawn

from the 2012 Medicare 5% SAF files. Results: Overall, 47,437 Medicare patients had 56,492 fractures and 2.5% of fractures were nonunion. Patients with healed fracture (age 75.0 +/- 12.7 SD) were older ($p < 0.0001$) than patients with nonunion (age 69.2 +/- 13.4 SD). The death rate among all Medicare beneficiaries was 4.8% per year, but fracture patients had an age and sex-adjusted death rate of 11.0% ($p < 0.0001$). Patients with fracture in 14 of 18 bones were significantly more likely to die within one year of fracture ($p < 0.0001$). Stepwise regression yielded a predictive nonunion model with 26 significant explanatory variables (all, $p <= 0.003$). Strength of this model was assessed using an area under the curve (AUC) calculation, and out-of-sample AUC = 0.710. Conclusions: A logistic model predicted nonunion with reasonable accuracy (AUC = 0.725). Within the Medicare population, nonunion patients were younger than patients who healed normally. Fracture was associated with increased risk of death within 1 year of fracture ($p < 0.0001$) in 14 different bones, confirming that geriatric fracture is a major public health issue. Comorbidities associated with increased risk of nonunion include past or current smoking, alcoholism, obesity or morbid obesity, osteoarthritis, rheumatoid arthritis, type II diabetes, and/or open fracture (all, multivariate $p < 0.001$). Nonunion prediction requires knowledge of 26 patient variables but predictive accuracy is currently comparable to the Framingham cardiovascular risk prediction. (C) 2016 Bioventus LLC. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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Z9 86
U1 0
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TI Non-synonymous WNT16 polymorphisms alleles are associated with different osteoarthritis phenotypes
SO RHEUMATOLOGY INTERNATIONAL
LA English
DT Article
DE WNT; Genetic association; Osteoarthritis; Bone; Cartilage; Joints
ID bone-mineral density; knee osteoarthritis; articular-cartilage; hip; prevalence; osteoporosis; pathogenesis; activation; deformity; fracture
AB Hereditary factors have a strong influence on osteoarthritis (OA). The Wnt pathway is involved in bone and cartilage homeostasis. Hence, we hypothesized that allelic variations of WNT16 could influence the OA phenotype. We studied 509 Caucasian patients undergoing joint replacement due to severe primary OA. Radiographs were used to classify the OA as atrophic or hypertrophic. Two nonsynonymous polymorphisms of WNT16 (rs2707466 and rs2908004) were analyzed. The association between the genotypes and the OA phenotype was analyzed by logistic regression and adjusted for age and body mass index. A genotype-phenotype association was found in the sex-stratified analysis. Thus, there was a significant difference in the genotypic frequencies of rs2707466 between hypertrophic and atrophic hip OA in males ($p = 0.003$), with overrepresentation of G alleles in the hypertrophic phenotype (OR 2.08; CI 1.28-3.38). An association in the same direction was observed between these alleles

and the type of knee OA, with G alleles being more common in the hypertrophic than in atrophic knee phenotypes (p = 0.008; OR 1.956, CI 1.19-3.19). Similar associations were found for the rs2908004 SNP, but it only reached statistical significance for knee OA (p = 0.017; OR 0.92, CI 0.86-0.989). This is the first study attempting to explore the association of genetic variants with the OA phenotype. These data suggest the need to consider the OA phenotype in future genetic association studies of OA.
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NR 38
TC 6
Z9 9
U1 0
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TI Association of Condylar Bone Quality with TMJ Osteoarthritis
SO JOURNAL OF DENTAL RESEARCH
LA English
DT Article
DE mandibular condyle; bone volume; cone beam computed tomography; micro-computed tomography; multivariate analysis; cross-sectional study
ID temporomandibular-joint; computed-tomography; mineral density; risk; osteoporosis; diagnosis; prevalence; morphology; disorders; growth
AB The etiology and treatment of temporomandibular joint (TMJ) osteoarthritis (TMJOA) remain complex and unclear. Based on clinical observations, we hypothesized that low condylar bone quality is significantly correlated with TMJOA and explored this association in a cross-sectional study with human patients. A

total of 254 postmenopausal female participants were included in this study. Radiographic findings from cone beam computed tomography (CBCT) and clinical symptoms were used to classify each TMJ data sample as healthy control (n = 124) or TMJOA (n = 130). Condylar bone mineral density (BMD) (computed tomography Hounsfield unit [CT HU]) and bone volume fraction (BV/TV) were measured and modeled as predictors of healthy control versus TMJOA status in multilevel logistic regression analyses. Both CT HU (adjusted odds ratio [AOR] = 0.9989, interquartile odds ratio [IOR] = 0.4206) and BV/TV (AOR= 0.8096, IOR = 0.1769) were negatively associated with TMJOA (P = 0.049, 0.011, respectively). To assess the diagnostic performance of CT HU and BV/TV for identification of TMJOA, receiver operating characteristic (ROC) curves were plotted. The estimated areas under the curve (AUC) were 0.6622 for BV/TV alone, 0.6074 for CT HU alone, and 0.7136 for CT HU and BV/TV together. The model incorporating CT HU and BV/TV together had a significantly higher AUC than the models using BV/TV alone (P = 0.038) or HU alone (P = 0.021). In conclusion, we found that low condylar bone quality was significantly correlated with TMJOA development and that condylar CT HU and BV/TV can be used together as a potential diagnostic tool for TMJOA. Careful clinical evaluation of the condyle coupled with appropriate radiographic interpretation would thus be critical for the early detection of TMJOA.
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TI Pulsed Electromagnetic Field at Different Stages of Knee Osteoarthritis in Rats Induced by Low-Dose Monosodium Iodoacetate: Effect on Subchondral Trabecular Bone Microarchitecture and Cartilage Degradation
SO BIOELECTROMAGNETICS
LA English
DT Article
DE osteoarthritis; pulsed electromagnetic field; subchondral bone; cartilage; X-ray microtomography
ID micro-computed tomography; biochemical markers; in-vitro; stimulation; model; chondrocytes; alendronate; degeneration; osteoporosis; metabolism
AB The aim of the study was to investigate the efficacy of pre-emptive, early, and delayed pulsed electromagnetic field (PEMF) treatment on cartilage and subchondral trabecular bone in knee osteoarthritis (OA) rats induced by low-dose monosodium iodoacetate (MIA). Seventy-five 12-week-old male Sprague-Dawley rats were assigned to five groups: OA (n = 30), pre-emptive PEMF (n - 10), early PEMF (n - 10), delayed PEMF (n - 10), and control (n - 15). Osteoarthritis was induced by injecting 0.2 mg MIA in rat's right knee joint. Control rats received a single sterile saline injection in the right knee. Male rats received pre-emptive (n = 10, day 0-end of week 4), early (n = 10, end of week 4-end of week 8), or delayed (n = 10, end of week 8-end of week 12) PEMF treatment (75 Hz, 1.6 mT). After 4, 8, and 12 weeks, rats were sacrificed at each time point and right knees were harvested. After sacrifice, micro-computed tomography, histology, and biomarker

analyses were performed. We found pre-emptive PEMF treatment preserved subchondral trabecular bone microarchitecture and prevented subchondral bone loss in MIA-induced OA rat model. Early and delayed PEMF treatment maintained subchondral trabeculae. PEMF treatment increased bone and cartilage formation, and decreased bone and cartilage resorption. Pre-emptive and early PEMF treatment had moderate effects on cartilage degradation. Time point of treatment initiation is crucial for treating OA. PEMF might become a potential biophysical treatment modality for osteoarthritis. (C) 2016 Wiley Periodicals, Inc.
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NR 42
TC 23
Z9 28
U1 1

U2 20
PU WILEY
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J9 BIOELECTROMAGNETICS
JI Bioelectromagnetics
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PT J
AU Yoshimura, N
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Nakamura, K
Tanaka, S
AF Yoshimura, Noriko
Muraki, Shigeyuki
Nakamura, Kozo
Tanaka, Sakae
TI Epidemiology of the locomotive syndrome: The research on osteoarthritis/osteoporosis against disability study 2005-2015
SO MODERN RHEUMATOLOGY
LA English
DT Review
DE Disability; Locomotive syndrome; Metabolic syndrome; Mild cognitive impairment; Osteoarthritis; Osteoporosis
ID diagnostic-criteria; society
AB Although locomotive organ disorders are major causes of disability and require support, little information is available regarding their epidemiology. Prevalence and co-existence of locomotive organ disorders including knee osteoarthritis (KOA),

lumbar spondylosis (LS), hip osteoarthritis, and osteoporosis have been determined from baseline results of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study. KOA, LS, and hip osteoarthritis overlap in the population, while KOA and LS co-exist in 42.0% of people. Mutual associations between locomotive organ disorders, metabolic syndrome components, and mild cognitive impairment were found using baseline and 3-year follow-up data from the ROAD study. Logistic regression analysis showed that hypertension, impaired glucose tolerance, and mild cognitive impairment increase the risk of KOA. Osteoporosis at L2-4 was significantly influenced by the presence of femoral neck osteoporosis, and vice versa. In turn, excess weight was inversely associated with the occurrence of femoral neck osteoporosis. Finally, data from the 3rd survey (7-year follow-up) were used to calculate the prevalence of the locomotive syndrome using tests proposed by the Japanese Orthopaedic Association for assessing the risk of developing locomotive syndrome. Subsequently, the age-sex prevalence of stage 1 and stage 2 locomotive syndrome was estimated at 69.8% and 25.1%, respectively.
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NR 21
TC 102
Z9 133
U1 1
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AU Padlina, I
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Lamy, O
AF Padlina, I.
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TI The lumbar spine age-related degenerative disease influences the BMD not the TBS: the Osteolaus cohort
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE BMD; Degenerative disease; Lumbar spine; TBS; Vertebral fracture
ID trabecular bone score; mineral density; fracture probability; women; osteoporosis; osteoarthritis; diagnosis; risk; men; prediction
AB We evaluated the influence of degenerative disease and fractured vertebra on lumbar spine bone mineral density (BMD) and trabecular bone score (TBS) in 1500 women aged 50-80 years. TBS was not affected by a degenerative disease. While BMD increases after 62.5 years, TBS continues to decline. TBS should play a leading role in lumbar spine evaluation. After menopause, lumbar spine (LS) BMD and TBS values decrease. Degenerative disease (DD) increases with age and affect LS BMD. The aim of this study was to measure changes in LS BMD and TBS in women 50 to 80 years old, taking into account the impact of fractured vertebrae and DD. LS BMD, TBS, and vertebral fracture assessment were evaluated in the OsteoLaus cohort (1500 women, 50-80 years old). The exams were analyzed following ISCD guidelines to identify vertebrae with fractures or DD (Vex). 1443 women were enrolled: mean age 66.7 +/- 11.7 years, BMI 25.7 +/- 4.4. LS BMD and TBS were weakly correlated (r2 = 0.16). The correlation (Vex excluded) between age and BMD was +0.03, between age and TBS -0.34. According to age group, LS BMD was 1.2 to 3.2% higher before excluding Vex ($p < 0.001$). TBS had an insignificant change of < 1% after excluding Vex. LS BMD (Vex) decreased by 4.6% between 52.5 and 62.5 years, and increased by 2.6% between 62.5 and 77.5 years. TBS (Vex excluded) values decreased steadily with age with an overall loss of 8.99% between 52.5 and 77.5 years. Spine TBS, femoral neck, and total hip BMD gradually decreased with age, reaching one SD between the oldest and youngest group. TBS is not affected

by DD. While BMD increases after 62.5 years, TBS continues to decline. For lumbar spine evaluation, in view of its independence from DD, TBS should play a leading role in the diagnosis in complement to BMD.
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NR 21
TC 64
Z9 72

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PU SPRINGER LONDON LTD
PI LONDON
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WC Endocrinology & Metabolism
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PT J
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TI Raman spectral characteristics of neck and head of femur in low-density lipoprotein receptor gene knockout mice submitted to treadmill aerobic training
SO JOURNAL OF PHOTOCHEMISTRY AND PHOTOBIOLOGY B-BIOLOGY
LA English
DT Article
DE Bone tissue; Hyperlipidemia; Raman spectroscopy; Principal component analysis
ID bone-mineral density; exercise; spectroscopy; health; osteoarthritis; osteoporosis; morphology; strength; rats

AB Hypercholesterolemia is associated with deterioration of bone tissue. Trough Raman spectroscopy, the present study aimed to assess the molecular changes in terms of mineral and organic bone-tissue remodeling in low density lipoprotein receptor gene knockout mice (LDLr - / -) submitted to treadmill aerobic training. In order to evaluate alterations in trabecular bone and cartilage surface, neck and head femoral were assessed into four groups: (CON, n = 7), the 1) animals did not perform any physical activity and had hypercholesterolemia (CON, n = 7); The trained groups where animals underwent a protocols of low, moderate and high training for 8 weeks and 4 times per week on a treadmill with progressive intensities: running speed (8-13 m/min) and time of exercise (20-60 min). These progressive intensities were needed to adjust the working load for the physical training to 2) 30-49% (LOW, n = 7), 3) 50-79% (MOD, n = 7), and 4) 80-100% (HIGH, n = 7) of the maximum running speed. Each group was examined for molecular changes in both bone phases (mineral and organic) using principal components analysis (PCA). All exercised groups showed a significant increase ($p < 0.05$) of bone remodeling in trabecular area and a higher content of proteins (organic content) in cartilage independently of physical activity intensity. Thus, this work demonstrated that physical training could act as a bone-protector factor in hyperlipidemic animal model as well as Raman technique associated with PCA analysis may be feasible methodology for assessment or monitoring of bone at the molecular level.
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U1 0
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AU Lund, B
Mygind-Klavsen, B
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Maagaard, N
Kraemer, O
Hölmich, P
Winge, S
Lind, M
AF Lund, Bent
Mygind-Klavsen, Bjarne
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Holmich, Per
Winge, Soren
Lind, Martin
TI Danish Hip Arthroscopy Registry (DHAR): the outcome of patients with femoroacetabular impingement (FAI)
SO JOURNAL OF HIP PRESERVATION SURGERY
LA English
DT Article
ID osteoarthritis; risk; pain; prevalence; management; scale; joint
AB The Danish Hip Arthroscopy Registry (DHAR) was initiated in January 2012 as a web-based prospective registry. The purpose of this study was to evaluate and report the first registry based outcome data of a national population with radiological and clinical femoroacetabular impingement (FAI) undergoing hip arthroscopic treatment. Our primary hypothesis was that patients undergoing hip arthroscopy would improve significantly in pain, quality of life and sports related outcome measurements in Patient Related Outcome Measures (PROM). Perioperative data and Patient Reported Outcome Measures (PROM) data from DHAR between January 2012 and November 2015 were extracted. Radiological pincer-type FAI was defined as LCE > 35 degrees and cam FAI as alphaangle > 55 degrees. These data were combined with FAI surgical data such as osteochondroplasty and labral repair or resection. PROMs consisting of HAGOS, EQ-5 D, HSAS and NRS pain scores were submitted online by the patients pre-operatively and at 1 and 2-years follow-up. 2054 FAI procedures in 1835 patients were included in this study (219 patients had bilateral procedures performed). HAGOS demonstrated significant improvement in all subscales at follow up. EQ-5 D demonstrated improvement after 1 and 2 years from 0.66 pre-op to 0.78 at 2 years. HSAS improved significantly from 2.5 to 3.3. Pain score data demonstrated improvement in NRS-rest 39 to 17 and NRS Walk 49 to 22 at follow-up. We conclude that patients with FAI undergoing hip arthroscopy experience improvement in pain, quality of life and also in function and sports related outcome measures during the first 2 years after surgery.
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NR 31
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Z9 66
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PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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TI Role of glucocorticoid-induced leucine zipper (GILZ) in inflammatory bone loss
SO PLOS ONE
LA English
DT Article
ID tumor-necrosis-factor; nf-kappa-b; rheumatoid-arthritis; transgenic mice; factor inhibitors; progenitor cells; synovial-fluid; tnf-alpha; therapy; osteoarthritis
AB TNF-alpha plays a key role in the development of rheumatoid arthritis (RA) and inflammatory bone loss. Unfortunately, treatment of RA with anti-inflammatory glucocorticoids (GCs) also causes bone loss resulting in osteoporosis. Our previous studies showed that overexpression of glucocorticoid-induced leucine zipper (GILZ), a mediator of GC's anti-inflammatory effect, can enhance osteogenic differentiation in vitro and bone acquisition in vivo. To investigate whether GILZ could antagonize TNF-alpha-induced arthritic inflammation and protect bone in mice, we generated a TNF-alpha-GILZ double transgenic mouse line (TNF-GILZ Tg) by crossbreeding a TNF-alpha Tg mouse, which ubiquitously expresses human TNF-alpha, with a GILZ Tg mouse, which expresses mouse GILZ under the control of a 3.6kb rat type I collagen promoter fragment. Results showed that overexpression of GILZ in bone marrow mesenchymal stem/progenitor cells protected mice from TNF-alpha-induced inflammatory bone loss and improved bone integrity (TNF-GILZ double Tg vs. TNF-alpha Tg, n = 12-15). However, mesenchymal cell lineage restricted GILZ expression had limited effects on TNF-alpha-induced arthritic inflammation as indicated by clinical scores and serum levels of inflammatory cytokines and chemokines.
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AU Gallo, J
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TI Inflammation and its resolution and the musculoskeletal system
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Review
DE fibroblasts; inflammation; innate lymphoid cells; macrophages; neutrophils; proresolving mediators
ID mast-cell subpopulations; regulatory t-cells; knee osteoarthritis; tissue-repair; disease; macrophages; homeostasis; mechanisms; immunity; innate
AB Inflammation, an essential tissue response to extrinsic/intrinsic damage, is a very dynamic process in terms of complexity and extension of cellular and metabolic involvement. The aim of the inflammatory response is to eliminate the pathogenic initiator with limited collateral damage of the inflamed tissue, followed by a complex tissue repair to the preinflammation phenotype. Persistent inflammation is a major contributor to the pathogenesis of many musculoskeletal diseases including ageing-related pathologies such as osteoporosis, osteoarthritis, and sarcopaenia. The translational potential of this article: Understanding the mechanisms of inflammation and its resolution is therefore critical for the development of effective regenerative, and therapeutic strategies in orthopaedics.
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PI AMSTERDAM
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SN 2214-031X
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J9 J ORTHOP TRANSL
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WC Orthopedics
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PT J
AU Zhu, Z
Laslett, LL
Jin, X
Han, W
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Wang, X
Lu, M
Cicuttini, F
Jones, G
Ding, C

AF Zhu, Z.
Laslett, L. L.
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TI Association between MRI-detected osteophytes and changes in knee structures and pain in older adults: a cohort study
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Knee osteoarthritis; Magnetic resonance imaging; Osteophytes; Knee pain; Knee structures abnormalities
ID early radiographic osteoarthritis; cartilage volume loss; imaging findings; surface-area; defects; prevalence; features; abnormality; progression; history
AB Objective: To describe cross-sectional and longitudinal associations between magnetic resonance imaging (MRI)-detected osteophytes (OPs) and knee structural abnormalities and knee pain in older adults. Method: A prospective population-based cohort study of 895 participants aged 50-80 years (mean age 62 years, 50% female) was performed. T1-or T2-weighted fat suppressed MRI was used to assess knee OPs, cartilage volume, cartilage defects and bone marrow lesions (BMLs) at baseline and after 2.6 years. Radiographically-detected OPs were scored according to the Osteoarthritis Research Society International (OARSI) atlas. Knee pain was assessed using a self-administered questionnaire at baseline, 2.6 and 5 years later. Results: 85% of participants had MRI-detected OPs at baseline, while 10% of participants had radiographically-detected OPs. Cross-sectionally, higher gardes of MRI-detected OPs in all compartments were significantly, independently and site-specifically associated with higher prevalences of cartilage defects and BMLs, lower cartilage volume and higher prevalence of knee pain. Longitudinally, higher gardes of baseline MRI-detected OPs site-specifically predicted greater risks of any increase in cartilage defects or BMLs, and loss of cartilage volume in medial and lateral tibiofemoral (LTF) and total compartments over 2.6 years in multivariable analyses. These significant associations were similar in those without radiographically-detected OPs. MTF and total OP scores were significantly associated with change in total knee pain over 2.6 and 5 years but these became non-significant after adjustment for cartilage defects and BMLs. Conclusion: MRI-detected knee OPs are common and appear to be clinically relevant to knee structural changes in older adults. (C) 2017 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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FU National Health and Medical Research Council of Australia [302204]; Tasmanian Community Fund [D0015018]; Arthritis Foundation of Australia [MRI06161]; University of Tasmania Institutional Research Grants Scheme [D0015019]
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TC 22
Z9 28
U1 0
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PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
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WC Orthopedics; Rheumatology
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PT J
AU Zhang, LB
Man, ZT
Li, W
Zhang, W
Wang, XQ
Sun, S
AF Zhang, Lai-Bo
Man, Zhen-Tao
Li, Wei
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Sun, Shui
TI Calcitonin protects chondrocytes from lipopolysaccharide-induced apoptosis and inflammatory response through MAPK/Wnt/NF-κB pathways
SO MOLECULAR IMMUNOLOGY
LA English
DT Article
DE Calcitonin; Lipopolysaccharide (LPS); Osteoarthritis; Bone morphogenetic protein 2 (BMP-2); MAPE/Wnt/NF-kappa B pathways
ID matrix-metalloproteinase expression; bone morphogenetic protein; c-reactive protein; cartilage degeneration; articular-cartilage; salmon-calcitonin; osteoarthritic cartilage; postmenopausal women; ii degradation; early-stage
AB Calcitonin (CT) is an anti-absorbent, which has long been used for treatment of osteoporosis. However, little information is available about the effects of CT on osteoarthritis (OA). This study was mainly aimed to explore the effects of CT on the treatment of OA, as well as the underlying mechanisms. Chondrocytes were isolated from immature mice and then were incubated with lipopolysaccharide (LPS), CT, small interfering (si) RNA against bone morphogenetic protein (BMP)-2, and/or the inhibitors of MAPK/Wnt/NF-kappa B pathway. Thereafter, cell viability, apoptosis, nitric oxide (NO) and inflammatory factors productions, and expression levels of cartilage synthesis protein key factors, cartilage-derived morphogenetic protein (CDMP) 1, SRY (sex-determining region Y)-box 9 protein (SOX9), and

MAPK/Wnt/NF-kappa B pathways key factors were determined. CT significantly reversed LPS-induced cell viability decrease, apoptosis increase, the inflammatory factors and NO secretion, the abnormally expression of cartilage synthesis proteins and the activation of MAPK/Wnt/NF-kappa B pathways ($P < 0.05$). In addition, we observed that administration of the inhibitors of MAPK/Wnt/NF-kappa B pathways statistically further increased the levels of CDMP1 and SOX9 ($P < 0.05$). Suppression of BMP-2 decreased the levels of CDMP1 and SOX9 and activated MAPK/Wnt/NF-kappa B pathways, and could partially abolish CT-modulated the expression changes in CDMP1 and SOX9, and MAPK/Wnt/NF-kappa B pathways key factors ($P < 0.05$). The results showed that CT protects chondrocytes from LPS-induced apoptosis and inflammatory response by regulating BMP-2 and thus blocking IVIAPK/Wnt/NF-kappa B pathways.

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NR 42
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Z9 46
U1 0
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PU PERGAMON-ELSEVIER SCIENCE LTD
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SC Biochemistry & Molecular Biology; Immunology
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PT J
AU Luo, YY
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TI Preventive effects of kudzu root on bone loss and cartilage degradation in

ovariectomized rat
SO AMERICAN JOURNAL OF TRANSLATIONAL RESEARCH
LA English
DT Article
DE Osteoporosis; osteoarthritis; bone absorption; cartilage degradation; kudzu; SERMs
ID hormone replacement therapy; articular-cartilage; postmenopausal women; estrogen; osteoarthritis; management; pathways; turnover; disease; health
AB The clinical utility of Traditional Chinese Medicine (TCM) herbs/roots extracts in osteoporosis (OP) and osteoarthritis (OA) has been described in multiple reports, but there have been few studies of TCM for preventing bone loss and cartilage degradation simultaneously. Six-month-old female Sprague-Dawley rats each were subjected to ovariectomized (OVX) or sham surgery and treated orally once daily with herbal extracts or vehicle. Body weight was recorded weekly, and blood samples were collected from fasting animals at different time points. Biochemical markers of bone resorption and cartilage degradation were analyzed. Changes in bone mineral density and calcium content were determined in the femoral center and femoral telocentric end of rats. Out of 56 TCM herbs/roots extracts, only kudzu root demonstrated consistent joint protective effects. OVX resulted in a marked increase in bone resorption and cartilage degradation, which could be significantly reversed by kudzu after three weeks of treatment. Compared to vehicle, kudzu induced a significant increase in bone mineral density in the femoral center and femoral telocentric end, and calcium content. The results show that kudzu exerts direct effects on articular cartilage in the OVX rat and can effectively prevent the acceleration of cartilage degradation induced by ovariectomy. Moreover, kudzu has demonstrated positive effects on metabolic health (cause a weight reduction) and may represent a possible treatment for OP and OA with high body mass index. Further studies are needed to investigate the potential effects of kudzu root in postmenopausal women.
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WC Oncology; Medicine, Research & Experimental
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PT J
AU Lowe, DB
Taylor, MJ
Hill, SJ
AF Lowe, Dianne B.
Taylor, Michael J.
Hill, Sophie J.
TI Associations between multimorbidity and additional burden for working-age adults with specific forms of musculoskeletal conditions: a cross-sectional study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Multimorbidity; Musculoskeletal conditions; Quality of life; Healthcare utilisation
ID quality-of-life; global burden; rheumatoid-arthritis; chronic disease; psychological distress; systematic analysis; co-morbidity; health-care; prevalence; comorbidity
AB Background: Multiple health conditions are increasingly a problem for adults with musculoskeletal conditions. However, multimorbidity research has focused

primarily on the elderly and those with a limited subset of musculoskeletal disorders. We sought to determine whether associations between multimorbidity and additional burden differ with specific forms of musculoskeletal conditions among working-age adults. Methods: Data were sourced from a nationally representative Australian survey. Specific musculoskeletal conditions examined were osteoarthritis; inflammatory arthritis; other forms of arthritis or arthropathies; musculoskeletal conditions not elsewhere specified; gout; back pain; soft tissue disorders; or osteoporosis. Multimorbidity was defined as the additional presence of one or more of the Australian National Health Priority Area conditions. Burden was assessed by self-reported measures of: (i) self-rated health (ii) musculoskeletal-related healthcare and medicines utilisation and, (iii) general healthcare utilisation. Associations between multimorbidity and additional health or healthcare utilisation burden among working-age adults (aged 18 - 64 years of age) with specific musculoskeletal conditions were estimated using logistic regression, adjusting for confounders. Interaction terms were fitted to identify whether there were specific musculoskeletal conditions where multimorbidity was more strongly associated with poorer health or greater healthcare utilisation than in the remaining musculoskeletal group. Results: Among working-age adults, for each of the specified musculoskeletal conditions, multimorbidity was associated with similar, increased likelihood of additional self-rated health burden and certain types of healthcare utilisation. While there were differences in the relationships between multimorbidity and burden for each of the specific musculoskeletal conditions, no one specific musculoskeletal condition appeared to be consistently associated with greater additional health burden in the presence of multimorbidity across the majority of self-rated health burden and healthcare use measures. Conclusions: For working-age people with any musculoskeletal conditions examined here, multimorbidity increases self-reported health and healthcare utilisation burden. As no one musculoskeletal condition appears consistently worse off in the presence of multimorbidity, there is a need to better understand and identify strategies that acknowledge and address the additional burden of concomitant conditions for working-age adults with a range of musculoskeletal conditions.
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DE Menopause; Systemic lupus erythematosus; Osteoarthritis; Rheumatoid arthritis
ID systemic-lupus-erythematosus; hormone-replacement-therapy; bone-mineral density; isolated pulmonary-hypertension; postmenopausal women; risk-factors; ovarian failure; double-blind; radiographic osteoarthritis; estrogen metabolites
AB Menopause occurs naturally in women at about 50 years of age. There is a wealth of data concerning the relationship of menopause to systemic lupus erythematosus, rheumatoid arthritis, and osteoarthritis; there are limited data

concerning other rheumatic diseases. Age at menopause may affect the risk and course of rheumatic diseases. Osteoporosis, an integral part of inflammatory rheumatic diseases, is made worse by menopause. Hormone replacement therapy has been studied; its effects vary depending on the disease and even different manifestations within the same disease. Cyclophosphamide can induce early menopause, but there is underlying decreased ovarian reserve in rheumatic diseases.
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TI Emerging roles for long noncoding RNAs in skeletal biology and disease
SO CONNECTIVE TISSUE RESEARCH
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DE Bone; cartilage; chondrocyte; long noncoding (lnc) RNAs; osteoarthritis; osteoblast; osteosarcoma
ID mesenchymal stem-cells; promotes osteoblast differentiation; potential therapeutic target; wide dna methylation; genome-wide; chondrogenic differentiation; gene-expression; bone-marrow; poor-prognosis; osteogenic differentiation
AB Normal skeletal development requires tight coordination of transcriptional networks, signaling pathways, and biomechanical cues, and many of these pathways are dysregulated in pathological conditions affecting cartilage and bone. Recently, a significant role has been identified for long noncoding RNAs (lncRNAs) in developing and maintaining cellular phenotypes, and improvements in sequencing technologies have led to the identification of thousands of lncRNAs across diverse cell types, including the cells within cartilage and bone. It is clear that lncRNAs play critical roles in regulating gene expression. For example, they can function as epigenetic regulators in the nucleus via chromatin modulation to control gene transcription, or in the cytoplasm, where they can function as scaffolds for protein-binding partners or modulate the activity of other coding and noncoding RNAs. In this review, we discuss the growing list of lncRNAs involved in normal development and/or homeostasis of the skeletal system, the potential mechanisms by which these lncRNAs might function, and recent improvements in the methodologies available to study lncRNA functions in vitro and in vivo. Finally, we address the likely utility of lncRNAs as biomarkers and therapeutic targets for diseases of the skeletal system, including osteoarthritis, osteoporosis, and in cancers of the skeletal system.
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NR 258
TC 90
Z9 100
U1 2
U2 41
PU TAYLOR & FRANCIS INC
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BP 116
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WC Cell Biology; Orthopedics
SC Cell Biology; Orthopedics
GA EL3LS
UT WOS:000394521200011
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PT J
AU Minisola, S
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TI Correction of vitamin D status by calcidiol: pharmacokinetic profile, safety, and biochemical effects on bone and mineral metabolism of daily and weekly dosage regimens
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Fracture; Hypovitaminosis D; Osteomalacia; Osteoporosis; Rickets; Vitamin D deficiency
ID randomized controlled-trial; serum 25-hydroxyvitamin d; d supplementation; postmenopausal women; osteoarthritis esceo; oral vitamin-d-3; european-society; economic-aspects; parathyroid-hormone; turnover markers
AB Rationale: Calcidiol can be employed to correct vitamin D deficiency. Main results: Calcidiol administered at daily and weekly regimens over a period of 3 months was able to successfully raise 25-hydroxyvitamin D levels without altering other markers related to bone and mineral metabolism. Significance: Calcidiol supplementation is effective and safe. Introduction The correction of vitamin D status is necessary to maintain an optimal mineral and skeletal homeostasis. Despite cholecalciferol (vitamin D-3) is the most commonly used drug for vitamin D supplementation, the more hydrophilic compound calcidiol (25-hydroxyvitamin D-3) can be employed at daily, weekly, and monthly regimens to reach in the short term the target levels of serum 25-hydroxyvitamin D [25(OH)D]. In the administration of different doses of calcidiol pharmacokinetic study (ADDI-D study), the efficacy and safety of daily and weekly dosages of calcidiol were tested. Methods A total of 87 Caucasian, community-dwelling, postmenopausal women, aged 55 years or older, with vitamin D inadequacy (serum 25(OH)D levels < 30 ng/ml, with mean 25(OH)D below 20 ng/ml, namely 16.5 +/- 7.5 ng/ml) were randomized to receive three different dosages of calcidiol: 20 mu g/day, 40 mu g/day, and 125 mu g/week for 3 months. The attained level of serum 25(OH)D was selected as primary endpoint to assess efficacy, while other parameters of mineral metabolism, (serum calcium, parathyroid hormone, phosphate, FGF23, urinary calcium, and markers of bone turnover) were assessed as secondary endpoints to establish safety. Results In all the three groups, serum 25(OH)D values significantly

and promptly rose and plateaued above the 30 ng/ml threshold remaining within safety interval after 14 days of treatment, with similar efficacy for the similar daily and weekly dose regimens. The different dosages were also equally effective in controlling secondary hyperparathyroidism. No significant changes in calcium and phosphate metabolism and in bone turnover markers were observed for any of the treatments, confirming the safety of this compound. Conclusions The results of this study demonstrate the short- and mid-term efficacy and safety on core parameters of mineral metabolism of different daily or weekly dosages of calcidiol when used to treat vitamin D inadequacy or deficiency in postmenopausal women. Further studies are needed to assess falls as primary outcome of calcidiol supplementation.
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NR 39
TC 34
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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TI Do Comorbidities Play a Role in Hand Osteoarthritis Disease Burden? Data from the Hand Osteoarthritis in Secondary Care Cohort
SO JOURNAL OF RHEUMATOLOGY
LA English
DT Article
DE HAND OSTEOARTHRITIS; COMORBIDITY; PATIENT-REPORTED OUTCOMES; DISABILITY; HAND PAIN; QUALITY OF LIFE
ID quality-of-life; knee osteoarthritis; rheumatology criteria; depression scale;

hospital anxiety; clinical-trials; health-status; pain; disability; impact
AB Objective. Because the association and its clinical relevance between comorbidities and primary hand osteoarthritis (OA) disease burden is unclear, we studied this in patients with hand OA from our Hand OSTeoArthritis in Secondary care (HOSTAS) cohort. Methods. Cross-sectional data from the HOSTAS study were used, including consecutive patients with primary hand OA. Nineteen comorbidities were assessed: 18 self-reported (modified Charlson index and osteoporosis) and obesity (body mass index = 30 kg/m(2)). Mean differences were estimated between patients with versus without comorbidities, adjusted for age and sex: for general disease burden [health-related quality of life (HRQOL), Medical Outcomes Study Short Form-36 physical component scale (0-100)] and disease-specific burden [self-reported hand function (0-36), pain (0-20; Australian/Canadian Hand OA Index), and tender joint count (TJC, 0-30)]. Differences above a minimal clinically important improvement/difference were considered clinically relevant. Results. The study included 538 patients (mean age 61 yrs, 86% women, 88% fulfilled American College of Rheumatology classification criteria). Mean (SD) HRQOL, function, pain, and TJC were 44.7 (8), 15.6 (9), 9.3 (4), and 4.8 (5), respectively. Any comorbidity was present in 54% (287/531) of patients and this was unfavorable [adjusted mean difference presence/absence any comorbidity (95% CI): HRQOL-4.4 (-5.8 to-3.0), function 1.9 (0.4-3.3), pain 1.4 (0.6-2.1), TJC 1.3 (0.4-2.2)]. Number of comorbidities and both musculoskeletal (e. g., connective tissue disease) and nonmusculoskeletal comorbidities (e. g., pulmonary and cardiovascular disease) were associated with disease burden. Associations with HRQOL and function were clinically relevant. Conclusion. Comorbidities showed clinically relevant associations with disease burden. Therefore, the role of comorbidities in hand OA should be considered when interpreting disease outcomes and in patient management.
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NR 50
TC 52
Z9 54
U1 0
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JI J. Rheumatol.
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WC Rheumatology
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TI Prevalence of Chronic Neck Pain, Low Back Pain, and Knee Pain and Their Related Factors in Community-Dwelling Adults in Iran A Population-based National Study
SO CLINICAL JOURNAL OF PAIN
LA English
DT Article
DE chronic musculoskeletal pain; low back pain; neck pain; knee pain; prevalence; odds ratio
ID chronic musculoskeletal pain; global burden; physical-activity; health-status; risk-factors; disease; osteoarthritis; epidemiology; osteoporosis; country
AB Background: Chronic musculoskeletal pain (CMP) is increasing in prevalence rapidly. Over the past 2 decades low back pain has been ranked globally as the primary cause of years lived with disability. The primary objective of this study was to investigate the prevalence of chronic neck pain (CNP), chronic low back pain (CLBP), and chronic knee pain (CKP) and their related risk factors in the national Iranian population. Methods: We analyzed data obtained through a cross-sectional, population-based survey of 7889 Iranians who were aged between 30 and 70 years. Results: The prevalence of CNP, CLBP, and CKP was 15.34%, 27.18%, and 29.97%, respectively. Female sex, aging, body mass index >= 25, Lur or Arab ethnicity, illiteracy, passive smoking, positive osteoporosis history, and low or high physical

activity levels were risk factors for CLBP, CNP, and CKP after adjustment for potential confounders. For example, in participants with a body mass index >= 30, odds ratios for CNP, CLBP, and CKP adjusted for age, sex, ethnicity, living area, education, employment status, smoking, and physical activity levels were 1.26 (95% confidence interval [CI], 1.04-1.52), 1.37 (95% CI, 1.17-1.59), and 1.64 (95% CI, 1.41-1.91), respectively. Conclusions: This is the first study investigating the prevalence of CNP, CLBP, and CKP in the national population of Iran. It shows some modifiable risk factors for CMP, and suggests that affordable planning for these risk factors can be valuable in preventing CMP globally. However, this is a cross-sectional study and future longitudinal studies in this field are necessary.
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NR 54
TC 68
Z9 76
U1 0
U2 36
PU LIPPINCOTT WILLIAMS & WILKINS
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PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
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J9 CLIN J PAIN
JI Clin. J. Pain
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AU Li, JJ
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AF Li, Jianjun
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Jing, Da
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Ding, Yin
Feng, Xue
TI Effects of low-intensity pulsed electromagnetic fields on bone microarchitecture, mechanical strength and bone turnover in type 2 diabetic db/db mice
SO SCIENTIFIC REPORTS
LA English
DT Article
ID ovariectomy-induced osteoporosis; affects osteoclast formation; hormone replacement therapy; knee osteoarthritis; leptin; transcription; osteogenesis; stimulation; model; gene
AB Type 2 diabetic patients have impaired bone quality, leading to increased fracture risk. Substantial evidence demonstrates that pulsed electromagnetic fields (PEMF) could resist osteopenia/osteoporosis induced by estrogen deficiency and disuse. However, the effects of PEMF on osteopenia/osteoporosis associated with diabetes, especially for more prevalent type 2 diabetes, remain poorly understood. We herein investigated the skeletal effects and mechanisms of PEMF (15 Hz, 20 Gs) on leptin receptor-deficient db/db mice with typical type 2 diabetic symptoms. Our mu CT results showed that 12-week PEMF exposure significantly improved both cancellous and cortical bone microarchitecture in db/db mice. Three-point bending and biomechanical indentation testing demonstrated that PEMF improved whole-bone structural properties and tissue-level material properties in db/db mice. PEMF significantly promoted bone formation in db/db mice evidenced by increased serum osteocalcin and bone mineral apposition rate, whereas PEMF exerted no observable alteration in bone resorption. Real-time PCR showed that PEMF upregulated tibial gene expression of osteoblastogenesis-related of canonical Wnt/beta-catenin signaling but not osteoclastogenesis-related RANKL-RANK signaling in db/db mice. Our findings demonstrate that PEMF improved bone quantity and quality with obvious anabolic activities in db/db mice, and imply that PEMF might become a clinically applicable treatment modality for improving bone quality in type 2 diabetic patients.
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NR 63
TC 28
Z9 33
U1 0
U2 31
PU NATURE PORTFOLIO
PI BERLIN
PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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J9 SCI REP-UK
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PD SEP 7
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DI 10.1038/s41598-017-11090-7
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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AU Roman-Blas, JA
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AF Roman-Blas, Jorge A.
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TI The combined therapy with chondroitin sulfate plus glucosamine sulfate or chondroitin sulfate plus glucosamine hydrochloride does not improve joint damage in an experimental model of knee osteoarthritis in rabbits
SO EUROPEAN JOURNAL OF PHARMACOLOGY
LA English
DT Article
DE Osteoarthritis; Cartilage damage; Synovial inflammation; Subchondral bone; Chondroitin sulfate; Glucosamine sulfate
ID subchondral bone; articular-cartilage; chronic arthritis; mineral density; osteoporosis; increases; synovitis; inflammation; combination; symptoms
AB Osteoarthritis is the most common chronic joint disorder especially during aging. Although with controversies, glucosamine, both in its forms of sulfate and hydrochloride, and chondroitin sulfate are commonly employed to treat osteoarthritis. Due to the modest improve in the symptoms observed in patients treated with these drugs alone, a formulation combining both agents has been considered. The discrepant results achieved for pain control or structural improvement in osteoarthritis patients has been attributed to the quality of chemical formulations or different bias in clinical studies. The current study has been designed to test the effects of two different combined formulations with adequate pharmaceutical grade of these drugs in osteoarthritic joints, and to explore the underlying mechanisms modulated by both formulations in different osteoarthritis target tissues. Knee osteoarthritis was surgically induced in experimental rabbits. Some animals received the combined therapy (CT) 1, (chondroitin sulfate 1200 mg/day + glucosamine sulfate 1500 mg/day), or the CT2 ((chondroitin sulfate 1200 mg/day + glucosamine hydrochloride 1500 mg/day). Neither CT1 nor CT2 significantly modified the cartilage damage or the synovial inflammation observed in osteoarthritic animals. Treatments were also unable to modify the presence of pro-inflammatory mediators, and the synthesis of metalloproteinases in the cartilage or in the synovium of osteoarthritic animals. Combined therapies did not modify the decrease in the subchondral bone mineral density observed in osteoarthritic rabbits. Therapies of chondroitin sulfate plus glucosamine sulfate or chondroitin sulfate plus glucosamine hydrochloride failed to improve structural damage or to ameliorate the inflammatory profile of joint tissues during experimental osteoarthritis.
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NR 34
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Z9 27
U1 1
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PI AMSTERDAM
PA PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
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JI Eur. J. Pharmacol.
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WC Pharmacology & Pharmacy
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PT J
AU Chu, JG
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AF Chu, Jian-Guo
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Tian, Fa-Ming
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Xiao, Ya-Ping
Shao, Li-Tao
Zhang, Ying-Ze
Zhang, Liu
TI Strontium ranelate causes osteophytes overgrowth in a model of early phase osteoarthritis
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Osteoarthritis; Strontium ranelate; Cartilage; Osteophytes; Subchondral bone; Micro-CT
ID cruciate ligament transection; subchondral bone; cartilage degradation; knee osteoarthritis; histological assessments; extracellular-matrix; articular-cartilage; rat model; degeneration; recommendations
AB Background: Osteoarthritis (OA) involves cartilage changes as well as modifications of subchondral bone and synovial tissues. Strontium ranelate (SR), an anti-osteoporosis compound, which is currently in phase III clinical trial for treatment of OA. Evidences suggest that SR preferably deposited in osteophyte, other than in subchondral bone in early phase of OA. This phenomenon raises concern about its utility for OA treatment as a disease-modifying drug. To evaluate the effect of SR on cartilage, subchondral bone mass and subchondral trabecular bone structure in medial meniscectomized (MNX) guinea pigs. Method: Thirty-six 3-month-old male Dunkin Hartley albino guinea pigs received either sham or medial meniscectomy operations. One week after the procedure, meniscectomized animals began 12 weeks of SR (625 mg/kg, daily) treatment by oral gavage for MNX + SR group, or normal saline for MNX + V group. All animals were euthanized 12 weeks later, cartilage degeneration and subchondral bone micro-architecture was analyzed. Results: Both OARSI scores (P = 0.523 for marcoscopic scores, P = 0.297 for histological scores) and Cartilage thickness (P = 0.335) in MNX + SR group were comparable to MNX + V group. However, osteophyte sizes were larger in MNX + SR group (P = 0.014), and collapsed osteophytes in MNX + SR group (7 by 12) were significantly more than in MNX + V group (1 by 12) (P = 0.027), while immunohistochemistry indicates catabolic changes in osteophyte/plateau junction. Micro-CT analysis showed bone mineral density (BMD) (P = 0.001), bone volume fraction (BV/TV) (P = 0.008), trabecular spacing (Tb.Sp) (P = 0.020), trabecular thickness (Tb.Th) (P = 0.012) and structure model index (SMI) (P = 0.005) levels to be significantly higher in the MNX + SR group than in the MNX + V group. Conclusions: SR (625 mg/kg/day) did not protect cartilage from degeneration in MNX guinea pigs but subchondral bone was significantly enhanced. In early phase

OA, SR administration causes osteophyte overgrowth, which may be related to incorporation into mineralizing osteophytes. This adverse effect is important for future studies of SR in OA.
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TI TGF-β Family Signaling in Connective Tissue and Skeletal Diseases
SO COLD SPRING HARBOR PERSPECTIVES IN BIOLOGY
LA English
DT Article
ID growth-factor-beta; bone morphogenetic protein; smooth-muscle-cells; camurati-engelmann-disease; van-buchem-disease; medial edge epithelium; transforming growth-factor-beta-1 expression; hereditary hemorrhagic telangiectasia; hyperostosis corticalis generalisata; progressive diaphyseal dysplasia
AB The transforming growth factor beta (TGF-beta) family of signaling molecules, which includes TGF-beta s, activins, inhibins, and numerous bone morphogenetic proteins (BMPs) and growth and differentiation factors (GDFs), has important functions in all cells and tissues, including soft connective tissues and the skeleton. Specific TGF-beta family members play different roles in these tissues, and their activities are often balanced with those of other TGF-beta family members and by interactions with other signaling pathways. Perturbations in TGF-beta family pathways are associated with numerous human diseases with prominent involvement of the skeletal and cardiovascular systems. This review focuses on the role of this family of signaling molecules in the pathologies of connective tissues that manifest in rare genetic syndromes (e.g., syndromic presentations of thoracic aortic aneurysm), as well as in more common disorders (e.g., osteoarthritis and osteoporosis). Many of these diseases are caused by or result in pathological alterations of the complex relationship between the TGF-beta family of signaling mediators and the extracellular matrix in connective tissues.

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WC Cell Biology
SC Cell Biology
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PT J
AU Patel, T
Milligan, J
Lee, J
AF Patel, Tejal
Milligan, Jamie
Lee, Joseph
TI Medication-related problems in individuals with spinal cord injury in a primary care-based clinic
SO JOURNAL OF SPINAL CORD MEDICINE
LA English
DT Article
DE Adverse drug reaction; Drug side effects; Pharmacists; Polypharmacy; Spinal cord injury
AB Objective: To determine the frequency of medical problems, reason for referral/primary complaint, products used, medication-related problems, and polypharmacy in patients with spinal cord injury (SCI) seen at an interprofessional primary care mobility clinic. Design: Retrospective review of medical records of patients with SCI for patient visits between August 2012 and March 2013. Methods: Data were abstracted from medical records of patients with SCI. Results: Of 74

patients who presented to the clinic, 19 had an SCI. Mean age was 46.7 years and 74% were male. Most frequent medical problems were depression/anxiety (37%), osteoporosis/osteopenia (26%), hypertension (21%), dyslipidemia (21%), and osteoarthritis (21%). Most common presenting complaints were pain (23%) and bowel/bladder issues (13%). Most common medication-related problems were untreated conditions (41%), ineffective medications (21%), adverse drug reactions (18%), and under-and over-dosage (each 9%). Patients with SCI most frequently used products to treat pain (68%), constipation (42%), muscle spasm (42%), hypertension (42%), and depression (37%). When including natural health products, vitamins and minerals, polypharmacy was seen in 74% of patients with SCI (63% when limited to prescription and over-the-counter medications). For patients with SCI in whose care a pharmacist collaborated, a mean of 3.2 medication-related problems per patient were identified compared with 1 per patient when the pharmacist was not involved. Conclusion: This study is the first to describe medication use, polypharmacy and medication-related problems in patients with SCI seen at an interprofessional primary care clinic. Use of high-risk medications, polypharmacy, and medication-related problems in patients with SCI suggest the need for collaborative interprofessional care that includes a pharmacist.
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AU Bini, G
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Bedini, R
Marinozzi, A
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AF Bini, G.

Bini, F.
Bedini, R.
Marinozzi, A.
Marinozzi, F.
TI A topological look at human trabecular bone tissue
SO MATHEMATICAL BIOSCIENCES
LA English
DT Article
DE CW-complex; Euler characteristic; Trabecular bone tissue; Kelvin cell
ID cancellous bone; quantification
AB Bone quality is affected by trabecular architecture at microscopic level. Various abnormalities of bone tissue lead to altered strength and to an increased susceptibility to fracture, such as Osteoporosis and Osteoarthritis, two major health burdens of our society. These are two complex musculoskeletal diseases that mainly concern bone tissue. In the last twenty years, there has been a growing interest in finding an appropriate topological model for the micro-architecture of trabecular bone tissue. In particular, we prove that these models involve general topological spaces. The appropriate notion to deal with is that of CW-complex. (C) 2017 Elsevier Inc. All rights reserved.
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PT J
AU Atik, OS
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AF Atik, O. Sahap
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TI Ulna fracture and medial meniscal tear resulting from dog-related injuries
SO EKLEM HASTALIKLARI VE CERRAHISI-JOINT DISEASES AND RELATED SURGERY
LA English
DT Article
DE Dog-related injuries; meniscus tear; ulna fracture
AB In this article, we present two middle-aged female patients with ulna fracture or medial meniscal tear resulting from dog-related injuries, which are not common. Both patients mentioned that pain started after their dogs pulled away their collar ropes strongly and suddenly. Both patients had postmenopausal osteoporosis and degenerative osteoarthritis. For this reason, ulna fracture and meniscus tear had developed with low-energy trauma resulting from dog-related injuries.
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NR 5
TC 3
Z9 3
U1 0
U2 1
PU TURKISH JOINT DISEASES FOUNDATION
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PA BUGDAY SOKAK 6-27, KAVAKLIDERE, ANKARA 06700, TURKEY
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PT J
AU Aguado-Maestro, I
Panteli, M
García-Alonso, M
García-Cepeda, I
Giannoudis, PV
AF Aguado-Maestro, Ignacio
Panteli, Michalis
Garcia-Alonso, Manuel
Garcia-Cepeda, Ignacio
Giannoudis, Peter V.
TI Hip osteoarthritis as a predictor of the fracture pattern in proximal femur fractures
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English

DT Article
DE Hip osteoarthritis; Hip fracture; Intracapsular; Extracapsular
ID bone-mineral density; femoral-neck; risk-factors; postoperative complications; elderly-women; osteoporosis; mortality; outcm; association; cohort
AB Introduction: Several authors have suggested a correlation between the fracture patterns of proximal femur fractures and the degree of hip osteoarthritis (HOA), but the current evidence to support this are insufficient. The aim of our study was to demonstrate whether there is an association between the grade of HOA and fracture pattern observed, in patients presenting with a fragility fracture of the proximal femur. Materials and methods: We contacted a retrospective review of all patients presenting to our institution with fragility fractures involving the proximal femur, between March 2012 and October 2013. Pathological fractures, high-energy injuries and patients with less than one year of follow-up were excluded from further analysis. Admission radiographs and severity of HOA were assessed according to Kellgren and Lawrence scale (minimal: Grades 1-2; severe: Grades 3-4). Fractures were classified according to AO/OTA classification. Results: A total of 1003 patients (725 females; 1003 fractures) met the inclusion criteria, having a mean age of 81.5 (46-106 years). With regards to fracture classification, 417 (41.6%) fractures were classified as extracapsular and 586 (58.4%) as intracapsular. A total of 939 (93.9%) patients presented with minimal HOA, whilst 61 (6.1%) of the patients presented with severe HOA. Of the 61 patients presenting with severe HOA, 42 patients (68.9%) sustained a 31A-interthrocanteric fracture and 19 patients (31.1%) sustained a 31B-intracapsular fracture. Regarding the patients presenting with minimal HOA (832 patients in total), 323 patients (38.8%) sustained 31A-intertrochanteric fracture and 509 patients (61.2%) sustained a 31B-intracapsular fracture. Patients presenting with severe HOA were found to have a statistically significant chance to present with an extracapsular fracture ($p < 0.01$). Conclusions: The degree of HOA is related to the fracture pattern in patients presenting following simple mechanical falls. More specifically, higher grades of HOA are associated with extracapsular fracture patterns, whereas lower grades of HOA are associated with intracapsular fracture patterns. (C) 2017 Elsevier Ltd. All rights reserved.
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NR 40
TC 20
Z9 24
U1 0
U2 5
PU ELSEVIER SCI LTD
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J9 INJURY
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WC Critical Care Medicine; Emergency Medicine; Orthopedics; Surgery
SC General & Internal Medicine; Emergency Medicine; Orthopedics; Surgery
GA FQ8OT
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PT J
AU Greenbaum, J

Wu, KH
Zhang, L
Shen, H
Zhang, JG
Deng, HW
AF Greenbaum, Jonathan
Wu, Kehao
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Shen, Hui
Zhang, Jigang
Deng, Hong-Wen
TI Increased detection of genetic loci associated with risk predictors of osteoporotic fracture using a pleiotropic cFDR method
SO BONE
LA English
DT Article
DE Osteoporosis; Association; Bone mineral density; Human genetics
ID bone-mineral density; genome-wide association; human height; polymorphisms; metaanalysis; osteoarthritis; determinant; population; disease; protein
AB Although GWAS have been successful in identifying some osteoporosis associated loci, the findings explain only a small fraction of the total genetic variance. In this study we use a recently developed novel pleiotropic conditional false discovery rate (cFDR) method to identify novel genetic loci associated with two risk traits for osteoporotic fracture (the clinical outcome and end result of osteoporosis), Height (HT) and Femoral Neck (FNK) BMD. The cFDR method allows us to improve the detection of associated variants by incorporating any potentially shared genetic mechanisms between the two associated traits. We analyzed the summary statistics from two GWAS meta-analyses for single nucleotide polymorphisms (SNPs) that are associated with HT and FNK BMD. Using the cFDR method, we show enrichment in the identification of SNPs associated with each trait conditioned on their strength of association with the second trait. The findings revealed 18 SNPs that are associated with both HT and FNK BMD, 4 of which had not previously been reported to play a role in bone health. The novel SNPs located at K1F1B and the intergenic region between FERD3L and TWISTNB are noteworthy as these genes may be associated with processes that are functionally important in bone metabolism. By leveraging GWAS results from related phenotypes we identified several novel loci that may contribute to the proportion of variability explained for each trait, although we cannot speculate about these potential contributions to heritability based on this analysis alone. (c) 2017 Elsevier Inc. All rights reserved.
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PT J

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TI Lumbar disc degeneration was not related to spine and hip bone mineral densities in Chinese: facet joint osteoarthritis may confound the association
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Lumbar spine; Bone mineral density; Disc degeneration; Facet joint osteoarthritis
ID osteoporosis; women; densitometry; discography; impact; mass; men; ct
AB A sample of 512 Chinese was studied and we observed that greater disc degeneration on MRI was associated with greater spine DXA BMD. Yet, this association may be confounded by facet joint osteoarthritis. BMD may not be a risk factor for lumbar disc degeneration in Chinese. Purpose Evidence suggested that lumbar vertebral bone and intervertebral disc interact with each other in multiple ways. The current paper aims to determine the association between bone mineral density (BMD) and lumbar disc degeneration using a sample of Chinese. Methods We studied 165 patients with back disorders and 347 general subjects from China. All subjects had lumbar spine magnetic resonance (MR) imaging and dual-energy X-ray absorptiometry (DXA) spine BMD studies, and a subset of general subjects had additional hip BMD measurements. On T2-weighted MR images, Pfirrmann score was used to evaluate the degree of lumbar disc degeneration and facet joint osteoarthritis was assessed as none, slight-moderate, and severe. Regression analyses were used to examine the associations between lumbar and hip BMD and disc degeneration, adjusting for age, gender, body mass index (BMI), lumbar region, and facet joint osteoarthritis. Results Greater facet joint osteoarthritis was associated with greater spine BMD ($P < 0.01$) in both patients and general subjects. For general subjects, greater spine BMD was associated with severe disc degeneration, controlling for age, gender, BMI, and lumbar region. When facet joint osteoarthritis entered the regression model, however, greater spine BMD was associated with greater facet joint osteoarthritis ($P < 0.01$) but not greater disc degeneration ($P > 0.05$). No statistical association was observed between spine BMD and lumbar disc degeneration in patients with back disorders ($P > 0.05$), and between hip BMD and disc degeneration in general subjects ($P > 0.05$). Conclusion

BMD may not be a risk factor for lumbar disc degeneration in Chinese. Facet joint osteoarthritis inflates DXA spine BMD measurements and therefore, may confound the association between spine BMD and disc degeneration.
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Z9 43
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PU SPRINGER LONDON LTD
PI LONDON
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WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
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PT J
AU Lu, N
Lu, JW
Zhou, CH
Zhong, FH
AF Lu, Ning
Lu, Jianwei
Zhou, Chenhe
Zhong, FuHua
TI Association between transforming growth factor-beta 1 gene single nucleotide polymorphisms and knee osteoarthritis susceptibility in a Chinese Han population
SO JOURNAL OF INTERNATIONAL MEDICAL RESEARCH
LA English
DT Article
DE Knee osteoarthritis; polymorphism; transforming growth factor-beta 1
ID bone-mineral density; growth-factor-beta-1; women; differentiation; tgf-beta-1;

epidemiology; osteoporosis; expression; aneurysms; receptor
AB Objective To investigate associations between single polymorphisms (SNPs) rs1800469 and rs1982073 in the transforming growth factor-1 gene (TGF-1) and knee osteoarthritis (OA) susceptibility in a Chinese Han population. MethodsTGF-1 rs1800469 and rs1982073 were genotyped in patients with knee OA and age- and sex-matched OA-free controls from a Chinese Han population. The association was further analyzed according to gender and age. Results A total of 765 patients with knee OA and 780 controls were included. CT and CT+CC genotypes of rs1982073, and variant C, were associated with a significantly increased risk of knee OA. Stratification analysis showed that the association between the OA risk and rs1982073 CT heterozygotes compared with TT homozygotes was stronger in females and those aged >65years. In contrast, CT, TT, and CT+TT genotypes of rs1800469 were not significantly associated with the risk of knee OA, even after further stratification analysis for gender and age. Conclusions The TGF-1 rs1982073 T to C change and the variant C genotype may contribute to knee OA risk in the Chinese Han population.
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PT J
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AF Coutts, Louise V.
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TI Local Variation in Femoral Neck Cortical Bone: In Vitro Measured Bone Mineral Density, Geometry and Mechanical Properties
SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE Bone mineral density; cortical bone; indentation; mechanical properties; osteoporosis
ID hip fracture; osteoarthritis; osteoporosis; microindentation; recommendations; variability; orientation; women; age
AB Age- and disease (osteoporotic fractured and osteoarthritic tissue)-related changes in the distribution of cortical bone were examined, using a multimodality approach, including measurement of local density, geometry and mechanical properties, where changes in these properties can give rise to instability and increasing probability of fracture. In contrast to the majority of previously reported research, this study also focuses on the characteristic non-circular femoral neck cross-sectional geometry and variation in bone mineral density (BMD) around the femoral neck. Twenty-two osteoarthritic and 7 osteoporotic femoral neck slices, collected from elective and trauma-related arthroplasty, and 16 cadaveric donor tissue controls were tested mechanically using Reference Point Indentation (BioDent (TM), Active Life Technologies, Santa Barbara, CA) and then scanned with in vitro-based radiography intended to replicate the dual-energy X-ray absorptiometry technique. All parameters were measured regionally around the

circumference of the femoral neck, allowing examination of spatial variability within the cortical bone. Fractured tissue was less resistant to indentation in the thinner superolateral segment compared to other segments and other groups. BMD around the fractured femoral necks appeared more consistent than that of nonfractured tissue, where BMD was reduced in the superolateral segment for the other groups. Cortical bone was thin in the superolateral segment for all groups except for the osteoarthritic group, and was thicker in the inferomedial segment for both osteoarthritic and fractured groups, resulting in the largest variation in buckling ratio (ratio of cortical bone diameter to cortical bone thickness) around the femoral neck for the fractured group. With age, healthy controls appeared to have lower inferomedial cortical thickness, whereas no significant differences in Reference Point Indentation measurements and density were observed. The study has highlighted several (both quality- and quantity-related) parameters that may be used to improve prediction of fracture risk.
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NR 23
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AU Corrado, A
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TI Osteoblast Role in Rheumatic Diseases
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
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DT Review
DE arthritis; osteoarthritis; osteoblast; osteoporosis; spondyloarthritis
ID necrosis-factor-alpha; subchondral bone osteoblasts; glucocorticoid-induced osteoporosis; ankylosing-spondylitis; beta-catenin; osteoclast differentiation; growth-factor; receptor activator; rank ligand; proinflammatory cytokines
AB Alterations in osteoblast growth, differentiation and activity play a role in the pathogenesis of several rheumatic diseases, such as rheumatoid arthritis, spondyloarthritides, osteoarthritis, and osteoporosis. In fact, in these rheumatic diseases, abnormal activity of Wnt signaling, receptor activator of nuclear factor-kappa B (RANK)-RANK ligand (RANKL)-osteoprotegerin (OPG) signaling, bone morphogenetic proteins (BMPs) pathway and other mechanisms have been described in osteoblasts. This review article is focused on current knowledge on the role of osteoblast dysregulation occurring in rheumatic diseases.
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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TI Immunoexpression of IGF1, IGF2, and osteopontin in craniofacial bone repair associated with autogenous grafting in rat models treated with alendronate sodium
SO CLINICAL ORAL INVESTIGATIONS
LA English
DT Article
DE Bisphosphonates; Rats; Bone healing; IGF1; IGF2; Osteopontin
ID risk-factors; insulin; osteonecrosis; jaw; resorption; implants; estrogen; density; cancer
AB The aim of this study was to verify the likely influence of presurgical administration of low doses of alendronate sodium in craniofacial bone repair and correlate the histological frame found on reparative tissue to the immunohistochemical presence of IGF1, IGF2, and osteopontin (OP). In total, 120 rats were randomly allocated into four groups: group C (control), group OA (autogenous bone), group B (bisphosphonates), and group OA-B (autogenous bone + bisphosphonates). Groups B and OA-B received alendronate sodium (ALN) 0.01 mg/kg subcutaneously on alternate days for 4 weeks. Groups C and OA received saline solution. Critical 5-mm defects were created in rat calvaria, which were filled with blood clot in groups C and B and with autogenous bone in groups OA and OA-B. The animals were euthanized at 15 or 30 days postoperatively. Histological analysis and immunohistochemistry of IGF1, IGF2, and OP proteins was performed. Immunohistochemistry evaluated the expression in cells and extracellular matrix. Groups C and B revealed healing predominantly characterized by connective tissue. In groups OA and OA-B, healing of connective tissue and neoformation of compact bone was observed. Expression of IGF1 an OP was present in all specimens. IGF1 expression in cells was more pronounced in groups OA and OA-B 15 days postoperatively. The expression of IGF2 was only observed in groups OA and OA-B, with greater intensity in group OA-B 30 days postoperatively. OP expression was only observed in cells and not in the extracellular matrix and

was more pronounced in group OA 15 days postoperatively. The application of systemic ALN at a dose of 0.01 mg/kg did not improve cranial bone matrix deposition. Nevertheless, the expression of IGF1 and OP and a slight marking of IGF2 were observed especially in groups OA and OA-B in the wound healing process. Future studies should assess higher doses of ALN to verify its influence on bone repair. The systemic use of ALN 0.01 mg/kg on alternate days 4 weeks prior to surgery did not interfere with bone repair.
C1 [Camati, Paulo Roberto; Giovanini, Allan Fernando; Schuanka, Cassiana Majewski; Giacomel, Maria Cecilia; de Araujo, Melissa Rodrigues; Zielak, Joao Cesar; Scariot, Rafaela; Deliberador, Tatiana Miranda] Univ Posit, Rua Prof Pedro Viriato Parigot de Sousa, BR-81280330 Curitiba, PR, Brazil.
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NR 39
TC 6
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AU Collin, PG
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TI Five common clinical presentations in the elderly: An anatomical review
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DE anatomy; ageing; geriatrics; fractures; spine; congestive heart failure; dementia; airway
ID age-related-changes; alzheimers-disease; computed-tomography; cellular basis; heart-failure; fractures; impact; adults; osteoarthritis; osteoporosis
AB Elderly patients face distinct health challenges and have an increased demand for specific medical procedures. As the aging population continues to increase, age-associated conditions such as congestive heart failure, hip fractures, spine degeneration, dementia, and airway compromise will increase in prevalence and procedures to correct these conditions will be increasingly performed. A clear understanding of the clinical anatomy of these diseases and procedures is imperative for anatomists and clinicians alike in order to best treat patients and continue to advance aging research and better teach future medical practitioners about the specific anatomy often involved in this group. The aging process mirrors in a variety of ways the common pathologies of the elderly, but it is key to draw the distinction between normal aging and pathology, particularly for congestive heart failure and dementia, in the clinical setting. This article aims to review the common presentations or procedures of the elderly and how the normal aging process is associated with the anatomy of these conditions or complications. Clin. Anat. 30:168-174, 2017. (c) 2017 Wiley Periodicals, Inc.

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TI Cementless Total Hip Arthroplasty in Octogenarians
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE total hip arthroplasty; cementless; octogenarians; outcome; complications
ID bone-mineral density; early failure rate; periprosthetic fractures; femoral fractures; replacement; older; osteoporosis; femur; joint; stem
AB Background: Although several studies indicate excellent results for cementless implants, controversy persists regarding its use in elderly patients. We determined to evaluate the outcome on patients aged over 80 years who were treated with cementless total hip arthroplasty for primary osteoarthritis of the hip. Methods: We assessed the data of 162 consecutive total hip arthroplasties in octogenarian patients (mean age 83 years, range 80-96 years). A control group was created, consisting of 342 patients aged younger than 80 years (mean age 65 years, range 37-79 years). The median follow-up of the cohort was 128.4 months (range 6-211). Results: Competing risk analyses revealed a cumulative implant survival of 98.1% at 5 and 10 years in the study group compared to 99.1% and 98.4% in the control

group, taking system exchange as the end point. No differences in regard to system exchange could be detected between the groups. A significantly worsened complication-free survival rate was evident in the octogenarian group. Osteoporosis was the most powerful risk factor that proved to have a significant negative impact on development of complications. Conclusion: Uncemented total hip arthroplasty is a viable option for the elderly patient. In this population sector, an excellent rate of implant survival can be expected. However, a significant increase of total complications in the octogenarian group could be detected, and was mainly caused by an elevated number of early postoperative complications. Osteoporosis turned out to be a strong risk factor in regard to complication-free survival. Surgeons should therefore be aware of this. (C) 2017 Elsevier Inc. All rights reserved.
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TI Patterns of Care Among Patients Referred to Rheumatologists in Ontario, Canada
SO ARTHRITIS CARE & RESEARCH
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DT Article
ID diagnosed rheumatoid-arthritis; early inflammatory arthritis; quality-of-care; performance-measures; management; physicians; symptoms; delay; onset; time
AB ObjectiveOur aim was to characterize referrals to rheumatologists, the early care management of patients with rheumatic diseases, and timeliness of care and treatment. MethodsWe conducted a retrospective observational study involving patients with first-time rheumatology referrals between 2000 and 2013 in the primary care Electronic Medical Record Administrative data Linked Database (EMRALD) in Ontario, Canada. Referrals were characterized in terms of diagnoses, patient demographics, diagnostic tests, treatment initiated by family physicians and rheumatologists, and other specialists seen prior to rheumatology consultation. Timeliness of referrals, rheumatologist consultations, and treatment were determined overall and for each diagnostic category. ResultsAmong 2,430 patients referred to a rheumatologist, 69% were female, with an average age of 53 years. The principal diagnosis associated with the referral included osteoarthritis (32%), systemic inflammatory rheumatic diseases (31%), regional musculoskeletal conditions (16%), chronic pain conditions (14%), osteoporosis (2%), and other/miscellaneous (5%). Family physicians most frequently prescribed nonsteroidal antiinflammatory drugs/cyclooxygenase 2 inhibitors (38%), and their pre-referral diagnostic testing practice varied considerably. The duration of time from symptom onset to rheumatology consultation varied by diagnoses, with the shortest being for patients with systemic rheumatic diseases; for rheumatoid arthritis (RA), the median time to consultation was 327 days. Most of the delay occurred prior to referral; 36% of RA patients initiated a disease-modifying

antirheumatic drug within 6 months of symptom onset. ConclusionApproximately 1 in 3 referrals to rheumatologists were for a systemic inflammatory rheumatic disease. We observed substantial delays to rheumatology consultations and variations in patterns of care that could be amenable to quality improvement interventions.
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NR 52
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Z9 32
U1 0
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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PT J
AU Awad, NK
Edwards, SL
Morsi, YS
AF Awad, Nasser K.
Edwards, Sharon L.
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TI A review of TiO2 NTs on Ti metal: Electrochemical synthesis, functionalization and potential use as bone implants
SO MATERIALS SCIENCE AND ENGINEERING C-MATERIALS FOR BIOLOGICAL APPLICATIONS
LA English
DT Review
DE Titanium implants; Osteogenesis; TiO2 nanotubes
ID biomedical applications; titania nanotubes; cell-adhesion; surface; growth; anodization; release; biocompatibility; mineralization; therapeutics
AB Degenerative diseases of bone such as osteoarthritis and osteoporosis can lead to bone fractures and immobility, compromising quality of life. Titanium (Ti)-based implants have been intensively investigated for bone repair, with these implants, demonstrating improved outcomes compared to stainless steel and cobalt-chrome alloys, owing to superior mechanical properties and biocompatibility. However, osseointegration between the Ti based implants and the surrounding bone tissue needs to be improved. Surface modification of Ti-based implants provides a solution for addressing this, with electrochemical anodization becoming a realistic approach for the fabrication of hierarchical structured for example nanotubes (NTs), implant surfaces. Using this technique, biocompatibility and osteogenesis of the implant may be improved, by providing an appropriate site for bone cell attachment. In this review, we discuss the anodization of Ti -based implants as an approach for creating titanium dioxide nanotubes (TiO2 NTs) on the implant surface. We further discuss the various ways of functionalizing the NT surface, to reduce post-operative infection and improve implant biocompatibility and osseointegration. (C) 2017 Elsevier B.V. All rights reserved.
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NR 63
TC 157
Z9 169
U1 4
U2 195
PU ELSEVIER
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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AU Yin, ZH
Wang, W
Han, J
Chen, K
Ma, JJ
AF Yin, Zhenhua
Wang, Wei
Han, Jian
Chen, Ke
Ma, Jianjun
TI Decreased trabecular bone deterioration of proximal tibiae and lumbar vertebrae

in postmenopausal women with osteoarthritis
SO EXPERIMENTAL AND THERAPEUTIC MEDICINE
LA English
DT Article
DE osteoarthritis; postmenopausal osteoporosis; bone morphometry; trabecular bone
ID mineral density; hip osteoarthritis; rheumatoid-arthritis; spine osteoarthritis; knee osteoarthritis; general-population; cancellous bone; femoral-head; osteoporosis; fractures
AB Osteoporosis and osteoarthritis (OA) are two common age-related skeletal disorders, which are associated with substantial morbidity and disability, particularly among elderly women. The present study was performed to investigate the trabecular bone deterioration of proximal tibiae and lumbar vertebrae in postmenopausal women with OA. The results demonstrated that the histomorphometric section of trabecular bone below the growth plate was markedly different between the healthy control and OA group. However, the loss of trabecular bone underneath the growth plate in the healthy control group was significantly worse than that of the OA group. Hematoxylin and eosin staining demonstrated the increased disconnection and separation of the trabecular bone network as well as the reduction of trabecular bone mass of primary and secondary spongiosa throughout the proximal metaphysis of tibia in the healthy control compared to the OA group; similar results were found when the same experiment was repeated on the lumbar vertebrae of healthy control subjects and OA patients from postmenopausal women. The biological properties of trabecular bone in the proximal tibia and lumbar vertebrae were measured in postmenopausal women with OA. Spearman's rank correlation analysis revealed that the bone volume fraction was both positively correlated with radiographic severity and Western Ontario McMaster University Osteoarthritis Index scores in in the proximal tibia and lumbar vertebrae from postmenopausal women with OA. In conclusion, the structural properties of the proximal tibia and lumbar vertebrae supported that an inverse correlation existed between postmenopausal women with OA and healthy controls. Moreover, there is an important protective mechanism of OA on trabecular microstructure in proximal tibiae and lumbar vertebrae from postmenopausal women.
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U1 1
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PI ATHENS
PA POB 18179, ATHENS, 116 10, GREECE
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PT J
AU Kruse, C
Eiken, P
Vestergaard, P
AF Kruse, Christian
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Vestergaard, Peter
TI Machine Learning Principles Can Improve Hip Fracture Prediction
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Osteoporosis; Fracture; Machine learning; FRAX; Prediction
ID osteoporotic fractures; risk; men; fit; bmd
AB Apply machine learning principles to predict hip fractures and estimate predictor importance in Dual-energy X-ray absorptiometry (DXA)-scanned men and women. Dual-energy X-ray absorptiometry data from two Danish regions between 1996 and 2006 were combined with national Danish patient data to comprise 4722 women and 717 men with 5 years of follow-up time (original cohort n = 6606 men and women). Twenty-four statistical models were built on 75% of data points through k-5, 5-repeat cross-validation, and then validated on the remaining 25% of data points to calculate area under the curve (AUC) and calibrate probability estimates. The best models were retrained with restricted predictor subsets to estimate the best subsets. For women, bootstrap aggregated flexible discriminant analysis ("bagFDA") performed best with a test AUC of 0.92 [0.89; 0.94] and well-calibrated probabilities following Na < ve Bayes adjustments. A "bagFDA" model limited to 11 predictors (among them bone mineral densities (BMD), biochemical glucose measurements, general practitioner and dentist use) achieved a test AUC of 0.91 [0.88; 0.93]. For men, eXtreme Gradient Boosting ("xgbTree")

performed best with a test AUC of 0.89 [0.82; 0.95], but with poor calibration in higher probabilities. A ten predictor subset (BMD, biochemical cholesterol and liver function tests, penicillin use and osteoarthritis diagnoses) achieved a test AUC of 0.86 [0.78; 0.94] using an "xgbTree" model. Machine learning can improve hip fracture prediction beyond logistic regression using ensemble models. Compiling data from international cohorts of longer follow-up and performing similar machine learning procedures has the potential to further improve discrimination and calibration.
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NR 28
TC 70
Z9 85
U1 2
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PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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PT J
AU Davies, MAM
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Kemp, SPT
Stokes, KA
Arden, NK
Newton, JL
AF Davies, Madeleine A. M.
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Delmestri, Antonella
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Newton, Julia L.
TI Health amongst former rugby union players: A cross-sectional study of morbidity and health-related quality of life
SO SCIENTIFIC REPORTS
LA English
DT Article
ID bone-mineral density; physical-activity; general-population; osteoarthritis; injury; eq-5d; risk; reliability; concussion; benefits
AB In the general population, physical activity is associated with improved health outcomes. However, long-term sports participation may be associated with adverse outcomes, particularly at the elite level. The aims of this study were to assess morbidity and health-related quality of life (HrQoL) amongst former rugby players, compared to an age-standardised general population sample. A cross-sectional study of former elite, male, rugby players (n = 259) was undertaken, and standardised morbidity ratios (SMR) calculated, assessing morbidity prevalence relative to English Longitudinal Study of Aging participants (ELSA, n = 5186). HrQoL, measured using the EQ-5D, was compared to a Health Survey for England (HSE, n = 2981) sample. In SMR analyses of participants aged 50+, diabetes was significantly lower amongst former players, (0.28, 95% CI 0.11-0.66), whereas osteoarthritis (4.00, 95% CI 3.32-4.81), joint replacement (6.02, 95% CI 4.66-7.77), osteoporosis (2.69, 95% CI 1.35-5.38), and anxiety (2.00, 95% CI 1.11-3.61) were significantly higher. More problems in HrQoL were reported amongst former players within the domains of mobility ($p < 0.001$), self-care ($p = 0.041$), usual activities ($p < 0.001$) and pain/discomfort ($p < 0.001$). Morbidity and HrQoL differ between players and the general population, with higher musculoskeletal morbidity and lower diabetes amongst former players. The magnitude of

musculoskeletal morbidity may warrant proactive osteoarthritis management within this population.
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Z9 56
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PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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J9 SCI REP-UK
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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UT WOS:000411998400001
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PT J
AU Teichtahl, AJ
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TI Associations between systemic bone mineral density and early knee cartilage changes in middle-aged adults without clinical knee disease: a prospective cohort study
SO ARTHRITIS RESEARCH & THERAPY
LA English

DT Article
DE Bone mineral density; Cartilage volume; Cartilage defects; Osteoarthritis; Knee
ID early radiographic osteoarthritis; inverse relationship; subchondral bone; surface-area; volume; osteoporosis; defects; determinants; progression; symptoms
AB Background: Osteoarthritis has a high prevalence in people with high bone mineral density (BMD). Nevertheless, whether high systemic BMD predates early structural features of knee osteoarthritis is unclear. This study examined the association between systemic BMD and knee cartilage defect progression and cartilage volume loss in middle-aged people without clinical knee disease. Methods: Adults (n = 153) aged 25-60 years had total body, lumbar spine, and total hip BMD assessed by dual-energy X-ray absorptiometry at baseline (2005-2008), and tibial cartilage volume and tibiofemoral cartilage defects assessed by magnetic resonance imaging at baseline and follow up (2008-2010). Results: Higher spine BMD was associated with increased risk for progression of medial (OR = 1.45, 95% CI 1.10, 1.91) and lateral (OR = 1.30, 95% CI 1.00, 1.67) tibiofemoral cartilage defects. Total hip BMD was also positively associated with the progression of medial (OR = 1.63, 95% CI 1.10, 2.41) and lateral (OR = 1.53, 95% CI 1.08, 2.18) tibiofemoral cartilage defects. Greater total body, spine, and total hip BMD were associated with increased rate of lateral tibial cartilage volume loss (for every 1 g/10 cm(2) increase in total body BMD: B = 0.44%, 95% CI 0.17%, 0.71%; spine BMD: 0.17%, 95% CI 0.04%, 0.30%; total hip BMD: 0.29%, 95% CI 0.13%, 0.45%), with no significant associations for medial tibial cartilage volume loss. Conclusion: In middle-aged people without clinical knee disease, higher systemic BMD was associated with increased early knee cartilage damage. Further work is needed to clarify the effect of systemic BMD at different stages of the pathway from health through to disease in knee osteoarthritis, as new therapies targeting bone are developed for the management of knee osteoarthritis.
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NR 38
TC 21
Z9 24
U1 1
U2 4
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 ARTHRITIS RES THER
JI Arthritis Res. Ther.
PD MAY 18
PY 2017
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DI 10.1186/s13075-017-1314-0
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WC Rheumatology
SC Rheumatology
GA EW2LR
UT WOS:000402328600001
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PT J
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TI Frailty in HIV infected people: a new risk factor for bone mineral density loss
SO AIDS
LA English
DT Article
DE bone mineral density; frailty; HIV
ID antiretroviral therapy; older women; phenotype; osteoporosis; fracture; men
AB Objective:The study aims to assess the association between bone mineral density (BMD) and frailty in a cohort of HIV-infected patients.Design:A cross-sectional study in an HIV outpatient unit where nearly 1000 patients are monitored.Methods:Study participants undergoing bone densitometry were proposed an evaluation of frailty using criteria of the Cardiovascular Health Study (CHS) and the Study of Osteoporotic Fractures (SOF). Frailty markers were weight-loss, self-reported exhaustion, physical activity, grip strength, chair stands, and slow gait. Patients' characteristics were collected from an electronic medical record. Associations of frailty with BMD and osteoporosis were tested using multivariate linear and logit regression models, respectively.Results:In total, 175 HIV-infected patients, 121 (69.14%) men, were analyzed. Prevalence of frailty markers, osteopenia, and osteoporosis were comparable among sexes. Despite a younger age, spinal and femoral neck BMD were lower in women ($P<0.05$). Linear regression model adjusting by age, duration of HIV follow-up, BMI, smoking status, osteoarthritis, osteoporosis treatment, and the age at menopause showed a negative association of spinal and femoral BMD with frailty according to SOF criteria in women ($P<0.05$). In men, SOF-defined frailty was associated with osteoporosis (odds ratio 28.79; 95% confidence interval 2.15-386.4) in a model adjusting for age, duration of HIV follow-up, CD4(+) nadir, CD4(+) T-cell count, tobacco consumption, exposure to tenofovir (TDF) and protease inhibitors. No significant associations were found between BMD and CHS-defined frailty.Conclusion:Our study shows that frailty according to SOF criteria is

associated with low spinal BMD values in female and osteoporosis in male HIV-infected patients. Copyright (C) 2017 Wolters Kluwer Health, Inc. All rights reserved.
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NR 15
TC 18
Z9 22
U1 1
U2 7
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
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JI Aids
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BP 1573
EP 1577
DI 10.1097/QAD.0000000000001507
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WC Immunology; Infectious Diseases; Virology
SC Immunology; Infectious Diseases; Virology
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UT WOS:000404914900009
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PT J
AU Giannini, S
Romagnoli, M
Barbadoro, P
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Muccioli, Giulio Maria Marcheggiani
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Grassi, Alberto
Zaffagnini, Stefano
TI Results at a minimum follow-up of 5 years of a ligaments-compatible total ankle replacement design
SO FOOT AND ANKLE SURGERY
LA English
DT Article
DE Ankle; Replacement; Arthritis; Trauma
ID long-term; arthroplasty; rates; osteoarthritis; complications; arthrodesis; mobility; motion; range
AB Background: A new design of 3-part ankle replacement was developed to achieve compatibility with the natural ligaments by allowing certain fibers to remain isometric during passive motion. Methods: We evaluate 75 ankle prostheses implanted from July 2003 to December 2008, at a mean follow-up 6.5 +/- 1.1 years (range 5-9 years). The mean age at surgery was 62 +/- 13 years (range 29-82). Results: The mean AOFAS scores achieved at pre-op and at last follow-up were

respectively 37 +/- 5 (23-45) and 78 +/- 8 (64-98). (p < 0.001). Clinical range of motion of the ankle measured by goniometer pre op was 1 degrees +/- 2 of dorsiflexion and 12 degrees +/- 4 degrees of plantarflexion; at last follow- up range of motion increased to 6 degrees +/- 5 degrees in dorsiflexion (p < 0.01) and 18 degrees +/- 7 degrees in plantarflexion (p < 0.05). Radiographs showed no loosening and little signs of radiolucency. Two revisions necessitated component removal, neither for implant loosening. The overall survival rate was 97.3%. Conclusions: Function and Range-of-motion showed significant improvements. These results demonstrate that ligaments-compatible shaped talar and tibial components, with a fully conforming interposed meniscal bearing, can provide satisfactory survival rates and clinical outcomes in the middle term. (C) 2017 European Foot and Ankle Society. Published by Elsevier Ltd. All rights reserved.
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U1 0
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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JI Foot Ankle Surg.
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SC Orthopedics
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PT J
AU Moya-Angeler, J
Lane, JM
Rodriguez, JA
AF Moya-Angeler, Joaquin
Lane, Joseph M.

Rodriguez, Jose A.
TI Metabolic Bone Diseases and Total Hip Arthroplasty: Preventing Complications
SO JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
LA English
DT Review
ID pagets-disease; osteogenesis imperfecta; replacement; osteoarthritis; management; fracture; osteonecrosis; osteoporosis; diagnosis; risk
AB Metabolic bone diseases are a diverse group of conditions characterized by abnormalities in calcium metabolism and/or bone cell physiology. These unbalanced processes can eventually lead to bony deformities and altered joint biomechanics, resulting in degenerative joint disease. Not infrequently, patients with metabolic bone diseases have restricting hip joint pain that ultimately necessitates hip arthroplasty. To minimize complications, the surgeon must consider the particular characteristics of these patients. The surgical and medical management of patients with metabolic bone diseases undergoing hip arthroplasty requires appropriate preoperative diagnosis, careful attention to the technical challenges of surgery, and strategies to maximize the long-term results of the surgical intervention, such as the use of bone anabolic and anticatabolic agents.
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U2 2
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AU Szeremeta, A
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AF Szeremeta, A.
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TI The association between insulin-like growth factor 1 (IGF-1), IGF-binding proteins (IGFBPs), and the carboxyterminal propeptide of type I procollagen (PICP) in pre- and postmenopausal women with rheumatoid arthritis
SO SCANDINAVIAN JOURNAL OF RHEUMATOLOGY
LA English
DT Article

ID bone turnover; cartilage destruction; biochemical markers; disease-activity; female-patients; serum-levels; factor-axis; osteoporosis; osteoarthritis; expression
AB Objectives: To assess the association between plasma levels of the insulin-like growth factor (IGF) system including IGF-1, IGF-binding proteins (IGFBPs) including IGFBP-1, total (t-)IGFBP-3 and functional (f-)IGFBP-3, and the carboxyterminal propeptide of type I procollagen (PICP) in pre- and postmenopausal women with rheumatoid arthritis (RA).Method: Plasma concentrations of IGF-1, IGFBP-1, t-IGFBP-3, f-IGFBP-3, and PICP were measured by immunoassay.Results: No significant difference was observed in plasma IGF-1 levels between pre- and postmenopausal subjects. Plasma levels of IGFBP-1 were elevated in RA. PICP and f-IGFBP-3 were greatly affected by menopausal status. Of the three IGFBPs tested, only f-IGFBP-3 plasma levels in RA women correlated negatively with age and disease duration. A positive correlation was demonstrated between PICP and erythrocyte sedimentation rate (ESR) in RA. Moreover, there was no correlation between PICP and IGF-1 and any of the IGFBPs in RA women.Conclusions: Considerable disruption of the IGF system in RA was found to be related to disease activity and duration. Changes in the IGF-IGFBP axis and PICP levels were different in pre- and postmenopausal women with RA. Elevated plasma PICP concentrations may indicate an increased rate of bone formation in postmenopausal RA women. Additionally, the observed changes in the IGF/IGFBP system did not affect bone formation during RA.
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NR 46
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Z9 4
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PU TAYLOR & FRANCIS LTD
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AU Lee, SY
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Ku, HC
AF Lee, Shih-Yi
Shih, Shou-Chuan
Leu, Yi-Shing
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Ku, Hui-Chun
TI Implications of Age-Related Changes in Anatomy for Geriatric-Focused Difficult Airways
SO INTERNATIONAL JOURNAL OF GERONTOLOGY
LA English
DT Review
DE difficult airways; difficult intubation; difficult mask ventilation; geriatric airway
ID impossible mask ventilation; endochondral ossification; chondrocyte apoptosis; predictive factors; older-adults; oral-mucosa; intubation; management; risk; laryngoscopy
AB The structure and function surrounding the airway change by the age, which may ultimately result in having anatomic features of difficult airways in the elderly. Hence, we reviewed the literature focusing on the age-related anatomic changes and accordingly to compare the characteristics of difficult airways. With age, teeth wear and loss, protein and collagen synthesis reduction, and bone loss and muscle atrophy results in aged face (chin protrusion, cheek retraction and drooping), jaw restriction (temporo-madibular joint disc displacement and osteoarthritis), neck and back stiffness, and kyphotic deformities (degeneration of spinal articular cartilage, intervertebral discs, and spinal osteoporosis). These age-related changes in anatomy are compatible with the predictors of a difficult airway. We hope that these age-related anatomic approaches will prospectively allow a detailed understanding of the hallmarks resulting in geriatric-focused difficult airways in the future studies. Copyright (C) 2017, Taiwan Society of Geriatric Emergency & Critical Care Medicine. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license.
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NR 62
TC 14
Z9 15
U1 1
U2 7
PU ELSEVIER TAIWAN
PI TAIPEI
PA RM N-412, 4F, CHIA HSIN BUILDING 11, NO 96, ZHONG SHAN N ROAD SEC 2, TAIPEI, 10449, TAIWAN
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J9 INT J GERONTOL
JI Int. J. Gerontol.
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
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PT J
AU Yoshimura, N
Muraki, S
Oka, H

Iidaka, T
Kodama, R
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Nakamura, K
Tanaka, S
Akune, T
AF Yoshimura, N.
Muraki, S.
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Iidaka, T.
Kodama, R.
Kawaguchi, H.
Nakamura, K.
Tanaka, S.
Akune, T.
TI Is osteoporosis a predictor for future sarcopenia or vice versa? Four-year observations between the second and third ROAD study surveys
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Incidence; Osteoporosis; Osteosarcopenia; Population-based cohort study; Sarcopenia
ID bioelectrical-impedance analysis; dwelling elderly subjects; skeletal-muscle mass; working group; older men; prevalence; community; association; epidemiology; definition
AB In a 4-year follow-up study that enrolled 1099 subjects aged ae60 years, sarcopenia prevalence was estimated at 8.2%. Moreover, the presence of osteoporosis was significantly associated with short-term sarcopenia occurrence, but the reciprocal relationship was not observed, suggesting that osteoporosis would increase the risk of osteoporotic fracture and sarcopenia occurrence. The present 4-year follow-up study was performed to clarify the prevalence, incidence, and relationships between sarcopenia (SP) and osteoporosis (OP) in older Japanese men and women. We enrolled 1099 participants (aged, ae60 years; 377 men) from the second survey of the Research on Osteoarthritis/Osteoporosis against Disability (ROAD) study (2008-2010) and followed them up for 4 years. Handgrip strength, gait speed, skeletal muscle mass, and bone mineral density were assessed. SP was defined according to the Asian Working Group for Sarcopenia. OP was defined based on the World Health Organization criteria. SP prevalence was 8.2% (men, 8.5%; women, 8.0%) in the second survey. In those with SP, 57.8% (21.9%; 77.6%) had OP at the lumbar spine L2-4 and/or femoral neck. SP cumulative incidence was 2.0%/year (2.2%/year; 1.9%/year). Multivariate regression analysis revealed that OP was significantly associated with SP occurrence within 4 years (odds ratio, 2.99; 95% confidence interval, 1.46-6.12; $p < 0.01$), but the reciprocal relationship was not significantly observed (2.11; 0.59-7.59; $p = 0.25$). OP might raise the short-term risk

of SP incidence. Therefore, OP would not only increase the risk for osteoporotic fracture but may also increase the risk for SP occurrence.
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NR 35
TC 146
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U1 1
U2 18
PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 0937-941X
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J9 OSTEOPOROSIS INT
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WC Endocrinology & Metabolism

SC Endocrinology & Metabolism
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PT J
AU Street, BD
Adkin, A
Gage, W
AF Street, Brian D.
Adkin, Allan
Gage, William
TI Reported balance confidence and movement reinvestment of younger knee replacement patients are more like younger healthy individuals, than older patients
SO GAIT & POSTURE
LA English
DT Article
DE Total knee replacement; Age-related differences; Balance confidence; Movement reinvestment; Functional mobility
ID joint replacement; community; pain; efficacy; surgery; falls
AB This study focused on differences between the rapidly growing younger (< 65 years old) and older (> 65 years old) total knee replacement (TKR) patients for measures of balance confidence, movement reinvestment, and functional mobility. Fifty-nine participants, including twenty-nine primary unilateral TKR patients (six months post-TKR) formed the four experimental groups: 1) Younger TKR Patient (YP), 2) Younger Control (YC), 3) Older TKR Patient (OP), and 4) Older Control (OC). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Oxford Knee Score (OKS), Activities-specific Balance Confidence scale (ABC), the Movement-Specific Reinvestment Scale (MSRS), and the Timed Up and Go (TUG) test were measured. The YP group reported a significantly lower WOMAC score ($p < 0.001$), and higher perceived knee joint function ($p = 0.001$), compared to the OP group. The YP group also reported significantly higher balance confidence ($p < 0.001$) and less movement reinvestment ($p = 0.001$) than the OP group. TUG durations revealed that the YP group had significantly higher functional mobility compared to the OP group ($p = 0.001$). The YP group did not differ from the YC group across any of these measures ($p > 0.05$). These results identify a clear distinction between younger and older TKR patients for fall risk and TKR outcome, which argues that age should be a factor clinicians take into account when addressing the management and care of individuals recovering from TKR.
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U2 2
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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JI Gait Posture
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WC Neurosciences; Orthopedics; Sport Sciences
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PT J
AU Kim, YH
Lee, JS
Park, JH
AF Kim, Y. H.
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Park, J. H.
TI Association between bone mineral density and knee osteoarthritis in Koreans: the Fourth and Fifth Korea National Health and Nutrition Examination Surveys
SO OSTEOARTHRITIS AND CARTILAGE

LA English
DT Article
DE Osteoarthritis; Bone density; Osteoporosis; Epidemiology; Aged
ID elderly-men; radiographic osteoarthritis; vitamin-d; women; osteoporosis; turnover; population; rotterdam; hip; incident
AB Objective: The objective of the study was to investigate the association of hip and lumbar spine (LS) bone mineral density (BMD) with the presence and severity of radiographic knee osteoarthritis (OA), including both men and women over 50 years of age, while adjusting for potential confounders. Design: Cross-sectional data from 5793 community-dwelling subjects (2491 men and 3302 women) aged >= 50 years in the Korea National Health and Nutrition Examination Surveys (KNHANES) were analyzed. BMDs for femoral neck (FN), total hip (TH), and LS were measured using dual-energy X-ray absorptiometry. Radiographic changes relating to OA were assessed using the Kellgren-Lawrence (KL) grading scale. The mean BMD, according to the presence of knee OA (KL grade >= 2) and the KL grades, were analyzed using the general linear models (GLM) adjusted for anthropometric and biochemical confounders. Results: Adjusted FN and LS BMD were significantly higher in subjects with knee OA (P = 0.036 and P = 0.001, respectively). Within the subjects with knee OA (KL grades 2, 3 and 4), adjusted FN and TH BMD decreased as the KL grades increased, while the adjusted LS BMD was not different. Among the subjects with KL grades of 0, 1 and 2, FN, TH and LS BMD increased as the KL grades increased. These inverted U-shaped associations between adjusted FN and TH BMD and KL grades were presented in both men and women. The proportion of osteoporosis (OP) was as high as 39.5% among subjects with KL grade 4. Conclusion: There is an inverse relationship between OP and the presence of knee OA, but there is a nonlinear and site-specific association between OP and the severity of knee OA. The relationship between the two diseases has to take into account potential covariates. (C) 2018 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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WC Orthopedics; Rheumatology
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PT J
AU Chen, J
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Xiao, J
Wang, XY
AF Chen, Jian
Gu, Yun-Tao
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TI Gastrodin reduces IL-1β-induced apoptosis, inflammation, and matrix catabolism in osteoarthritis chondrocytes and attenuates rat cartilage degeneration in vivo
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Gastrodin; NF-kappa B; Inflammation; Apoptosis; Osteoarthritis
ID nf-kappa-b; stress-induced apoptosis; articular-cartilage; oxidative stress; inhibition; metabolism; mediators; disease; metalloproteinase; osteoporosis
AB Therapeutics for osteoarthritis (OA) are intended to restore chondrocyte function and inhibit cell apoptosis. Previous studies have shown that gastrodin had anti-apoptotic and anti-inflammatory effects. However, little is known about whether gastrodin has protective effects against the processes of OA. We studied the potential effects of gastrodin on chondrocytes and the underlying mechanisms. Our results showed that gastrodin could prevent chondrocyte apoptosis induced by IL-1 beta. Additionally, gastrodin suppressed the nuclear factor kappa B (NF-kappa B) pathway, decreased the release of inflammatory mediators (IL-6, TNF-alpha), and reduced matrix catabolism in IL-1 beta-treated chondrocytes. Furthermore, gastrodin ameliorated rat cartilage degeneration in an OA model of knee joints in vivo, suggesting its potential as a candidate therapeutic for OA.
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WC Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Research & Experimental Medicine; Pharmacology & Pharmacy

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AU Tsiklauri, L
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TI Visfatin alters the cytokine and matrix-degrading enzyme profile during osteogenic and adipogenic MSC differentiation
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoporosis; Osteoarthritis; Fragility fracture; Adipokines; Adipogenesis; Osteogenesis; Mesenchymal stem cell
ID mesenchymal stem-cells; rheumatoid-arthritis; bone-marrow; stromal cells; leptin; resistin; disease; osteoclastogenesis; adiponectin; resorption

AB Objectives: Age-related bone loss is associated with bone marrow adiposity. Adipokines (e.g., visfatin, resistin, leptin) are adipocyte-derived factors with immunomodulatory properties and might influence differentiation of bone marrow-derived mesenchymal stem cells (MSC) in osteoarthritis (OA) and osteoporosis (OP). Thus, the presence of adipokines and MMPs in bone marrow and their effects on MSC differentiation were analyzed. Methods: MSC and ribonucleic acid (RNA) were isolated from femoral heads after hip replacement surgery of OA or osteoporotic femoral neck fracture (FF) patients. Bone structural parameters were evaluated by microcomputed tomography (mCT). MSC were differentiated towards adipocytes or osteoblasts with/without adipokines. Gene expression (adipokines, bone marker genes, MMPs, TIMPs) and cytokine production was evaluated by realtime-polymerase chain reaction (realtime-PCR) and enzymelinked immunosorbent assay (ELISA). Matrix mineralization was quantified using Alizarin red S staining. Results: mCT showed an osteoporotic phenotype of FF compared to OA bone (reduced trabecular thickness and increased ratio of bone surface vs volume of solid bone). Visfatin and leptin were increased in FF vs OA. Visfatin induced the secretion of IL-6, IL-8, and MCP-1 during osteogenic and adipogenic differentiation. In contrast to resistin and leptin, visfatin increased MMP2 and MMP13 during adipogenesis. In osteogenically differentiated cells, MMPs and TIMPs were reduced by visfatin. Visfatin significantly increased matrix mineralization during osteogenesis, whereas collagen type I expression was reduced. Conclusion: Visfatin-mediated increase of matrix mineralization and reduced collagen type I expression could contribute to bone fragility. Visfatin is involved in impaired bone remodeling at the adipose tissue/bone interface through induction of proinflammatory factors and dysregulated MMP/TIMP balance during MSC differentiation. (c) 2018 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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NR 49
TC 35
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PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
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PT J
AU Westby, MD
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Jones, CA
AF Westby, M. D.
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TI Development of quality indicators for hip and knee arthroplasty rehabilitation
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Knee arthroplasty; Hip arthroplasty; Quality; Indicators; Rehabilitation
ID post-acute rehabilitation; of-care; health-care; replacement surgery; united-states; exercise; osteoarthritis; physiotherapy; interventions; metaanalysis
AB Objective: To develop quality indicators (QIs) reflecting the minimum acceptable standard of rehabilitation care before and after elective total hip arthroplasty (THA) and total knee arthroplasty (TKA) for osteoarthritis (OA). Methods: Informed by high quality evidence and using a modified RAND-UCLA Delphi approach, an 18-member Canadian panel of clinicians, researchers and patients considered 81 proposed QIs (40 for THA, 42 for TKA) addressing rehabilitation before and after elective THA and TKA. Panelists rated QIs for their importance and validity on a 9-point Likert scale through two rounds of online rating interspersed with a moderated and anonymous online discussion forum. Those QIs with median ratings of similar to 7 for importance and validity with no disagreement based on the inter-percentile range adjusted for symmetry were included in the final sets. Results: Fifteen panelists from seven provinces and varied practice settings completed the Delphi process. Of the 81 plus one additional QIs (total of 82), 67 (82%) were rated as both important and valid (31 for THA, 36 for TKA). For THA, 14 pre-op, six acute and eight post-acute QIs were accepted. For TKA, 16 pre-op, 10 acute and eight post-acute indicators were accepted. Two of three 'across-continuum' QIs were rated appropriate for both procedures. Conclusion: This work represents the first QIs with which to measure, report and benchmark quality of care in patients receiving rehabilitation before and after THA/TKA surgery. The QIs will be further tested for reliability and feasibility before being widely disseminated in clinical settings and used to assess care gaps. (c) 2018

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NR 49
TC 24
Z9 25
U1 0
U2 10
PU ELSEVIER SCI LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
PD MAR 15
PY 2018
VL 26
IS 3
BP 370
EP 382
DI 10.1016/j.joca.2017.10.020
PG 13
WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA FY6IX
UT WOS:000426949700011
PM 29292095
DA 2026-02-10
ER

PT J
AU Wang, JH
Wu, YJ
Tee, BL
Lo, RY
AF Wang, Jen-Hung
Wu, Ya-Ju
Tee, Boon Lead
Lo, Raymond Y.
TI Medical Comorbidity in Alzheimer's Disease: A Nested Case-Control Study
SO JOURNAL OF ALZHEIMERS DISEASE
LA English
DT Article
DE Alzheimer's disease; cholinesterase inhibitors; comorbidity; dementia; nested case-control studies
ID diabetes-mellitus; glucose-levels; risk-factors; dementia; epidemiology; pathology; prevalence; insulin; impact; care
AB Background: Little is known about the distribution of medical comorbidities in Alzheimer's disease (AD). Objective: We aimed to describe the comorbidity pattern of AD in a nested case-control study. Methods: Incident AD cases were identified by International Classification of Diseases codes in a random sample of 2 million individuals in Taiwan National Health Insurance program during 2001-2011. We further restricted cases to those treated with AD drugs of approved reimbursement. We sampled a set of age-and sex-matched control subjects (2: 1 ratio) and employed conditional logistic regression to estimate the associations between pre-specified 14 comorbidities and AD. The clusters of multiple chronic diseases

were then identified by exploratory factor analysis. Results: A total of 2,618 AD cases were identified during 2001-2011 with a mean age of 76.1 years and female preponderance (59%). The most common 5 comorbidities in AD were hypertension (55.1%), osteoarthritis (38.2%), depression (32.3%), diabetes mellitus (DM) (25.7%), and cerebrovascular disease (CVD) (22.7%). After adjusting for age and sex, DM, osteoporosis, depression, and CVD were significantly associated with AD. The number of comorbidity was 3-fold greater in the AD group. The cluster of hypertension, DM, and hyperlipidemia was the most common combination in old age, whereas the cluster osteoarthritis and osteoporosis was the only multimorbidity pattern significantly associated with AD. Conclusion: Multimorbidity is common in AD. Depression, CVD, osteoporosis, and DM are associated with incident AD, supporting that their co-existence is a typical feature of AD at old age. Comorbidity care should be integrated into current management for patients with AD.
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NR 38
TC 81
Z9 89
U1 0
U2 19
PU IOS PRESS
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PA NIEUWE HEMWEG 6B, 1013 BG AMSTERDAM, NETHERLANDS
SN 1387-2877

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J9 J ALZHEIMERS DIS
JI J. Alzheimers Dis.
PD JUN 15
PY 2018
VL 63
IS 2
BP 773
EP 781
DI 10.3233/JAD-170786
PG 9
WC Neurosciences
SC Neurosciences & Neurology
GA GD9KG
UT WOS:000430831000029
PM 29660933
DA 2026-02-10
ER

PT J
AU Boyde, A
AF Boyde, A.
TI Evaluation of laser ablation microtomy for correlative microscopy of hard tissues
SO JOURNAL OF MICROSCOPY
LA English
DT Article
DE Bone; enthesis; ligament; osteoarthritis; osteoporosis; tendon
ID articular calcified cartilage; backscattered electron; undecalcified bone; subchondral bone; soft-tissue; osteoarthritis; immunohistochemistry; protrusions; imperfecta; density
AB Laser ablation machining or microtomy (LAM) is a relatively new approach to producing slide mounted sections of translucent materials. We evaluated the method with a variety of problems from the bone, joint and dental tissues fields where we require thin undecalcified and undistorted sections for correlative light microscopy (LM) and backscattered electron scanning electron microscopy (BSE SEM). All samples were embedded in poly-methylmethacrlate (PMMA) and flat block surfaces had been previously studied by BSE-SEM and confocal scanning light microscopy (CSLM). Most were also studied by X-yay microtomography (XMT). The block surface is stuck to a glass slide with cyanoacrylate adhesive. Setting the section thickness and levelling uses inbuilt optical coherence tomographic imaging. Tight focusing of near-infrared laser radiation in the sectioning plane gives extreme intensities causing photodisruption of material at the focal point. The laser beam is moved by a fast scanner to write a cutting line, which is simultaneously moved by an XY positioning unit to create a sectioning

plane. The block is thereby released from the slide, leaving the section stuck to the slide. Light, wet polishing on the finest grade (4000 grit) silicon carbide polishing paper is used to remove a 1-2 m thick damaged layer at the surface of the section. Sections produced by laser cutting are fine in quality and superior to those produced by mechanical cutting and can be thinner than the voxel' in most laboratory X-ray microtomography systems. The present extensive pilot studies have shown that it works to produce samples which we can study by both light and electron microscopy.
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NR 35
TC 8
Z9 10
U1 0
U2 19
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0022-2720
EI 1365-2818
J9 J MICROSC-OXFORD
JI J. Microsc.
PD JUL 15
PY 2018
VL 271
IS 1
BP 17
EP 30
DI 10.1111/jmi.12689
PG 14
WC Microscopy
SC Microscopy
GA GJ8LF
UT WOS:000435640500003
PM 29485196
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ER

PT J
AU Bokhari, RA
Lau, SF
Mohamed, S
AF Bokhari, Rubiatul Adawiyah
Lau, Seng Fong

Mohamed, Suhaila
TI Orthosiphon stamineus (Misai Kucing) ameliorated postmenopausal osteoporosis in rat model
SO MENOPAUSE-THE JOURNAL OF THE NORTH AMERICAN MENOPAUSE SOCIETY
LA English
DT Article
DE Bone histomorphometry; Orthosiphon stamineus; Osteoporosis; Ovariectomy; Postmenopausal; Rat
ID osteoarthritis; turnover; estrogen; collagen; extract
AB Objective:Orthosiphon stamineus (OS) or Misai Kucing (Java tea) is a popular herbal supplement from Southeast Asia for various metabolic, age-related diseases. This study investigated the potential use of OS leaf extracts to ameliorate osteoporosis in ovariectomized rats.Methods:Fifty-six female Sprague-Dawley rats were randomly allocated into eight groups (n=7): SHAM (healthy sham control); OVX (ovarietomized) nontreated rats (negative control); OVX+Remifemin (100mg/kg body weight), and 2% green tea extract (positive controls); OVX+OS 50% ethanolic and aqueous extracts, both at either 150 or 300mg/kg. After 16 weeks, the rats' bones and blood were evaluated for osteoporosis indicators (protein and mRNA expressions), micro-computed tomography for bone histomorphometry, and three-point bending test for tibia mechanical strength.Results:The extracts dose-dependently and significantly (P<0.05) improved bone strength and flexibility, bone mineral density, bone formation protein markers (P1NP), and bone histomorphometry. All extracts reduced the inflammation biomarker (interleukin-6). The extracts up-regulated osteoblastogenesis (bone morphogenetic protein-2) and collagen-1 synthesis (collagen type 1 alpha-1) mRNA expressions, and down-regulated bone resorption (TNFSF11 and nuclear factor-kappa B) mRNA expressions. Both the water and 50% ethanolic extract were effective. The effective dose is equivalent to 25 to 50mg/kg extract for humans.Conclusions:The extract showed bone-protective and antiosteoporotic effects (improving bone strength, flexibility, bone density, and bone morphometry) by reducing inflammation and the bone resorption biomarkers, while enhancing bone formation biomarkers and collagen synthesis.
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NR 31
TC 4
Z9 5
U1 0
U2 14
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA

SN 1072-3714
EI 1530-0374
J9 MENOPAUSE
JI Menopause-J. N. Am. Menopause Soc.
PD FEB 15
PY 2018
VL 25
IS 2
BP 202
EP 210
DI 10.1097/GME.0000000000000980
PG 9
WC Obstetrics & Gynecology
SC Obstetrics & Gynecology
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UT WOS:000424082900014
PM 28926512
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ER

PT J
AU Hmida, B
Boudokhane, S
Migaou, H
Kalai, A
Jellad, A
Ben Salah, Z
AF Hmida, Badii
Boudokhane, Soumaya
Migaou, Houda
Kalai, Amine
Jellad, Anis
Ben Salah, Zohra
TI Postpartum sacral stress fracture associated with mechanical sacroiliac joint disease: A case report
SO MEDICINE
LA English
DT Article
DE osteoarthritis; postpartum; sacroiliac joint; sacrum; stress fracture
ID insufficiency fractures; low-back; pregnancy; osteoporosis; pain
AB Rationale:Stress fractures of the sacrum and mechanical sacroiliac joint disease can occur not only during pregnancy but also postpartum. Mechanical sacroiliac joint disease is common in patients with low back pain but often misdiagnosed by practitioners. The association of the 2 conditions has not been studied yet.Patient

concerns:A 37-year-old woman physiatrist presented with 8-week history of persistent low back and left buttock pain that started in the third trimester of her pregnancy.Diagnoses:Laboratory investigation, dual-energy x-ray absorptiometry, magnetic resonance imaging, and CT of the pelvic region were performed. The patient was diagnosed with postpartum sacral stress fracture associated with mechanical sacroiliac joint disease.Interventions:Treatment consisted in pain killers and tailored to a nonweight-bearing period of 3 months.Outcomes:Painful symptoms disappeared and the patient was able to walk and perform other daily activities normally.Lessons:Clinician should be aware of the clinical context and the possible association of these 2 conditions in order to undertake an early and appropriate treatment.
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NR 15
TC 7
Z9 7
U1 0
U2 3
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0025-7974
EI 1536-5964
J9 MEDICINE
JI Medicine (Baltimore)
PD AUG 15
PY 2018
VL 97
IS 32
BP
EP
DI 10.1097/MD.0000000000011735
PG 2
WC Medicine, General & Internal
SC General & Internal Medicine
GA GR0ZJ
UT WOS:000442254400018
PM 30095627
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PT J
AU Yang, SQ
   Duan, XH
AF Yang, Shaoqing
   Duan, Xiaohong
TI Epigenetics, Bone Remodeling and Osteoporosis
SO CURRENT STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE Epigenetic; DNA methylation; histone modification; bone remodeling; osteoblastogenesis; osteoclastogenesis; osteoporosis
ID histone deacetylase inhibitors; mesenchymal stem-cells; de-novo methylation; dna methylation; osteogenic differentiation; osteoclast differentiation; in-vivo; receptor activator; osteocalcin gene; osteoblast
AB Background: Osteoporosis is a common degenerative bone disease which is

characterized with decreased bone strength and increased risk of fracture. The abnormal bone metabolism homeostasis, especially in osteoclastic function, takes a fundamental role in osteoporosis pathogenesis. In the past decade, epigenetic regulation of bone homeostasis are widely investigated and considered as a vital factor in the regulation of the differentiation and functions of osteoblasts, osteoclasts and osteocytes. The relationship between osteoporosis and epigenetic regulations has gradually become as an important issue in the mechanism study of osteoporosis. Objective: In this review, we summarize the recent progresses of epigenetic regulation mechanism in bone development and remodeling, and emphasize the epigenetic features of osteoporosis and the potent therapy application of epigenetic drugs for osteoporosis. Conclusion: DNA methylation and histone modification regulated bone development and remodeling via affecting both osteoblastogenesis and osteoclastogenesis. And the abnormal epigenetic status is relevant to bone disease such as osteoporosis and osteoarthritis. Several inhibitors of DNMTs or HDACs exhibit a potential application for osteoporosis, and the side effects of these drugs should also be considered in the future applications.
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TI Physical activity participation and the risk of chronic diseases among South Asian adults: protocol for a systematic review and meta-analysis
SO SYSTEMATIC REVIEWS
LA English
DT Review
DE Physical activity; Chronic diseases; Systematic review; South Asia; Adults
ID coronary-heart-disease; noncommunicable diseases; all-cause; interventions; prevention; mortality; time
AB Background: Chronic diseases contribute to about half of the adult disease burden in the South Asian region. Meanwhile, physical activity levels are declining despite the global evidence of its role in the prevention of chronic diseases. While there are a plethora of systematic reviews on the effects of physical activity on chronic diseases, there has not yet been a synthesis of the evidence concerning the nature of this relationship among people living in South Asian countries incorporating multiple chronic diseases and a focus on physical activity domains. The aim of this protocol is to describe the rationale and methods for a systematic review of published research to identify the association between physical activity

and selected chronic diseases and their markers and analysis of the strength of association with a focus on physical activity domains among South Asian adults 40 years and older. Methods: Nine electronic databases including Medline, PsycINFO, Embase, CENTRAL, CINAHL Plus, AgeLine, SPORTDiscus, Scopus and Web of Science will be systematically searched for papers reporting the association between physical activity and selected chronic diseases (type 2 diabetes mellitus, breast cancer, colorectal cancer, coronary heart disease, stroke, vascular diseases and musculoskeletal diseases (osteoarthritis, osteoporosis, back and neck pain)) and their markers using predefined search terms. Searches will be limited to peer-reviewed, English language papers with a quantitative design. In addition, a manual search of references of relevant systematic reviews as well as citations and references of eligible studies will also be carried out. The methodological appraisal will be performed using the National Institutes of Health quality assessment checklist for observational studies and the Effective Public Health Practice Project quality assessment tool for intervention studies. The overall quality of evidence for the study outcomes across the study designs will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. The review results will be presented in the form of narrative synthesis, and a random effects meta-analysis is planned depending on the nature of included studies and available data. Discussion: This review will summarise the strength of the association between physical activity and selected chronic diseases and their markers among South Asian adults 40 years or older. The findings will provide an evidence base to guide public health policy and interventions in the South Asian region and to inform future research to address the rising burden of chronic diseases.
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AF Chen, Jie-Hua
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TI Role of advanced glycation end products in mobility and considerations in possible dietary and nutritional intervention strategies
SO NUTRITION & METABOLISM
LA English
DT Review
DE Advanced glycation end products (AGEs); Mobility; AGEs inhibitors; Dietary intervention strategies
ID maillard reaction-products; renal-failure patients; experimental diabetic-retinopathy; n-epsilon-carboxymethyllysine; leukemia inhibitory factor; low-density-lipoprotein; protein cross-linking; oxidative stress; skin autofluorescence; in-vitro
AB Advanced glycation end products (AGEs), a group of compounds that are formed by non-enzymatic reactions between carbonyl groups of reducing sugars

and free amino groups of proteins, lipids or nucleic acids, can be obtained exogenously from diet or formed endogenously within the body. AGEs accumulate intracellularly and extracellularly in all tissues and body fluids and can cross-link with other proteins and thus affect their normal functions. Furthermore, AGEs can interact with specific cell surface receptors and hence alter cell intracellular signaling, gene expression, the production of reactive oxygen species and the activation of several inflammatory pathways. High levels of AGEs in diet as well as in tissues and the circulation are pathogenic to a wide range of diseases. With respect to mobility, AGEs accumulate in bones, joints and skeletal muscles, playing important roles in the development of osteoporosis, osteoarthritis, and sarcopenia with aging. This report covered the related pathological mechanisms and the potential pharmaceutical and dietary intervention strategies in reducing systemic AGEs. More prospective studies are needed to determine whether elevated serum AGEs and/or skin autofluorescence predict a decline in measures of mobility. In addition, human intervention studies are required to investigate the beneficial effects of exogenous AGEs inhibitors on mobility outcomes.

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PM 30337945
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PT J
AU Gao, B
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TI Local delivery of tetramethylpyrazine eliminates the senescent phenotype of

bone marrow mesenchymal stromal cells and creates an anti-inflammatory and angiogenic environment in aging mice
SO AGING CELL
LA English
DT Article
DE bone marrow niche; bone marrow stem; progenitor cells; cellular senescence; EZH2-H3K27me3; H-type vessel; tetramethylpyrazine
ID analog cxc195 protects; cellular senescence; stem-cells; osteogenic differentiation; induced apoptosis; osteoarthritis; osteoporosis; methylation; dysfunction; homeostasis
AB Aging drives the accumulation of senescent cells (SnCs) including stem/progenitor cells in bone marrow, which contributes to aging-related bone degenerative pathologies. Local elimination of SnCs has been shown as potential treatment for degenerative diseases. As LepR(+) mesenchymal stem/progenitor cells (MSPCs) in bone marrow are the major population for forming bone/cartilage and maintaining HSCs niche, whether local elimination of senescent LepR(+) MSPCs delays aging-related pathologies and improves local microenvironment need to be well defined. In this study, we performed local delivery of tetramethylpyrazine (TMP) in bone marrow of aging mice, which previously showed to be used for the prevention and treatment of glucocorticoid-induced osteoporosis (GIOP). We found the increased accumulation of senescent LepR(+) MSPCs in bone marrow of aging mice, and TMP significantly inhibited the cell senescent phenotype via modulating Ezh2-H3k27me3. Most importantly, local delivery of TMP improved bone marrow microenvironment and maintained bone homeostasis in aging mice by increasing metabolic and anti-inflammatory responses, inducing H-type vessel formation, and maintaining HSCs niche. These findings provide evidence on the mechanisms, characteristics and functions of local elimination of SnCs in bone marrow, as well as the use of TMP as a potential treatment to ameliorate human age-related skeletal diseases and to promote healthy lifespan.
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NR 46
TC 53
Z9 62
U1 0
U2 39
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1474-9718
EI 1474-9726
J9 AGING CELL
JI Aging Cell
PD JUN 15
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VL 17
IS 3
BP
EP
DI 10.1111/acel.12741
PG 12
WC Cell Biology; Geriatrics & Gerontology
SC Cell Biology; Geriatrics & Gerontology
GA GF4VQ
UT WOS:000431962300008
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PT J
AU Barastegui, D
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TI Assessing long-term return to play after hip arthroscopy in football players evaluating risk factors for good prognosis
SO KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY
LA English
DT Article
DE Groin pain; Hip arthroscopy; Soccer; Return to play
ID professional hockey players; femoroacetabular impingement; follow-up; sport; outcm; athlete; league; osteoarthritis; microfracture; management
AB Groin pain is the third most common disease in football players and has often been associated with hip pathology such as femoroacetabular impingement and labral lesions. Hip arthroscopy offers possibilities of function restoration via minimally invasive procedures. The aim of this study is to evaluate professional football player's injuries and their return to play after hip arthroscopy for FAI and labral injuries. Patients that underwent hip arthroscopy between 2009 and 2014 were selected retrospectively. From this population, only professional soccer players competing at national level were included (Tegner 10). Arthroscopic surgery was proposed in patients with persistent pain. All patients were assessed for VAS score preoperatively and at 3, 6, 12 and 24 months post-op. HOS (sport and DLA) and mHHS tests were performed at the same time periods. All patients were men with a mean age of 26.5 +/- 7.1 years old. Preoperative VAS (7.4 +/- 1.3), HOS ADL (67.7 +/- 5.5), HOS sport (37.6 +/- 18.7) and mHHS (72.5 +/- 8.8) showed improved scores during long-term follow-up. Time to return to play was 10.8 months (SD +/- 4.3), with range between 4 and 20 months. Mean follow-up was 45.4 +/- 15.6 months (range from 26 to 72 months). No differences were observed between non-active and active patients at final follow-up with respect to chondral lesions, but significant differences were observed with reference to management of the labrum ($p = 0.031$), where a higher rate of labrectomies existed among inactive patients and a higher rate of suture among active patients. Hip arthroscopy is a safe procedure with very good return to play results, but for optimized return to football one should consider patient age at the time of surgery, the condition of the labrum and low scores on the Harris Hip Score (mHHS) and HOS (sport version)

as predictive factors for poor prognosis. Level of evidence IV.
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NR 26
TC 26
Z9 27
U1 1
U2 6
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 0942-2056
EI 1433-7347
J9 KNEE SURG SPORT TR A
JI Knee Surg. Sports Traumatol. Arthrosc.
PD MAR 15
PY 2018
VL 26
IS 3
BP 963
EP 968
DI 10.1007/s00167-017-4573-z
PG 6
WC Orthopedics; Sport Sciences; Surgery
SC Orthopedics; Sport Sciences; Surgery
GA FX5DZ
UT WOS:000426099600040
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PT J
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AF Su, Peihong
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TI Mesenchymal Stem Cell Migration during Bone Formation and Bone Diseases Therapy
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE mesenchymal stem cells; migration; bone formation; bone diseases; therapy
ID hypoxia-inducible factor-1-alpha; endothelial growth-factor; in-vitro; osteogenic differentiation; fracture repair; synovial-fluid; nod/scid mice; stromal cells; marrow; cxcr4
AB During bone modeling, remodeling, and bone fracture repair, mesenchymal stem cells (MSCs) differentiate into chondrocyte or osteoblast to comply bone formation and regeneration. As multipotent stem cells, MSCs were used to treat bone diseases during the past several decades. However, most of these implications just focused on promoting MSC differentiation. Furthermore, cell migration is also a key issue for bone formation and bone diseases treatment. Abnormal MSC migration could cause different kinds of bone diseases, including osteoporosis. Additionally, for bone disease treatment, the migration of endogenous or exogenous MSCs to bone injury sites is required. Recently, researchers have paid more and more attention to two critical points. One is how to apply MSC migration to bone disease therapy. The other is how to enhance MSC migration to improve the therapeutic efficacy of bone diseases. Some considerable outcomes showed that enhancing MSC migration might be a novel trick for reversing bone loss and other bone diseases, such as osteoporosis, fracture, and osteoarthritis (OA). Although plenty of challenges need to be conquered, application of endogenous and exogenous MSC migration and developing different strategies to improve therapeutic efficacy through enhancing MSC migration to target tissue might be the trend in the future for bone disease treatment.
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NR 97
TC 190
Z9 213

U1 2
U2 76
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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EI 1422-0067
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JI Int. J. Mol. Sci.
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DI 10.3390/ijms19082343
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
GA GR7LE
UT WOS:000442869800195
PM 30096908
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PT J
AU Han, JK
Gao, W
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AF Han, Jiakai
Gao, Wei
Su, Dongyue
Liu, Yang
TI Gypenoside inhibits RANKL-induced osteoclastogenesis by regulating NF-B, AKT, and MAPK signaling pathways
SO JOURNAL OF CELLULAR BIOCHEMISTRY
LA English
DT Article
DE gypenoside(GP); osteoporosis; osteoclast differentiation; receptor activator of nuclear factor-B ligand (RANKL)
ID c-fos; differentiation; activation; cells; nfatc1; matrix-metalloproteinase-9; osteoporosis; induction; mechanism; erk
AB Gypenoside (GP) is one of the most pharmacologically active components in

Gynostemma pentaphyllum and possesses neuroprotective, anticancer, anti-oxidant, anti-inflammatory, anti-diabetic, and anti-osteoarthritis effects. However, the involvement of GP the osteoclast differentiation has not yet been investigated. In the present study, we examined the effect of GP on receptor activator of nuclear factor-B ligand (RANKL)-induced osteoclast formation. Our results demonstrated that GP significantly inhibited the formation of osteoclast, as well as suppressed the expression of osteoclastogenesis-related marker proteins in RANKL-stimulated bone marrow macrophages (BMMs). For molecular mechanisms, GP inhibited RANKL-induced NF-B and MAPK activation and AKT phosphorylation in BMMs. Collectively, these findings suggest that GP inhibits RANKL-induced osteoclastogenesis via regulating NF-B, AKT, and MAPK signaling pathways. Therefore, GP may be a potential agent in the treatment of osteoclast-related diseases such as osteoporosis.

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NR 30
TC 22
Z9 25
U1 0
U2 22
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0730-2312
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J9 J CELL BIOCHEM
JI J. Cell. Biochem.
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BP 7310
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WC Biochemistry & Molecular Biology; Cell Biology
SC Biochemistry & Molecular Biology; Cell Biology
GA GU3OB
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PT J
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AF Kosik-Bogacka, Danuta, I
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Prokopowicz, Adam
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TI Calcium, magnesium, zinc and lead concentrations in the structures forming knee joint in patients with osteoarthritis
SO JOURNAL OF TRACE ELEMENTS IN MEDICINE AND BIOLOGY
LA English
DT Article
DE Trace elements; Cartilage; Anterior cruciate ligament; Meniscus; Osteoarthritis
ID bone-mineral density; age-related-changes; hip-replacement surgery; element contents; trace-elements; serum magnesium; hypertension; meniscus; cadmium; osteoporosis
AB The aim of the study was to investigate the relationships between the concentrations of calcium (Ca), magnesium (Mg), zinc (Zn), and lead (Pb) in cartilage, anterior cruciate ligament, and meniscus samples obtained following knee joint surgery in patients with osteoarthritis in northwestern Poland. Furthermore, we examined the relationships between the concentrations of these metals in the studied parts of the knee joint and the influences of gender, age, BMI and hypertension. We found significantly higher concentrations of Ca, Mg, and Zn in the cartilage of men than in women and a significantly higher Pb concentration in the meniscus of the men. We also found a higher concentration of Pb in the cartilage of patients over 65 years of age. There were no differences in the concentrations of the studied metals between patients with and without hypertension. There was no relationship between Ca, Mg, Zn, and Pb levels in analyzed materials and BMI. Furthermore, we noted some new interactions between metals in the studied structures of the knee joint. The results reported in the study shows the influence of age, gender and BMI on the Ca, Mg, Zn and Pb in the studied structures of the knee joint.
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NR 61
TC 23
Z9 25
U1 2
U2 23
PU ELSEVIER GMBH
PI MUNICH
PA HACKERBRUCKE 6, 80335 MUNICH, GERMANY
SN 0946-672X
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J9 J TRACE ELEM MED BIO
JI J. Trace Elem. Med. Biol.
PD JUN 15
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WC Biochemistry & Molecular Biology; Endocrinology & Metabolism
SC Biochemistry & Molecular Biology; Endocrinology & Metabolism
GA GY5PV
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Yu, Wen-Xuan
Wong, Ka-Chun
Yao, Xin-Sheng
Wong, Man-Sau
TI Oleanolic Acid Exerts Osteoprotective Effects and Modulates Vitamin D Metabolism
SO NUTRIENTS
LA English
DT Article
DE oleanolic acid; ovariectomised; aging; osteoporosis; calcium; vitamin D
ID ligustri-lucidi extract; intestinal calcium-absorption; bone-mineral density; parathyroid-hormone; 1,25-dihydroxyvitamin d-3; 25-hydroxyvitamin d-3; ethanol extract; gene-expression; 1-alpha-hydroxylase gene; d supplementation
AB Oleanolic acid (OA) is a triterpenoid with reported bone anti-resorption activities. The present study aimed to characterize its bone protective effects in vivo and to study its effects on vitamin D metabolism, both in vivo and in vitro. OA significantly increased bone mineral density, improved micro-architectural properties, reduced urinary Ca excretion, increased 1,25(OH)(2)D-3 and renal CYP27B1 mRNA expression in mature C57BL/6 ovariectomised (OVX) mice. OA also improved bone properties, Ca balance, and exerted modulatory effects on renal CYP27B1 and CYP24A1 expressions in aged normal female Sprague-Dawley rats. In addition, OA significantly increased renal CYP27B1 mRNA and promoter activity, and suppressed CYP24A1 mRNA and protein expressions in human proximal tubule HKC-8 cells. OA exerted bone protective effects in mature OVX mice and aged female rats. This action on bone might be, at least in part, associated with its effects on Ca and vitamin D metabolism. The present findings suggest that OA is a potential drug candidate for the management of postmenopausal osteoporosis.
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U1 2
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PU MDPI
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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J9 NUTRIENTS
JI Nutrients
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TI Validation of the German version of the Kujala score in patients with patellofemoral instability: a prospective multi-centre study
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article
DE Kujala score; Patellofemoral instability; Validation; Kujala patellofemoral score; Patellofemoral pain syndrome (PFPS); Questionnaire
ID sulcus-deepening trochleoplasty; anterior knee pain; recurrent patellar dislocations; osteoarthritis outcome score; cultural-adaptation; trochlear dysplasia; follow-up; ligament reconstruction; translation; scale
AB The Kujala score is the most frequently used questionnaire for patellofemoral disorders like pain, instability or osteoarthritis. Unfortunately, we are not aware of a validated German version of the Kujala score. The aim of our study was the translation and linguistic validation of the Kujala score in German-speaking patients with patella instability and the assessment of its measurement characteristics. The German Kujala score was developed in several steps of translation. In addition to healthy controls, the Kujala German was assessed in consecutive patients undergoing reconstruction of the medial patellofemoral ligament for recurrent patellar dislocations. Pre-op, 6 and 12 months postop the patients completed the Kujala German score, the KOOS, the Lysholm score, a VAS Pain, and the SF-12v2 scores. In addition, there was a Kujala German Score retest preop after a 1-week interval. We found high reliability in terms of internal consistency for the Kujala score (Cronbach's alpha = 0.87). Convergent validity with the KOOS (symptom r = 0.65, pain r = 0.78, ADL r = 0.74, sports/recreation r = 0.84, quality of life r = 0.70), the Lysholm score (r = 0.88) and the SF-12 physical component summary score (r = 0.79) and VAS pain (r = - 0.71) was also very high. Discriminant validity in terms of correlation with the SF-12 mental component summary Score was satisfactory (r = 0.14). In conclusion, the German version of the Kujala score proved to be a reliable and valid instrument in the setting of a typical patellofemoral disease treated with a standard patellofemoral procedure.
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NR 49
TC 47
Z9 52
U1 0
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TI Impact of Osteoarthritis on Household Catastrophic Health Expenditures in Korea
SO JOURNAL OF KOREAN MEDICAL SCIENCE
LA English
DT Article
DE Osteoarthritis; Health Expenditure; Households
ID of-pocket costs; policy; care; prescription; coverage
AB Background: Osteoarthritis (OA) is a disease of old age whose prevalence is increasing. This study explored the impact of OA on household catastrophic health expenditure (CHE) in Korea. Methods: We used data on 5,200 households from the Korea Health Panel Survey in 2013 and estimated annual living expenses and out-of-pocket (OOP) payments. Household CHE was defined when a household's total OOP health payments exceeded 10%, 20%, 30%, or 40% of the household's capacity to pay. To compare the OOP payments of households with OA individuals and those without OA, OA households were matched 1:1 with households containing a member with other chronic disease such as neoplasm, hypertension, heart disease, cerebrovascular disease, diabetes, or osteoporosis. The impact of OA on CHE was determined by multivariable logistic analysis. Results: A total of 1,289 households were included, and households with and without OA patients paid mean annual OOP payments of $2,789 and $2,607, respectively. The prevalence of household CHE at thresholds of 10%, 20%, 30%, and 40% were higher in households with OA patients than in those without OA patients (P<0.001). The presence of OA patients in each household contributed significantly to CHE at thresholds of10% (odds ratio [OR], 1.48; 95% confidence interval [CIL 1.16-1.87), 20% (OR, 1.29; 95% Cl, 1.014.66), and 30% (OR, 1.37; 95% CI, 1.05-1.78), but not of 40% (OR, 1.17; 95% CI, 0.87-1.57). Conclusion: The presence of OA patients in Korean households is significantly related to CHE. Policy makers should try to reduce OOP payments in households with OA patients.
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PU KOREAN ACAD MEDICAL SCIENCES
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PA 302 75 DONG DU ICHON, DONG YONGSAN KU, SEOUL 140 031, SOUTH KOREA
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JI J. Korean Med. Sci.
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WC Medicine, General & Internal
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TI Influence of scanner, powder application, and adjustments on CAD-CAM crown misfit
SO JOURNAL OF PROSTHETIC DENTISTRY
LA English
DT Article
ID marginal fit; ceramic crowns; internal fit; system; restorations; experience; thickness; future; 3d
AB Statement of problem. The manufacturers of computer-aided design and computer-aided manufacturing (CAD-CAM) systems emphasize that new technologies can improve the marginal fit of dental crowns. However, data supporting this claim are limited. Purpose. The purpose of this in vitro study was to investigate the differences among the following fabrication methods on the marginal discrepancy of dental crowns: intraoral optical scanners, powder application, and adjustments of intaglio surface. Material and methods. A single human premolar was fixed on a typodont and prepared to receive crowns prepared by the CEREC CAD-CAM system. Three fabrication techniques were used: digital scans using the CEREC Bluecam scanner with titanium dioxide powder (TDP), digital scans using the CEREC Omnicam scanner without TDP, and digital scans using the Omnicam scanner with TDP. Five experimental groups (n=10) were designated: Bluecam (group B), Bluecam with adjustments (group BA), Omnicam (group 0), Omnicam with adjustments (group OA), and Omnicam with TDP (group OP). The specimens were scanned using microcomputed tomography to measure the vertical, horizontal, and internal fit and volumetric 3-dimensional (3D) internal fit values of each luting space. The paired t test was used to evaluate mean marginal fit change after adjustments within the same group. One-way analysis of variance and post hoc tests were used to compare groups B, 0, and OP (alpha=.05). Results. Mean vertical fit values standard deviations of group B=29.5 +/- 13.2 mu m; BA=26.9 +/- 7.7 mu m; 0=149.4 64.4 mu m; 0A=49.4 +/- 12.7 mu m; and OP=33.0 +/- 8.3 mu m. Adjustments in the intaglio surface and TDP application statistically influenced the vertical fit of group 0 (P<.001). The percentage of vertical fit values <75 mu m in group B=89.3%, BA=92.7%, O=31.0%, OA=73.5%, and OP=92.0%. Mean horizontal fit values for group B=56.2 +/- 21.5 mu m; 85.8 +/- 44.4 mu m for group BA; 77.5 +/- 11.8 mu m for group 0; 102.5 +/- 16.2 mu m for group OA; and 91.4 +/- 19.4 mu m for group OP. Results from group B were significantly different from those of the other test groups (P<.05). The percentages of horizontal misfit were 61.2% in group B; 73.5% in group BA; 88.1% in group O; 92.4% in group OA; and 85.0% in group OP. Volumetric 3D internal fit values in group B were 9.4 +/- 1.3 mm(3); 10.7 +/- 1.0 mm(3) in group BA; 11.8 +/- 2.1 mm(3) in group O; 11.0 +/- 1.3 mm(3) in group OA; and 9.6 +/- 0.9 mm(3) in group OP. The overall results from groups B and OP were better than those of group O, with regard to vertical misfit and volumetric 3D internal fit. Conclusions. Different intraoral optical scanners, powder application, and internal adjustments influenced the marginal discrepancy of crowns. Crowns fabricated using the Omnicam system had significantly higher vertical discrepancy and volumetric 3D internal fit than those fabricated using the

Bluecam scanner with TDP. Adjustments of the intaglio surface improved the vertical fit of crowns made using the Omnicam scanner; however, TDP application before Omnicam scanning improved the vertical fit as well as the volumetric 3D internal fit value of the luting space of crowns.
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AU Srivastava, RK
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TI Immunoporosis: Immunology of Osteoporosis-Role of T Cells
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE immunoporosis; osteoimmunology; bone loss; T lymphocytes; osteoporosis
ID osteoclastic bone-resorption; in-vivo; immune-system; rheumatoid-arthritis; parathyroid-hormone; helper-cells; tnf-alpha; inflammatory diseases; peripheral-blood; synovial-fluids

AB The role of immune system in various bone pathologies, such as osteoporosis, osteoarthritis, and rheumatoid arthritis is now well established. This had led to the emergence of a modern field of systems biology called as osteoimmunology, an integrated research between fields of immunology and bone biology under one umbrella. Osteoporosis is one of the most common inflammatory bone loss condition with more than 200 million individuals affected worldwide. T helper (Th) cells along with various other immune cells are major players involved in bone homeostasis. In the present review, we specifically discuss the role of various defined T lymphocyte subsets (Th cells comprising Th1, Th2, Th9, Th17, Th22, regulatory T cells, follicular helper T cells, natural killer T cells, gamma delta T cells, and CD8(+) T cells) in the pathophysiology of osteoporosis. The study of the specific role of immune system in osteoporosis has now been proposed by our group as "immunoporosis: the immunology of osteoporosis" with special emphasis on the role of various subsets of T lymphocytes. The establishment of this new field had been need of the hour due to the emergence of novel roles of various T cell lymphocytes in accelerated bone loss observed during osteoporosis. Activated T cells either directly or indirectly through the secretion of various cytokines and factors modulate bone health and thereby regulate bone remodeling. Several studies have summarized the role of inflammation in pathogenesis of osteoporosis but very few reports had delineated the precise role of various T cell subsets in the pathobiology of osteoporosis. The present review thus for the first time clearly highlights and summarizes the role of various T lymphocytes in the development and pathophysiology of osteoporosis, giving birth to a new field of biology termed as "immunoporosis". This novel field will thus provide an overview of the nexus between the cellular components of both bone and immune systems, responsible for the observed bone loss in osteoporosis. A molecular insight into the upcoming and novel field of immunoporosis would thus leads to development of innovative approaches for the prevention and treatment of osteoporosis.
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TI Low risk for hip fracture and high risk for hip arthroplasty due to osteoarthritis among Swedish farmers
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Arthroplasty; Epidemiology; Hip fracture; Occupation; Osteoarthritis; Osteoporosis; Physical activity; Sweden
ID body-mass index; physical-activity; knee osteoarthritis; men; population; women; work; occupation; metaanalysis; association
AB We aimed to study the risk of hip fracture and risk of hip arthroplasty among farmers in Sweden. Our results indicate that farming, representing an occupation with high physical activity, in men is associated with a lower risk of hip fracture but an increased risk of hip arthroplasty. Introduction The risks of hip fracture and hip arthroplasty are influenced by factors including socioeconomic status, education, urbanization, latitude of residence, and physical activity. Farming is an occupation encompassing rural living and high level of physical activity. Therefore, we aimed to study the risk of hip fracture and risk of hip arthroplasty among farmers in Sweden. Methods We studied the risk of hip fracture, and hip arthroplasty due to primary osteoarthritis, in all men and women aged 35 years or more in Sweden between 1987 and 2002. Documented occupations were available in 3.5 million individuals, of whom 97,136 were farmers. The effects of age, sex, income, education, location of residence, and occupation on risk of hip fracture or hip arthroplasty were examined using a modification of Poisson regression. Results A total of 4027 farmers and 93,109 individuals with other occupations sustained a hip fracture,

while 5349 farmers and 63,473 others underwent a hip arthroplasty. Risk of hip fracture was higher with greater age, lower income, lower education, higher latitude, and urban area for all men and women. Compared to all other occupations, male farmers had a 20% lower age-adjusted risk of hip fracture (hazard ratio (HR) 0.80, 95% CI 0.77-0.84), an effect that was not seen in female farmers (HR 0.96, 95% CI 0.91-1.01). Both male and female farmers had a higher age-adjusted risk for hip arthroplasty. Conclusions Our results indicate that farming, representing an occupation with high physical activity, in men is associated with a lower risk of hip fracture but an increased risk of hip arthroplasty.
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NR 47
TC 8
Z9 12
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U2 4
PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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PT J
AU Soki, FN
Yoshida, R
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AF Soki, Fabiana N.
Yoshida, Ryu
Paglia, David N.
Duong, Le T.
Hansen, Marc F.
Drissi, Hicham
TI Articular cartilage protection in Ctsk-/- mice is associated with cellular and molecular changes in subchondral bone and cartilage matrix
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Article
ID adult rhesus-monkeys; cathepsin-k; gene-expression; ovariectomized monkeys; odanacatib treatment; knee osteoarthritis; mouse model; hip; mineralization; degeneration
AB Osteoarthritis (OA) is a degenerative disease and a major cause of chronic disability in aging individuals. Cathepsin K (CatK), encoded by the Ctsk gene, has been implicated in the pathogenesis of pycnodysostosis and osteoporosis. The use of a selective inhibitor of CatK was recently shown to delay OA progression in rabbits. However, the cellular mechanisms underlying these protective effects remain unexplored. We examined articular cartilage maintenance and joint bone remodeling using Ctsk null mice (Ctsk(-/-)) which underwent destabilization of the

medial meniscus (DMM). We found that Ctsk(-/-) mice displayed delayed remodeling of subchondral and calcified cartilage by osteoclasts and chodroclasts respectively in DMM-induced osteoarthritis. While WT mice displayed a more severe OA phenotype than Ctsk(-/-) mice at 16 weeks, higher subchondral bone volume and lower trabecular spacing were also observed in surgically-induced OA joints of Ctsk(-/-) mice. However, no differences were seen in non-surgical controls. During OA progression, TRAP(+) osteoclast numbers were increased in both WT and Ctsk(-/-) mice. However, Ctsk(-/-) mice had fewer physis-derived chondroclasts than WT when OA was present. These data suggest that CatK may differentially regulate chondroclastogenesis in the growth plate. Targeted PCR arrays of RNA harvested from laser captured osteoclasts in the subchondral bone and chondroclasts in the growth plate demonstrated differential expression of Atp6v0d2, Tnfrsf11a, Ca2, Calcr, Ccr1, Gpr68, Itgb3, Nfatc1, and Syk genes between WT and Ctsk(-/-) mice at 8- and 16-weeks post-DMM. Our data provide insight into the cellular mechanisms by which cathepsin K deletion delays OA progression in mice.
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PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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TI Subchondral bone fragility with meniscal tear accelerates and parathyroid hormone decelerates articular cartilage degeneration in rat osteoarthritis model
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article

DE osteoarthritis; subchondral bone; articular cartilage; parathyroid hormone; cartilage degeneration
ID cruciate ligament transection; experimental mouse models; knee-joint instability; synovial mast-cells; endochondral ossification; transcription factor-2; strontium ranelate; controlled-trial; teriparatide; osteoporosis
AB The aims of this study were to investigate the influence of subchondral bone fragility (SBF) on the progression of the knee osteoarthritis by using a novel rat model, and to examine the preventive effect of parathyroid hormone (PTH) on cartilage degeneration. First, 40 rats were assigned to the following four groups: Sham, SBF, Medial meniscal tear (MMT), and MMT+SBF groups. In SBF and MMT+SBF groups, we induced SBF by microdrilling the subchondral bone. Second, 10 additional rats were randomly assigned to the following two groups: MMT+SBF+saline and MMT+SBF+PTH groups. Osteoarthritic changes in the articular cartilage and subchondral bone were evaluated using safranin-O/fast green staining, matrix metalloproteinase-13 (MMP-13), and type X collagen immunohistochemistry, toluidine blue staining, and micro-CT scanning. The combination of SBF and meniscal tear increased the number of mast cells in the subchondral bone, and led to the abnormal subchondral bone microarchitecture, such as abnormally decreased trabecular number and increased trabecular thickness, compared with meniscal tear alone. Moreover, SBF with meniscal tear enhanced articular cartilage degeneration and increased the expression of MMP-13 and type X collagen, compared with meniscal tear alone. The administration of PTH decreased the number of mast cells in the subchondral bone and improved the microstructural parameters of the subchondral bone, and delayed the progression of articular cartilage degeneration. These results suggest that SBF is one of the factors underlying the osteoarthritis development, especially in knees with traumatic osteoarthritis, and that the administration of PTH is a potential therapeutic treatment for preventing OA progression. (c) 2017 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 36:1959-1968, 2018.
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FU Ministry of Education of Japan [15H04955]; Asahi-Kasei Pharmaceutical Co.; Grants-in-Aid for Scientific Research [15H04955] Funding Source: KAKEN
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AU Rizzoli, R
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TI Benefits and safety of dietary protein for bone health-an expert consensus paper endorsed by the European Society for Clinical and Economical Aspects of Osteopororosis, Osteoarthritis, and Musculoskeletal Diseases and by the International Osteoporosis Foundation
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Review
DE Acid-base homeostasis; Bone mineral density; Bone turnover; Dairy products; Fracture; Osteoporosis
ID postmenopausal chinese women; randomized controlled-trial; hip fracture risk; potassium citrate supplementation; net acid excretion; growth-factor-i; mineral density; older men; milk supplementation; vitamin-d
AB A summary of systematic reviews and meta-analyses addressing the benefits and risks of dietary protein intakes for bone health in adults suggests that dietary protein levels even above the current RDA may be beneficial in reducing bone loss and hip fracture risk, provided calcium intakes are adequate. Several systematic reviews and meta-analyses have addressed the benefits and risks of dietary protein intakes for bone health in adults. This narrative review of the literature summarizes and synthesizes recent systematic reviews and meta-analyses and highlights key messages. Adequate supplies of dietary protein are required for optimal bone growth and maintenance of healthy bone. Variation in protein intakes within the "normal" range accounts for 2-4% of BMD variance in adults. In older people with osteoporosis, higher protein intake (ae<yen> 0.8-g/kg body weight/day, i.e., above the current RDA) is associated with higher BMD, a slower rate of bone loss, and reduced risk of hip fracture, provided that dietary calcium intakes are adequate. Intervention with dietary protein supplements attenuate age-related BMD decrease and reduce bone turnover marker levels, together with an increase in IGF-I and a decrease in PTH. There is no evidence that diet-derived acid load is deleterious for bone health. Thus, insufficient dietary protein intakes may be a more severe problem than protein excess in the elderly. Long-term, well-controlled randomized trials are required to further assess the influence of dietary protein intakes on fracture risk.
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TI Guidelines for the conduct of pharmacological clinical trials in hand osteoarthritis: Consensus of a Working Group of the European Society on Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English
DT Review
DE Hand osteoarthritis; Clinical trials; Guidelines; Pharmacological treatment
ID systematic literature search; radiographic scoring methods; community-dwelling adults; erosive osteoarthritis; physical function; radiological assessment; functional disability; general-population; finger joints; task-force
AB Objectives: To gather expert opinion on the conduct of clinical trials that will facilitate regulatory review and approval of appropriate efficacious pharmacological treatments for hand osteoarthritis (OA), an area of high unmet clinical need. Methods: The European Society on Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal diseases (ESCEO) organized a working group under the auspices of the International Osteoporosis Foundation (IOF) and the World Health Organization (WHO). Results: This consensus guideline is intended to provide a reference tool for practice, and should allow for better standardization of the conduct of clinical trials in hand OA. Hand OA is a heterogeneous disease affecting different, and often multiple, joints of the thumb and fingers. It was recognized that the various phenotypes and limitations of diagnostic criteria may make the results of hand OA trials difficult to interpret. Nonetheless, practical recommendations for the conduct of clinical trials of both symptom and structure modifying drugs are outlined in this consensus statement, including guidance on study design, execution, and analysis. Conclusions: While the working group acknowledges that the methodology for performing clinical trials in hand OA will evolve as knowledge of the disease increases, it is hoped that this guidance will support the development of new pharmacological treatments targeting hand OA. (C) 2018 The Authors. Published by Elsevier HS Journals, Inc.
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NR 62
TC 24
Z9 28
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PU W B SAUNDERS CO-ELSEVIER INC
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PT J
AU Kodama, R
Muraki, S
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TI Serum levels of matrix metalloproteinase-3 and autoantibodies related to rheumatoid arthritis in the general Japanese population and their association with osteoporosis and osteoarthritis: the ROAD study
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Biomarkers; Matrix metalloproteinase-3; Osteoporosis; Rheumatoid arthritis; Osteoarthritis
ID citrullinated peptide antibody; hand osteoarthritis; american-college; human skin; prevalence; mmp-3; biomarkers; criteria; disease; damage
AB To purpose of this study was to reveal the mean levels and positive proportion of serological markers related to rheumatoid arthritis, and clarify their relationship

with osteoporosis and hand osteoarthritis (OA). A total of 1546 participants from the third survey of the research on osteoarthritis/osteoporosis against disability study were enrolled in the current study. Using participant blood samples, the levels of anti-cyclic citrullinated protein (CCP) antibody, rheumatoid factor (RF), matrix metalloproteinase-3 (MMP-3), C-reactive protein (CRP), and high-sensitivity CRP (hsCRP) were measured. Subjects with higher than normal levels were defined as being positive. Osteoporosis was defined according to the recommendations set by World Health Organization criteria in 1994. Radiographic hand OA was evaluated using the modified Kellgren-Lawrence (KL) scale. The positive proportion of anti-CCP antibody, RF, MMP-3, CRP, and hsCRP was 1.8, 7.1, 15.0, 6.7, and 6.4%, respectively. MMP-3 was associated with age, and was significantly higher in men than in women. Positive MMP-3 was not significantly related to osteoporosis or severe hand OA (KL grade >= 3) after adjustment for other factors including age, sex, and body mass index. The results from this study clarified the values and positive proportion of RA-related markers and revealed their relationship with osteoporosis and hand OA.
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NR 39
TC 5
Z9 6
U1 0
U2 7
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JI J. Bone Miner. Metab.
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WC Endocrinology & Metabolism; Medicine, Research & Experimental
SC Endocrinology & Metabolism; Research & Experimental Medicine
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AU Peng, MZ
Wang, YG
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Li, T
Zhou, XJ
Xiao, M
Wang, JW
AF Peng, Mingzheng
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Xu, Yan
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Li, Tao
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Wang, Jinwu
TI Interleukin-35 Inhibits TNF-α-Induced Osteoclastogenesis and Promotes Apoptosis via Shifting the Activation From TNF Receptor-Associated Death Domain (TRADD)-TRAF2 to TRADD-Fas-Associated Death Domain by JAK1/STAT1
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Article
DE TNF-alpha; osteoclast; apoptosis; FADD; interleukin-35
ID nf-kappa-b; bone-marrow-cells; rankl-induced osteoclastogenesis; rheumatoid-arthritis; signaling complex; mediated osteoclastogenesis; up-regulation; in-vitro; t-cells; il-35
AB Over-activated osteoclasts derived from myeloid or peripheral blood monocytes by inflammatory cytokines results in osteoporosis, osteoarthritis, and other bone erosion-related diseases. Interleukin 35 (IL-35) is a novel anti-inflammatory and immunosuppressive factor. This study investigated the effect of IL-35 on TNF-alpha-induced osteoclastogenesis. In the presence of IL-35, this process was detected by Tartrate-Resistant Acid Phosphatase (TRAP) staining, F-actin staining, and bone resorption assays. The effects of IL-35 on TNF-alpha-induced apoptosis were demonstrated by TUNEL staining, cell viability assays, and flow cytometry. Moreover, a microarray was performed to detect the effect of IL-35 on TNF-alpha-activated phosphatase kinase. The effect of IL-35 on the TNF-alpha-mediated activation of NF-kappa B, MAPK, TRAF2, RIP1, Fas-associated death domain (FADD), and caspase3 was further investigated. In addition, a murine calvarial osteolysis model was established via the subcutaneous injection of TNF-alpha onto the calvaria, and histological analysis was subsequently performed. As a result, IL-35 inhibited TNF-ainduced osteoclast formation and bone resorption in vitro and osteolysis calvaria in vivo. NFATc1, c-fos, and TRAP were downregulated by IL-35 through the inhibition of NF-kappa B and MAPK, during which JAK1/STAT1 was activated. Moreover, based on TUNEL staining and flow cytometry, IL-35 was shown to enhance TNF-alpha-induced osteoclast apoptosis. Meanwhile, FADD and cleaved-caspase 3 were increased in cells treated with TNF-alpha and IL-35, whereas the DNA-binding activity of NF-kappa B was

increased in TNF-alpha-treated cells, but was decreased in cells treated with both TNF-alpha and IL-35. In conclusion, IL-35 inhibits TNF-alpha-induced osteoclastogenesis and promotes apoptosis by activating JAK1/STAT1 and shifting activation from TNF receptor-associated death domain (TRADD)-TRAF2/RIP1-NF-kappa B to TRADD-FADD-caspase 3 signaling.
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TI Changes in Local Bone Density in Early Thumb Carpometacarpal Joint Osteoarthritis
SO JOURNAL OF HAND SURGERY-AMERICAN VOLUME
LA English
DT Article
DE Hounsfield units; osteoarthritis; thumb
ID x-ray absorptiometry; hounsfield units; mineral density; pinch strength; osteoporosis; scans; women; grip
AB Purpose Thumb carpometacarpal (CMC) osteoarthritis (OA) represents a major source of functional morbidity. The effects of early CMC OA on loading and use patterns potentially lead to changes in local bone density and microarchitecture. Hounsfield units (HU), a quantitative attenuation coefficient obtained from computed tomography (CT) scans, have been shown to be a reliable marker of bone density. We hypothesized that early CMC OA is associated with lower local bone density about the CMC joint as assessed by HU. Methods We examined HU units from CT scans in 23 asymptomatic subjects and 91 patients with early CMC OA. The HU measurements were obtained within cancellous portions of the trapezium, capitate, first and third metacarpal bases, and distal radius. Linear regression models, with age and sex included as covariates, were used to assess the relationship between CMC OA and HU values at each anatomical site. Results Early OA patients had significantly lower HU than asymptomatic subjects within the trapezium (mean, 377 HU vs 436 HU) and first metacarpal bases (265 HU vs 324 HU). No significant group differences were noted at the capitate, third metacarpal, or distal radius. Male sex and younger age were associated with significantly higher HU at all the anatomical sites, except the first metacarpal base, where age had no significant effect. Conclusions Subjects presenting with early CMC OA had significantly lower bone density as assessed with HU at the thumb CMC joint (trapezium and first metacarpal base). Early thumb CMC OA and discomfort may lead to diminished loading across the basal joint, producing focal disuse osteopenia. These findings in symptomatic early arthritis suggest a relationship between symptoms, functional use of the CMC joint, and local bone density.
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NR 22
TC 13
Z9 15
U1 0
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PT J
AU Raybould, G
Babatunde, O
Evans, AL
Jordan, JL
Paskins, Z
AF Raybould, Grace
Babatunde, Opeyemi
Evans, Amy L.
Jordan, Joanne L.
Paskins, Zoe
TI Expressed information needs of patients with osteoporosis and/or fragility fractures: a systematic review
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Review
DE Information needs; Osteoporosis; Education; Communication
ID health literacy; decision aid; hip fracture; adherence; women; perceptions; medication; management; risk; osteoarthritis
AB This systematic review identified patients have unmet information needs about the nature of osteoporosis, medication, self-management and follow-up. Clinician knowledge and attitudes appear to be of key importance in determining whether these needs are met. Unmet information needs appear to have psychosocial consequences and result in poor treatment adherence. Purpose Patient education

is an integral component of the management of osteoporosis, yet patients are dissatisfied with the information they receive and see this as an area of research priority. This study aimed to describe and summarise the specific expressed information needs of patients in previously published qualitative research. Methods Using terms relating to osteoporosis, fragility fracture and information needs, seven databases were searched. Articles were screened using predefined inclusion and exclusion criteria. Full-text articles selected for inclusion underwent data extraction and quality appraisal. Findings were drawn together using narrative synthesis. Results The search identified 11,024 articles. Sixteen empirical studies were included in the review. Thematic analysis revealed three overarching themes relating to specific information needs, factors influencing whether information needs are met and the impact of unmet information needs. Specific information needs identified included the following: the nature of osteoporosis/fracture risk; medication; self-management and understanding the role of dual energy x-ray absorptiometry and follow-up. Perceived physician knowledge and attitudes, and the attitudes, beliefs and behaviours of patients were important factors in influencing whether information needs were met, in addition to contextual factors and the format of educational resources. Failure to elicit and address information needs appears to be associated with poor treatment adherence, deterioration of the doctor-patient relationship and important psychosocial consequences. Conclusion This is the first study to describe the information needs of patients with osteoporosis and fracture, the impact of this information gap and possible solutions. Further research is needed to co-design and evaluate educational interventions with patients.
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FU Arthritis Research UK Centre in Primary Care grant [18139]; INSPIRE from Keele University School of Medicine (Wellcome Trust)
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ANKYLOSING SPONDYLITIS, V0, P0
NR 50
TC 46
Z9 55
U1 0
U2 12
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
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AU Pirosa, A
Gottardi, R
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Alexander, Peter G.
Tuan, Rocky S.
TI Engineering in-vitro stem cell-based vascularized bone models for drug screening and predictive toxicology
SO STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE tissue engineering; vascularized bone; three-dimensional microphysiological systems; biomaterial; scaffold; preclinical model; bioreactors
ID endothelial progenitor cells; nitric-oxide synthase; perfusion bioreactor system; microvessel-like structures; beta-tricalcium phosphate; porous ceramic scaffolds; growth-factor delivery; large animal-models; fluid shear-stress; calcium-phosphate
AB The production of veritable in-vitro models of bone tissue is essential to understand the biology of bone and its surrounding environment, to analyze the pathogenesis of bone diseases (e.g., osteoporosis, osteoarthritis, osteomyelitis, etc.), to develop effective therapeutic drug screening, and to test potential therapeutic strategies. Dysregulated interactions between vasculature and bone cells are often related to the aforementioned pathologies, underscoring the need for a bone model that contains engineered vasculature. Due to ethical restraints and limited prediction power of animal models, human stem cell-based tissue engineering has gained increasing relevance as a candidate approach to overcome the limitations of animals and to serve as preclinical models for drug testing. Since bone is a highly vascularized tissue, the concomitant development of vasculature and mineralized matrix requires a synergistic interaction between osteogenic and endothelial precursors. A number of experimental approaches have been used to achieve this goal, such as the combination of angiogenic factors and three-dimensional scaffolds, prevascularization strategies, and coculture systems. In this review, we present an overview of the current models and approaches to generate in-vitro stem cell-based vascularized bone, with emphasis on the main challenges of vasculature engineering. These challenges are related to the choice of

biomaterials, scaffold fabrication techniques, and cells, as well as the type of culturing conditions required, and specifically the application of dynamic culture systems using bioreactors.
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TI PROFILE OF PATIENTS WITH OSTEOPOROTIC FRACTURES AT A TERTIARY ORTHOPEDIC TRAUMA CENTER
SO ACTA ORTOPEDICA BRASILEIRA
LA English
DT Article
DE Osteoporotic fractures; Osteoporosis; Epidemiology; Diagnosis; Bone density; Prevalence
ID subsequent fracture; osteoarthritis; prevalence
AB Objective: To evaluate the profile of patients with osteoporotic fractures treated at a tertiary orthopedic hospital. Methods: Using questionnaires, 70 patients with osteoporotic fractures (OF) were compared with 50 outpatients with multiple osteoarthritis (OA) followed through an outpatient clinic. Results: The OF group was older ($p < 0.001$), less heavy ($p=0.003$), had lower BMI ($p=0.006$), was more likely to be white ($p=0.011$), was less likely to be married ($p=0.008$), and had previous falls, previous fractures, old fractures (>1 year), falls in the last 12 months, fractures due to falls, and needed more assistance ($p < 0.05$). They also had lower Lawton & Brody Instrumental Activities of Daily Living scores ($p < 0.05$) and reported less lower limb disability, foot pathology, muscle weakness, hypothyroidism, and vitamin D intake than patients in the OA group. White race, previous falls, and previous fractures increase the risk of osteoporotic fractures by 10.5, 11.4, and 4.1 times, respectively. The chance of fracture dropped 29% for each one-unit increase in Lawton & Brody IADL score. Married participants had fewer fractures than participants with other marital status. Conclusion: Together, race, marital status, previous falls, foot pathologies, previous fractures, and IADL scores define the profile of patients with osteoporotic fractures.

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WC Orthopedics
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PT J
AU Rabelo, GD
Roux, JP
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AF Rabelo, Gustavo Davi
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TI Cortical Fractal Analysis and Collagen Crosslinks Content in Femoral Neck After Osteoporotic Fracture in Postmenopausal Women: Comparison with Osteoarthritis
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Cortical bone; Osteoporosis; Femoral neck; Lacunarity; Fractal dimension
ID trabecular bone-structure; biomechanical property; nonenzymatic glycation;

structural basis; proximal femur; lacunarity; strength; mature
AB The femoral neck (FN) has been previously characterized by thinner cortices in osteoporotic fracture (HF) when compared to hip osteoarthritis (HOA). The purposes of this study were to complete the previous investigations on FNs from HF and HOA by analyzing the complexity of the cortical structure and to approach the intrinsic properties of cortical bone by assessing the collagen crosslink contents. FN samples were obtained during arthroplasty in 35 postmenopausal women (HF; n = 17; mean age 79 +/- 2 years; HOA; n = 18; mean age 66 +/- 2 years). The cortical fractal dimension (Ct.FD) and lacunarity (Ct.Lac) derived from high-resolution peripheral quantitative tomography (isotropic voxel size: 82 mu m) images of FN by using Ctan software and Fraclac running in ImageJ were analyzed. The collagen crosslinks content [pyridinoline, deoxypyridinoline, pentosidine (PEN)] were assessed in cortical bone. Ct.FD was significantly lower ($p < 0.0001$) in HF than HOA reflecting a decreased complexity and was correlated to the age and BMD. In two sub-groups, BMD- and age-matched, respectively, Ct.FD remained significantly lower in HF than HOA ($p < 0.001$). Ct.Lac was not different between HF and HOA. PEN content was two times higher in HF than HOA ($p < 0.0001$) independently of age. In conclusion, FN with HF was characterized by a less complex cortical texture and higher PEN content than HOA. In addition to the decreased bone mass and BMD previously reported, these modifications contribute to the lower bone quality in HF than HOA in postmenopausal women.
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PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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JI Calcif. Tissue Int.
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WC Endocrinology & Metabolism
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PT J
AU Al-Qattan, MM
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AF Al-Qattan, Mohammad M.
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TI Fibromodulin: Structure, Physiological Functions, and an Emphasis on its Potential Clinical Applications in Various Diseases
SO JCPSP-JOURNAL OF THE COLLEGE OF PHYSICIANS AND SURGEONS PAKISTAN
LA English
DT Review
DE Fibromodulin; Proteoglycans; Structure; Function; Disease; Human; Scarless healing
ID temporomandibular-joint osteoarthritis; extracellular-matrix; growth-factor; transforming growth-factor-beta-1; proteoglycan fibromodulin; collagen fibrillogenesis; differential expression; intervertebral discs; articular-cartilage; angiogenic factors
AB Fibromodulin (FMOD) is one of the small leucine-rich proteoglycans. A search of the literature did not reveal any paper that specifically reviews the potential clinical applications of FMOD in the management of human diseases. First, the structure and physiological functions of FMOD were reviewed. Then its potential clinical applications in various diseases including diseases of the skin, tendons,

joints, intervertebral discs, blood vessels, teeth, uterus, bone and kidney were reviewed. FMOD is able to switch the adult response to skin wounding to the desired fetal response of scarless healing. Lowered levels of FMOD would be desirable in the management of tendinopathy, uterine fibroids, tumors resistant to radiotherapy, glioblastomas, small-cell lung cancer, and primary liver/lung fibrosis. In contrast, increased levels of FMOD would be desirable in the management of acute tendon injuries, osteoarthritis, rheumatoid arthritis, temporo-mandibular disease, joint laxity, intervertebral disc disease, neo-intimal hyperplasia of vein grafts, teeth caries, periodontal disease, endometrial atrophy, osteoporosis and diabetic nephropathy. Furthermore, FMOD may be used as a prognostic marker of cerebrovascular events in patients undergoing carotid endarterectomy and a marker for prostatic cancer. Finally, the use of FMOD in the treatment of symptomatic endometrial atrophy should be explored in women who are unable to use the standard estrogen management for endometrial atrophy. The review concluded that clinical trials in humans should be initiated to investigate the potential therapeutic effects of FMOD.
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NR 68
TC 17
Z9 17
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PU COLL PHYSICIANS & SURGEONS PAKISTAN
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JI JCPSP-J. Coll. Physicians Surg.
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PT J
AU Zhong, FH
Lu, JW
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AF Zhong, Fuhua
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Wang, Yangxin
Song, Hongpu
TI Genetic variation of SMAD3 is associated with hip osteoarthritis in a Chinese Han population
SO JOURNAL OF INTERNATIONAL MEDICAL RESEARCH
LA English
DT Article
DE Hip osteoarthritis; single nucleotide polymorphism; SMAD3; Chinese Han; case-control study; PCR
ID single nucleotide polymorphisms; knee osteoarthritis; susceptibility; women; epidemiology; osteoporosis
AB Objective This study was performed to investigate the association between genetic variation in SMAD3 and hip osteoarthritis (OA) in a Chinese Han population. Methods The frequency of two single nucleotide polymorphisms of SMAD3, rs1470002 and rs12901499, was examined in 500 patients with hip OA and 1080 healthy controls in a Chinese Han population. Further analysis was performed according to sex and age. Results We detected statistically significant differences in the allele frequency and genotype between the hip OA and healthy control groups. The frequency of the GA+GG and GA genotypes of rs12901499 and the G variant were much higher in patients with hip OA than in healthy controls. This association was also present when the participants were stratified by sex and age. However, there was no significant association between the risk of hip OA and the presence of rs1470002 GA, AA, or GA+AA genotypes, even after sex- and age-stratified analysis. Conclusions The SMAD3 SNP rs12901499 GA genotype and G variant may increase the risk of hip OA in Chinese Han patients.
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PT J
AU Blanc-Petitjean, P
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AF Blanc-Petitjean, P.
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TI Factors affecting rotation of occiput posterior position during the first stage of labor
SO JOURNAL OF GYNECOLOGY OBSTETRICS AND HUMAN REPRODUCTION
LA English
DT Article
DE First stage of labor; Intrapartum care; Occiput posterior position; Oxytocin; Rotation
ID manual rotation; transverse positions; epidural analgesia; operative delivery; cesarean delivery; fetal position; association; risk; 2nd-stage; impact
AB Introduction. - Fetal occiput posterior (OP) positions account for 15 to 20% of cephalic presentations and are associated with poorer maternal and neonatal

outcomes than occiput anterior (OA) positions. The aim of this study was to identify maternal, neonatal and obstetric factors associated with rotation from OP to OA position during the first stage of labor. Material and methods. - This secondary analysis of a multicenter randomized controlled trial (EVADELA) included 285 laboring women with ruptured membranes and a term fetus in OP position. After excluding women with cesarean deliveries before full dilatation, we compared two groups according to fetal head position at the end of the first stage of labor: those with and without rotation from OP to OA position. Factors associated with rotation were assessed with univariate and multivariate analyses using multilevel logistic regression models. Results. - The rate of anterior rotation during the first stage was 49.1%. Rotation of the fetal head was negatively associated with excessive gestational weight gain (adjusted odds ratio [aOR]: 0.37, 95% confidence interval [CI]: 0.17-0.80), macrosomia (aOR: 0.35, 95% CI: 0.14-0.90), direct OP position (aOR: 0.24, 95% CI: 0.09-0.65), and prelabor rupture of membranes (aOR: 0.40, 95% CI: 0.19-0.86). Oxytocin administration was the only factor positively associated with fetal head rotation (aOR: 2.17, 95% CI: 1.20-3.91). Discussion. - Oxytocin administration may affect rotation of OP positions during the first stage of labor. Further studies should be performed to assess the risks and benefits of its utilization for managing labor with a fetus in OP position. (C) 2018 Elsevier Masson SAS. All rights reserved.
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TC 10
Z9 10
U1 0
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JI J. Gynecol. Obstet. Hum. Reprod.
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WC Obstetrics & Gynecology
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PT J
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TI Is it possible that the pathogenesis of osteoarthritis could start with subchondral trabecular bone loss like osteoporosis?
SO EKLEM HASTALIKLARI VE CERRAHISI-JOINT DISEASES AND RELATED SURGERY

LA English
DT Article
DE Bone mineral densitometry; osteoarthritis; osteoporosis; subchondral bone loss; trabecular thickness
ID mineral density
AB Objectives: This study aims to investigate the role of subchondral trabecular bone thickness in the mechanism of knee osteoarthritis and the correlation of osteoarthritis and osteoporosis pathogenesis. Patients and methods: The study included 62 patients (9 males, 53 females, mean age 66.7 years; range, 50 to 84 years) with osteoarthritk All radiographs were evaluated according to Kellgren and Lawrence classification. The bone mineral density of the patients was measured and bone samples were collected from all patients included in the study during the surgical procedure and investigated pathologically. Results: Osteoarthritis grade and trabecular bone thickness were correlated with each other. Trabecular thickness rate was higher in patients with severe osteoarthritis, whereas trabecular thickness rate was statistically significantly lower than the mean in patients with mild osteoarthritis (p=0.045). Conclusion: Trabecular thickness rate was significantly lower in the mild grade of osteoarthritis compared to the severe grade. As the level of osteoarthritis increased, the number of patients with osteoporosis decreased.
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U2 11
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TI Pro-inflammatory dietary pattern is associated with fractures in women: an eight-year longitudinal cohort study
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Aged; Dietary Inflammatory Index; Fracture; Inflammation; Osteoporosis
ID c-reactive protein; bone-mineral density; independent risk-factor; hip fracture; vertebral fractures; postmenopausal women; mediterranean diet; physical-activity; index; markers
AB In this study, during 8 years of follow-up, we reported that higher dietary inflammatory index values were associated with a higher risk of incident fractures in women, but not in men, after adjusting for potential confounders. Inflammation is a key risk factor for many adverse outcomes in older people. While diet is a potential source of inflammation, little is known about the impact of inflammatory diet on fractures. Thus, we investigated whether higher Dietary Inflammatory Index (DII)(TM) A (R) scores are associated with fractures in a cohort of North American people. This longitudinal study with a follow-up of 8 years included 3648 participants (1577 males and 2071 females; mean age = 60.6 years) with/at risk of knee osteoarthritis participating with in the Osteoarthritis Initiative. DII scores were calculated using the validated Block Brief 2000 Food Frequency Questionnaire, categorized into sex-specific quintiles. Information on fractures was obtained through self-reported history of fractures at hip, spine, and forearm. The relationship between baseline DII score and incident fracture was assessed through a Cox's regression analysis, adjusted for potential baseline confounders, and reported as hazard ratios (HRs). During 8 years of follow-up, 560 individuals developed fractures (15.4%). Adjusting for 10 potential confounders, women in the highest DII score quintile (i.e., most pro-inflammatory diet) had a significantly higher risk for fractures (HR = 1.46; 95% CI = 1.02-2.11) compared to women in the lowest quintile. An increase in one standard deviation of DII scores significantly

predicted fracture onset in women (adjusted HR = 1.14; 95% CI = 1.02-1.27). The association between DII score and fractures was not significant among men or in the sample as whole. Pro-inflammatory diet is associated with a higher incidence of fractures in women but not men.
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NR 47
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Z9 33
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U2 14
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TI Racial differences in comorbidity profile among patients with chronic obstructive

pulmonary disease
SO BMC MEDICINE
LA English
DT Article
DE COPD; Comorbidity; Race; Ethnicity
ID cardiovascular-disease; united-states; lung-function; copd; mortality; exacerbation; population; obesity; anemia; cohort
AB Background: Chronic obstructive pulmonary disease (COPD) is often accompanied by multiple comorbidities, which are associated with an increased risk of exacerbation, a poor health-related quality of life, and high mortality. However, differences in comorbidity profile by race and ethnicity in COPD patients have not been fully elucidated. Methods: Participants aged 40 to 79 years with spirometry-defined COPD from the U.S. National Health and Nutrition Examination Survey (NHANES) (2007-2012) and from the Korea NHANES (2007-2015) were analyzed to compare the prevalence of comorbidities by race and ethnicity group. Comorbidities were defined using questionnaire data, physical exams, and laboratory tests. Results: Non-Hispanic Whites had the highest prevalence of dyslipidemia (65.5%), myocardial infarction (6.2%), osteoarthritis (40.1%), and osteoporosis (13.6%), while non-Hispanic Blacks had the highest prevalence of asthma (24.0%), hypertension (70.2%), stroke (7.3%), diabetes mellitus (DM) (23.3%), anemia (16.4%), and rheumatoid arthritis (11.9%). Compared to non-Hispanic Whites, non-Hispanic Blacks had a significantly higher prevalence of hypertension, stroke, DM, anemia, and rheumatoid arthritis after adjusting for age, sex, body mass index, and smoking status, while Hispanics had a significantly higher prevalence of DM and anemia, and Koreans had significantly lower prevalences of all comorbidities except stroke, DM, and anemia. Conclusions: COPD-related comorbidities varied significantly by race and ethnicity, and different strategies may be required for the optimal management of COPD and its comorbidities in different race and ethnicity groups.
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TI Scoping review of priority setting of research topics for musculoskeletal conditions
SO BMJ OPEN
LA English
DT Review
ID primary-care research; of-the-art; american orthopedic foot; ankle research priority; low-back-pain; research agenda; clinical-research; chiropractic profession; research prioritization; research council
AB Objective Describe research methods used in priority-setting exercises for musculoskeletal conditions and synthesise the priorities identified. Design Scoping review. Setting and population Studies that elicited the research priorities of

patients/consumers, clini cians, researchers, policy-makers and/or funders for any musculoskeletal condition were included. Methods and analysis We searched MEDLINE and EMBASE from inception to November 2017 and the James Lind Alliance top 10 priorities, Cochrane Priority Setting Methods Group, and Cochrane Musculoskeletal and Back Groups review priority lists. The reported methods and research topics/questions identified were extracted, and a descriptive synthesis conducted. Results Forty-nine articles fulfilled our inclusion criteria. Methodologies and stakeholders varied widely (26 included a mix of clinicians, consumers and others, 16 included only clinicians, 6 included only consumers or patients and in 1 participants were unclear). Only two (4%) reported any explicit inclusion criteria for priorities. We identified 294 broad research priorities from 37 articles and 246 specific research questions from 17 articles, although only four (24%) of the latter listed questions in an actionable format. Research priorities for osteoarthritis were identified most often (n=7), followed by rheumatoid arthritis (n=4), osteoporosis (n=4) and back pain (n=4). Nearly half of both broad and specific research priorities were focused on treatment interventions (n=116 and 111, respectively), while few were economic (n=8, 2.7% broad and n=1, 0.4% specific), implementation (n=6, 2% broad and n=4, 1.6% specific) or health services and systems research (n=15, 5.1% broad and n=9, 3.7% specific) priorities. Conclusions While many research priority-setting studies in the musculoskeletal field have been performed, methodological limitations and lack of actionable research questions limit their usefulness. Future studies should ensure they conform to good priority-setting practice to ensure that the generated priorities are of maximum value.
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TI Evidence for Ongoing Modeling-Based Bone Formation in Human Femoral Head Trabeculae via Forming Minimodeling Structures: A Study in Patients with Fractures and Arthritis
SO FRONTIERS IN ENDOCRINOLOGY
LA English

DT Article
DE modeling-based bone formation; forming minimodeling structures; femoral head; bone histomorphometry; femoral neck fracture; rheumatoid arthritis; hip osteoarthritis
ID vertebral cancellous bone; microcallus formations; rheumatoid-arthritis; sedimentation-rate; dialysis patients; osteoid seams; cortical bone; osteoporosis; osteocytes; disease
AB Bone modeling is a biological process of bone formation that adapts bone size and shape to mechanical loads, especially during childhood and adolescence. Bone modeling in cortical bone can be easily detected using sequential radiographic images, while its assessment in trabecular bone is challenging. Here, we performed histomorphometric analysis in 21 bone specimens from biopsies collected during hip arthroplasty, and we proposed the criteria for histologically identifying an active modeling-based bone formation, which we call a "forming minimodeling structure" (FMiS). Evidence of FMiSs was found in 9 of 20 specimens (45%). In histomorphometric analysis, bone volume was significant higher in specimens displaying FMiSs compared with the specimens without these structures (BV/TV, 31.7 10.2 vs. 23.1 3.9%; $p < 0.05$). Osteoid parameters were raised in FMiS-containing bone specimens (OV/BV, 2.1 +/- 1.6 vs. 0.6 +/- 0.3%; $p < 0.001$, OS/BS, 23.6 +/- 15.5 vs. 7.6 +/- 4.2%; $p < 0.001$, and O.Th, 7.4 mu m +/- 2.0 vs. 5.2 +/- 1.0; $p < 0.05$). Our results showed that the modeling-based bone formation on trabecular bone surfaces occurs even during adulthood. As FMiSs can represent histological evidence of modeling-based bone formation, understanding of this physiology in relation to bone homeostasis is crucial.
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PT J
AU Cornelis, FMF

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TI ANP32A regulates ATM expression and prevents oxidative stress in cartilage, brain, and bone
SO SCIENCE TRANSLATIONAL MEDICINE
LA English
DT Article
ID n-acetyl cysteine; genome-wide association; ataxia-telangiectasia; knee osteoarthritis; deficient mice; chondrocyte hypertrophy; histone acetylation; clinical-parameters; antioxidant enzymes; articular-cartilage
AB Osteoarthritis is the most common joint disorder with increasing global prevalence due to aging of the population. Current therapy is limited to symptom relief, yet there is no cure. Its multifactorial etiology includes oxidative stress and overproduction of reactive oxygen species, but the regulation of these processes in the joint is insufficiently understood. We report that ANP32A protects the cartilage against oxidative stress, preventing osteoarthritis development and disease progression. ANP32A is down-regulated in human and mouse osteoarthritic cartilage. Micro-array profiling revealed that ANP32A protects the joint by promoting the expression of ATM, a key regulator of the cellular oxidative defense. Antioxidant treatment reduced the severity of osteoarthritis, osteopenia, and cerebellar ataxia features in Anp32a-deficient mice, revealing that the ANP32A/ATM axis discovered in cartilage is also present in brain and bone. Our findings indicate that modulating ANP32A signaling could help manage oxidative stress in cartilage, brain, and bone with therapeutic implications for osteoarthritis, neurological disease, and osteoporosis.
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AF Lindstrom, Erik
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TI Nonclinical and clinical pharmacological characterization of the potent and selective cathepsin K inhibitor MIV-711
SO JOURNAL OF TRANSLATIONAL MEDICINE
LA English
DT Article
DE Cathepsin K; Osteoarthritis; CTX-I; NTX-I; CTX-II; Subchondral bone; Cartilage
ID bone turnover; knee osteoarthritis; postmenopausal osteoporosis; biochemical markers; controlled-trial; double-blind; collagen; expression; biomarkers; cartilage
AB Background: Cathepsin K is an attractive therapeutic target for diseases in which bone resorption is excessive such as osteoporosis and osteoarthritis (OA). The current paper characterized the pharmacological profile of the potent and selective cathepsin K inhibitor, MIV-711, in vitro and in cynomolgus monkeys, and assessed translation to human based on a single dose clinical study in man. Methods: The potency and selectivity of MIV-711 were assessed in vitro using recombinant enzyme assays and differentiated human osteoclasts. MIV-711 was administered to healthy cynomolgus monkeys (3-30 mu mol/kg, p.o.). Plasma levels of MIV-711 and the bone resorption biomarker CTX-I were measured after single dose experiments, and urine levels of CTX-I, NTX-I and CTX-II biomarkers were measured after repeat dose experiments. The safety, pharmacokinetics and pharmacodynamics (serum CTX-I) of MIV-711 were assessed in human healthy subjects after single ascending doses from 20 to 600 mg. Results: MIV-711 was a potent inhibitor of human cathepsin K (K-i: 0.98 nmol/L) with > 1300-fold selectivity towards other human cathepsins. MIV-711 inhibited human osteoclast-mediated bone resorption with an IC50 value of 43 nmol/L. Single oral doses of MIV-711 to monkeys reduced plasma levels of CTX-I in a dose-dependent fashion by up to 57% at trough. The effect on CTX-I was linearly correlated to the plasma exposure of MIV-711, while the efficacy duration outlasted plasma exposure. Repeat oral dosing with MIV-711 also reduced urinary levels of the bone resorption biomarkers CTX-I (by 93%) and NTX-I (by 71%) and the cartilage degradation biomarker CTX-II (by 71%). MIV-711 was safe and well-tolerated when given as single ascending doses to healthy subjects. MIV-711 reduced serum CTX-I levels in a dose-dependent manner by up to 79% at trough. The relationship between MIV-711 exposure and effects on these biomarkers in humans was virtually identical when compared to the corresponding monkey data. Conclusions: MIV-711 is a potent and selective cathepsin K inhibitor with dose-dependent effects on biomarkers of bone and cartilage degradation in monkey and human. Taken together, MIV-711 shows promise for the treatment of bone and cartilage related disorders in humans, such as OA.
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TI Emerging role of extracellular vesicles in musculoskeletal diseases
SO MOLECULAR ASPECTS OF MEDICINE
LA English
DT Review
DE Exosomes; Muscular dystrophy; Osteoporosis; Osteoarthritis; microRNA
ID synovial fibroblasts; osteogenic differentiation; matrix-metalloproteinase; muscle; expression; micrornas; myogenesis; mechanism; exosm; osteoarthritis
AB Research into the biology of extracellular vesicles (EVs), including exosomes and microvesicles, has expanded significantly with advances in EV isolation techniques, a better understanding of the surface markers that characterize exosomes and microvesicles, and greater information derived from eomics approaches on the proteins, lipids, mRNAs, and microRNAs (miRNAs) transported by EVs. We have recently discovered a role for exosome-derived miRNAs in age-related bone loss and osteoarthritis, two conditions that impose a significant public health burden on the aging global population. Previous work has also revealed multiple roles for EVs and their miRNAs in muscle regeneration and congenital myopathies. Thus, EVs appear to be involved in a number of degenerative conditions that impact the musculoskeletal system, indicating that the musculoskeletal system is an excellent model for investigating the role of EVs in tissue maintenance and repair. This review highlights the role of EVs in bone, skeletal muscle, and joint health, including both normal tissue metabolism as well as tissue injury repair and regeneration. A consistent theme that emerges from study of musculoskeletal EVs is that various miRNAs appear to mediate a number of key pathological processes. These findings point to a potential therapeutic opportunity to target EV-derived

miRNAs as a strategy for improving musculoskeletal function. (c) 2017 Elsevier Ltd. All rights reserved.
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TI Profile of osteoarthritic patients undergoing hip or knee arthroplasty, a step toward a definition of the "need for surgery"
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
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DT Article
DE Osteoarthritis; Hip; Knee; Arthroplasty; Treatment
ID total joint arthroplasty; quality-of-life; preoperative radiographic severity; european-society; economic-aspects; relevant outcm; physical function; health-status; replacement; osteoporosis

AB Aims The objective of this study is to characterize, based on clinical, radiographic, health-related, quality-of-life-related, and demographic variables, the profile of a large, homogeneous, cohort of patients undergoing knee or hip arthroplasty, in a public hospital. Current regulatory guidelines for structure-modifying agent are not clear regarding hard clinical endpoint. The "need for surgery" has been suggested as a potential relevant outcome, but, until now, it is poorly defined. By characterizing a large number of patients who undergo total hip or total knee replacement, this paper aims at providing a contribution to the better definition of the "need for surgery" in advanced OA of the lower limbs. Methods Consecutive patients who underwent primary knee arthroplasty (KA) or hip arthroplasty (HA) between December 2008 and February 2013, in an academic hospital, and who were diagnosed with hip or knee osteoarthritis (OA) (ACR criteria). Data collected at baseline included demographic and clinical data; Kellgren-Lawrence radiological grading; Western Ontario and Mc Master Universities Arthritis Index (WOMAC); EuroQol five dimensions questionnaire and EuroQol visual analog scale; and 36-item Short Form Health Survey. Results 626 subjects were included, 346 with hip OA and 280 with knee OA. Significant differences between subjects in need of an HA or of a KA were seen in terms of age (66.5 years versus 65 for hip), duration of complaints (2188 days versus 1146.5 for hip), BMI (28.68 kg/mA(2) versus 27.07), radiological status (severe OA were found in 79.85% in knee group and 68.73% in hip group), comorbidities (FCI higher in knee group), traumatic of surgical history (37 versus 6%), and health-related quality of life and function (patients with HA had a poorer clinical status regarding WOMAC and WOMAC subscale). Conclusion Significant differences were observed between patients undergoing KA or HA. These differences might be useful to better understand the "need for surgery" status in these indications. This concept may help to define responders and failures to pharmacological treatment of OA.
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TI State of the art of bioimplants manufacturing: part I
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ID 316l stainless-steel; mechanical-property; biomedical applications; powder-metallurgy; corrosion behavior; titanium; laser; implants; surface; fatigue
AB Bioimplants are becoming increasingly important in the modern society due to the fact of an aging population and associated issues of osteoporosis and osteoarthritis. The manufacturing of bioimplants involves an understanding of both mechanical engineering and biomedical science to produce biocompatible products with adequate lifespans. A suitable selection of materials is the prerequisite for a long-term and reliable service of the bioimplants, which relies highly on the comprehensive understanding of the material properties. In this paper, most biomaterials used for bioimplants are reviewed. The typical manufacturing processes are discussed in order to provide a perspective on the development of manufacturing fundamentals and latest technologies. The review also contains a discussion on the current measurement and evaluation constraints of the finished bioimplant products. Potential future research areas are presented at the end of this paper.
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TI Current methods of preventing aseptic loosening and improving osseointegration of titanium implants in cementless total hip arthroplasty: a review
SO JOURNAL OF INTERNATIONAL MEDICAL RESEARCH
LA English
DT Article
DE Osseointegration; titanium implant; cementless hip arthroplasty; aseptic loosening; osteoarthritis; surgery
ID intensity pulsed ultrasound; bone regeneration; stem; risk; revision; failure; replacement; migration; register; alloys
AB Hip osteoarthritis is the most common joint disorder, and is represented by a

degenerative process, resulting in pain and functional impairment. If conservative treatment for hip osteoarthritis fails, the only remaining option is hip arthroplasty. Despite good survival of implants, loosening of components is the most common complication. This leads to revision surgeries, which are technically demanding, expensive, and result in a low satisfaction rate. Uncemented hip replacements require proper osseointegration for increased survival. Physical characteristics of implants include biocompatibility, Young's modulus of elasticity, strength, and corrosion resistance, and each influence fixation of implants. Moreover, implant surface treatments, pore size, pore density, and femoral stem design should be appropriately selected. Patients' optimization of obesity, osteoporosis, cardiovascular disease, psychotic disorders, and smoking cessation are associated with a higher survival of implants. Surgical factors, such as approach, drilling and rasping, acetabular bone coverage, acetabular cup positioning, and implant size, also affect survival of implants. Avoiding drugs, which may impair osseointegration of implants, and having an appropriate rehabilitation protocol are important. Future directions include anabolic and anti-catabolic bone-acting drugs to enhance osseointegration of implants. Comprehensive knowledge of the factors mentioned above is important for preventing aseptic loosening, with important socioeconomic consequences.
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TI A Conceptual Model for the Evaluation of Surgical Missions
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LA English
DT Article
ID total joint replacement; total knee replacement; quality-of-life; functional status; physical-activity; pain management; global burden; total hip; health; dominican
AB Background: Medical missions to low and middle-income countries are increasingly frequent, with an estimated 6,000 trips sponsored by U.S. organizations accounting for approximately 200,000 surgical cases and $250 million in costs annually. However, these missions have received little critical evaluation. This paper describes the research program Operation Walk (Op-Walk) Boston, and proposes an evaluation model for similar surgical missions. Methods: We propose an evaluation model, borrowing from the work of Donabedian and enriched by evidence from our research program. The model calls for evaluation of the salient contextual factors (culture and beliefs), system management (structure, process, and outcomes), and sustainability of the program's interventions. We used these domains to present findings from the quantitative and qualitative research work of Op-Walk Boston. Results: Op-Walk's qualitative research findings demonstrated that cultural factors are important determinants of patients' perceptions of arthritis etiology, physical activity patterns, and treatment preferences. Quantitative assessments documented that Dominican patients had worse lower-extremity functional status (mean Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC] function score of 33.6) and pain preoperatively than patients undergoing total hip or knee replacement in the U.S. (WOMAC function score of 43.3 to 54), yet they achieved excellent outcomes (50-point improvement), comparable to those of their U.S. counterparts. Assessments of the quality and sustainability of the Op-Walk program showed that the quality of care provided by Op-Walk Boston meets Blue Cross Blue Shield Centers of Excellence (Blue Distinction) criteria, and that sustainable changes were transferred to the host hospital. Conclusions: Our proposed model offers a method for formal assessment of medical missions that addresses the call for evidence of their merit. We suggest that surgical missions adopt quantitative and qualitative strategies to document their impact, identify areas of improvement, and justify program continuation, growth, and support.
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TI MicroRNAs in orthopaedic research: Disease associations, potential therapeutic applications, and perspectives
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DE MicroRNAs (miRNAs); cartilage; bone; skeletal development; osteoarthritis
ID mesenchymal stem-cells; lumbar disc degeneration; osteogenic differentiation; chondrocyte apoptosis; bone-formation; molecular characterization; intraarticular injection; extracellular vesicles; expression profiles; noncoding rnas
AB MicroRNAs (miRNAs) are small non-coding RNAs that function to control many cellular processes by their ability to suppress expression of specific target genes. Tens to hundreds of target genes may be affected by one miRNA, thereby resulting in modulation of multiple pathways in any given cell type. Therefore, altered expression of miRNAs (i.e., during tissue development or in scenarios of disease or cellular stress) can have a profound impact on processes regulating cell differentiation, metabolism, proliferation, or apoptosis, for example. Over the past 5-10 years, thousands of reports have been published on miRNAs in cartilage and bone biology or disease, thus highlighting the significance of these non-coding RNAs in regulating skeletal development and homeostasis. For the purpose of this review, we will focus on miRNAs or miRNA families that have demonstrated function in vivo within the context of cartilage, bone or other orthopaedic-related

tissues (excluding muscle). Specifically, we will discuss studies that have utilized miRNA transgenic mouse models or in vivo approaches to target a miRNA with the aim of altering conditions such as osteoarthritis, osteoporosis and bone fractures in rodents. We will not discuss miRNAs in the context skeletal cancers since this topic is worthy of a review of its own. Overall, we aim to provide a comprehensive description of where the field currently stands with respect to the therapeutic potential of specific miRNAs to treat orthopaedic conditions and current technologies to target and modify miRNA function in vivo. (c) 2017 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 36:33-51, 2018.
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NR 207
TC 26
Z9 31
U1 0
U2 20
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0736-0266
EI 1554-527X
J9 J ORTHOP RES
JI J. Orthop. Res.
PD JAN 15
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VL 36
IS 1
BP 33
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PG 19
WC Orthopedics
SC Orthopedics
GA FY3PF
UT WOS:000426732700004
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PT J
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Barattini, DF
Pricop, M
Rosu, S
AF Guadagna, Simone
Barattini, Dionisio Franco
Pricop, Marius
Rosu, Serban
TI Oral hyaluronan for the treatment of knee osteoarthritis: a systematic review
SO PROGRESS IN NUTRITION

LA English
DT Review
DE Hyaluronic acid; Oral treatments; Dietary supplement; Knee; Osteoarthritis; Objective measures
ID molecular-weight hyaluronan; extract-containing supplement; comb extract; double-blind; clinical-trial; pain; acid; hyalgan(r); absorption; adults
AB Study Objectives: Osteoarthritis (OA) is the most common chronic condition of the joints, affecting approximately 27 million of people in the US and its prevalence is predicted to grow. Recently, symptomatic slowacting drugs for osteoarthritis (SYSADOA) have been vastly studied and have generated considerable interest among clinicians and the public. In particular, the use of oral hyaluronic acid (HA) treatments for knee pain has been the source of much research and it is now widely adopted in the clinic for its safety and relative low cost. The aim of this study is to discuss the efficacy of oral HA in treating knee OA based on the most recent data from the literature as well as to encourage the use of objective measures to determine more effectively the efficacy of current therapies for knee OA. Methods: We searched the PubMed database up to 23/01/2018 based on data from randomized, double-blind, placebo-controlled trials, non-controlled trials and cohort studies conducted in adult subjects. The search words used contained the terms: oral hyaluronan (HA) and knee osteoarthritis (OA). We selected 15 relevant reports. The review was registered on PROSPERO (International prospective register of systematic reviews), registration number CRD42018104127. Results: Companies in Japan, US and Europe produced different oral supplements containing HA in various formulations, which have been tested in clinical trials. The vast majority of the studies analyzed found significant improvements of scores including VAS, WOMAC, JKOM and SF-36v2 in patients with moderate knee OA after short (1 - 4 months) daily treatments with oral HA preparations, compared to placebo-treated controls. Interestingly, few studies proposed the use of objective measures to evaluate the efficacy of HA treatments with ultrasonography and an isokinetic dynamometer, but they obtained modest and controversial results. Conclusions: Current clinical data on oral HA products for the treatment of mild to moderate knee OA are promising and in line with The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) recommendation to use SYSADOA. However, more high-quality research with larger sample sizes and longer exposures to the oral treatment is needed to confirm these data. Particularly, more effort is required to standardize the treatments (final dose of HA, molecular weight of HA and presence of other active molecules) and to assess the results on patients with objective measures.
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NR 35
TC 6
Z9 8
U1 0
U2 24
PU MATTIOLI 1885
PI FIDENZA
PA VIA DELLA LODESANA 649-SX, FIDENZA, 43046 PR, ITALY
SN 1129-8723
EI
J9 PROG NUTR
JI Prog. Nutr.
PD DEC 15
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VL 20
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WC Nutrition & Dietetics
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PT J
AU Hohloch, L
Kim, S
Mehl, J
Zwingmann, J
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Bode, G
AF Hohloch, Lisa
Kim, Suchung
Mehl, Julian
Zwingmann, Jorn
Feucht, Matthias J.
Eberbach, Helge

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Suedkamp, Norbert
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TI Customized post-operative alignment improves clinical outcome following medial open-wedge osteotomy
SO KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY
LA English
DT Article
DE High tibial osteotomy; Varus deformity; Osteoarthritis; Cartilage defect; Correction angle
ID high tibial osteotomy; autologous chondrocyte implantation; varus knee; cartilage regeneration; survivorship analysis; limb alignment; osteoarthritis; defects; compartment; evolution
AB Purpose High tibial osteotomy (HTO) has gained more importance in the treatment of cartilage damage or osteoarthritis of the medial compartment with concurrent varus deformity. Concerning the extent of axis correction, various different views exist. The aim of this study was to evaluate the effect of the size of axis correction on functional outcome in patients undergoing a valgus HTO. Methods From 2005 to 2013, 156 patients with an underlying varus deformity and cartilage damages or unicompartimental osteoarthritis of the medial compartment were treated by HTO. Retrospectively patients were allocated into three different groups according to the degree of axis correction. For this purpose, three adjacent areas, respectively, comprising 5% of the tibial plateau were defined. Limits of those areas were set as follows: with the medial border representing the 0% point and the lateral border representing the 100 point, the three areas were separated according to their limiting intersection points (group A 50-55%, group B 55-60%, group C > 60%). For comparison of the functional outcomes, standardized measures and scores were used (pre-OP: VAS, Lysholm; post-OP: VAS, Lysholm, KOOS). Analysis of the pre- and post-operatively recorded X-rays was effected by means of a planning software (mediCAD, Hectec GmbH, Germany), and statistical analysis was carried out using SPSS Statistics 21.0 (IBM Corp., Armonk, USA). A p value of 0.05 was considered statistically significant. Results Thirty-nine patients were allocated to group A, 50 patients to group B and 67 to group C. Pre-operatively, patients in each group were of a homogenous constitution. In the groups A-C, HTO proved to reduce the VAS score and to increase the Lysholm score ($p < 0.001$). Regarding outcome parameters, group A showed significantly better results in terms of increased Lysholm ($p = 0.049$) and KOOS pain score ($p = 0.043$). In patients treated by HTO and ACI implantation for medial compartment lesions, the best results were achieved in group A which was of statistical significance in comparison of the Lysholm ($p = 0.006$) and VAS score ($p = 0.045$) of groups A and C. In this subgroup, the size of the post-operative valgus angle significantly correlated with the final VAS score (PC 0.364; $p = 0.013$), final Lysholm score (PC - 0.390; $p = 0.007$) and KOOS4 (PC - 0.356; $p = 0.014$). Conclusion HTO for varus deformity in patients with concomitant cartilage damage or osteoarthritis

of the medial compartment is a reliable treatment option with satisfying functional outcome. Precise pre-operative planning regarding individual factors in each patient is mandatory; a pathology-based extent of correction leads to a favourable clinical outcome and to a significant reduction in pain.
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NR 45
TC 39
Z9 48
U1 0
U2 3
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 0942-2056
EI 1433-7347
J9 KNEE SURG SPORT TR A
JI Knee Surg. Sports Traumatol. Arthrosc.
PD SEP 15

PY 2018
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BP 2766
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DI 10.1007/s00167-017-4731-3
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WC Orthopedics; Sport Sciences; Surgery
SC Orthopedics; Sport Sciences; Surgery
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UT WOS:000441912100027
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PT J
AU del Real, A
Riancho-Zarrabeitia, L
López-Delgado, L
Riancho, JA
AF del Real, Alvaro
Riancho-Zarrabeitia, Leyre
Lopez-Delgado, Laura
Riancho, Jose A.
TI Epigenetics of Skeletal Diseases
SO CURRENT OSTEOPOROSIS REPORTS
LA English
DT Review
DE Epigenetics; DNA methylation; Fractures; Adaptation; micro RNA; Histones
ID vitamin-d status; dna methylation; osteogenic differentiation; bone mass; histone deacetylases; multiple-myeloma; noncoding rnas; developmental origins; childhood growth; stem-cells
AB Purpose of Review Epigenetic mechanisms modify gene activity in a stable manner without altering DNA sequence. They participate in the adaptation to the environment, as well as in the pathogenesis of common complex disorders. We provide an overview of the role of epigenetic mechanisms in bone biology and pathology. Recent Findings Extensive evidence supports the involvement of epigenetic mechanisms (DNA methylation, post-translational modifications of histone tails, and non-coding RNAs) in the differentiation of bone cells and mechanotransduction. A variety of epigenetic abnormalities have been described in patients with osteoporosis, osteoarthritis, and skeletal cancers, but their actual pathogenetic roles are still unclear. A few drugs targeting epigenetic marks have been approved for neoplastic disorders, and many more are being actively investigated. Summary Advances in the field of epigenetics underscore the

complex interactions between genetic and environmental factors as determinants of osteoporosis and other common disorders. Likewise, they help to explain the mechanisms by which prenatal and post-natal external factors, from nutrition to psychological stress, impact our body and influence the risk of later disease.
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NR 100
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Z9 19
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PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
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PT J
AU Xiao, Y
Li, B
Liu, J
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Li, Bing

Liu, Jun
TI miRNA-27a regulates arthritis via PPAR in vivo and in vitro
SO MOLECULAR MEDICINE REPORTS
LA English
DT Article
DE microRNA-27a; arthritis; PPAR; IGFBP-5
ID human osteoarthritis chondrocytes; knee osteoarthritis; rat model; signaling pathway; apoptosis; cartilage; gamma; expression; efficacy; matrix
AB The present study investigated the role of microRNA (miR)-27a in the development of arthritis and its mechanism of action. Initially, collagen was used to develop an in vivo rat model of arthritis. Changes in the miRs in the rats were analyzed. It was subsequently observed that miR-27a expression was reduced in patients with arthritis, compared with the control group. In the present study an in vitro miR-27a overexpression model of arthritis was established and it was observed that miR-27a increased the proliferation of osteoblast-like cells in vitro. miR-27a overexpression promoted osteogenic differentiation, increased alkaline phosphatase (ALP) and osteoporosis (OST) content, induced insulin-like growth factor binding protein-5 (IGFBP-5) protein expression, reduced inflammation and suppressed peroxisome proliferator-activated receptor (PPAR) and matrix metalloproteinase-17 (MMP-17) protein expression in arthritis. However, miR-27a downregulation inhibited osteogenic differentiation, increased inflammation and PPAR and MMP-17 protein expression and suppressed ALP and OST content in an in vitro model of arthritis. The PPAR inhibitor reduced the function of miR-27a downregulation on arthritis. Therefore the results of the present study revealed that miR-27a regulates arthritis via PPAR.
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Choi, JS
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Kim, In-Young
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Park, Dong-Chan
Moon, Seung-Bae
Cho, Hyung-Rae
Bashir, Khawaja Muhammad Imran
Ku, Sae Kwang
Choi, Jae-Suk
TI Anti-osteoporotic effects of mixed compositions of extracellular polymers isolated from Aureobasidium pullulans and Textoria morbifera in ovariectomized mice
SO BMC COMPLEMENTARY AND ALTERNATIVE MEDICINE
LA English
DT Article
DE Anti-osteoporotic effect; Aureobasidium pullulans; -Glucans; Exopolymer; Textoria morbifera
ID beta-glucan; dendropanax-morbifera; bone loss; induced-osteoarthritis;

antidiabetic activity; alveolar bone; green tea; rats; mouse; polycan
AB BackgroundExtracellular polymeric substances isolated from Aureobasidium pullulans (EAP), containing specifically 13% -1,3/1,6-glucan, have shown various favorable bone-preserving effects. Textoria morbifera Nakai (TM) tree has been used as an ingredient in traditional medicine and tea for various pharmacological purposes. Thus, the present study was aimed to examine the synergistic anti-osteoporotic potential of mixtures containing different proportions of EAP and TM compared with that of the single formulations of each herbal extract using bilateral ovariectomized (OVX) mice, a renowned rodent model for studying human osteoporosis.MethodsThirty five days after bilateral-OVX surgery, 9 combinations of EAP:TM (ratios=1:1, 1:3, 1:5, 1:7, 1:9, 3:1, 5:1, 7:1, 9:1) and single separate formulations of EAP or TM were supplied orally, once a day for 35days at a final concentration of 200mg/kg. Variations in body weight gains during the experimental periods, as well as femur weights, bone mineral density (BMD), bone strength (failure load), and mineral content (calcium [Ca] and inorganic phosphorus [IP]) following sacrifice were measured. Furthermore, histomorphometric and histological profile analyses of serum biochemical parameters (osteocalcin content and bone specific alkaline phosphatase [bALP] activity) were conducted following sacrifice. Femurs histomorphometric analyses were also conducted for bone resorption, structure and mass. The results for the mixed formulations of EAP:TM and separate formulations were compared with those of risedronate sodium (RES).ResultsThe EAP:TM (3:1) formulation synergistically enhanced the anti-osteoporotic potential of individual EAP or TM formulations, possibly due to enhanced variety of the active ingredients. Furthermore, the effects of EAP:TM were comparable to those of RES (2.5mg/kg) treatment.ConclusionThe results of this study suggest that, the EAP:TM (3:1) combination might act as a new pharmaceutical agent and/or health functional food substance for curing osteoporosis in menopausal women.
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NR 70
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U1 0
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SC Integrative & Complementary Medicine
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AU Kakutani, R
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Endo, Naoto
TI Rapidly Destructive Arthrosis of Bilateral Humeral Heads Caused by Subchondral Insufficiency Fracture
SO ACTA MEDICA OKAYAMA

LA English
DT Article
DE rapidly destructive arthrosis; differential diagnosis; humeral head replacement; osteoporosis; shoulder joint
ID shoulder
AB The bilateral shoulder pain of an 81-year-old Japanese woman due to falls persisted despite celecoxib treatment, and plain X-rays later showed bilateral collapsed humeral heads. After ruling out osteoarthritis, infectious arthritis, crystal-induced arthritis, neuropathic arthropathy, and osteonecrosis, we diagnosed bilateral shoulder joint rapidly destructive arthrosis (RDA). Lumbar bone mineral density showed very low T-score (-4.1). Primary osteoporosis was observed. Histology of biopsied humeral head indicated the features of fracture healing process: callus formation and osteodasts without empty lacunae. Her history thus included an insufficiency fracture due to severe osteoporosis. Bilateral humeral head replacement was performed; her shoulder joint function improved. This case is extremely rare in that RDA was caused by simultaneous bilateral shoulder joint collapse within a very short time, with minimal or low mechanical stress and severe osteoporosis.
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CR DIEPPE P, 1985, CLIN RHEUM DIS, V11, P367
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PT J
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TI Mid-term results with a neck-preserving femoral stem for total hip arthroplasty
SO HIP INTERNATIONAL
LA English
DT Article
DE Femoral neck preservation; hip; short stem; stem; THA; total hip arthroplasty
ID survival; implants; design
AB Introduction: This prospective study aims to evaluate the mid-term clinical and radiological performance of a new short, neck-preserving femoral stem in total hip arthroplasty (THA). Patients and methods: 178 consecutive patients (190 hips) underwent THA from November 2008 to July 2016. Mean follow-up is 62.4 months. Women make up 41% of the cohort at a mean age of 50 +/- 4 years, with primary hip osteoarthritis as the main complaint. All patients underwent radiological

evaluation using the modified Gruen method, and clinical assessment via the Harris Hip Score (HHS), preoperatively and at 1, 6, 12, 24, 60, 80 and 106 months post-op. Results: A mean HHS increase (from 50 +/- 12 points preoperatively to 96 +/- 4 at 62 months), together with painless articular improvement, was present at 6 months postoperatively indicating early functional recovery. Effective osteointegration and primary stability were present on radiographic analysis, without evidence of stress shielding or stem mal-positioning: subsidence amounting to <1 mm was present in 40% of implants immediately after surgery, with subsequent stabilisation within 6 months in all cases. Metaphyseal trabecular re-orientation in absence of symptomatic cortical hypertrophy or progressive radiolucency indicates physiological load transfer in the proximal femur. Stem-related revision surgery was necessary for 1.05% of all implants due to fracture and infection. No loosening, dislocations or mechanical failures were reported. Conclusions: All patients show excellent functional recovery and clinical outcomes at 62 months, demonstrating the role optimal primary stability and physiological joint reconstruction play in ensuring stable secondary fixation and long-term survival of a short, neck-preserving stem.
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WC Orthopedics
SC Orthopedics
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PT J
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TI Development and Pilot Testing of Multimedia Patient Education Tools for Patients With Knee Osteoarthritis, Osteoporosis, and Rheumatoid Arthritis
SO ARTHRITIS CARE & RESEARCH
LA English
DT Article
ID knowledge questionnaire pkq; quality-of-life; health literacy; entertainment education; randomized-trial; decision aids; responsiveness; validity; association; reliability
AB ObjectiveWe developed and tested multimedia patient education tools (video tools) for patients with knee osteoarthritis (OA), osteoporosis (OP), and rheumatoid arthritis (RA). MethodsWe followed an edutainment model, incorporating educational patient story lines. The goals were designed to make the programs both didactic and entertaining, with navigation and graphic user interfaces as simple as possible. We created both English and Spanish language versions. Once the video tool was finalized, 60 patients, 20 per disease, were shown the tool and interviewed. Disease knowledge was our primary outcome, and decision conflict, disease management, and acceptability were secondary outcomes. ResultsWe observed statistically significant differences in pre- to postintervention knowledge questionnaire scores (before and after viewing the video tool) (OA: P = 0.03, OP: P

= 0.01, and RA: P < 0.0001). Most participants felt they gained clarity on disease duration, symptoms, and the time medication takes to start acting; were encouraged to see their doctor regularly; and were more aware about taking their medications. In terms of acceptability, most patients in all disease groups found the length and amount of information presented in the video tools to be just right, and the presentation to be balanced. In terms of comprehension, all participants provided a favorable evaluation of the video tool; all found the video easy to use, the vocabulary easy to understand, and the materials to be well organized. ConclusionMultimedia tools that incorporate videos may help patients better understand and manage their disease. Patient involvement in the development process is essential to ensure relevant content and usability.
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TC 33
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U2 13
PU WILEY
PI HOBOKEN
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WC Rheumatology
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PT J
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AF Ghazi, Cameron
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TI Social cognitive or learning theory use to improve self-efficacy in

musculoskeletal rehabilitation: A systematic review and meta-analysis
SO PHYSIOTHERAPY THEORY AND PRACTICE
LA English
DT Article
DE Patient education; therapeutic exercise; movement rehabilitation
ID total knee replacement; functional recovery; health behavior; older women; pain; osteoarthritis; limitations; management; exercise; program
AB Objective: To review the rehabilitation research methodological quality and intervention effectiveness of studies that used social cognitive or learning theory principles to improve self-efficacy in patients with orthopedic or musculoskeletal conditions. Design: A systematic literature review and meta-analysis of peer reviewed studies published in English was performed using the OVID and SPORTDiscus databases. Initial search terms were social cognitive theory or social learning theory combined with rehabilitation. Results: From the 25 total studies that contributed to this review, 23 contributed patient outcome information and 20 contributed to effect size determination. Of 1947 total study participants, most (n=1537, 78.9%) were women. Participants were primarily late middle-age (64.8 +/- 17years). Studies included participants with hip or knee osteoarthritis (OA) or who were post-hip or knee arthroplasty (11/25, 44%), post-femur or tibia fracture (6/25, 24%), adults in assisted living or inpatient rehabilitation facilities (2/25, 8%), independent community dwelling older adults (2/25, 8%), college-age recreational athletes post-sports injury (2/25, 8%), older women with osteoporosis risk (1/25, 4%) or middle-aged adults post-traumatic hand injury (1/25, 4%). For the 20 studies that contributed to effect size determination, a large overall mean effect size (Cohen's d=0.98, 95% CI 0.42-1.86) was observed. Conclusions: Studies that used social cognitive or learning theory principles to improve self-efficacy in patients with orthopedic or musculoskeletal conditions generally displayed moderate to large effect sizes supporting this intervention. Sound research methodological quality and low risk of intervention-related injury or other adverse events were also generally observed. Findings suggest that these interventions may also benefit individuals with conditions that have not progressed to end-stage salvage surgery such as younger, more athletically active individuals for knee OA prevention.
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AU Li, GW
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TI Enhancing research publications and advancing scientific writing in health research collaborations: sharing lessons learnt from the trenches
SO JOURNAL OF MULTIDISCIPLINARY HEALTHCARE
LA English
DT Article
DE research publication; scientific writing; health research collaboration
ID randomized controlled-trial; individual patient data; hip osteoarthritis; protocol; biostatistics; osteoporosis; metaanalysis; prevention; adherence; framework
AB Background: Disseminating research protocols, processes, methods or findings via peer-reviewed publications has substantive merits and benefits to various stakeholders. Purpose: In this article, we share strategies to enhance research publication contents (ie, what to write about) and to facilitate scientific writing (ie, how to write) in health research collaborations. Methods: Empirical experience sharing. Results: "lb enhance research publication contents, we encourage identifying appropriate opportunities for publications, publishing protocols ahead of results papers, seeking publications related to methodological issues,

considering justified secondary analyses, and sharing academic process or experience. To advance writing, we suggest setting up scientific writing as a goal, seeking an appropriate mentorship, making full use of scientific meetings and presentations, taking some necessary formal training in areas such as effective communication and time and stress management, and embracing the iterative process of writing. Conclusion: All the strategies we share are dependent upon each other; and they advocate gradual academic accomplishments through study and training in a "success-breeds-success" way. It is expected that the foregoing shared strategies in this paper, together with other previous guidance articles, can assist one with enhancing research publications, and eventually one's academic success in health research collaborations.
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TI Multimodal imaging of undecalcified tissue sections by MALDI MS and μXRF
SO ANALYST
LA English
DT Article
ID mass-spectrometry; biological samples; trace-elements; ion formation; peptides; support; matrix; lipids; plants; brain
AB Matrix-assisted laser desorption/ionisation mass spectrometric imaging (MALDI MSI) is a technique that provides localized information on intact molecules in a sample. Micro X-ray fluorescence (mu XRF) imaging allows the examination of the spatial distribution of elements in a sample without any morphological changes. These methods have already been applied separately to different tissues, organs, plants and bacterial films, but, to the best of our knowledge, they have yet to be coupled in a multimodal analysis. In this proof-of-principle study, we established and tested sample preparation strategies, allowing the multimodal analysis of lipids (sphingomyelin and phosphatidylcholines) and elements relevant to bone structures as calcium, phosphorous and sulphur in the very same sample section of a chicken phalanx without tissue decalcification. The results of the investigation of such parameters as adhesive tapes supporting tissue sections, and the sequence of the imaging experiments are presented. We show specific lipid distributions in skin, cartilage, muscle, nail, and the intact morphology of bone by calcium and phosphorus imaging. A combination of molecular and elemental imaging was achieved, thus, providing now for the first time the possibility of gathering MALDI MSI and mu XRF information from the very same sample without any washing steps omitting therefore the analytical artifacts that inevitably occur in approaches using consecutive tissue sections. The proposed combination can benefit in research studies regarding bone diseases, osteoporosis, osteoarthritis, cartilage failure, bone/tendon distinguishing, where elemental and lipid interaction play an essential role.
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TC 37
Z9 42
U1 4
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PU ROYAL SOC CHEMISTRY
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TI Higher Rates of Operative Delivery and Maternal and Neonatal Complications in Persistent Occiput Posterior Position with a Large Head Circumference: A Retrospective Cohort Study
SO FETAL DIAGNOSIS AND THERAPY
LA English
DT Article
DE Head circumference; Instrumental delivery; Occiput posterior position; Operative delivery; Prolonged second stage of labor
ID anal-sphincter injury; fetal position; labor; risk; association; 2nd-stage
AB Introduction: We investigated whether large head circumference (HC) combined with persistent occiput posterior (OP) position is associated with higher rates of operative delivery and obstetric and neonatal complications than OP deliveries without large HC or in occiput anterior (OA) position. Materials and Methods: Term singleton deliveries in our centers from January 2010 to December 2014, delivered in cephalic OA (n = 41,038) or OP position (n = 1,740), were assessed. We compared delivery modes, maternal and neonatal complications in OA versus OP deliveries, and HC >= 90th centile versus HC <90th centile in persistent OP position. Results: Persistent OP position combined with HC >= 90th centile was associated with higher rates of vacuum extraction and unplanned cesarean delivery than HC <90th centile in OP position (20.1 vs. 17.2%, OR 1.53 [95% CI 0.99-2.36], and 23.4 vs. 9.2%, OR 3.326 [95% CI 2.17-5.11], respectively). Rates of prolonged second stage of labor and neonatal intensive care unit admission were also increased compared to those in either OA position with HC >= 90th centile or OP

position with HC <90th centile. Discussion: Large HC combined with OP position is associated with higher rates of operative delivery and prolonged second stage of labor compared to OP delivery with HC <90th centile. HC might be included with other measures to assess women in labor, as it is associated with fetal outcomes in OP deliveries. (C) 2017 S. Karger AG, Basel
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TI Usefulness of bone microarchitectural and geometric DXA-derived parameters in haemophilic patients
SO HAEMOPHILIA
LA English
DT Article
DE bone mineral density; bone strain; dual energy X-ray absorptiometry; haemophilia; haemophilia joint health score; hip structural analysis; trabecular bone score
ID mineral density; hip fracture; knee osteoarthritis; lumbar spine; score; strength; risk; osteoporosis; strategy; children
AB Introduction Haemophilia is a recessive X-linked inherited bleeding disorder, whose typical symptom is spontaneous intra-articular haemorrhage leading to joint damage, which can be quantified by the Haemophilia Joint Health Score (HJHS). Arthropathy and other characteristics of haemophilic patients may reduce bone mineral density (BMD), increasing the risk for fragility fractures, which also may occur due to bone quality impairment. Aim Methods To evaluate bone quantity by BMD and bone quality by Trabecular Bone Score (TBS), bone strain (BS) and hip structural analysis (HSA) in a haemophilic population, and to relate these parameters to general and specific risk factors for osteoporosis and to HJHS. Seventy haemophilic patients >= 18 years were enrolled. Densitometric derived lumbar spine and femoral BMD with TBS, BS and HSA were performed. Data regarding risk factors for osteoporosis, presence of arthroprosthesis or arthrodesis were collected, and HJHS was calculated. A Z-score <=-2.0 defined a low bone mass. Results Conclusions Overall, a reduced bone mass was present in 52 patients at the femur and in 38 at the lumbar spine. Lumbar spine BMD, TBS and BS did not correlate with HJHS. HSA bone geometric parameters correlated negatively with HJHS. BMD and HSA correlated with some risk factors for osteoporosis, namely HIV and its therapy, hepatitis C and smoking. Haemophilic patients showed a reduced

BMD at lumbar spine and/or femur. Femoral bone density and geometry correlated with HJHS. The microarchitecture of the trabecular vertebral bone seemed to be not influenced by the haemophilic joint damage.
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NR 39
TC 26
Z9 29
U1 0
U2 0
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1351-8216
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PT J
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TI Bone Health and Natural Products-An Insight
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE phytochemicals; osteoporosis; bone disorders; osteoclast; osteoblast
ID stimulates osteoblast differentiation; ovariectomy-induced osteoporosis; nf-kappa-b; postmenopausal osteoporosis; osteogenic differentiation; signaling pathway; ugonin k; in-vivo; osteoarthritis; cells
AB Bone metabolism involves a complex balance between matrix deposition, mineralization, and resorption. Numerous evidences have revealed that dietary components and phytoconstituents can influence these processes, through inhibition of bone resorption, thus exhibiting beneficial effects on the skeleton. Various traditional herbal formulae in ayurvedic and Chinese medicine have shown demonstrable benefits in pharmacological models of osteoporosis. The present review discusses normal bone metabolism and disorders caused by bone disruption, with particular reference to osteoporosis and current therapeutic treatment. Furthermore the effects of constituents from natural products on bone tissue are explained, with relevant evidences of efficacy in various experimental

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NR 67
TC 67
Z9 74
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TI Obesity, Metabolic Syndrome, and Musculoskeletal Disease: Common Inflammatory Pathways Suggest a Central Role for Loss of Muscle Integrity
SO FRONTIERS IN PHYSIOLOGY
LA English
DT Review
DE joint diseases; muscle; bone; tendon; NFkB; MAPK
ID diet-induced obesity; glycation end-products; high-fat diet; necrosis-factor-alpha; skeletal-muscle; gut microbiota; adipose-tissue; knee osteoarthritis; sarcopenic obesity; oxidative stress
AB Inflammation can arise in response to a variety of stimuli, including infectious agents, tissue injury, autoimmune diseases, and obesity. Some of these responses are acute and resolve, while others become chronic and exert a sustained impact on the host, systemically, or locally. Obesity is now recognized as a chronic low-grade, systemic inflammatory state that predisposes to other chronic conditions including metabolic syndrome (MetS). Although obesity has received considerable attention regarding its pathophysiological link to chronic cardiovascular conditions and type 2 diabetes, the musculoskeletal (MSK) complications (i.e., muscle, bone, tendon, and joints) that result from obesity-associated metabolic disturbances are less frequently interrogated. As musculoskeletal diseases can lead to the worsening of MetS, this underscores the imminent need to understand the cause and effect relations between the two, and the convergence between inflammatory pathways that contribute to MSK damage. Muscle mass is a key predictor of longevity in older adults, and obesity-induced sarcopenia is a significant risk factor for adverse health outcomes. Muscle is highly plastic, undergoes regular remodeling, and is responsible for the majority of total body glucose utilization, which when impaired leads to insulin resistance. Furthermore, impaired muscle integrity, defined as persistent muscle loss, intramuscular lipid accumulation, or connective tissue deposition, is a hallmark of metabolic dysfunction. In fact, many common inflammatory pathways have been implicated in the pathogenesis of the interrelated tissues of the musculoskeletal system (e.g., tendinopathy, osteoporosis, and osteoarthritis). Despite these similarities, these diseases are rarely evaluated in a comprehensive manner. The aim of this review is to summarize the common pathways that lead to musculoskeletal damage and disease that result from and contribute to MetS. We propose the overarching hypothesis that there is a central role for muscle damage with chronic exposure to an obesity-inducing diet. The inflammatory consequence

of diet and muscle dysregulation can result in dysregulated tissue repair and an imbalance toward negative adaptation, resulting in regulatory failure and other musculoskeletal tissue damage. The commonalities support the conclusion that musculoskeletal pathology with MetS should be evaluated in a comprehensive and integrated manner to understand risk for other MSK-related conditions. Implications for conservative management strategies to regulate MetS are discussed, as are future research opportunities.
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TI The contribution of thoracic vertebral deformity and arthropathy to trunk pain in patients with chronic obstructive pulmonary disease (COPD)
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DT Article
DE Pain; Chronic obstructive pulmonary disease; Vertebral deformity; Arthropathy; Thoracic vertebrae; Osteoporosis
ID back-pain; physical-activity; ct; osteoarthritis; epidemiology; osteoporosis; mortality; fracture; people; cancer
AB Background: Pain, commonly localized to the trunk in individuals with COPD, may be due to osteoporosis-related vertebral deformity and chest wall hyper-expansion causing misalignment of joints between the ribs and vertebrae. The purpose of this study was to determine if thoracic vertebral deformity and arthropathy were independent contributors to trunk pain in COPD patients compared to people with a significant smoking history. Method: Participants completed the Brief Pain Inventory (BPI) on the same day as chest CT scans and spirometry. Current and ex-smokers were separated into COPD (n=91) or non-COPD (n=80) groups based on spirometry. Subsequently, CT images were assessed for thoracic vertebral deformity, bone attenuation values, and arthropathy

of thoracic vertebral joints. Results: The trunk area was the most common pain location in both COPD and non-COPD groups. Thoracic vertebral deformity and costotransverse joint arthropathy were independent contributors to trunk pain in COPD patients (adjusted OR=3.55 and 1.30, respectively) whereas alcohol consumption contributed to trunk pain in the non-COPD group (adjusted OR=0.35 in occasional alcohol drinkers; 0.08 in non-alcohol drinkers). The spinal deformity index and the number of narrowed disc spaces were significantly positively related to the BPI intensity, interference, and total scores significantly in COPD patients. Conclusion: Trunk pain, at least in part, is caused by thoracic vertebral deformity, and costotransverse and intervertebral arthropathy in patients living with COPD. The results of this study provided the foundation for the management of pain, which requires further exploration.
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TI Mesenchymal Stem Cells in the Musculoskeletal System: From Animal Models to Human Tissue Regeneration?
SO STEM CELL REVIEWS AND REPORTS

LA English
DT Review
DE Musculoskeletal system; Mesenchymal stem cells; Bone; Muscles; Synovium; Regenerative medicine; Osteoarthritis; Osteoporosis
ID skeletal-muscle regeneration; side population cells; bone-marrow; satellite cells; stromal cells; intraarticular injection; progenitor cells; clinical-trial; joint disease; in-vivo
AB The musculoskeletal system includes tissues that have remarkable regenerative capabilities. Bone and muscle sustain micro-damage throughout the lifetime, yet they continue to provide the body with the support that is needed for everyday activities. Our current understanding is that the regenerative capacity of the musculoskeletal system can be attributed to the mesenchymal stem/ stromal cells (MSCs) that reside within its different anatomical compartments. These MSCs can replenish various tissues with progenitor cells to form functional cells, such as osteoblasts, chondrocytes, myocytes, and others. However, with aging and in certain disorders of the musculoskeletal system such as osteoarthritis or osteoporosis, this regenerative capacity of MSCs appears to be lost or diverted for the production of other non-functional cell types, such as adipocytes and fibroblasts. In this review, we shed light on the tissue sources and subpopulations of MSCs in the musculoskeletal system that have been identified in animal models, discuss the mechanisms of their anti-inflammatory action as a prerequisite for their tissue regeneration and their current applications in regenerative medicine. While providing up-to-date evidence of the role of MSCs in different musculoskeletal pathologies, in particular in osteoporosis and osteoarthritis, we share some thoughts on their potential as diagnostic markers in musculoskeletal health and disease.
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TI Cost Effectiveness of Intra-Articular Hyaluronic Acid and Disease-Modifying Drugs in Knee Osteoarthritis
SO PHARMACOECONOMICS
LA English
DT Review

ID alongside clinical-trials; european-society; economic-aspects; glucosamine sulfate; hip osteoarthritis; african-americans; symptomatic knee; prevalence; osteoporosis; classification
AB Background The place of disease-modifying osteoarthritis drugs (DMOADs) and intra-articular hyaluronic acid (IAHA) in the therapeutic arsenal for knee osteoarthritis (OA) remains uncertain. Indeed, these treatments have demonstrated symptomatic efficacy but no efficacy for disease modification. Objective This report reviews the cost effectiveness of IAHA and DMOADs used in the treatment of knee OA. Methods A systematic literature search of the MEDLINE, Scopus, EMBASE and Cochrane databases was performed independently by two rheumatologists who used the same predefined eligibility criteria to identify relevant articles. Papers without abstracts and in languages other than English or French were excluded. Extracted costs were annualised and converted to 2015 euros (sic) using the Consumer Price Index of the relevant countries and the 2013 Purchasing Power Parities between these countries and the European Union average. Results A total of 95 abstracts were selected, and 13 articles were considered for the review: nine articles on IAHA and four on DMOADs. Only one article directly compared different IAHA compounds. Articles showed substantial heterogeneity in methodological approaches. The incremental cost-effectiveness ratios (ICERs) ranged from (sic)4000 to (sic)57,550 and from (sic)240 to (sic)53,225 per quality-adjusted life-year (QALY) gained for DMOADs and IAHA, respectively. Conclusions This review highlights substantial heterogeneity between studies, ranging from a cost saving (or dominating) position to very high ICERs, far above the acceptability threshold of (sic)50,000/QALY. Additional research is needed to determine reliable and robust ICER estimates for knee OA therapies.
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TI Age-Related Changes in Femoral Head Trabecular Microarchitecture
SO AGING AND DISEASE
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DT Article
DE micro computed tomography (mu-CT); osteoporosis; aging; microarchitecture; trabecular bone; femoral head
ID bone-mineral density; postmenopausal women; cancellous bone; structural basis; iliac crest; x-ray; mechanical-property; hip osteoarthritis; osteoporosis; fracture
AB Osteoporosis is a prevalent bone condition, characterised by low bone mineral density and increased fracture risk. Currently, the gold standard for identifying osteoporosis and increased fracture risk is through quantification of bone mineral density using dual energy X-ray absorption. However, many studies have shown that bone strength, and consequently the probability of fracture, is a combination of both bone mass and bone 'quality' (architecture and material chemistry). Although the microarchitecture of both non-fracture and osteoporotic bone has been previously investigated, many of the osteoporotic studies are constrained by factors such as limited sample number, use of ovariectomised animal models, and lack of male and female discrimination. This study reports significant differences in bone quality with respect to the microarchitecture between fractured and non-fractured human femur specimens. Micro-computed tomography was utilised to investigate the microarchitecture of femoral head trabecular bone from a relatively large cohort of non-fracture and fracture human donors. Various microarchitectural parameters have been determined for both groups, providing an understanding of the differences between fracture and non -fracture material. The microarchitecture of non-fracture and fracture bone tissue is shown to be significantly different for many parameters. Differences between sexes also exist, suggesting differences in remodelling between males and females in the fracture group. The results from this study will, in the future, be applied to develop a fracture model which encompasses bone density, architecture and material chemical properties for both female and male tissues.
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TI Oleanolic acid exerts bone protective effects in ovariectomized mice by inhibiting osteoclastogenesis
SO JOURNAL OF PHARMACOLOGICAL SCIENCES
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DT Article
DE Postmenopausal osteoporosis (POP); Oleanolic acid (OA); Ovariectomy (OVX); Osteoclastogenesis; Bone resorption
ID differentiation; activation; therapy
AB Postmenopausal osteoporosis (POP) is quite prevalent and many new drugs are under development to obtain better therapeutic outcomes. Oleanolic acid (OA) has been reported to prevent bone loss in ovariectomized (OVX) rats by stimulating osteoblastogenesis. One previous study has demonstrated that acetate of OA suppressed lipopolysaccharides (LPS)-induced bone loss in mice. However, the role of OA in the receptor activator of nuclear factor kappa-B ligand (RANKL)-mediated osteoclastogenesis is still not elucidated. Here we show that OA dose-dependently inhibits RANKL-mediated osteoclastogenesis and the formation of functional osteoclasts without impairing the viability and osteoclastic potential in bone marrow macrophages (BMMs). Moreover, OA administration attenuates bone loss in OVX mice by inhibiting osteoclast's densities. Mechanistically, OA does not affect RANKL-induced activation of the NF-kappa B, JNK, p38, ERK and Alt pathways, but inhibits the expression of the nuclear factor of activated T-cells c1(NFATc1) and c-Fos. Moreover, OA significantly suppresses the expression of RANKL-activated

osteoclast genes encoding matrix metalloproteinase 9 (MMP9), Cathepsin K(Ctsk), tartrate-resistant acid phosphatase (TRAP) and carbonic anhydrase ll (Car2). This work has elucidated the molecular mechanism of OA in RANKL-mediated osteoclastogenesis and revealed the promising potential of OA to be further developed as a new drug to prevent and treat POP. (C) 2018 The Authors. Production and hosting by Elsevier B.V. on behalf of Japanese Pharmacological Society.
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NR 40
TC 35
Z9 39
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WC Pharmacology & Pharmacy
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PT J
AU Mahmood, H
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Espino, DM
AF Mahmood, Humaira
Shepherd, Duncan E. T.
Espino, Daniel M.
TI Surface damage of bovine articular cartilage-off-bone: the effect of variations in underlying substrate and frequency
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Articular cartilage; Bone mineral density; Damage; Frequency; Mechanical loading; Osteoarthritis
ID radiographic knee osteoarthritis; mineral density; subchondral bone; unconfined compression; osteoporosis; women; joint; hand; indentation; association
AB BackgroundChanges in bone mineral density have been implicated with the onset of osteoarthritis, but its role in inducing failure of articular cartilage mechanically is unclear. This study aimed to determine the effect of substrate density, as the underlying bone, on the surface damage of cartilage-off-bone, at frequencies associated with gait, and above.MethodsBovine articular cartilage samples were tested off-bone to assess induced damage with an indenter under a

compressive sinusoidal load range of 5-50N at frequencies of 1, 10 and 50Hz, corresponding to normal and above normal gait respectively, for up to 10,000cycles. Cartilage samples were tested on four underlying substrates with densities of 0.1556, 0.3222, 0.5667 and 0.6000g/cm(3). India ink was applied to identify damage as cracks, measured across their length using ImageJ software. Linear regression was performed to identify if statistical significance existed between substrate density, and surface damage of articular cartilage-off-bone, at all three frequencies investigated (p<0.05).ResultsSurface damage significantly increased (p<0.05) with substrate density at 10Hz of applied frequency. Crack length at this frequency reached the maximum of 10.959.12mm (mean +/- standard deviation), across all four substrates tested. Frequencies applied at 1 and 50Hz failed to show a significant increase (p>0.05) in surface damage with an increase in substrate density, at which the maximum mean crack length were 3.01 +/- 3.41mm and 5.65 +/- 6.54mm, respectively. Crack formation at all frequencies tended to form at the periphery of the cartilage specimen, with multiple straight-line cracking observed at 10Hz, in comparison to single straight-line configurations produced at 1 and 50Hz.Conclusions p id= Par4 The effect of substrate density on the surface damage of articular cartilage-off-bone is multi-factorial, with an above-normal gait frequency. At 1Hz cartilage damage is not associated with substrate density, however at 10Hz, it is. This study has implications on the effects of the factors that contribute to the onset of osteoarthritis.
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NR 61
TC 10
Z9 10
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U2 6
PU BMC
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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PT J
AU Woisetschläger, M
Spångeus, A
AF Woisetschlager, Mischa
Spangeus, Anna
TI Model for improved correlation of BMD values between abdominal routine Dual energy CT data and DXA scans
SO EUROPEAN JOURNAL OF RADIOLOGY
LA English
DT Article
DE Osteoporosis; Bone mass density; Dual-energy CT; DXA; Osteoarthritis of the spine; Aortic calcium score
ID computed-tomography; screening tool; osteoporosis; density; osteoarthritis; colonography; fragility; system
AB Background: Osteoporosis is a common but underdiagnosed and undertreated disease causing severe morbidity and economic burden. The gold standard for detection of osteoporosis is DXA (dual energy x-ray absorptiometry), which is a dedicated examination for osteoporosis. Dual energy CT (DECT) examinations are increasingly used in daily routine for a wide variety of diagnoses. In the present study, we wanted to examine whether vBMD (volume bone mass density) could be evaluated as a side product in non-contrast as well as contrast phases as well as to evaluate a correction model taking known shortcomings for DXA into account. Methods: A total of 20 patients, i.e. 79 vertebrae (one excluded due to vertebral fracture), mean age 71 years (range 43-85) with a mean BMI (body mass index) of 26 (range 17-33) were examined with both abdominal/pelvic DECT as well as DXA. Furthermore, aortic calcium was measured as well as the presence of osteoarthritis of the spine (OAS) and osteoarthritis in facet joints (OAF) with a 5-grade scaling system. Results: A significant correlation was found between DXA BMD and vBMD from DECT with no contrast (WNC) ($r=0.424$, $p=0.001$), and with venous contrast (WVC) ($r=0.402$, $p < 0.001$), but no significant correlation was found with arterial contrast (WAC). Using multivariate linear regression with DXA BMD as dependent, two models were created combining DECT WNC, aortic calciumscore (ACS), OAS and BMI yielding an R-2 = 0.616 (model 1) and replacement of WNC to WVC a R-2 = 0.612 (model 2). The Pearson correlation between DXA and predictive DXA BMD value of model 1 was $r=0.785$ ($p < 0.001$) and model 2 $r=0.782$ ($p < 0.001$). Conclusion: There is a correlation between DXA BMD and DECT in non-contrast and venous contrast scans but not in arterial scans. The correlation is further improved by quantifying the degree of different confounding factors (osteoarthritis

of the spine, body mass index and aortic calcium score) and taking these into account in an explanatory model. Future software solutions with DECT data as input data might be able to automatically measure the BMD in the trabecular bone as well as measuring the confounding factors automatically in order to obtain spinal DXA comparable BMD values.
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10.1016/j.jacr.2015.04.018
NR 22
TC 8
Z9 11
U1 0
U2 4
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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JI Eur. J. Radiol.
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WC Radiology, Nuclear Medicine & Medical Imaging
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PT J
AU Yu, YL
Shen, XK
Luo, Z
Hu, Y
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AF Yu, Yonglin
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TI Osteogenesis potential of different titania nanotubes in oxidative stress microenvironment
SO BIOMATERIALS
LA English
DT Article
DE TiO2 nanotubes; Oxidative stress; ITG alpha 5 beta 1; Wnt signals; Osteogenesis
ID osteoblast differentiation; tio2 nanotubes; bone-formation; stem-cells; growth; alpha(5)beta(1); proliferation; improvement; topography; mechanisms
AB Oxidative stress is commonly existed in bone degenerative disease (osteoarthritis, osteoporosis etc.) and some antioxidants had great potential to enhance osteogenesis. In this study, we aim to investigate the anti-oxidative properties of various TiO2 nanotubes (TNTs) so to screen the desirable size for improved osteogenesis and reveal the underlying molecular mechanism in vitro. Comparing cellular behaviors under normal and oxidative stress conditions, an interesting conclusion was obtained. In normal microenvironment, small TNTs were beneficial for adhesion and proliferation of osteoblasts, but large TNTs greatly increased osteogenic differentiation. However, after H2O2 (300 mu M) treatment (mimicking oxidative stress), only large TNTs samples demonstrated superior cellular behaviors of increased osteoblasts' adhesion, survival and differentiation when comparing with those of native titanium (control). Molecular results revealed that oxidative stress resistance of large nanotubes was closely related to the high expression of integrin alpha 5 beta 1 (ITG alpha 5 beta 1), which further up-regulated the production of anti-apoptotic proteins (p-FAK, p-Akt, p-FoxO3a and Bcl2) and down-regulated the expression of pro-apoptotic protein (Bax). Moreover, we found that Wnt signals (Wnt3a, Wnt5a, Lrp5, Lrp6 and beta-catenin) played an important role in promoting osteogenic differentiation of osteoblasts under oxidative condition. (C) 2018 Elsevier Ltd. All rights reserved.
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PT J
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TI Inappropriate claims from non-equivalent medications in osteoarthritis: a position paper endorsed by the European Society for Clinical and Economic

Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Chondroitin sulfate; Glucosamine; Symptomatic slow-acting drugs for osteoarthritis; Knee; Osteoarthritis
ID crystalline glucosamine sulfate; knee osteoarthritis; double-blind; avocado/soybean unsaponifiables; chondroitin sulfate; symptomatic efficacy; hip osteoarthritis; global burden; task-force; placebo
AB Osteoarthritis (OA) is a progressive joint disease, that occurs frequently in the aging population and is a major cause of disability worldwide. Both glucosamine and chondroitin are biologically active molecules that are substrates for proteoglycan, an essential component of the cartilage matrix. Evidence supports the use of glucosamine and chondroitin as symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) with impact on OA symptoms and disease-modifying effects in the long term. Glucosamine and chondroitin are administered in exogenous form as a sulfate salt and multiple formulations of these agents are available, both as prescription-grade products and nutritional supplements. However, while all preparations may claim to deliver a therapeutic level of glucosamine or chondroitin not all are supported by clinical evidence. Only patented crystalline glucosamine sulfate (pCGS) is shown to deliver consistently high glucosamine bioavailability and plasma concentration in humans, which corresponds to demonstrated clinical efficacy. Similarly, clinical evidence supports only the pharmaceutical-grade chondroitin sulfate. The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) advocates, through careful consideration of the evidence base, that judicious choice of glucosamine and chondroitin formulation is essential to maximize clinical benefit, patient adherence and satisfaction with treatment. In future, the ESCEO recommends that complex molecules with biological activity such as pCGS may be treated as "biosimilars" akin to the European Medicines Agency guidance on biological medicinal products. It seems likely that for all other complex molecules classed as SYSADOAs, the recommendation to use only formulations clearly supported by the evidence-base should apply.
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TI Unassisted quiet standing and walking after crutch usage in patients with total hip replacements: Does crutch length matter?
SO GAIT & POSTURE
LA English
DT Article
DE Unaided gait; Static stability; Hip arthroplasty; Crutch length setup; Rehabilitation
ID ground reaction forces; spatiotemporal gait parameters; exercise program; older; people; speed; aids; osteoarthritis; arthroplasty; variability
AB Background: Crutch use is prescribed early in the rehabilitation process following total hip replacement (THR) surgery to improve safety and promote return to active living. Research question: Purpose of this study was to understand mid-term effects of crutch length setup on quiet standing and walking two months post-op when crutch use was no longer required. Methods: Thirty patients were evaluated 2 months post-surgery when they had been walking without crutch for a month. The patients had previously been assigned randomly to elbow flexed (EF) or elbow extended (EE) crutch set-ups and evaluated 3 days post-surgery. Quiet standing stability was assessed with participants standing in a comfortable position with each foot on separated force platforms, facing forward for 10 s. In addition, participants walked on the laboratory path, instrumented with motion tracking system and force platforms. For the quiet standing trial, centre of pressure measure, acromial height and lower limbs load bearing symmetry were evaluated. For the walking trial, spatiotemporal and ground reaction force (GRF) parameters were evaluated together with side symmetry indices. Results: Results showed no significant differences in any standing trial variables between groups. For walking, GRF parameters and symmetry indices were similar for both groups. However, increased base of support width, reduced self-selected walking speed and stride length were found for the EF group. Significance: This study showed that crutch set-up influenced gait after patients started to walk unassisted. Patients that previously used crutch adjusted according to the EE setup, demonstrated a more efficient gait with higher self-selected speed and longer and narrower stride. Clinicians may use these results for a proper crutch height adjustment, which improves walking and, in turn, functional recovery in post THR patients.
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NR 40
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Z9 7
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TI Fetal rotation during vacuum extractions for prolonged labor: a prospective cohort study
SO ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA
LA English
DT Article
DE delivery; fetal rotation; prolonged labor; ultrasound; vacuum extraction
ID persistent occiput posterior; assisted vaginal delivery; head position; intrapartum sonography; instrumental delivery; cesarean delivery; 2nd-stage; ultrasound; outcm; forceps
AB IntroductionThe aim of the study was to investigate fetal head rotation during vacuum extraction. Material and methodsWe conducted a prospective cohort study from November 2013 to July 2016 in seven European hospitals. Fetal head position was determined with transabdominal or transperineal ultrasound and categorized

as occiput anterior (OA), occiput transverse (OT) or occiput posterior (OP) position. Main outcome was the proportion of fetuses rotating during vacuum extraction. Secondary outcomes were conversion of delivery method, duration of vacuum extraction, umbilical artery pH <7.10 and agreement between clinical and ultrasound assessments. ResultsThe study population comprised 165 women. During vacuum extraction 117/119 (98%) remained in OA and two fetuses rotated to OP position. Rotation from OT to OA position occurred in 14/19 (74%) and to OP position in 5/19 (26%). Rotation from OP to OA position occurred in 15/25 (60%), and 10/25 (40%) fetuses remained in OP position. Delivery information was missing in two cases. The conversion rate from vacuum extraction to cesarean section or forceps was 10% in the OA group vs. 23% in the non-OA group; p<0.05. The estimated duration of vacuum extraction was significantly shorter in OA fetuses, 7min vs. 10min (log rank test p<0.01). There was no significant difference in umbilical artery pH <7.10 between OA and non-OA position. Cohens Kappa of agreement between clinical and ultrasound assessments was 0.42 (95% CI 0.26-0.57). ConclusionMost fetuses in OP or OT positions rotated to OA position during vacuum extraction, but the proportion of failed vacuum extractions remained high.
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TI Nonstandard Lumbar Region in Predicting Fracture Risk
SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE Bone mineral density; femoral neck; fracture risk prediction; lumbar spine; osteoporosis
ID bone-mineral density; osteoporotic fractures; multiple sites; femoral-neck; spine bmd; women; men; frax; hip; osteoarthritis
AB Femoral neck (FN) bone mineral density (BMD) is the most commonly used skeletal site to estimate fracture risk. The role of lumbar spine (LS) BMD in fracture risk prediction is less clear due to osteophytes that spuriously increase LS BMD, particularly at lower levels. The aim of this study was to compare fracture predictive ability of upper L1-L2 BMD with standard L2-L4 BMD and assess whether the addition of either LS site could improve fracture prediction over FN BMD. This study comprised a prospective cohort of 3016 women and men over 60 yr from the Dubbo Osteoporosis Epidemiology Study followed up for occurrence of minimal trauma fractures from 1989 to 2014. Dual-energy X-ray absorptiometry was used to measure BMD at L1-L2, L2-L4, and FN at baseline. Fracture risks were estimated using Cox proportional hazards models separately for each site. Predictive performances were compared using receiver operating characteristic curve analyses. There were 565 women and 179 men with a minimal trauma fracture during a mean of 11 +/- 7 yr. L1-L2 BMD T-score was significantly lower than L2-L4 T-score in both genders ($p < 0.0001$). L1-L2 and L2-L4 BMD models had a similar fracture predictive ability. LS BMD was better than FN BMD in predicting vertebral fracture risk in women [area under the curve 0.73 (95% confidence interval, 0.68-0.79) vs 0.68 (95% confidence interval, 0.62-0.74), but FN was superior for hip fractures prediction in both women and men. The addition of L1-L2 or L2-L4 to FN BMD in women increased overall and vertebral predictive power compared with FN BMD alone by 1% and 4%, respectively ($p < 0.05$). In an elderly population, L1-L2 is as good as but not better than L2-L4 site in predicting fracture risk. The addition of LS BMD to FN BMD provided a modest additional benefit in overall fracture risk. Further studies in individuals with spinal degenerative disease are needed.
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TI Vitamin D Receptor in Muscle Atrophy of Elderly Patients: A Key Element of Osteoporosis-Sarcopenia Connection
SO AGING AND DISEASE
LA English
DT Article
DE Vitamin d receptor; polymorphisms; sarcopenia; osteoporosis; osteoarthritis; aging
ID bone-mineral density; cdx-2 polymorphism; satellite cells; gene; osteoarthritis; association; mechanisms; expression; genotype; fracture
AB In this study, we investigated the relationship between sarcopenia (evaluated in term of fibers atrophy), vitamin d receptor protein expression and TaqI/Cdx2/FokI VDR genotypes in an Italian cohort of osteoporosis(n=44) and osteoarthritis (n=55) patients. Muscle biopsies were fixed and investigated by both immunohistochemistry (vitamin d receptor expression) and transmission electron microscopy (satellite stem cells niches). Vitamin d receptor polymorphisms were studied on DNA extracted from muscle paraffin sections. For the first time, we reported that aging differently affects the VDR activation in OA and OP patients. In particular, while in OP patients we observed a significant reduction of VDR positive myonuclei with age, no "age effect" was observed in OA patients. The frequent activation of VDR could explain the lower number of atrophic fiber that we observed in OA patients respect to OP. From genetic point of view, we showed a putative association among polymorphisms FokI and Cdx2 of VDR gene, vitamin d receptor activation and the occurrence of sarcopenia. Altogether these data open new prospective for the prevention and cure of age-related muscle disorders.
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PU INT SOC AGING & DISEASE
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PT J
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AF Runge, William O.
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TI Bone changes after short-term whole body vibration are confined to cancellous bone
SO JOURNAL OF MUSCULOSKELETAL & NEURONAL INTERACTIONS
LA English
DT Article
DE Vibration; Osteoporosis; Osteoarthritis; Biomechanics; Rats
ID postmenopausal women; mechanical signals; muscle strength; mineral density; frequency; osteoarthritis; quality; rat; identification; degeneration
AB Objective: This study assessed femur properties in 80 adult female rats exposed to a range of whole body vibration amplitudes at 45 Hz over five weeks. Our hypothesis was that an optimal amplitude for whole body vibration would be apparent and would result in increased bone strength. Methods: Animals were treated in five amplitude groups (0 g. 0.15 g, 0.3 g, 0.6 g, and 1.2 g peak), for 15 minutes per day, five days per week, for five weeks. Femur strength was assessed via: (1) three-point bending of the shaft, (2) cantilever bending of the neck, and (3) indentation of distal cancellous bone. Femoral bone mineral density, plasma prostaglandin E2 (PGE(2)) concentrations, cartilage thickness, and histopathologic properties were measured. Results: Vibration doubled (P=0.039) cancellous bone stiffness in the 0.6 g and 1.2 g groups and induced a 74% increase in PGE(2) concentrations (P=0.007). However, femoral densitometry and strength of the neck and shaft were unchanged and the cancellous bone indentation strength did not differ statistically (P=0.084). Cartilage thickness of vibrated groups at the medial condyle did not increase significantly (P=0.142) and the histopathologic grade did not change. There was no definitive optimal vibration amplitude. Conclusion: The benefits of vibration therapy over five weeks were confined to cancellous bone.
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TI Flavopiridol Protects Bone Tissue by Attenuating RANKL Induced Osteoclast Formation
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE flavopiridol; CDK9; osteoclast; bone resorption; NF-kappa B
ID nf-kappa-b; inducible gene-expression; transcriptional elongation; signaling pathway; p-tefb; inhibition; resorption; cartilage; osteoarthritis; osteoporosis
AB Bone resorption and homeostasis is carried out by osteoclasts, whose differentiation and activity are regulated by the RANK/RANKL axis. Our previous studies using a mouse model of joint injury show that joint trauma induces local inflammation followed by bone remodeling. The transcription factor cyclin-dependent kinase 9 (CDK9) is the major regulator of inflammation, as CDK9 inhibitor flavopiridol effectively suppress injury-induced inflammatory response. The objective of this study was to investigate the underlying mechanism through which flavopiridol regulates bone resorption. The effects of CDK9 inhibition, by the specific-inhibitor flavopiridol, on bone resorption were determined in vivo using two distinct and clinically relevant bone remodeling models. The first model

involved titanium particle-induced acute osteolysis, and the second model was ovariectomy-induced chronic osteoporosis. The effects and mechanism of CDK9 inhibition on osteoclastogenesis were examined using in vitro culture of bone marrow macrophages (BMMs). Our results indicated that flavopiridol potently suppressed bone resorption in both in vivo bone-remodeling models. In addition, CDK9 inhibition suppressed in vitro osteoclastogenesis of BMM and reduced their expression of osteoclast-specific genes. Finally, we determined that flavopiridol suppressed RANKL signaling pathway via inhibition of p65 phosphorylation and nuclear translocation of NF-kappa B. Summary, CDK9 is a potential therapeutic target to prevent osteolysis and osteoporosis by flavopiridol treatment.
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TI Kiwi omnicup handheld versus Mityvac M-style conventional vacuum system: a retrospective observational study
SO JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
LA English
DT Article
DE Conventional vacuum system; hand-held vacuum system; Kiwi omnicup; M-style Mityvac cup; vacuum assisted delivery
ID randomized controlled-trial; postpartum hemorrhage; extraction; delivery; cup
AB Introduction: To improve the choice of vacuum-assisted delivery (VAD) system, we compared the outcomes of Kiwi handheld system and Mityvac M-style conventional system (both use disposable plastic cups).Materials and methods: Retrospective observational study with data collection from electronic medical records. The study was conducted at a tertiary medical center, with approximately 7000 deliveries annually. Categorical and continuous variables were analyzed using chi-square test and t-test, respectively. p value<.05 was considered significant. The main outcomes assessed were the overall failure rate of each system, failure rates for occipito-anterior (OA) versus occipito-transverse/occipito-anterior (OT/OP) positions, +1 versus +2 fetal stations, and early maternal/neonatal outcomes.Results: During a 10-month period, there were 507 (8.4%) attempted VADs, 36 failed (7.1%), and eight (1.5%) converted to cesarean section. Of these, 364 were Kiwi-assisted and 143 Mityvac-assisted. Background characteristics were similar. The handheld system had more failures overall (9.6 versus 0.7%), at OA (7.6 versus 0.9%), and non-OA positions (17.3% versus none), at +1 (13.25 versus 0.96%) and at +2/3 stations (6.1% versus none), than the conventional system did, respectively. There was a higher rate of early post-partum hemorrhage (15.3 versus

7.4%) in the conventional group. Both systems had similar rates of third/fourth degree perineal tears, shoulder dystocia and adverse neonatal outcomes.Conclusions: Our results suggest more failures with Kiwi compared to Mityvac, overall and at any fetal position/station, without a significant difference in adverse outcome profile.
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PT J
AU Chen, CH
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Kuo, YJ
AF Chen, Chia-Hsien
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TI Sintered dicalcium pyrophosphate treatment attenuates estrogen deficiency-associated disc degeneration in ovariectomized rats
SO DRUG DESIGN DEVELOPMENT AND THERAPY
LA English
DT Article
DE sintered dicalcium pyrophosphate; ovariectomy; disc degeneration; matrix metalloprotease; inflammation
ID knee osteoarthritis; subchondral bone; articular-cartilage; osteoporosis; alendronate; osteoclast; expression; cells; model; osteopenia
AB Background: Estrogen deficiency is associated with musculoskeletal disorders. Sintered dicalcium pyrophosphate (SDCP) is a novel antiosteoporotic agent. In this

study, we examined its use for restoration of bone quality and attenuation of disc degeneration in ovariectomy rats. Methods: Sixty female Sprague Dawley rats were randomly divided into 3 groups, namely sham group undergoing sham surgery, ovariectomy (OVX) group receiving an equivalent volume of isotonic sodium chloride solution, and OVX/SDCP group orally administered with 0.25 mg/mL SDCP. Animals were sacrificed at 3 and 6 months post ovariectomy and lumbar vertebrae and intervertebral discs were harvested. Bone mineral density, micro-computed tomography analysis, and biomechanical testing were performed to assess bone quality. Histological analysis with hematoxylin and eosin, Alcian blue, and Masson's trichrome stain were conducted to determine disc degeneration. Immunohistochemistry and real-time PCR were carried out to measure the expressions of aggrecan, type I collagen, type II collagen, and MMP-1, MMP-3, and MMP-13. Results: SDCP improved bone quality as observed by the results of increased bone mineral density and stiffness in OVX rats. The improvement in disc degeneration induced by estrogen withdrawal was associated with reduced gene expressions of MMPs and increased production of collagen type II. Conclusion: SDCP prevents osteoporosis and meliorates disc degeneration in OVX rats. It represents a favorable therapeutic agent for osteoporotic and osteoarthritic conditions in clinical practice.
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AF Whitney, Daniel G.
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TI Noncommunicable disease and multimorbidity in young adults with cerebral palsy
SO CLINICAL EPIDEMIOLOGY
LA English
DT Article
DE cerebral palsy; noncommunicable disease; multimorbidity; osteoporosis; osteoarthritis; cardiovascular disease; diabetes; pulmonary disease
ID spinal-cord-injury; physical-activity; sedentary behavior; older-adults; children; muscle; health; risk; individuals; population
AB Purpose: Individuals with cerebral palsy (CP) are at increased risk for frailty and chronic disease due to factors experienced throughout the lifespan, such as excessive sedentary behaviors and malnutrition. However, little is known about noncommunicable diseases (NCDs) and multimorbidity profiles in young adults with CP. The study objective was to compare NCD and multimorbidity profiles between young adults with and without CP. Methods: A clinic-based sample of adults (18-30 years) with (n=452) and without (n=448) CP was examined at the University of Michigan Medical Center. The prevalence and predictors of 13 NCDs were evaluated, including existing diagnoses or historical record of musculoskeletal, cardiometabolic, and pulmonary morbidities. The level of motor impairment was determined by the Gross Motor Function Classification System (GMFCS) and stratified by less vs more severe motor impairment (GMFCS I-III vs IV-V). Logistic regression was used to determine the odds of NCD morbidity and multimorbidity in adults with CP compared to adults without CP, and for GMFCS IV-V compared to GMFCS I-III in those with CP, after adjusting for age, sex, body mass index, and smoking. Results: Adults with CP had a higher prevalence of osteopenia, osteoporosis, hypertension, myocardial infarction, hyperlipidemia, asthma, and multimorbidity compared to adults without CP, and higher odds of musculoskeletal (odds ratio [OR]: 6.97) and cardiometabolic morbidity (OR: 1.98), and multimorbidity (OR: 2.67). Adults with CP with GMFCS levels IV-V had a higher prevalence of osteopenia/osteoporosis, osteoarthritis, hypertension, other cardiovascular conditions, pulmonary embolism, and multimorbidity, and higher odds of musculoskeletal (OR: 3.41), cardiometabolic (OR: 2.05), pulmonary morbidity (OR: 1.42), and multimorbidity (OR: 3.45) compared to GMFCS I-III. Conclusion: Young adults with CP have a higher prevalence of chronic NCDs and multimorbidity compared to young adults without CP, which is pronounced in those with more severe motor impairment. These findings reiterate the importance of early screening for prevention of NCDs in CP.
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NR 44
TC 101
Z9 113
U1 0
U2 9
PU DOVE MEDICAL PRESS LTD
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AU Hu, ZB
Wei, B
Wu, SK
Sun, JC
Xiang, M
Zhang, ZM
AF Hu, Zi-Bing
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Wu, Shao-Ke
Sun, Jie-Cong
Xiang, Min
Zhang, Zhong-Min
TI Changes in bone mineral density and bone metabolic indexes in ankylosing spondylitis mouse model complicated with osteoporosis
SO EXPERIMENTAL AND THERAPEUTIC MEDICINE
LA English
DT Article
DE ankylosing spondylitis; osteoporosis; bone mineral density; bone metabolism
ID vertebral fractures; induced arthritis
AB Changes in bone mineral density and bone metabolic indexes in a model of ankylosing spondylitis (AS) mice complicated with osteoporosis (OP) were investigated. BLAB/c mice were used as the subjects. AS was induced using proteoglycan, and OP was induced using tail suspension method. The mice were randomly divided into four groups: AS group, OP group, AS + OP group and negative control group. Changes in bone mineral density, bone strength, serum calcium (Ca), phosphorus, alkaline phosphatase (ALP) and tartrate-resistant acid phosphatase (TRACP), in mice of each group were detected and compared. There were statistically significant differences in bone mineral density and bone strength

among groups. Compared with the negative control group, bone mineral density and bone strength in the AS, the OP and the AS + OP groups were significantly decreased, and the lowest bone mineral density and bone strength were found in the AS + OP group ($P<0.05$). There were no significant differences in bone mineral density and bone strength between the AS group and the OP group. Significant differences in serum Ca, ALP and TRACP but not in serum phosphorus were found among groups. Compared with the control group, serum levels of Ca and TRACP in the AS, the OP and the AS + OP groups were significantly increased, while levels of ALP were obviously decreased ($P<0.05$). Bone destruction in AS mice complicated with osteoarthritis was more serious than that in mice with simple AS.
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PA POB 18179, ATHENS, 116 10, GREECE
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PT J
AU Ikemoto, T
Arai, YC
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Arai, Young-Chang
TI Locomotive syndrome: clinical perspectives
SO CLINICAL INTERVENTIONS IN AGING
LA English
DT Review
DE locomotive syndrome; long-term care; frailty; sarcopenia; functional disability;

osteoarthritis; spondylosis; osteoporosis
ID bone-mineral density; quality-of-life; physical performance-measures; syndrome risk test; elderly-people; cognitive impairment; musculoskeletal pain; body-composition; muscle strength; older adults
AB The deterioration of locomotive components, which comprise bones, joints, and intervertebral discs, and muscles and nerves, can lead to symptoms such as pain, limitations in the range of joint mobility, malalignment, impaired balance, and difficulty walking. Locomotive syndrome (LoS) was proposed by the Japanese Orthopedic Association in 2007 as a concept for people who are at a high risk of developing a musculoskeletal ambulation disability attributed to locomotor organs. Although many international articles related to LoS have been published, an international consensus of this concept seems to be lacking. This review article on LoS introduces the concept, the related assessment methods, and the condition's prevalence based on the most up-to-date literature, and discusses discrimination from frailty and sarcopenia, relevance to musculoskeletal problems, management plan, and future directions. Familiarity with recent evidence would be useful for the health care providers in an aging society to educate individuals with LoS or pre-LoS and to maintain their well-being and prevent them from requiring long-term care.
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PA PO BOX 300-008, ALBANY, AUCKLAND 0752, NEW ZEALAND
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PT J
AU Tantowi, NACA
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AF Tantowi, Nur Adeelah Che Ahmad
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TI Ficus deltoidea Prevented Bone Loss in Preclinical Osteoporosis/Osteoarthritis Model by Suppressing Inflammation
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Ficus deltoidea; Osteoporosis; Osteoarthritis; Microstructure; NF-kappa beta; TNF-alpha
ID nf-kappa-b; nonsteroidal antiinflammatory drugs; articular-cartilage; subchondral bone; rat models; fracture; osteoarthritis; risk; microarchitecture; osteoporosis
AB Osteoporosis (OP) and osteoarthritis (OA) are debilitating musculoskeletal diseases of the elderly. Ficus deltoidea (FD) or mistletoe fig, a medicinal plant, was pre-clinically evaluated against OP- and OA-related bone alterations, in postmenopausal OA rat model. Thirty twelfth-week-old female rats were divided into groups (n=6). Four groups were bilateral ovariectomized (OVX) and OA-induced by intra-articular monosodium iodoacetate (MIA) injection into the right knee joints. The Sham control and OVX-OA non-treated groups were given deionized water. The three other OVX-OA groups were orally administered daily with FD extract (200, 400mg/kg) or diclofenac (5mg/kg) for 4weeks. The rats' bones and blood were evaluated for protein and mRNA expressions of osteoporosis and inflammatory indicators, and micro-CT computed tomography for bone microstructure. The non-treated OVX-OA rats developed severe OP bone loss and bone microstructural damage in the subchondral and metaphyseal regions, supported by reduced serum bone formation markers (osteocalcin, osteoprotegerin) and increased bone resorption markers (RANKL and CTX-I). The

FD extract significantly ($p<0.05$) mitigated these bone microstructural and biomarker changes by dose-dependently down-regulating pro-inflammatory NF-, TNF-, and IL-6 mRNA expressions. The FD extract demonstrated good anti-osteoporotic properties in this OP/OA preclinical model by stimulating bone formation and suppressing bone resorption via anti-inflammatory pathways. This is among the few reports relating the subchondral bone plate and trabecular thickening with the metaphyseal trabecular osteopenic bone loss under osteoporotic-osteoarthritis conditions, providing some insights on the debated inverse relationship between osteoporosis and osteoarthritis.
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NR 50
TC 20
Z9 24
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PI NEW YORK
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J9 CALCIFIED TISSUE INT
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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PT J
AU Xu, YE
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AF Xu Yier
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TI High-throughput metabolomics investigates anti-osteoporosis activity of oleanolic acid via regulating metabolic networks using ultra-performance liquid chromatography coupled with mass spectrometry
SO PHYTOMEDICINE
LA English
DT Article
DE Oleanolic acid; Osteoporosis; Metabolomics; Metabolites; Pathway
ID bone-mineral density; disease; women; men
AB Background: Osteoporosis has brought about heavy socio-economic burden in

the morbidity and medical expenses associated with osteoporosis treatment and various restrictions on behavior of their social roles. Oleanolic acid (OA) is an anti-osteoporosis natural product, but molecular mechanisms of therapeutic effect are not still well known. Purpose: In this study, we explore anti-osteoporosis activity of oleanolic acid and predict the underlying mechanisms by metabolomics strategy. Methods: SD rats were intraperitoneal injection with prednison for once to establish osteoporosis model. Using metabolomics strategy based on ultra-performance liquid chromatography coupled with quadrupole time-offlight/ mass spectrometry (UPLC-TOF/MS), serum samples of 24 rats were analyzed to seek differential metabolites and pathway associated with OA treatment of osteoporosis. In addition, the effect of OA on osteoporosis rats was also evaluated by clinical biochemistry indicators and bone density analysis. Results: Clinical biochemistry indicators and bone density of lumbar and femur were reversed by OA treatment. A total of 25 potential biomarkers were identified in the rats model of glucocorticoid-induced osteoporosis, and oleanolic acid have a regulatory effect on 17 of them that related to some vital metabolic pathway such as linoleic acid metabolism, valine, leucine and isoleucine biosynthesis, phenylalanine, tyrosine and tryptophan biosynthesis as well as cysteine and methionine metabolism. The ingenuity pathway analysis (IPA) platform is applied to further understanding the relationship between metabolic changes and therapeutic effect of OA, which the disordered state carbohydrate metabolism, molecular transport and lipid metabolism in glucocorticoid-induced osteoporosis rats are mainly ameliorated by oleanolic acid. Conclusion: Metabolomics provides a novel method to investigate the anti-osteoporosis effects of OA and probe into the potential mechanisms, and will contributes to the development of new drugs.
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NR 27
TC 20
Z9 23
U1 1
U2 55
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PA OFFICE JENA, P O BOX 100537, 07705 JENA, GERMANY
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WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
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TI The effect of Chinese martial arts Tai Chi Chuan on prevention of osteoporosis: A systematic review
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Review
DE Bone mineral density; Osteoporosis; Prevention; Tai Chi Chuan
ID bone-mineral density; randomized controlled-trial; postmenopausal women; older-adults; muscle strength; exercise; balance; falls; risk; osteoarthritis
AB Background/Objective: Tai Chi Chuan (TCC) is suggested to have beneficial effects on the musculoskeletal system. The aim of this systematic review is to evaluate the evidence of the effect of TCC on bone mineral density (BMD) and its potential for prevention of osteoporosis. Methods: A literature search was conducted using PubMed, Embase, and Cochrane databases from inception to January 2017. Randomized controlled studies, case-control trials, prospective cohort studies, and cross-sectional studies which evaluated the effect of TCC on BMD were selected without any subject or language restriction. Results: Nine articles met the inclusion criteria, including seven randomized controlled trials (RCTs), one case-control trial (CCT), and one cross-sectional study, encompassing a

total of 1222 participants. Five studies showed statistically significant improvements in BMD after TCC, three studies showed nonsignificant intergroup differences, and one study provided no statistical evaluation of results. The studies with nonsignificant results tended to have a shorter total duration of TCC practice. Apart from dual-energy X-ray absorptiometry (DXA), two studies additionally used peripheral quantitative computed tomography (pQCT) which showed statistically significant positive effects of TCC on preventing osteoporosis. Conclusion: TCC is beneficial to BMD and may be a cost-effective and preventive measure of osteoporosis. This beneficial effect is better observed in long-term TCC practice. (C) 2018 The Authors. Published by Elsevier (Singapore) Pte Ltd on behalf of Chinese Speaking Orthopaedic Society.
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Z9 52
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PU ELSEVIER SCIENCE BV
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TI Pitfalls in the measurement of muscle mass: a need for a reference standard
SO JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE
LA English
DT Article
DE Lean mass; Muscle mass; Lean body mass; Reference standard
ID x-ray absorptiometry; electrical-impedance myography; in-vivo precision; cell lung-cancer; body-composition; skeletal-muscle; bioelectrical-impedance; serological biomarkers; bioimpedance analysis; adipose-tissue
AB BackgroundAll proposed definitions of sarcopenia include the measurement of muscle mass, but the techniques and threshold values used vary. Indeed, the literature does not establish consensus on the best technique for measuring lean body mass. Thus, the objective measurement of sarcopenia is hampered by limitations intrinsic to assessment tools. The aim of this study was to review the methods to assess muscle mass and to reach consensus on the development of a reference standard. MethodsLiterature reviews were performed by members of the

European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis working group on frailty and sarcopenia. Face-to-face meetings were organized for the whole group to make amendments and discuss further recommendations. ResultsA wide range of techniques can be used to assess muscle mass. Cost, availability, and ease of use can determine whether the techniques are better suited to clinical practice or are more useful for research. No one technique subserves all requirements but dual energy X-ray absorptiometry could be considered as a reference standard (but not a gold standard) for measuring muscle lean body mass. ConclusionsBased on the feasibility, accuracy, safety, and low cost, dual energy X-ray absorptiometry can be considered as the reference standard for measuring muscle mass.

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NR 90
TC 590
Z9 658
U1 1
U2 81

PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 2190-5991
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J9 J CACHEXIA SARCOPENI
JI J. Cachexia Sarcopenia Muscle
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WC Geriatrics & Gerontology; Medicine, General & Internal
SC Geriatrics & Gerontology; General & Internal Medicine
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PT J
AU Fernandez-Rebollo, E
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AF Fernandez-Rebollo, Eduardo
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Wagner, Wolfgang
TI Primary Osteoporosis Is Not Reflected by Disease-Specific DNA Methylation or Accelerated Epigenetic Age in Blood
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE OSTEOPOROSIS; DNA METHYLATION; EPIGENETIC; AGING; BIOMARKER

ID epigenome-wide association; mesenchymal stem-cells; bone-mineral density; dvo-guideline; osteoarthritis; mutations; fracture; therapy; risk; life
AB Osteoporosis is an age-related metabolic bone disease. Hence, osteoporotic patients might suffer from molecular features of accelerated aging, which is generally reflected by specific age-associated DNA methylation (DNAm) changes. In this study, we analyzed genomewide DNAm profiles of peripheral blood from patients with manifest primary osteoporosis and non-osteoporotic controls. Statistical analysis did not reveal any individual CG dinucleotides (CpG sites) with significant aberrant DNAm in osteoporosis. Subsequently, we analyzed if age-associated DNAm patterns are increased in primary osteoporosis (OP). Using three independent age-predictors we did not find any evidence for accelerated epigenetic age in blood of osteoporotic patients. Taken together, osteoporosis is not reflected by characteristic DNAm patterns of peripheral blood that might be used as biomarker for the disease. The prevalence of osteoporosis is age-associatedbut it is not associated with premature epigenetic aging in peripheral blood. (c) 2017 American Society for Bone and Mineral Research.
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NR 32
TC 39
Z9 44
U1 1
U2 10
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0884-0431
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J9 J BONE MINER RES
JI J. Bone Miner. Res.

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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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AF Lv, Chen
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Huang, Lintuo
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TI Glucosamine promotes osteoblast proliferation by modulating autophagy via the mammalian target of rapamycin pathway
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Autophagy; Glucosamine; Osteoblast; mTOR; Proliferation
ID bone mass; osteoporosis; cells; protects; cancer
AB Glucosamine is effective in the treatment of osteoarthritis; however, its effect on osteoporosis remains unclear. Decreased activity of osteoblasts is the main cause of osteoporosis. Here, we examined the effects of glucosamine on osteoblasts. The potential underlying mechanisms were explored. The results showed that

glucosamine had a biphasic effect on the viability of hFOB1.19 osteoblasts. At low concentrations (<0.6 mM), glucosamine induced hFOB1.19 cell proliferation, whereas at high concentrations (>0.8 mM) it induced apoptosis. The autophagy inhibitor 3-methyladenine (3-MA) was used to verify that glucosamine modulated hFOB1.19 cell viability via autophagy. The induction of apoptosis by high concentrations of glucosamine was significantly exacerbated by 3-MA, whereas the promotion of cell proliferation by low concentrations of glucosamine was significantly suppressed by 3-MA. Autophagy was examined by western blot detection of autophagy-related proteins including LC3, Beclin-1, and SQSTM1/p62 and by immunofluorescence analysis of autophagosomes. Glucosamine activated autophagy in a time-and concentration-dependent manner. Investigation of the underlying mechanism showed that glucosamine inhibited the phosphorylation of m-TOR in a concentration-dependent manner within 48 h, and rapamycin significantly inhibited the phosphorylation of m-TOR. These results demonstrated that glucosamine promoted hFOB1.19 cell proliferation and increased autophagy by inhibiting the m-TOR pathway, suggesting its potential as a therapeutic agent for osteoporosis.
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NR 31
TC 27
Z9 35
U1 2
U2 34
PU ELSEVIER FRANCE-EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER
PI ISSY-LES-MOULINEAUX
PA 65 RUE CAMILLE DESMOULINS, CS50083, 92442 ISSY-LES-MOULINEAUX, FRANCE
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PT J
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AF Rodrigues, T. A.
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TI Strontium ranelate as a possible disease-modifying osteoarthritis drug: a systematic review
SO BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH
LA English
DT Review
DE Osteoarthritis; Strontium ranelate; Treatment; Pain; Symptoms
ID knee osteoarthritis; subchondral bone; osteoporosis; hip; risk; progression; management; arthritis; cartilage; outcm
AB Considering that osteoarthritis (OA) is the most prevalent joint disease worldwide, multiple pharmacological treatments have been proposed to alter the articular structure with potential benefit in the progression of the disease. The so-called disease-modifying OA drugs have been frequently investigated but conclusive findings are rare. Strontium ranelate (SrRan) is a drug usually prescribed to treat osteoporosis, with proven effects in decreasing the risk of fractures and possible effect in reducing the progression of OA. The objective of this review was to demonstrate the current panorama of knowledge on the use of SrRan in clinical and experimental models, clarifying its mechanisms of action and describing possible anti-nociceptive and anti-inflammatory effects. The systematic review was based on the PRISMA statement and included articles that are indexed in scientific databases. Fifteen studies were included: seven pre-clinical and eight clinical studies. Despite the limited number of studies, the results suggest a positive effect of SrRan in patients with OA, through changes in functional capacity and reduction of progression of morphological parameters and joint degradation, with moderate quality of evidence for those clinical outcomes. Novel studies are necessary to elucidate the molecular targets of SrRan, focusing on anti-inflammatory effects and histological changes promoted by SrRan, which seemed to reduce the progression of OA in the experimental and clinical studies.
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J9 BRAZ J MED BIOL RES
JI Brazilian J. Med. Biol. Res.
PD JUN 15
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VL 51
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BP
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WC Biology; Medicine, Research & Experimental
SC Life Sciences & Biomedicine - Other Topics; Research & Experimental Medicine
GA GJ7DO
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PT J
AU Yoon, C
Chang, MJ
Chang, CB
Song, MK
Shin, JH
Kang, SB
AF Yoon, Chan
Chang, Moon Jong
Chang, Chong Bum
Song, Min Kyu
Shin, Jae Hoon
Kang, Seung-Baik
TI Medial Tibial Periprosthetic Bone Resorption and Its Effect on Clinical Outcomes After Total Knee Arthroplasty: Cobalt-Chromium vs Titanium Implants

SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE total knee arthroplasty; implant material; implant design; periprosthetic bone resorption; radiolucent line; bone mineral density
ID mineral density changes; high-viscosity cement; follow-up; standard radiographs; proximal tibia; replacement; component; design; tray; fixation
AB Background: Recently, concerns arose over the medial tibial bone resorption of a novel cobalt-chromium implant. This study aimed at investigating the effects of tibial component material, design, and patient factors on periprosthetic bone resorption and at determining its association with clinical outcomes after total knee arthroplasty (TKA). Methods: A total of 462 primary TKAs using 5 types of implants were included. To evaluate tibial periprosthetic bone resorption, we assessed radiolucent lines and change in bone mineral density at the medial tibial condyle (BMDMT). Factors related to bone resorption were assessed using regression analysis. Clinical outcomes were also evaluated with respect to periprosthetic bone resorption. Results: Compared to titanium implants, cobalt-chromium implants showed a higher incidence of complete radiolucent lines (23.1% vs 7.9% at 2 years post-TKA) and a greater degree of BMDMT reduction. However, there was no significant difference between the implants made of the same material. Increased medial tibial bone resorption was associated with male sex, osteoporosis, larger preoperative varus deformity, longer follow-up period, and lower body mass index. The periprosthetic bone resorption was not associated with clinical outcomes including changes in range of motion and Western Ontario and McMaster Universities Osteoarthritis Index score. Furthermore, no cases warranted additional surgery. Conclusion: Periprosthetic bone resorption was associated with implant material but not with implant design. Moreover, patient factors were related to the medial tibial bone resorption post-TKA. However, the periprosthetic bone resorption was not associated with short-term clinical outcomes. We contend that researchers should incorporate integrative considerations when developing and assessing novel implants. (C) 2018 Elsevier Inc. All rights reserved.
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WC Orthopedics
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PT J
AU González-Chica, DA
Vanlint, S
Hoon, E
Stocks, N
AF Gonzalez-Chica, David Alejandro
Vanlint, Simon
Hoon, Elizabeth
Stocks, Nigel
TI Epidemiology of arthritis, chronic back pain, gout, osteoporosis, spondyloarthropathies and rheumatoid arthritis among 1.5 million patients in Australian general practice: NPS MedicineWise MedicineInsight dataset
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Pain; chronic; Back pain; Musculoskeletal; Arthritis; Epidemiology; Population health
ID global burden; chronic diseases; prevalence; osteoarthritis; impact; management; perception; health
AB Background: Previous estimates for the prevalence of musculoskeletal conditions (MSK) and chronic pain in Australia have been based on self-report. We aimed to determine the prevalence and distribution of arthritis, chronic back pain, gout, osteoporosis, spondyloarthropathies and rheumatoid arthritis and current consultations for chronic pain among adults attending Australian general practice, and describe their distribution according to sociodemographic characteristics and presence of co-morbidities. Methods: We investigated 1,501,267 active adult patients (57.6% females; 22.5% >= 65y) evaluated between 2013 and 2016 and

included in the MedicineInsight database (a National Prescribing Service MedicineWise program), a large general practice data program that extracts longitudinal de-identified electronic medical record data from 'active' patients in over 550 practices. Three main groups of outcomes were investigated: 1) "prevalence" of arthritis, chronic back pain, gout, osteoporosis, spondyloarthropathies, and/or rheumatoid arthritis between 2000 and 2016; 2) "current" diagnosis/encounter for the same conditions occurring between 2013 and 2016, and; 3) "current" consultations for chronic pain of any type occurring between 2013 and 2016. Results: The combined "prevalence" of the investigated MSK (diagnosis between 2000 and 2016) among adults attending Australian general practice was 16.8% (95% CI 15.9; 17.7) with 21.3% (95% CI 20.2; 22.4) of the sample consulting for chronic pain between 2013 and 2016. The investigated MSK with the highest "prevalence" were arthritis (9.5%) and chronic back pain (6.7%). Patients with some of these MSK attended general practices more frequently than those without these conditions (median 2.0 and 1.0 contacts/year, respectively). The "prevalence" of the investigated MSK and "current" consultations for chronic pain increased with age, especially in women, but chronic pain remained stable at 22% for males aged > 40 years. The investigated MSK and chronic pain were more frequent among those in lower socioeconomic groups, veterans, Aboriginal and Torrent Strait Islanders, current and ex-smokers, and patients with chronic obstructive pulmonary disease or heart failure. Conclusions: The investigated MSK are more frequent among lower socioeconomic groups and the elderly. Based on information collected from adults attending Australian general practices, MedicineInsight provided similar estimates to those obtained from population-based studies, with the advantage of being based on medical diagnosis and including a national sample.
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CR Australian Institute of Health and Welfare, 2014, ARTHRITIS SERIES, V18, P0
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NR 42
TC 57
Z9 59
U1 0
U2 15
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN 1471-2474
EI
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD JAN 18
PY 2018
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DI 10.1186/s12891-018-1941-x
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
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PM 29347932
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PT J
AU Chen, SM
Peng, YJ
Wang, CC
Su, SL
Salter, DM
Lee, HS
AF Chen, Shu-Mei
Peng, Yi-Jen
Wang, Chih-Chien
Su, Sui-Lung
Salter, Donald M.

Lee, Herng-Sheng
TI Dexamethasone Down-regulates Osteocalcin in Bone Cells through Leptin Pathway
SO INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
LA English
DT Article
DE osteocalcin downregulation; dexamethasone; osteoblast
ID glucocorticoid-induced osteoporosis; body-weight; receptor; osteoarthritis; osteogenesis; obesity; marrow; tissue; mice; mass
AB Glucocorticoid therapy, especially at higher doses, is associated with significant adverse side effects including osteoporosis. Leptin, secreted from adipose tissue, has diverse effects on bone tissue regulation. As glucocorticoids stimulate leptin synthesis and secretion directly in adipose tissue we hypothesised that dexamethasone (DEX) induced osteoporosis may, in part, be mediated by an osteoblast dependent leptin-leptin receptor pathway. Human bone cells expressed leptin and leptin receptors (Ob-Ra and Ob-Rb). DEX increased leptin, Ob-Ra and Ob-Rb expression in a dose-dependent manner while decreasing expression of osteocalcin. In the presence of leptin, Cbfa1 and osteonectin expression showed no significant change, whereas osteocalcin expression was decreased. Recombinant human quadruple antagonist leptin suppressed DEX-induced osteocalcin downregulation. The signaling pathway involved up-regulation of JAK2. In conclusion, upregulation of leptin and Ob-Rb in human bone cells by DEX is associated with down-regulation of osteocalcin expression. The down regulation of osteocalcin by DEX was partially through a leptin autocrine/paracrine loop. Adverse effects of DEX on the skeleton may be modified by targeting leptin signaling pathways.
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PT J
AU Lespessailles, E
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Chapurlat, R
AF Lespessailles, Eric
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Chapurlat, Roland
TI Contribution of high resolution peripheral quantitative CT to the management of bone and joint diseases
SO JOINT BONE SPINE
LA English
DT Review
DE High resolution peripheral quantitative; computerized tomography; Bone microarchitecture; Osteoporosis; Fragility fracture; Therapy; Erosion; Porosity
ID distal radius; rheumatoid-arthritis; hr-pqct; postmenopausal women; cortical porosity; computed-tomography; trabecular bone; geometric-property; cancellous bone; skeletal sites
AB Many imaging modalities have been described to diagnose and monitor osteoporosis (OP), osteoarthritis and inflammatory rheumatic diseases. Over the last ten years, High Resolution peripheral Quantitative Computerized Tomography (HR-pQCT) was shown to be a precise and non invasive technique to study bone and joint diseases in clinical research. It allows the study of both cortical and trabecular bone microarchitecture at the distal tibia and radius, and further applications have been developed such as the study of mechanical properties by the finite element analysis. Thus, in case-control and cross-sectional studies, microarchitecture parameters discriminated fractured individuals independently of areal BMD. Also, microstructure parameters can predict incident fracture in postmenopausal women. In metabolic diseases associated with bone fragility, HR-pQCT may also be used to explore bone changes. In joint disease studies, HR-pQCT was a remarkable tool to assess bone erosion and joint space narrowing at the hand. This article gives an overview of this imaging technique. (C) 2017 Societe francaise de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.
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AU Haj-Mirzaian, A
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AF Haj-Mirzaian, A.
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TI Bisphosphonates intake and its association with changes of periarticular bone area and three-dimensional shape: data from the Osteoarthritis Initiative (OAI)
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Bisphosphonates; Periarticular bone; Osteoarthritis; 3T MRI; Knee
ID subchondral bone; knee osteoarthritis; progression
AB Objective: To determine the association between bisphosphonate treatment with the change of periarticular bone area and three-dimensional (3D) shape in participants of the Osteoarthritis Initiative (OAI) study. Design: Using propensity score (PS) matching method in females, 48 bisphosphonate users and 105 non-users, who were matched for osteoarthritis (OA) and osteoporosis (OP) related factors were included. Baseline and 24-month magnetic resonance imaging (MRI)-based periarticular bone area and 3D shape measurements were used. The association between bisphosphonate intake and 24-month interval changes of the periarticular bone area and 3D shape were evaluated using paired Wilcoxon signed rank test. We used conditional logistic regression models for determining the association between bisphosphonate intake and periarticular bone change, defined using the standard deviation of difference (SDD) and reliable change index (RCI) methods. P-values have been adjusted for multiple comparisons using Benjamini & Hochberg procedure and false discovery rate (FDR)-adjusted P-values were reported. Results: The 24-month interval increases in the periarticular bone area in medial side of tibia were significantly greater in non-users than users

(FDR-adjusted P-value: 0.002). There was an approaching significance trend for lower medial tibial periarticular bone area expansion in bisphosphonate users in comparison with non-users (For 1SDD change, odds ratio 95% confidence interval (OR (95% CI)): 0.514 (0.271-0.975), FDR-adjusted P-value: 0.085) (For 1.96RCI change, OR (95% CI): 0.552 (0.309-0.986), FDR-adjusted P-value: 0.085). Conclusions: Bisphosphonate intake was associated with a reduction in the odds (approaching but not achieving significance) of expansion periarticular bone area, specifically in the medial tibial sub-region. Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.
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WC Orthopedics; Rheumatology
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PT J
AU Tomori, Y
Motoda, N
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AF Tomori, Yuji
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TI Preiser disease after repeated local glucocorticoid injections A case report
SO MEDICINE
LA English
DT Article
DE aseptic avascular necrosis; glucocorticoid; Preiser disease; scaphoid; steroid; wrist
ID idiopathic avascular necrosis; radial wedge osteotomy; femoral-head; induced osteonecrosis; induced osteoporosis; steroid treatment; rabbits; vascularity; bone; wrist
AB Rationale: Preiser disease or avascular necrosis (AVN) of the scaphoid causes intolerable wrist pain and malalignment of the carpal bones. In previously reported cases, patients have had a history of steroid use for systemic illness such as autoimmune hemolytic anemia, systemic lupus erythematosus, or renal transplantation, or have had other risk factors, such as smoking, alcoholism, or infection. In particular, systemic glucocorticoid therapy has been most commonly associated with the disease. Although there are reports of AVN of the scaphoid induced by systemic glucocorticoids, no prior report has associated AVN of the carpal bones with repeated local injections of glucocorticoids. Patient concerns: We present a case in which it was strongly suspected that AVN of the scaphoid was induced by repeated local glucocorticoid injections. The patient had no history of excessive alcohol use, smoking, or trauma, except for local repeated steroid injections. Diagnoses: Initially, she had diagnosed with de Quervain's disease and was treated by repeated local glucocorticoid injections followed by surgery for de Quervain's disease. Five years after surgery for de Quervain's disease, the patient presented at our hospital with sudden onset of intolerable pain in her right wrist without a history of trauma. In spite of nonsurgical treatment with rest, immobilization, analgesia, and surgery, her wrist pain was not improved. After further repeated local steroid injections in her wrist, radiographs, and magnetic resonance imaging of her wrist showed the AVN of the scaphoid. Interventions: Surgery was performed and the fragmented proximal scaphoid and the entire lunate were resected. Outcomes: The diagnosis was confirmed according to the histopathological examination of the proximal scaphoid bone, which showed the characteristic of AVN of the scaphoid. At follow-up evaluation, radiographs of the right wrist showed no progression of osteoarthritis. The patient had no tenderness or residual pain at the wrist and had no desire to pursue additional surgery. Lessons: We have presented a case with AVN of the scaphoid, which was strongly suspected to be associated with the repeated local steroid injections. Further studies are required to more fully elucidate the association between AVN of the scaphoid and repeated local steroid injections.
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NR 35
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PU LIPPINCOTT WILLIAMS & WILKINS
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JI Medicine (Baltimore)
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ER

PT J
AU Bruyère, O
AF Bruyere, Olivier
TI Pharmaceutical-grade chondroitin sulfate in the management of knee osteoarthritis
SO EXPERT OPINION ON PHARMACOTHERAPY
LA English
DT Review
DE Knee osteoarthritis; treatment; pain; function; chondroitin sulfate
ID glucosamine sulfate; consensus statement; european-society; economic-aspects; double-blind; placebo; trial; recommendations; osteoporosis; esceo
AB Introduction: Chondroitin Sulfate (CS) is a drug which is available as pharmaceutical-grade and nutriceutical-grade products, with important variations in preparation, composition, purity and therapeutic effects. Previous studies using pharmaceutical-grade CS suggested that the compound improves pain and function and delays structural progression in knee osteoarthritis (OA), whereas discrepant results were observed when lower grade preparations were investigated.Areas covered: The recently published chondroitin versus celecoxib versus Placebo Trial (CONCEPT) assessed the symptomatic effect of pharmaceutical-grade CS 800 mg/day in symptomatic knee OA.Expert opinion:This prospective, randomized, 6-month, 3-arm, double-blind, double-dummy, placebo and celecoxib (200 mg/day) - controlled trial involved 604 patients aged above 50years with primary knee OA. This study showed that CS is superior to placebo and similar to celecoxib in reducing pain and improving function in Kellgren-Lawrence grade 1-3 patients supporting the role of pharmaceutical-grade CS as a potential first-line treatment for the management of patients with mild to moderate knee OA.
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NR 17
TC 5
Z9 7
U1 4
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PU TAYLOR & FRANCIS LTD
PI ABINGDON
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PT J
AU Chen, JQ
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AF Chen, Jianquan
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TI mTOR signaling in skeletal development and disease
SO BONE RESEARCH
LA English
DT Review
ID bone mass; immunosuppressant rapamycin; mammalian protein; binding partner; growth; activation; osteoblast; autophagy; complex; rictor
AB The mammalian/mechanistic target of rapamycin (mTOR) is a serine/threonine protein kinase that integrates inputs from nutrients and growth factors to control many fundamental cellular processes through two distinct protein complexes mTORC1 and mTORC2. Recent mouse genetic studies have established that mTOR pathways play important roles in regulating multiple aspects of skeletal development and homeostasis. In addition, mTORC1 has emerged as a common effector mediating the bone anabolic effect of Igf1, Wnt and Bmp. Dysregulation of mTORC1 could contribute to various skeletal diseases including osteoarthritis and osteoporosis. Here we review the current understanding of mTOR signaling in skeletal development and bone homeostasis, as well as in the maintenance of articular cartilage. We speculate that targeting mTOR signaling may be a valuable approach for treating skeletal diseases.
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Z9 167
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PU SPRINGERNATURE
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON, N1 9XW, ENGLAND
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J9 BONE RES
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TI Chronic Medical Conditions and CA125 Levels among Women without Ovarian Cancer
SO CANCER EPIDEMIOLOGY BIOMARKERS & PREVENTION
LA English
DT Article
ID antigen 125 levels; serum ca-125; heart-failure; tumor-markers; carbohydrate antigen-125; inflammatory activation; high-risk; prostate; lung; epidemiology
AB Background: Randomized trials using the biomarker cancer antigen (CA) 125, with or without pelvic ultrasound, have failed to show a clear benefit of general population screening for ovarian cancer. In part, this may be due to a lack of information about conditions, besides ovarian cancer, that can alter CA125 levels and affect specificity or sensitivity. We evaluated the association between common medical conditions and CA125 levels among women without ovarian cancer. Methods: We used data and specimens from 2,004 women without ovarian cancer who participated in the New England Case Control study between 1992 and 2008. Participants completed in-person interviews and donated blood samples at enrollment. We measured CA125 using the CA12511 assay and calculated the association between medical conditions and log-transformed CA125 using linear regression. Results: The median age of participants was 53 years and 1,119 (56%) were postmenopausal. The average CA125 level was 14.5 units/nil, for premenopausal and 11.7 for postmenopausal women. Among premenopausal women, CA125 was significantly lower for women with colon polyps (P = 0.06) and hysterectomy (P = 0.01) and significantly higher with endometriosis (P 0.05). CA125 was also significantly higher in premenopausal women with coronary artery disease (CVD) (P < 0.01, n 2 cases) but not among postmenopausal with CM (n 79). Furthermore, among postmenopausal women, CA1.25 was significantly lower for women with osteoporosis, hypercholesterolemia, and osteoarthritis (P = 0.03, 0.02, and 0.01 respectively) and higher for women with a history of inflammatory bowel disease (P = 0.04). Conclusions: Several chronic diseases are associated with CA125, which could influence the interpretation of CA125 in the context of ovarian cancer screening. Impact: Consideration of chronic medical conditions may he necessary to interpret CA125 values. (C) 2018 AACR.
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NR 48

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Z9 52
U1 0
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PU AMER ASSOC CANCER RESEARCH
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J9 CANCER EPIDEM BIOMAR
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TI Real-world retrospective cohort study ARCTIC shows burden of comorbidities in Swedish COPD versus non-COPD patients
SO NPJ PRIMARY CARE RESPIRATORY MEDICINE
LA English
DT Article
ID obstructive pulmonary-disease; economic burden; prevalence; outcm; risk
AB This study aimed to generate real-world evidence to assess the burden of comorbidities in COPD patients, to effectively manage these patients and optimize the associated healthcare resource allocation. ARCTIC is a large, real-world, retrospective cohort study conducted in Swedish COPD patients using electronic medical record data collected between 2000 and 2014. These patients were studied for prevalence of various comorbidities and for association of these comorbidities with exacerbations, mortality, and healthcare costs compared with an age-, sex-, and comorbidities-matched non-COPD reference population. A total of 17,479 patients with COPD were compared with 84,514 non-COPD reference population. A significantly higher prevalence of various comorbidities was observed in COPD patients 2 years post-diagnosis vs. reference population, with the highest percentage increase observed for cardiovascular diseases (81.8% vs. 30.7%). Among the selected comorbidities, lung cancer was relatively more prevalent in COPD patients vs. reference population (relative risk, RR = 5.97, $p < 0.0001$). Ischemic heart disease, hypertension, depression, anxiety, sleep disorders, osteoporosis, osteoarthritis, and asthma caused increased mortality rates in COPD patients. Comorbidities that were observed to be significantly associated with increased number of severe exacerbations in COPD patients included heart failure, ischemic heart disease, depression/anxiety, sleep disorders, osteoporosis, lung cancer, and stroke. The cumulative healthcare costs associated with comorbidities over 2 years after the index date were observed to be significantly higher in COPD patients ((sic) 27,692) vs. reference population ((sic) 5141) ($p < 0.0001$). The data support the need for patient-centered treatment strategies and targeted healthcare resource allocation to reduce the humanistic and economic burden associated with COPD comorbidities.
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TI Clodronate in the management of different musculoskeletal conditions
SO MINERVA MEDICA
LA English
DT Review

DE Clodronic acid; Osteoporosis; Osteoarthritis; Arthroplasty
ID bone-mineral density; regional-pain-syndrome; breast-cancer patients; cyclical intravenous clodronate; randomized controlled-trials; induced ovarian failure; total hip-arthroplasty; total knee patients; syndrome type-i; double-blind
AB INTRODUCTION: Clodronic acid is a non-nitrogen-containing bisphosphonate largely used from some decades in the prevention and treatment of postmenopausal and secondary osteoporosis. In addition to antiresorptive activity, clodronate has shown anti-inflammatory and analgesic properties, and modulatory effects on bone and cartilage metabolism. EVIDENCE ACQUISITION: A literature review has been conducted to characterize the mechanism of action of clodronate and to retrieve available evidence about the use of clodronate in primary and secondary osteoporosis, and its potential role in other musculoskeletal conditions and orthopedic surgery. EVIDENCE SYNTHESIS: The efficacy and safety of the available clodronate formulations (oral, intravenous and intramuscular) in the prevention and treatment of postmenopausal and secondary osteoporosis, including corticosteroid-induced osteoporosis and bone mass loss secondary to endocrine, gastrointestinal and neoplastic diseases, have been demonstrated in a variety of clinical trials. The analgesic, anti-inflammatory, bone-and chondro-modulating properties of clodronate have allowed to expand its use in other musculoskeletal conditions to those currently approved. Clodronate has proven to be beneficial in the treatment of osteoarthritis of the knee and of the hand, in the management of complex regional pain syndrome, and in the peri-and postoperative phase in subjects undergoing arthroplasty. CONCLUSIONS: The analysis of the available literature has shown that clodronate has relevant musculoskeletal effects beyond the antiresorptive activity. Further research is needed to better position clodronate therapy in the management of these conditions and to define the optimal formulation and dose regimen in any of the tested new indications.
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TI Effect of Total Flavonoids of Rhizoma drynariae on Tibial Dyschondroplasia by Regulating BMP-2 and Runx2 Expression in Chickens
SO FRONTIERS IN PHARMACOLOGY
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DT Article
DE Rhizoma drynariae; tibial dyschondroplasia; BMP-2; Runx2; gene expression
ID bone morphogenetic protein-2; liver oxidative stress; osteoblast differentiation; growth-plate; in-vitro; cells; toxicity; apigenin
AB Tibial dyschondroplasia (TD) is an abnormality of the growth cartilage that occurs in chickens and other rapidly growing avian species. This disease not only cause huge economic losses, but also greatly affects animal welfare. The total flavonoids of Rhizoma drynariae (TFRD) has been used to cure wide variety of diseases including bone fractures and osteoarthritis and osteoporosis. However, less information is available about the using of TFRD against the TD. The aim of this study was to determine the effect of TFRD on TD by regulating BMP-2 and Runx2 in chickens. A total of 200 birds were randomly divided into control, TD, TD recovery (TDR), and TFRD groups. All the groups were given standard diet with an addition of thiram (50 mg/kg) from days 3 to 7 in TD, TDR, and TFRD groups in order to induce TD in chickens. After the induction of TD, the birds of TFRD group were fed standard diet with the addition of TFRD at 20 mg/kg. Clinical results conveyed that TFRD can improve the growth performance of the TD chickens and recover normal activity, and it is more obvious than TDR. Gene expressions of BMP-2 and Runx2 were down-regulated during the development of the disease and were up-regulated obviously after TFRD treatment. In conclusion, TFRD not only decreased the mortality rate but also increased the growth performance of TD in chickens. In conclusion, TFRD plays important role in improving the growth performance, adjusting the relevant physiological indicators, and regulating BMP-2 and Runx2 in chickens.
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TI Both Oleanolic Acid and a Mixture of Oleanolic and Ursolic Acids Mimic the Effects of Fructus ligustri lucidi on Bone Properties and Circulating 1,25-Dihydroxycholecalciferol in Ovariectomized Rats
SO JOURNAL OF NUTRITION
LA English
DT Article
DE bone; calcium; Fructus ligustri lucidi; oleanolic acid; ursolic acid
ID ethanol extract; calcium balance; mineral density; gene-expression; improvement; differentiation; kinetics; cells
AB Background: Oleanolic acid (OA) and ursolic acid (UA) are major chemical constituents found in Fructus ligustri lucidi (FLL), a Chinese herb previously shown to increase bone properties and modulate calcium-vitamin D metabolism in rats. OA and UA have been reported to exert osteoprotective effects in vitro. Objective: The present study was designed to determine whether OA or OA + UA mimicked the effects of FLL on bone and calcium homeostasis using ovariectomized rats. Methods: Three-month-old ovariectomized Sprague-Dawley rats were stabilized for 2 mo and randomly assigned to 4 groups offered the same amount (15-17 g/d) of a control diet or experimental diets containing FLL (18.8 g/kg), OA (0.67 g/kg), or OA (0.67 g/kg) + UA (0.22 g/kg) for 6 wk. Serum was obtained formeasurement of 1,25-dihydroxycholecalciferol [1,25(OH)(2)D-3] and bones were collected for micro-CT analysis. Calcium balance was measured at weeks 1 and 6. A calcium kinetic study using Ca-45 was conducted at week 6 and modeled using WinSAAM software. Results: Compared with the control group, rats fed the FLL-, OA-, and OA

+ UA-enriched diets had better bone properties and 51%, 31%, and 27% higher serum 1,25(OH)(2)D-3 concentrations at week 6, respectively. These variables did not differ between the treatments. Calcium balance was not affected by diet at either week 1 or week 6. Kinetic modeling predicted that FLL and OA + UA diet-fed rats had 9% and 15% less endogenous excretion of calcium, respectively, compared with the control group. All 3 treatments resulted in a higher calcium mass of compartment 3 because of changes in transfer rate between compartments 2 and 3, and were positively associated with the serum 1,25(OH)(2)D-3 concentration (R-2 = 0.28; P < 0.01). Conclusion: Similar to FLL, OA and OA + UA increase bone properties, serum 1,25(OH)(2)D-3 concentration, and calcium use in ovariectomized rats, suggesting their potential role in management of osteoporosis.
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NR 30
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TI Cross-Validation of Arthroplasty Records Between Arthroplasty and Hospital Discharge Registers, Self-Reports, and Medical Records Among a Cohort of 14,220 Women
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE arthroplasty; osteoarthritis; validation studies; cohort studies; registers; self-report
ID hip
AB Background: There are no actual validation studies of the Finnish Arthroplasty Register (FAR), and only a few studies about the accuracy of self-reported hip and knee arthroplasty exist. Therefore, we examine how reliably total hip (THA) and knee (TKA) arthroplasties can be identified from multiple data sources, including self-reports, the hospital discharge register, the arthroplasty register, and medical records. Methods: Data from the FAR and from the Finnish Hospital Discharge Register (FHDR) during the years 1980-2010 were cross-checked to identify all THA and TKA events for the Kuopio Osteoporosis Risk Factor and Prevention Study cohort (n = 14,220). Unclear events were further checked from the medical records. After establishing a gold standard, by referring to confirmed THAs and TKAs, we examined the validity of self-reports in identifying the prevalent population with THA/TKA and in identifying incident THA/TKA. Results: Completeness of 2820 total arthroplasty events was 96.1% in FAR and 98.3% in FHDR. The self-reports had 95.1% sensitivity and 92.9% positive predictive value (PPV) to identify population with THA and for TKA sensitivity was 94.6% and PPV 95.2%. Self-reports' sensitivity of finding the actual surgery events was 65.3% and PPV 85.4% for THA and for TKA sensitivity was 62.9% and PPV 83.4%. Conclusion: The best way to identify THAs and TKAs in Finland is to combine data from the FAR and the FHDR. Self-reports can be considered as suitable to identify the prevalent population with THA/TKA, and they do not work as well to identify the actual surgery events. (C) 2018 Elsevier Inc. All rights reserved.
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PT J
AU Kuriyan, R
AF Kuriyan, Rebecca
TI Body composition techniques
SO INDIAN JOURNAL OF MEDICAL RESEARCH
LA English
DT Review
DE Adiposity; anthropometry; body composition; DEXA; hydrodensitometry; hydrometry; models; muscle mass
ID air displacement plethysmography; south indian children; x-ray absorptiometry; mass index cutoffs; fat-free mass; waist circumference; asian indians; 4-compartment model; adipose-tissue; cellular-level
AB Body composition is known to be associated with several diseases, such as cardiovascular disease, diabetes, cancers, osteoporosis and osteoarthritis. Body composition measurements are useful in assessing the effectiveness of nutritional interventions and monitoring the changes associated with growth and disease conditions. Changes in body composition occur when there is a mismatch between nutrient intake and requirement. Altered body composition is observed in conditions such as wasting and stunting when the nutritional intake may be inadequate. Overnutrition on the other hand leads to obesity. Many techniques are available for body composition assessment, which range from simple indirect measures to more sophisticated direct volumetric measurements. Some of the methods that are used today include anthropometry, tracer dilution, densitometry,

dual-energy X-ray absorptiometry, air displacement plethysmography and bioelectrical impedance analysis. The methods vary in their precision and accuracy. Imaging techniques such as nuclear magnetic resonance imaging and computed tomography have become powerful tools due to their ability of visualizing and quantifying tissues, organs, or constituents such as muscle and adipose tissue. However, these methods are still considered to be research tools due to their cost and complexity of use. This review was aimed to describe the commonly used methods for body composition analysis and provide a brief introduction on the latest techniques available.
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TI Preoperative dual-energy X-ray absorptiometry and FRAX in patients with lumbar spinal stenosis
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
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DT Article
DE Lumbar spinal stenosis; DXA; FRAX; Osteoporosis; Bone mineral density
ID bone-mineral density; walking capacity; osteoporosis; diagnosis; osteoarthritis; performance; prevalence; fixation; surgery; quality
AB BackgroundOsteoporosis implies an increased risk of complications after orthopedic surgery. For the mostly elderly group of patients undergoing lumbar spinal stenosis surgery (LSS), it is important to include skeletal health evaluation in the preoperative planning. The aim of this study was to assess spine and femoral neck (FN) bone mineral density (BMD) in LSS patients and to evaluate whether the

World Health Organization (WHO) fracture risk assessment tool (FRAX) can identify patients with reduced BMD levels in the spine.MethodsThe study involved 65 LSS patients and 53 patients with hip osteoarthritis (HOA) for comparison. BMD was measured with dual-energy X-ray absorptiometry (DXA) in the lumbar spine in three projections: anterior-posterior (AP), lateral and lateral-mid (the mid-portion of the vertebrae), and FN. The LSS patients filled out the FRAX questionnaire.ResultsIn the LSS group, 43% of the women and 8% of the men were classified as being osteoporotic/osteopenic by AP spine measurement. The corresponding proportions using the lateral spine T-score -2.5 were 87% and 57%, respectively, and 82% and 53%, respectively, for the FN. The FN BMD T-score was significantly lower in the LSS group compared with the HOA group. The FRAX questionnaire identified 40% of the LSS patients with a moderate/high risk of sustaining an osteoporotic fracture within 10years, with or without simultaneous FN BMD, while 71% of these patients were classified as being osteoporotic with DXA lateral spine measurement.ConclusionIt is common with osteoporosis/osteopenia in patients undergoing spine surgery, and the identification may influence the surgical treatment why the evaluation of BMD is important preoperatively. FRAX evaluation could not replace DXA measurement of the spine regarding the identification of osteoporosis patients in the preoperative planning phase.

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NR 29
TC 5
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 J ORTHOP SURG RES
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PT J
AU Sawada, Y
Sugimoto, A
Osaki, T
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AF Sawada, Yoko
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TI Ajuga decumbens stimulates mesenchymal stem cell differentiation and regenerates cartilage in a rabbit osteoarthritis model
SO EXPERIMENTAL AND THERAPEUTIC MEDICINE
LA English
DT Article
DE Ajuga decumbens; anti-inflammation; cartilage regeneration; mesenchymal stem cell; osteoarthritis; osteogenesis
ID glucosamine hydrochloride; chondrocytes; injury; tissue; osteoporosis; expression; arthritis; sulfate; repair; bone
AB In a previous study by our group, Ajuga decumbens extract (ADE) was demonstrated to decrease the number of osteoclasts in subchondral bone and to have a synergistic effect with glucosamine in improving cartilaginous injuries in a rabbit model of osteoarthritis. In the present study, a concentrate of the useful fraction of ADE, termed extra ADE (EADE), which includes higher concentrations of the active component 20-hvdroxyecdysone, was evaluated for its efficacy to accelerate the healing of experimental cartilage injury. Cartilage injuries were surgically induced in rabbits by creating three holes; one in the articular cartilage of the medial trochlea and two in the trochlear sulcus of the distal femur. The rabbits were divided into the following four groups (n=3 in each): Control, ADR (0.5 g/kg), low dosage EADE (0.05 g/kg; low EADE) and high dosage EADE (0.5 g/kg; high EADE). ADE and EADE were dissolved in tap water and each dosage was orally administered every day for 3 weeks. At the end of the experimental period, histological analysis indicated that the cartilage matrix was regenerated in the low and high EADE groups. On counting of cells in the histological specimens, it was determined that the mean number of osteoclasts per 100 osteoblasts in subchondral bone was lower in the high EADE group compared with the control group. Furthermore, the results indicated that treatment with EADE (1-100 mu g/ml) stimulated chondrogenic differentiation of mesenchymal stem cells and induced proteoglycan production to a greater extent than the control in vitro. EADE treatment (10 and 100 mu g/ml) was also observed to significantly attenuate

interleukin-l beta-induced prostaglandin R2 production in chondrocytes (P<0.05). In summary, the results of the present study suggest that EADE may have greater curative sffects on bone injiury compared with the currently used therapeutic ADE.
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AU Vrtacnik, P
Zupan, J
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AF Vrtacnik, Peter
Zupan, Janja
Mlakar, Vid
Kranjc, Tilen
Marc, Janja
Kern, Barbara
Ostanek, Barbara
TI Epigenetic enzymes influenced by oxidative stress and hypoxia mimetic in osteoblasts are differentially expressed in patients with osteoporosis and

osteoarthritis
SO SCIENTIFIC REPORTS
LA English
DT Article
ID bone; disease; angiogenesis; receptors; tissue; genes; model; mice
AB Epigenetic mechanisms including posttranslational histone modifications and DNA methylation are emerging as important determinants of bone homeostasis. With our case-control study we aimed to identify which chromatin-modifying enzymes could be involved in the pathology of postmenopausal osteoporosis and osteoarthritis while co-regulated by estrogens, oxidative stress and hypoxia. Gene expression of HAT1, KAT5, HDAC6, MBD1 and DNMT3A affected by oxidative stress and hypoxia in an in vitro qPCR screening step performed on an osteoblast cell line was analysed in trabecular bone tissue samples from 96 patients. Their expression was significantly reduced in patients with postmenopausal osteoporosis and osteoarthritis as compared to autopsy controls and significantly correlated with bone mineral density and several bone histomorphometry-derived parameters of bone quality and quantity as well as indicators of oxidative stress, RANK/RANKL/OPG system and angiogenesis. Furthermore, oxidative stress increased DNA methylation levels at the RANKL and OPG promoters while decreasing histone acetylation levels at these two genes. Our study is the first to show that higher expression of HAT1, HDAC6 and MBD1 is associated with superior quantity as well as quality of the bone tissue having a more favourable trabecular structure.
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AU Al-Zaghal, A
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TI Applications of PET Imaging in the Evaluation of Musculoskeletal Diseases Among the Geriatric Population
SO SEMINARS IN NUCLEAR MEDICINE
LA English
DT Review
ID positron-emission-tomography; early-stage osteoarthritis; f-18-sodium fluoride pet; fdg-pet; diagnosing infection; f-18-fdg pet/ct; bone; f-18-fluoride; inflammation; metabolism
AB Medical imaging plays a particularly important role in the care of elderly patients, in whom complex symptomatology and a high prevalence of musculoskeletal diseases necessitate sensitive imaging modalities. MRI is the most commonly used imaging modality in the evaluation of various musculoskeletal disorders. The integration of positron emission technique and computed tomography as well as magnetic resonance imaging allows for generating complimentary data for accurate and quantitative diagnosis. This article highlights the implementations of molecular imaging probes in the assessment of prevalent musculoskeletal disorders among geriatric population with emphasis on osteoarthritis, osteoporosis, diabetic foot, and prosthetic joint infections. We also discuss the sensitivity of FDG-PET imaging in differentiating polymyalgia

rheumatica from other diseases that have similar clinical presentation. (C) 2018 Published by Elsevier Inc.
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NR 62
TC 17
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PU W B SAUNDERS CO-ELSEVIER INC
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J9 SEMIN NUCL MED
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SC Radiology, Nuclear Medicine & Medical Imaging
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AU Yoshimura, N
Muraki, S
Oka, H
Iidaka, T
Kodama, R
Horii, C
Kawaguchi, H
Nakamura, K
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AF Yoshimura, N.
Muraki, S.
Oka, H.
Iidaka, T.
Kodama, R.
Horii, C.
Kawaguchi, H.
Nakamura, K.
Akune, T.
Tanaka, S.
TI Do sarcopenia and/or osteoporosis increase the risk of frailty? A 4-year observation of the second and third ROAD study surveys
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Frailty; Incidence; Osteoporosis; Population-based cohort study; Sarcopenia
ID bioelectrical-impedance analysis; dwelling elderly subjects; muscle; mass; association; consensus; adults
AB In this 4-year follow-up study including 1083 subjects (60years), the prevalence of frailty was estimated to be 5.6%; osteoporosis was found to be significantly associated with frailty. Moreover, the presence of both osteoporosis and sarcopenia increased the risk of frailty compared to the presence of osteoporosis or sarcopenia alone.IntroductionThis study aims to examine the contribution of sarcopenia and osteoporosis to the occurrence of frailty using 4-year follow-up information of a population-based cohort study.MethodsThe second survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study was conducted between 2008 and 2010; 1083 subjects (aged 60years, 372 men, 711 women) completed all examinations on frailty, sarcopenia, and osteoporosis, which were defined using Fried's definition, Asian Working Group for Sarcopenia criteria, and WHO criteria, respectively. The third survey was conducted between 2012 and 2013; 749 of 1083 individuals enrolled from the second survey (69.2%, 248 men, 501 women) completed assessments identical to those in the second survey.ResultsThe prevalence of frailty in the second survey was 5.6% (men, 3.8%; women, 6.6%). The cumulative incidence of frailty was 1.2%/year (men, 0.8%/year;

women, 1.3%/year). After adjustment for confounding factors, logistic regression analysis indicated that osteoporosis was significantly associated with the occurrence of frailty (odds ratio, 3.07; 95% confidence interval, 1.26-7.36; p=0.012). Moreover, the occurrence of frailty significantly increased according to the presence of osteoporosis and sarcopenia (odds ratio vs. neither osteoporosis nor sarcopenia: osteoporosis alone, 2.50; osteoporosis and sarcopenia, 5.80).ConclusionsPreventing osteoporosis and coexistence of osteoporosis and sarcopenia may help reduce the risk of frailty.
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NR 30
TC 41
Z9 46
U1 1
U2 24
PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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JI Osteoporosis Int.
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WC Endocrinology & Metabolism
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PT J
AU Gao, YP
Ge, W
AF Gao, Yanpan
Ge, Wei
TI The histone methyltransferase DOT1L inhibits osteoclastogenesis and protects against osteoporosis
SO CELL DEATH & DISEASE
LA English
DT Article
ID bone-resorption; cell-migration; in-vitro; differentiation; osteoarthritis; activation; autophagy; nfatc1; fusion; degradation
AB Osteoclasts are absorptive cells that play a critical role in homeostatic bone remodeling and pathological bone resorption. Emerging evidence suggests an important role of epigenetic regulation in osteoclastogenesis. In this study, we investigated the role of DOT1L, which regulates gene expression epigenetically by histone H3K79 methylation (H3K79me), during osteoclast formation. Using RANKL-induced RAW264.7 macrophage cells as an osteoclast differentiation model, we found that DOT1L and H3K79me2 levels were upregulated during osteoclast differentiation. Small molecule inhibitor-(EPZ5676 or EPZ004777) or short hairpin RNA-mediated reduction in DOT1L expression promoted osteoclast differentiation and resorption. In addition, DOT1L inhibition increased osteoclast surface area and accelerated bone-mass reduction in a mouse ovariectomy (OVX) model of osteoporosis without alter osteoblast differentiation. DOT1L inhibition increase reactive oxygen species (ROS) generation and autophagy activity, and cell migration in pre-osteoclasts. Moreover, it strengthened expression of osteoclast fusion and resorption-related protein CD9 and MMP9 in osteoclasts derived from RAW264.7. Our findings support a new mechanism of DOT1L-regulated, H3K79me2-mediated, epigenetic regulation of osteoclast differentiation, implicating DOT1L as a new therapeutic target for osteoclast dysregulation-induced disease.
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WC Cell Biology
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PT J
AU Schimmel, M
Srinivasan, M
McKenna, G
Müller, F
AF Schimmel, Martin
Srinivasan, Murali
McKenna, Gerald
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TI Effect of advanced age and/or systemic medical conditions on dental implant survival: A systematic review and meta-analysis
SO CLINICAL ORAL IMPLANTS RESEARCH
LA English
DT Review
DE aging; Alzheimer's disease; bisphosphonates; cancer; cardiovascular disease; chronic obstructive pulmonary disease; cirrhosis of the liver; dementia; dental implants; depression; diabetes mellitus; geriatric; hypertensive heart disease; hyposalivation; ischemic heart disease; lower respiratory infections; medication-related osteonecrosis of the jaw; meta-analysis; neurocognitive impairment; osteoarthritis; Parkinson's disease; radiotherapy; respiratory diseases; stroke; systematic review
ID bisphosphonate-related osteonecrosis; type-2 diabetes-mellitus; oral bisphosphonates; loading protocols; follow-up; osseointegrated implants; edentulous patients; irradiated patients; parkinsons-disease; neck-cancer
AB Objectives: This review evaluated implant survival in geriatric patients (>= 75 years) and/or the impact of systemic medical conditions. Materials and Methods: Systematic literature searches were performed to identify studies reporting on geriatric subjects with dental implants and on implant patients who had any of the seven most common systematic conditions among geriatric patients. Meta-analyses were performed on the postloading implant survival rates. The impact of systemic medical conditions and their respective treatment was qualitatively analyzed. Results: A total of 6,893 studies were identified; of those, 60

studies were included. The fixed-effects model revealed an overall implant survival of 97.3% (95% CI: 94.3, 98.7; studies = 7) and 96.1% (95% CI: 87.3, 98.9; studies = 3), for 1 and 5 years, respectively. In patients with cardiovascular disease, implant survival may be similar or higher compared to healthy patients. High implant survival rates were reported for patients with Parkinson's disease or diabetes mellitus type II. In patients with cancer, implant survival is negatively affected, namely by radiotherapy. Patients with bone metastases receiving high-dose antiresorptive therapy (ART) carry a high risk for complications after implant surgery. Implant survival was reported to be high in patients receiving low-dose ART for treatment of osteoporosis. No evidence was found on implant survival in patients with dementia, respiratory diseases, liver cirrhosis, or osteoarthritis. Conclusions: Implant prostheses in geriatric subjects are a predictable treatment option with a very high rate of implant survival. The functional and psychosocial benefits of such intervention should outweigh the associated risks to common medical conditions.
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NR 102
TC 136
Z9 168
U1 4
U2 41
PU WILEY
PI HOBOKEN

PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0905-7161
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J9 CLIN ORAL IMPLAN RES
JI Clin. Oral Implant. Res.
PD OCT 15
PY 2018
VL 29
IS
BP 311
EP 330
DI 10.1111/clr.13288
PG 20
WC Dentistry, Oral Surgery & Medicine; Engineering, Biomedical
SC Dentistry, Oral Surgery & Medicine; Engineering
GA GZ0SA
UT WOS:000449074000020
PM 30328186
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ER

PT J
AU Katchy, AU
Ezeobi, I
Katchy, SC
AF Katchy, A. U.
Ezeobi, I.
Katchy, S. C.
TI Acetabular Reconstruction Using a Cage in Complex Primary Total Hip Replacement in a Developing Country: An Assessment of Early Functional Outcome
SO NIGERIAN JOURNAL OF CLINICAL PRACTICE
LA English
DT Article
DE Acetabular defect; clinical outcome; complex primary total hip replacement; DePuy antiprotrusio cage
ID traumatic posterior dislocation; follow-up; revision arthroplasty; pelvic discontinuity; surgical technique; minimum 5-year; allograft bone; deficiency; components; classification
AB Background: Acetabular reconstruction following bone loss is a major challenge facing the arthroplasty surgeon. Traditionally, the armamentarium for the treatment of large bone defects (Paprosky Type 2C or 3) included antiprotrusio cages (APC). The aim of this study is to determine the pattern of presentation and assess the early functional outcome of patients who had undergone acetabular reconstruction using APC in complex primary total hip replacement (THR). Patients

and Method: Between November 2008 and November 2015, 38 THR were carried out in 35 patients who required acetabular reconstruction, at Davidson and Judith Consultants Clinics Enugu, Nigeria. Results: There were 25 males and 10 females, with a ratio of 2.5:1. The average age of the patients was 61.33 +/- 6.92 with a range of 56 to 72. The mean pre-op Harris score was 49.02 +/- 2.3. The mean post-op Harris hip score (HSS) was 88.75 +/- 10 ($P < 0.001$) at one year and 92.25 +/- 13 ($P < 0.001$) at 5 years. The etiology showed that most (52.63%) of our patients had primary osteoarthritis with Type 3 acetabular defect. Two (5.26%) patients had the following complications: dislocation (2.63%) and screw breakage (2.63%). The minimum follow-up period was 5 years. Discussion: After follow-up at 1 year and 5 years, the hips showed significant improvement concerning pain, gait, and mobility based on HHS and were able to return to their various professions. Conclusion: APC provides a satisfactory solution for patients who present with acetabular deficiency in complex primary THR.
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NR 29
TC 0
Z9 0
U1 0
U2 1
PU WOLTERS KLUWER MEDKNOW PUBLICATIONS
PI MUMBAI
PA WOLTERS KLUWER INDIA PVT LTD , A-202, 2ND FLR, QUBE, C T S NO 1498A-2 VILLAGE MAROL, ANDHERI EAST, MUMBAI, 400059, INDIA
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J9 NIGER J CLIN PRACT
JI Niger. J. Clin. Pract.
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DI 10.4103/njcp.njcp_136_18
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WC Medicine, General & Internal
SC General & Internal Medicine

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PM 30156203
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ER

PT J
AU Kroker, A
Manske, SL
Mohtadi, N
Boyd, SK
AF Kroker, Andres
Manske, Sarah L.
Mohtadi, Nicholas
Boyd, Steven K.
TI A study of the relationship between meniscal injury and bone microarchitecture in ACL reconstructed knees
SO KNEE
LA English
DT Article
DE HR-pQCT; Bone microarchitecture; Knee; Meniscus repair; Meniscectomy; Anterior cruciate ligament reconstruction
ID anterior cruciate ligament; subchondral bone; articular-cartilage; mineral density; partial meniscectomy; cancellous bone; high prevalence; soccer players; osteoarthritis; model
AB Background: Anterior cruciate ligament (ACL) tears increase the risk of developing knee osteoarthritis. This risk increases further with concurrent meniscus injury. The role of bone changes during knee osteoarthritis development are not well-understood, but may be important to its etiology. Purpose: To explore the effects of ACL tears on bone mineral density (BMD) and bone microarchitecture at five years post-op and their relationship to meniscal pathology, using high-resolution peripheral quantitative computed tomography (HR-pQCT). Methods: Twenty-eight participants with unilateral ACL reconstructions five years prior and no evidence of clinical or radiographic osteoarthritis were recruited. All participants represented one of three meniscus statuses: meniscus intact, meniscus repair, or meniscectomy. BMD and bone microarchitecture of the subchondral bone plate and adjacent trabecular bone were assessed using HR-pQCT, and percent-differences between the injured and contralateral knee were determined. Results: Subchondral bone plate thickness in the lateral femoral condyle was higher in the reconstructed knee (9.0%, $p = 0.002$), driven by the meniscus repair and meniscectomy groups (15.2% to 15.4%, $p < 0.05$). Trabecular BMD was lower in the reconstructed knee in the medial femoral condyle (-4.8% to 7.6%, $p < 0.05$), driven by all meniscus statuses. In the lateral compartments, few differences in trabecular bone were found. However, accounting for meniscus status, the meniscus intact

group had lower trabecular BMD throughout both femur and tibia. Conclusions: Five years post-op, reconstructed knees demonstrated detectable differences in BMD and bone microarchitecture, despite having normal radiographs. Meniscus damage affected primarily the lateral compartment, warranting further investigation to determine if these changes relate to osteoarthritis development (C) 2018 Elsevier B.V. All rights reserved.
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NR 48
TC 12
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U1 0
U2 2
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 0968-0160
EI 1873-5800
J9 KNEE
JI Knee
PD OCT 15
PY 2018
VL 25
IS 5
BP 746
EP 756
DI 10.1016/j.knee.2018.07.004
PG 11
WC Orthopedics; Sport Sciences; Surgery
SC Orthopedics; Sport Sciences; Surgery
GA GW6VB
UT WOS:000447100600003
PM 30115589
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ER

PT J
AU Chen, WJ
Mo, SY
Luo, G
Wang, YY
Deng, XH
Zhu, J
Zhao, W
AF Chen, Wenji
Mo, Shiyan
Luo, Gui
Wang, Yanyan
Deng, Xiaohu
Zhu, Jian
Zhao, Wei
TI Progressive pseudorheumatoid dysplasia with new-found gene mutation of Wntl

inducible signaling pathway protein 3
SO PEDIATRIC RHEUMATOLOGY
LA English
DT Article
DE Progressive pseudorheumatoid dysplasia; Wntl inducible signaling pathway protein 3
ID wisp3 mutations; arthropathy
AB Background: As one kind of osteochondrodysplasia, progressive pseudorheumatoid dysplasia (PPD) is also known as spondyloepiphyseal dysplasia tarda with progressive arthropathy or arthropathy progressive pseudorheumatoid of childhood. PPD is a very rare disease, especially in China, and has an estimated prevalence of 1/1000000 due to lacking definite prevalence survey. It is an autosomal recessive disorder caused by gene mutation of Wntl inducible signaling pathway protein 3 (WISP3). Its basic pathological change is persistent degeneration and loss of articular cartilage in multiple joints. Its clinical appearances include bone enlargement, platyspondyly, irregular endplate, secondary osteoarthritis, extensive osteoporosis, joint rigidity and function loss. Clinical diagnosis of PPD is made based on clinical appearance and imaging examinations, whereas its definite diagnosis depends on gene sequencing. PPD has no severe effect on life span, but causes high disability rate and very poor prognosis. There are only case reports with limited information in China. Case presentation: One female patient was diagnosed as PPD and secondary osteoarthritis. She had typical clinical appearance and imaging examinations, and received individualized therapeutic regimens. She had a gene mutation (c.72delT, p.T24TfsX4) of WISP3. This gene mutation has not been reported by previous literatures and included in Single Nucleotide Polymorphism Database. Conclusions: As the first time, this paper reported a patient with PPD caused by new-found gene mutation (c.72delT, p.T24TfsX4) of WISP3.
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CR Gao YS, 2013, JCR-J CLIN RHEUMATOL, V19, P138, DOI 10.1097/RHU.0b013e318289bf35
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NR 12
TC 5
Z9 6
U1 0
U2 3
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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EI
J9 PEDIATR RHEUMATOL
JI Pediatr. Rheumatol.
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WC Pediatrics; Rheumatology
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PT J
AU Yoo, JI
Kim, MJ
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AF Yoo, Jun-Il
Kim, Mi-Ji
Na, Jae-Bum
Chun, Yun-Hong
Park, Young-Jin
Park, Yongwhi
Hah, Young-Sool
Ha, Yong-Chan
Park, Ki Soo
TI Relationship between endothelial function and skeletal muscle strength in community dwelling elderly women
SO JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE
LA English
DT Article
DE Sarcopenia; Endothelial function; EndoPAT
ID sarcopenic obesity; disease; risk; prevalence; consensus
AB Background The aim of this study is to determine whether there is correlation between endothelial function and skeletal muscle function measured by hand grip strength in elderly women. Methods Results This cross-sectional study used data of NAMGARAM-2 cohort. The NAMGARAM-2 cohort consisted of a group of people living in three rural communities. They were enrolled for studies on activity limitation due to age-related musculoskeletal disorders including knee osteoarthritis, osteoporosis, and sarcopenia. They were residents aged 40 years or older. They agreed to participate in this cohort from March 2016 to May 2017. Peripheral endothelial function was assessed by reactive hyperaemia-peripheral arterial tonometry using EndoPAT2000 system. Hand grip strength was measured using a digital hand dynamometer. Endothelial function index assessed by EndoPAT was worse in the low grip strength group than that in the normal group of elderly women (1.54 +/- 0.51 in the low grip strength group vs. 1.77 +/- 0.67 in the normal group, P = 0.003). There was a positive correlation between hand grip strength and endothelial function (r = 0.176, P = 0.007). On stepwise multivariate analysis, endothelial dysfunction (reactive hyperaemia-peripheral arterial tonometry index < 1.67) significantly increased the risk of low hand grip strength (odds ratio = 2.019; 95% confidence interval = 1.107-3.682; P = 0.022). Conclusions Endothelial function and skeletal muscle strength had a significant correlation in elderly women, providing additional support for the relevant role of vascular system in sarcopenia.
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NR 30
TC 39
Z9 45
U1 1
U2 8
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 2190-6009
EI
J9 J CACHEXIA SARCOPENI
JI J. Caxhexia Sarcopenia Muscle
PD DEC 15
PY 2018
VL 9
IS 6
BP 1034
EP 1041
DI 10.1002/jcsm.12340
PG 8
WC Geriatrics & Gerontology; Medicine, General & Internal
SC Geriatrics & Gerontology; General & Internal Medicine
GA HA5SO

UT WOS:000450338100003
PM 30084166
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PT J
AU Hung, CC
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Fu, SH
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AF Hung, Chih-Chien
Wang, Chen-Yu
Fu, Shau-Huai
Yang, Rong-Sen
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TI Effects of anti-osteoporosis medications on total hip arthroplasty risks in osteoporotic patients with hip osteoarthritis in Taiwan: a nationwide cohort study
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Osteoporosis; Hip osteoarthritis; Total hip arthroplasty; Anti-osteoporosis medications
ID health insurance research; bone-marrow lesions; knee osteoarthritis; cartilage degradation; oarsi recommendations; biochemical markers; consensus; bisphosphonates; replacement; progression
AB A Summary This nationwide cohort study examined the potential disease-modifying effect of anti-osteoporosis medication on hip osteoarthritis. The results revealed that the usage of anti-osteoporosis medication is not associated with decreased risk in undergoing total hip arthroplasty in patient with hip osteoarthritis. Purpose This study aimed to assess the association between use of anti-osteoporosis medications (AOMs) and the risk of undergoing total hip arthroplasty (THA) in patients with hip osteoarthritis (OA). Methods Using the 2008-2013 National Health Insurance Research Database, we identified patients who were first diagnosed as having hip OA. All identified patients were followed until THA, death of any cause, or December 31, 2013, whichever occurred first. All AOM exposures were divided into three categories: bisphosphonates use, non-bisphosphonates use, and no use of AOMs and assessed in a time-varying manners. The primary outcome was THA. The secondary outcome was the differences in the longitudinal utilization of NSAIDs between AOM users and non-users. Time-dependent Cox proportional hazards models were used to investigate the effect of AOM use on the risk of THA. Results We identified 35,870 patients who were first diagnosed as having hip OA and had no history of AOM use between 2009 and 2012. Among them, 3162 and 1667 patients had their first

prescription of bisphosphonates and other non-bisphosphonates AOMs during the follow-up period. Mean age of bisphosphonates users, non-bisphosphonates users, and non-users was 75.62, 76.84, and 67.39 years, respectively. Bisphosphonates or non-bisphosphonates users did not show significant change when compared to non-users in terms of risk of undergoing THA [adjusted hazard ratio (aHR) 0.972, 95% confidence interval (CI) 0.743-1.273; aHR 0.926, 95% CI 0.672-1.277]. Conclusion Our results showed that the use of AOMs is not associated with decreased risk of THA in patients with hip OA.
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NR 46
TC 9
Z9 9
U1 0
U2 8
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 1862-3522
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J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
PD OCT 10
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IS 1
BP
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DI 10.1007/s11657-018-0522-9
PG 13
WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
GA GW5KE
UT WOS:000446970900002
PM 30306268
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PT J
AU Chen, Q
Bao, NR
Yao, QQ
Li, ZY
AF Chen, Qiang
Bao, Nirong
Yao, Qingqiang
Li, Zhi-Yong
TI Fractal dimension: A complementary diagnostic indicator of osteoporosis to bone mineral density
SO MEDICAL HYPOTHESES

LA English
DT Article
DE Osteoporosis; Diagnostic indicator; Fractal dimension; Bone mineral density
ID trabecular bone; postmenopausal women; risk; microarchitecture; osteoarthritis; radiographs; outcm; disease
AB Morbidity of osteoporosis is increasing as the world population grows and ages, but bone mineral density (BMD) as a common-used diagnostic indicator is not omnipotent in predicting the bone fragility. According to the definition of osteoporosis by World Health Organization (WHO), the present hypothesis proposes an additional fractal-dimension indicator less than 3 to measure the structural change of bones, and further to diagnose osteoporotic patients with complications, to which BMD is insensitive. Literature reports support that the fractal dimension is more sensitive than BMD in specific cases. The hypothesis shows a promise not only in improving the accuracy of screening osteoporotic patients as a complementary indicator to BMD, but also in evaluating mechanical properties of osteoporotic bone and bone-repair effect of bone tissue engineering.
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 0306-9877
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J9 MED HYPOTHESES
JI Med. Hypotheses
PD JUL 15
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WC Medicine, Research & Experimental
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PT J
AU Rizou, S
Chronopoulos, E
Ballas, M
Lyritis, GP
AF Rizou, S.
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Ballas, M.
Lyritis, G. P.
TI Clinical manifestations of osteoarthritis in osteoporotic and osteopenic postmenopausal women
SO JOURNAL OF MUSCULOSKELETAL & NEURONAL INTERACTIONS
LA English
DT Article
DE Osteoarthritis; Osteoporosis; Osteopenia; Postmenopausal Woman; Bone Mineral Density
ID neck-pain-questionnaire; bone-mineral density; fracture risk; epidemiology; prevalence; impact
AB Objective: We investigated the frequency of clinical manifestations of osteoarthritis in women with low BMD. Methods: This prospective epidemiological study investigated the degree of osteoarthritic pain and functional disability in symptomatic joints of a randomly selected population of postmenopausal Greek women aged >45 years with osteoporosis or osteopenia. Degree of osteoarthritic impairment (none, mild, moderate or severe) was classified at the knee, hip, neck or hand using a site-specific internationally validated osteoarthritis questionnaire. Results: 3000 women were included with mean age of 66.7 years. Osteoporosis was more common than osteopenia. Mild osteoarthritic impairment was most prevalent. An inverse relationship between severity of osteoarthritic impairment and mean femoral neck T-score was observed, regardless of site. There was a significant difference in mean femoral neck T-score between patients with severe osteoarthritic impairment and those with no, mild, or moderate impairment. This was also observed when lumbar spine BMD results were pooled. Conclusions: Most postmenopausal women with low BMD suffer from osteoarthritic impairment, with an inverse association between severity of osteoarthritic impairment and mean

femoral neck T-score. Mean lumbar spine or femoral neck T-scores of patients with severe osteoarthritic impairment were significantly lower than those of patients with less impairment.
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TI Advanced Therapy Medicinal Products: A Guide for Bone Marrow-derived MSC Application in Bone and Cartilage Tissue Engineering
SO TISSUE ENGINEERING PART B-REVIEWS
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DT Review
DE ATMPs; GMP; mesenchymal stromal cells; bone tissue engineering; cartilage tissue engineering
ID mesenchymal stem-cells; autologous chondrocyte implantation; sinus floor augmentation; collagen-based scaffold; cyclic tensile strain; platelet-rich plasma;

chondrogenic differentiation; osteogenic differentiation; articular-cartilage; stromal cells
AB Millions of people worldwide suffer from trauma- or age-related orthopedic diseases such as osteoarthritis, osteoporosis, or cancer. Tissue Engineering (TE) and Regenerative Medicine are multidisciplinary fields focusing on the development of artificial organs, biomimetic engineered tissues, and cells to restore or maintain tissue and organ function. While allogenic and future autologous transplantations are nowadays the gold standards for both cartilage and bone defect repair, they are both subject to important limitations such as availability of healthy tissue, donor site morbidity, and graft rejection. Tissue engineered bone and cartilage products represent a promising and alternative approach with the potential to overcome these limitations. Since the development of Advanced Therapy Medicinal Products (ATMPs) such as TE products requires the knowledge of diverse regulation and an extensive communication with the national/international authorities, the aim of this review is therefore to summarize the state of the art on the clinical applications of human bone marrow-derived stromal cells for cartilage and bone TE. In addition, this review provides an overview of the European legislation to facilitate the development and commercialization of new ATMPs.
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TI In vivo identification of Bmp2-correlation networks during fracture healing by means of a limb-specific conditional inactivation of Bmp2
SO BONE
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DT Article

DE Bmp2; Fracture healing; Co-expression; Differential gene expression; Conditional knockout; Networks
ID bone morphogenetic proteins; factor-beta superfamily; candidate genes; knee osteoarthritis; messenger-rna; expression; association; defects; osteoporosis; polymorphism
AB Bmp2 is known to play an essential role in the initiation of fracture healing via periosteal activation. Specifically, activation and subsequent differentiation of periosteal progenitor cells requires Bmp2 signaling for activation of the osteo-chondrogenic pathway. Here, we explored the interactive transcriptional gene-gene interplays between Bmp2 and 150 known candidate genes during fracture repair. We constructed the interactive Bmp2 signaling pathways in vivo, by comparing gene expression levels prior and 24 h post femur fracture, in presence (wild type) and in absence of Bmp2 (Bmp2c/c;Prx1::cre limb-specific conditional knockout). Twenty-six differentially expressed genes (pre- vs. post-fracture), which demonstrated high correlations within each experimental condition, were used to construct the co-expression networks. Topological dynamic shifts across different co-expression networks characterized the 26 differentially expressed genes as non-redundant focal linking hubs, redundant connecting hubs, periphery genes, or non-existent. Top-ranked up- or down-regulated genes were identified and discussed. Protein-protein interactions in public databases support our findings. Thus, the co-expression networks from this study can be used for future experimental hypotheses.
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TI Electrochemical surface-enhanced Raman scattering measurement on ligand capped PbS quantum dots at gap of Au nanodimer
SO SPECTROCHIMICA ACTA PART A-MOLECULAR AND BIOMOLECULAR SPECTROSCOPY
LA English
DT Article
DE EC-SERS; PbS quantum dots; Surface modification; Two-dimensional correlation spectroscopy
ID single-molecule; fatty-acid; oleic-acid; spectroscopy; sers; nanoparticles; gold; nanocrystals; electrodes; medicine
AB The vibrational characteristics of ligand-capped lead sulfide (PbS) quantum dots (QDs) were clarified via electrochemical surface-enhanced Raman spectroscopy (EC-SERS) using a hybridized system of gold (Au) nanodimers and PbS Qps under electrochemical potential control. Enhanced electromagnetic field caused by the coupling of QDs with plasmonic Au nanodimers allowed the characteristic behavior of the ligand oleic acid (OA) on the PbS Op surface to be detected under electrochemical potential control. Binding modes between the QDs and OA

molecules were characterized using synchronous two-dimensional correlation spectra at distinct electrochemical potentials, confirming that the bidentate bridging mode was probably the most stable mode even under relatively negative potential polarization. Changes in binding modes and molecular orientations resulted in fluctuations in EC-SERS spectra. The present observations strongly recommend the validity of the QD-plasmonic nanostructure coupled system for sensitive molecular detection via EC-SERS. (C) 2018 Elsevier B.V. All rights reserved.
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TI Comparison of a Patient-Centered Weight Loss Program starting before versus after knee replacement: A pilot study
SO OBESITY RESEARCH & CLINICAL PRACTICE
LA English
DT Article
DE Weight loss; Surgery; Intervention
ID total hip; physical-activity; arthroplasty; osteoarthritis; obesity; outcm; health; disease; surgery
AB Background: Most patients risk gaining weight in the years after knee replacement, adding further concern to a population that is mostly overweight/obese prior to surgery. Objective: Via a randomised pilot study, we assessed changes in weight during a Patient Centered Weight Loss Program (PACE) initiated either before or after knee replacement, while simultaneously examining

the feasibility of recruiting and retaining participants over 26 weeks. Methods: Recruitment outreach was made to 133 patients scheduled for knee replacement. Sixteen participants were randomised to a 14-session weight loss program that started either <6 weeks before surgery (PACE) or at 12 weeks post-op (Delayed PACE). Repeated measures ANOVAs were used to examine preliminary changes in weight, function, patient-reported outcomes, and physical activity across time (baseline/pre-op, 12 and 26 weeks after surgery) and group. Results: Retention was 75% and 69% at 12 and 26 weeks after surgery, respectively. Weight significantly decreased across the 26 weeks (P< 0.001). A group by time interaction (A= 0.03) demonstrated Delayed PACE [-7.6 +/- 5.9 kg (-7.9 +/- 5.9%)] lost significantly more weight than PACE [-2.5 +/- 2.7 kg (-2.6 +/- 2.6%)] participants at 26 weeks. Significant improvements across time were seen for all function and patient reported outcomes, however activity did not change. Conclusion: Conducting a behavioural intervention was challenging but feasible in a knee replacement population, with preliminary evidence suggesting that initiating a program 12 weeks after surgery produces greater weight losses at 26 weeks compared to a program starting before knee replacement. (C) 2018 Asia Oceania Association for the Study of Obesity. Published by Elsevier Ltd. All rights reserved.
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TI Trends and Determinants of Osteoporosis Treatment and Screening in Patients With Rheumatoid Arthritis Compared to Osteoarthritis
SO ARTHRITIS CARE & RESEARCH
LA English
DT Article
ID united-states; prevention; fracture; women; management; care; therapy; risk; men; disparity
AB Objective. To profile osteoporosis (OP) care in patients with rheumatoid arthritis (RA) over the past decade. Methods. Patients with RA or osteoarthritis (OA) were followed from 2003 through 2014. OP care was defined as receipt of OP treatment (with the exception of calcium/vitamin D) or screening (OPTS). Adjusted trends over followup, and the factors associated with OP care, were examined using multivariable Cox proportional hazards. Results. OPTS was reported in 67.4% of 11,669 RA patients and in 64.6% of 2,829 OA patients during a median (interquartile range) 5.5 (2-9) years of followup. In patients for whom treatment was recommended by the 2010 American College of Rheumatology (ACR) glucocorticoid-induced OP (GIOP) guidelines (48.4% of RA patients and 17.6% of OA patients), approximately 55% overall reported OP medication use. RA patients were not more likely to undergo OPTS compared to OA patients (hazard ratio 1.04 [95% confidence interval 0.94-1.15]). Adjusted models showed a stable trend for OPTS between 2004 and 2008 compared to 2003, with a significant downward trend after 2008 in both RA and OA patients. Factors associated with receipt of OP care in RA patients were older age, postmenopausal state, prior fragility fracture or diagnosis of OP, any duration of glucocorticoid treatment, and use of biologic agents. Conclusion. Approximately half of RA patients for whom treatment was indicated never received an OP medication. OP care in RA patients was not better than in OA patients, and the relative risk of the application of this care has been decreasing in RA and OA patients since 2008 without improvement after the release of the 2010 ACR GIOP guideline.
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U1 0
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PU WILEY
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 ARTHRIT CARE RES
JI Arthritis Care Res.
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PT J
AU Deng, S
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AF Deng, Shuang
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Nie, Zhi-Gang
Chen, Sen
Peng, Hao
TI Sesamin Protects the Femoral Head From Osteonecrosis by Inhibiting ROS-Induced Osteoblast Apoptosis in Rat Model
SO FRONTIERS IN PHYSIOLOGY
LA English
DT Article
DE sesamin; ONFH; dexamethasone; ROS; apoptosis
ID endothelial dysfunction; hypertensive-rats; cell-line; stress; activation; osteocytes; signal
AB Glucocorticoids intake has become the most common pathogenic factor for osteonecrosis of the femoral head (ONFH). Annually, tens of millions of patients suffer from pain related to ONFH. Researchers have proposed several underlying mechanisms of ONFH, including osteocyte apoptosis, cell differentiation disorder, and angiogenesis hindrance. Sesamin, isolated from Sesamum indicum seeds, was reported could affect osteocyte inflammation and differentiation in osteoarthritis and osteoporosis. We investigated the underlying influence of sesamin on ONFH rat model. Fifteen male Sprague-Dawley rats were randomly divided into three groups. The ONFH model group only received the methylprednisolone (MPS) and lipopolysaccharide (LPS) injection to promote the development of ONFH. The sesamin treatment group was injected with sesamin, MPS, and LPS. The control group was untreated. Rats from above groups were sacrificed 4 weeks later. The effect of sesamin on ONFH rats was validated by H&E staining. TUNEL staining

showed that femoral head necrosis was attenuated by sesamin. Furthermore, the phosphorylation of Akt was increased and the downstream cellular apoptosis signal pathway was inhibited. Intracellular ROS level was decreased after sesamin treatment. In conclusion, our findings suggest that sesamin protects the femoral head from osteonecrosis by inhibiting ROS-induced osteoblast apoptosis.
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NR 41
TC 33
Z9 38
U1 1
U2 23
PU FRONTIERS MEDIA SA
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AU Onder, G
Vetrano, DL
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TI Accounting for frailty when treating chronic diseases
SO EUROPEAN JOURNAL OF INTERNAL MEDICINE
LA English
DT Review
DE Frailty; Chronic diseases; Multimorbidity; Personalized medicine
ID older-adults; predict frailty; blood-pressure; health; pain; prevalence; impact; women; risk; osteoporosis
AB Chronic diseases are considered to be major determinants of frailty and it could be hypothesized that their treatment may counteract the development of frailty. However, the hypothesis that intensive treatment of chronic diseases might reduce the progression of frailty is poorly supported by existing studies. In contrast, some evidence suggests that intensive treatment of chronic diseases may increase negative health outcomes in frail older adults. In particular, if treatment of symptoms related to chronic diseases (i.e. pain in osteoarthritis, dyspnoea in respiratory disease, motor symptoms in Parkinson disease) might potentially reverse frailty, the benefits related to preventive pharmacological treatment of chronic diseases (i.e. antihypertensive treatment) in patients with prevalent frailty is not certain. In particular, several factors might alter the risk/benefit ratio of a given treatment in persons with frailty. These include: exclusion of frail persons from clinical studies, reduced life expectancy in frail persons, increased susceptibility to iatrogenic events, and functional deficits associated with frailty. Therefore, frailty acts as an effect modifier, by modifying the risks and benefits of chronic disease treatments. This hypothesis must be considered and tested in future clinical intervention studies and clinical guidelines should provide specific recommendations for the treatment of frail people, underlining the pros and the cons of pharmacological treatment and possible targets for therapy in this

population. Meanwhile, in older patients, the prescribing process should be individualized and flexible.
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NR 37
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Z9 90
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PU ELSEVIER SCIENCE BV
PI AMSTERDAM
PA PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
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WC Medicine, General & Internal
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PT J
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TI Sex disparities in health and health care utilization after Parkinson diagnosis: Rethinking PD associated disability
SO PARKINSONISM & RELATED DISORDERS
LA English
DT Article
DE Parkinson disease; Comorbidity; Gender; Epidemiology; Health services; Disparities
ID brain-stimulation surgery; medicare claims data; gender-differences; nonmotor symptoms; disease; women; accuracy; outcm; men
AB Objective: To examine sex differences and trends in comorbid disease and

health care utilization in individuals with newly diagnosed Parkinson disease (PD). Design: Retrospective cohort study. Participants: Over 133,000 Medicare beneficiaries with a new PD diagnosis in 2002 followed through 2008. Methods: We compared the prevalence and cumulative incidence of common medical conditions, trends in survival and health care utilization between men and women with PD. Results: Female PD patients had higher adjusted incidence rate ratio (IRR) of depression (IRR: 1.28, 1.25-1.31), hip fracture (IRR: 1.51, 1.45-1.56), osteoporosis (3.01, 2.92-3.1), and rheumatoid/osteoarthritis (IRR: 1.47,1.43-1.51) than men. In spite of greater survival, women with PD used home health and skilled nursing facility care more often, and had less outpatient physician contact than men throughout the study period. Conclusions: Women experience a unique health trajectory after PD diagnosis as suggested by differing comorbid disease burden and health care utilization compared to men. Future studies of sex differences in care needs, care quality, comorbidity related disability, PD progression, and non-clinical factors associated with disability are needed to inform research agendas and clinical guidelines that may improve quality survival for women with PD. (C) 2017 Elsevier Ltd. All rights reserved.
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CR Unknown -, 2001, INTERNATIONAL CLASSIFICATION OF FUNCTIONING, V0, P0
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NR 26
TC 28
Z9 31
U1 0
U2 3
PU ELSEVIER SCI LTD
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JI Parkinsonism Relat. Disord.
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WC Clinical Neurology
SC Neurosciences & Neurology
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PT J
AU Rossi, LMM
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AF Montagner Rossi, Lia Mara
Copes, Rafaela Martinez
Dal Osto, Leo Canterle
Flores, Clovis
Comim, Fabio Vasconcellos
Premaor, Melissa Orlandin
TI Factors related with osteoporosis treatment in postmenopausal women
SO MEDICINE
LA English
DT Article
DE bone densitometry; information; osteoporosis; post-menopause; treatment
ID bisphosphonate therapy; health plan; bone mass; persistence; adherence; fracture; determinants; medication; brazil; drugs
AB Although fractures had high mortality and morbidity, many studies proved that fracture risk might be decreased by pharmacological therapy, although a low treatment adherence rate is observed. The aim of this study was to identify factors associated with osteoporosis treatment in postmenopausal women. A

cross-sectional study was carried out from March to August 2013 at the primary care setting. Postmenopausal women were recruited. A standardized questionnaire was applied. Women who were using at least one of the following drugs at the moment of the survey were considered as current treatment: bisphosphonates, raloxifene, estrogen, calcitonin, teriparatide, or strontium ranelate. Women who had used any of the mentioned medications before the study were considered as past treatment. Of the 1025 women included in the study, 8% were on current treatment, 5.7% had past treatment, and 86.3% had not received treatment. Treated women (either current or past) had a higher rate of osteoarthritis, had more falls, had higher education level, presented a higher rate of private health insurance, and received more information about osteoporosis. They also had more dual-energy x-ray absorptiometry (DXA) scans and were more frequently diagnosed with osteoporosis by these DXA scans. The factors independently associated with treatment in the regression analysis were the DXA scan itself, the diagnosis of osteoporosis by DXA, and information about osteoporosis. Current and past treatments of osteoporosis were associated with DXA and information. These results suggest that some measures to inform women about osteoporosis and or even the popularization of DXA scans could improve the treatment.
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NR 33
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U2 9
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TI Age trajectoreis of musculoskeletal morbidities in adults with cerebral palsy
SO BONE
LA English
DT Article
DE Cerebral palsy; Osteoporosis; Arthritis
ID disabilities monitoring network; hip fracture; young-adults; ambulatory ability; muscle pathology; united-states; bone mass; children; prevalence; disease
AB Background: Individuals with cerebral palsy (CP) are at an increased risk for age-related morbidities due to functional impairments, maladapted growth, and altered body composition. While musculoskeletal (MSK) def lcits are present in children, little is understood about MSK morbidity throughout the lifespan in those with CP. The purpose of this study was to examine the age-related trajectories of

MSK morbidity and multimorbidity throughout adulthood in those with CP. Methods: A clinic-based sample of adults with CP (n = 1395; <= 18 years) was examined to determine prevalence of MSK morbidities at the University of Michigan Medical Center. Logistic regression was used to determine the effects of age on individual MSK morbidities and multimorbidity (i.e., <= 2 morbidities) after adjusting for sex, race, weight, and smoking. Results: With the 18-30 year age group as Lhe reference, the adjusted odds of osteopenia was lower in the 41-50 and > 50 year age groups, the odds of osteoporosis and rheumatoid arthritis was higher in 41-50 and > 50 year age groups, and the odds of osteoarthritis was higher in 31-40, 41-50, and > 50 year age groups. The adjusted odds of MSK multimorbidity increased substantially with increasing age for 31-40 year olds (OR 1 919; 95% CI 1.05-3.52), 41-50 year olds (OR 4.30; 95% CI 2.40-7.69), and > 50 year olds (OR 6.05; 95% CI 3.56-10.27). Conclusions: Adults with CP are at high risk for MSK morbidities across all ages. Future studies are needed to examine the global aging trajectories of MSK health among adults with CP. Study findings highlight the importance of maximizing MSK accretion, and developing programs to assist individuals with CP and their care givers to maintain MSK mass and function throughout the lifespan.

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TI Prevention of articular cartilage degeneration in a rat model of monosodium iodoacetate induced osteoarthritis by oral treatment with Withaferin A
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Chondrocytes; Cartilage; Osteoarthritis; Interleukin-1 beta; Monosodium iodoacetate
ID il-1-beta-induced inflammatory response; chondrocytes; mice; bone; disease; injury; mineralization; ossification; osteoporosis; hypertrophy

AB Withaferin A (WFA), a highly oxygenated withanolide is used for anti-osteoporotic, fracture healing, obesity control as medicine and dietary supplement in Ayurveda and Unani medicine but its potential remains to be investigate for the osteoarthritis studies. In the present study, chondro-protective effects of WFA, under in vitro and in vivo conditions were evaluated. In-vitro pharmacological activity of WFA was tested on rat articular chondrocytes through MTT, DPPH, different staining, FACS and translation studies. In-vivo studies of WFA were evaluated through monosodium iodoacetate (MIA) induced osteoarthritis studies. DPPH assay, alcian blue and toluidine blue staining indicated the chondrogenic potential of WFA. Similarly, WFA enhance chondrogenesis through up-regulation of SOX9 protein. In addition, WFA reduced the ROS generation, mitochondrial depolarization and apoptosis induced by inflammatory cytokines IL-1 beta and TNF-alpha. Furthermore, WFA treatment in MIA treated rats alleviated cartilage erosion and improvement in sub-chondral bone micro-architecture by decrease in Tissue volume (similar to 32%), and trabecular bone pattern factor (similar to 28%). Taken together, our study provides convincing evidence for the candidature of WFA (10 mg kg(-1) day(-1)) as a potential agent for the treatment of cartilage degenerative diseases like osteoarthritis.
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Z9 22
U1 0
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PA 65 RUE CAMILLE DESMOULINS, CS50083, 92442 ISSY-LES-MOULINEAUX, FRANCE
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PT J
AU Liu, CL
Liu, C
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AF Liu, Chenglei
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TI Relationship Between Subchondral Bone Microstructure and Articular Cartilage in the Osteoarthritic Knee Using 3T MRI
SO JOURNAL OF MAGNETIC RESONANCE IMAGING
LA English
DT Article
ID magnetic-resonance images; in-vivo mri; trabecular bone; topological analysis; resolution regime; tesla; microarchitecture; osteoporosis; arthritis; fracture
AB Background: The importance of subchondral bone in the pathogenesis of osteoarthritis (OA) has drawn interest. Purpose: To investigate subregional trabecular bone microstructural features and to determine the relationship between cartilage and trabecular bone in the osteoarthritic human knee. Study Type: Prospective study. Subjects: In all, 92 knees were enrolled and divided into three groups: without OA, mild OA, and severe OA. Sequence: A sagittal 3D balanced fast field echo (3D B- FFE) sequence and FatSat 3D fast field echo (3D-FFE) sequence at 3T MRI. Assessment: The trabecular bone in 12 sites of the knee joint was evaluated using digital topological analysis, and the cartilage thickness in four sites was calculated. Statistical Test: Trabecular bone and cartilage parameters between groups were compared using analysis of variance (ANOVA) with

Bonferroni adjustment, and their correlations were analyzed using Pearson's correlation coefficient. Results: Within both femoral condyles, the trabecular bone structure deteriorated in mild OA, showing a lower bone volume fraction (BVF) (0.15 to 0.12, P< 0.05), higher erosion index (EI) (2.25 to 2.28, P< 0.01), and a lower plate- to- rod ratio (SCR) (6.22 to 5.96, P< 0.05). Within medial and lateral tibia, deterioration in the trabecular bone was also observed, demonstrating a lower BVF (0.15 to 0.12 P< 0.05) and a higher EI (2.25 to 2.61, P< 0.05). Cartilage attrition mainly occurred in the medial joint. Extensive correlations were found between the medial cartilage thickness and subregional trabecular parameters. There was mainly a positive correlation with both femoral BVFs (r> 0.3, P< 0.05), and a negative correlation with the tibia SCR (r<- 0.2, P< 0.05). Data Conclusion: In the early stage of OA, trabecular bone osteoporotic changes were observed in both femoral condyles and the tibia. Based on a strong correlation with the medial cartilage thickness, the trabecular structural topological analysis may be useful for elucidating OA onset and progression. Level of Evidence: 2 Technical Efficacy: Stage 2
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JI J. Magn. Reson. Imaging
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WC Radiology, Nuclear Medicine & Medical Imaging
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AF Zhao, Hongxia
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Dong, Xin
Su, Jiacan
TI Integrative Bone Metabolomics-Lipidomics Strategy for Pathological Mechanism of Postmenopausal Osteoporosis Mouse Model
SO SCIENTIFIC REPORTS
LA English
DT Article

ID osteoblast proliferation; mass-spectrometry; mineral density; differentiation; metabonomics; insulin; acid; osteoarthritis; intervention; metabolism
AB Osteoporosis, characterized by bone mass reduction and increased fractures, has become a global health problem that seriously affects the health of people, especially postmenopausal women; however, the current pathogenesis of postmenopausal osteoporosis (PMOP) has not been thoroughly elucidated to date. In this study, bilateral ovariectomy was performed to establish an OVX mouse model of osteoporosis. UPLC-Q-TOF-MS-based lipidomics in combination with metabolomics were used to analyze the femur tissue of osteoporosis mice. We found that 11 polar metabolites and 93 lipid metabolites were significantly changed and were involved in amino acid metabolism, nucleotide metabolism and lipid metabolism. Among the lipids, fatty acyls, glycerolipids, glycerophospholipids, sphingolipids and sterols showed robust changes. These results revealed that several metabolic disorders caused by changes in the hormone levels in OVX, especially disordered lipid metabolism, are closely related to the imbalance between bone resorption and formation and may underlie the development of PMOP. The data generated via lipidomics and metabolomics presented in this study shows good applicability and wide coverage in the construction of the metabolic profile of bone tissue. Therefore, this approach may provide the pathway focusing and data support at the metabolite level for the in-depth mechanism of PMOP.
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Z9 90
U1 3
U2 44
PU NATURE PORTFOLIO
PI BERLIN
PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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J9 SCI REP-UK
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WC Multidisciplinary Sciences

SC Science & Technology - Other Topics
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AU Veronese, N
Punzi, L
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TI Sarcopenic osteoarthritis: a new entity in geriatric medicine?
SO EUROPEAN GERIATRIC MEDICINE
LA English
DT Review
DE Sarcopenia; Osteoarthritis; Physical performance; Therapy
ID serum 25-hydroxyvitamin d; vitamin-d supplementation; quality-of-life; knee osteoarthritis; physical frailty; orthostatic hypotension; mediterranean diet; hypovitaminosis d; european project; economic-aspects
AB Purpose Osteoarthritis, a disease characterized by cartilage degradation, abnormal subchondral bone remodeling and some grade of inflammation, and sarcopenia, a condition of low muscle mass associated with reduced strength and function, are prevalent disorders in older adults. In this review, we examine what is known about the relationship between osteoarthritis and sarcopenia, with particular focus on the older population. We also discuss how osteoarthritis and sarcopenia may interact and affect each other in clinical progression and the potential benefits from developing treatments that address such muscular-skeletal interaction. Methods We searched in Pubmed and Scopus through a combination of search and MESH terms, for osteoarthritis and sarcopenia. Results Even if more literature is needed, there is increasing evidence that decline in lower limb muscle strength is associated with knee or hip osteoarthritis in a pathological network of pain, altered joint stability, maladapted postures and defective neuromuscular communication. At the cellular levels, chondrocytes and myoblasts share common pathways, and the close anatomical location of both cell types also suggest the possibility of paracrine communication. Conclusions Sarcopenia and osteoarthritis

are significantly intercorrelated and in the near future should be considered as an only entity, as we have recently proposed for sarcopenia and osteoporosis. The treatment of both sarcopenia and osteoarthritis is based on physical exercise and nutritional interventions with the aim of improving cartilage, bone and muscle health. Future studies are needed, particularly to know the exact prevalence of sarcopenia in people with osteoarthritis, its peculiar consequences and the most appropriate treatments.
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NR 79
TC 18
Z9 20
U1 0
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PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 EUR GERIATR MED
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PT J
AU Tada, M
Inui, K
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AF Tada, Masahiro
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Koike, Tatsuya
TI Abatacept might increase bone mineral density at femoral neck for patients with

rheumatoid arthritis in clinical practice: AIRTIGHT study
SO RHEUMATOLOGY INTERNATIONAL
LA English
DT Article
DE Rheumatoid arthritis; Bone mineral density; Bone mineral markers; Osteoporosis; Abatacept
ID antitumor necrosis factor; double-blind; risk; methotrexate; efficacy; safety; classification; osteoporosis; multicenter; metabolism
AB We investigated the influence of abatacept (ABT) on bone mineral density (BMD) and bone metabolic markers (BMMs) in patients with rheumatoid arthritis (RA) compared to other biologic disease-modifying anti-rheumatic drugs (bDMARDs). This prospective, comparative, non-randomized study (the AIRTIGHT study; UMIN000005570) investigated the effects of ABT and other bDMARDs on bone metabolism. A total of 165 RA patients were divided into ABT (n = 50) and non-ABT (n = 115). We evaluated percentage changes in BMD (%Delta BMD) at the lumbar spine and femoral neck using dual-energy X-ray absorptiometry. Urinary levels of cross-linked N-telopeptide of type I collagen (uNTx) and bone-specific alkaline phosphatase (BAP) were used as markers of bone resorption and formation, respectively. No significant differences in 1-year completion rates were seen between ABT (64%) and non-ABT (72%; p = 0.387). The %Delta BMD at the femoral neck was significantly higher in the ABT group (0.97%) than in the non-ABT group (- 2.19%; p = 0.026). Whereas, no significant difference in %Delta BMD at the lumbar spine was observed between groups (ABT, - 0.40%; Non-ABT, - 1.67%; p = 0.524). No significant differences were observed in changes to uNTx or BAP. ABT treatment was significantly associated with increased BMD at the femoral neck (odds ratio (OR) 8.84; 95% CI 1.08-72.4; p = 0.04), and baseline lumbar osteoarthritis was significantly associated with BMD at the lumbar spine (OR 2.97; 95% CI 1.23-7.13; p = 0.02). The efficacy of ABT for increasing BMD at the femoral neck was superior to that of other bDMARDs. ABT may offer good efficacy for improving BMD at the femoral neck in patients with RA.
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NR 27
TC 35
Z9 42
U1 0
U2 2
PU SPRINGER HEIDELBERG
PI HEIDELBERG

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PT J
AU Mys, K
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AF Mys, Karen
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TI Quantification of bone microstructure in the wrist using cone-beam computed tomography
SO BONE
LA English
DT Article
DE Cone-beam computed tomography; Bone parameters; Micro-computed tomography; Medical imaging processing; Quantification
ID resolution; ct; accuracy; microarchitecture
AB Due to the rising life expectancy, bone diseases (e g osteoporosis, osteoarthritis) and trauma (e.g. fracture) have become an important socio-economic burden Accurate visualization and quantification of the bone micro structure in vivo is seen as an important step to enhance diagnosis and treatment. Micro-computed tomography (microCT) has become the gold standard in three-dimensional (3D) imaging of trabecular bone structure. Yet, usage is limited

to ex vivo analyses, hence, it cannot be used to evaluate bone and bone adaptive responses in a patient High-resolution peripheral computed tomography (HR-pQCT) is considered the best technique to measure the bone microarchitecture in vivo By design HR pQCT is limited to scanning extremities, such as the distal radius and distal tibia with a limited field of view and long scanning time (similar to 2a 3 mm for a stack of 0.9 cm). Cone-beam computed tomography (CBCT) is a promising alternative with a much larger field of view. Yet, CBCT is challenged by artefacts that reduce image contrast, such that it is currently being used for qualitative evaluation only. Therefore, the aims of this work were first to enhance image contrast and second to determine the accuracy of high-resolution CBCT for bone microarchitectural assessment. Trapezia of nineteen female arthritic patients were scanned twice ex vivo, once using CBCT (NewTom 5G, Cefla, Verona, Italy) at a nominal voxel size of 75 mu m and once using microCT (SkyScan 1172, Bruker, Kontich, Belgium) at a voxel size of 19 84 mu m. The CBCT-scans were reconstructed following 2 protocols: (1) using the commercial software delivered with the scanner and (2) using in-house developed software After reconstruction and image processing, the images were segmented using adaptive thresholding Bone morphometry parameters including bone volume (BV), total tissue volume (TV), bone volume fraction (BV/TV), bone surface density (BS/ TV), trabecular thickness (Tb.Th), trabecular separation (Tb Sp) and trabecular number (Tb N) were calculated Statistical evaluations were made at a significance level of 5%. Significant correlations were found between the CBCT based bone parameters and the microCT based parameters with R-2 > 0.68 The in house reconstructed software outperformed the commercial software. Smaller bias (overestimation of TbTh decreased from 114.24% to 59.96%) as well as higher correlations were observed for the in-house processed images. Still, a significant overestimation was observed for BV/TV and Tb. Th and an underestimation for Tb.N. We conclude that our CBCT image reconstruction improved image contrast which allowed for an accurate quantification of trabecular bone microarchitecture.

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NR 23
TC 30
Z9 31
U1 0
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PU ELSEVIER SCIENCE INC
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PA STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA
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J9 BONE
JI Bone
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WC Endocrinology & Metabolism
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PT J
AU Telleria, JJM
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AF Telleria, Jessica J. M.
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Chiodo, Christopher P.
Smith, Jeremy T.
TI Prevalence of Vitamin D Deficiency in Patients With Talar Osteochondral Lesions
SO FOOT & ANKLE INTERNATIONAL
LA English
DT Article
DE talus; osteochondral lesion; vitamin D; deficiency; hypovitaminosis D
ID united-states; talus; fractures; season; ankle; osteoarthritis; skin; osteoporosis; population; dissecans
AB Background: Vitamin D deficiency affects over 1 billion people worldwide and is common in foot and ankle patients. The prevalence in those with osteochondral lesions of the talus (OLTs) is unknown. This study identified the prevalence and risk factors for hypovitaminosis D in patients with an OLT. Methods: Serum 25(OH)D levels were obtained from patients presenting with an OLT from May to November during 2007 to 2016. Hypovitaminosis D was defined as 25(OH)D less than 30 ng/mL (75 nmol/L). Patients presenting with an acute ankle sprain (AS) during the same months served as a control group. Specific medical risk factors for hypovitaminosis D were recorded. The final OLT population included 46 patients (31 women [67.4%]; mean [SD] age 43.6 [14.8] years). The comparison AS group had 40 patients (32 women [80.0%]; mean [SD] age 56.2 [13.0] years). Results: The mean (SD) 25(OH)D in the OLT and AS cohorts were 31.2 (12.6) ng/mL and 37.1 (13.5) ng/mL, respectively (P = .039). Hypovitaminosis D was identified in 54% of the OLT population and 28% of the AS population (P = .012). Conclusion: Hypovitaminosis D is intimately related to decreased bone mineral density. This study identified a significantly higher rate of hypovitaminosis D in patients with an OLT compared to a cohort of AS patients. These findings suggest that when patients present with an OLT, health care providers should consider evaluating for and treating hypovitaminosis D. Level of Evidence: Level III, comparative study.
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AU Lavrador, P

Gaspar, VM
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TI Bioinspired bone therapies using naringin: applications and advances
SO DRUG DISCOVERY TODAY
LA English
DT Review
ID nf-kappa-b; controlled-release strategy; natural-products; rat model; osteoporosis; mechanisms; differentiation; angiogenesis; cartilage; expression
AB The use of natural compounds for treating chronic bone diseases holds remarkable potential. Among these therapeutics, naringin, a flavanone glycoside, represents one of the most promising candidates owing to its multifaceted effect on bone tissues. This review provides an up-to-date overview on naringin applications in the treatment of bone disorders, such as osteoporosis and osteoarthritis, and further highlights its potential for stem cell pro-osteogenic differentiation therapies. A critical perspective on naringin clinical translation is also provided. The topic is discussed in light of recently developed biomaterial-based approaches that potentiate its bioavailability and bioactivity. Overall, the reported pro-osteogenic, antiresorptive and antiadipogenic properties establish this flavanone as an exciting candidate for application in bone tissue engineering and regenerative medicine.
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AU Lv, HZ
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TI Multivariate analysis of factors related to radiographic knee osteoarthritis based

on the comparison between football players and matched nonsportsmen
SO INTERNATIONAL ORTHOPAEDICS
LA English
DT Article
DE Knee osteoarthritis; Osteoporosis; Joint wear; Body mass density
ID joint; arthritis; hip
AB Purpose Knee osteoarthritis (KOA) is the most common joint pathology worldwide and a major cause of later disability. It is unknown if the bone mass density (BMD) is correlated with KOA. This study aimed to investigate the prevalence of radiographic KOA among retired professional football players by comparing with matched nonsportsmen, and assess the correlation between BMD and KOA. Methods A cross-sectional, descriptive study was performed on a group of retired professional football players without history of knee injury. A control group of nonsporting volunteers was matched to the football player group in terms of age, height, weight, and body mass index (BMI). Uni- and multivariate analyses were performed to identify risk factors for KOA and predictors for knee function. Results Eighty-six retired male professional football players, with a mean age of 53 (51-58) years and an average period of professional career of 19.8 +/- 6.3 years, were enrolled into the study group. Eighty-six subjects were included in the control group. Radiographic KOA was more common in the control group (45.3%) than in the study group (15.1%;chi(2) = 18.633, P < 0.001). While the HSS, IKS score, and BMD of spine, femoral neck, and trochanter were all higher among sportsmen than the nonsportsmen (z = 10.250, z = 10.450, z = 7.237, z = 8.826, z = 8.776, all P < 0.001). Independent risk factors for ROA were age (55-60 + years, aOR 9.159, P < 0.001) and BMD (decrease, aOR 16.226, P = 0.001; osteoporosis, aOR 8.176, P = 0.005). The mathematical model of multiple linear regression for the HSS and IKS score were Y = 127.217-3.334 age + 8.971 BMD + 4.752 occupation and Y = 57.784-3.022 age + 7.241 BMD + 4.730 occupation, respectively. Conclusions This study reveals that low BMD and advanced age are independent risk factors for KOA. High BMD and regular exercise have a positive impact on knee function as evaluated with the use of HSS and IKS. Our findings guarantee further study to investigate the possibility that KOA may be caused by low BMD.
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AF Fang, Michele
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TI Race, Bundled Payment Policy, and Discharge Destination After TKA: The Experience of an Urban Academic Hospital
SO GERIATRIC ORTHOPAEDIC SURGERY & REHABILITATION
LA English
DT Article
DE payment reform; primary knee arthroplasty; racial disparity; discharge destination; readmission
ID total joint arthroplasty; care; disparity; medicare; outcm; knee
AB Background: Total knee arthroplasty (TKA) provides good clinical outcomes for the treatment of end-stage osteoarthritis; however, discharge destination after TKA has major implications on postoperative adverse outcomes and readmissions. With the initiation of Bundled Payments for Care Improvement (BPCI), it is unclear how racial disparities in discharge destination after TKA will be affected by the new bundled payment for TKA. Methods: Bundled Payments for Care Improvement was implemented in July 01, 2014, at the University of Pennsylvania. We compared differences during early implementation (July 1, 2014, to, March 30, 2016) and during late policy implementation (April 1, 2016, to February 28, 2017) in patient characteristics (including race: African American [AA], white, and other race), discharge destination (skilled nursing facility [SNF], inpatient rehabilitation facility, home, home with home health, or other), and outcomes. Results: We identified 2276 patients who underwent TKA (43.8% AA, 48.2% white, and 8.0% other race). African American patients were more likely to be discharged to SNF as opposed to home than white patients both during the early BPCI (AA: 53.0%, n = 320; white: 32.4%, n = 210, P < .05) and late BPCI implementation (AA: 44.4%, n = 169, white:

26.9%, n = 120, P < .05), though all races showed trends to decreasing SNF use during the late BPCI implementation. Discussion: There were no significant differences in readmissions, length of stay, mortality, or intensive care unit days during early and late implementation of BPCI or when AA patients were compared to white patients. Conclusion: We found no significant changes in racial variations in discharge destination and outcomes after elective TKA. Bundled Payments for Care Improvement has encouraged better preoperative preparation of patients and discharge planning; however, payment reforms alone might not be sufficient to address variation in post-op management following elective surgery.
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TI Treadmill Running Ameliorates Destruction of Articular Cartilage and Subchondral Bone, Not Only Synovitis, in a Rheumatoid Arthritis Rat Model
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE treadmill running; exercise; articular cartilage; rheumatoid arthritis; collagen-induced arthritis; pro-inflammatory cytokine; cnnexin43; osteoporosis
ID induced osteoarthritis; monoclonal-antibody; expression; alpha; methotrexate; connexin-43; recommendations; interleukin-6; infliximab; exercise
AB We analyzed the influence of treadmill running on rheumatoid arthritis (RA) joints using a collagen-induced arthritis (CIA) rat model. Eight-week-old male Dark Agouti rats were randomly divided into four groups: The control group, treadmill group (30 min/day for 4 weeks from 10-weeks-old), CIA group (induced CIA at 8-weeks-old), and CIA + treadmill group. Destruction of the ankle joint was evaluated by histological analyses. Morphological changes of subchondral bone were analyzed by -CT. CIA treatment-induced synovial membrane invasion, articular cartilage destruction, and bone erosion. Treadmill running improved these changes. The synovial membrane in CIA rats produced a large amount of tumor necrosis factor- and Connexin 43; production was significantly suppressed by treadmill running. On -CT of the talus, bone volume fraction (BV/TV) was significantly decreased in the CIA group. Marrow star volume (MSV), an index of bone loss, was significantly increased. These changes were significantly improved by treadmill running. Bone destruction in the talus was significantly increased with CIA and was suppressed by treadmill running. On tartrate-resistant acid phosphate and alkaline phosphatase (TRAP/ALP) staining, the number of osteoclasts around the pannus was decreased by treadmill running. These findings indicate that treadmill running in CIA rats inhibited synovial hyperplasia and joint destruction.
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Z9 26
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN 1422-0067
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J9 INT J MOL SCI
JI Int. J. Mol. Sci.
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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PT J
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AF Song, Yuanzheng
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TI Bone quality, and the combination and penetration of cement-bone interface A comparative micro-CT study of osteoarthritis and rheumatoid arthritis
SO MEDICINE
LA English
DT Article
DE bone-cement interface; bone quality; micro-CT; osteoarthritis; rheumatoid arthritis
ID mineral density; cancellous bone; bristol oa500; femoral-head; osteoporosis; disease; model; micromechanics; progression; frequency
AB To compare the microstructure, bone quality, and the combination and penetration of cement-bone interface in tissue specimens from patients with osteoarthritis (OA) and rheumatoid arthritis (RA). A total of 80 femoral condyle tissue specimens from 20 OA patients (40 condyles) and 20 RA patients (40 condyles) who underwent total knee arthroplasty at the Department of Orthopaedics in Tengzhou Central People's Hospital were collected between January 2017 and September 2017. According to the random number table method, 20 specimens from the OA group were defined as group A, and 20 specimens in the RA group were defined as group B The bone quality parameters were measured by micro-CT. The remaining 20 specimens in the OA group and the remaining 20 specimens in the RA group were defined as group C and group D, the cement-bone interfaces were established by the self-made bone cement compression device, and were analyzed by micro-CT. Micro-CT measurement revealed that the bone volume fraction (BV/TV), trabecular thickness (Tb.Th), and trabecular number (Tb.N) in group A were significantly higher than those in group B (all $P < .05$). The bone surface/bone volume (BS/BV), structure model index (SMI), trabecular separation (Tb.Sp), and degree of anisotropy (DA) in group A were significantly lower than those in group B (all $P < .05$). The penetration depth of bone cement in group D was significantly greater than those in group C via x-ray detection. The bone quality of OA patients is better than that of RA patients, but the combination and penetration of cement-bone interface of RA patients are better than that of OA patients. The findings advance our understanding of knee prosthesis and have important clinical implications, but they require validations in future studies with larger sample sizes.

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PU LIPPINCOTT WILLIAMS & WILKINS
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J9 MEDICINE
JI Medicine (Baltimore)
PD AUG 15
PY 2018
VL 97
IS 35
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WC Medicine, General & Internal
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TI Extracorporeal shock wave treatment can normalize painful bone marrow edema in knee osteoarthritis A comparative historical cohort study
SO MEDICINE
LA English
DT Article
DE alendronate; bone marrow edema; MRI; osteoarthritis; pain; shock wave
ID necrotic femoral heads; intravenous ibandronate; transient osteoporosis; pressure measurements; core decompression; subchondral bone; hip; therapy; rabbits; expression
AB Bone marrow edema (BME) represents a reversible but highly painful finding in magnetic resonance imaging (MRI) of patients with knee osteoarthritis. The aim of this retrospective study was to evaluate the efficacy of extracorporeal shock wave treatment (ESWT) on painful BME in osteoarthritis of the knee. This study focuses on people who had early-to-mid stage osteoarthritis with knee pain and MRI findings of BME. Patients who underwent ESWT treatment or prescribed alendronate treatment in our department were analyzed. Knee pain and function were measured using the visual analog scale (VAS) for pain and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC), respectively. The degree of BME was measured with MRI scans. A total of 126 patients who received ESWT treatment (Group A, n=82) or alendronate treatment (Group B, n=44) were included. All patients were followed up clinically and radiographically for a minimum of 12 months. The mean follow-up was 23.5 months (range, 12-38 months). The VAS and WOMAC score decreased more significantly after treatment in Group A than that in Group B (P<.01) within 3 months. In 6-month MRI follow-ups, there was higher incidence of distinct reduction and complete regression of BME of the affected knee in Group A than that in Group B (P<.01). ESWT is an effective, reliable, and noninvasive treatment in patients with painful BME in osteoarthritis of the knee followed by a rapid normalization of the MRI appearance. It has the potential to shorten the natural course of this disease.
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PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
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J9 MEDICINE
JI Medicine (Baltimore)
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WC Medicine, General & Internal
SC General & Internal Medicine
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TI Ultrastructural change of the subchondral bone increases the severity of cartilage damage in osteoporotic osteoarthritis of the knee in rabbits
SO PATHOLOGY RESEARCH AND PRACTICE
LA English
DT Article
DE Osteoarthritis; Osteoporosis; Subchondral bone; Cartilage; Scanning electron microscopy
ID tougu xiaotong capsule; articular-cartilage; experimental-model; pathogenesis;

prevalence; morphology; hip
AB Osteoporotic osteoarthritis is a phenotype of osteoarthritis (OA) manifested as fragile and osteoporotic subchondral bone. However, the ultrastructural features of subchondral bone in osteoporosis OA have not been determined. The study was aimed to investigate the ultrastructural dynamic changes of subchondral bone in osteoporotic OA model and how the ultrastructural damage in the subchondral bone caused by osteoporosis deteriorated the cartilage damage in OA. Eighteen rabbits were equally randomized to three groups, including the control, the OA and the osteoporotic OA groups. The structural changes of cartilage were evaluated by HE and safranin-O fast green staining, the Mankin's grading system was used to assess the stage of OA progression. And microstructural or ultrastructural changes in subchondral bone were assessed by micro-computed tomography or by scanning electron microscopy. According to the changes of cartilage histopathology, the OA group was in the early pathological stage of OA while the osteoporotic OA group was in the middle stage of OA based on Mankin's grading system. In addition, the damage of cartilage surface, reduction in the number of chondrocytes and the matrix staining were more increased in the osteoporotic OA group compared to the OA group. Compared to the OA group, the subchondral bone in the microstructure and ultrastructure in the osteoporotic OA group showed more microfracture changes in trabecular bone with more destructions of the tree-like mesh. Moreover, the collagen fibers were random rough with a fewer amount of bone lacunae in subchondral cortical plate in the osteoporotic OA group compared to the OA group. These findings indicated that the subchondral bone ultrastructure in the osteoporotic OA model was characterized by the destruction of the network structure and collagen fibers. The subchondral bone ultrastructural damage caused by osteoporosis may change mechanical properties of the upper cartilage and aggravate OA cartilage. Therefore, early diagnosis and treatment of osteoporosis is of great significance to prevent early OA from further developing osteoporotic OA.
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NR 40
TC 19
Z9 24
U1 0
U2 32
PU ELSEVIER GMBH
PI MUNICH
PA HACKERBRUCKE 6, 80335 MUNICH, GERMANY
SN 0344-0338
EI
J9 PATHOL RES PRACT
JI Pathol. Res. Pract.
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BP 38
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PG 6
WC Pathology
SC Pathology
GA GB5EN
UT WOS:000429086000006
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ER

PT J
AU Anderson, KB
Holloway-Kew, KL
Mohebbi, M
Kotowicz, MA
Hans, D
Pasco, JA
AF Anderson, Kara B.
Holloway-Kew, Kara L.
Mohebbi, Mohammadreza
Kotowicz, Mark A.
Hans, Didier
Pasco, Julie A.
TI Is trabecular bone score less affected by degenerative-changes at the spine than lumbar spine BMD?
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Trabecular bone score; Men; Lumbar spine degenerative-changes; Bone mineral density
ID predicts osteoporotic fractures; mineral density; geelong osteoporosis; tbs; men; women; microarchitecture; osteoarthritis; osteopenia; diagnosis
AB It has been established that degenerative-changes at the spine elevate bone mineral density at the lumbar spine. This study in men reports that trabecular bone score may be less affected by spinal degenerative-changes.PurposeA recent tool for assessing trabecular microarchitecture at the lumbar spine, trabecular bone score (TBS), provides information about bone health complementary to lumbar spine areal BMD (here referred to as BMD). In men, mean BMD increases with increasing age due to degenerative-changes at the spine including osteophytes and aortic calcification. The aim of this study was to investigate whether TBS is similarly affected by the presence of degenerative-changes in men.MethodsThis study included 728 men aged 40-90years enrolled in the Geelong Osteoporosis Study. Lumbar spine DXA scans (Lunar Prodigy) were used to determine TBS retrospectively (TBS iNsight software, Version 2.2), and for identification of degenerative-changes. Using multivariable regression techniques, the relationships between TBS or BMD and degenerative-changes were assessed, further adjusting for age and weight. The difference between each of the two methods was examined through testing interactions between method, degenerative-changes and age.ResultsOf 728 men, 439 (60.3%) were identified as having one or more degenerative-changes at the lumbar spine. Adjusted mean TBS was 1.219 (1.203-1.232) and 1.196 (1.179-1.212) for those with and without degenerative-changes, respectively. Adjusted mean BMD was 1.317g/cm(2)

(1.297-1.336) and 1.198g/cm(2) (1.173-1.223) for those with and without degenerative-changes, respectively. Partial r(2) for degenerative-changes in the model for TBS was 0.076 and for BMD, 0.257 (both p<0.05). The three-way interaction between method, degenerative-changes and age was significant (p=0.05) indicating significant effect of artefacts on the standardised values, affected by age and method.ConclusionThis study suggests that TBS is less affected by degenerative-changes at the spine than is BMD. Thus, TBS may prove useful in the assessment of fracture risk in men with degenerative-changes at the spine.
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10.1007/s00774-007-0793-5
NR 17
TC 41
Z9 45
U1 0
U2 4
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 1862-3522
EI 1862-3514
J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
PD NOV 16
PY 2018
VL 13
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BP
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DI 10.1007/s11657-018-0544-3
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WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
GA HA7YY
UT WOS:000450504200002
PM 30446835
DA 2026-02-10
ER

PT J
AU Parratte, S
Ollivier, M
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AF Parratte, S.
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TI Primary total knee arthroplasty for acute fracture around the knee
SO ORTHOPAEDICS & TRAUMATOLOGY-SURGERY & RESEARCH
LA English
DT Review

DE Distal femur fracture; Proximal tibia fracture; Total knee arthroplasty; Elderly; Osteoporosis; Adult
ID distal femoral fractures; elderly-patients; supracondylar fractures; osteoporotic fractures; hip fracture; revision; replacement; management; femur; mortality
AB Relatively poor results have been reported with open reduction and internal fixation of complex fractures around the knee in elderly osteoporotic patients, and primary total knee arthroplasty (TKA) has been proposed as an alternative solution. While limiting the number of procedures, it meets two prerequisites: (1) to save the patient's life, thanks to early weight-bearing, to limit decubitus complications; and (2) to save knee function and patient autonomy, thanks to early knee mobilization. There are 3 main indications: complex articular fractures in elderly patients with symptomatic osteoarthritis prior to fracture; complex articular fractures of the tibial plateau in elderly patients whose bone quality makes internal fixation hazardous; and major destruction of the distal femur in younger patients. Although admitted in emergency, these patients require adequate preoperative management, including a multidisciplinary approach to manage comorbidities, control of anemia and pain, and assessment and management of vascular and cutaneous conditions. Preoperative planning is crucial, to order appropriate implants and materials that may be needed intraoperatively. Surgical technique is based on the basic principles of revision surgery as regards choice of implant, steps of reconstruction, bone defect management and implant fixation. For complex fractures of the distal femur, primary temporary reduction is a useful "trick", to determine the level of the joint line and femoral rotation. Complementary internal fixation may be required incase of diaphyseal extension of the fracture and to prevent inter-prosthetic fractures. In the literature, the results of primary TKA for fracture are encouraging and better than for secondary TKA after failure of non-operative treatment or internal fixation, with lower rates of revision and complications, earlier full weight-bearing and better functional results. Loss of autonomy is, however, frequent, and 1-year mortality is high, especially following complex femoral fractures in the elderly. (c) 2017 Elsevier Masson SAS. All rights reserved.
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NR 26
TC 33
Z9 51
U1 1

U2 7
PU ELSEVIER MASSON, CORPORATION OFFICE
PI PARIS
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EI
J9 ORTHOP TRAUMATOL-SUR
JI Orthop. Traumatol.-Surg. Res.
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WC Orthopedics; Surgery
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ER

PT J
AU Hu, H
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AF Hu, He
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Li, Wei
Liu, Caiyun
Guo, Ai
TI Osteoactivin inhibits dexamethasone-induced osteoporosis through up-regulating integrin β1 and activate ERK pathway
SO BIOMEDICINE & PHARMACOTHERAPY
LA English

DT Article
DE BMSC; ERK; Intergrin beta 1; Osteoactivin; Osteoporosis
ID mesenchymal stem-cells; osteoclast differentiation; regeneration; expression; plays
AB Backgrounds: Dexamethasone (Dex) is widely used in autoimmune diseases and inflammation treatment. A sever side effect of prolonged exposure to Dex is increased risk of osteoporosis (OP) or even femoral head necrosis, which would cause much suffer to patients. To reveal the mechanism behind this phenomenon, provide therapeutic guidance and potential target, we analyzed the inhibitory mechanism of Dex on osteogenesis of rat-BMSC. Methods: Rat BMSC were obtained and characterized with FACS analysis. Osteogenesis and adipogenesis abilities were detected with Oil-O-Red staining, Alizarin Red staining and ALP activity analysis. These BMSC were then treated with Dex in combination with recombinant OA or not and detected for osteogenesis related gene expression with qRT PCR. Protein interaction and expression were detected by Co-Immunoprecipitation and western blot. Results: Osteoactivin (OA) could promote integrin beta 1 expression and interact with this protein physically, leading to ERK activation and promoting osteogenesis related genes' expression including Runx2, Coll a and OCN in BMSC. Dex, however, could block expression of several upstream genes of OA and decrease OA mRNA and protein level, and eventually suppress integrin beta 1 ERK activation and lead to decreased osteogenesis, which could finally develop into OP. Conclusion: Recombinant OA treated BMSC exerted better osteogenesis potency even with Dex administration. This is because additional OA in medium counter-acts with Dex's influence and rescued osteoblast differentiation via up-regulating integrin beta 1 and activate ERK/MAPK pathway which promotes osteogenesis. Hence, OA/integrin beta 1 could serve as potential therapeutic target for OP.
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NR 21
TC 27
Z9 34
U1 2
U2 38
PU ELSEVIER FRANCE-EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER
PI ISSY-LES-MOULINEAUX
PA 65 RUE CAMILLE DESMOULINS, CS50083, 92442 ISSY-LES-MOULINEAUX, FRANCE
SN 0753-3322
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J9 BIOMED PHARMACOTHER
JI Biomed. Pharmacother.
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WC Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Research & Experimental Medicine; Pharmacology & Pharmacy
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ER

PT J
AU Park, ES
Ahn, SS
Jung, SM
Song, J
Park, YB
Lee, SW
AF Park, Eun Seong
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TI Application of 2012 EULAR/ACR criteria for polymyalgia rheumatica to Korean patients previously classified by Chuang and Hunder criteria or Healey criteria
SO INTERNATIONAL JOURNAL OF RHEUMATIC DISEASES
LA English
DT Article
DE classification criteria; polymyalgia rheumatica; reclassification
AB Aim: To apply 2012 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) criteria to Korean patients previously classified as polymyalgia rheumatica (PMR) by Chuang and Hunder criteria or Healey criteria and investigated whether they might be still reclassified as PMR or not. Methods: We retrospectively reviewed the medical records of 113 previously classified PMR patients. We applied 2012 EULAR/ACR criteria without ultrasonography to PMR patients, and fulfilment required at least 4 points. We evaluated odds ratios (OR) using logistic regression analyses. Results: The mean age was 61.7 years. Seventy-one patients (62.8%) fulfilled Chuang and Hunder criteria, and 113 patients (100%) met Healey criteria. When we applied 2012 EULAR/ACR criteria, 98 patients fulfilled essential items (>= 50 years, bilateral shoulder aching and abnormal C-reactive protein or erythrocyte sedimentation rate), and only 80 patients

achieved points >= 4. Eight patients fulfilling the criteria exhibited higher frequencies of all the detailed items than those who did not. In multivariate logistic regression analysis, absence of rheumatoid factor or anti-citrullinated peptide antibodies was the only independent contributing item to the fulfilment of 2012 EULAR/ACR criteria (OR 23.571, 95% CI 6.357-87.407, P < .001). When we reclassified 33 excluded patients, the most common newly classified disease was generalized osteoarthritis (24.2%), followed by osteoporosis with compression fracture (15.2%). Conclusion: Eighty of 113 patients (81.6%) previously classified by Chuang and Hunder criteria or Healey criteria fulfilled 2012 EULAR/ACR criteria for PMR.
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NR 12
TC 2
Z9 3
U1 0
U2 0
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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JI Int. J. Rheum. Dis.
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WC Rheumatology
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PT J
AU Wang, YZ
Kou, JQ
Zhang, HN
Wang, CY
Li, HY
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Zhang, YT
AF Wang, Yingzhen
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Zhang, Haining
Wang, Changyao
Li, Haiyan
Ren, Yuanzhong
Zhang, Yongtao
TI The renin-angiotensin system in the synovium promotes periarticular osteopenia in a rat model of collagen-induced arthritis
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Article
DE Periarticular osteopenia; Rheumatoid arthritis; Renin-angiotensin system; Synovial tissue; Bone metabolism; Perindopri
ID rheumatoid-arthritis; converting enzyme; therapeutic target; type-1 receptor; bone; differentiation; inhibitor; rankl; osteoporosis; mechanisms
AB Periarticular osteopenia is the most specific hallmark of rheumatoid arthritis

(RA). The renin-angiotensin system (RAS) in the synovium has been found to participate in the pathogenic process of RA. This study examined whether and how RAS regulates periarticular osteopenia in RA. The synovial tissues from patients with RA and osteoarthritis (OA) were prepared. Female Sprague-Dawley rats were treated with either saline, bovine type II collagen (CII) to induce arthritis (CIA), or CII combined with perindopril, an inhibitor of angiotensin-converting enzyme (ACE). Expressions of RAS components, including AT1R, AT2R and ACE, in human and rat synovial tissues were detected. Bone mass of rat joints was examined. Levels of RANKL, OPG and DKK-1 in rat synovium and expressions of TRAF6 and beta-catenin in rat bone were examined. The results showed that AT1R, AT2R and ACE in human and rat synovium were up-regulated, but the increased ACE in rat synovial tissues was abrogated by perindopril. While CIA rats displayed increased bone resorption and decreased bone formation, perindopril treatment almost completely abrogated the RAS-mediated osteopenia, indicating that inhibition of ACE reduced the joint damages in rats. The expressions of RANKL and DKK-1 increased in CIA rats as compared with those in the control; TRAF6 was up-regulated and beta-catenin was down-regulated in the bone tissues of CIA rats. The changes were then reversed by the use of perindopril. Our findings demonstrate that RAS in the synovium promotes periarticular osteopenia by increasing bone resorption and decreasing bone formation through modulating the RANKL/RANK/TRAF6 and Wnt/beta-catenin pathways.
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TI The effects of POSS particles on the flame retardancy of intumescent polypropylene composites and the structure-property relationship
SO POLYMER DEGRADATION AND STABILITY
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DT Article
DE Polypropylene; Flame retardant; POSS; Intumescence
ID polyhedral oligomeric silsesquioxane; mechanical-property; thermal-degradation; fire retardancy; polymer nanocomposites; ammonium polyphosphate; physical-property; epoxy-resin; behavior; flammability
AB In the current study, the effects of four different POSS nanoparticles on the flame retardant properties of intumescent PP were investigated through mass-loss calorimetry (MLC), limiting oxygen index (LOI) test and UL-94 ratings. In addition,

the structure-property relationship was enlightened via thermal, morphological and mechanical tests. The four different POSS types, namely aminopropyl isobutyl-POSS (A-POSS), octaphenyl-POSS (OP-POSS), octaammonium-POSS (OA-POSS) and trissulfonic acid propyl-POSS (TS-POSS), were used. The ratio of ammonium polyphosphate (APP) to pentaerythritol (PER) was kept constant and the POSS content was varied as 0.5%, 1% and 3%. The MLC, LOI and UL-94 tests revealed that the addition of POSS particles had adjuvant on the flame retardant properties of PP/IFR system. All POSS nanoparticles showed their highest adjuvant effect at the lowest concentration of 0.5 wt%. The highest UL-94 rating and the highest LOI values were achieved in the presence of OA-POSS and TS-POSS. The ceramic layer formation was monitored using scanning electron microscopy (SEM) and FTIR on the char residues. The thermal properties of PP/IFR/POSS composites were obtained via differential scanning calorimeter and thermo-gravimetric analysis. The inline melt flow properties were observed via vertical force measurements. The fracture morphology was investigated using SEM. Mechanical tests showed that the yield strengths of the composites were lower than that of pristine PP; in contrast, the elongation at break and the impact strength of composites enhanced in A-POSS and TS-POSS based composites.
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TI Exposure Duration Is a Determinant of the Effect of Sinusoidal Electromagnetic Fields on Peak Bone Mass of Young Rats
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DE Sinusoidal electromagnetic fields; Exposure duration; Osteoblasts; Peak bone mass; Bone mineral density
ID mesenchymal stem-cells; magnetic-field; double-blind; osteogenic differentiation; knee osteoarthritis; clinical-trial; in-vitro; mineralization; osteoporosis; stimulation
AB We proposed a three-step strategy to obtain the optimal therapeutic parameters, which is composed of large-scale screening at cellular level, verification in animal experiments, and confirmation by a clinical trial. The objective of the current study was to test the feasibility of our strategy. Newborn rat calvarial osteoblasts were treated by 50 Hz 1.8 mT sinusoidal electromagnetic fields (SEMFs) with 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 h/days, respectively. The osteogenic differentiation and maturation of the osteoblast were assayed and compared to obtain the optimal duration. One-month-old growing rats were then treated by the same SEMFs with 0.5, 1.5, and 2.5 h/days, respectively, and the peak bone mass was analyzed after 2 months. It was found that the optimal exposure duration to promote the osteogenic differentiation and maturation of osteoblasts was 1.5 h/days, judging by the increasing degrees of ALP activity, calcified nodules formed, the gene and protein expression levels of Runx-2, BMP-2, and Col-I, as well as the expression levels of signaling proteins of the BMP-2/Smad1/5/8 pathway. The highest increase of peak bone mass after 2 months was also obtained by 1.5 h/days, judging by the results of X-ray dual-energy absorptiometry, mechanical property analysis, micro-CT scanning, and serum bone turnover marker examinations. The above results indicated that exposure duration is a determinant for the therapeutic effect of EMFs, and the optimal therapeutic effects only can be obtained by the optimal exposure duration.
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NR 45
TC 7
Z9 9
U1 0
U2 17
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
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PT J
AU Beaudart, C
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TI Quality of life assessment in musculo-skeletal health
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Quality of life; Musculo-skeletal health; Sarcopenia; Osteoporosis; Osteoarthritis; Frailty
ID rheumatoid-arthritis; older-people; osteoporotic fractures; vertebral fractures; incident fractures; physical frailty; clinical-trials; mortality risk; global burden; hip fracture
AB Musculoskeletal disorders affect morbidity, quality of life and mortality, and represent an increasing economic and societal burden in the context of population aging and increased life expectancy. Improvement of quality of life should be one of the priorities of any interventions to prevent and treat musculoskeletal disorders in the ageing population. Two main approaches, namely generic and disease-specific instruments, can be applied to measure health-related quality of life. Among the generic tools available in scientific literature, the short form 36 questionnaire (SF-36) and the Euroqol five item questionnaire (EQ-5D) are two of the most popular questionnaires used to quantify the health related quality of life in people with musculoskeletal disorders. However, because generic tools may not always be able to detect subtle effects of a specific condition on quality of life, a specific tool is highly valuable. Specific tools improve the ability to clinically characterize quality of life in subjects with a specific musculoskeletal disorder, as well as the capacity to assess changes over time in the QoL of these subjects. The recent development of specific tools should help to validate preventive and therapeutic interventions in this field.
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NR 88
TC 98
Z9 116
U1 0
U2 16
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 AGING CLIN EXP RES
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WC Geriatrics & Gerontology
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PT J
AU Kirzner, N
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AF Kirzner, Nathan
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TI Reverse shoulder arthroplasty vs BIO-RSA: clinical and radiographic outcomes at short term follow-up
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH

LA English
DT Article
DE Reverse shoulder arthroplasty; BIO-RSA; Scapular insufficiency fractures; Scapular notching; Functional outcomes
ID glenohumeral osteoarthritis; prosthesis; fractures; cuff; classification; complications; reliability; arthritis; revision; design
AB BackgroundBony increased-offset reverse shoulder arthroplasty (BIO-RSA) may address issues such as inferior scapular notching, prosthetic instability and limited postoperative shoulder rotation; all of which have been reported with the standard RSA and attributed to the medialized design. We hypothesised that this lateralization may increase the rate of scapular stress fractures.MethodsA retrospective review of prospectively collected data was performed on patients who had undergone a RSA between January 2013 and October 2016. A comparative cohort study was designed to compare patients with a standard Grammont-style RSA to those with a BIO-RSA using the same implant. Functional outcome was measured by the American Shoulder and Elbow Surgeons (ASES) Shoulder Score, the Subjective Shoulder Value (SSV), the Western Ontario Osteoarthritis of the Shoulder (WOOS) index and pain scores. Radiographs were obtained for all patients and examined for the presence of scapular fracture as well as scapular notching and graft incorporation.ResultsA total of forty patients (22 patients in the standard RSA cohort and 18 with BIO-RSA) were included in the study. Patient characteristics (including age, gender, length of follow-up, dominant side and osteoporosis) were similar in both groups ($p>0.05$). The average postoperative follow-up was 20months (range 12-48months). There was bone graft incorporation in all BIO-RSA patients at the final radiological follow-up, with no evidence of graft resorption. The overall scapular stress fracture rate was 12.5% (9.1% in the standard RSA and 16.7% in the BIO-RSA). The rates were similar in both cohorts ($p=0.64$). All fractures were managed conservatively. To determine whether the presence of a scapular stress fracture had an influence on outcomes, the cohort was divided into cases with and without fracture. Patients with a stress fracture had worse ASES ($p=0.028$) and WOOS ($p=0.048$) scores. Additionally, osteoporosis was present more commonly in the fracture group (80% vs 17%; $p=0.01$). A statistically significant difference was identified when comparing the rates of scapular notching between standard RSA and BIO-RSA cohorts (68% vs 33%; $p=0.028$). Furthermore, when notching was present, significantly worse outcome scores were present in all outcome measures ($p<0.001$).ConclusionThe BIO-RSA technique was associated with an increase in scapular stress fracture rate when compared to the standard RSA; however, this was not found to be significant. Furthermore, both techniques resulted in similar improvements in the measured functional outcomes. BIO-RSA, however, was associated with a lower scapular notching rate, justifying further evaluation of this technique.Level of evidenceRetrospective cohort study, level III
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NR 32
TC 36
Z9 43
U1 0
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PI LONDON
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TI Osteoimmunology: The Nexus between bone and immune system
SO FRONTIERS IN BIOSCIENCE-LANDMARK
LA English
DT Article
DE Osteoimmunology; Osteoblasts; Osteoclasts; Bone loss; Treg cell; Th17 cell; Ovariectomy; Osteoporosis; RA; Osteoarthritis; Review
ID growth-factor-beta; kappa-b ligand; tumor-necrosis-factor; regulatory t-cells; phosphoinositide 3-kinase p110-delta; natural-killer-cells; rheumatoid-arthritis; receptor activator; dendritic cells; estrogen deficiency
AB Osteoimmunology is an interdisciplinary research field which combines the existing fields of osteology (bone biology) and immunology under one umbrella. The observation that contributed enormously to the emergence of osteoimmunology as an independent field of investigation was the enhanced bone loss in various inflammatory bone diseases such as rheumatoid arthritis, osteoporosis and periodontitis. T helper cells (Th1, Th2, Treg and Th17) along with various other immune cells (B cells, DC, macrophages etc.) are actively involved in bone homeostasis. The present review thus provides an overview of the nexus between these two prominent systems (Bone and Immune system) of an organism, which reside in a common niche (bone marrow) and thus cross-commumcate to modulate their respective development. Investigations in the field of osteoimmunology thus promise the advent of new era in the field with novel therapeutics for bone loss in various inflammatory conditions. A molecular insight into the field of osteoimmunology can lead to novel approaches for the prevention and treatment of diverse inflammatory conditions such as osteoporosis, rheumatoid arthritis and osteoarthritis.
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TI Nrf2 as a therapeutic target for rheumatic diseases
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DT Article
DE Nrf2; Rheumatic conditions; Rheumatoid arthritis; Systemic lupus erythematosus; Osteoarthritis; Osteoporosis
ID nf-kappa-b; erythroid 2-related factor-2; systemic-lupus-erythematosus; human osteoarthritis chondrocytes; t-cell-activation; heme oxygenase-1; nlrp3 inflammasome; antioxidant response; signaling pathway; oxidative stress
AB Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) is a master regulator of cellular protective processes. Rheumatic diseases are chronic conditions characterized by inflammation, pain, tissue damage and limitations in function. Main examples are rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis and osteoporosis. Their high prevalence constitutes a major health problem with an important social and economic impact. A wide range of evidence indicates that Nrf2 may control different mechanisms involved in the physiopathology of rheumatic conditions. Therefore, the appropriate expression and balance of Nrf2 is necessary for regulation of oxidative stress, inflammation, immune responses, and cartilage and bone metabolism. Numerous studies have demonstrated that Nrf2 deficiency aggravates the disease in experimental models while Nrf2 activation results in immunoregulatory and anti-inflammatory effects. These reports reinforce the increasing interest in the pharmacologic regulation of Nrf2 and its potential

applications. Nevertheless, a majority of Nrf2 inducers are electrophilic molecules which may present off-target effects. In recent years, novel strategies have been sought to modulate the Nrf2 pathway which has emerged as a therapeutic target in rheumatic conditions.
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NR 100
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Thornton, Wendy Loken
TI The role of illness burden in theory of mind performance among older adults
SO EXPERIMENTAL AGING RESEARCH
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DT Article
ID cognitive function; executive function; age-differences; hypertension; guidelines; management
AB Background/Study Context: Theory of Mind (ToM) reflects the ability to reason about mental states in order to understand and predict behavior. Research has identified links between increased pulse pressure, a measure of vascular health, and reduced cognitive ToM in older adults. However, the relationships between other vascular and nonvascular conditions and reduced ToM are unknown. We examined (1) illnesses as predictors of cognitive and affective ToM and (2) neurocognitive mediators of illness burden and ToM. Methods: We used hierarchical regression and mediation to investigate the effects of vascular illness burden (hypertension, Type 2 diabetes, high cholesterol, and high pulse pressure) and nonvascular illness burden (osteoporosis, osteoarthritis, rheumatoid arthritis, and thyroid dysfunction) on cognitive and affective ToM in N = 86 community-dwelling older adults (59 females; 27 males, M age = 71.74 years). Results: Vascular illness burden emerged as a significant predictor of older adults' cognitive ToM (R-2 = .43, p < .001), and this relationship was mediated by executive functioning. Nonvascular illness burden did not predict cognitive nor affective ToM in this sample. Conclusion: Our findings highlight the specific importance of considering vascular health as a risk factor for declines in ToM in later life. Further elucidation of the associations between health, neurocognition, and ToM will be valuable in developing effective interventions for older adults given the high prevalence of vascular illness in later life.
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TI A long-lasting bisphosphonate partially protects periprosthetic bone, but does not enhance initial stability of uncemented femoral stems: A randomized placebo-controlled trial of women undergoing total hip arthroplasty
SO JOURNAL OF BIOMECHANICS
LA English
DT Article
DE Total hip arthroplasty; Radiostereometric analysis; Bone mineral density; Bisphosphonates; Postmenopausal osteoporosis
ID early implant migration; yearly zoledronic acid; double-blind; follow-up; mineral density; radiostereometric analysis; postmenopausal women; 2-year rsa; fixation; osteoarthritis
AB Low bone quality may compromise the success of cementless total hip arthroplasty in high-risk patients such as elderly women. Zoledronic acid is a long-lasting antiresorptive agent, which is known to reduce short-term periprosthetic bone loss. However, its effect on femoral stem stability is not well known. Forty-nine female patients with a mean age of 68 years (range, 51-85 years) scheduled to undergo cementless total hip arthroplasty due to osteoarthritis were randomized in this double-blind, placebo controlled trial to receive a single postoperative infusion of zoledronic acid or placebo. Patients were evaluated for up to four years postoperatively for femoral stem migration measured by radiostereometric analysis, bone mineral density (BMD) measured by dual X-ray absorptiometry, functional recovery, and patient-reported outcome scores. Implant survival was determined at nine years postoperatively. Zoledronic acid did not reduce the femoral stem migration that occurred predominantly during the settling period of the first 3-6 months. Subsequently, all femoral stems were radiographically osseointegrated. Zoledronic acid maintained periprosthetic BMD, while the expected loss of periprosthetic bone during the first 12 months was

found in controls. Thereafter, periprosthetic BMD of Gruen zone 7 decreased even in the zoledronic acid group but remained 14.6% higher than that in the placebo group at four years postoperatively. Functional recovery was comparable across the groups. At nine years postoperatively, no revision arthroplasty had been performed. In conclusion, in women at high-risk for low BMD, zoledronic acid had a long-lasting, partially protective effect on periprosthetic bone loss, but the treatment did not enhance the initial femoral stem stability. (C) 2018 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license.
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TI Integrating genome-wide DNA methylation and mRNA expression profiles identified different molecular features between Kashin-Beck disease and primary osteoarthritis
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Article
DE Kashin-Beck disease; Osteoarthritis; Methylation; Gene expression
ID susceptibility gene; articular-cartilage; abnormal expression; skeletal growth; chondrocytes; association; china; glycosaminoglycans; osteoporosis; metabolism
AB Background: Kashin-Beck disease (KBD) is an endemic osteochondropathy of unknown etiology. Osteoarthritis (OA) is a form of degenerative joint disease sharing similar clinical manifestations and pathological changes to articular cartilage with KBD. Methods: A genome-wide DNA methylation profile of articular cartilage from five KBD patients and five OA patients was first performed using the Illumina Infinium HumanMethylation450 BeadChip. Together with a previous gene expression profiling dataset comparing KBD cartilage with OA cartilage, an integrative pathway enrichment analysis of the genome-wide DNA methylation and the mRNA expression profiles conducted in articular cartilage was performed by InCroMAP software. Results: We identified 241 common genes altered in both the DNA methylation profile and the mRNA expression profile of articular cartilage of KBD versus OA, including CHST13 (NM_152889, fold-change = 0.5979, P-methy = 0.0430), TGFBR1 (NM_004612, fold-change = 2.077, P-methy = 0.0430), TGFBR2 (NM_001024847, fold-change = 1.543, P-methy = 0.037), TGFBR3 (NM_001276, fold-change = 0.4515, P-methy = 6.04 x 10(-4)), and ADAM12 (NM_021641, fold-change = 1.9768, P-methy = 0.0178). Integrative pathway enrichment analysis identified 19 significant KEGG pathways, including mTOR signaling (P = 0.0301), glycosaminoglycan biosynthesis-chondroitin sulfate/dermatan sulfate (P = 0.0391), glycosaminoglycan biosynthesis-keratan sulfate (P = 0.0278), and PI3K-Akt signaling (P = 0.0243). Conclusion: This study identified different molecular features between Kashin-Beck disease and primary osteoarthritis and provided novel clues for clarifying the pathogenetic differences between KBD and OA.
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TI Oleanolic Acid and Ursolic Acid Improve Bone Properties and Calcium Balance and Modulate Vitamin D Metabolism in Aged Female Rats
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE oleanolic acid; ursolic acid; bone protection; calcium balance; vitamin D metabolism; aged rats
ID fructus-ligustri-lucidi; parathyroid-hormone; ethanol extract; 25-hydroxyvitamin d-3; 1,25-dihydroxyvitamin d-3; mineral density; gene-expression; in-vitro; osteoblast differentiation; 1-alpha-hydroxylase gene
AB Oleanolic acid (OA) and ursolic acid (UA) are the major chemical constituents in Fructus Ligustri Lucidi (FLL), a kidney-tonifying Chinese herb that is previously shown to improve bone properties and enhance calcium balance in aged female rats. The present study was designed to study if OA and UA act as the active ingredients in FLL to exert the positive effects on bone and mineral metabolism in aged rats. Aged (13-month-old) Sprague-Dawley female rats were randomly assigned to four groups with oral administration of drug or vehicle treatment for 12 weeks: medium calcium diet (MCD, 0.6% calcium), high calcium diet (HCD, 1.2% calcium), MCD + FLL (700 mg/kg/day), MCD + OA (23.6 mg/kg/day) + UA (8.6 mg/kg/day). A group of mature (3-month-old) female rats fed with MCD was

included as positive control. The results demonstrated that FLL and OA+UA increased bone mineral density and improved microarchitectural properties of aged female rats. The osteoprotective effects of FLL and OA+UA might be, at least in part, associated with their actions on enhancing calcium balance and suppressing age-induced secondary hyperparathyroidism in aged female rats. FLL and OA+UA also significantly induced renal CYP27B1 protein expression and OA+UA treatment decreased CYP24A1 mRNA and protein expressions in aged female rats. In addition, FLL and OA+UA significantly increased the promoter activity, mRNA and protein expressions of renal CYP27B1 in vitro in human proximal tubule HKC-8 cells. The present findings suggest that OA+UA can be regarded as the active ingredients of FLL and might be a potential drug candidate for prevention and treatment of osteoporosis.
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TI MRI-detected osteophytes of the knee: natural history and structural correlates of change
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Article
DE Osteoarthritis; Magnetic resonance imaging; Osteophyte; Natural history
ID radiographically diagnosed osteophytes; population-based cohort; cartilage volume loss; older-adults; imaging findings; surface-area; joint space; osteoarthritis; association; pain
AB BackgroudThe natural history of semi-quantitative magnetic resonance imaging (MRI)-detected osteophytes (MRI-detected OPs) has not been described and it is unknown whether knee structural abnormalities can predict MRI-detected OP change over time. Thus, the aim of current study is to describe the natural history of knee MRI-detected OP, and to determine if knee structural abnormalities are associated with change of MRI-detected OP in a longitudinal study of older adults.MethodsRandomly selected older adults (n = 837, mean age 63years) had MRI at baseline and 413 of them had MRI 2.6years later to measure MRI-detected OP, cartilage defects, cartilage volume, bone marrow lesions (BMLs), meniscal extrusion, infrapatellar fat pad (IPFP) quality score/maximum area and effusion-synovitis.ResultsOver 2.6years, average MRI-detected OP score increased significantly in all compartments. The total MRI-detected OP score remained stable in 53% of participants, worsened (1-point increase) in 46% and decreased in 1%. Baseline cartilage defects (RR, 1.25-1.35), BMLs (RR, 1.16-1.17), meniscal extrusion (RR, 1.22-1.33) and IPFP quality score (RR, 1.08-1.20) site-specifically and independently predicted an increase in MRI-detected OP (p values all 0.05), after adjustment for covariates. Presence of IPFP abnormality was significantly associated with increased MRI-detected OPs but became non-significant after adjustment for other structural abnormalities. Total (RR, 1.27) and suprapatellar pouch effusion-synovitis (RR, 1.22) were both associated with increased MRI-detected OPs in the lateral compartment only (both p<0.04).ConclusionKnee MRI-detected OPs are common in older adults and are likely to progress. The association between

baseline structural abnormalities and worsening MRI-detected OPs suggest MRI-detected OP could be a consequence of multiple knee structural abnormalities.
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NR 49
TC 12
Z9 15
U1 0
U2 6
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN 1478-6354
EI 1478-6362
J9 ARTHRITIS RES THER
JI Arthritis Res. Ther.
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PY 2018
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IS
BP
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DI 10.1186/s13075-018-1734-5
PG 11
WC Rheumatology
SC Rheumatology
GA GX9IU
UT WOS:000448116300001
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TI Risk factors for nonunion of bone fracture in pediatric patients An inception cohort study of 237,033 fractures
SO MEDICINE
LA English
DT Article
DE cardiovascular disease; fracture nonunion; opioid use; risk factors; scaphoid fractures; tobacco smoking; vitamin D deficiency
ID atypical femoral fractures; shaft fractures; limb fractures; children; bisphosphonates; pain; osteoporosis; metaanalysis; management; initiation
AB Adult fracture nonunion risk is related to injury severity and surgical technique, yet nonunion is not fully explained by these risk factors alone; biological risk factors are also important. We test a hypothesis that risk factors associated with pediatric fracture nonunion are similar to adult nonunion risk factors. Inception cohort study in a large payer database of pediatric fracture patients (0-17 years) in the United States in calendar year 2011. Continuous enrollment in the database was required for 12 months, to allow time to capture a nonunion diagnosis. The final database collated demographic descriptors, treatment procedures as per Current Procedural Terminology (CPT) codes, comorbidities as per International Statistical Classification of Diseases and Related Health Problems (ICD-9) codes, and drug prescriptions as per National Drug Code Directory (Red Book) codes. Logistic regression was used to calculate odds ratios (ORs) for variables associated with nonunion. Among 237,033 pediatric fractures in 18 bones, the nonunion rate was 0.85%. Increased nonunion risk was associated with increasing age, male gender, high body-mass index, severe fracture (e.g., open fracture, multiple fractures), and tobacco smoking (all, P < .0001). Nonunion rate varied with fracture location; scaphoid, neck of femur, and tibia/fibula were most likely to go to nonunion. Nonunion ORs were significantly increased for risk factors including; surgical procedure, cardiovascular disease, Vitamin D deficiency, osteoarthritis, osteoporosis, and opioid prescription (all, multivariable P < .001). Nonunion is rare in pediatric patients, but nonunion risk increases with increasing age. We confirm a hypothesis that risk factors for pediatric nonunion are similar to adult nonunion risk factors. Scaphoid fractures in adolescents have nearly the same risk of nonunion as in adults. Opioids should be used cautiously in pediatric patients, as they are associated with a significant and substantial elevation of nonunion risk.
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CR Antonova E, 2013, BMC MUSCULOSKEL DIS, V14, P0, DOI 10.1186/1471-2474-14-42
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NR 37
TC 39
Z9 44
U1 0
U2 12
PU LIPPINCOTT WILLIAMS & WILKINS
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PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
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J9 MEDICINE
JI Medicine (Baltimore)
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WC Medicine, General & Internal
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TI Prevalence and co-existence of locomotive syndrome, sarcopenia, and frailty: the third survey of Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Disability; Locomotive syndrome; Sarcopenia; Frailty; Co-existence
ID bioelectrical-impedance analysis; dwelling elderly subjects; older-adults; association; mass; consensus; decline
AB This study aimed to estimate the prevalence of locomotive syndrome, sarcopenia, and frailty and clarify their co-existence in a population-based cohort. The third survey of Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study was conducted between 2012 and 2013, examining 963 subjects (aged >= 60 years; 321 men, 642 women). Locomotive syndrome, sarcopenia, and frailty were defined using three tests proposed by Japanese Orthopaedic Association, Asian Working Group for Sarcopenia criteria, and Fried's definition, respectively. Prevalence of locomotive syndrome stages 1 and 2 were 81.0% (men, 80.4%; women, 81.3%) and 34.1% (men, 30.5%; women, 35.8%), respectively, and those of sarcopenia and frailty were 8.7% (men, 9.7%; women, 8.3%) and 4.5% (men, 2.8%; women, 5.3%), respectively. Locomotive syndrome stage 1, sarcopenia, and frailty co-existed in 2.1%; 6.5% had locomotive syndrome stage 1 and sarcopenia, 2.4% had locomotive syndrome stage 1 and frailty, while none had sarcopenia and frailty. Locomotive syndrome stage 1 presented alone in 70.0%, sarcopenia in 0.1%, and no frailty. The remaining 18.9% had none of these conditions. Co-existence of locomotive syndrome stage 2, sarcopenia, and frailty

was observed in 2.0%; 5.0% had locomotive syndrome stage 2 and sarcopenia, 2.2% had locomotive syndrome stage 2 and frailty, and 0.1% had sarcopenia and frailty. Locomotive syndrome stage 2, sarcopenia, and frailty alone, presented in 24.9%, 1.7%, and 0.2%, respectively. The remaining 64.0% had none of these conditions. Most subjects with sarcopenia and/or frailty also had locomotive syndrome. Preventing locomotive syndrome may help prevent frailty and sarcopenia and subsequent disability.
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NR 31
TC 90
Z9 108
U1 0
U2 18
PU SPRINGER JAPAN KK
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SN 0914-8779
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J9 J BONE MINER METAB
JI J. Bone Miner. Metab.
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WC Endocrinology & Metabolism; Medicine, Research & Experimental
SC Endocrinology & Metabolism; Research & Experimental Medicine
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PT J
AU Yuenyongviwat, V
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AF Yuenyongviwat, V
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TI Effect of glucosamine sulfate on intraocular pressure in patients with knee osteoarthritis: A prospective randomized controlled trial
SO JOURNAL FRANCAIS D OPHTALMOLOGIE
LA English
DT Article
DE Knee osteoarthritis; Crystalline glucosamine sulfate; Intraocular pressure; Osteoarthritis
ID european-society; economic-aspects; osteoporosis; management
AB Purpose. Glucosamine sulfate is one of the treatment options for patients with osteoarthritis of the knee. It has been postulated that glucosamine sulfate affects intraocular pressure (10P), This study aimed to evaluate the effect of crystalline glucosamine sulfate on 10P in patients with osteoarthritis of the knee. Methods. Forty-two patients with osteoarthritis of the knee were randomized into two groups. The first group of patients received 1500 mg of crystalline glucosamine sulfate once daily for 6 months and the conventional treatment protocol. The second group of patients received only the conventional treatment protocol. 10P was recorded at the start of the study and at 6 weeks, 3 months, 6 months, and 9 months. Results. The patient demographic data were not different between the two groups. There were no differences in the 10Ps between the groups ($P > 0.05$) nor differences in baseline 10Ps within each group compared with each follow-up visit ($P > 0.05$). Conclusions. Glucosamine sulfate is still an option without significant concern over elevated 10P in patients with osteoarthritis of the knee and normal ocular pressure. (C) 2019 Elsevier Masson SAS. All rights reserved.
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NR 9
TC 2
Z9 3
U1 0
U2 8
PU MASSON EDITEUR
PI MOULINEAUX CEDEX 9
PA 21 STREET CAMILLE DESMOULINS, ISSY, 92789 MOULINEAUX CEDEX 9, FRANCE
SN 0181-5512
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J9 J FR OPHTALMOL
JI J. Fr. Ophthamol.
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BP 711
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WC Ophthalmology
SC Ophthalmology

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PT J
AU Xia, WB
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TI East meets West: current practices and policies in the management of musculoskeletal aging
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review

DE Osteoarthritis; Osteoporosis; Sarcopenia; FRAX; Prevention; Treatment
ID bone turnover markers; nonsteroidal antiinflammatory drugs; chinese postmenopausal women; hydroxy-beta-methylbutyrate; vitamin-d supplementation; serum 25-hydroxyvitamin d; knee osteoarthritis; muscle strength; hyaluronic-acid; global burden
AB Healthy aging is defined as the process of developing and maintaining the functional ability that enables wellbeing in older age. Healthy aging is dependent upon intrinsic capacity, a composite of physical and mental capacities, and the environment an individual inhabits and their interactions with it. Maintenance of musculoskeletal health during aging is a key determinant of functional ability. Sarcopenia, osteoporosis and osteoarthritis, are a triad of musculoskeletal diseases of aging that are major contributors to the global burden of disease and disability worldwide. The prevention and management of these disorders is of increasing importance with pressure mounting from the aging population. In a new initiative, the Chinese Medical Association, Chinese Society of Osteoporosis and Bone Mineral Research, and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases jointly organized a symposium to discuss current practices and policies in the management of musculoskeletal aging. The meeting allowed experts from Europe and China to share their experience and recommendations for the management of these three major diseases. Discussing and analyzing similarities and differences in their practice should lead, through a mutual enrichment of knowledge, to better management of these diseases, in order to preserve intrinsic capacity and retard the age-related degradation of physical ability. In future, it is hoped that sharing of knowledge and best practice will advance global strategies to reduce the burden of musculoskeletal disease and promote healthy aging tailored to meet the individual patient's needs.
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TI Biodegradable polymers: an update on drug delivery in bone and cartilage diseases
SO EXPERT OPINION ON DRUG DELIVERY
LA English
DT Review
DE Bone diseases; cartilage diseases; biodegradable polymers; drug delivery systems; controlled drug release; targeted drug delivery; tissue engineering
ID mesenchymal stem-cells; autologous chondrocyte implantation; sustained-release formulation; thickness chondral defects; collagen-induced arthritis; in-vitro characterization; growth-factor receptor; rheumatoid-arthritis; plga nanoparticles; targeted delivery
AB Introduction: The unique structure of bone and cartilage makes the systemic delivery of free drugs to those connective tissues very challenging. Consequently, effective and targeted delivery for bone and cartilage is of utmost importance. Engineered biodegradable polymers enable designing carriers for a targeted and temporal controlled release of one or more drugs in concentrations within the therapeutic range. Also, tissue engineering strategies can allow drug delivery to advantageously promote the in situ tissue repair. Areas covered: This review article highlights various drug delivery systems (DDS) based on biodegradable biomaterials to treat bone and/or cartilage diseases. We will review their applications in osteoporosis, inflammatory arthritis (namely osteoarthritis and rheumatoid arthritis), cancer and bone and cartilage tissue engineering. Expert opinion: The increased knowledge about biomaterials science and of the pathophysiology of diseases, biomarkers, and targets as well as the development of innovative tools has led to the design of high value-added DDS. However, some challenges persist and are mainly related to an appropriate residence time and a controlled and sustained release over a prolonged period of time of the therapeutic agents. Additionally, the poor prediction value of some preclinical animal models hinders the translation of many formulations into the clinical practice.
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TI PROFILE OF PATIENTS WITH OSTEOPOROTIC FRACTURES AND FACTORS THAT DECREASE PREVENTION
SO ACTA ORTOPEDICA BRASILEIRA
LA English
DT Article
DE Osteoporotic Fractures; Osteoporosis; Epidemiology; Prevalence; Secondary Prevention
ID implementation; people; models; care
AB Objective: To evaluate the epidemiological profile of patients with osteoporotic fractures compared to patients with osteoarthritis (OA) and identify factors that diminish adherence to secondary prevention. Methods: A total of 108 patients with osteoporotic fractures (OF) were compared to 86 patients with OA. Results: Patients in the OF group were older ($p < 0.001$); had a lower body mass index ($p < 0.001$); were less literate ($p = 0.012$); were more frequently Caucasian ($p = 0.003$); were less frequently married ($p < 0.001$); experienced more falls, cognitive deficiency, previous fractures, old fracture, falls in the last year, and fall fractures; needed more help and took more medicine for osteoporosis ($p < 0.05$); and showed less pathology in the feet, muscle weakness, less vitamin D intake, and lower Katz & Lawton scores ($p < 0.001$). Factors that increased the chance of nonadherence included older age ($p = 0.020$), falls ($p = 0.035$), cognitive deficiency ($p = 0.044$), and presence of depression/apathy/confusion ($p < 0.001$). Conclusion: Patient age, ethnicity, marital status, previous falls, foot pathologies, muscle weakness, previous fractures, use of vitamin D, use of osteoporosis drugs, and lower Katz & Lawton scale score defined the OF group. Factors that increased the chance of nonadherence included older age, sedative use, cognitive disorders, and symptoms of depression/apathy/confusion.
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NR 20
TC 4
Z9 4
U1 0
U2 4
PU ATHA COMUNICACAO & EDITORA
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J9 ACTA ORTOP BRAS
JI Acta Ortop. Bras.
PD MAR-APR 15
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DI 10.1590/1413-785220192702214727
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WC Orthopedics
SC Orthopedics
GA HR1IC
UT WOS:000462883600004
PM 30988654
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PT J
AU Rupp, M
Anastasopoulou, L
Wintermeyer, E
Malhaan, D
El Khassawna, T
Heiss, C
AF Rupp, Markus
Anastasopoulou, Lydia
Wintermeyer, Elke
Malhaan, Deeksha
El Khassawna, Thaqif
Heiss, Christian
TI Predatory journals: a major threat in orthopaedic research
SO INTERNATIONAL ORTHOPAEDICS
LA English
DT Review
DE Predatory journals; Legitimate publishing; Open access
AB Predatory publishing is a major threat to contemporary publishing, as it offers 'to unaware scientist's',a quick open-access publication against fees without peer-review procedures.. Lack of peer-review leads to unethical practices, as plagiarism, publication of unscientific falsified data, and even unsafe clinical practices. As these journals threaten the credibility of academic publishing,

significant work has been done from many scientific teams, in the last years, in establishing discriminating criteria between predatory and legitimate publishing. In the present review, we include mechanisms used by predatory editors to convince eager researchers to submit to their journals. We also provide useful links giving information about potential predatory journals and publishers, as well as scholarly writing. Joining the efforts of different scientific disciplines which compiled green lists with journals in their field, we conducted a green list with genuine orthopaedic research journals based on the directory of open-access journals (DOAJ) and Thomson Reuters journal citation reports. Ninety-six legitimate orthopaedic journals were identified based on the Thomson Reuters journal citation reports. One hundred thirty hits were found on the DOAJ site using the keywords orthopaedics, orthopedics, sports medicine, musculoskeletal, trauma, traumatology, osteoarthritis, osteoporosis, cartilage, bone, hand, shoulder, knee, hip, foot, wound. Twenty-one journals on the DOAJ site occurred overlapping with keywords. Researchers and clinicians in the field of orthopaedics are advised to use all available tools in order to recognize predatory practices and avoid publishing in predatory journals.
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NR 52
TC 28
Z9 35
U1 0
U2 22
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 0341-2695
EI 1432-5195
J9 INT ORTHOP
JI Int. Orthop.
PD MAR 15
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VL 43
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EP 517
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WC Orthopedics
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UT WOS:000460590900001
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PT J
AU Falling, C
Stebbings, S
Baxter, GD
Gearry, RB
Mani, R
AF Falling, Carrie
Stebbings, Simon
Baxter, George D.
Gearry, Richard B.
Mani, Ramakrishnan
TI Musculoskeletal Pain in Individuals With Inflammatory Bowel Disease Reflects Three Distinct Profiles
SO CLINICAL JOURNAL OF PAIN
LA English
DT Article
DE musculoskeletal pain; central sensitization; inflammatory bowel disease
ID latent class analysis; quality-of-life; central sensitization; extraintestinal manifestations; questionnaire; comorbidity; classification; osteoarthritis; subgroups; diagnosis
AB Objectives: Pain affects over 70% of individuals with inflammatory bowel disease (IBD), with abdominal and musculoskeletal pain representing the most common symptoms. Musculoskeletal pain in IBD is reported to be associated with multiple clinical features, however the scope and nature of pain is not well understood. Primary aims were to identify subgroups of musculoskeletal pain in individuals with IBD based on clinical features of pain and assess how these subgroups differ in aspects of demographics, comorbidity, and IBD characteristics. Methods: Cross-sectional online survey was performed on adults with IBD. Domains included: demographics, comorbidity, and clinical IBD and pain features. Latent class analysis was used to identify subgroups with similar attributes of: pain (severity, location, interference, and quality), IBD (activity, quality of life, and abdominal pain), and symptoms related to central sensitization. Correlation and regression analyses were used to profile identified subgroups. Results: Of 305 included participants, 208 indicated the presence of musculoskeletal pain. Three identified subgroups were characterized as "mixed mechanism," "central mechanism," and "regional and remission." Between subgroup differences included: total comorbidity score (P=0.005), osteoarthritis (P=0.027), osteoporosis (P=0.045), depression (P=0.001), anxiety (P=0.025), and chronic fatigue syndrome (P=0.020). Sex and age were identified as confounders for depression and anxiety. Conclusions: Study results suggest multiple mechanisms contributing to pain experiences in IBD, to include central mechanisms. Features related to demographics, extraintestinal manifestations, IBD subtype, and clinical IBD features were not predictors of subgroup membership. However, total comorbidity

demonstrated association with pain subgroups in this population.
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NR 61
TC 14
Z9 16
U1 0
U2 2
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0749-8047
EI 1536-5409
J9 CLIN J PAIN
JI Clin. J. Pain
PD JUL 15
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VL 35
IS 7
BP 559
EP 568
DI 10.1097/AJP.0000000000000698
PG 10
WC Anesthesiology; Clinical Neurology
SC Anesthesiology; Neurosciences & Neurology
GA IC5ST
UT WOS:000471029300001
PM 30829736
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PT J
AU Pawlak, Z
Mrela, A
Kaczmarek, M
Cieszko, M
Urbaniak, W
AF Pawlak, Zenon
Mrela, Aleksandra
Kaczmarek, Mariusz
Cieszko, Mieczyslaw
Urbaniak, Wieslaw
TI Natural joints: Boundary lubrication and antiphospholipid syndrome (APS)
SO BIOSYSTEMS

LA English
DT Article
DE Articular cartilage degradation; Phospholipids deactivation; Antiphospholipid syndrome (APS); beta(2)-Glycoprotein I, beta(2)-GPI as deactivator; Friction coefficient
ID domain-i
AB The paper shows that osteoporosis (OA) changes the SF content and the lipid profile substantially. To estimate the implication of the lipid environment in case the articular cartilage (AC) changes, we measured friction coefficient normal samples, with early and late stages of (OA). During joint inflammation and osteoarthritis, enzymatically activated beta(2)-Glycoprotein I is transformed into antibody conformation. Our hypothesis about cartilage degradation of PL bilayers by antibodies (beta(2)-Glycoprotein I) is considering antiphospholipid syndrome (APS), which was not discussed in the literature before. Deactivated PL molecule has no ability to form bilayers, lamellar phases, and liposomes. The phospholipid content in synovial fluid (SF) during joint inflammation, osteoarthritis, and rheumatoid arthritis is significantly higher (2-3 times) above the normal concentration of PL, and has a poor boundary-lubricating ability is deactivated.
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NR 23
TC 11
Z9 11
U1 1
U2 15
PU ELSEVIER SCI LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
SN 0303-2647
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J9 BIOSYSTEMS
JI Biosystems
PD MAR 15
PY 2019
VL 177
IS
BP 44
EP 47
DI 10.1016/j.biosystems.2018.10.018
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WC Biology; Mathematical & Computational Biology
SC Life Sciences & Biomedicine - Other Topics; Mathematical & Computational Biology
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PT J
AU van Wijnen, AJ
Westendorf, JJ
AF van Wijnen, Andre J.
Westendorf, Jennifer J.
TI Epigenetics as a New Frontier in Orthopedic Regenerative Medicine and Oncology
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Review
DE bone; cartilage; skeletal development; osteoarthritis; osteoporosis; chromatin; oncohistones
ID giant-cell tumor; dna hydroxymethylation; histone modifications; skeletal growth; bone-formation; ezh2; cartilage; mutations; gene; differentiation
AB Skeletal regenerative medicine aims to repair or regenerate skeletal tissues using pharmacotherapies, cell-based treatments, and/or surgical interventions. The field is guided by biological principles active during development, wound healing, aging, and carcinogenesis. Skeletal development and tissue maintenance in adults represent highly intricate biological processes that require continuous adjustments in the expression of cell type-specific genes that generate, remodel, and repair the skeletal extracellular matrix. Errors in these processes can facilitate musculoskeletal disease including cancers or injury. The fundamental molecular mechanisms by which cell type-specific patterns in gene expression are established and retained during successive mitotic divisions require epigenetic control, which we review here. We focus on epigenetic regulatory proteins that control the mammalian epigenome at the level of chromatin with emphasis on proteins that are amenable to drug intervention to mitigate skeletal tissue degeneration (e.g., osteoarthritis and osteoporosis). We highlight recent findings on a number of druggable epigenetic regulators, including DNA methyltransferases (e.g., DNMT1, DNMT3A, and DNMT3B) and hydroxylases (e.g., TET1, TET2, and TET3), histone methyltransferases (e.g., EZH1, EZH2, and DOT1L) as well as histone deacetylases (e.g., HDAC3, HDAC4, and HDAC7) and histone acetyl readers (e.g., BRD4) in relation to the development of bone or cartilage regenerative drug therapies. We also review how histone mutations lead to epigenomic catastrophe and cause musculoskeletal tumors. The combined body of molecular and genetic studies focusing on epigenetic regulators indicates that these proteins are critical for normal skeletogenesis and viable candidate drug targets for short-term local pharmacological strategies to mitigate musculoskeletal tissue degeneration. (c) 2019 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 37:1465-1474, 2019.
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FU National Institutes of Health [R01 AR68103, AR049069]; Regenerative Medicine Minnesota [RMM 101617 DS006]; National Institute of Arthritis and Musculoskeletal and Skin Diseases [R01AR049069] Funding Source: NIH RePORTER
CR Allen HL, 2010, NATURE, V467, P832, DOI 10.1038/nature09410
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TI European guidance for the diagnosis and management of osteoporosis in postmenopausal women
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DT Article
DE Bone mineral density; Diagnosis of osteoporosis; Fracture risk assessment; FRAX; Health economics; Treatment of osteoporosis
ID bone-mineral density; vertebral fracture risk; estrogen plus progestin; vitamin-d supplementation; increased cardiovascular risks; health technology-assessment; hormone replacement therapy; zoledronic acid treatment; monthly oral ibandronate; liaison service models
AB Guidance is provided in a European setting on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis.IntroductionThe International Osteoporosis Foundation and European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis published guidance for the diagnosis and management of osteoporosis in 2013. This manuscript updates these in a European setting.MethodsSystematic reviews were updated.ResultsThe following areas are reviewed: the role of bone mineral density measurement for the diagnosis of osteoporosis and assessment of fracture risk; general and pharmacological management of osteoporosis; monitoring of treatment; assessment of fracture risk; case-finding strategies; investigation of patients; health economics of treatment. The update includes new information on the evaluation of bone microstructure evaluation in facture risk assessment, the role of FRAX (R) and Fracture Liaison Services in secondary fracture prevention, long-term effects on fracture risk of dietary intakes, and increased fracture risk on stopping drug treatment.ConclusionsA platform is provided on which specific guidelines can be developed for national use.
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AU Lewis, R
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TI Strategies for optimising musculoskeletal health in the 21st century
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Review
DE Ageing; Musculoskeletal health; Musculoskeletal disorders; Global burden; Joint diseases; Osteoarthritis (OA); Rheumatoid arthritis (RA); Low back pain (LBP); Osteoporosis (OP); Sarcopenia; Obesity; Type II diabetes; Metabolic disease
ID nonsteroidal antiinflammatory drugs; quality-of-life; knee osteoarthritis; chondroitin sulfate; rheumatoid-arthritis; articular-cartilage; global burden; gait analysis; animal-model; chronic pain
AB We live in a world with an ever-increasing ageing population. Studying healthy ageing and reducing the socioeconomic impact of age-related diseases is a key research priority for the industrialised and developing countries, along with a better mechanistic understanding of the physiology and pathophysiology of ageing that occurs in a number of age-related musculoskeletal disorders. Arthritis and musculoskeletal disorders constitute a major cause of disability and morbidity globally and result in enormous costs for our health and social-care systems. By gaining a better understanding of healthy musculoskeletal ageing and the risk factors associated with premature ageing and senescence, we can provide better care and develop new and better-targeted therapies for common musculoskeletal disorders. This review is the outcome of a two-day multidisciplinary, international workshop sponsored by the Institute of Advanced Studies entitled "Musculoskeletal Health in the 21st Century" and held at the University of Surrey from 30th June-1st July 2015. The aim of this narrative review is to summarise current knowledge of musculoskeletal health, ageing and disease and highlight strategies for prevention and reducing the impact of common musculoskeletal diseases.
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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TI Cost-effectiveness evaluation of glucosamine for osteoarthritis based on simulation of individual patient data obtained from aggregated data in published studies
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Osteoarthritis; Cost-effectiveness; Glucosamine
ID knee osteoarthritis; double-blind; european-society; economic-aspects; sulfate; recommendations; osteoporosis; progression; management; symptoms
AB BackgroundThe economic evaluation of treatments usually requires access to individual patient data, which is difficult to obtain. Moreover, in osteoarthritis, health utility scores are unavailable and can be assessed only using a validated equation model based on various clinical data. We aimed to develop and validate a methodology to simulate individual health utility scores from aggregated clinical data available in published studies to calculate the cost-effectiveness of different glucosamine preparations (i.e., crystalline glucosamine sulfate, glucosamine sulfate, and glucosamine hydrochloride) used for osteoarthritis.MethodsWe developed a method to simulate individual utility values and validated the model by comparing the results obtained with the simulation and the results of one trial where the utility scores are available. Then, we simulated the utility scores of 10 published trials that used different glucosamine preparations. The utility estimates were used to calculate the quality-adjusted life year (QALY) using the area-under-the-curve method. Costs were for the glucosamine product only. The incremental cost/effectiveness ratio (ICER) was then calculated.ResultsThe values of utility scores calculated from data sources and those simulated with the model were similar. From 10 studies where utility was simulated, four used crystalline glucosamine sulfate, and six used other formulations. The ICER revealed that compared to placebo, crystalline glucosamine sulfate only was cost-effective at all

time points and up to 3years with a median ICER of 5347.2Euro/QALY at month 3, 4807.2Euro/QALY at month 6 and 11535.5Euro/QALY at year 3. The use of other formulations was not cost-effective.ConclusionUsing a new model to simulate individual health utility scores of patients included in ten published trials, ICER analysis showed that the use of crystalline glucosamine sulfate is cost-effective, while other formulations were not. The results confirm the importance of the formulation of glucosamine products.
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NR 29
TC 14
Z9 17
U1 0
U2 5
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 1594-0667
EI 1720-8319
J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
PD JUN 15
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VL 31
IS 6
BP 881
EP 887
DI 10.1007/s40520-019-01138-1
PG 7
WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA IB4WG
UT WOS:000470272200017

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ER

PT J
AU Gladish, JI
Powell, DW
Queen, RM
AF Gladish, Jonathan It
Powell, Douglas W.
Queen, Robin M.
TI The effects of total ankle arthroplasty on postural stability and loading symmetry in quiet stance
SO JOURNAL OF BIOMECHANICS
LA English
DT Article
DE Ankle; Arthritis; Balance; Postural stability; Arthroplasty
ID body-weight distribution; balance; instability; osteoarthritis; reliability; falls
AB Ankle osteoarthritis is a debilitating condition affecting about 1% of the population with approximately 50,000 new instances annually. One treatment is total ankle arthroplasty (TAA), however, its effects on balance are not well understood. This study analyzed balance over a two-year period following TAA. 408 subjects (177 left, 231 right ankles) diagnosed with end-stage ankle osteoarthritis performed quiet standing trials while center of pressure (COP) data were collected. Data were compared across three time points (pre-op, 1-year, and 2-years post-op) and between surgical and non-surgical limbs using a linear mixed model with significance set at P=0.05. COP excursions in the feet-together condition were not significantly different between limbs after 2 years in anteroposterior or mediolateral directions (P = 0.06, 0.08) after being significantly different between limbs in the anteroposterior (P=0.014) and mediolateral direction (P<0.001) pre-op. The vertical ground reaction force significantly decreased across time in the non-surgical limb, while reciprocally increasing in the surgical limb (P<0.001). After 2 years, no significant difference in vertical ground reaction force between limbs existed (P= 0.20). Limb asymmetry indices decreased at each time point in both conditions (all P < 0.001) and were not significantly different from zero after 2 years in the feet-together condition (P = 0.290). In conclusion, surgical limb balance improved compared to pre-op, resulting in increased symmetry between limbs after 2 years. Vertical ground reaction forces on both limbs converge and limb asymmetry indices approach zero two years post-op. Differences in the COP excursion-loading symmetry relationship between limbs could be useful for identifying instability in other pathologies. (C) 2018 Elsevier Ltd. All rights reserved.
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NR 40
TC 4
Z9 4
U1 0
U2 4
PU ELSEVIER SCI LTD
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PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
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J9 J BIOMECH
JI J. Biomech.
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WC Biophysics; Engineering, Biomedical
SC Biophysics; Engineering
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PT J
AU O'Connell, NE
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TI Incidence of osteoarthritis, osteoporosis and inflammatory musculoskeletal diseases in adults with cerebral palsy: A population-based cohort study
SO BONE
LA English
DT Article
DE Cerebral palsy; Osteoarthritis; Osteoporosis; Inflammatory museuloskeletal diseases; Incidence
ID practice research datalink; young-adults; issue; risk; pain
AB Background People with cerebral palsy (CP) may be at increased risk of musculoskeletal conditions due to various factors including malnutrition and abnormal levels of skeletal loading. This study aimed to compare the incidence of osteoporosis, osteoarthritis and inflammatory musculoskeletal diseases between adults with and without CP. Methods: A population based cohort study was conducted using data from the Clinical Practice Research Datalink collected between 1987 and 2015. Adults with CP were matched to adults without CP for age, sex and general practice. Cox models, stratified by matched set and adjusted for potential confounders, were fitted to compare the risk of osteoporosis,

osteoarthritis and inflammatory musculoskeletal diseases. Results: 1705 adults with CP were matched to 5115 adults without CP. Adults with CP had an increased risk of osteoporosis in unadjusted (Hazard Ratio (HR) 3.67, 95% Confidence Interval (CI) 2.32 to 5.80, p < 0.001) and adjusted (HR 6.19, 95% CI 3.37 to 11.39, p < 0.001) analyses. No evidence of increased risk of inflammatory musculoskeletal diseases was observed in unadjusted or adjusted analyses. For osteoarthritis no evidence of increased risk was seen in the unadjusted analysis, but evidence of an increased risk was seen when the analysis was adjusted for alcohol consumption, smoking status, and mean yearly general practice (GP) visits (HR 1.54, 95% CI 1.17 to 2.02, p < 0.001). Conclusions: After accounting for potential confounding variables, we found that CP is associated with increased risk of osteoporosis and osteoarthritis. These findings provide the strongest epidemiological evidence to date for increased risk of osteoporosis and osteoarthritis in people with CP, and highlight need for clinical awareness of such conditions in this population.
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NR 33
TC 32
Z9 38
U1 1
U2 9
PU ELSEVIER SCIENCE INC
PI NEW YORK
PA STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA
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J9 BONE
JI Bone

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DI 10.1016/j.bone.2019.05.007
PG 6
WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA IG1MI
UT WOS:000473555300005
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ER

PT J
AU Atik, OS
Sezgin, EA
Tepedelenlioglu, HE
AF Atik, O. Sahap
Sezgin, Erdem Aras
Tepedelenlioglu, H. Emre
TI The role of biomarkers in osteoarthritis and osteoporosis for early diagnosis and monitoring prognosis
SO EKLEM HASTALIKLARI VE CERRAHISI-JOINT DISEASES AND RELATED SURGERY
LA English
DT Review
ID biological markers
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NR 8
TC 6
Z9 7
U1 0
U2 3
PU TURKISH JOINT DISEASES FOUNDATION
PI KAVAKLIDERE
PA BUGDAY SOKAK 6-27, KAVAKLIDERE, ANKARA 06700, TURKEY
SN 1305-8282
EI 1309-0313
J9 EKLEM HAST CERRAHISI
JI Eklem Hast. Cerrahisi
PD JUN 15
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WC Orthopedics; Surgery
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UT WOS:000475356700018
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PT J
AU Karam, N
Lavoie, JF
St-Jacques, B
Bouhanik, S
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AF Karam, Nancy
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TI Bone-Specific Overexpression of PITX1 Induces Senile Osteoporosis in Mice Through Deficient Self-Renewal of Mesenchymal Progenitors and Wnt Pathway Inhibition
SO SCIENTIFIC REPORTS
LA English
DT Article
ID acute lymphoblastic-leukemia; transcription factor; hindlimb; cells; children; fracture; repair; ptx1
AB The cellular and molecular mechanisms underlying senile osteoporosis remain poorly understood. In this study, transgenic mCol1 alpha 1-Pitx1 mice overexpressing paired-like homeodomain 1(PITX1), a homeobox transcription factor, rapidly develop a severe type-II osteoporotic phenotype with significant reduction in bone mass and biomechanical strength similar to that seen in humans and reminiscent of the phenotype previously observed in Sca-1(Ly6 alpha)-nu II mice. PITX1 plays a critical role in hind limb formation during fetal development, while loss of expression is associated with primary knee/hip osteoarthritis in aging humans. Through in vivo and in vitro analyses, we demonstrate that Pitxl directly regulates the self-renewal of mesenchymal progenitors and indirectly regulates osteoclast differentiation through the upregulation of Wnt signaling inhibitors DKK1, SOST, and GSK3-beta. This is confirmed by elevated levels of plasma DKK1 and the accumulation of phospho-beta-catenin in transgenic mice osteoblasts. Furthermore, overexpressed Pitxl in mice osteoblasts results in severe repression of Sca-1 (Ly6 alpha) that was previously associated with senile osteoporosis. Our study is the first to demonstrate the novel roles of PITX1 in senile osteoporosis where PITX1 regulates the self-renewal of mesenchymal stem cells or progenitor cells through Sca-1 (Ly6 alpha) repression and, in addition, inhibits the Wnt signaling pathway.
C1 [Karam, Nancy; Lavoie, Jean-Francois; St-Jacques, Benoit; Bouhanik, Saadallah; Franco, Anita; Ladoul, Nihad; Moreau, Alain] St Justine Univ Hosp, Res Ctr, Viscogliosi Lab Mol Genet Musculoskeletal Dis, Montreal, PQ H3T 1C5, Canada.
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CR Atkins GJ, 2011, J BONE MINER RES, V26, P1425, DOI 10.1002/jbmr.345

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NR 30
TC 9
Z9 13
U1 0
U2 5
PU NATURE PORTFOLIO
PI BERLIN
PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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J9 SCI REP-UK
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WC Multidisciplinary Sciences
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PT J
AU Yoshimura, Y
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Arikawa-Hirasawa, Eri
Machida, Shuichi
Naito, Hisashi
Hamada, Chieko
Kominami, Eiki
TI A nationwide observational study of locomotive syndrome in Japan using the ResearchKit: The Locomonitor study
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English
DT Article
ID population; osteoarthritis/osteoporosis; association; disability; apple

AB Background: We developed the Locomonitor application (app), the world's first iOS app to study locomotive syndrome, using the ResearchKit and examined the prevalence and risk factors for locomotive syndrome in Japanese general individuals 20-69 years old in a nationwide cross-sectional observational study. Methods: The participants were recruited from February to August 2016. The outcome measures for the locomotive function were evaluated by locomotive syndrome risk tests (LSRTs) using the Locomonitor app. The chi-squared test, a linear-by-linear association trend analysis, and Spearman's correlation test were performed as statistical analyses. Results: A total of 2177 subjects from all prefectures in Japan were included (average 42.2 years old). The Locomo25 and Stand-Up test scores in female participants and the Two-Step test scores in male participants showed age-dependent deterioration. In the overall population, the incidence of Locomo stage 1 and 2, as evaluated by the Locomo25, Stand-Up test or Two-Step test, was 30.2% and 29.2%, respectively. In subjects without locomotive syndrome (40.5%), LSRT scores showed age-dependent deterioration in both sexes. Locomotive syndrome in participants with a body mass index (BMI) of >25 kg/m(2) was more frequent than in those with a BMI of <25 kg/m(2) (age- and gender-adjusted odds ratio [OR] 1.344 [95% confidence interval {CI} 1.03-1.75, p = 0.027]). Locomotive syndrome in participants with an exercise habit was less frequent than in those without an exercise habit (age- and gender-adjusted OR 0.499 [95% CI 1333-0.755, p < 0.0001]). Conclusions: The Locomonitor app, a newly developed remote platform, revealed that approximately 20% 30% of Japanese individuals 20-69 years old in the general population met the definition of locomotive syndrome. Locomotive syndrome in participants with obesity was more frequent than those without obesity, while locomotive syndrome in participants with an exercise habit was less frequent than those without an exercise habit. (C) 2019 The Japanese Orthopaedic Association. Published by Elsevier B.V. All rights reserved.
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TI Correlation between hip osteoarthritis and proximal femoral fracture site: could it be protective for intracapsular neck fractures? A retrospective study on 320 cases
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Extracapsular fractures; Hip osteoarthritis; Intracapsular fractures; Proximal femur fractures
ID bone-mineral density; risk; falls; classification; osteoporosis; reliability; pattern; knee
AB A Summary Proximal femoral fractures affect elderly people, showing high

morbidity and mortality incidence resulting in a major economic burden on national healthcare systems. Understanding the causes of these injuries is of paramount importance to prevent the serious consequences of these fractures. Introduction Hip osteoarthritis and proximal femoral fractures mainly affect elderly patients. Several authors, in their studies, tried to document a correlation between these conditions, but the results are conflicting. The aim of this study was to evaluate the relationship between hip osteoarthritis and the fracture site. Secondly, to evaluate if the grade of osteoarthritis could influence the fracture pattern. Methods A retrospective study on 320 patients admitted for hip fracture between June 2015 and December 2016 was carried on. Radiographic images were evaluated, assessing the type of fracture, presence and grade of osteoarthritis according to Kellgren-Lawrence and Tonnis classifications, and their correlations. Results Osteoarthritis was found to affect the fracture site showing a higher prevalence among subjects with extracapsular than those with intracapsular fractures ($p<0.00001$). Patients with radiographic signs of arthritis had mainly trochanteric fracture. Conversely, patients without arthritis more frequently presented a femoral neck fracture. This correlation was even more significant as the severity of the OA increased. Conclusions Results support the hypothesis that hip osteoarthritis could represent a protective factor for intracapsular fractures and a risk factor for trochanteric ones. The severity of arthritis is also associated with the fracture pattern.
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PT J
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TI Changes in quality of life in patients with postmenopausal osteoporosis receiving weekly bisphosphonate treatment: a 2-year multicenter study in Japan
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Osteoporosis; Bisphosphonate; Persistence; Quality of life; Pain
ID high-risk; alendronate; fracture; level
AB We investigated changes in quality of life (QOL), including pain, in Japanese women aged55years who were diagnosed as having osteoporosis at 265 centers across Japan and treated continuously with once-weekly bisphosphonates for 24months. In 2650 evaluable patients, a significant improvement in QOL was observed from 3months after enrollment onward and maintained throughout the 2-year observation period. A significant improvement in scores was observed for all domains of the Euro QOL 5 Dimension (EQ-5D), and the pain, health perception, and posture, figure domains of the Japanese Osteoporosis QOL Questionnaire (JOQOL). Factors identified as significantly contributing to QOL change were fractures within the year before enrollment, presence of spondylosis deformans, presence of osteoarthritis, use of activated vitamin D-3, and age based on the JOQOL, and presence of spondylosis deformans, use of activated vitamin D-3, and

age based on the EQ-5D. The results suggested that the patients' perception of treatment effects, such as improvement in pain, contributes to treatment continuation. Osteoporosis patients should be informed that continuous treatment with once-weekly bisphosphonates can lead to a significant improvement in QOL regardless of concomitant locomotor diseases, to encourage them to remain on treatment. In conclusion, continuous bisphosphonate treatment improved the QOL even in patients with locomotor diseases, and the concomitant use of activated vitamin D-3 may also facilitate further improvement in QOL.
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TI Assessment of Muscle Function and Physical Performance in Daily Clinical Practice: A position paper endorsed by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Review
DE Muscle function; Muscle strenght; Physical performance; Daily practice; Sarcopenia
ID dwelling older-people; chair-stand test; test-retest reliability; gait speed; grip strength; handgrip strength; walk test; usual-pace; go test; validity
AB It is well recognized that poor muscle function and poor physical performance are strong predictors of clinically relevant adverse events in older people. Given the large number of approaches to measure muscle function and physical performance, clinicians often struggle to choose a tool that is appropriate and validated for the population of older people they deal with. In this paper, an overview of different methods available and applicable in clinical settings is proposed. This paper is based on literature reviews performed by members of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) working group on frailty and sarcopenia. Face-to-face meetings were organized afterwards where the whole group could amend and discuss the recommendations further. Several characteristics should be considered when choosing a tool: (1) purpose of the assessment (intervention, screening, diagnosis); (2) patient characteristics (population, settings, functional ability, etc.); (3) psychometric properties of the tool (test-retest reliability, inter-rater reliability, responsiveness, floor and ceiling effects, etc.); (4) applicability of the tool in clinical settings (overall cost, time required for the examination, level of training, equipment, patient acceptance, etc.); (5) prognostic reliability for relevant clinical outcomes. Based on these criteria and the available evidence, the expert group advises the use of grip strength to measure muscle strength and the use of 4-m gait speed or the Short Physical Performance Battery test to measure physical performance in daily practice. The tools proposed are relevant for the assessment of muscle weakness and physical performance. Subjects with low values should receive additional diagnostic workups to achieve a full diagnosis of the underlying condition responsible (sarcopenia, frailty or other).
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TC 384
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AF Weidner, Hilary
Gao, Victor Yuan
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McTague, Sean
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TI CK2.3, a Mimetic Peptide of the BMP Type I Receptor, Increases Activity in Osteoblasts over BMP2
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DT Article
DE osteoporosis; femoral head; osteoarthritis; BMP2; CK2.3; BMD
ID bone-mineral density; postmenopausal women; osteoporosis; protein-2; management; fractures; spine; age
AB Bone is one of the most important organs in the human body. It provides structure, function, and protection for other vital organs; therefore, bone maintenance and homeostasis are critical processes. As humans age, their bone mineral density decreases, which leads to diseases like osteoporosis. This disease affects one in two women and one in five men aged 50 and over. As the aging population increases, the interest and significance of studying this debilitating bone disease becomes more relevant. Current therapeutic products for osteoporosis have many side effects and can be taken for a limited number of years. Most therapeutic products only focus on decreasing bone resorption, not increasing bone formation. Bone morphogenetic protein 2 is an essential growth factor that drives osteoblast differentiation and activity and is essential for bone formation. However, usage in the clinic is unsuccessful due to several side effects. Recently, a signaling disparity in bone marrow stromal cells within the bone morphogenetic protein pathway that led to decreased bone morphogenetic protein 2 responsiveness was identified in patients diagnosed with osteoporosis. However, it is unclear how other cell populations, especially osteoblasts, which are key players in bone remodeling, are affected and whether the bone morphogenetic protein pathway is affected during osteoporosis. Our research group designed a novel peptide, casein kinase 2.3, that acts downstream of the bone morphogenetic receptor type Ia and increases bone mineralization in murine cells and primary bovine osteoblasts. The aim of the study presented here was to compare the responsiveness of osteoblasts to bone morphogenetic protein 2 and casein kinase 2.3, especially in patients diagnosed with osteoporosis. Mature osteoblasts were extracted from patients diagnosed with osteoporosis or osteoarthritis from Christiana Care Hospital in Newark, Delaware. They were stimulated with either bone morphogenetic protein 2 or casein kinase 2.3, and their effect on osteoblast activity was determined. The osteoporotic patients showed no mineralization response to bone morphogenetic protein 2 stimulation, while the osteoarthritis patients significantly responded to bone morphogenetic protein 2 stimulation. Furthermore, markers for osteoblast activity were increased by casein kinase 2.3, which was in sharp contrast to bone morphogenetic protein 2. This further

supports a major bone morphogenetic protein signaling disparity in both the elderly and those suffering with osteoporosis. Both patient types did significantly respond to casein kinase 2.3. Further analysis of the bone morphogenetic protein pathway could lead to new therapeutic products for osteoporosis.
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TI Mitochondria and cellular senescence: Implications for musculoskeletal ageing
SO FREE RADICAL BIOLOGY AND MEDICINE
LA English
DT Review
DE Cellular senescence; Senotherapies; Senolytics; Mitochondria; Ageing; Sarcopenia; Osteoporosis; Osteoarthritis
ID dna-damage; skeletal-muscle; life-span; satellite cells; secretory phenotype; stem-cells; dysfunction; tissue; contributes; accumulation
AB Musculoskeletal ageing and its associated diseases are major contributors to the loss of independence and reduced quality of life in older people. Several recent studies indicate that cellular senescence is a contributor to age-related loss of function in various organs including muscle, bones and joints. Importantly, these studies indicate that therapies targeting specifically senescent cells have great therapeutic potential in improving musculoskeletal health during ageing. Senescent cells are characterised by dramatic changes in mitochondrial function, metabolism and homeostasis. Mitochondrial dysfunction has been shown to contribute to senescence and the SASP. Here we review the role of cellular senescence in musculoskeletal ageing as well as the potential mechanisms by which mitochondrial dysfunction may impact on the induction and development of the senescent phenotype.
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TI The Association between Frailty and Disability among the Elderly in Rural Areas of Korea
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DT Article
DE disability; elderly; frailty; rural
ID older-adults; impairment
AB Background: The rapid increase in the elderly population in Korea is associated with an expanded burden of health problems. The purpose of this study was to investigate the association between frailty and physical disability among Koreans using the frailty index, which was developed to assess health conditions in elderly people. Methods: We included 503 elderly people from the Namgaram-II cohort. We used the Korean version of the Kaigo-Yobo checklist as our frailty assessment tool. For the disability assessment tool, we used the Korean version of the 12-item World Health Organization Disability Assessment Schedule (WHODAS-12). We fit multiple linear regression models for men and women for each section. Our models also included variables for musculoskeletal diseases that are known to be associated with frailty, such as sarcopenia, osteoporosis, and radiologic knee osteoarthritis. Results: After correcting for social demographic characteristics, blood profiles, high blood pressure, and diabetes, the Kaigo-Yobo results showed a significant difference in frailty between men (1.53 +/- 0.74) and women (2.60 +/- 0.77), and WHODAS-12 also showed a significant difference between men (6.59 +/- 5.08) and women (15.99 +/- 5.70). After correcting for social demographic characteristics, blood profiles, high blood pressure, and diabetes, Kaigo-Yobo and WHODAS-12 were significantly associated with each other among both men (beta = 2.667) and women (beta = 3.200) ($p < 0.001$). Conclusions: The study results show an association between frailty and disability among elderly people in rural areas. Therefore, prevention should occur at the pre-frailty stage of a person's life to prevent further disability. Also, disability welfare programs should be provided to elderly people who present with frailty.

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TI Diallyl disulfide alleviates inflammatory osteolysis by suppressing osteoclastogenesis via NF-κB-NFATc1 signal pathway
SO FASEB JOURNAL
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DE natural products; osteoclast; bone resorption
ID nf-kappa-b; rankl-induced osteoclastogenesis; cell-cell fusion; bone-resorption; receptor activator; in-vitro; differentiation; ligand; modulation; mechanisms
AB Skeletal homeostasis is closely effectuated by the regulation of bone formation and bone resorption. Osteoclasts are multinuclear giant cells responsible for bone resorption. Overactivated osteoclasts and excessive bone resorption result in various lytic bone diseases, such as osteoporosis, osteoarthritis, periprosthetic infection, and inflammatory aseptic loosening of orthopedic implants. In consideration of the severe side effects caused by the currently available drugs, exploitation of novel drugs has gradually attracted attention. Because of its anti-inflammatory, antioxidant, and antitumor capacities, diallyl disulfide (DADS), a major oil-soluble organosulfur ingredient compound derived from garlic, has been widely researched. However, the effects of DADS on osteoclasts and lytic bone diseases are still unknown. In this study, we investigated the effects of DADS on receptor activator of NF-kappa B ligand (RANKL)- and LPS-mediated osteoclastogenesis, LPS-stimulated proinflammatory cytokines related to osteoclasts, and LPS-induced inflammatory osteolysis. The results showed that DADS significantly inhibited RANKL-mediated osteoclast formation, fusion, and bone resorption in a dose-dependent manner via inhibiting the NF-kappa B and signal transducer and activator of transcription 3 signaling and restraining the interaction of NF-kappa B p65 with nuclear factor of activated T cells cytoplasmic 1. Furthermore, DADS also markedly suppressed LPS-induced osteoclastogenesis and reduced the production of proinflammatory cytokines with LPS stimulation to indirectly mediate osteoclast formation. Consistent with the in vitro results, DADS prevented the LPS-induced severe bone loss by blocking the osteoclastogenesis. All of the results indicate that DADS may be a potential and exploitable drug used for preventing and impeding osteolytic lesions.-Yang, J., Tang, R., Yi, J., Chen, Y., Li, X., Yu, T., Fei, J. Diallyl disulfide alleviates inflammatory osteolysis by suppressing osteoclastogenesis via NF-kappa B-NFATc1 signal pathway.
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TI Adjuvant denosumab in postmenopausal patients with hormone receptor-positive breast cancer (ABCSG-18): disease-free survival results from a randomised, double-blind, placebo-controlled, phase 3 trial
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LA English
DT Article
ID plus zoledronic acid; clinical-practice; bone loss; therapy; women; bisphosphonates; inhibitor; rankl; metaanalysis; prevention
AB Background In postmenopausal women with hormone receptor-positive, early-stage breast cancer, treatment with adjuvant aromatase inhibitors is the standard of care, but it increases risk for osteoporosis and fractures. Results from the ABCSG-18 trial showed that use of denosumab as an adjuvant to aromatase inhibitor therapy significantly reduced clinical fractures. Disease-free survival outcomes from ABCSG-18 have not yet been reported. Methods Postmenopausal patients with early, hormone receptor-positive, non-metastatic adenocarcinoma of the breast, who had completed their initial adjuvant treatment pathway (surgery, radiotherapy, or chemotherapy, or a combination) and were receiving adjuvant aromatase inhibitors, were enrolled at 58 trial centres in Austria and Sweden into this prospective, double-blind, placebo-controlled, phase 3 trial. With permuted block randomisation (block sizes 2 and 4, stratified by previous aromatase inhibitor use, total lumbar spine bone mineral density score at baseline, and type of centre),

patients were assigned (1: 1) to receive subcutaneous denosumab (60 mg) or matching placebo every 6 months during aromatase inhibitor therapy. The primary endpoint (previously reported) was the time to first clinical fracture after randomisation. The secondary endpoint reported here is disease-free survival (defined as time from randomisation to first evidence of local or distant metastasis, contralateral breast cancer, secondary carcinoma, or death from any cause) in the intention-to-treat population. This study is registered with EudraCT (number 2005-005275-15) and ClinicalTrials.gov (number NCT00556374), and is ongoing for long-term follow-up. Findings Between Dec 18, 2006, and July 22, 2013, 3425 eligible patients were enrolled and randomly assigned; 1711 to the denosumab group and 1709 to the placebo group (with five others withdrawing consent). After a median followup of 73 months (IQR 58-95), 240 (14.0%) patients in the denosumab and 287 (16.8%) in the placebo group had disease-free survival events. Disease-free survival was significantly improved in the denosumab group versus the placebo group (hazard ratio 0.82, 95% CI 0.69-0.98, Cox p=0.0260; descriptive analysis, without controlling for multiplicity). In the denosumab group, disease-free survival was 89.2% (95% CI 87.6-90.8) at 5 years and 80.6% (78.1-83.1) at 8 years of follow-up, compared with 87.3% (85.7-89.0) at 5 years and 77.5% (74.8-80.2) and 8 years in the placebo group. No independently adjudicated cases of osteonecrosis of the jaw or confirmed atypical femoral fractures were recorded. The total number of adverse events was similar in the denosumab group (1367 [including 521 serious] adverse events) and the placebo group (1339 [515 serious]). The most common serious adverse events were osteoarthritis (62 [3.6%] of 1709 in the denosumab group vs 58 [3.4%] of 1690 in the placebo group), meniscus injury (23 [1.3%] vs 24 [1.4%]), and cataract (16 [0.9%] vs 28 [1.7%]). One (< 0.1%) treatment-related death (due to pneumonia, septic kidney failure, and cardiac decompensation) occurred in the denosumab group. Interpretation Denosumab constitutes an effective and safe adjuvant treatment for patients with postmenopausal hormone receptor-positive early breast cancer receiving aromatase inhibitor therapy. Copyright (c) 2019 Elsevier Ltd. All rights reserved.
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TI Appropriateness of clinical criteria for the use of SYmptomatic Slow-Acting Drug for OsteoArthritis (SYSADOA). A Delphi Method Consensus initiative among experts in Italy
SO EUROPEAN JOURNAL OF PHYSICAL AND REHABILITATION MEDICINE
LA English
DT Article
DE Osteoarthritis; Delphi technique; Consensus
ID knee osteoarthritis; glucosamine sulfate; double-blind; injection therapy; management; placebo; guidelines; replacement; chondroitin; efficacy
AB BACKGROUND: Osteoarthritis (OA) is a theme currently representing an emerging topic for its increasing incidence. It is well known that it is a chronic

disease that could lead to important long-lasting disability; this generates increasing costs for the health care system. OA treatment options vary: localization, etiology, grading and symptomatology should be considered before choosing the most adequate therapy. Currently, a modern approach to managing OA involves SYmptomatic Slow-Acting Drug for OsteoArthritis(SYSADOAs). However, while all preparations may claim to deliver a therapeutic level of glucosamine or chondroitin, not all of them are supported by clinical evidence. Recently the European Society for Clinical and Economic aspects of Osteoporosis, Osteoarthritis and musculoskeletal diseases (ESCEO), produced an evidenced based document providing practitioners with the latest clinical and economic information, thereby allowing them to optimize the management of knee OA. According to this report, only crystalline glucosamine sulphate and the pharmaceutical-grade chondroitin sulphate are considered as effective in the first line approach to treating knee OA as an alternative drug to acetaminophen. However, some OA guidelines do not agree are not concordant in recommending the use of SYSADOA, perhaps because they are generally considered as a class and distinctions among formulations are not made. AIM: Aim of this study was to identify the main aspects involved in patient selection, the choice of therapeutic agents and the safety profile in using SYSADOA. DESIGN: Delphi method Consenus Statement. POPULATION: Italian Physicians having expertise in Ostcoarthritis management. METHODS: A committee of 11 experts from Italian universities, public hospitals, territorial services. research institutes and patient associations was set up. Sixty-three clinicians from a large number of Italian medical centers specialized in osteoarthritis management took part in a Delphi process which was aimed at obtaining consensus statements among the participants. RESULTS: Large consensus was obtained for statements grouped under the following main themes: treatment indications; drug/medical devices choice; treatment efficacy. CONCLUSIONS: Results from the Italian consensus on appropriateness of OA therapies in osteoarthritis seems to be in line with the stepwise approach proposed by the ESCEO algorithm, where crystalline glucosamine sulphate shows greater clinical efficacy than other glucosamine-based formulations, according to several independent meta-analyses. CLINICAL REHABILITATION IMPACT: This study may be used as a practical reference tool to help Italian physicians treat osteoarthritis patients using SYSADOA.
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TI Recent advances in functional nanostructured materials for bone-related diseases
SO JOURNAL OF MATERIALS CHEMISTRY B
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DT Review
ID selective drug-delivery; mesenchymal stem-cells; in-vitro; thermoresponsive hydrogels; osteogenic differentiation; thermosensitive hydrogel; extracellular-matrix; oxide nanoparticles; pulmonary delivery; hyaluronic-acid
AB Bone-related diseases seriously threaten people's health and research studies have been dedicated towards searching for new and effective treatment methods. Nanotechnologies have opened up a new field in recent decades and nanostructured materials, which exist in a variety of forms, are considered to be promising materials in this field. This article reviews the most recent progress in the development of nanostructured materials for bone-related diseases, including osteoporosis, osteoarthritis, bone metastasis, osteomyelitis, myeloma, and bone defects. We highlight the advantages and functions of nanostructured materials, including sustained release, bone targeting, scaffolding in bone tissue engineering, etc., in bone-related diseases. We also include the remaining challenges of these emerging materials.
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TI Microsimulation model for the health economic evaluation of osteoporosis interventions: study protocol
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DT Article
ID core diabetes model; quality-of-life; cost-effectiveness; dubbo osteoporosis;

clinical-outcm; residual lifetime; fracture; risk; men; validation
AB Introduction Osteoporosis is a systemic skeletal disease that is characterised by reduced bone strength and increased fracture risk. Osteoporosis-related fractures impose enormous disease and economic burden to the society. Although many treatments and health interventions are proven effective to prevent fractures, health economic evaluation adds evidence to their economic merits. Computer simulation modelling is a useful approach to extrapolate clinical and economic outcomes from clinical trials and it is increasingly used in health economic evaluation. Many osteoporosis health economic models have been developed in the past decades; however, they are limited to academic use and there are no publicly accessible health economic models of osteoporosis. Methods and analysis We will develop the Australian osteoporosis health economic model based on our previously published microsimulation model of osteoporosis in the Chinese population. The development of the model will follow the recommendations for the conduct of economic evaluations in osteoporosis by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases and the US branch of the International Osteoporosis Foundation. The model will be a state-transition semi-Markov model with memory. Clinical parameters in the model will be mainly obtained from the Dubbo Osteoporosis Epidemiology Study and the health economic parameters will be collected from the Australian arm of the International Costs and Utilities Related to Osteoporotic Fractures Study. Model transparency and validates will be tested using the recommendations from Good Research Practices in Modelling Task Forces. The model will be used in economic evaluations of osteoporosis interventions including pharmaceutical treatments and primary care interventions. A user-friendly graphical user interface will be developed, which will connect the user to the calculation engine and the results will be generated. The user interface will facilitate the use of our model by people in different sectors. Ethics and dissemination No ethical approval is needed for this study. Results of the model validation and future economic evaluation studies will be submitted to journals. The user interface of the health economic model will be publicly available online accompanied with a user manual.
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TI Nanomedicines for improved targetability to inflamed synovium for treatment of rheumatoid arthritis: Multi-functionalization as an emerging strategy to optimize therapeutic efficacy
SO JOURNAL OF CONTROLLED RELEASE
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DT Review
DE Nanomedicines; Multi-functionalization; Extended plasma half-life; Improved targetability and synovial internalisation; Receptor-mediated endocytosis; Superior therapeutic efficacy
ID solid lipid nanoparticles; nf-kappa-b; adjuvant-induced arthritis; collagen-induced arthritis; vasoactive-intestinal-peptide; modifying antirheumatic drugs; folate-targeted nanoparticles; antigen-induced arthritis; necrosis-factor-alpha; saint-o-sm
AB Owing to its intricate autoimmune pathophysiology and significant risks of progression to other rheumatic comorbidities (i.e., osteoporosis and osteoarthritis), a plausible therapeutic regimen is mandatory for early-stage management of rheumatoid arthritis (RA). Nevertheless, the conventional therapeutic agents particularly the corticosteroids and disease-modifying anti-rheumatic drugs (DMARDs) have shown grander success in the treatment of RA; however, long-term use of these agents is also associated with serious adverse events. To combat these issues and optimize therapeutic efficacy, nanotechnology-based interventions have been emerged as viable option. While, nanomedicines signposted superiority over the conventional pharmacological moieties; there are still many pharmacokinetic and pharmacodynamic challenges to nanomedicines following their intravenous or infra-articular administration. To circumvent these challenges, significant adaptations such as PEGylation, surface conjugation of targeting ligand(s), and site-responsive behavior (i.e., pH-, biochemical-, or thermal-responsiveness) have been implemented. Besides, multi-functionalization of nanomedicines has been emerging as an exceptional strategy to overcome pharmacokinetic challenges, improve targetability to inflamed synovium, maximise internalisation into the

activated macrophages, and improved therapeutic outcomes for treatment of RA. Therefore, this review aims to conceptualize and recapitulate the substantial evidences regarding the pharmacokinetic and pharmacodynamic superiority of multi-functionalized nanomedicines over the naked nanomedicines for site-selective targeting to inflamed synovium and rational treatment of RA and other rheumatic co-morbidities. Pharmaceutical sustainability of the multi-functionalized nanomedicines for improved biocompatibility, profound interaction with the targeting tissue/cells/sub-cellular domain, and diminished systemic toxicity has also been pondered.
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AU Yang, YM
Lei, H
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TI Effect of the PTHrP(1-34) analog abaloparatide on inducing chondrogenesis involves inhibition of intracellular reactive oxygen species production
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS
LA English
DT Article
DE Abaloparatide; Osteoarthritis; Chondrogenesis; Mesenchymal stem cells; Reactive oxygen species
ID parathyroid-hormone; oxidative stress; cell-death; differentiation; hypertrophy; culture
AB Osteoarthritis (OA) is a degenerative joint disease characterized by a progressive loss of articular cartilage. Mesenchymal stem cells transplanted to damaged tissues are promising for OA cartilage repair. However, these cells are poor survival after transplantation and acquire hypertrophic properties during chondrogenic induction. Parathyroid hormone-related protein (PTHrP) promotes chondrogenesis and suppresses chondrocyte hypertrophic differentiation. Additionally, PTHrP was reported to have antioxidant effects. The synthetic PTHrP(1-34) analog abaloparatide (ABL) is a newly approved drug for osteoporosis therapy. It is unknown whether ABL stimulates chondrogenesis and affects intracellular reactive oxygen species (ROS) production. By using mouse embryonic

limb bud mesenchymal stem cells in micromass culture as an in vitro model of chondrogenic differentiation, we found that mesenchymal stem cells in micromass cultures spontaneously produced ROS, and N-acetyl-L-cysteine, a potent antioxidant, enhanced chondrogenesis. The effect of ABL on stimulation of chondrogenesis is involved in its inhibition of intracellular ROS generation. These novel findings support the use of ABL for the damaged cartilage regeneration. (C) 2019 Elsevier Inc. All rights reserved.
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TI Vitamin K as a Powerful Micronutrient in Aging and Age-Related Diseases: Pros and Cons from Clinical Studies
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE vitamin K; vitamin K-dependent proteins; cardiovascular diseases; skeletal health; inflammaging; pathological calcification; inflammation
ID matrix gla-protein; bone-mineral density; hormone replacement therapy; community-dwelling adults; vascular smooth-muscle; coronary-heart-disease; postmenopausal women; menaquinone-7 supplementation; hemodialysis-patients; older-adults
AB Vitamin K is a multifunctional micronutrient implicated in age-related diseases such as cardiovascular diseases, osteoarthritis and osteoporosis. Although vitamin K-dependent proteins (VKDPs) are described to have a crucial role in the pathogenesis of these diseases, novel roles have emerged for vitamin K, independently of its role in VKDPs carboxylation. Vitamin K has been shown to act as an anti-inflammatory by suppressing nuclear factor kappa B (NF-kappa B) signal transduction and to exert a protective effect against oxidative stress by blocking the generation of reactive oxygen species. Available clinical evidences indicate that a high vitamin K status can exert a protective role in the inflammatory and mineralization processes associated with the onset and progression of age-related diseases. Also, vitamin K involvement as a protective super-micronutrient in aging and inflammaging is arising, highlighting its future use in clinical practice. In this review we summarize current knowledge regarding clinical data on vitamin K in skeletal and cardiovascular health, and discuss the potential of vitamin K supplementation as a health benefit. We describe the clinical evidence and explore molecular aspects of vitamin K protective role in aging and age-related diseases, and its involvement as a modulator in the interplay between pathological calcification and inflammation processes.
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Z9 60
U1 0
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
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Bougault, Carole
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TI Design, synthesis and biological evaluation of inhibitors of cathepsin K on dedifferentiated chondrocytes
SO BIOORGANIC & MEDICINAL CHEMISTRY
LA English
DT Article
DE Azanitrile; Cathepsin K inhibitors; Chondrocyte; Dedifferentiation; Osteoarthritis
ID azadipeptide nitrile inhibitors; human articular chondrocytes; cartilage formation; highly potent; osteoporosis; expression; odanacatib; redifferentiation; degeneration; quantity
AB Selective proteinase inhibitors have demonstrated utility in the investigation of cartilage degeneration mechanisms and may have clinical use in the management of osteoarthritis. The cysteine protease cathepsin K (CatK) is an attractive target for arthritis therapy. Here we report the synthesis of two cathepsin K inhibitors (CKIs): racemic azanitrile derivatives CKI-E and CKI-F, which have better inhibition properties on CatK than the commercial inhibitor odanacatib (ODN). Their IC50 values and inhibition constants (K-i) have been determined in vitro. Inhibitors demonstrate differential selectivity for CatK over cathepsin B, L and S in vitro, with Ki amounting to 1.14 and 7.21 nM respectively. We analyzed the effect of these racemic inhibitors on viability in different cell types. The human osteoblast-like cell line MG63, MOVAS cells (a murine vascular smooth muscle cell line) or murine primary chondrocytes, were treated either with CKI-E or with CKI-F, which were not toxic at doses of up to 5 mu M. Primary chondrocytes subjected to several passages were used as a model of phenotypic loss of articular chondrocytes, occurring in osteoarthritic cartilage. The efficiency of CKIs regarding CatK inhibition and their specificity over other proteases were validated in primary chondrocytes subjected to several passages. Racemic CKI-E and CKI-F at 0.1 and 1 mu M significantly inhibited CatK activity in dedifferentiated chondrocytes, even better than the commercial CatK inhibitor ODN. The enzymatic activity of other proteases such as matrix metalloproteinases or aggrecanases were not affected. Taken together, these findings support the possibility to design CatK inhibitors for preventing cartilage degradation in different pathologies.
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NR 52
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Song, Chunli
TI Exosomal long noncoding RNAs in aging and age-related diseases
SO IUBMB LIFE
LA English
DT Review
DE age-related diseases; aging; exosomes; lncRNAs
ID emerging role; potential biomarkers; transferrin receptor; mediated transfer; senescent cells; up-regulation; cancer; micrornas; vesicles; proliferation
AB Molecules secreted by cells into the internal environment during aging, including those secreted in exosomes, have long been a matter of concern. Those cells that absorb exosomes, also known as recipient cells, exhibit certain phenotypic changes because of the regulatory role of functional molecules (including proteins and nucleic acids) released in exosomes. Involvement of

noncoding RNAs (ncRNAs) in the regulation of aging has received increasing attention, and long ncRNAs (lncRNAs) have become one of the research hotspots in recent years. LncRNAs carried by exosomes play a role in intercellular communication between adjacent and distant cells. Moreover, exosomal lncRNAs promote the decline of organ functions and the development of age-related diseases, including atherosclerosis, Type 2 diabetes, osteoporosis, osteoarthritis, rheumatoid arthritis, Parkinson's disease, multiple sclerosis, and cancer. Here, we review the regulatory roles of exosomal lncRNAs in aging and age-related diseases.
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NR 105
TC 25
Z9 28
U1 0
U2 23
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1521-6543
EI 1521-6551
J9 IUBMB LIFE
JI IUBMB Life
PD DEC 15
PY 2019
VL 71
IS 12
BP 1846
EP 1856
DI 10.1002/iub.2141
PG 11
WC Biochemistry & Molecular Biology; Cell Biology
SC Biochemistry & Molecular Biology; Cell Biology
GA JL6SW
UT WOS:000495661000002
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ER

PT J
AU Iapichino, MC
AF Iapichino, M. C.
TI Tapentadol prolonged release for pain control in a frail obese patient: a case report
SO EUROPEAN REVIEW FOR MEDICAL AND PHARMACOLOGICAL SCIENCES
LA English
DT Article
DE Tapentadol; Fragile patients; Chronic pain; Rehabilitation

ID oxycodone controlled-release; opioid therapy; double-blind; osteoarthritis; management; efficacy; moderate; safety; disease; burden
AB We present the case of a 59-year-old woman with third-grade obesity and severe comorbidities including osteoporosis, dyslipidemia, diabetes mellitus, hypertension, night eating following bariatric biliary-intestinal by-pass surgery, severe fibromyalgia, poly-arthrosis, lumbar disc herniation in L5S1, sleep disorders and sleep apnea syndrome, and emotional disorders with anxiety and depression, who suffered from chronic pain unresponsive to a combination of multiple analgesics. After a period of metabolic and nutritional rehabilitation. analgesic treatment with tapentadol prolonged release (PR) was started and gradually increased to a daily dose of 300 mg with optimal pain control and a marked improvement in the quality of life and autonomy. Therapy suspension was followed by rebound pain with a worsening in functional capacity, and thus, the patient requested a new rehabilitation treatment, with new benefits. Analgesia is of paramount importance in fragile patients who are undergoing a rehabilitation period, in order to improve compliance with the rehabilitation protocols and increase the success of behavioral therapy. Tapentadol PR can be an effective analgesic therapy for pain control in several settings. Its peculiar tolerability profile improves the acceptability of tapentadol, even in patients with multiple previous analgesic treatments.
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NR 25
TC 0
Z9 1
U1 0
U2 3
PU VERDUCI PUBLISHER
PI ROME
PA VIA GREGORIO VII, ROME, 186-00165, ITALY
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EI
J9 EUR REV MED PHARMACO
JI Eur. Rev. Med. Pharmacol. Sci.
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WC Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
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PT J
AU Xie, BP
Shi, LY
Li, JP
Zeng, Y

Liu, W
Tang, SY
Jia, LJ
Zhang, J
Gan, GX
AF Xie, Bao-ping
Shi, Li-ying
Li, Jin-ping
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Liu, Wei
Tang, Si-yuan
Jia, Lu-juan
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Gan, Guo-xing
TI Oleanolic acid inhibits RANKL-induced osteoclastogenesis via ER alpha/miR-503/RANK signaling pathway in RAW264.7 cells
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Oleanolic acid; Osteoclasts; Estrogen receptor alpha (ER alpha); Methylpiperidino pyrazole; MicroRNA-503; Osteoporosis
ID estrogen-receptor-alpha; bone loss; differentiation; expression; microrna
AB Oleanolic acid (OA) has recently become a research hotspot in the treatment of many human diseases, especially osteoporosis and arthritis. However, the mechanisms are not elucidated completely. We aimed to elucidate the target and the mechanism via which OA inhibited osteoclast differentiation. We used TRAP staining and toluidine blue dye to test OA effect on osteoclastogenesis and bone resorption respectively. We detected the expression level of osteoclast differentiation related genes, estrogen receptor alpha (ER alpha) and miR-503. We blocked ER alpha with its specific blocker, methylpiperidino pyrazole (MPP). We antagonized the function of miR-503 with antagomir-503-5p. RT-PCR and ELISA kits were used to investigate the effects of OA on miR-503 formation and maturation-relevant enzymes Dicer and Drosha at gene and protein levels. The data suggested that OA inhibited osteoclastogenesis and bone resorption. OA upregulated ER alpha and miR-503 expression levels, inhibited RANK expression. MPP significantly attenuated the OA effect including inhibiting osteoclastogenesis, inhibiting bone resorption and up-regulating miR-503 expression. It showed that ER alpha was the target of OA and OA up-regulated miR-503 expression through ER alpha. Antagomir-503-5p inhibited the function of miR-503 and attenuated the inhibition of OA on osteoclastogenesis, suggesting that OA inhibited osteoclast by up-regulating miR-503 expression. In addition, OA up-regulated miR-503 by up-regulating Dicer expression. In conclusion, OA inhibits RANKL-induced osteoclastogenesis via ER alpha/miR-503/ RANK signaling pathway in RAW264.7 cells.

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Z9 52
U1 0
U2 27
PU ELSEVIER FRANCE-EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER
PI ISSY-LES-MOULINEAUX
PA 65 RUE CAMILLE DESMOULINS, CS50083, 92442 ISSY-LES-MOULINEAUX, FRANCE
SN 0753-3322
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J9 BIOMED PHARMACOTHER
JI Biomed. Pharmacother.
PD SEP 15
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WC Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Research & Experimental Medicine; Pharmacology & Pharmacy
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PT J
AU Myszka, A
Kubicka, AM
Tomczyk, J
AF Myszka, Anna
Kubicka, Anna M.
Tomczyk, Jacek
TI The mechanical hypothesis of septal aperture formation tested in an early medieval population from Ostrow Lednicki (Poland)
SO JOURNAL OF ANATOMY
LA English
DT Article
DE brachialis muscle; entheses; supratrochlear foramen; triceps muscle; ulna
ID musculoskeletal stress markers; coronoid-olecranon septum; supratrochlear foramen; entheseal changes; humerus; age; perforation; fractures; death
AB The aetiology of septal aperture formation is still an open question. The influence of bone robusticity, osteoarthritis, osteoporosis, and the size and shape of ulnar processes has been discussed. Some researchers have shown that weaker muscles lead to greater joint hypermobility, the impingement of ulnar processes on the humeral lamina, and, consequently, septal aperture formation. Assuming this theory is correct, the question is whether flexion or extension or both play a role in septal lamina perforation. The aim of the study was to examine the mechanical hypothesis of septal aperture formation in samples of skeletal material derived from an early medieval cemetery in Ostrow Lednicki (Poland). A total of 136 pairs of bones (humeri and ulnae) were examined. Septal aperture was scored as present or absent. Entheseal changes in ulna were used as markers of activity patterns, especially involving elbow extension and flexion. Entheseal changes were assessed based on a three-point rating scale. A significant negative correlation between septal aperture and triceps muscles was noted in right bones in females (tau = -0.331) and in both sexes combined (tau = -0.322). The relationship between septal aperture and the brachialis muscle was positive but non-significant. This means that looser triceps lead to greater looseness of the elbow, greater protrusion of the olecranon process, and consequent septal aperture formation. Different results were obtained for the brachialis, which may suggest that forearm flexion does not significantly affect septal lamina perforation.
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NR 62
TC 5
Z9 7

U1 0
U2 13
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 J ANAT
JI J. Anat.
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WC Anatomy & Morphology
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PT J
AU Kim, WB
Kim, BR
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Han, EY
Nam, KW
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Kim, JH
AF Kim, Won Bin
Kim, Bo Ryun
Kim, Sang Rim
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Nam, Kwang Woo
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TI Comorbidities in Patients With End-Stage Knee OA: Prevalence and Effect on Physical Function

SO ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION
LA English
DT Article
DE Comorbidity; Knee; Osteoarthritis; Quality of life; Rehabilitation
ID 6-minute walk test; muscle strength; quadriceps strength; older-adults; reported outcm; national-health; lumbar spine; total hip; osteoarthritis; disability
AB Objective: To investigate the prevalence of comorbidities and their effect on physical function, quality of life (QOL), and pain, in patients with end-stage knee osteoarthritis (OA). Design: A cross-sectional study. Setting: A rehabilitation facility at university hospital. Participants: Patients (N = 577; 503 women and 74 men) diagnosed with end-stage knee OA between October 2013 and June 2018. Intervention: Not applicable. Main Outcome Measures: Comorbidities were as follows: osteoporosis, presarcopenia, degenerative spine disease, diabetes, and hypertension. All patients completed the following performance-based physical function tests: stair-climbing test (SCT), 6-minute walk test (6MWT), timed Up and Go (TUG) test, and gait analysis. Self-reported physical function and pain were measured using Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) and a visual analog scale (VAS), respectively, and self-reported QOL was measured using EuroQoL 5 dimensions (EQ-5D) questionnaire. Results: Univariate analyses revealed that patients with osteoporosis had significantly higher scores in SCT ascent, SCT descent, TUG, WOMAC pain tests, and lower scores in 6MWT, gait speed, and cadence tests than those without osteoporosis. Patients with presarcopenia recorded higher scores in SCT ascent, TUG, EQ-5D, and lower scores in 6MWT and gait speed tests than those without presarcopenia. Patients with degenerative spine disease showed higher scores in WOMAC pain and lower scores in gait speeds than those without degenerative spine disease. Patients with diabetes showed higher scores in SCT ascent than those without diabetes, and patients with hypertension showed lower scores in 6MWT than those without hypertension. After adjusting age, sex, and body mass index, SCT descent retained significant association with osteoporosis, SCT ascent showed independent association with presarcopenia and diabetes, and WOMAC pain revealed significant association with degenerative spine disease. Conclusion: The results confirm associations between comorbidities, performance-based and self-reported physical functions, and QOL in patients with end-stage knee OA. (C) 2019 by the American Congress of Rehabilitation Medicine
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NR 55
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Z9 15
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WC Rehabilitation; Sport Sciences
SC Rehabilitation; Sport Sciences
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PT J
AU Adams, J
McIntyre, E
Frawley, J
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AF Adams, Jon
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TI Formal and informal healthcare behaviours of women with chronic illness: A cross-sectional analysis of 1925 women
SO INTERNATIONAL JOURNAL OF CLINICAL PRACTICE
LA English
DT Article
ID alternative medicine; self-care; complementary; adults
AB Aim: To describe the healthcare behaviours of Australian women (45 years and over) diagnosed with a chronic illness. Methods: This is a cross-sectional sub-study of the 45 and Up Study-the largest study of healthy ageing conducted in the Southern Hemisphere-including 1,932 Australian women (45 years and older) with a self-reported diagnosis of either depression, asthma, diabetes, osteoarthritis or osteoporosis. Questionnaires were posted to eligible participants between September and December 2016 and included self-reported use of formal and

informal health services and healthcare behaviours, and health practitioner recommendations and monitoring of informal care. Descriptive statistics were used to describe the sample characteristics and chi-square tests assessed associations between variables. Results: The average age of participants was 69. We found that 53.7% of the women used informal healthcare products or practices for their chronic illness (eg exercise, nutritional supplements). These women were significantly (P < 0.001) more likely to consult with all types of health practitioners, compared with women not using informal healthcare. Physical activity and nutritional supplements were the most commonly recommended product or practice by all healthcare practitioners. However, informal healthcare behaviours were not regularly recommended or monitored by health practitioners. Conclusions: Women use a range of informal products and practices to manage chronic illness, but many fail to communicate with their health practitioners about such use. Future research should consider how to encourage better communication between health practitioners and patients related to informal healthcare for chronic illness to help ensure safe, effective, coordinated patient management.
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NR 32
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Z9 5
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PT J
AU Luo, J
Sun, P
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Xiao, JR
AF Luo, Jian
Sun, Peng
Siwko, Stefan
Liu, Mingyao
Xiao, Jianru
TI The role of GPCRs in bone diseases and dysfunctions
SO BONE RESEARCH
LA English
DT Review
ID protein-coupled-receptor; hormone-releasing-hormone; genome-wide association; adolescent idiopathic scoliosis; fatty-acid receptor; metabotropic glutamate-receptor; regulates osteoclast function; calcium-sensing receptor; prostaglandin-e receptor; glucagon-like peptide-1
AB The superfamily of G protein-coupled receptors (GPCRs) contains immense structural and functional diversity and mediates a myriad of biological processes upon activation by various extracellular signals. Critical roles of GPCRs have been established in bone development, remodeling, and disease. Multiple human GPCR mutations impair bone development or metabolism, resulting in osteopathologies. Here we summarize the disease phenotypes and dysfunctions caused by GPCR gene mutations in humans as well as by deletion in animals. To date, 92 receptors (5 glutamate family, 67 rhodopsin family, 5 adhesion, 4 frizzled/taste2 family, 5 secretin family, and 6 other 7TM receptors) have been associated with bone diseases and dysfunctions (36 in humans and 72 in animals). By analyzing data from these 92 GPCRs, we found that mutation or deletion of different individual GPCRs could induce similar bone diseases or dysfunctions, and the same individual GPCR mutation or deletion could induce different bone diseases or dysfunctions in different populations or animal models. Data from human diseases or dysfunctions

identified 19 genes whose mutation was associated with human BMD: 9 genes each for human height and osteoporosis; 4 genes each for human osteoarthritis (OA) and fracture risk; and 2 genes each for adolescent idiopathic scoliosis (AIS), periodontitis, osteosarcoma growth, and tooth development. Reports from gene knockout animals found 40 GPCRs whose deficiency reduced bone mass, while deficiency of 22 GPCRs increased bone mass and BMD; deficiency of 8 GPCRs reduced body length, while 5 mice had reduced femur size upon GPCR deletion. Furthermore, deficiency in 6 GPCRs induced osteoporosis; 4 induced osteoarthritis; 3 delayed fracture healing; 3 reduced arthritis severity; and reduced bone strength, increased bone strength, and increased cortical thickness were each observed in 2 GPCR-deficiency models. The ever-expanding number of GPCR mutation-associated diseases warrants accelerated molecular analysis, population studies, and investigation of phenotype correlation with SNPs to elucidate GPCR function in human diseases.

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TI A chronological map of 308 physical and mental health conditions from 4 million

individuals in the English National Health Service
SO LANCET DIGITAL HEALTH
LA English
DT Article
ID pathophysiology; diseases; profile; asthma; onset; care
AB Background To effectively prevent, detect, and treat health conditions that affect people during their lifecourse, health-care professionals and researchers need to know which sections of the population are susceptible to which health conditions and at which ages. Hence, we aimed to map the course of human health by identifying the 50 most common health conditions in each decade of life and estimating the median age at first diagnosis. Methods We developed phenotyping algorithms and codelists for physical and mental health conditions that involve intensive use of health-care resources. Individuals older than 1 year were included in the study if their primary-care and hospital-admission records met research standards set by the Clinical Practice Research Datalink and they had been registered in a general practice in England contributing up-to-standard data for at least 1 year during the study period. We used linked records of individuals from the CALIBER platform to calculate the sex-standardised cumulative incidence for these conditions by 10-year age groups between April 1, 2010, and March 31, 2015. We also derived the median age at diagnosis and prevalence estimates stratified by age, sex, and ethnicity (black, white, south Asian) over the study period from the primary-care and secondary-care records of patients. Findings We developed case definitions for 308 disease phenotypes. We used records of 2 784 138 patients for the calculation of cumulative incidence and of 3 872 451 patients for the calculation of period prevalence and median age at diagnosis of these conditions. Conditions that first gained prominence at key stages of life were: atopic conditions and infections that led to hospital admission in children (<10 years); acne and menstrual disorders in the teenage years (10-19 years); mental health conditions, obesity, and migraine in individuals aged 20-29 years; soft-tissue disorders and gastro-oesophageal reflux disease in individuals aged 30-39 years; dyslipidaemia, hypertension, and erectile dysfunction in individuals aged 40-59 years; cancer, osteoarthritis, benign prostatic hyperplasia, cataract, diverticular disease, type 2 diabetes, and deafness in individuals aged 60-79 years; and atrial fibrillation, dementia, acute and chronic kidney disease, heart failure, ischaemic heart disease, anaemia, and osteoporosis in individuals aged 80 years or older. Black or south-Asian individuals were diagnosed earlier than white individuals for 258 (84%) of the 308 conditions. Bone fractures and atopic conditions were recorded earlier in male individuals, whereas female individuals were diagnosed at younger ages with nutritional anaemias, tubulointerstitial nephritis, and urinary disorders. Interpretation We have produced the first chronological map of human health with cumulative-incidence and period-prevalence estimates for multiple morbidities in parallel from birth to advanced age. This can guide clinicians, policy makers, and researchers on how to formulate differential diagnoses, allocate resources, and target research priorities on the basis of the knowledge of who gets

which diseases when. We have published our phenotyping algorithms on the CALIBER open-access Portal which will facilitate future research by providing a curated list of reusable case definitions. Copyright (C) 2019 The Author(s). Published by Elsevier Ltd.
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TI Radiofrequency echographic multi-spectrometry for the in-vivo assessment of bone strength: state of the art-outcomes of an expert consensus meeting organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
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DT Review
DE Bone strength assessment; Osteoporosis diagnosis; Fracture risk; REMS; Ultrasound; Lumbar spine; Femoral neck
ID finite-element-analysis; quantitative computed-tomography; fracture risk prediction; mineral density; hip fracture; lumbar spine; score tbs; fragility fractures; proximal femur; older men
AB Purpose The purpose of this paper was to review the available approaches for bone strength assessment, osteoporosis diagnosis and fracture risk prediction, and to provide insights into radiofrequency echographic multi spectrometry (REMS), a non-ionizing axial skeleton technique. Methods A working group convened by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis met to review the current image-based methods for bone strength assessment and fracture risk estimation, and to discuss the clinical perspectives of REMS. Results Areal bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) is the consolidated indicator for osteoporosis diagnosis and fracture risk assessment. A more reliable fracture risk estimation would actually require an improved assessment of bone strength, integrating also bone quality information. Several different approaches have been proposed, including additional DXA-based parameters, quantitative computed tomography, and quantitative ultrasound. Although each of them showed a somewhat improved clinical performance, none satisfied all the requirements for a widespread routine employment, which was typically hindered by unclear clinical usefulness, radiation doses, limited accessibility, or inapplicability to spine and hip, therefore leaving several clinical needs still unmet. REMS is a clinically available technology for osteoporosis diagnosis and fracture risk assessment through the estimation of BMD on the axial skeleton reference sites. Its automatic processing of unfiltered ultrasound signals provides accurate BMD values in view of fracture risk assessment. Conclusions New approaches for improved bone strength and fracture risk estimations are needed for a better management of osteoporotic patients. In this context, REMS represents a valuable approach for osteoporosis diagnosis and fracture risk prediction.
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Z9 88
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TI Chondrocyte enlargement is a marker of osteoarthritis severity
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Chondrocyte size; Hypertrophic markers; Cartilage
ID cartilage; differentiation; hypertrophy; growth; bone
AB Objective: We aimed to assess whether an increase in chondrocyte size might be a feature of the articular cartilage (AC) hypertrophic-like phenotype both in experimental and in human osteoarthritis (OA). The anatomical location of these enlarged cells in the cartilage layers was also evaluated. Methods: Experimental OA was carried out in female rabbits alone or in combination with osteoporosis (OPOA). The rabbits were subjected to destabilization knee surgery to develop OA. Osteoporosis was induced with ovariectomy and methylprednisolone administration. Human OA samples obtained from knee replacement surgery were also studied. Cartilage lesions and chondrocyte size were assessed in AC sections. Immunostaining of type-X collagen and metalloproteinase-13 were used as markers of the AC hypertrophic transformation. Both the cell size and the gene expression of type-X collagen were further analyzed in primary murine chondrocyte cultures. Results: Compared to healthy AC, chondrocyte size was increased both in experimental and in human OA, in correlation with the severity of cartilage damage. No differences in chondrocyte size were found between deeper or more superficial regions of AC. In cell cultures, accretion of hypertrophic markers and cell enlargement were found to occur synchronized. Conclusions: We observed an enhancement in the mean size of chondrocytes at the OA cartilage, which showed correlation with cartilage damage, both in human and in experimental OA. The enlarged chondrocytes were homogeneously distributed throughout the AC.

Our results suggest that chondrocyte size could be a reliable measure of disease progression, of potential use in the histopathological assessment of OA cartilage.
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TI Xian-Ling-Gu-Bao induced inflammatory stress rat liver injury: Inflammatory and oxidative stress playing important roles
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article

DE Xian Ling Gu Bao; Osteoarthritis; Hepatotoxicity; Inflammation factor; Oxidative stress
ID necrosis-factor-alpha; kupffer cell activation; toll-like receptors; fatty liver; cartilage degeneration; cytochrome-p450 2e1; endotoxin levels; 1st multicenter; herbal fufang; double-blind
AB Ethnopharmacological relevance: Xian-Ling-Gu-Bao (XLGB) Fufang is an herbal formula that has been used in clinical settings to treat osteoporosis, osteoarthritis, aseptic bone necrosis, and climacteric syndrome. Despite its uses, XLGB treatment has been linked to potential liver injury. To date, there is a lack of clear demonstration of such toxicity in animal models. Aim of the study: As animal models fail to reproduce the XLGB hepatotoxicity reported in humans, because human hepatocytes are clearly more sensitive to XLGB, this study was designed to investigate a more reliable animal model of such toxicity. Materials and methods: We randomized rats into five groups, as follows: CON (control), XLGB, lipopolysaccharide (LPS), L-XLGB/LPS (XLGB, 0.125 g/kg; LPS, 0.1 mg/kg), and XLGB/LPS (XLGB, 1.25 g/kg; LPS, 0.1 mg/kg). These groups were treated with 0.5% sodium carboxymethyl cellulose (CMC-Na), XLGB suspension, normal saline, or LPS. The first administration of XLGB [0.125 g/kg or 1.25 g/kg, by mouth (PO)] or its solvent (0.5% CMC-Na) was delivered, and then food was removed. Twelve hours after the first administration of XLGB, rats received LPS [0.1 mg/kg, intravenously (IV)] or saline control. After 30 min, a second administration of XLGB (0.125 g/kg or 1.25 g/kg, PO) or solvent was administered. The rats were anesthetized at 12 h or 24 h following the second administration of XLGB. Liver function was evaluated by measuring liver weight, liver microscopy, serum biochemistry and plasma microRNA-122 (miR-122). The plasma levels of 27 cytokines were measured to evaluate inflammation. Moreover, the expression of cytochrome P450 2E1 (CYP2E1), nicotinic adenine dinucleotide phosphate (NADPH) oxidase and inducible nitric oxide synthase (iNOS) at protein levels were observed; immunofluorescence and immunohistochemistry were used to confirmed the hepatotoxicity of XLGB. Results: Hepatotoxicity in male rats with moderate inflammation induced by XLGB was indicated by liver histopathology, serum biochemical analysis, serum miR-122 levels, and immunofluorescent assessments. We observed significant increases in liver weight and liver indexes in male rats with moderate inflammation in response to XLGB. Histopathological assessment further showed that extensive hepatocellular necrosis and inflammatory infiltration were evident in rats co-treated with XLGB/LPS. The levels of serum transaminases [alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT)], total bilirubin (TBIL) and triglyceride (TG), which are markers of liver function, were also significantly increased by XLGB/LPS treatment. Similarly, miR-122 was significantly elevated in XLGB/LPS treated rats relative to other groups. An immunofluorescent assessment showed extensive apoptosis in hepatocytes from these co-treated rats. What is more, XLGB can dose-dependently induce liver injury in male rats with moderate inflammation. Hepatic CYP2E1, neutrophil chemotactic factor (NCF-1), iNOS, and NOX-2 (an NADPH oxidase subunit) levels were increased in response to

XLGB treatment, and staining for DMPO nitrone adducts further showed elevated oxidative stress level in XLGB/LPS-treated rats relative to the other experimental groups. Conclusion: LPS and XLGB co-treatment in rats led to marked hepatotoxicity. This toxicity was associated with disrupted lipid metabolism, extensive liver necrosis and inflammatory infiltration, apoptosis, and expression of oxidative stress-related proteins. These results demonstrate a valuable model for the study of iDILI in the context XLGB treatment, and further provide insights into the potential mechanisms by which XLGB may induce hepatotoxicity in humans.
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NR 76
TC 21
Z9 27

U1 1
U2 36
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
SN 0378-8741
EI 1872-7573
J9 J ETHNOPHARMACOL
JI J. Ethnopharmacol.
PD JUL 15
PY 2019
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IS
BP
EP
DI 10.1016/j.jep.2019.111910
PG 11
WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
SC Plant Sciences; Pharmacology & Pharmacy; Integrative & Complementary Medicine
GA IE1CS
UT WOS:000472124100009
PM 31026554
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PT J
AU Hsu, H
Kung, PT
Ku, MC
Lan, JL
Chou, WY
Tsai, WC
AF Hsu, Huan
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Ku, Ming-Chou
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Tsai, Wen-Chen
TI Do rheumatoid arthritis patients have more major complications and length of stay after lower extremities fracture surgery? A nationwide data with propensity score matching

SO MEDICINE
LA English
DT Article
DE hospitalization length; lower extremities fracture surgery; major complication; rheumatoid arthritis
ID charlson comorbidity index; total knee arthroplasty; hip fracture; risk; mortality; outcm; osteoarthritis; epidemiology; osteoporosis; predictors
AB Patients with rheumatoid arthritis (RA) have a high risk of cardiovascular diseases and fractures. This retrospective cohort study explored whether patients with RA face higher complication risks or longer hospital stays than other patients when they had a lower limb fracture that required the surgery. Patients aged >45 years who received lower limb fracture surgeries between 2005 and 2012 were selected from the National Health Insurance Research Database, and 10 related variables including sex and age were used in propensity score matching to pair RA patients with non-RA patients in a 1:4 ratio. The final study sample comprised 1109 patients with RA and 4436 non-RA patients. The results indicated that 5.57% of the study sample had postoperative complications, accounting for 5.05% of patients with RA and 5.70% of the control group. After conditional logistic regression analysis was performed, the risk of major complications has no significant differences between patients with RA and the control group (odds ratio [OR] = 0.87; 95% confidence interval [CI]: 0.61-1.24; P>.05). However, the comorbidity severity score exerted a significant effect on complications; patients with scores = 3 were 2.78 times more likely to experience complications (OR=2.78; 95% CI 1.52-5.07). When considering different types of complications, patients with RA were less likely to be exposed to the risk of stroke (OR=0.48). After controlling all related factors, no significant differences were observed in the complication risks or deaths between the 2 groups (P>.05). Regarding hospitalization length, the average stay for all patients was 8.12 days; after controlling related factors, the hospitalization length for patients with RA was 0.97 times that of the control group, which was nonsignificant (P>.05). These results may provide some information to healthcare professionals when providing treatments.
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NR 46
TC 2
Z9 2
U1 0
U2 4
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0025-7974
EI 1536-5964
J9 MEDICINE
JI Medicine (Baltimore)
PD JUL 15
PY 2019
VL 98
IS 27
BP
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DI 10.1097/MD.0000000000016286
PG 10
WC Medicine, General & Internal
SC General & Internal Medicine
GA IQ4QQ
UT WOS:000480735700074
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PT J
AU Kanis, JA
Cooper, C
Rizzoli, R
Reginster, JY
AF Kanis, J. A.
Cooper, C.
Rizzoli, R.
Reginster, J. -Y.
TI Executive summary of the European guidance for the diagnosis and management of osteoporosis in postmenopausal women
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Review
DE Bone mineral density; Diagnosis of osteoporosis; Fracture risk assessment; FRAX; Health economics; Treatment of osteoporosis
AB A guidance on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis was recently published in Osteoporosis International as a joint effort of the International Osteoporosis Foundation and European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (Kanis et al. in Osteoporos Int 10.1007/s00198-018-4704-5, 2018). This manuscript updates the previous guidelines document, published in 2013 (Kanis et al. in Osteoporos Int 24:23-57, 2013) and is written in a European perspective. The present article reports and summarizes the main recommendations included in this 2018 guidance document.
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CR Kanis J, 2018, OSTEOPOROS INT, V0, P0
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NR 2
TC 76
Z9 78
U1 1
U2 23
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 0171-967X
EI 1432-0827
J9 CALCIFIED TISSUE INT
JI Calcif. Tissue Int.
PD MAR 15
PY 2019
VL 104
IS 3
BP 235
EP 238
DI 10.1007/s00223-018-00512-x
PG 4
WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA HP0UG
UT WOS:000461381400001
DA 2026-02-10
ER

PT J
AU Almeida, M

Porter, RM
AF Almeida, Maria
Porter, Ryan M.
TI Sirtuins and FoxOs in osteoporosis and osteoarthritis
SO BONE
LA English
DT Article
DE Aging; Autophagy; Chondrocytes; Osteoblasts; Osteoclasts; Osteocytes; Oxidative stress; Senescence; ROS; Wnt signaling
ID transcription factor foxo3a; oxidative stress; beta-catenin; articular chondrocytes; cellular senescence; gene-expression; bone-formation; cartilage homeostasis; mammalian sirtuins; forkhead proteins
AB The sirtuin family of NAD-dependent protein deacetylases promotes longevity and counteracts age-related diseases. One of the major targets of Sirtuins are the FoxO family of transcription factors. FoxOs play a major role in the adaptation of cells to a variety of stressors such as oxidative stress and growth factor deprivation. Studies with murine models of cell-specific loss- or gain-of-function of Sirtuins or FoxOs and with Sirtuinl stimulators have provided novel insights into the function and signaling of these proteins on the skeleton. These studies have revealed that both Sirtuins and FoxOs acting directly in cartilage and bone cells are critical for normal skeletal development, homeostasis and that their dysregulation might contribute to skeletal disease. Deacetylation of FoxOs by Sirtl in osteoblasts and osteoclasts stimulates bone formation and inhibits bone resorption, making Sirtl ligands promising therapeutic agents for diseases of low bone mass. While a similar link has not been established in chondrocytes, Sirtl and FoxOs both have chondroprotective actions, suggesting that Sirtl activators may have similar efficacy in preventing cartilage degeneration due to aging or injury. In this review we summarize these advances and discuss their implications for the pathogenesis of age-related osteoporosis and osteoarthritis.
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TI Secreted Frizzled-related proteins (sFRPs) in osteo-articular diseases: much more than simple antagonists of Wnt signaling?
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ID fibroblast-like synoviocytes; endochondral ossification; cartilage degradation; osteoblast function; mesenchymal cells; gene-expression; bone; osteoarthritis; frzb; inhibitor
AB Osteo-articular diseases are characterized by a dysregulation of joint and/or bone homeostasis. These include diseases affecting the joints originally, such as osteoarthritis and rheumatoid arthritis, or the bone, such as osteoporosis. Inflammation and the involvement of Wingless-related integration site (Wnt) signaling pathways are key pathophysiological features of these diseases resulting in tissue degradation by matrix-degrading enzymes, namely matrix metalloproteinases (MMPs) and a disintegrin and metalloproteinases with thrombospondin motifs (ADAMTs), secreted by the joint resident cells and/or by infiltrating immune cells. Activation of Wnt signaling pathways is modulated by different families of proteins, including Dickkopfs and the secreted Frizzled-related proteins (sFRPs). The sFRP family is composed of five secreted glycoproteins in mammals that regulate Wnt signaling in the extracellular compartment. Indeed, sFRPs are able to bind both to the soluble Wnt ligands and to their cell membrane receptors, the Frizzled proteins. Their expression profile is altered in osteo-articular diseases, suggesting that they could account for the abnormal activation of Wnt pathways. In the present article, we review how sFRPs are more than simple antagonists of the Wnt signaling pathways and discuss their pathophysiological relevance in the context of osteo-articular diseases. We detail their Wnt-dependent and their Wnt-independent roles, with a particular emphasis on their ability to modulate the inflammatory response and extracellular matrix (ECM) remodeling. We also discuss their potential therapeutic use with a focus on bone remodeling, osteo-articular cancers, and tissue engineering.
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TI Fracture types affect clinical outcomes of patients managed within the fracture liaison and osteoporosis medication management services
SO SCIENTIFIC REPORTS
LA English
DT Article
ID hip fracture; practice framework; mortality; capture; reduce
AB Osteoporosis medication in fragility fracture patients is associated with better outcomes. However, limited studies have investigated whether fracture types affect outcomes among patients undergoing treatment. We performed a secondary data analysis on participants from a fracture liaison service and an osteoporosis medication management service. Participants (n = 974) were regrouped into hip fracture (HF), vertebral fracture (VF), HF + VF, and NO HF/VF groups at baseline. Bivariate and multivariate logistic regressions were performed to identify baseline correlates on one-year mortality, incident refractures, and falls. Baseline characteristics were different among fracture groups. The HF group was oldest, with the lowest body mass index (BMI), lowest FRAX (R) T-score and had the highest 10-year fracture risk. After intervention, the HF group still had the highest mortality, but the HF + VF group had the highest refracture and incident fall rates. In the multivariate regression analysis, prevalent HF and VF, lower BMI and albumin level, and having chronic kidney disease or cancer were associated with higher mortality rates. HF + VF patients had the highest refracture risk. Prevalent HF and VF, older age and higher BMI, and having cancer or osteoarthritis were associated with a greater fall risk. HF and VF are associated with adverse outcomes, even under an optimal fracture care.
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TI Algorithm for the Use of Biochemical Markers of Bone Turnover in the Diagnosis, Assessment and Follow-Up of Treatment for Osteoporosis
SO ADVANCES IN THERAPY
LA English
DT Article
DE Algorithm; Bone; Bone biomarker; CTX; Osteoporosis; P1NP; Rheumatology
ID postmenopausal women; fracture risk; double-blind; international osteoporosis; vertebral fractures; metabolism markers; randomized-trial; denosumab; teriparatide; risedronate
AB Introduction Increased biochemical bone turnover markers (BTMs) measured in serum are associated with bone loss, increased fracture risk and poor treatment adherence, but their role in clinical practice is presently unclear. The aim of this consensus group report is to provide guidance to clinicians on how to use BTMs in patient evaluation in postmenopausal osteoporosis, in fracture risk prediction and in the monitoring of treatment efficacy and adherence to osteoporosis medication. Methods A working group with clinical scientists and osteoporosis specialists was invited by the Scientific Advisory Board of European Society on Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Results Serum bone formation marker PINP and resorption marker beta CTX-I are the preferred markers for evaluating bone turnover in the clinical setting due to their specificity to bone, performance in clinical studies, wide use and relatively low analytical variability. BTMs cannot be used to diagnose osteoporosis because of low sensitivity and specificity, but can be of value in patient evaluation where high values may indicate the need to investigate some causes of secondary osteoporosis. Assessing serum levels of beta CTX-I and PINP can improve fracture prediction slightly, with a gradient of risk of about 1.2 per SD increase in the bone marker in addition to clinical risk factors and bone mineral density. For an individual patient, BTMs are not useful in projecting bone loss or treatment efficacy, but it is recommended that serum PINP and beta CTX-I be used to

monitor adherence to oral bisphosphonate treatment. Suppression of the BTMs greater than the least significant change or to levels in the lower half of the reference interval in young and healthy premenopausal women is closely related to treatment adherence. Conclusion In conclusion, the currently available evidence indicates that the principal clinical utility of BTMs is for monitoring oral bisphosphonate therapy.
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Z9 105
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TI Harnessing a Novel Inhibitory Role of miR-16 in Osteogenesis by Human Mesenchymal Stem Cells for Advanced Scaffold-Based Bone Tissue Engineering
SO TISSUE ENGINEERING PART A
LA English
DT Article
DE nonviral delivery; miRNA miR-16; scaffold; osteogenesis; human mesenchymal stem cells
ID collagen-based scaffolds; positive regulation; gene delivery; in-vitro; differentiation; regeneration; proliferation; expression; nanohydroxyapatite; micrornas
AB MicroRNA (miRNA) therapeutics is increasingly being developed to either target bone-related diseases such as osteoporosis and osteoarthritis or as the basis for novel bone tissue engineering strategies. A number of miRNAs have been reported as potential osteo-therapeutics but no consensus has yet been established on the optimal target. miR-16 has been studied extensively in nonosteogenic functions and used as functionality reporter target in the development of nonviral miRNA delivery platforms. This study hypothesized that miR-16 may also play an inhibitory role in osteogenesis due to its ability to directly target Smad5 and AcvR2a. This study thus aimed to assess the potential of miR-16 inhibition to increase osteogenesis in human mesenchymal stem cells (hMSCs) using a previously established miRNA delivery platform composed of nanohydroxyapatite (nHA) particles as nonviral vectors in combination with collagen-nHA scaffolds designed specifically for bone repair. Initial results showed that antagomiR-16 delivery efficiently increased the relative levels of both putative targets and Runx2, the key transcription factor for osteogenesis, while also increasing osteocalcin levels. Furthermore, significant increases in mineral calcium deposition by hMSCs were found in both monolayer and most importantly in scaffold-based osteodifferentiation studies, ultimately demonstrating that miR-16 inhibition further enhances the therapeutic potential of a scaffold with known potential for bone repair applications and thus holds significant therapeutic potential as a novel bone tissue engineering strategy. Furthermore, we suggest that harnessing the additional functions known to miR-16 by incorporating either its enhancers or inhibitors to tissue-specific tailored scaffolds provides exciting opportunities for a diverse range of therapeutic indications.
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TI Exercise as a prescription for patients with various diseases
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DT Review
DE Diseases; Exercise prescription; Patients
ID quality-of-life; low-back-pain; randomized controlled-trial; high-intensity interval; chronic heart-failure; coronary-artery-disease; chronic kidney-disease; obstructive pulmonary-disease; rotator cuff tendinopathy; breast-cancer patients
AB A growing understanding of the benefits of exercise over the past few decades has prompted researchers to take an interest in the possibilities of exercise therapy. Because each sport has its own set of characteristics and physiological complications that tend to occur during exercise training, the effects and underlying mechanisms of exercise remain unclear. Thus, the first step in probing the effects of exercise on different diseases is the selection of an optimal exercise protocol. This review summarizes the latest exercise prescription treatments for 26 different diseases: musculoskeletal system diseases (low back pain, tendon injury, osteoporosis, osteoarthritis, and hip fracture), metabolic system diseases (obesity, type 2 diabetes, type 1 diabetes, and nonalcoholic fatty liver disease), cardio-cerebral vascular system diseases (coronary artery disease, stroke, and chronic heart failure), nervous system diseases (Parkinson's disease, Huntington's disease, Alzheimer's disease, depression, and anxiety disorders), respiratory system diseases (chronic obstructive pulmonary disease, interstitial lung disease, and after lung transplantation), urinary system diseases (chronic kidney disease and after kidney transplantation), and cancers (breast cancer, colon cancer, prostate cancer, and lung cancer). Each exercise prescription is displayed in a corresponding table. The recommended type, intensity, and frequency of exercise prescriptions are summarized, and the effects of exercise therapy on the prevention and rehabilitation of different diseases are discussed. (C) 2019 Published by Elsevier B.V. on behalf of Shanghai University of Sport.
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ID oligomeric matrix protein; mild cognitive impairment; c-terminal telopeptide; alzheimers-disease; turnover markers; ii collagen; serum sclerostin; skeletal-muscle; biochemical markers; synovial-fluid
AB Specific hallmarks are thought to underlie the ageing process and age-related functional decline. In this viewpoint, we put forward the hypothesis that disturbances in the process of tissue maintenance are an important common denominator that may lie in between specific hallmarks of ageing (i.e. damage and responses to damage) and their ultimate (patho)physiological consequences (i.e. functional decline and age-related disease). As a first step towards verifying or falsifying this hypothesis, it will be important to measure biomarkers of tissue maintenance in future studies in different study populations. The main aim of the current paper is to discuss potential biomarkers of tissue maintenance that could be used in such future studies. Among the many tissues that could have been chosen to explore our hypothesis, to keep the paper manageable, we chose to focus on a selected number of tissues, namely bone, cartilage, muscle, and the brain, which are important for mobility and cognition and affected in several common age-related diseases, including osteoporosis, osteoarthritis, sarcopenia, and neurodegenerative diseases. Furthermore, we discuss the advantages and limitations of potential biomarkers for use in (pre)clinical studies. The proposed biomarkers should be validated in future research, for example by measuring these in humans with different rates of ageing.
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TI Mechanistic insights into the inhibition mechanism of cysteine cathepsins by chalcone-based inhibitors-a QM cluster model approach
SO STRUCTURAL CHEMISTRY
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DT Article
DE Cysteine protease; Catalytic dyad; Inhibition mechanism; QM cluster; DFT; Chalcone
ID michael reaction acceptors; cystatin-c; catalytic mechanism; drug discovery; emerging roles; proteases; reactivity; inducers; disease; cancer
AB Cathepsins are the most abundant cysteine proteases involved in many physiological processes. The imbalance between the natural cysteine protease inhibitors and cathepsins leads to many pathological conditions such as cancer, osteoporosis, and osteoarthritis. Thus, cysteine cathepsins have turn out to be an attractive therapeutic target for the development of new inhibitors. In this paper, the computational study of the inhibition mechanism of cysteine protease by chalcone-based inhibitors has been carried out by means of quantum chemical calculations by employing DFT method. The present study exposes how the processes of activation of the reactive centers of the chalcone derivatives and the nucleophilic attack by the cysteine residue at the electrophilic reactive site of the chalcone take place in the catalytic active site. The obtained results reveal that the inhibition reaction proceeds in a stepwise manner and the attack of the cysteine residue will be either at carbonyl carbon C32 (pathway 1) or beta-carbon C33 (pathway 2). The low positive activation (5.61 and 4.58 kcal/mol) and reaction (1.60 and 9.70 kcal/mol) energies corresponding to both the pathways along with the

positive backward difference (2)rho(r) values for C32/33-S6 bonds imply that the overall reaction is endothermic and the nature of inhibitor is reversible covalent.
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NR 59
TC 6
Z9 6
U1 0
U2 10
PU SPRINGER/PLENUM PUBLISHERS
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 1040-0400
EI 1572-9001
J9 STRUCT CHEM
JI Struct. Chem.
PD OCT 15
PY 2019
VL 30
IS 5
BP 1779
EP 1793
DI 10.1007/s11224-018-1273-3
PG 15
WC Chemistry, Multidisciplinary; Chemistry, Physical; Crystallography
SC Chemistry; Crystallography
GA IY2KD
UT WOS:000486218300023
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ER

PT J
AU Prince, JM
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AF Prince, Joel M.
Bernatz, James T.
Binkley, Neil
Abdel, Matthew P.
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TI Changes in femoral bone mineral density after total knee arthroplasty: a systematic review and meta-analysis
SO ARCHIVES OF OSTEOPOROSIS

LA English
DT Review
DE Bone mineral density; Bone loss; Femur; Total knee arthroplasty; Meta-analysis; Periprosthetic fracture
ID x-ray absorptiometry; 1-year follow-up; distal femur; total hip; periprosthetic fracture; replacement; osteoarthritis; epidemiology; prevalence; osteoporosis
AB BackgroundBone loss after total knee arthroplasty (TKA) may lead to periprosthetic fractures that are associated with significant costs (morbidity, economic, etc.) and pose a challenge to operative fixation. This meta-analysis quantifies the change in bone mineral density (BMD) of the distal femur after primary TKA.MethodsA systematic review of six databases was performed by two independent reviewers. Studies that reported bone density after knee arthroplasty were identified and inclusion/exclusion criteria was applied. Data were extracted and analyzed using the Comprehensive Meta-Analysis Software.ResultsFourteen studies were included in the analysis. The average decrease in BMD was 0.09 [0.05, 0.13], 0.14 [0.08, 0.20], 0.16 [0.10, 0.23], and 0.16 [0.12, 0.20] g/cm(2) at 3, 6, 12, and 24months, respectively, corresponding to a 9.3%, 13.2%, 15.8%, and 15.4% BMD loss. A high degree of heterogeneity existed between the studies (I-2>90% at most time points).ConclusionIn summary, there is a rapid and significant 15% decrease in BMD in the first 6months after TKA that is sustained to 24months. Better understanding regarding how perioperative optimization of bone health may affect BMD loss and the incidence of periprosthetic fracture is essential.Level of evidenceTherapeutic Level II.
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NR 42
TC 34
Z9 37
U1 0
U2 7
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 1862-3522
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J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
PD FEB 23
PY 2019
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BP
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DI 10.1007/s11657-019-0572-7
PG 11
WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
GA HM3QY
UT WOS:000459390300001
PM 30798359
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ER

PT J
AU Rehling, T
Bjorkman, ASD
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Molsted, S
AF Rehling, Thomas
Bjorkman, Anne-Sofie Dam
Andersen, Marie Borring
Ekholm, Ola
Molsted, Stig
TI Diabetes Is Associated with Musculoskeletal Pain, Osteoarthritis, Osteoporosis, and Rheumatoid Arthritis
SO JOURNAL OF DIABETES RESEARCH
LA English
DT Article
ID physical-activity; alcohol-consumption; danish adults; exercise; management; hba(1c); health; risk
AB Aim. To investigate the associations between diabetes and musculoskeletal pain, osteoarthritis, osteoporosis, and rheumatoid arthritis. Methods. Self-reported data were provided by the nationwide Danish National Health Survey 2013. Inclusion criteria were age >= 40 years and known diabetes status. The exposure variable was diabetes, and the outcome variables included musculoskeletal pain during the last 14 days in three body sites (back/lower back, limbs, and shoulder/neck), osteoarthritis, osteoporosis, and rheumatoid arthritis. Logistic regression analyses adjusted for age, gender, BMI, education, marital status, and physical activity were performed. Results. 9,238 participants with diabetes were 65.6 +/- 11.0 (mean +/- SD) years old; 55.6% were males. 99,980 participants without diabetes were 59.2 +/- 11.8 years old; 46.7% were males. Diabetes was associated with back/lower back pain (OR 1.2 (CI 95% 1.1-1.2), p<0.001), pain in the limbs (1.4 (1.3-1.4), p<0.001), shoulder/neck pain (1.2 (1.1-1.3), p<0.001), osteoarthritis (1.3 (1.2-1.4), p<0.001), osteoporosis (1.2 (1.1-1.4), p=0.010), and rheumatoid arthritis (1.6 (1.4-1.7), p<0.001). In participants with diabetes, physical activity was associated with reduced pain (e.g., back/lower back pain (0.7 (0.6-0.7), p<0.001)). Conclusion. Diabetes was associated with elevated odds of having musculoskeletal pain. Diabetes was also associated with elevated odds of having osteoarthritis, osteoporosis, and rheumatoid arthritis. The most frequent disease in individuals with diabetes was osteoarthritis. The reported pain may have negative impacts on the level of physical activity. Health-care professionals should remember to inform patients with diabetes that musculoskeletal pain, osteoarthritis, osteoporosis, and rheumatoid arthritis are not contraindications to exercise training.
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NR 33
TC 70
Z9 84
U1 0
U2 9
PU HINDAWI LTD
PI LONDON
PA ADAM HOUSE, 3RD FLR, 1 FITZROY SQ, LONDON, W1T 5HF, ENGLAND
SN 2314-6745
EI 2314-6753
J9 J DIABETES RES
JI J. Diabetes Res.
PD DEC 6
PY 2019
VL 2019
IS
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EP
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PG 6
WC Endocrinology & Metabolism; Medicine, Research & Experimental
SC Endocrinology & Metabolism; Research & Experimental Medicine
GA JX0HP
UT WOS:000503425300001
PM 31886282
DA 2026-02-10
ER

PT J
AU Zeng, DH
Yao, PB
Zhao, H
AF Zeng, Dehui
Yao, Pingbo
Zhao, Hong
TI P2X7, a critical regulator and potential target for bone and joint diseases
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English

DT Review
DE bone cancer; osteoporosis; P2X7 receptor; rheumatoid arthritis; the stress fracture injury
ID nf-kappa-b; collagen-induced arthritis; p2x(7) receptor; mineral density; rheumatoid-arthritis; extracellular nucleotides; functional polymorphisms; purinergic receptors; nlrp3 inflammasome; fluid shear
AB Abundant evidence indicted that P2X7 receptor show a essential role in human health and some human diseases including hypertension, atherosclerosis, pulmonary inflammation, tuberculosis infection, psychiatric disorders, and cancer. P2X7 receptor also has an important role in some central nervous system diseases such as neurodegenerative disorders. Recently, more research suggested that P2X7 receptor also plays a crucial role in bone and joint diseases. But the effect of P2X7 receptor on skeletal and joint diseases has not been systematically reviewed. In this article, the role of P2X7 receptor in skeletal and joint diseases is elaborated. The activation of P2X7 receptor can ameliorate osteoporosis by inducing a fine balance between osteoclastic resorption and osteoblastic bone formation. The activation of P2X7 receptor can relieve the stress fracture injury by increasing the response to mechanical loading and inducing osteogenesis. But the activation of P2X7 receptor mediates the cell growth and cell proliferation in bone cancer. In addition, the activation of P2X7 receptor can aggravate the process of some joint diseases such as osteoarthritis, rheumatoid arthritis, and acute gouty arthritis. The inhibition of P2X7 receptor can alleviate the pathological process of joint disease to some extent. In conclusion, P2X7 receptor may be a critical regulator and therapeutic target for bone and joint diseases.
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FU National Natural Science Foundation of Hunan province [2018JJ6122, 2018JJ2339]; Hunan Province Education Department Science and Research Project [16C1395, 16C1393]; 13th Five-Year Plan of Hunan Province Education Science [XJK17BGD070]
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TI Promoting mobility and healthy aging in men: a narrative review
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Review
DE Aging; Falls; Male mobility; Osteoporosis; Sarcopenia
ID dwelling older-adults; bone-mineral density; vitamin-d supplementation; fish-oil

supplementation; sarcopenic obesity; muscle mass; physical function; adaptive response; american-college; national-health
AB Maintaining mobility is an important aspect of health and well-being in older men. This literature review describes several modifiable and nonmodifiable risk factors impacting bone, muscle, and joint health. Exercise and nutritional interventions may help to prevent the progressive deterioration in bones, muscles, and joints impacting mobility in later life. Limitations in mobility are increasingly recognized as a major public health problem due to an aging population and growing number of older individuals affected by disabling comorbidities. Despite increasing numbers and debilitating consequences, there are no guidelines providing recommendations on strategies to maintain mobility for healthy aging among older men. This narrative review aims to fill this literature gap. PubMed, Scopus, and Google Scholar databases were searched using predefined search terms. Primary studies, exploratory analyses, cross-sectional surveys, meta-analyses, evidence-based clinical reviews, and guidelines from nationally recognized societies focusing on mobility in older men and key elements including bone, muscle and joint health, and balance were selected. Several modifiable and nonmodifiable risk factors have been reported in the literature that impact bone, muscle, and joint health and predispose older men to falls and fractures. The most common conditions impacting bones, muscles, and joints are osteoporosis, sarcopenia, and osteoarthritis, respectively. In addition to being key contributors to disability in the elderly, these conditions are all associated with a higher mortality risk. Although more studies are required, current evidence supports the use of various nonpharmacological (mainly exercise and nutrition) and/or pharmacological treatment modalities to help prevent and/or reverse these conditions. Incorporating lifestyle interventions involving exercise and nutrition at a younger age can help prevent the age-related, progressive deterioration in bones, muscles, and joints that can reduce mobility in later life. Established barriers to physical activities (e.g., poor health, social isolation) in men are important to consider for optimizing outcomes.
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TI Role of Epigenomics in Bone and Cartilage Disease
SO JOURNAL OF BONE AND MINERAL RESEARCH
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DT Review
DE EPIGENETICS; DNA METHYLATION; MICRORNA; LONG NON-CODING RNA; HISTONE; EPIGENOMEWIDE ASSOCIATION STUDIES; OSTEOPOROSIS; OSTEOARTHRITIS

ID mesenchymal stem-cells; differentially methylated regions; wide dna methylation; long noncoding rna; osteogenic differentiation; gene-expression; histone deacetylases; osteoblast differentiation; articular chondrocytes; microrna regulation
AB Phenotypic variation in skeletal traits and diseases is the product of genetic and environmental factors. Epigenetic mechanisms include information-containing factors, other than DNA sequence, that cause stable changes in gene expression and are maintained during cell divisions. They represent a link between environmental influences, genome features, and the resulting phenotype. The main epigenetic factors are DNA methylation, posttranslational changes of histones, and higher-order chromatin structure. Sometimes non-coding RNAs, such as microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), are also included in the broad term of epigenetic factors. There is rapidly expanding experimental evidence for a role of epigenetic factors in the differentiation of bone cells and the pathogenesis of skeletal disorders, such as osteoporosis and osteoarthritis. However, different from genetic factors, epigenetic signatures are cell- and tissue-specific and can change with time. Thus, elucidating their role has particular difficulties, especially in human studies. Nevertheless, epigenomewide association studies are beginning to disclose some disease-specific patterns that help to understand skeletal cell biology and may lead to development of new epigenetic-based biomarkers, as well as new drug targets useful for treating diffuse and localized disorders. Here we provide an overview and update of recent advances on the role of epigenomics in bone and cartilage diseases. (c) 2019 American Society for Bone and Mineral Research.
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TI Executive summary of European guidance for the diagnosis and management of osteoporosis in postmenopausal women
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Bone mineral density; Diagnosis of osteoporosis; Fracture risk assessment; FRAX; Health economics; Treatment of osteoporosis
AB A guidance on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis was recently published in Osteoporosis International as a joint effort of the International Osteoporosis Foundation and European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (Kanis et al. Osteoporos Int, 10.1007/s00198-018-4704-5, 2018). This manuscript updates the previous guideline document, published in 2013 (Kanis et al. Osteoporos Int 24:23-57, 2013) and is written from a European perspective. The present article reports and summarizes the main recommendations included in this 2018 guidance document (Fig.1).
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TI Translational Insights into Extremely Low Frequency Pulsed Electromagnetic Fields (ELF-PEMFs) for Bone Regeneration after Trauma and Orthopedic Surgery
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Review
DE extremely low frequency pulsed electromagnetic fields (ELF-PEMF); bone regeneration; fracture healing; spinal fusion; osteoporosis; bone mineral density; osteoarthritis; pain; bone cells
ID ovariectomy-induced osteoporosis; double-blind trial; electrical-stimulation; knee osteoarthritis; osteogenic differentiation; osteoclast formation; osteoblast differentiation; growth stimulation; signaling pathway; calcium-channels
AB The finding that alterations in electrical potential play an important role in the mechanical stimulation of the bone provoked hype that noninvasive extremely low frequency pulsed electromagnetic fields (ELF-PEMF) can be used to support healing of bone and osteochondral defects. This resulted in the development of many ELF-PEMF devices for clinical use. Due to the resulting diversity of the ELF-PEMF characteristics regarding treatment regimen, and reported results, exposure to ELF-PEMFs is generally not among the guidelines to treat bone and osteochondral defects. Notwithstanding, here we show that there is strong evidence for ELF-PEMF treatment. We give a short, confined overview of in vitro studies investigating effects of ELF-PEMF treatment on bone cells, highlighting likely mechanisms. Subsequently, we summarize prospective and blinded studies, investigating the effect of ELF-PEMF treatment on acute bone fractures and bone fracture non-unions, osteotomies, spinal fusion, osteoporosis, and osteoarthritis. Although these studies favor the use of ELF-PEMF treatment, they likewise demonstrate the need for more defined and better controlled/monitored treatment modalities. However, to establish indication-oriented treatment regimen, profound knowledge of the underlying mechanisms in the sense of cellular pathways/events triggered is required, highlighting the need for more systematic studies to unravel optimal treatment conditions.
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TI Results of a 6-week treatment with 10 mg prednisolone in patients with hand osteoarthritis (HOPE): a double-blind, randomised, placebo-controlled trial
SO LANCET
LA English
DT Article
ID nonsteroidal antiinflammatory drugs; induced osteoporosis; criteria; risk
AB Background Hand osteoarthritis is a prevalent joint condition that has a high burden of disease and an unmet medical need for effective therapeutic options. Since local inflammation is recognised as contributing to osteoarthritic complaints, the Hand Osteoarthritis Prednisolone Efficacy (HOPE) study aimed to investigate

the efficacy and safety of short-term prednisolone in patients with painful hand osteoarthritis and synovial inflammation. Methods The HOPE study is a double-blind, randomised, placebo-controlled trial. We recruited eligible adults from rheumatology outpatient clinics at two sites in the Netherlands. Patients were considered eligible if they had symptomatic hand osteoarthritis and signs of inflammation in their distal and proximal interphalangeal (DIP/PIP) joints. For inclusion, patients were required to have four or more DIP/PIP joints with osteoarthritic nodes; at least one DIP/PIP joint with soft swelling or erythema; at least one DIP/PIP joint with a positive power Doppler signal or synovial thickening of at least grade 2 on ultrasound; and finger pain of at least 30 mm on a 100-mm visual analogue scale (VAS) that flared up during a 48-h non-steroidal anti-inflammatory drug (NSAID) washout (defined as worsening of finger pain by at least 20 mm on the VAS). Eligible patients were randomly assigned (1:1) to receive 10 mg prednisolone or placebo orally once daily for 6 weeks, followed by a 2-week tapering scheme, and a 6-week follow-up without study medication. The patients and study team were masked to treatment assignment. The primary endpoint was finger pain, assessed on a VAS, at 6 weeks in participants who had been randomly assigned to groups and attended the baseline visit. This study is registered with the Netherlands Trial Registry, number NTR5263. Findings We screened patients for enrolment between Dec 3, 2015, and May 31, 2018. Patients completed baseline visits and started treatment between Dec 14, 2015, and July 2, 2018, and the last study visit of the last patient was Oct 4, 2018. Of 149 patients assessed for eligibility, 57 (38%) patients were excluded (predominantly because they did not meet one or several inclusion criteria, most often because of an absence of synovial inflammation or of flare-ups after NSAID washout) and 92 (62%) patients were eligible for inclusion. We randomly assigned 46 (50%) patients to receive prednisolone and 46 (50%) patients to receive placebo, all of whom were included in the modified intention-to-treat analysis of the primary endpoint. 42 (91%) patients in the prednisolone group and 42 (91%) in the placebo group completed the 14-week study. The mean change between baseline and week 6 on VAS-reported finger pain was -21.5 (SD 21.7) in the prednisolone group and -5.2 (24.3) in the placebo group, with a mean between-group difference (of prednisolone vs placebo) of -16.5 (95% CI -26.1 to -6.9; p=0.0007). The number of non-serious adverse events was similar between the groups. Five serious adverse events were reported during our study: one serious adverse event in the prednisolone group (a myocardial infarction) and four serious adverse events in the placebo group (an infected traumatic leg haematoma that required surgery, bowel surgery, atrial fibrillation that required a pacemaker implantation, and symptomatic uterine myomas that required a hysterectomy). Four (4%) patients discontinued the study because of an adverse event: one (2%) patient receiving prednisolone (for a myocardial infarction) and three (7%) patients receiving placebo (for surgery of the bowel and for an infected leg haematoma and for Lyme disease arthritis of the knee). Interpretation Treatment with 10 mg prednisolone for 6 weeks is efficacious and safe for the treatment of patients with painful hand osteoarthritis and signs of

inflammation. The results of our study provide clinicians with a new short-term treatment option for patients with hand osteoarthritis who report a flare-up of their disease. Copyright (C) 2019 Elsevier Ltd. All rights reserved.
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AF Hambright, William S.
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TI Murine models of accelerated aging and musculoskeletal disease
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DE Mouse models; Progeria; Musculoskeletal diseases; Accelerated aging; Senescence; Stem cells
ID nf-kappa-b; senescent secretory phenotype; cellular senescence; dna-repair; heterochronic parabiosis; progeroid syndrome; mouse model; early-onset; bone loss; cells
AB The primary risk factor for most musculoskeletal diseases, including osteoarthritis, osteoporosis and sarcopenia, is aging. To treat the diverse types of musculoskeletal diseases and pathologies, targeting their root cause, the aging process itself, has the potential to slow or prevent multiple age-related musculoskeletal conditions simultaneously. However, the development of approaches to delay onset of age related diseases, including musculoskeletal pathologies, has been slowed by the relatively long lifespan of rodent models of aging. Thus, to expedite the development of therapeutic approaches for age-related musculoskeletal disease, the implementation of mouse models of accelerated musculoskeletal aging are of great utility. Currently there are multiple genetically diverse mouse models that mirror certain aspects of normal human and mouse aging. Here, we provide a review of some of the most relevant murine models of accelerated aging that mimic many aspects of natural musculoskeletal aging, highlighting their relative strengths and weaknesses. Importantly, these

murine models of accelerated aging recapitulate phenotypes of musculoskeletal age-related decline observed in humans.
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ID mesenchymal stem-cells; extracellular vesicles; osteogenic differentiation; knee osteoarthritis; femoral-head; cartilage; osteoporosis; apoptosis; fracture; protein
AB Exosomes, which mediate cell-to-cell communications and provide a novel insight into information exchange, have drawn increasing attention in recent years. The homeostasis of bone metabolism is critical for bone health. The most common bone diseases such as osteoporosis, osteoarthritis and bone fractures have apparent correlations with exosomes. Accumulating evidence has suggested the potential regenerative capacities of stem cell-derived exosomes. in this review, we summarise the pathophysiological mechanism, clinical picture and therapeutic effects of exosomes in bone metabolism. We introduce the advantages and challenges in the application of exosomes. Although the exact mechanisms remain unclear, miRNAs seem to play major roles in the exosome.
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NR 124
TC 41
Z9 46
U1 4
U2 57
PU BENTHAM SCIENCE PUBL LTD
PI SHARJAH
PA EXECUTIVE STE Y-2, PO BOX 7917, SAIF ZONE, 1200 BR SHARJAH, U ARAB EMIRATES
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J9 CURR PHARM DESIGN
JI Curr. Pharm. Design
PD JUN 15
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BP 4536
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DI 10.2174/1381612825666191127114054
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WC Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
GA KB0QE
UT WOS:000506204200007
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ER

PT J
AU Deng, S
Nie, ZG
Peng, PJ
Liu, Y
Xing, S
Long, LS
Peng, H
AF Deng, Shuang
Nie, Zhi-gang

Peng, Pu-ji
Liu, Yang
Xing, Sai
Long, Lin-sheng
Peng, Hao
TI Decrease of GSK3β Ser-9 Phosphorylation Induced Osteoblast Apoptosis in Rat Osteoarthritis Model
SO CURRENT MEDICAL SCIENCE
LA English
DT Article
DE osteonecrosis of the femoral head; GSK3 beta; phosphorylation; apoptosis; dexamethasone
ID glycogen-synthase kinase-3-beta; glucocorticoid-induced osteoporosis; femoral-head; osteonecrosis; pathway; family
AB Nowadays, the cumulative intake of glucocorticoids has become the most common pathogenic factor for non-traumatic osteonecrosis of the femoral head (ONFH). Apoptosis of osteoblasts is considered as the main reason of ONFH at the molecular level. Glycogen synthase kinase 3 (GSK3) is an important regulator of cellular differentiation and apoptosis pathway, which can modulate the balance between osteoblasts and osteoclasts. Several studies have reported about its function in osteoporosis, but little is known about it in osteonecrosis. In our study, lipopolysaccharide and methylprednisolone were utilized to establish a rat ONFH model. The phosphorylation of GSK3 Ser-9 was decreased in the model. Western blotting examination of -catenin, Bcl-2, Bax and caspase-3 revealed that the osteoblasts were apoptotic. In dexamethasone (Dex)-incubated primary osteoblasts, the expression profile of GSK3 phosphorylation and apoptotic factors were consistent with those in the rat ONFH model. To further investigate the regulation of osteonecrosis caused by GSK3, the expression and function of GSK3 were inhibited in Dex-incubated primary osteoblasts. The knockdown of GSK3 by siRNA decreased the expression of Bax and cleaved caspase-3, but increased Bcl-2 and -catenin. On the other hand, selective inhibition of GSK3 function by LiCl counteracted the activation of caspase-3 induced by Dex. Our work is the first study about the GSK3 phosphorylation in ONFH, and provides evidence for further therapeutic methods.
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FU National Natural Science Foundation of China [81672154]
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NR 28
TC 15
Z9 18
U1 0
U2 7
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA

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EI 2523-899X
J9 CURR MED SCI
JI Curr. Med. Sci.
PD FEB 15
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IS 1
BP 75
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WC Medicine, Research & Experimental
SC Research & Experimental Medicine
GA HO7RS
UT WOS:000461146900011
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PT J
AU Mourad, C
Omoumi, P
Malghem, J
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AF Mourad, Charbel
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TI Conventional Radiography of the Hip Revisited: Correlation with Advanced Imaging
SO MAGNETIC RESONANCE IMAGING CLINICS OF NORTH AMERICA
LA English
DT Article
DE Hip; Osteonecrosis; Osteoarthritis; Bone marrow edema; Radiography; MR imaging
ID femoral-head; transient osteoporosis; pelvic radiographs; adult hip; osteoarthritis; osteonecrosis; fractures; bone; weightbearing; patterns
AB This review proposes a structured approach to analyzing conventional radiographs of adult hips by focusing on alterations of radiological bone density, femoral head contours, and the joint space. Conventional radiography enables detecting subtle changes in cortical contours and joint space width due to its high spatial resolution. It is limited to the detection of cortical changes in areas to which the x-ray beam is tangent. It has reduced sensitivity for the detection of trabecular

bone and medullary changes. Radiographic findings in common hip disorders, such as osteoarthritis, osteonecrosis, transient osteoporosis, and subchondral insufficiency fractures, are correlated to changes on MR imaging and computed tomography.
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NR 56
TC 5
Z9 6
U1 0
U2 8
PU W B SAUNDERS CO-ELSEVIER INC
PI PHILADELPHIA
PA 1600 JOHN F KENNEDY BOULEVARD, STE 1800, PHILADELPHIA, PA 19103-2899 USA
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J9 MAGN RESON IMAGING C
JI Magn. Reson. Imaging Clin. N. Am.
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VL 27
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BP 661
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WC Radiology, Nuclear Medicine & Medical Imaging
SC Radiology, Nuclear Medicine & Medical Imaging
GA JL8SM
UT WOS:000495797400008
PM 31575399
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PT J
AU Hewlett, J
Kenney, J
AF Hewlett, Jim
Kenney, John
TI Innovations in functional and rehabilitative knee bracing
SO ANNALS OF TRANSLATIONAL MEDICINE
LA English
DT Review
DE Functional knee bracing; functional rehabilitative knee bracing; posterior cruciate ligament bracing (PCL bracing); anterior cruciate ligament bracing (ACL bracing); osteoarthritis bracing (OA bracing); post-op extension deficit bracing
ID posterior cruciate ligament; pneumatic brace; injury; strength; forces

AB New knee brace designs are available that have the potential to improve patient outcomes relative to traditional bracing. For the indications of post-knee injury/surgery recovery, conservative management of knee osteoarthritis (OA), total knee arthroplasty (TKA) pre-habilitation, and the treatment of post-surgical extension deficits/flexion contractures, innovative new bracing designs merit review and discussion. The researchers requested information from industry brace manufacturers, and from the information received, have selected those products considered significant improvements over traditional functional brace designs for review in this article. Clinical research supporting the benefits of the innovative products listed in the article have been cited when available. The authors are both Certified Orthotists with over 50 years of combined knee bracing experience.
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NR 14
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PA FLAT-RM C 16F, KINGS WING PLAZA 1, NO 3 KWAN ST, SHATIN, HONG KONG 00000, PEOPLES R CHINA
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J9 ANN TRANSL MED
JI ANN. TRANSL. MED.
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WC Oncology; Medicine, Research & Experimental
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PT J
AU Franco-Trepat, E
Guillán-Fresco, M
Alonso-Pérez, A
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Gómez, R
AF Franco-Trepat, Eloi
Guillan-Fresco, Maria
Alonso-Perez, Ana
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TI Visfatin Connection: Present and Future in Osteoarthritis and Osteoporosis
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Review
DE osteoarthritis; osteoporosis; cartilage; bone; inflammation; catabolism; visfatin; NAMPT; TLR4; metabolic alterations

ID bone-mineral density; colony-enhancing factor; nicotinamide phosphoribosyltransferase nampt; type-2 diabetes-mellitus; visceral adipose-tissue; nad(+) salvage pathway; infrapatellar fat pad; morbidly obese women; gene-expression; articular chondrocytes
AB Musculoskeletal pathologies (MSPs) such as osteoarthritis (OA) and osteoporosis (OP), are a set of disorders that cause severe pain, motion difficulties, and even permanent disability. In developed countries, the current incidence of MSPs reaches about one in four adults and keeps escalating as a consequence of aging and sedentarism. Interestingly, OA and OP have been closely related to similar risk factors, including aging, metabolic alterations, and inflammation. Visfatin, an adipokine with an inflammatory and catabolic profile, has been associated with several OA and OP metabolic risk factors, such as obesity, insulin resistance, and type II diabetes. Furthermore, visfatin has been associated with the innate immune receptor toll-like receptor 4 (TLR4), which plays a key role in cartilage and bone inflammatory and catabolic responses. Moreover, visfatin has been related to several OA and OP pathologic features. The aim of this work is to bring together basic and clinical data regarding the common role of visfatin in these pathologies and their major shared risk factors. Finally, we discuss the pitfalls of visfatin as a potential biomarker and therapeutic target in both pathologies.
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TI Endorsement by Central European experts of the revised ESCEO algorithm for the management of knee osteoarthritis
SO RHEUMATOLOGY INTERNATIONAL
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DT Article
DE NSAID; Osteoarthritis; Paracetamol; Safety; SYSADOA
ID nonsteroidal antiinflammatory drugs; cyclooxygenase-2 inhibitors; economic-aspects; adverse events; metaanalysis; safety; glucosamine; outcm; risk; osteoporosis
AB Osteoarthritis (OA) is characterized by deterioration of the joints and associated

with considerable pain and disability. OA is a chronic disease that requires intervention with both non-pharmacological and pharmacological treatment modalities and, inevitably, disease progression may necessitate successive treatments throughout the course of the disease. There is increasing data on the shortfalls of current pharmacological treatment of OA, and safety concerns associated with analgesic therapy use in OA arising from increasing evidence of gastrointestinal, cardiovascular, hepatic and renal adverse events with paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs). Consequently, symptomatic slow-acting drugs for OA (SYSADOAs) may now be considered as a first-line treatment for knee OA, with a particular emphasis placed on the outstanding benefit: risk ratio of pharmaceutical-grade glucosamine and chondroitin sulfate formulations. In this short communication we review recent publications concerned with the safety of paracetamol, NSAIDs and SYSADOAs. Greater understanding of the benefits and limitations of current medications will lead to better disease management in OA. Furthermore, adherence to guideline recommendations across Europe and internationally, such as those from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO), will promote evidence-based medicine and patient-centric care, ultimately leading to greater physician and patient satisfaction.

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TC 23
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U1 0
U2 9
PU SPRINGER HEIDELBERG
PI HEIDELBERG
PA TIERGARTENSTRASSE 17, D-69121 HEIDELBERG, GERMANY
SN 0172-8172
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J9 RHEUMATOL INT
JI Rheumatol. Int.
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WC Rheumatology
SC Rheumatology
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UT WOS:000471206100001
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PT J
AU Dretakis, K
Igoumenou, VG
AF Dretakis, Konstantinos
Igoumenou, Vasilios G.
TI The role of parathyroid hormone (PTH) and vitamin D in falls and hip fracture type
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Parathyroid hormone (PTH); 25 (OH) vitamin D; Hip fracture type; Falls
ID bone-mineral density; d deficiency; risk-factors; elderly-women; d level; association; prevention; neck; osteoarthritis; epidemiology
AB Background Fragility fractures of the hip are associated with high morbidity and mortality, and represent a rather devastating consequence of osteoporosis. Hip fractures are traditionally investigated as a whole, although it has been recently implied that distinct pathogenic mechanisms may lead either to trochanteric or subcapital fractures. Aims To investigate whether differences exist by hip fracture type with respect to serum 25(OH)D (vitamin D) and parathyroid hormone (PTH) levels, in addition to epidemiological and demographic data, including history of falls. Methods The inclusion criteria were met by 116 patients [48 men and 68 women; mean age 80.8 +/- 8.5 (range 62-94) years]. Patients were analyzed according to hip fracture type, history of falls, and vitamin D and PTH status. Results Older age, recurrent falls, serum levels of PTH > 65 pg/ml, and severe vitamin D deficiency were found to be associated with trochanteric fractures. Additionally, older age, female gender, PTH > 65 pg/ml, and severe vitamin D deficiency were related to recurrent falls. Meanwhile, patients with absence of PTH response to low vitamin D levels, were not repeated fallers and suffered mostly from subcapital fractures. Discussion and conclusion Elevated PTH levels predispose both to falls and trochanteric fractures, while vitamin D-deficient patients with normal PTH levels are mostly related to subcapital fractures. It is thereby indicated that different pathophysiological processes lie behind subcapital and trochanteric fractures. A better understanding of these mechanisms may assist in the development of prevention strategies for individuals recognized at risk for falls and either type of hip fracture.

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NR 47
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PA 233 SPRING ST, NEW YORK, NY 10013 USA
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ER

PT J
AU Fischbacher, M
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AF Fischbacher, Melanie
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TI The influence of antiresorptive bone medication on the effect of high-intensity resistance and impact training on osteoporotic fracture risk in postmenopausal women with low bone mass: protocol for the MEDEX-OP randomised controlled trial
SO BMJ OPEN
LA English
DT Article
DE bone mineral density; exercise; fracture prevention; osteoporosis; Pilates; resistance training
ID quality-of-life; mineral density; muscular strength; test-performance; grip strength; improves bone; exercise; alendronate; therapy; balance
AB Introduction Antiresorptive medications increase bone density and decrease vertebral fracture, while high-intensity resistance and impact training (HiRIT) increases balance, bone and muscle strength decreasing risk for falls and fractures. Medications are typically prescribed by doctors and exercise by exercise specialists, frequently in isolation. Objective Our primary aim is to determine the effect of an 8-month HiRIT programme with or without osteoporosis medications on bone mineral density (BMD) of the spine and hip in postmenopausal women with low bone mass. Methods and analysis One hundred and sixty postmenopausal women with low bone mass will be recruited from the community to participate in an 8-month randomised controlled trial. Participants will be on stable doses of

antiresorptive bone medication for at least 12 months (n=80) or have not taken bone medications for at least 12 months (n=80). Participants will be block randomised, stratified by medication intake, to twice-weekly 40-min supervised sessions of HiRIT or a low-intensity exercise programme (control). Primary outcomes include change in lumbar spine and total hip areal bone mineral density. Secondary outcomes include whole body, femoral neck and forearm BMD, proximal femur bone geometry and volumetric density, vertebral morphology, body composition, anthropometry, physical function, posture, rate of falls, osteoarthritis symptoms, pelvic floor health, quality of life, physical activity enjoyment, resting blood pressure, safety and compliance. All outcomes will be assessed at baseline and 8months and intention-to-treat and per-protocol analyses will be conducted. Repeated measure analysis of covariance will be used to determine intervention effects on outcome measures, controlling for initial values, compliance and other variables found to differ between groups at baseline. Ethics and dissemination The study has been approved by Griffith University Human Research Ethics Committee (Ref: 2017/739). Results will be reported in peer-reviewed journals and at conferences.
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PI LONDON
PA BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND
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WC Medicine, General & Internal
SC General & Internal Medicine
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PT J
AU Narloch, J
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AF Narloch, Jerzy
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TI Osteoarthritis Changes Hip Geometry and Biomechanics Regardless of Bone Mineral DensityA Quantitative Computed Tomography Study
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE quantitative computed tomography; hip; osteoarthritis; osteoporosis
ID x-ray absorptiometry; proximal femur; cortical bone; postmenopausal women; knee osteoarthritis; fracture risk; femoral-neck; clinical-use; osteoporosis; spine
AB We aimed to compare proximal femur geometry and biomechanics in postmenopausal women with osteoarthritis (OA) and/or osteoporosis (OP), using quantitative computed tomography (QCT). A retrospective analysis of QCT scans of the proximal femur of 175 postmenopausal women was performed. Morphometric and densitometric data of the proximal femur were used to evaluate its biomechanics. We found, 21 had a normal bone mineral density (BMD), 72 had osteopenia, and 81 were diagnosed with OP. Radiographic findings of hip OA were seen in 43.8%, 52.8%, and 39.5% of the normal BMD, osteopenic, and OP groups, respectively ($p < 0.05$). OA was significantly correlated with total hip volume ($r = 0.21$), intertrochanteric cortical volume ($r = 0.25$), and trochanteric trabecular volume ($r = 0.20$). In each densitometric group, significant differences in hip geometry and BMD were found between the OA and non-OA subgroups. Hip OA and OP often coexist. In postmenopausal women, these diseases coexist in 40% of cases. Both OA and OP affect hip geometry and biomechanics. OA does so regardless of densitometric status. Changes are mostly reflected in the cortical bone. OA leads to significant changes in buckling ratio (BR) in both OP and non-OP

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NR 44
TC 3
Z9 4
U1 0
U2 4
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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WC Medicine, General & Internal
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PT J
AU Ramos, AL
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Albrecht, K
AF Ramos, Andres Luque
Redeker, Imke
Hoffmann, Falk
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TI Comorbidities in Patients with Rheumatoid Arthritis and Their Association with Patient-reported Outcomes: Results of Claims Data Linked to Questionnaire Survey
SO JOURNAL OF RHEUMATOLOGY
LA English
DT Article
DE EPIDEMIOLOGY; HEALTHCARE; COMORBIDITY; DEPRESSION; RHEUMATOID ARTHRITIS
ID evidence-based recommendations; cardiovascular risk-factors; prevalence; depression; health; osteoporosis; management; psoriasis; ability; cohort
AB Objective. To investigate the prevalence of comorbidities in a population-based cohort of persons with rheumatoid arthritis (RA) compared to matched controls and to examine their association with patient-reported outcomes in a survey sample. Methods. Data of 96,921 persons with RA [International Classification of Diseases, 10th ed (ICD-10) M05/M06] and 484,605 age-and sex-matched controls without RA of a German statutory health fund were studied regarding 26 selected

comorbidities (ICD-10). A self-reported questionnaire, comprising joint counts [(tender joint count (TJC), swollen joint count (SJC)], functional status (Hannover Functional Ability Questionnaire), effect of the disease (Rheumatoid Arthritis Impact of Disease), and well-being (World Health Organization 5-item Well-Being Index; WHO-5) was sent to a random sample of 6193 persons with RA, of whom 3184 responded. For respondents who confirmed their RA (n = 2535), associations between comorbidities and patient-reported outcomes were analyzed by multivariable linear regression. Results. Compared to controls, all investigated comorbidities were more frequent in persons with RA (mean age 63 yrs, 80% female). In addition to cardiovascular risk factors, the most common were osteoarthritis (44% vs 21%), depression (32% vs 20%), and osteoporosis (26% vs 9%). Among the survey respondents, 87% of those with 0-1 comorbidity but only 77% of those with >= 8 comorbidities were treated by rheumatologists. Increasing numbers of comorbidities were associated with poorer values for TJC, SJC, function, and WHO-5. Conclusion. Compared to a matched population, persons with RA present with increased prevalence of numerous comorbidities. Patients with RA and multimorbidity are at risk of insufficient rheumatological care and poorer patient-reported outcomes.

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NR 28
TC 84
Z9 100
U1 0
U2 10
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AU Ota, S
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TI Symptomatic bone marrow lesions induced by reduced bone mineral density in middle-aged women: a cross-sectional Japanese population study
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Article
DE Bone marrow lesion; Bone mineral density; Bone markers; Knee osteoarthritis
ID knee osteoarthritis; biochemical markers; pain; osteoporosis; turnover; association; biomarkers; prevalence; serum; hip
AB BackgroundThe etiology of bone marrow lesions (BMLs) without knee osteoarthritis (KOA) and their association with bone fragility are unclear. We aimed to investigate the association between BMLs, bone mineral density (BMD), and bone markers in women without radiographic evidence of KOA.MethodsThis single-center cross-sectional study in a Japanese population included 266 women without radiographic evidence of KOA, which was defined as a Kellgren-Lawrence grade <2. All participants underwent coronal and sagittal T2-weighted fat-suppressed magnetic resonance imaging of their right knee. BML severity was scored according to the Whole-Organ MRI Scoring method. BMD was measured by

dual-energy X-ray absorptiometry of the forearm. Levels of bone markers (bone-alkaline phosphatase [BAP], type I procollagen N-terminal propeptide [PINP], cross-linked N-telopeptide of type I collagen [NTx], and tartrate-resistant acid phosphatase-5b [TRACP-5b]), pentosidine, and homocysteine were assessed in the serum. Knee symptoms were evaluated on the basis of the Knee injury and Osteoarthritis and Outcome Score (KOOS). Participants were divided into symptomatic knee and asymptomatic knee groups on the basis of their KOOS according to the classification criteria for early KOA. Multiple linear regression analysis was performed to evaluate the relationship between BMLs, BMD, and bone markers.ResultsThe prevalence of BML was 35.3%. Age and some bone marker levels (BAP, PINP, NTx, and TRACP-5b) were higher, and all KOOS subscale scores and BMD were lower in participants with BMLs than in those without BMLs. On multiple linear regression analysis, BMD was negatively associated with BMLs (p=0.014) in participants with symptomatic knees. There was no such association in participants with asymptomatic knees (p=0.918). Among the bone markers, BAP (p=0.006) and PINP (p=0.043) were positively associated with BMLs in participants with symptomatic knees, while BAP (p=0.038) and TRACP-5b (p=0.011) were positively associated with BMLs in participants with asymptomatic knees.ConclusionsIn symptomatic Japanese women without radiographic evidence of KOA, BMD is negatively associated and some bone markers are positively associated with BMLs after adjustment for age and BMI. Thus, maintaining systemic bone metabolism could contribute to BML prevention in patients with pre-radiographic KOA.
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NR 48
TC 25
Z9 28
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PI LONDON
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TI Preoperative Systemic Bone Quality Does Not Affect Tibial Component Migration in Knee Arthroplasty: A 2-Year Radiostereometric Analysis of a Hundred Consecutive Patients
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE RSA; bone mineral density; migration; knee arthroplasty; bone turnover markers
ID total hip-arthroplasty; outcome score koos; mineral density; trabecular metal; osteoarthritis; rsa; osteoporosis; fixation; cementation; stability
AB Background: Bone quality and other preoperative predictive factors may affect implant migration and the survival of knee arthroplasty. Methods: In a prospective cohort of 100 consecutive patients (65 women) at a mean age of 67.7 years (range 39-87 years), we investigated preoperative predictors of postoperative tibial component migration in cemented and cementless total knee arthroplasties or cemented unicompartmental knee arthroplasty. Predictors consisted of Knee Injury and Osteoarthritis Outcome Score (KOOS) and Oxford Knee Score, questionnaires, bone turnover markers of CTX and P1NP, systemic bone mineral density (BMD), and knee osteoarthritis (OA) grade. Tibial component migration was measured with radiostereometry postoperative, at 1 and 2 years of follow-up. Results: Between 1 and 2 years, 19 tibial components migrated continuously (maximum total point motion [MTPM] > 0.2 mm). In general, there was no difference in age, body mass

index, BMD, KOOSs, or OA grade between patients with continuous tibial migration compared to patients without continuous migration (P > .11). However, cementless tibial components with continuous migration had a lower KOOS pain score (more pain), lower vitamin D, and a higher bone turnover (CTX) value than patients without continuous migration. There was no association between the BMD and MTPM at 1-year follow-up regardless of prothesis type (P > .17). Patients with osteoporosis and normal BMD had similar mean tibial component MTPM at 2 years (3 prostheses combined; P = .34). Conclusion: Migration of tibial components inserted with or without bone cement was not affected by the preoperative bone quality in terms of systemic BMD, bone turnover markers, and OA grade in the knee. (C) 2019 Elsevier Inc. All rights reserved.
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TI An updated algorithm recommendation for the management of knee

osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English
DT Article
DE Algorithm; Recommendations; GRADE; Treatment; Knee osteoarthritis
ID nonsteroidal antiinflammatory drugs; intraarticular hyaluronic-acid; life setting trials; quality-of-life; crystalline glucosamine sulfate; individual patient data; g-f 20; double-blind; chondroitin sulfate; hip osteoarthritis
AB Objectives: The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) sought to revisit the 2014 algorithm recommendations for knee osteoarthritis (OA), in light of recent efficacy and safety evidence, in order to develop an updated stepwise algorithm that provides practical guidance for the prescribing physician that is applicable in Europe and internationally. Methods: Using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process, a summary of evidence document for each intervention in OA was provided to all members of an ESCEO working group, who were required to evaluate and vote on the strength of recommendation for each intervention. Based on the evidence collected, and on the strength of recommendations afforded by consensus of the working group, the final algorithm was constructed. Results: An algorithm for management of knee OA comprising a stepwise approach and incorporating consensus on 15 treatment recommendations was prepared by the ESCEO working group. Both "strong" and "weak" recommendations were afforded to different interventions. The algorithm highlights the continued importance of non-pharmacological interventions throughout the management of OA. Benefits and limitations of different pharmacological treatments are explored in this article, with particular emphasis on safety issues highlighted by recent literature analyses. Conclusions: The updated ESCEO stepwise algorithm, developed by consensus from clinical experts in OA and informed by available evidence for the benefits and harms of various treatments, provides practical, current guidance that will enable clinicians to deliver patient-centric care in OA practice. (C) 2019 The Authors. Published by Elsevier Inc.
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PT J
AU Lindsey, RC
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AF Lindsey, Richard C.
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TI Vitamin C effects on 5-hydroxymethylcytosine and gene expression in osteoblasts and chondrocytes: Potential involvement of PHD2
SO PLOS ONE
LA English
DT Article
ID bone-mineral density; ascorbic-acid; proteasomal degradation; alkaline-phosphatase; osterix expression; prolyl hydroxylase; in-vitro; differentiation; collagen; activation
AB Vitamin C (ascorbic acid, AA) is a well-known regulator of bone and cartilage metabolism. However, the mechanisms of AA's action in these tissues are only partly understood. In this study, we confirmed that AA contributes to bone and cartilage metabolism by showing decreased articular cartilage and trabecular bone in AA-deficient spontaneous fracture (sfx) mutant mice. In vitro, we found that AA exerts differential effects on chondrocyte and osteoblast differentiation. Since AA is known to increase levels of 5-hydroxymethylcytosine (5-hmC) and induce DNA demethylation via the ten-eleven translocases (TETs), and since prolyl hydroxylase domain-containing protein 2 (PHD2), a known mediator of AA's effects in these tissues, is part of the same enzyme family as the TETs, we next investigated whether increases in 5-hmC might mediate some of these effects. All TETs and PHDs are expressed in chondrocytes and osteoblasts, and PHD2 is localized in both

the cytoplasm and nucleus of the cell, lending plausibility to the hypothesis of altered 5-hmC content in these cells. We found that AA treatment increased levels of 5-hmC in both cell types globally, notably including promoter regions of osteoblast differentiation genes. Furthermore, inhibition of PHD2 decreased 5-hmC levels in chondrocyte differentiation gene promoters, and knockdown of Phd2 in chondrocytes reduced global 5-hmC levels, suggesting for the first time that PHD2 may itself directly mediate increases in 5-hmC in chondrocyte and osteoblast genes. Further investigation of this mechanism could lead to novel therapeutic approaches to treat debilitating diseases such as osteoarthritis and osteoporosis.
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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TI Increased Risk of Musculoskeletal Disorders and Mental Health Problems in Retired Professional Jockeys: A Cross-Sectional Study
SO INTERNATIONAL JOURNAL OF SPORTS MEDICINE
LA English
DT Article
DE osteoarthritis; osteoporosis; anxiety; depression; athlete; chronic disease
ID body-mass index; weight; sport; age; prevalence; osteoarthritis; comorbidity; concussion; depression; height
AB To examine the prevalence of chronic disease and mental health problems in retired professional, male jockeys compared to an age-matched reference population. A cross-sectional study comparing data from a cohort of retired professional jockeys with an age-matched general population sample. Male participants (age range: 50-89 years old) were used to compare health outcomes of self-reported physician-diagnosed conditions: heart disease, stroke, diabetes, hypertension, osteoporosis, osteoarthritis, depression and anxiety between study populations. Conditional logistic regression models were used to estimate associations between study groups and health outcome. In total, 810 participants (135 retired professional male jockeys and 675 participants from the reference population) were included, with an average age of 64.7 +/- 9.9 years old. Increased odds of having osteoporosis (OR=6.5, 95%CI 2.1-20.5), osteoarthritis (OR=7.5, 95%CI 4.6-12.2), anxiety (OR=2.8, 95%CI 1.3-5.9) and depression (OR=2.6, 95%CI 1.3-5.7) were seen in the retired professional jockeys. No differences were found for the remaining health outcomes. Retired professional jockeys had increased odds of musculoskeletal disease and mental health problems compared to the general population. Understanding the prevalence of chronic disease and mental health problems in retired professional jockeys will help inform screening and intervention strategies for jockeys.

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NR 35
TC 9
Z9 9
U1 0
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PU GEORG THIEME VERLAG KG
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Rabenda, Veronique
Rizzoli, Ren
Scholte-Voshaar, Marieke
Vlaskovska, Mila
Reginster, Jean-Yves
TI Practical guidance for engaging patients in health research, treatment guidelines and regulatory processes: results of an expert group meeting organized by the World Health Organization (WHO) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Outcomes research; Patient engagement; Patient preference; Regulatory process; Treatment guidelines
ID discrete-choice experiment; public involvement; drug development; core set; preferences; engagement; partners
AB There is increasing emphasis on patient-centred research to support the development, approval and reimbursement of health interventions that best meet patients' needs. However, there is currently little guidance on how meaningful patient engagement may be achieved. An expert working group, representing a wide range of stakeholders and disciplines, was convened by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the World Health Organization (WHO). Through a structured, collaborative process the group generated practical guidance to facilitate optimal patient engagement in clinical development and regulatory decisions. Patient engagement is a relational process. The principles outlined in this report were based on lessons learned through applied experience and on an

extensive dialogue among the expert participants. This practice guidance forms a starting point from which tailoring of the approach to suit different chronic diseases may be undertaken.
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NR 54
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PG 11
WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
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TI Open-Source Remote Gait Analysis: A Post-Surgery Patient Monitoring Application
SO SCIENTIFIC REPORTS
LA English
DT Article
ID cruciate ligament reconstruction; transitional care; anterior; osteoarthritis; kinematics; asymmetry; mechanics; strength; kinetics; walking
AB Critical to digital medicine is the promise of improved patient monitoring to allow assessment and personalized intervention to occur in real-time. Wearable sensor-enabled observation of physiological data in free-living conditions is integral to this vision. However, few open-source algorithms have been developed for analyzing and interpreting these data which slows development and the realization of digital medicine. There is clear need for open-source tools that analyze free-living wearable sensor data and particularly for gait analysis, which provides important biomarkers in multiple clinical populations. We present an open-source analytical platform for automated free-living gait analysis and use it to investigate a novel, multi-domain (accelerometer and electromyography) asymmetry measure for quantifying rehabilitation progress in patients recovering from surgical reconstruction of the anterior cruciate ligament (ACL). Asymmetry indices extracted from 41,893 strides were more strongly correlated ($r = -0.87$, $p < 0.01$) with recovery time than standard step counts ($r = 0.25$, $p = 0.52$) and significantly differed between patients 2- and 17-weeks post-op ($p < 0.01$, effect size: 2.20-2.96), and controls ($p < 0.01$, effect size: 1.74-4.20). Results point toward future use of this open-source platform for capturing rehabilitation progress and, more broadly, for free-living gait analysis.
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Z9 53
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PU NATURE PORTFOLIO
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PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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TI Ipriflavone attenuates the degeneration of cartilage by blocking the Indian hedgehog pathway
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Article
DE Ipriflavone; Osteoarthritis; Indian hedgehog; Chondrocyte hypertrophy
ID growth-plate; osteoblast differentiation; postmenopausal women; signaling pathway; osteoarthritis; recommendations; osteoporosis; cyclopamine; combination; prevention
AB BackgroundTo determine if ipriflavone, a novel and safe inhibitor of Indian hedgehog (Ihh) signaling, can attenuate cartilage degeneration by blocking the Ihh

pathway.MethodsHuman chondrocytes were used to evaluate Ihh signaling, cell proliferation, apoptosis, gene, and protein expression of chondrocytes by cell proliferation and apoptosis assays, real-time qPCR, and Western blotting at 48h after ipriflavone treatment. Human cartilage explants were further used to validate the cell culture results. The effects of ipriflavone on cartilage degeneration in vivo were assessed using the rat ACLT OA model. Two-month-old male SD rats were randomized into 3 groups (n=75): (1) sham, (2) ACLT alone, and (3) ACLT+ ipriflavone. Ipriflavone was administered intragastrically at 24h after ACLT for 6weeks. The extent of OA progression was evaluated by the OARSI score and immunohistochemistry at 12weeks after surgery. The Ihh signaling pathway and OA-related genes were quantified by real-time PCR.ResultsCell proliferation in the cells treated with ipriflavone was increased to 36.40%1.32% (5M) and 28.54%+/- 0.74% (10M) from 11.99%+/- 0.35% (DMSO) ($P<0.001$), and apoptosis was decreased to 12.64%+/- 3.7% (5M) and 15.18%+/- 3.13% (10M) from 25.76%+/- 5.1% (DMSO) ($P<0.05$). Ipriflavone blocked Runx-2 mainly through the Smo-Gli2 pathway. A similar result was found in the cartilage explant culture. Ihh signaling in vivo was inhibited in animals treated with ipriflavone. Safranin-O staining revealed a less cartilage damage with lower OARSI scores ($P<0.05$) in the ipriflavone-treated animals compared with untreated animals. The gene expression of Smo and Gli2 was inhibited significantly by ipriflavone ($P<0.05$). The OA-related gene and protein type X, MMP-13, and type II collagen-C fragment were reduced, while type II collagen and Agg were increased in the ipriflavone-treated animals ($P<0.05$).Conclusions Catabolic genes were disrupted by blocking the Ihh pathway. This finding suggests that disruption of Ihh signaling with ipriflavone provides chondral protection in rat posttraumatic OA.

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NR 41
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Imamura, Tomoaki
TI The impact of musculoskeletal diseases on the presence of locomotive syndrome
SO MODERN RHEUMATOLOGY
LA English
DT Article
DE Hypertension; locomotive syndrome; low back pain; musculoskeletal disease;

osteoporosis
ID quality-of-life; back muscle strength; elderly-people; body-mass; osteoarthritis; osteoporosis; association; population; knee; dysfunction
AB Objectives: We assessed the impact of musculoskeletal diseases, depressive mental state, and hypertension on locomotive syndrome, a condition of reduced mobility requiring nursing care. Since locomotive syndrome is a major public health issue that needs attention, its relationship with functional inconvenience in performing daily activities was also investigated. Methods: We conducted a cross-sectional study using an Internet panel survey, comprising 747 persons aged 30-90 years. Demographics, personal medical history, and daily activity data were assessed. The 25-question Geriatric Locomotive Function Scale was used to diagnose locomotive syndrome. Stepwise linear regression analysis and logistic regression analysis were conducted to evaluate the association between locomotive syndrome, musculoskeletal diseases, and functional inconvenience. Results: Aging, osteoporosis, and low back pain significantly increased the risk of locomotive syndrome, followed by knee osteoarthritis and lumbar spinal stenosis. Locomotive syndrome was significantly related to depressive mental state and hypertension, and led to functional inconvenience in Seiza sitting, cleaning, shopping, and strolling. Conclusion: Locomotive syndrome was associated with functional inconvenience in performing common daily activities involving the lower extremities and spine. Osteoporosis and aging were significantly associated with locomotive syndrome. The risk of locomotive syndrome may be decreased by treating comorbid osteoporosis and instituting exercise and diet-related modifications.
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NR 38
TC 23
Z9 26
U1 1
U2 14
PU TAYLOR & FRANCIS LTD
PI ABINGDON
PA 2-4 PARK SQUARE, MILTON PARK, ABINGDON OR14 4RN, OXON, ENGLAND
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J9 MOD RHEUMATOL
JI Mod. Rheumatol.

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WC Rheumatology
SC Rheumatology
GA HH2LT
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PT J
AU Li, Y
Xie, B
Jiang, ZQ
Yuan, BB
AF Li, Ying
Xie, Bing
Jiang, Zhiqiang
Yuan, Binbin
TI Relationship between osteoporosis and osteoarthritis based on DNA methylation
SO INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL PATHOLOGY
LA English
DT Article
DE Osteoporosis; osteoarthritis; mitochondria; DNA methylation
ID gene-expression; bone; epigenetics; mechanisms; fractures
AB The aim of this study was to investigate the relationship between osteoporosis and osteoarthritis by analyzing the DNA methylation in osteoporosis and osteoarthritis. The cancellous bone specimens were collected from a total of 12 hospitalized patients and divided into the osteoporosis group (OA), the osteoarthritis group (OP), the osteoporosis combined with osteoarthritis group (OA & OP), and the normal control group (N). The cancellous bone specimens of each group were detected and the differences in gene expression profiles by the MeDIP-chip technique were compared. Compared with Group OA & OP, the methylation levels in Group OA and Group OP were statistically higher, $P < 0.05$. In the microarray analysis, a total of 1,222 sites occurred hypermethylation. The analysis targeting the differentially expressed genes between Group OA & OP and Group N revealed that group OA and group OP had 4 common genes: PPIL3, NIF3L1, SMTN, and CALHM2. The level of genomic methylation is lower in the

patients with osteoporosis and/or osteoarthritis. The common difference between osteoarthritis and osteoporosis is reflected in some specific promoters, which may participate in the processes of diseases through different pathways.
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NR 23
TC 12
Z9 16
U1 0
U2 6
PU E-CENTURY PUBLISHING CORP
PI MADISON
PA 40 WHITE OAKS LN, MADISON, WI 53711 USA
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J9 INT J CLIN EXP PATHO
JI Int. J. Clin. Exp. Pathol.
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WC Oncology; Pathology
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PT J
AU Wang, QL
Li, HF
Wang, DP
Liu, ZY
Xia, WW
Xu, LL
Yu, S
AF Wang, Q-L
Li, H-F
Wang, D-P
Liu, Z-Y
Xia, W-W

Xu, L-L
Yu, S.
TI Effect of GGCX on the differentiation function of osteoporosis bone marrow mesenchymal stem cells through regulating TGFβ/smad signaling pathway
SO EUROPEAN REVIEW FOR MEDICAL AND PHARMACOLOGICAL SCIENCES
LA English
DT Article
DE Osteoporosis; GGCX; BMSC; TGF beta/smad signaling pathway; Differentiation
ID gla-rich protein; association
AB OBJECTIVE: Osteoporosis (OP) has a high incidence and can be found in multiple age groups. The bone marrow mesenchymal stem cells (BMSCs) have the potential for self-renewal and multi-directional differentiation, which are often used for investigating the differentiation function of osteoporosis bone marrow mesenchymal stem cells. gamma-glutamyl carboxylase (GGCX) is a carboxylase-related carboxylase and was observed to be abnormally expressed in osteoarthritis. However, the role and related mechanisms of GGCX in OP have not been fully elucidated. This work aimed to evaluate the effect of GGCX on the differentiation function of BMSCs. PATIENTS AND METHODS: Sprague-Dawley rats were randomly divided into the OP group prepared by ovariectomy and sham group. GGCX expression was tested by enzyme-linked immunosorbent assay (ELISA). BMSCs were isolated from OP rats and transfected with pcDNA-GG-CX plasmids. BMSC proliferation was detected by tetrazolium salt colorimetry (MTT) assay. The osteogenic and adipogenic differentiation of BMSCs was analyzed by alizarin red staining and oil red O staining. The ALP activity was determined by alkaline phosphatase (ALP) activity colorimetric assay. Real time-PCR was used to test the expressions of osteogenesis-related genes RUNX2 and OPN mRNA. Western blot was adopted to assess the TGF beta/smad signaling pathway activity. RESULTS: GGCX expression was significantly decreased in the serum of OP rats compared with the sham group ($p < 0.05$). The transfection of pcDNA-GGCX plasmid significantly promoted BMSC cell proliferation, increased calcified nodule formation, inhibited adipogenic differentiation, enhanced ALP activity, elevated RUNX2, and OPN mRNA expressions, and upregulated TGF beta 1, Smad2, and Smad7 expressions ($p < 0.05$). CONCLUSIONS: GGCX secretion is reduced in osteoporosis. GGCX can regulate osteoporosis via promoting the TGF beta/smad signaling pathway, facilitating BMSCs osteogenic differentiation, and inhibiting BMSCs adipogenic differentiation.
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Z9 21
U1 0
U2 10
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PA VIA GREGORIO VII, ROME, 186-00165, ITALY
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WC Pharmacology & Pharmacy
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PT J
AU McIntyre, E
Lauche, R
Frawley, J
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AF McIntyre, Erica
Lauche, Romy
Frawley, Jane
Sibbritt, David
Reddy, Prasuna
Adams, Jon
TI Physical activity and depression symptoms in women with chronic illness and the mediating role of health-related quality of life
SO JOURNAL OF AFFECTIVE DISORDERS
LA English
DT Article
DE Depression; Health behaviour; Exercise; Women's health; Quality of life; Chronic disease
ID psychological distress; older-adults; exercise; hardiness; care; association; prevalence; impact
AB Background: The aim of this study was to determine the impact of physical activity on depression symptom severity in women 45 years and older with a chronic illness diagnosis, and explore relations between physical activity and psychological and health-related characteristics predicting depression symptoms.

Methods: 1932 women diagnosed with one of five chronic illnesses: asthma, depression, diabetes, osteoarthritis, or osteoporosis participated in a sub-study of the 45 and Up Study-a cross-sectional study of people aged 45 years and older. The survey included items measuring demographics, depression symptoms, health-related quality of life (HRQoL), health-related hardiness, sleep quality, and health behaviours, such as physical activity. Results: A multiple regression model explained 43% of the variance in depression symptoms (R-2 = 0.43, F (18) = 61.72, p < .001); intensity of physical activity was a significant predictor of depression symptoms (p < .001), and HRQoL was found to explain the most variance (B = -10.00) in depression symptoms. Mediation analysis confirmed that HRQoL partially mediated the relation between physical activity and depression symptoms; however, the effect was very small. Limitations: Cross-sectional data and self-report measures limit the implications of the findings. Conclusion: Women with chronic illness engaging in more vigorous physical activity had less severe depression symptoms. Findings suggest that improving HRQoL is critical to the prevention and management of depression symptoms in women with chronic illness. Psychological and health-related factors that influence HRQoL, such as sleep quality and health-related hardiness, are important clinical considerations for health practitioners.
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NR 45
TC 17
Z9 24
U1 2
U2 40
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 0165-0327
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J9 J AFFECT DISORDERS
JI J. Affect. Disord.
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WC Clinical Neurology; Psychiatry
SC Neurosciences & Neurology; Psychiatry
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UT WOS:000467801200036
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PT J
AU Grote, C
Reinhardt, D
Zhang, MC
Wang, JX
AF Grote, Caleb
Reinhardt, Daniel
Zhang, Mingcai
Wang, Jinxi
TI Regulatory mechanisms and clinical manifestations of musculoskeletal aging
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Review

DE musculoskeletal aging; sarcopenia; osteoporosis; osteoarthritis; tendinopathy
ID human articular-cartilage; age-related-changes; different fiber types; dna-damage; bone mass; stem-cells; cellular senescence; skeletal-muscle; cross-linking; life-span
AB Aging is the strongest risk factor for degenerative bone and joint diseases. Clinical therapies for age-related musculoskeletal disorders face significant challenges as their pathogenic mechanisms remain largely unclear. This review article focuses on the recent advances in the understanding of regulatory mechanisms of musculoskeletal aging and their clinical relevance. We begin with the prevalence and socioeconomic impacts of major age-related musculoskeletal disorders such as sarcopenia, osteoporosis, osteoarthritis, and degenerative tendinopathy. The current understanding of responsible biological mechanisms involved in general aging is then summarized. Proposed molecular, cellular, and biomechanical mechanisms relevant to the clinical manifestations of aging in the musculoskeletal system are discussed in detail, with a focus on the disorders affecting muscle, bone, articular cartilage, and tendon. Although musculoskeletal aging processes share many common pathways with the aging of other body systems, unique molecular and cellular mechanisms may be involved in the aging processes of musculoskeletal tissues. Advancements in the understanding of regulatory mechanisms of musculoskeletal aging may promote the development of novel treatments for age-related musculoskeletal disorders. Finally, future research directions for major musculoskeletal tissues including functional interaction between the tissues and their clinical relevance to age-related musculoskeletal disorders are highlighted in the Future Prospects section. (c) 2019 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 37:1475-1488, 2019.
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TI Recommendations for the Reporting of Harms in Manuscripts on Clinical Trials Assessing Osteoarthritis Drugs: A Consensus Statement from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
SO DRUGS & AGING
LA English
DT Article
ID single intraarticular injection; topical diclofenac solution; randomized controlled-trial; adverse event assessment; vehicle tdt 064; double-blind; knee osteoarthritis; hyaluronic-acid; glucosamine sulfate; hand osteoarthritis
AB BackgroundThere is strong evidence of under-reporting of harms in manuscripts on randomized controlled trials (RCTs) compared with the volume of raw data retrieved from these trials. Many guidelines have been developed to tackle this, but they have failed to address some important issues that would allow for standardization and transparency. As a consequence, harms reporting in manuscripts remains suboptimal.ObjectiveThe European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) aimed to deliver accurate recommendations for better reporting of harms in clinical trials manuscripts on anti-osteoarthritis (OA) drugs. These could help to better inform clinicians on harms recorded in RCTs and further help researchers conducting meta-analyses.MethodsUsing the outcomes of several systematic reviews on the safety of anti-OA drugs, we summarized the ways in which harms have been reported in OA RCT manuscripts to date. Next, we drafted some recommendations and initiated a modified Delphi process that involved a panel of clinicians and clinical researchers to build an expert consensus on recommendations from the ESCEO for the reporting of harms in future manuscripts

on RCTs assessing anti-OA drugs.ResultsThese recommendations emphasize that all treatment-emergent adverse events (AEs) should always be taken into account for harms reporting, with no frequency threshold, and describe how specific AEs should be reported; they also provide a list of the most relevant organ systems to be considered according to each class of drug for reporting of harms within the results section of a manuscript. Irrespective of the drug, the ESCEO recommends that total, severe and serious AEs and withdrawals due to AEs should always be reported; guidance on the reporting of specific events pertaining to each category is provided. The ESCEO also recommends the reporting of information on drug effect on biological parameters, with specific guidance.ConclusionsThese recommendations may contribute to improve transparency in the field of safety of anti-OA medications. Pharmaceutical companies developing drugs for OA, and researchers conducting clinical trials, are encouraged to comply with them when reporting harms-related results in manuscripts on RCTs. The ESCEO also encourages journals to refer to the ESCEO recommendations in their instructions to authors for the publication of manuscripts on trials of anti-OA medications.
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TI Increased rates of knee arthroplasty and cost of patients with meniscal tears treated with arthroscopic partial meniscectomy versus non-operative management
SO KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY
LA English
DT Article
DE Meniscal tear; Meniscectomy; Knee arthroscopy; Knee; Total knee replacement; Total knee arthroplasty
ID anterior cruciate ligament; osteoarthritis; surgery; injury; prevalence; outcm; 5-year; repair; trial; risk
AB PurposeThe purpose of this study was to determine the cost of arthroscopic partial meniscectomy (APM), one of the most common surgeries performed by orthopaedic surgeons, and the associated rate of progression to knee arthroplasty (KA) compared to patients treated non-operatively after diagnosis of meniscal tear.MethodsUtilizing data mining software (PearlDiver, Colorado Springs, CO), a national insurance database of approximately 23.5million orthopaedic patients was queried for patients diagnosed with a meniscal tear. Patients were classified by treatment: non-operative and arthroscopic partial meniscectomy and were followed after initial diagnosis for cost and progression to knee arthroplasty.ResultsThere were 176,407 subjects in the non-op group and 114,194 subjects in the arthroscopic partial meniscectomy group. Arthroscopic partial meniscectomy generated more cost than non-operative ($3842.57 versus $411.05, P<0.001). Arthroscopic partial meniscectomy demonstrated greater propensity to need future knee arthroplasty (11.4% at 676days) than those treated non-operatively (9.5% at 402 days) (P<0.001). Female patients demonstrated a higher rate of progression to knee arthroplasty in the arthroscopic partial meniscectomy and non-operative groups (P<0.001).ConclusionCompared to non-operative treatment for meniscal tears, arthroscopic partial meniscectomy is more expensive and does not appear to decrease the rate of progression to knee arthroplasty. Patients undergoing arthroscopic partial meniscectomy yielded on average a delay of only 9months (274days) before undergoing knee arthroplasty. Female patients experienced a significantly higher rate of progression to knee arthroplasty. The authors recognize the limitations of this type of study including its retrospective nature, reliance upon accurate coding and billing information, and the inability to determine whether symptoms including mechanical locking played a role in the decision to perform an APM.Level of evidenceIV.
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JI Knee Surg. Sports Traumatol. Arthrosc.
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TI Metformin; an old antidiabetic drug with new potentials in bone disorders
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Review
DE Metformin; Diabetes; AMPK; Bone disorders; Bone cancers
ID activated protein-kinase; type-2 diabetes-mellitus; x-ray absorptiometry; mineral density; skeletal-muscle; postmenopausal women; fracture risk; in-vivo; osteoblast differentiation; glucose-uptake
AB The prevalence of diabetes mellitus especially type 2 diabetes mellitus is increasing all over the world. In addition to cardiomyopathy and nephropathy, diabetics are at higher risk of mortality and morbidity due to greater risk of bone fractures and skeletal abnormalities. Patients with diabetes mellitus have lower bone quality in comparison to their non-diabetic counterparts mainly because of hyperglycemia, toxic effects of advanced glycosylation end-products (AGEs) on bone tissue, and impaired bone microvascular system. AGEs may also contribute to the development of osteoarthritis further to osteoporosis. Therefore, glycemic control in diabetic patients is vital for bone health. Metformin, a widely used antidiabetic drug, has been shown to improve bone quality and decrease the risk of fractures in patients with diabetes in addition to glycemic control and improving insulin sensitivity. AMP activated protein kinase (AMPK), the key molecule in metformin antidiabetic mechanism of action, is also effective in signaling pathways involved in bone physiology. This review, discusses the molecules linking diabetes and bone turnover, role of AMPK in bone metabolism, and the effect of metformin as an activator of AMPK on bone disorders and malignancies.
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AU Yik, JH
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TI Perioperative pregabalin does not reduce opioid requirements in total knee arthroplasty
SO KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY
LA English
DT Article
DE Total knee arthroplasty; Pregabalin; Morphine; Preoperative; Analgesia; Pain score
ID postoperative pain; controlled-trial; oral pregabalin; analgesia; management; single; gabapentin; efficacy; morphine; hip
AB PurposeThe purpose of this prospective, randomized, double-blinded, placebo-controlled study was to determine if pregabalin, when given perioperatively in addition to patient-controlled analgesia morphine, paracetamol and etoricoxib, is effective in reducing morphine requirements and moderating pain scores after primary total knee arthroplasty. We hypothesize that there would be no difference in postoperative opioid requirements, postoperative pain scores, and functional scores with the use of perioperative pregabalin.MethodsEighty-seven patients who underwent primary total knee arthroplasty were randomised and allocated to two groups. One group received capsules containing pregabalin 75mg, and the other a placebo-one capsule before surgery and one capsule once per night up till postoperative day 2. Multimodal analgesia provided for all patients in this study included femoral nerve block, intravenous patient-controlled analgesia (morphine), paracetamol and etoricoxib. The primary outcome of patient's pain control was based on the measurement of cumulative morphine consumption during the first 72h postoperatively.ResultsPregabalin did not reduce the cumulative or effective morphine consumption at 48h and 72h post-operation. There were also no significant differences noted in pain scores at 48h and 72h after surgery, functional range of motion of the operated knee at 72h post-op, or outcomes recorded on

the Knee Society Score (KSS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and 36-Item Short Form Survey (SF-36) questionnaires at 3 and 6months post-op. None of the patients demonstrated common adverse reactions to pregabalin.ConclusionThis study showed no reduction in postoperative opioid requirements, or improvement in early postoperative pain scores or functional outcomes at 6months, with perioperative use of pregabalin. Orthopaedic surgeons may consider this when selecting an analgesic regimen for their patients.Level of evidenceII.
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DE Bulgaria; Rheumatology; Vasculitis; Osteoarthritis; Rheumatoid arthritis; Spondylitis; Systemic lupus erythematosus; Scleroderma; Myositis; Biologics
ID systemic-lupus-erythematosus; society classification criteria; american-college; eular recommendations; ankylosing-spondylitis; double-blind; arthritis; management; disease; rheumatism
AB Our aim was to appraise publications from Bulgaria, to assess their global impact, and to describe features and challenges unique to the rheumatology practice in Bulgaria characterized by stringent cost constraints. The Scopus database was queried on 25th July 2018 and data on the number of published documents, their Hirsch-indices and citations number were extracted. Published Bulgarian guidelines for the management of rheumatic diseases and the presented data on Bulgarian Rheumatology Society were identified based on prior knowledge of the authors. From all the identified 1082 document the most extensively researched areas were rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), osteoporosis, and osteoarthritis (OA). For the last five years (from Jan 2013 to 25th July 2018) the number of publications was 293. We found that Bulgaria's international scientific collaboration in the field of rheumatology is focused on a handful of countries mainly from Europe. Although Bulgarian rheumatologists have access to costly biologic agents for treating their patients with rheumatic diseases, their funding may not be granted according to the current recommendations of European League against Rheumatism (EULAR) and national guidelines for the management of rheumatic diseases. Although the western world clearly dominates the production of scientific publications in rheumatology, Bulgarian rheumatology may present another perspective for diagnosis and management of patients with rheumatic diseases in a cost-stringent environment. Nevertheless, both rheumatology science and practice in Bulgaria still have a long way to go to take its deserved place among the other European countries.
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AF Catelli, Danilo S.
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TI Modified gait patterns due to cam FAI syndrome remain unchanged after surgery
SO GAIT & POSTURE
LA English
DT Article
DE Femoroacetabular impingement syndrome; Osteochondroplasty; Muscle forces; Hip contact forces; Kinetics; Kinematics; Gait parameters
ID hip muscle strength; femoroacetabular impingement; surgical dislocation; biomechanics; arthroscopy; kinematics; walking; joint; osteoarthritis; individuals
AB Background: In order to reduce the development of hip osteoarthritis related to cam-type femoroacetabular impingement syndrome (FAIS), corrective surgery has evolved to become a safe and effective treatment. Although corrective surgery produces high level of patient satisfaction, it is still unclear how it affects muscle and hip contact forces during level walking. Research question: The purpose was to compare the muscle force contributions and hip contact forces in patients before and after surgical correction for cam FAIS with healthy control (CTRL) individuals during level walking. Methods: Eleven male patients with symptomatic cam-type morphology, who underwent hip osteochondroplasty, had their level walking recorded pre- and at 2-year postoperatively. The patients were sex-, age-, BMI-matched to 11 CTRL individuals. Sagittal and frontal hip kinematics and kinetics were computed and, subsequently, muscle and hip contact forces were estimated using musculoskeletal modelling and static optimization. Results: Patient-reported outcomes improved postoperatively. The pre- and postoperative FAIS walked slower and with shorter steps than the CTRL. Postoperative biceps femoris (CTRL: 0.35 +/- 0.13 N/BW; pre-op: 0.28 +/- 0.11 N/BW; post-op: 0.20 +/- 0.07 N/BW) and semimembranosus forces (CTRL: 0.77 +/- 0.24 N/BW; pre-op: 0.66 +/- 0.24 N/BW; post-op: 0.41 +/- 0.14 N/BW) were lower at ipsilateral foot-strike. Postoperative rectus femoris force (CTRL: 1.73 +/- 0.35 N/BW; pre-op: 1.44 +/- 0.24 N/BW; post-op: 1.18 +/- 0.23 N/BW) was lower than the other two groups, and the pre- and postoperative FAIS had lower iliacus (CTRL: 1.17 +/- 0.18 N/ BW; pre-op: 0.93 +/- 0.16 N/BW; post-op: 0.94 +/- 0.21 N/BW) and psoas (CTRL: 1.55 +/- 0.24 N/BW; pre-op: 1.14 +/- 0.38 N/BW; post-op: 1.10 +/- 0.46 N/BW) muscle forces at contralateral foot-strike compared with the CTRL. Pre- and postoperative FAIS

demonstrated lower peak hip contact loading resultant than the CTRL. Significance: The altered gait parameters observed in the preoperative FAIS was not restored after surgery, and was still away from the CTRL. It is possible that the reduced dynamic muscle forces of the biceps femoris, semimembranosus and rectus femoris postoperatively were associated with the protected mechanism that involved the iliopsoas preoperatively. This is an indication that the gait adaptations affected by the FAIS do not restore to normal after surgical correction at the 2-years follow-up.
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Z9 40
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TI Risk Factors for Poor Functional Recovery, Mortality, Recurrent Fractures, and Falls Among Patients Participating in a Fracture Liaison Service Program
SO JOURNAL OF THE AMERICAN MEDICAL DIRECTORS ASSOCIATION

LA English
DT Article
DE Body mass index; chronic kidney disease; fall; fracture liaison service; osteoporosis
ID hip fracture; body-mass; burden; health; women; care
AB Objective: A fracture liaison service (FLS) for patients with fractures is a promising approach for improving outcomes, but barriers to the successful implementation of an FLS remain. The factors influencing the outcomes of patients already receiving FLS care are unclear. Design: A prospective multicenter cohort study. Settings and participants: Patients with incident hip and clinical vertebral fractures treated at 2 institutions between January 2014 and June 2016 were prospectively enrolled. Demographic profiles, comorbidities, prior fracture experiences, T scores, Fracture Risk Assessment Tool (FRAX) scores, and serum markers were examined. Measures: Self-reported functional status (at the 4th month), mortality, recurrent fractures, and falls (at the 2-year follow-up). Results: Of 712 patients screened for eligibility, 600 (84%) participants (age 78 +/- 10 years) were enrolled in the FLS program. At 4 months, 58%, 53%, and 60% of the participants reported improved mobility, self-care, and daily activities after FLS care, respectively. After 2 years, 85 (14%) died, 36 (6%) developed recurrent fractures, and 199 (33%) had 1 or more fall episodes. Multivariate logistic regression showed that neurologic disorders, heart disease, and diabetes were associated with a decreased probability of functional recovery. Cox regression showed that older age and chronic kidney disease (CKD) were predictive of increased mortality, whereas heart disease was correlated with an increased refracture risk. Older age and cancer or osteoarthritis were associated with a higher risk of falls. Importantly, a higher body mass index predicted a lower risk of mortality and a higher probability of improved self-care but a higher risk of fall at follow-up. Conclusions/Implications: We discovered that comorbidities including CKD, heart disease, cancer, and osteoarthritis could influence short-term functional changes, survival, and the risk of refractures or falls among patients participating in FLSs. These factors are expected to aid in prognosis estimation and management planning for those with fractures. (C) 2018 AMDA - The Society for Post-Acute and Long-Term Care Medicine.
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TC 17
Z9 21
U1 0
U2 9
PU ELSEVIER SCIENCE INC
PI NEW YORK
PA STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA
SN 1525-8610
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J9 J AM MED DIR ASSOC
JI J. Am. Med. Dir. Assoc.

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WC Geriatrics & Gerontology
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ER

PT J
AU Jain, MV
Rajpura, A
Kumar, VS
Shaw, D
Al Najjar, M
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Jackson, Richard
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TI Functional outcome of total hip arthroplasty after a previous hip arthroscopy: a retrospective comparative cohort study
SO HIP INTERNATIONAL
LA English
DT Article
DE Hip arthroscopy; total hip arthroplasty
ID knee arthroscopy; impingement; trends; age

AB Background: Despite patients demonstrating significant short-term clinical improvement from a hip arthroscopy (HA), a number of patients progress to significant osteoarthritis of the hip requiring total hip arthroplasty (THA). This study aims to evaluate if there is any difference in the functional outcome of patients undergoing THA after a previous hip arthroscopy compared to patients undergoing THA for primary osteoarthritis of the hip. Methods: Between 2010 and 2013, in a group of 414 patients who underwent hip arthroscopy, we identified 18 patients who underwent a subsequent uncemented THA. These formed the study group. During the same period, 625 patients underwent an uncemented THA performed for primary OA, of which 63 patients were matched to the study group for age, follow-up and implants used. These formed the control group. Pre-op and post-op Oxford Hip Scores (OHS) were recorded for all patients. Results: A mean follow-up of 26.5 and 26.3months was observed in the study and control groups respectively. The median (interquartile ranges) preoperative OHS were 14 (8.25, 17.0) and 18.5 (13.25, 24.75) in the 2 groups. Corresponding postoperative scores were 40 (31.25, 45) and 46 (43, 48). Median difference between the preoperative and postoperative OHS was 27 (19, 31) and 25 (18.25, 31). Adjusting for the pre-treatment scores, the postoperative scores in the study arm were significantly lower than for the control arm with an estimate (SE) of -0.464 (p = 0.012). Post-hoc power analysis showed that the study was sufficiently powered to detect a meaningful difference in scores. Conclusion: Total hip arthroplasty after hip arthroscopy leads to satisfactory functional outcomes. However, the functional outcome in this group is significantly worse than in a matched cohort of patients undergoing THA for osteoarthritis. There was no difference in the rate of complications between the 2 groups.
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10.1007/s00402-011-1352-z
NR 19
TC 7
Z9 7
U1 0
U2 3
PU SAGE PUBLICATIONS LTD
PI LONDON
PA 1 OLIVERS YARD, 55 CITY ROAD, LONDON EC1Y 1SP, ENGLAND
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J9 HIP INT
JI Hip Int.
PD JUL 15
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WC Orthopedics
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PT J
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TI Effectiveness of home based intervention program in reducing mortality of hip fracture patients: A non-randomized controlled trial
SO ARCHIVES OF GERONTOLOGY AND GERIATRICS
LA English
DT Article
DE Intervention; Hip fracture; Postoperative; Mortality; Mobility; Comanaged care
ID osteoarthritis index womac; western-ontario-university; elderly-patients; nutritional-status; surgical fixation; surgery; predictors; population; exercise; women
AB Purpose: The study was done to investigate whether a postoperative intervention program is effective in reducing mortality and improving mobility in two comparative hip fracture patients over one year postoperatively. Methods: A non-randomized controlled trial study with an intervention group of hip fracture patients and historical control group with 12 months follow up. One hundred twenty four admitted hip fracture patients to the Trauma Unit of Assiut University Hospitals, aged 50 years and older were included from 1st July to 31st December 2014. They were divided into 64 and 60 patients as intervention and control groups respectively. Weight, height and bone mineral density were measured and baseline characteristics were taken. The intervention was a postoperative care program in the form of education sessions with an explanatory leaflet on discharge for nutrition and physical exercise program at home. Follow up phone calls were done at 3 months, 6 months and one year postoperatively by one assessor. Physical mobility was assessed by 24 items Western Ontario And McMaster Universities Osteoarthritis Index (WOMAC). Results: Mortality was significantly higher in the control group, WOMAC score was significantly better among intervention group through follow up. By multivariate Cox survival analysis, advancing age, no intervention, osteoporosis, postoperative complications, chest infections and heart attacks were significant predictors for mortality. Conclusion: A significant improvement in mobility and reduction of mortality was achieved by application of

a postoperative care program that could be incorporated into the hip fracture patients' care pathway.
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NR 44
TC 11
Z9 11
U1 1
U2 20
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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JI Arch. Gerontol. Geriatr.
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BP 8
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PG 10
WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA HJ5WE
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PT J
AU Oshiro, CES
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AF Oshiro, Caryn E. S.
Frankland, Timothy B.
Rosales, A. Gabriela
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TI Fall Ascertainment and Development of a Risk Prediction Model Using Electronic Medical Records
SO JOURNAL OF THE AMERICAN GERIATRICS SOCIETY
LA English
DT Article
DE adults; falls; risk; EMR
ID older-people; adults
AB OBJECTIVES To examine the use of electronic medical record (EMR) data to ascertain falls and develop a fall risk prediction model in an older population. DESIGN Retrospective longitudinal study using 10 years of EMR data (2004-2014). A series of 3-year cohorts included members continuously enrolled for a minimum

of 3 years, requiring 2 years pre-fall (no previous record of a fall) and a 1-year fall risk period. SETTING Kaiser Permanente Hawaii, an ambulatory setting. PARTICIPANTS A total of 57 678 adults, age 60 years and older. MEASUREMENTS Initial EMR searches were guided by current literature and geriatricians to understand coding sources of falls as our outcome. Falls were captured by two coding sources: International Classification of Diseases, Ninth Revision (ICD-9) codes (E880-889) and/or a fall listed as a "primary reason for visit." A comprehensive list of EMR predictors of falls were included into prediction models enabling statistical subset selection from many variables and modeling by logistic regression. RESULTS Although 72% of falls in the training data set were coded as "primary reason for visit," 22% of falls were coded as ICD-9 and 6% coded as both. About 80% were reported in face-to-face encounters (eg, emergency department). A total of 2164 individuals had a fall in the risk period. Using the 13 key predictors (age, comorbidities, female sex, other mental disorder, walking issues, Parkinson's disease, urinary incontinence, depression, polypharmacy, psychotropic and anticonvulsant medications, osteoarthritis, osteoporosis) identified through LASSO regression, the final model had a sensitivity of 67%, specificity of 69%, positive predictive value of 8%, negative predictive value of 98%, and area under the curve of .74. CONCLUSION This study demonstrated how the EMR can be used to ascertain falls and develop a fall risk prediction model with moderate sensitivity/specificity. Concurrent work with clinical providers to enhance fall documentation will improve the ability of the EMR to capture falls and consequently may improve the model to predict fall risk.
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NR 24
TC 33
Z9 36
U1 1
U2 19
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0002-8614
EI 1532-5415
J9 J AM GERIATR SOC
JI J. Am. Geriatr. Soc.
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BP 1417
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WC Geriatrics & Gerontology; Gerontology
SC Geriatrics & Gerontology
GA IH2DE
UT WOS:000474304600017
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PT J
AU Yamada, H
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AF Yamada, Hiroaki
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TI Study of the cartilage matrix production-promoting effect of chicken leg extract and identification of the active ingredient
SO NUTRITION RESEARCH AND PRACTICE
LA English
DT Article
DE Osteoarthritis; phenylalanyl-hydroxyproline; cartilage; chicken leg
ID articular-cartilage; osteoarthritis; digestion; efficient; peptides; pepsin
AB BACKGROUND/OBJECTIVES: Osteoarthritis (OA) is a major public health issue in Japan and other countries, and foods that prevent or treat OA are in strong demand. Proteins and peptides in chicken meat and bones are known for being rich in functional and nutritional ingredients for the improvement of osteoporosis. We speculated that chicken legs, a food consumed in many regions of the world, may also contain such ingredients. In this study, we aim to (i) evaluate the effect of chicken leg extract (CLE) on the promotion of cartilage matrix production and (ii) identify the active ingredient in CLE that contributes to this function. MATERIALS/METHODS: Artificial CLE digest was prepared, and the acid mucopolysaccharide production-promoting activity of the CLE digest was

evaluated by alcian blue staining of ATDC5 cells. CLE was orally administered to rabbits with burr holes in the knee joint of the femur, and the degree of regeneration of cartilage matrix was evaluated. Furthermore, we investigated orally administered CLE-derived peptides in human plasma using LC-MS. From measuring the acid mucopolysaccharide production-promotion activity of these peptides, a molecule considered to be an active ingredient in the CLE digest was identified. RESULTS: CLE digest promoted acid mucopolysaccharide production and facilitated regeneration of cartilage matrix in in vitro and in vivo experiments. Four peptides including phenylalanyl-hydroxyproline (Phe-Hyp) were detected as CLE-derived peptides in human plasma. The effect of CLE was inferred to be due to Phe-Hyp, which was confirmed to be present in the CLE digest. CONCLUSIONS: It was shown that CLE stimulated the production of articular cartilage matrix both in vitro and in vivo, and that CLE could be an effective food for preventing or treating OA. Furthermore, only Phe-Hyp was confirmed as the active compound in the CLE digest, suggesting that the activity of CLE was due to Phe-Hyp.
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NR 25
TC 5
Z9 6
U1 0
U2 8
PU KOREAN NUTRITION SOC
PI SEOUL
PA 804 KST CTR, 635-4 YEOGSAM-SONG KANGNAM-KU, SEOUL, 135-703, SOUTH KOREA
SN 1976-1457
EI 2005-6168
J9 NUTR RES PRACT
JI Nutr. Res. Pract.
PD DEC 15
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IS 6
BP 480
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WC Nutrition & Dietetics
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GA JU8RT
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AU Pucci, S
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TI Clusterin silencing restores myoblasts viability and down modulates the inflammatory process in osteoporotic disease
SO JOURNAL OF TRANSLATIONAL MEDICINE
LA English
DT Article
DE Clusterin (CLU); Osteoporosis; Osteoarthritis; Sarcopenia; Muscle waist; Osteoporosis marker
ID skeletal-muscle; isoforms; protein; bone
AB Background: Targeting new molecular pathways leading to Osteoporosis (OP) and Osteoarthritis (OA) is a hot topic for drug discovery. Clusterin (CLU) is a glycoprotein involved in inflammation, proliferation, cell death, neoplastic disease, Alzheimer disease and aging. The present study focuses on the expression and the role of CLU in influencing the decrease of muscle mass and fiber senescence in OP-OA condition. Methods: Vastus lateralis muscle biopsies were collected from 20 women with OP undergoing surgery for fragility hip fracture and 20 women undergoing arthroplasty for hip osteoarthritis. Results: We found an overexpression of CLU in degenerated fibers in OP closely correlated with interleukin 6 (IL6) and histone H4 acetylation level. Conversely, in OA muscle tissues we observed a weak expression of CLU but no nuclear histone H4 acetylation. Ex vivo studies on isolated human myoblasts confirmed CLU overexpression in OP as compared to OA ($p<0.001$). CLU treatment of isolated OP and OA myoblasts showed: modulation of proliferation, morphological changes, increase of histone H4 acetylation and induction of myogenin (MYOG) activation in OP myoblast only. In OP condition, functional knockdown of CLU by siRNA restores proliferative myoblasts capability

and tissue damage repair, carried out by an evident upregulation of Transglutaminase 2 (TGM2). We also observed downmodulation of CX3CR1 expression with consequent impairing of the inflammatory infiltrate recruitment. Conclusions: Results obtained suggest a potential role of CLU in OP by influencing myoblasts terminal differentiation, epigenetic regulation of muscle cell differentiation and senescence. Moreover, CLU silencing points out its role in the modulation of tissue damage repair and inflammation, proposing it as a new diagnostic marker for muscle degeneration and a potential target for specific therapeutic intervention in OP related sarcopenia.
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NR 42
TC 16
Z9 16
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U2 13
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AU Ng, QX
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AF Ng, Qin Xiang
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Lim, Donovan Yutong
Sivalingam, Vivekanandan
TI Clinical Role of Aspirin in Mood Disorders: A Systematic Review
SO BRAIN SCIENCES
LA English
DT Review
DE aspirin; anti-inflammatory; psychiatry; mood disorder; depression; bipolar;

systematic review
ID low-dose aspirin; primary prevention; depression; risk; minocycline; lithium; metaanalysis; dysfunction; microglia; secretion
AB Worldwide, depression and bipolar disorder affect a large and growing number of people. However, current pharmacotherapy options remain limited. Despite adequate treatment, many patients continue to have subsyndromal symptoms, which predict relapse in bipolar illness and often result in functional impairments. Aspirin, a common nonsteroidal anti-inflammatory drug (NSAID), has purported beneficial effects on mood symptoms, showing protective effects against depression in early cohort studies. This systematic review thus aimed to investigate the role of aspirin in mood disorders. Using the keywords (aspirin or acetylsalicy* or asa) and (mood or depress* or bipolar or mania or suicid*), a comprehensive search of PubMed, EMBASE, Medline, PsycINFO, Clinical Trials Register of the Cochrane Collaboration Depression, Anxiety and Neurosis Group (CCDANTR), Clinicaltrials.gov and Google Scholar databases found 13,952 papers published in English between 1 January 1988 and 1 May 2019. A total of six clinical studies were reviewed. There were two randomized, placebo-controlled, double-blind trials and populations drawn from two main cohort studies (i.e., the Geelong Osteoporosis Study and the Osteoarthritis Initiative study). Using a random-effects model, the pooled hazard ratio of the three cohort studies was 0.624 (95% confidence interval: 0.0503 to 1.198, p = 0.033), supporting a reduced risk of depression with aspirin exposure. Overall, the dropout rates were low, and aspirin appears to be well-tolerated with minimal risk of affective switch. In terms of methodological quality, most studies had a generally low risk of bias. Low-dose aspirin (80 to 100 mg/day) is safe, well-tolerated and potentially efficacious for improving depressive symptoms in both unipolar and bipolar depression. Due to its ability to modulate neuroinflammation and central nervous system processes, aspirin may also have valuable neuroprotective and pro-cognitive effects that deserve further exploration. Further randomized, controlled trials involving the adjunctive use of aspirin should be encouraged to confirm its therapeutic benefits.
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NR 39
TC 22
Z9 24
U1 1
U2 12
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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EI 2076-3425
J9 BRAIN SCI
JI Brain Sci.
PD NOV 15
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VL 9
IS 11
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DI 10.3390/brainsci9110296
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WC Neurosciences
SC Neurosciences & Neurology
GA JV3NV
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Nenes, A.
Mihalopoulos, N.
TI Yearlong variability of oxidative potential of particulate matter in an urban Mediterranean environment
SO ATMOSPHERIC ENVIRONMENT
LA English
DT Article
DE Oxidative potential; Reactive oxygen species; DTT assay; Particulate matter; Toxicity; Urban aerosol
ID oxygen species activity; organic aerosol composition; ultrafine particles pm0.25; humic-like substances; water-soluble pm2.5; reactive oxygen; chemical-composition; los-angeles; dithiothreitol dtt; redox activity
AB The oxidative potential (OP) of fine and coarse fractions of ambient aerosols was studied in the urban environment of Athens, Greece. OP was quantified using a dithiothreitol (DTT) assay, applied to the water soluble fraction of aerosol that was extracted from 361 fine and 84 coarse mode of 24-h and 12-h filter samples over a one-year period. During the cold period, samples were collected on a 12-h basis, to assess the impact of night-time biomass burning emissions from domestic heating on OP. The chemical characteristics of aerosols were measured in parallel using an Aerosol Chemical Speciation Monitoring (ACSM) and a 7-wavelength Aethalometer. A source apportionment analysis on the ACSM data resulted in the identification of organic aerosol (OA) factors on a seasonal basis. A good correlation of OP with NO3-, NH4+, BC (Black Carbon), Organics and LV-OOA (low volatility oxygenated OA) was found during winter, revealing the importance of combustion and aging processes for OP. During the summertime, a good correlation between OP and SO4-2 and NH4+ indicates its association with

regional aerosol - thus the importance of oxidative aging that reduces its association with any characteristic source. Multiple regression analysis during winter revealed that highly oxygenated secondary aerosol (LV-OOA) and, to a lesser extent, fresh biomass burning (BBOA) and fossil fuel HOA) organic aerosol, are the prime contributors to the OP of fine aerosol, with extrinsic toxicities of 54 +/- 22 pmol min(-1) mu g(-1), 28 +/- 7 and 17 +/- 4 pmol min(-1) mu g(-1), respectively. In summer, OP cannot be at- tributed to any of the identified components and corresponds to a background aerosol value. In winter however, the regression model can reproduce satisfactorily the water soluble DTT activity of fine aerosol, providing a unique equation for the estimation of aerosol OP in an urban Mediterranean environment.
C1 [Paraskevopoulou, D.; Bougiatioti, A.; Stavroulas, I.; Lianou, M.; Liakakou, E.; Gerasopoulos, E.; Nenes, A.; Mihalopoulos, N.] Natl Observ Athens, Inst Environm Res & Sustainable Dev, 1 Metaxa & Vas Pavlou, Athens 15236, Greece.
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DT Review
DE -glutamyl carboxylase (GGCX); steroid and xenobiotic receptor (SXR); pregnane X receptor (PXR); osteoporosis; osteoarthritis; sarcopenia; osteocalcin; matrix Gla protein (MGP); Gla-rich protein (GRP)
ID gamma-carboxyglutamic acid; xenobiotic receptor sxr; matrix gla protein; single nucleotide polymorphism; pregnane x receptor; bone-formation; hip-fracture; undercarboxylated osteocalcin; circulating levels; androgen receptor
AB Vitamin K is a fat-soluble vitamin that was originally found as an essential factor for blood coagulation. With the discovery of its role as a co-factor for -glutamyl carboxylase (GGCX), its function for blood coagulation was understood as the activation of several blood coagulation factors by their -carboxylation. Over the last two decades, other modes of vitamin K actions have been discovered, such as the regulation of transcription by activating the steroid and xenobiotic receptor (SXR), physical association to 17-Hydroxysteroid dehydrogenase type 4 (17-HSD4), covalent modification of Bcl-2 antagonist killer 1 (Bak), and the modulation of protein kinase A (PKA) activity. In addition, several epidemiological studies have revealed that vitamin K status is associated with some aging-related diseases including osteoporosis, osteoarthritis, and sarcopenia. Clinical studies on single nucleotide polymorphisms of GGCX suggested an association between higher GGCX activity and bone protective effect, while recent findings using conditional knockout mice implied that a contribution in protective effect for bone loss by GGCX in osteoblastic lineage was unclear. GGCX in other cell lineages or in other tissues might play a protective role for osteoporosis. Meanwhile, animal experiments by our groups among others revealed that SXR, a putative receptor for vitamin K, could be important in the bone metabolism. In terms of the cartilage

protective effect of vitamin K, both GGCX- and SXR-dependent mechanisms have been suggested. In clinical studies on osteoarthritis, the -carboxylation of matrix Gla protein (MGP) and gla-rich protein (GRP) may have a protective role for the disease. It is also suggested that SXR signaling has protective role for cartilage by inducing family with sequence similarity 20a (Fam20a) expression in chondrocytes. In the case of sarcopenia, a high vitamin K status in plasma was associated with muscle strength, large muscle mass, and high physical performance in some observational studies. However, the basic studies explaining the effects of vitamin K on muscular tissue are limited. Further research on vitamin K will clarify new biological mechanisms which contribute to human longevity and health through the prevention and treatment of aging-related musculoskeletal disorders.
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DE Peripheral arterial disease; Ankle Brachial Index; Amputation
ID ankle-brachial index; cardiovascular-disease; arm index; mortality; risk; prevalence; epidemiology; predictor
AB Introduction: Peripheral vascular disease is defined as narrowing of blood vessels that restricts blood flow. Atherosclerosis is the most common etiology followed by vasculitis, dysplastic syndromes, degenerative diseases, thrombosis, and thromboembolism. The mortality rate at diagnosis is 4%-6%. Atherosclerotic peripheral vascular disease and leg amputation from such condition increase the mortality rate to 30%, and the 5-year survival rate is less than 30%. Thus, disease severity and extent of peripheral vascular disease must be evaluated and presented. Materials and Method: Between January 2005 and March 2018,98 patients underwent surgery for acute arterial occlusion owing to chronic peripheral arterial disease were evaluated according to the Fontaine Classification, demographic characteristics, concomitant disease, physical examination findings, type of surgery and amputation and mortality rates, and its causes were analyzed. Results: None of the patients (n=98) presented with Fontaine stage I disease. Because peripheral arterial disease is usually observed in the elderly population, elderly patients with several health problems at advanced age are more likely to undergo extremity amputation. It can be reduced by including the ankle brachial index examination in any outpatient clinic. Other stages of the disease were also evaluated in detail. Conclusion: ABI examination should be included in the systemic examination for patients aged>70 years. Currently, lumbar hernia, osteoporosis or osteoarthritis are also observed in such patients, and the clinical signs of peripheral arterial disease are masked. Due to these diseases, the diagnosis of peripheral arterial disease is delayed.
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TC 1
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PU GUNES KITABEVI LTD STI
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PT J
AU Sun, XH
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AF Sun, Xiuhong
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TI Effect of Mir-663 on the Differentiation of Bone Marrow Mesenchymal Stem Cells in Inflammatory Environment Through Regulating Oxidative Stress and Transforming Growth Factor β1
SO JOURNAL OF BIOMATERIALS AND TISSUE ENGINEERING
LA English
DT Article
DE Mir-663; Osteoarthritis; TGF-beta 1; Oxidative Stress; Inflammatory Factor
ID osteogenic differentiation; replacement
AB BMSCs are beneficial for the treatment of Osteoarthritis (OA). Mir-663 involves in various diseases. However, the role of Mir-663 in the differentiation of BMSCs in an inflammatory environment remains unclear. Rat BMSCs were isolated and divided into control group, and inflammation group which was treated with 1 mu g/ml lipopolysaccharide (LPS), Mir-663 group and Mir-663 siRNA groups which was respectively transfected with Mir-663 plasmid and Mir-663 siRNA into LPS-treated BMSCs followed by analysis of the survival rate of BMSC by MTT, Caspase 3 activity, ALP activity, expression of osteogenic genes Runx2 and OP by Real time PCR, ROS content and SOD activity, TGF-beta 1 level by Real time PCR and ELISA, TNF-alpha and IL-1 beta, secretion by ELISA. LPS treatment significantly increased Mir-663 expression, inhibited cell proliferation, increased Caspase 3 activity, and inhibited ALP activity. Meanwhile it also significantly decreased Runx2 and OP expression, increased ROS content, decreased SOD activity and TGF-beta 1 expression as well

as elevated TNF-alpha and IL-1 beta secretion compared to control (P < 0005); Mir-663 plasmid transfection can further promote the above changes (P < 0005); whereas, Mir-663 siRNA could reverse the above changes (P < 0005). Mir-663 expression was increased in BMSCs in inflammatory environment. Down-regulation of Mir-663 expression can regulate oxidative stress, up-regulate TGF-,1 level, inhibit the secretion of TNF-alpha and IL-1 beta, and promote the proliferation and osteogenic differentiation of BMSCs in inflammatory environment.
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JI J. Biomater. Tissue Eng.
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TI Recommendations for the conduct of economic evaluations in osteoporosis: outcomes of an experts' consensus meeting organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the US branch of the International Osteoporosis Foundation
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Cost-effectiveness; Economic evaluation; Osteoporosis; Recommendations; Reference case
ID cost-effectiveness analyses; fracture risk reduction; quality-of-life; postmenopausal women; excess mortality; hip fracture; vertebral fractures; older women; health; impact

AB Economic evaluations are increasingly used to assess the value of health interventions, but variable quality and heterogeneity limit the use of these evaluations by decision-makers. These recommendations provide guidance for the design, conduct, and reporting of economic evaluations in osteoporosis to improve their transparency, comparability, and methodologic standards.IntroductionThis paper aims to provide recommendations for the conduct of economic evaluations in osteoporosis in order to improve their transparency, comparability, and methodologic standards.MethodsA working group was convened by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis to make recommendations for the design, conduct, and reporting of economic evaluations in osteoporosis, to define an osteoporosis-specific reference case to serve a minimum standard for all economic analyses in osteoporosis, to discuss methodologic challenges and initiate a call for research. A literature review, a face-to-face meeting in New York City (including 11 experts), and a review/approval by a larger group of experts worldwide (including 23 experts in total) were conducted.ResultsRecommendations on the type of economic evaluation, methods for economic evaluation, modeling aspects, base-case analysis and population, excess mortality, fracture costs and disutility, treatment characteristics, and model validation were provided. Recommendations for reporting economic evaluations in osteoporosis were also made and an osteoporosis-specific checklist was designed that includes items to report when performing an economic evaluation in osteoporosis. Further, 12 minimum criteria for economic evaluations in osteoporosis were identified and 12 methodologic challenges and need for further research were discussed.ConclusionWhile the working group acknowledges challenges and the need for further research, these recommendations are intended to supplement general and national guidelines for economic evaluations, improve transparency, quality, and comparability of economic evaluations in osteoporosis, and maintain methodologic standards to increase their use by decision-makers.
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NR 65
TC 67
Z9 77
U1 0
U2 11
PU SPRINGER LONDON LTD
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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TI Osteoporosis Is Common and Undertreated Prior to Total Joint Arthroplasty
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE osteoporosis; arthroplasty; total hip arthroplasty; total knee arthroplasty; bone health
ID total hip-arthroplasty; periprosthetic femoral fractures; bone-mineral density; knee arthroplasty; women; osteoarthritis; epidemiology; component
AB Background: Osteoporosis is common in total joint arthroplasty (TJA) patients and likely contributes to the increasing incidence of periprosthetic fracture. Despite this, the prevalence of osteoporosis in patients undergoing elective TJA is inadequately studied. We hypothesize that preoperative osteoporosis is underrecognized and undertreated in the TJA population. The purpose of this study is to report preoperative osteoporosis screening rates and prevalence prior to TJA and rates of pharmacologic osteoporosis treatment in the TJA population. Methods: This is a retrospective case series of 200 consecutive adults (106F, 94M) aged 48-92 years who underwent elective TJA (100 total hip, 100 total knee) at a single tertiary-care center. Charts were retrospectively reviewed to determine preoperative osteoporosis risk factors, prior dual-energy X-ray absorptiometry (DXA) testing, and prior osteoporosis pharmacotherapy. Fracture risk was estimated using the Fracture Risk Assessment Tool and the National Osteoporosis Foundation criteria for screening and treatment were applied to all patients. Results: One hundred nineteen of 200 patients (59.5%) met criteria for DXA testing. Of these 119, 21 (17.6%) had DXA testing in the 2 years prior to surgery, and 33% had osteoporosis by T-score. Forty-nine patients (24.5%) met National Osteoporosis Foundation criteria for pharmacologic osteoporosis treatment, and 11 of these 49 received a prescription for pharmacotherapy within 6 months before or after surgery. Conclusion: One quarter of TJA patients meet criteria to receive osteoporosis medications, but only 5% receive therapy preoperatively or postoperatively. This lack of preoperative osteoporosis screening and treatment may contribute to periprosthetic fracture risk. (c) 2019 Elsevier Inc. All rights reserved.
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TI Timing metabolism in cartilage and bone: links between circadian clocks and tissue homeostasis
SO JOURNAL OF ENDOCRINOLOGY
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DT Review
DE circadian clock; articular cartilage; bone; metabolism
ID rev-erb-alpha; gene-expression; diurnal-variation; rheumatoid-arthritis; ppar-gamma; osteoarthritic chondrocytes; prednisone chronotherapy; suprachiasmatic nucleus; transcription factor; knee osteoarthritis
AB The circadian system in mammals is responsible for the temporal coordination

of multiple physiological and behavioural processes that are necessary for homeostasis. In the skeleton, it has long been known that metabolic functions of chondrocytes, osteoblasts and osteoclasts exhibit intrinsic circadian rhythms. In addition, results from animal models reveal a close connection between the disruption of circadian rhythms and skeletal disorders such as rheumatoid arthritis, osteoarthritis and osteoporosis. In this review, we summarise the latest insights into the genetic and biochemical mechanisms linking cartilage and bone physiology to the circadian clock system. We also discuss how this knowledge can be utilised to improve human health.
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NR 192
TC 17
Z9 20
U1 2
U2 33
PU BIOSCIENTIFICA LTD
PI BRISTOL
PA STARLING HOUSE, 1600 BRISTOL PARKWAY N, BRISTOL, ENGLAND
SN 0022-0795
EI 1479-6805
J9 J ENDOCRINOL
JI J. Endocrinol.
PD DEC 15
PY 2019
VL 243
IS 3
BP R29
EP R46
DI 10.1530/JOE-19-0256
PG 18
WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA JS5UL
UT WOS:000500371300001
PM 31470415
DA 2026-02-10
ER

PT J
AU Liang, KY
Ou, XJ
Huang, XK
Lan, QF
AF Liang, Kaiyong
Ou, Xiaojuan
Huang, Xukai
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TI Adrenocortical hypofunction with simultaneous primary aldosteronism A case report
SO MEDICINE
LA English
DT Article
DE adenoma; adrenal; aldosteronism; cortical hypofunction; diabetes

ID adrenal-tumors; immunoassay; diagnosis; cortisol
AB Rationale: Cases of adrenocortical hyperfunction combined with primary aldosteronism have been reported in the literature, and the underlying mechanism involves the secretion of aldosterone and glucocorticoids by a tumor or an adenoma. However, adrenocortical hypofunction and coexisting primary aldosteronism have not been reported until now. Herein, we report a case of adrenocortical hypofunction combined with primary aldosteronism. Patient concerns: A 66-year-old Chinese woman with rheumatoid arthritis who had been diagnosed with secondary adrenal insufficiency and was taking prednisone acetate tablets for replacement treatment presented to our department. She also had type 2 diabetes mellitus, osteoporosis, bilateral knee osteoarthritis, and lumbar vertebral compression fracture. She had previously developed tuberculosis, which had been cured. Diagnosis: The cortisol and adrenocorticotropic hormone rhythm indicated cortisol dysfunction in the patient. A 64-slice computed tomography and magnetic resonance imaging both showed bilateral adrenal hyperplasia. A postural stimulation test indicated a high level of aldosteronism and a high aldosterone-to-renin ratio (ARR, supine position: aldosterone 1788.73pg/mL, ARR 146.62; upright position: aldosterone 2916.21pg/mL, ARR 92.29). The captopril test showed the aldosterone level decreased by 364.70pg/mL 1hour after administration of captopril (from 2153.28 to 1788.58pg/mL). The decline in aldosterone level was approximately 16.90% (i.e., <30%), and the ARR was still >40. Based on the above-mentioned findings, we diagnosed the patient with adrenocortical hypofunction with primary aldosteronism. Interventions: We administered spironolactone 20 mg twice daily and continued the glucocorticoid replacement therapy. Outcomes: One week after diagnosis, the patient had an aldosterone level of 2201.16pg/mL, plasma renin activity of 3.88ng/mL/h, and an ARR of 56.7 (upright position). Her blood pressure was maintained within the normal range. Lessons: Although adrenocortical hypofunction with primary aldosteronism is rare, cases of primary aldosteronism complicated with hypercortisolism are occasionally encountered. Hence, whenever possible, we recommend testing both aldosterone and cortisol levels in all patients with adrenal dysfunction.
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NR 13
TC 0
Z9 1
U1 0
U2 4
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0025-7974
EI 1536-5964
J9 MEDICINE
JI Medicine (Baltimore)
PD MAR 15
PY 2019
VL 98
IS 13
BP
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DI 10.1097/MD.0000000000015033
PG 4
WC Medicine, General & Internal
SC General & Internal Medicine
GA HX3UX
UT WOS:000467319800053
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PT J
AU Lin, LW
Tsai, FH
Lan, WC
Cheng, YD
Lee, SC
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AF Lin, Li-Wei
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Lan, Wan-Cheng
Cheng, Yih-Dih
Lee, Sheng-Chi
Wu, Chi-Rei
TI Steroid-Enriched Fraction of Achyranthes bidentata Protects Amyloid β Peptide 1-40-Induced Cognitive Dysfunction and Neuroinflammation in Rats
SO MOLECULAR NEUROBIOLOGY
LA English
DT Article
DE Achyranthes bidentata; Ecdysterone; A beta 1-40; Oxidative stress; Neuroinflammation; ERK; NF-kappa B pathway; Hippocampus
ID cascade hypothesis; memory impairment; nitric-oxide; in-vitro; cells; apoptosis; disease; chondrocytes; inflammation; involvement
AB The roots of Achyranthes bidentata Blume (AB) is commonly used in the treatment of osteoporosis and dementia in traditional Chinese medicine. Pharmacological reports evidenced that AB possessed anti-osteoarthritis effects. However, there is little literature about the anti-dementia activities of AB. The present study was designed to prepare steroid-enriched fraction of AB (ABS) and investigate whether ABS can protect from cognitive dysfunction and neuroinflammation against A beta 1-40-induced Alzheimer's disease (AD) model in rats. ABS only contained 135.11 +/- 4.28mg of ecdysterone per gram. ABS (50mg/kg) reversed the dysfunction of exploratory activity and memory function on plus-maze and Morris water maze caused by A beta 1-40 in rats. ABS (50mg/kg) also decreased amyloid deposition, neurofibrillary tangle, neural damage, activated astrocyte, and microglial caused by A beta 1-40. Furthermore, ABS reversed the phenomenon of neural oxidative damage and neuroinflammation, including the higher levels of MDA and cytokines, and the lower activities of antioxidant enzymes and GSH levels caused by A beta 1-40 in rat cortex and hippocampus. Finally, ABS restored the activation of ERK pathway and decreased NF-kappa B phosphorylation and translocation altered by A beta 1-40. ABS alone (50mg/kg) promoted cognitive function, activated brain antioxidant defense system, and decreased brain TNF-alpha levels in sham group. Therefore, ABS has the cognition-promoting and antidementia potential. Steroids especial ecdysterone are major active components of AB. The action mechanism is due to decreasing oxidative stress and neuroinflammation through modulating ERK pathway, NF-kappa B phosphorylation, and translocation in A beta 1-40-induced AD rat model.
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NR 43
TC 29
Z9 30
U1 0
U2 27
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 0893-7648
EI 1559-1182
J9 MOL NEUROBIOL
JI Mol. Neurobiol.
PD AUG 15
PY 2019
VL 56
IS 8
BP 5671

EP 5688
DI 10.1007/s12035-018-1436-7
PG 18
WC Neurosciences
SC Neurosciences & Neurology
GA IJ1QK
UT WOS:000475673100029
PM 30666561
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ER

PT J
AU Zhai, GJ
Pelletier, JP
Liu, M
Aitken, D
Randell, E
Rahman, P
Jones, G
Martel-Pelletier, J
AF Zhai, Guangju
Pelletier, Jean-Pierre
Liu, Ming
Aitken, Dawn
Randell, Edward
Rahman, Proton
Jones, Graeme
Martel-Pelletier, Johanne
TI Activation of The Phosphatidylcholine to Lysophosphatidylcholine Pathway Is Associated with Osteoarthritis Knee Cartilage Volume Loss Over Time
SO SCIENTIFIC REPORTS
LA English
DT Article
ID synovial-fluid; human plasma; progression; phospholipase-a2; quantification; osteoporosis; replacement; degradation; thickness; symptoms
AB To identify serum biomarker(s) for predicting knee cartilage volume loss overtime, we studied 139 knee osteoarthritis (OA) patients from a previous 24-month clinical trial cohort. Targeted metabolomic profiling was performed on serum collected at baseline. The pairwise metabolite ratios as proxies for enzymatic reaction were calculated and used in the analysis. Cartilage volume loss between baseline and 24 months was assessed quantitatively by magnetic resonance imaging (MRI). Data revealed an association between the serum ratio of lysophosphatidylcholine 18:2 (lysoPC 18:2) to phosphatidylcholine 44:3 (PC44:3) and the cartilage volume loss in the lateral compartment (beta = -0.21 +/- 0.04, p =

8.53*10(-7)) and with joint degradation markers, COMP (r = 0.32, p =0.0002) and MMP1 (r = 0.26, p = 0.002). The significance remained after adjustment for age, sex, BMI, diabetes, hypertension, dyslipidemia, and the treatment taken in the original study. As the ratio indicated the over activation of the conversion pathway of PC to lysoPC catalyzed by phospholipase A(2) (PLA(2)), we assessed and found that a specific PLA(2), PLA(2)G5, was significantly increased in human OA cartilage and synovial membrane (85% and 19% respectively, both p < 0.04) compared to controls, and its overexpression correlated with IL-6 (r = 0.63, p = 0.0008). Our data suggest that the serum lysoPC 18:2 to PC44:3 ratio is highly associated with a greater risk of cartilage volume loss of the knee and warrants further investigation in an independent cohort.
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NR 47
TC 38
Z9 45
U1 1
U2 10
PU NATURE PORTFOLIO
PI BERLIN
PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
SN 2045-2322
EI
J9 SCI REP-UK
JI Sci Rep
PD JUL 4
PY 2019
VL 9
IS
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EP
DI 10.1038/s41598-019-46185-w
PG 10
WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
GA IH1AE
UT WOS:000474222900005
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PT J
AU Honvo, G
Bruyère, O
Reginster, JY
AF Honvo, Germain
Bruyere, Olivier
Reginster, Jean-Yves
TI Update on the role of pharmaceutical-grade chondroitin sulfate in the symptomatic management of knee osteoarthritis
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH

LA English
DT Article
DE Osteoarthritis; Chondroitin; Pain; Function; Safety; Treatment
ID slow-acting drugs; double-blind; european-society; economic-aspects; placebo; recommendations; osteoporosis; hip; tolerability; progression
AB Osteoarthritis (OA) is the most prevalent musculoskeletal disease and a major cause of negative relevant outcomes, associated with an ever-increasing societal burden. Pharmaceutical-grade chondroitin sulfate (CS) was repeatedly reported to reduce pain and improve function in patients with knee OA. This treatment was also shown to be cost-effective, compared to placebo, up to 24months. However, controversies still persist regarding the usefulness of CS for patients with knee OA, mainly due to inconsistent reports from various clinical trials. In this literature review, we aimed to summarize the main most recent findings on the efficacy and safety of CS in OA. Based on the results of studies presenting a low risk of bias, the most recent meta-analysis shows that only the pharmaceutical-grade CS may be considered as an appropriate background treatment for the management of knee OA. Evidence from another recent meta-analysis, using data from full safety reports, confirms the good safety profile of CS in OA. This new evidence on efficacy and safety suggests that recommendations for the use of CS in patients with knee OA cannot be extrapolated to other low-grade preparations as generics, nutraceutical-grade or over-the-counter preparations.
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NR 30
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PA 233 SPRING ST, NEW YORK, NY 10013 USA
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AU Qadir, A
Gao, YG
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Tian, Y
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AF Qadir, Abdul
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Miao, Zhiping
Qian, Airong
TI Non-Viral Delivery System and Targeted Bone Disease Therapy
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE non-viral delivery system; cationic lipids; bone targeting moieties;

bisphosphonates; bone therapeutic agents
ID mediated gene delivery; drug-delivery; calcium-phosphate; cathepsin-k; in-vitro; osteoclast differentiation; plasmid dna; nanoparticles; resorption; bisphosphonate
AB Skeletal systems provide support, movement, and protection to the human body. It can be affected by several life suffering bone disorders such as osteoporosis, osteoarthritis, and bone cancers. It is not an easy job to treat bone disorders because of avascular cartilage regions. Treatment with non-specific drug delivery must utilize high doses of systemic administration, which may result in toxicities in non-skeletal tissues and low therapeutic efficacy. Therefore, in order to overcome such limitations, developments in targeted delivery systems are urgently needed. Although the idea of a general targeted delivery system using bone targeting moieties like bisphosphonates, tetracycline, and calcium phosphates emerged a few decades ago, identification of carrier systems like viral and non-viral vectors is a recent approach. Viral vectors have high transfection efficiency but are limited by inducing immunogenicity and oncogenicity. Although non-viral vectors possess low transfection efficiency they are comparatively safe. A number of non-viral vectors including cationic lipids, cationic polymers, and cationic peptides have been developed and used for targeted delivery of DNA, RNA, and drugs to bone tissues or cells with successful consequences. Here we mainly discuss such various non-viral delivery systems with respect to their mechanisms and applications in the specific targeting of bone tissues or cells. Moreover, we discuss possible therapeutic agents that can be delivered against various bone related disorders.
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NR 124
TC 23
Z9 25
U1 2
U2 33
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PI BASEL
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
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AU Bartels, S
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TI Low bone density and high morbidity in patients between 55 and 70 years with displaced femoral neck fractures: a case-control study of 50 patients vs 150 normal controls
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Femoral neck fracture; Bone mineral density; Comorbidity; Osteoporosis
ID hip fracture; internal-fixation; risk-factors; young; age; hemiarthroplasty; arthroplasty; epidemiology; osteoporosis; metaanalysis
AB Background A displaced femoral neck fracture (FNF) in patients 55-70 years is a serious injury with a high risk of treatment failure and the optimal surgical treatment remains unclear. We aimed to describe characteristics of fracture patients compared to a sample from the normal population. Methods Fifty patients aged 55-70 years with a displaced FNF were gender- and age- matched with a control group of 150 persons without a hip fracture using computergenerated randomization and the Norwegian National Population Register. To reduce the risk

of spurious selection bias, the sample size of the control group was trebled compared to the fracture group. Dual-energy x-ray absorptiometry (DXA) was performed. Demographics and hip function (Harris Hip Score, Oxford Hip Score, and Hip Dysfunction and Osteoarthritis Outcome Score) were collected. Results There were more than 75% women in both groups. The mean age was 64.5 years in the fracture group and 65.1 in the control group. Results for DXA measured for lumbar spine, total hip and the femoral neck showed that patients with displaced FNF were significantly more osteoporotic. Fracture patients had significantly lower body mass index, higher Charlson comorbidity index (CCI), and higher ASA (American Society of Anesthesiologists) score than the control group. No clinically relevant differences in hip function were found. There were 48% smokers in the fracture group compared to 10% in the control group. The odds ratio for obtaining a displaced FNF was high if the patients suffered from osteoporosis, smoked or had several comorbidities. Conclusions This study showed that patients aged 55-70 years with a displaced femoral neck fracture had lower bone density and higher comorbidity compared with a gender- and age-matched population without femoral neck fractures. This suggests that this patient group is epidemiologically similar to older patients with femoral neck fractures.
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TI Diagnosis and Management of Paget's Disease of Bone in Adults: A Clinical Guideline
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DT Article
DE PAGET'S DISEASE OF BONE; ANTIRESORPTIVES; RADIONUCLIDE BONE SCANS; ALP; BISPHOSPHONATES
ID giant-cell tumor; distemper virus transcripts; total hip-arthroplasty; measles-virus; double-blind; disodium etidronate; bisphosphonate treatment; intravenous pamidronate; symptomatic management; familial aggregation
AB An evidence-based clinical guideline for the diagnosis and management of Paget's disease of bone (PDB) was developed using GRADE methodology, by a Guideline Development Group (GDG) led by the Paget's Association (UK). A systematic review of diagnostic tests and pharmacological and nonpharmacological treatment options was conducted that sought to address several key questions of clinical relevance. Twelve recommendations and five conditional recommendations were made, but there was insufficient evidence to address eight of the questions posed. The following recommendations were identified as the most important: 1) Radionuclide bone scans, in addition to targeted radiographs, are recommended as a means of fully and accurately defining the extent of metabolically active disease in patients with PDB. 2) Serum total alkaline phosphatase (ALP) is recommended as a first-line biochemical screening test in combination with liver function tests in

screening for the presence of metabolically active PDB. 3) Bisphosphonates are recommended for the treatment of bone pain associated with PDB. Zoledronic acid is recommended as the bisphosphonate most likely to give a favorable pain response. 4) Treatment aimed at improving symptoms is recommended over a treat-to-target strategy aimed at normalizing total ALP in PDB. 5) Total hip or knee replacements are recommended for patients with PDB who develop osteoarthritis in whom medical treatment is inadequate. There is insufficient information to recommend one type of surgical approach over another. The guideline was endorsed by the European Calcified Tissues Society, the International Osteoporosis Foundation, the American Society of Bone and Mineral Research, the Bone Research Society (UK), and the British Geriatric Society. The GDG noted that there had been a lack of research on patient-focused clinical outcomes in PDB and identified several areas where further research was needed. (c) 2019 The Authors. Journal of Bone and Mineral Research Published by Wiley Periodicals Inc.
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TI Integrins in Osteocyte Biology and Mechanotransduction
SO CURRENT OSTEOPOROSIS REPORTS
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DT Review
DE Osteocyte; Integrin; Mechanotransduction; Osteoporosis; Osteoarthritis; Bone metastasis
ID focal adhesion kinase; mechanical stimulation; signaling pathways; bone-cells; molecular-mechanisms; strain amplification; gene-expression; down-regulation; primary cilium; fluid-flow
AB Purpose of ReviewOsteocytes are the main mechanosensitive cells in bone. Integrin-based adhesions have been shown to facilitate mechanotransduction, and therefore play an important role in load-induced bone formation. This review outlines the role of integrins in osteocyte function (cell adhesion, signalling, and mechanotransduction) and possible role in disease.Recent FindingsBoth beta(1) and beta(3) integrins subunits have been shown to be required for osteocyte mechanotransduction. Antagonism of these integrin subunits in osteocytes resulted in impaired responses to fluid shear stress. Various disease states (osteoporosis, osteoarthritis, bone metastases) have been shown to result in altered integrin expression and function.SummaryOsteocyte integrins are required for normal cell function, with dysregulation of integrins seen in disease. Understanding the mechanism of faulty integrins in disease may aid in the creation of novel therapeutic approaches.
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TI PLGA scaffold carrying icariin to inhibit the progression of osteoarthritis in rabbits
SO ROYAL SOCIETY OPEN SCIENCE
LA English
DT Article
DE electrospinning; icariin; osteoarthritis; cartilage degeneration; subchondral bone
ID subchondral bone; osteogenic differentiation; articular-cartilage; gene-expression; chondrocytes; cells; osteoporosis; osteopontin; degradation; collagen
AB Icariin, the main effective component extracted from epimedium, has been shown to stimulate osteogenic differentiation and bone formation and to increase synthesis of the cartilage extracellular matrix. However, there has been little study on the effects of icariin on osteoarthritis. In this study, we loaded icariin onto poly(lactic-co-glycolic acid) (PLGA) electrospinning. The aim of this study was to explore a composite scaffold and to inhibit the progression of osteoarthritis. Our main experimental results demonstrated that the PLGA/icariin composite spinning scaffold had higher hydrophilicity, and icariin was released slowly and steadily from the scaffold. According to the results of an MTT test, immunofluorescence staining, an alkaline phosphate activating assay and a real-time polymerase chain reaction (RT-PCR) assay, the PLGA/icariin composite scaffold had good biocompatibility. In models of osteoarthritis, the results of a RT-PCR assay indicated that the PLGA/icariin scaffold promoted the synthesis of the extracellular matrix. The results of X-ray microtomography and histological evaluation demonstrated that the PLGA/icariin scaffold maintained the functional morphology of articular cartilage and inhibited the resorption of subchondral bone trabeculae. These findings indicated that the PLGA and icariin composite scaffold has therapeutic potential for use in the treatment of osteoarthritis.
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AU Lehtovirta, S
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TI Defective WNT signaling may protect from articular cartilage deterioration - a quantitative MRI study on subjects with a heterozygous WNT1 mutation
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE WNT signaling; WNT1; Osteoporosis; Osteoarthritis; Radiology
ID t-2 relaxation-times; focal knee lesions; early osteoarthritis; adiabatic t-1-rho; regional-analysis; spatial-patterns; t2 measurements; bone; association; osteoporosis
AB Objective: WNT signaling is of key importance in chondrogenesis and defective WNT signaling may contribute to the pathogenesis of osteoarthritis and other cartilage diseases. Biochemical composition of articular cartilage in patients with aberrant WNT signaling has not been studied. Our objective was to assess the knee articular cartilage in WNT1 mutation-positive individuals using a 3.0T MRI unit to measure cartilage thickness, relaxation times, and texture features. Design: Cohort comprised mutation-positive (N = 13; age 17-76 years) and mutation-negative (N = 13; 16-77 years) subjects from two Finnish families with autosomal dominant WNT1 osteoporosis due to a heterozygous missense mutation c.652T>G (p.C218G) in WNT1. All subjects were imaged with a 3.0T MRI unit and assessed for cartilage thickness, T2 and T1 rho relaxation times, and T2 texture features contrast,

dissimilarity and homogeneity of T2 relaxation time maps in six regions of interest (ROIs) in the tibiofemoral cartilage. Results: All three texture features showed opposing trends with age between the groups in the medial tibiofemoral cartilage (P = 0.020-0.085 for the difference of the regression coefficients), the mutation-positive individuals showing signs of cartilage preservation. No significant differences were observed in the lateral tibiofemoral cartilage. Cartilage thickness and means of T2 relaxation time did not differ between groups. Means of T1r relaxation time were significantly different in one ROI but the regression analysis displayed no differences. Conclusions: Our results show less age-related cartilage deterioration in the WNT1 mutation-positive than the mutation-negative subjects. This suggests, that the WNT1 mutation may alter cartilage turnover and even have a potential cartilage-preserving effect. (C) 2019 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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U1 0
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AF Yildirim, Mustafa Aziz
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TI RELATIONSHIP BETWEEN OSTEOARTHRITIS AND OSTEOPOROSIS IN HOMOLOGOUS JOINTS
SO ACTA MEDICA MEDITERRANEA

LA English
DT Article
DE Bone mineral density; Coxarthrosis; Osteoporosis
ID bone-mineral density; postmenopausal women; inverse relationship; knee osteoarthritis; fracture; hip
AB Introduction: Osteoarthritis and osteoporosis are the two most common musculoskeletal diseases. We investigated whether there is an inverse relationship between osteoarthritis and osteoporosis for the right and left hips. Material and methods: Sixty-six postmenopausal women were included in this study. The subjects were divided into two groups, the osteoarthritis and control groups (n = 33 each), according to whether they had hip osteoarthritis. In the osteoarthritis group, subjects were blindly graded using the Kellgren- Lawrence system and divided into a right hip osteoarthritis group (n = 29) and a left hip osteoarthritis group (n = 32) according to the affected hip joint. The bone mineral density of both hips was measured using dual-energy X-ray ahvorptiometry. Physical activity was assessed using the International Physical Activity Questionnaire. Results: A correlation between the presence of osteoarthritis and bone loss at the femoral neck was observed for the right hip (R = -0,302, p = 0.017), whereas no significant correlation was observed for the left hip. Osteoarthritis in the right hip was associated with older age and higher right femoral neck bone mineral density (R2 = 0368). The odds ratio for the radiographic presence of right hip osteoarthritis was 55678.5 per unit difference in bone mineral density of the right femoral neck. Conclusion: Although the right and left hips are homologous joints, the present study revealed an inverse relationship between OA and OP only for the right hip, indicating that the relationship between osteoarthritis and osteoporosis should be assessed using a joint-by-joint approach
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AU Heikkinen, J
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TI Depressive disorders, anxiety disorders and subjective mental health in common musculoskeletal diseases: A review
SO MATURITAS
LA English
DT Review
DE Depressive disorder; Anxiety disorders; Mental health; Subjective well-being; Life satisfaction; Musculoskeletal diseases
ID bone-mineral density; reported life satisfaction; 15-year follow-up; quality-of-life; low-back; work disability; risk; metaanalysis; dissatisfaction; osteoarthritis
AB Globally, musculoskeletal diseases (MSDs) and mental disorders are the leading causes of disability, but their mutual relationships have been little studied. The objective of the current review is to summarize the evidence on the relationships between depressive and anxiety disorders, subjective mental health and common MSDs in adults aged 45 years and over. A review of studies published in English, identified using MEDLINE, was conducted. Search terms included spinal stenosis, intervertebral disc displacement, osteoarthritis, osteoporosis, depressive disorder, anxiety disorders, mental health, subjective well-being, subjective quality of life, life satisfaction and personal satisfaction. A total of 287 records were initially identified, and an additional 190 records were identified from their reference lists. Eight studies were considered eligible and were, thus, included in the current review. The

included studies reported that: 1) major depressive disorder is associated with chronic back pain; 2) anxiety disorders are associated with cervical or lumbar disc herniation; 3) mood and anxiety disorders are associated with lower bone mineral density in men; 4) life satisfaction and its improvement prevent bone loss in postmenopausal women; and 5) quality of life reduces progressively as the number of osteoporotic fractures increases. In conclusion, common MSDs are associated with mental disorders and subjective mental health in adults aged 45 years or more, but longitudinal research is needed.
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TI Identification of Novel Loci Associated With Hip Shape: A Meta-Analysis of Genomewide Association Studies
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE HIP SHAPE; OSTEOARTHRITIS; HIP FRACTURE RISK; DXA; GWAS
ID susceptibility loci; parathyroid-hormone; noncoding elements; indian hedgehog; factor sox9; differentiation; osteoarthritis; risk; abnormality; prediction
AB We aimed to report the first genomewide association study (GWAS) meta-analysis of dual-energy X-ray absorptiometry (DXA)-derived hip shape, which is thought to be related to the risk of both hip osteoarthritis and hip fracture. Ten hip shape modes (HSMs) were derived by statistical shape modeling using SHAPE software, from hip DXA scans in the Avon Longitudinal Study of Parents and Children (ALSPAC; adult females), TwinsUK (mixed sex), Framingham Osteoporosis Study (FOS; mixed), Osteoporotic Fractures in Men study (MrOS), and Study of Osteoporotic Fractures (SOF; females) (total N = 15,934). Associations were adjusted for age, sex, and ancestry. Five genomewide significant ($p < 5 \times 10(-9)$, adjusted for 10 independent outcomes) single-nucleotide polymorphisms (SNPs) were associated with HSM1, and three SNPs with HSM2. One SNP, in high linkage disequilibrium with rs2158915 associated with HSM1, was associated with HSM5 at genomewide significance. In a look-up of previous GWASs, three of the identified SNPs were associated with hip osteoarthritis, one with hip fracture, and five with height. Seven SNPs were within 200 kb of genes involved in endochondral bone formation, namely SOX9, PTHrP, RUNX1, NKX3-2, FGFR4, DICER1, and HHIP. The SNP adjacent to DICER1 also showed osteoblast cis-regulatory activity of GSC, in which mutations have previously been reported to cause hip dysplasia. For three of the lead SNPs, SNPs in high LD ($r(2) > 0.5$) were identified, which intersected with open chromatin sites as detected by ATAC-seq performed on embryonic mouse proximal femora. In conclusion, we identified eight SNPs independently associated with hip shape, most of which were associated with height and/or mapped close to endochondral bone formation genes, consistent with a contribution of processes involved in limb growth to hip shape and pathological sequelae. These findings raise the possibility that genetic studies of hip shape might help in understanding potential pathways involved in hip osteoarthritis and hip fracture. (c) 2018 The Authors. Journal of Bone and Mineral Research Published by Wiley Periodicals, Inc.
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TI Association between cam-type femoroacetabular impingement and osteitis pubis in non-athletic population on magnetic resonance imaging
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Femoroacetabular impingement; Osteitis pubis; Magnetic resonance imaging
ID femoral-head; alpha angle; groin pain; hip; osteoarthritis; management; motion; hernia
AB Background Osteitis pubis (OP) is a common source of groin and extra-articular hip pain and is associated with intra-articular hip pathology. In this study, we aimed to determine the prevalence of osteitis pubis on magnetic resonance imaging (MRI) in non-athletic patients with cam-type femoroacetabular impingement (FAI). Methods This retrospective cross-sectional study included 178 subjects: 90 patients with cam-type FAI diagnosed by MRI and 88 subjects used as a control group. Additionally, their MRI data were analyzed for the characteristics of osteitis pubis, with severity graded from minimal to severe on a four-point scale. Results A total of 98 patients and 88 controls were studied. Seventy-two males (80%) and 18 females (20%) were the patient group, whereas 71 males (80.68%) and 17 females (19.32%) were the control group. The mean alpha angle of the patients with FAI was 65.8 +/- 3.3 degrees in the right side and 66.2 +/- 3.2 degrees in the left side, whereas in the control group, it was 47 +/- 5.6 degrees in the right side and 47.8 +/- 5.2 degrees in the left side. Alpha angle measurements were significantly higher in the patient group than the control group ($p < 0.001$). A statistically significant increase in the prevalence of osteitis pubis was found in patients with

cam-type FAI (45.56%) compared to control subjects (5.68%) ($p < 0.001$). Conclusions This study demonstrated that the frequency of osteitis pubis was increased in non-athletic patients with FAI syndrome. Further studies are required to determine whether these findings reflect the clinical symptoms in patients with hip pain.
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AF Tong, Xiaoyang
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TI The Effect of Exercise on the Prevention of Osteoporosis and Bone Angiogenesis

SO BIOMED RESEARCH INTERNATIONAL
LA English
DT Review
ID pathway
AB Physical activity or appropriate exercise prevents the development of osteoporosis. However, the exact mechanism remains unclear although it is well accepted that exercise or mechanical loading regulates the hormones, cytokines, signaling pathways, and noncoding RNAs in bone. Accumulating evidence has shown that bone is a highly vascularized tissue, and dysregulation of vasculature is associated with many bone diseases such as osteoporosis or osteoarthritis. In addition, exercise or mechanical loading regulates bone vascularization in bone microenvironment via the modulation of angiogenic mediators, which play a crucial role in maintaining skeletal health. This review discusses the effects of exercise and its underlying mechanisms for osteoporosis prevention, as well as an angiogenic and osteogenic coupling in response to exercise.
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TI A Jack of All Trades: Impact of Glucocorticoids on Cellular Cross-Talk in Osteoimmunology
SO FRONTIERS IN IMMUNOLOGY
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DT Review
DE glucocorticoids; glucocorticoid receptor; osteoporosis; arthritis; inflammation; fracture healing; conditional knockout mice
ID induced leucine-zipper; toll-like receptor; 11-beta-hydroxysteroid dehydrogenase type-1; synovial lining macrophages; suppress bone-formation; necrosis-factor-alpha; osteophyte formation; endogenous glucocorticoids; skeletal-muscle; mast-cells
AB Glucocorticoids (GCs) are known to have a strong impact on the immune system, metabolism, and bone homeostasis. While these functions have been long investigated separately in immunology, metabolism, or bone biology, the understanding of how GCs regulate the cellular cross-talk between innate immune cells, mesenchymal cells, and other stromal cells has been garnering attention rather recently. Here we review the recent findings of GC action in osteoporosis, inflammatory bone diseases (rheumatoid and osteoarthritis), and bone regeneration during fracture healing. We focus on studies of pre-clinical animal models that enable dissecting the role of GC actions in innate immune cells, stromal cells, and bone cells using conditional and function-selective mutant mice of the GC receptor (GR), or mice with impaired GC signaling. Importantly, GCs do not only directly affect cellular functions, but also influence the cross-talk between mesenchymal and immune cells, contributing to both beneficial and adverse effects of GCs. Given the importance of endogenous GCs as stress hormones and the wide prescription of pharmaceutical GCs, an improved understanding of GC action is decisive for tackling inflammatory bone diseases, osteoporosis, and aging.
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Yuan, PW
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Wang, KZ
AF Wang, Weizhuo
Huang, Mengdi
Hui, Yigeng
Yuan, Puwei
Guo, Xiong
Wang, Kunzheng
TI Cryptotanshinone inhibits RANKL-induced osteoclastogenesis by regulating ERK and NF-κB signaling pathways
SO JOURNAL OF CELLULAR BIOCHEMISTRY
LA English
DT Article
DE Cryptotanshinone; extracellular signal-regulated kinase; NF-kappa B; osteoclast differentiation; osteoclastogenesis; osteoporosis
ID receptor activator; c-fos; osteoporosis; prevention; differentiation; protects
AB Osteoporosis (OS) is one of the most common healthy problems characterized by low bone mass. Osteoclast, the primary bone-resorbing cell, is responsible for destructive bone diseases including osteoporosis (OS). Cryptotanshinone (CTS), an active component extracted from the root of Salvia miltiorrhiza bunge, has been shown to prevent the destruction of cartilage and the thickening of subchondral bone in mice osteoarthritis models. However, its molecular mechanism in osteoclastogenesis needs to be determined. The aim of the current study was to explore the effect of CTS on osteoclastogenesis and further evaluate the underlying mechanism. Our results showed that CTS inhibited receptor activator of NF-kappa B ligand (RANKL)-induced the increase in tartrate-resistant acid phosphatase (TRAP) activity in bone marrow-derived macrophages (BMMs). In addition, the expressions of osteoclastogenesis-related marker proteins and nuclear factor of activated T-cells (NFAT) activation were suppressed by CTS treatment in BMMs. Furthermore, CTS attenuated RANKL-induced ERK phosphorylation and NF-kappa B

activation in BMMs. These findings indicated that CTS inhibited RANKL-induced osteoclastogenesis by inhibiting ERK phosphorylation and NF-kappa B activation in BMMs. Thus, CTS may function as an inhibitor of osteoclastogenesis and may be considered as an alternative medicine for the prevention and treatment of OS.
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PU WILEY
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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WC Biochemistry & Molecular Biology; Cell Biology
SC Biochemistry & Molecular Biology; Cell Biology
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TI Nirogacestat suppresses RANKL-Induced osteoclast formation in vitro and attenuates LPS-Induced bone resorption in vivo
SO EXPERIMENTAL CELL RESEARCH
LA English
DT Article
DE Nirogacestat; Osteoclasts; RANKL; Bone resorption; Notch2
ID nf-kappa-b; induced osteolysis; notch2; osteoporosis; differentiation; activation; expression; prevention; mutations; roles
AB Bone resorption, initiated by osteoclasts (OCs), plays an essential role in bone homeostasis. The abnormalities of bone resorption may induce a series of diseases, including osteoarthritis, osteoporosis and aseptic peri-implant loosening. Nirogacestat (PF-03084014, PF), a novel gamma-secretase inhibitor, has been used in phase II clinical trial for treatment of desmoid tumor. However, whether it has the therapeutic effect on abnormal bone resorption remains to be evaluated. In this study, we investigated the role of PF in the regulation of receptor activator of nuclear factor-kB ligand (RANKL)-induced osteoclastogenesis in vitro, and the lipopolysaccharide (LPS)-induced bone resorption in vivo. It was found that PF could suppress the formation of osteoclasts from bone marrow macrophages (BMMs) without causing cytotoxicity, inhibit bone resorption and downregulate the mRNA level of osteoclast-specific markers, including calcitonin receptor (CTR), tartrate resistant acid phosphatase (TRAP), cathepsin K (CTSK), dendritic cell-specific transmembrane protein (Dc-stamp), Atp6v0d2 (V-ATPase d2) and nuclear factor of activated T-cells cytoplasmic 1 (NFATc1). Furthermore, Notch2 signaling, as well as RANKL-induced AKT signaling was significantly inhibited in BMMs. Consistent with in vitro observation, we found that PF greatly ameliorated LPS-induced bone resorption. Taken together, our study demonstrated that PF has a great potential to be used in management of osteolytic diseases.
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PA 525 B STREET, STE 1900, SAN DIEGO, CA 92101-4495 USA
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WC Oncology; Cell Biology
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AF Kim, Bo Young
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Jung, Ju-Yang
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Kim, Sang Hyon
Kwon, Seong-Ryul
Suh, Chang-Hee
Kim, Sung-Soo
TI Clinical Impact of the Fracture Risk Assessment Tool on the Treatment Decision for Osteoporosis in Patients with Knee Osteoarthritis: A Multicenter Comparative Study of the Fracture Risk Assessment Tool and World Health Organization Criteria
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE osteoporosis; fracture; fracture risk assessment tool; knee osteoarthritis
ID bone-mineral density; prevalence; women; hip; population; intervention; association; thresholds; burden; female
AB Background: To compare the frequency of high-risk osteoporotic fracture in patients with knee OA (OA) using the fracture risk assessment tool (FRAX) and the bone mineral density (BMD). Methods: We retrospectively assessed 282 Korean patients with knee OA who visited five medical centers and 1165 healthy controls (HCs) aged >= 50 years without knee OA. After matching for age, sex, and body mass index, 478 subjects (239 patients with knee OA and 239 HCs) were included. Results: Based on the BMD, the frequency of osteoporosis was 40.2% in patients with knee OA and 36.4% in HCs. The predicted mean FRAX major osteoporotic

fracture probabilities calculated with or without femur neck BMD differed significantly between the knee OA and HCs (6.9 +/- 3.8% versus 6.1 +/- 2.8%, p = 0.000 and 8 +/- 3.6% versus 6.8 +/- 2.3%, p < 0.001, respectively). The mean FRAX hip fracture probabilities calculated with or without femur neck BMD differed significantly in the knee OA and HCs (2.1 +/- 2.4% versus 1.7 +/- 1.8%, p = 0.006 and 3 +/- 2.3% versus 2.4 +/- 1.6%, p < 0.001, respectively). Conclusion: Our study suggests that FRAX may have a clinical impact on treatment decisions to reduce osteoporotic facture in patients with knee OA.
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NR 30
TC 8
Z9 10
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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TI Magnetic resonance imaging T1 and T2 mapping provide complementary information on the bone mineral density regarding cancellous bone strength in the femoral head of postmenopausal women with osteoarthritis
SO CLINICAL BIOMECHANICS
LA English
DT Article
DE MRI T1 mapping; MRI T2 mapping; Cancellous bone; Bone strength; Bone marrow
ID marrow adipose-tissue; osteoporosis; mri; collagen; fractures; volume; spine; age
AB Background Since bone mass is not the only determinant of bone strength, there has been increasing interest in incorporating the bone quality into fracture

risk assessments. We aimed to examine whether the magnetic resonance imaging (MRI) T1 or T2 mapping value could provide information that is complementary to bone mineral density for more accurate prediction of cancellous bone strength. Methods: Four postmenopausal women with hip osteoarthritis underwent 3.0-T MRI to acquire the T1 and T2 values of the cancellous bone of the femoral head before total hip arthroplasty. After the surgery, the excised femoral head was portioned into multiple cubic cancellous bone specimens with side of 5 mm, and the specimens were then subjected to microcomputed tomography followed by biomechanical testing. Findings: The T1 value positively correlated with the yield stress (sigma(y)) and collapsed stress (sigma(c)). The T2 value did not correlate with the yield stress, but it correlated with the collapsed stress and strength reduction ratio (sigma(c),/sigma(y)), which reflects the progressive re-fracture risk. Partial correlation coefficient analyses, after adjusting for the bone mineral density, showed a statistically significant correlation between T1 and yield stress. The use of multiple coefficients of determination by least squares analysis emphasizes the superiority of combining the bone mineral density and the MRI mapping values in predicting the cancellous bone strength compared with the bone mineral density-based prediction alone. Interpretation: The MRI T1 and T2 values predict cancellous bone strength including the change in bone quality.
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TI Toxicity of cadmium in musculoskeletal diseases
SO ENVIRONMENTAL TOXICOLOGY AND PHARMACOLOGY
LA English
DT Review
DE Cadmium; Osteoarthritis; Osteoporosis; Rheumatoid arthritis; Oxidative stress
ID scalp hair samples; environmental exposure; bone-resorption; population; level; osteomalacia; association; tissue; risk; zinc
AB Epidemiological studies have reported that exposure to toxic metals like cadmium (Cd) may promote the development of musculoskeletal diseases, such as osteoporosis, rheumatoid arthritis (RA), and osteoarthritis (OA), among others. The objective of this review is to summarize the molecular mechanisms of inflammation and oxidative stress activated by Cd at the bone level, particularly in osteoporosis, RA, and OA. Cadmium can increase bone resorption, affect the activity of osteoclasts and calcium (Ca) absorption, and impair kidney function, which favors the development of osteoporosis. In the case of RA, Cd interferes with the activity of antioxidant proteins, like superoxide dismutase (SOD) and catalase (CAT). It also promotes an inflammatory state, inducing the process of citrullination, which affects the proteins of immune response. On the other hand, accumulation of Cd in the tissues and blood of smokers has been related to the development of some musculoskeletal diseases. Therefore, knowing the negative impact of Cd toxicity at the articular level can help understand the damage mechanisms it produces, leading to the development of such diseases.
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TI Comparative Analyses of Pharmaceuticals or Food Supplements Containing Chondroitin Sulfate: Are Their Bioactivities Equivalent?
SO ADVANCES IN THERAPY
LA English
DT Article
DE Chondroitin sulfate; Food supplements; Glucosamine; HPAE-PAD; Human primary chondrocytes; Human primary synoviocytes; Keratan sulfate; NF-kappa B mediated inflammation pathway; OA in vitro model; Rheumatology
ID residual keratan sulfate; task-force; knee osteoarthritis; standing-committee; european-society; economic-aspects; in-vitro; management; recommendations; osteoporosis
AB Introduction Oral supplementation of chondroitin sulfate (CS) and glucosamine (GlcN), symptomatic slow-acting molecules, is recommended by European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis and

Musculoskeletal Diseases (ESCEO) and other European Union (EU) guidelines for the restoration of the articular cartilage surface in patients affected by osteoarthritis (OA). They are commercialized as pharmaceutical grade products and as food supplements in combination with plant extracts hyaluronic acid, methylsulfonylmethane, and other components. Food supplements do not need to undergo the strict regulatory controls of pharmaceutical grade products; thus, composition and contaminants that could be present may not be evidenced before commercialization and these uncertainties may give rise to concerns about the bioactivity of these formulations. Methods In this paper 10 different food supplements (FS) from diverse European countries were analyzed in comparison with two pharmaceutical grade products (Ph) using updated analytical approaches and biochemical cell-based assays. The purity, the titer, and the origin of CS in Ph and FS samples were initially assessed in order to successively compare the biological function. Both food supplements and pharmaceutical formulations were tested in vitro, using the same final CS concentration, on primary chondrocytes and synoviocytes in terms of (i) cell viability, (ii) activation of the NF-kappa B-mediated inflammation pathway, (iii) cartilage oligomeric matrix protein (COMP-2), IL-6, and IL-8 production. Results All the FS presented a certain insoluble fraction; the CS and the GlcN contents were lower than the declared ones in 9/10 and 8/10 samples, respectively. All FS contained keratan sulfate (KS) at up to 50% of the total glycosaminoglycan amount declared on the label. Primary cells treated with the samples diluted to present the same CS concentration in the medium showed cytotoxicity in 7/10 FS while Ph preserved viability and reduced NF-kappa B, COMP-2, and secreted inflammatory cytokines. Conclusion Among all samples tested, the pharmaceutical grade products demonstrated effective modulation of biomarkers counteracting the inflammation status and improving viability and the physiological condition of OA human primary chondrocyte and synoviocyte cells. In contrast to that, most FS were cytotoxic at the tested concentrations, and only 3/10 of them showed similarities to Ph sample behavior in vitro. Funding This work was partially supported by PON01_1226 NUTRAFAST, MIUR Ministero dell'Universita e della Ricerca Scientifica. Bioteknet financed two short-term grants for graduate technicians. The journal's Rapid Service and Open Access fees were funded by IBSA CH.
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TI POSS Hybrid Robust Biomass IPN Hydrogels with Temperature Responsiveness
SO POLYMERS
LA English
DT Article
DE octa-ammonium POSS; sodium alginate; hydrogels; temperature responsiveness
ID double-network hydrogels; biocompatibility evaluation; alginate; delivery; release; design
AB In order to improve the performance of traditional sodium alginate (SA) hydrogels cross-linked by Ca2+ ions to meet greater application demand, a strategy was designed to structure novel SA-based gels (named OP-PN gels) to achieve both stimulus responsiveness and improved mechanical strength. In this strategy, the SA chains are co-cross-linked by CaCl2 and cationic octa-ammonium polyhedral oligomeric silsesquioxane (Oa-POSS) particles as the first network, and an organically cross-linked poly(N-isopropyl acrylamide) (PNIPA) network is introduced into the gels as the second network. Several main results are obtained from the synthesis and characterization of the gels. For OP-PN gels, their properties depend on the content of both uniformly dispersed Oa-POSS and PNIPA network directly. The increased Oa-POSS and PNIPA network content significantly improves both the strength and resilience of gels. Relatively, the increased Oa-POSS is greatly beneficial to the modulus of gels, and the increased PNIPA network is more favorable to advancing the tensile deformation of gels. The gels with hydrophilic PNIPA network exhibit better swelling ability and remarkable temperature responsiveness, and their volume phase transition temperature can be adjusted by altering the content of Oa-POSS. The deswelling rate of gels increases gradually with the increase of POSS content due to the hydrophobic Si-O skeleton of POSS. Moreover, the enhanced drug loading and sustained release ability of the target drug bovine serum albumin displays great potential for this hybrid gel in the biomedical field.
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TI Compressive behaviour of uniaxially aligned individual mineralised collagen fibres at the micro- and nanoscale
SO ACTA BIOMATERIALIA
LA English
DT Article
DE Mineralised collagen fibre; In situ micromechanical testing; Nanoscale deformation mechanisms; SAXS/XRD; Failure analysis; Compressive strength
ID turkey leg tendon; x-ray-diffraction; mechanical-property; cortical bone; elastic property; hierarchical structure; in-situ; micropillar compression; deformation mechanisms; load-transfer
AB The increasing incidence of osteoporotic bone fractures makes fracture risk prediction an important clinical challenge. Computational models can be utilised to facilitate such analyses. However, they critically depend on bone's underlying hierarchical material description. To understand bone's irreversible behaviour at the micro- and nanoscale, we developed an in situ testing protocol that allows us to directly relate the experimental data to the mechanical behaviour of individual mineralised collagen fibres and its main constitutive phases, the mineralised collagen fibrils and the mineral nanocrystals, by combining micropillar compression of single fibres with small angle X-ray scattering (SAXS) and X-ray diffraction (XRD).

Failure modes were assessed by SEM. Strain ratios in the elastic region at fibre, fibril and mineral levels were found to be approximately 22:5:2 with strain ratios at the point of compressive strength of 0.23 +/- 0.11 for fibril-to-fibre and 0.07 +/- 0.01 for mineral-to-fibre levels. Mineral-to-fibre levels showed highest strain ratios around the apparent yield point, fibril-to-fibre around apparent strength. The mineralised collagen fibrils showed a delayed mechanical response, contrary to the mineral phase, which points towards preceding deformations of mineral nanocrystals in the extrafibrillar matrix. No damage was measured at the level of the mineralised collagen fibre which indicates an incomplete separation of the mineral and collagen, and an extrafibrillar interface failure. The formation of kink bands and the gradual recruitment of fibrils upon compressive loading presumably led to localised strains. Our results from a well-controlled fibrillar architecture provide valuable input for micromechanical models and computational non-linear bone strength analyses that may provide further insights for personalised diagnosis and treatment as well as bio-inspired implants for patients with bone diseases. Statement of significance Musculoskeletal diseases such as osteoporosis, osteoarthritis or bone cancer significantly challenge health care systems and make fracture risk prediction and treatment optimisation important clinical goals. Computational methods such as finite element models have the potential to optimise analyses but highly depend on underlying material descriptions. We developed an in situ testing set-up to directly relate experimental data to the mechanical behaviour of bone's fundamental building block, the individual mineralised collagen fibre and its main constituents. Low multilevel strain ratios suggest high deformations in the extrafibrillar matrix and energy dissipation at the interfaces, the absence of damage indicates both an incomplete separation between mineral and collagen and an extrafibrillar interface failure. The formation of kink bands in the fibril-reinforced composite presumably led to localised strains. The deformation behaviour of a well-controlled fibrillar architecture provides valuable input for nonlinear bone strength analyses. (C) 2019 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.
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TI Efficacy of Chondroitin Sulfate in Patients with Knee Osteoarthritis: A Comprehensive Meta-Analysis Exploring Inconsistencies in Randomized, Placebo-Controlled Trials
SO ADVANCES IN THERAPY
LA English
DT Review
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AB IntroductionThere are some controversies about treatment modalities in

osteoarthritis (OA), including chondroitin sulfate (CS). The objective of this study was to determine whether CS is effective at alleviating pain and improving function in patients with knee OA and to identify the factors that explain inconsistencies in clinical trial results.MethodsWe conducted a systematic review of randomized, placebo-controlled trials, searching the databases Medline, Cochrane central register for controlled trials and Scopus. Random effects meta-analysis was then performed, using tau(2) and I-2 statistics to assess heterogeneity. The pain and Lequesne index (LI) scores were expressed as standardized mean differences (SMDs), with a 95% confidence interval (CI). Heterogeneity was explored by stratifying the analyses according to pre-specified study-level characteristics and assessing the sources of funnel plot asymmetry.ResultsThe inclusion criteria yielded 18 trials. Overall, CS significantly but inconsistently reduced pain (SMD: - 0.63; 95% CI: - 0.91, - 0.35; I-2=94%) and improved function (SMD: - 0.82; 95% CI: - 1.31, - 0.33; I-2=95%). When limiting the analysis to studies with a low risk of bias, the pharmaceutical grade CS of IBSA origin showed a greater reduction in pain (SMD: - 0.25; 95% CI: - 0.34, - 0.16; I-2=75%) and function (SMD: - 0.33; 95% CI: - 0.47, - 0.20; I-2=53%, p=0.07) compared with the other preparations (SMDPain: - 0.08; 95% CI: - 0.19, + 0.02; I-2=20%; SMDFunction: - 0.18; 95% CI: - 0.36, +0.01; I-2=0%). Assessing funnel plot asymmetry in the studies with a low risk of bias, we found strong correlations between the treatment effects and study size (pain: r(S)=0.93; LI: r(S)=0.86; p<0.05). Ultimately, there was no residual heterogeneity in the CS effects when the smallest studies were removed from the analyses.ConclusionThis new meta-analysis suggests that CS provides a moderate benefit for pain and has a large effect on function in knee OA, however with large inconsistency. The risks of bias, brand and study size were the factors explaining heterogeneity among the clinical trial results.
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TI European chondroitin sulfate and glucosamine food supplements: A systematic quality and quantity assessment compared to pharmaceuticals
SO CARBOHYDRATE POLYMERS
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DT Article
DE Chondroitin sulfate; Food supplement; Glucosamine; Keratan sulfate; HPAE-PAD; NF-kB mediated inflammation pathway
ID keratan sulfate; economic-aspects; task-force; osteoarthritis; formulations; osteoporosis; hyaluronan; management; society; knee
AB Chondroitin sulfate and glucosamine, commercialized as anti-osteoarthritis food supplements, do not undergo the strict quality controls of pharmaceuticals. In this paper a systematic multi-analytical approach was designed to analyse 25 food supplements from 8 European countries compared to 2 pharmaceuticals by using high performance anion-exchange chromatography with pulsed amperometric detection, size exclusion chromatography with triple detector array, capillary electrophoresis, mono and bi-dimensional NMR. Furthermore the biological activity was assessed on in vitro human synoviocyte and chondrocyte primary cell models. Most of the samples (over 19 out of 25) showed lower condroitin sulfate and glucosamine contents than the declared ones (up to -60.3%) while all of them showed a KS contamination (up to 47.1%). Mixed animal origin chondroitin sulfate and multiple molecular weight species were determined in more than 32% of the samples. Only 1 on 5 biologically screened samples had an effective action in vitro almost comparable to the pharmaceuticals.
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NR 38
TC 53
Z9 58
U1 2
U2 60
PU ELSEVIER SCI LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
SN 0144-8617
EI 1879-1344
J9 CARBOHYD POLYM
JI Carbohydr. Polym.
PD OCT 15
PY 2019
VL 222
IS
BP
EP
DI 10.1016/j.carbpol.2019.114984
PG 12
WC Chemistry, Applied; Chemistry, Organic; Polymer Science
SC Chemistry; Polymer Science
GA II8EP
UT WOS:000475425500024
PM 31320062
DA 2026-02-10
ER

PT J
AU Liu, KF
Liu, Y
Xu, YT
Nandakumar, KS
Tan, HJ
He, CH
Dang, WZ
Lin, JH
Zhou, C
AF Liu, Kaifei
Liu, Ying

Xu, Yanting
Nandakumar, Kutty Selva
Tan, Huijing
He, Chonghua
Dang, Wenzhen
Lin, Jiahe
Zhou, Chun
TI Asperosaponin VI protects against bone destructions in collagen induced arthritis by inhibiting osteoclastogenesis
SO PHYTOMEDICINE
LA English
DT Article
DE Asperosaponin VI; Osteoclasts; CIA; Bone erosion; Signaling pathway
ID adhesion kinase; differentiation; resorption; mice; osteoarthritis; mechanisms; nfat
AB Background: Bone destructive diseases like rheumatoid arthritis (RA), osteoporosis and bone metastatic tumors are mainly mediated by over-activated osteoclasts. Asperosaponin VI (AVI), isolated from the rhizome of Dipsacus asper, belongs to triterpenoid saponins. It has multiple physiological activities but its effects on RA, especially on osteoclast differentiation and activation are still unclear. Purpose: Explore the protective role of AVI on collagen induced arthritis (CIA) in vivo and RANKL induced osteoclastogenesis in vitro. Methods: The effects of AVI on cell viability and RANKL-induced osteoclastogenesis, actin ring formation, bone resorption activity as well as on osteoclast specific gene and protein expression were tested using bone marrow derived monocytes (BMMs). Paws from CIA mice were used for micro-CT, HE and TRAP staining, real-time PCR and western blot. Sera were used for cytokine analysis by ELISA. The signaling pathways were detected using western blot, real-time PCR and immunofluorescence assay. Results: AVI significantly inhibited RANKL-induced osteoclast formation and bone resorption activity by suppressing the formation of actin ring. It also inhibited the expression of various osteoclatogenesis marker genes and signaling pathways. AVI protected arthritis in vivo by suppressing inflammation and bone loss. Conclusion: AVI exerts its anti-osteoclastogenic activity both in vitro and in vivo by inhibiting RANKL-induced osteoclast differentiation and function. Thus, our studies demonstrate a potential therapeutic role for AVI in preventing or inhibiting RANKL-mediated osteolytic bone diseases.
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FU National Natural Science Foundation of China [81601926]; Guangzhou science and technology project [201804010009]; Scientific research platform and project of Guangdong Education department [2017KQNCX257]
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NR 38
TC 36
Z9 39
U1 5
U2 39
PU ELSEVIER GMBH
PI MUNICH
PA HACKERBRUCKE 6, 80335 MUNICH, GERMANY
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EI 1618-095X
J9 PHYTOMEDICINE
JI Phytomedicine
PD OCT 15
PY 2019
VL 63
IS
BP
EP
DI 10.1016/j.phymed.2019.153006
PG 11
WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
SC Plant Sciences; Pharmacology & Pharmacy; Integrative & Complementary Medicine
GA JR5YD
UT WOS:000499699300012
PM 31299594
DA 2026-02-10
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PT J
AU Whitney, DG
AF Whitney, Daniel G.
TI Prevalence of High-Burden Medical Conditions Among Young and Middle-Aged

Adults With Pediatric-Onset Medical Conditions: Findings From US Private and Public Administrative Claims Data
SO INTERNATIONAL JOURNAL OF HEALTH POLICY AND MANAGEMENT
LA English
DT Article
DE Clinical Epidemiology; Pediatric-Onset Medical Conditions; Noncommunicable Diseases; United States
ID life-years dalys; global burden; systematic analysis; disease; disability; multimorbidity; injury
AB Adults with pediatric-onset medical conditions (POMCs) are susceptible to early development of high-burden medical conditions. However, research pertaining to this topic is lacking, which is vital information that could assist in health benefit planning and administration. The purpose of this study was to determine the prevalence of high-burden medical conditions among privately and publicly insured adults with POMCs, as compared to adults without POMCs, from the US. Data from 2016 were extracted from Optum Clinformatics (R) Data Mart (private insurance) and a random 20% sample from Medicare fee-for-service (public insurance). International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes were used to identify 18-64-year-old beneficiaries with POMCs, as well as several high-burden medical conditions, including pain, fracture, mood affective disorders, anxiety disorders, ischemic heart diseases, cerebrovascular diseases, hypertensive and other cardiovascular diseases, type 2 diabetes, osteoporosis, osteoarthritis, chronic obstructive pulmonary diseases, liver diseases, and cancer. Privately and publicly insured adults with POMCs had higher prevalence of all medical conditions compared to adults without POMCs. Publicly insured adults with POMCs had higher prevalence of all medical conditions compared to privately insured adults with POMCs, except for the lower prevalence of pain and cancer. When stratified by the category of POMCs (eg, musculoskeletal, circulatory), privately and publicly insured groups tended to have higher prevalence of most (private) or all (public) medical conditions compared to adults without POMCs. Adults with POMCs have higher prevalence of several high-burden medical conditions compared to adults without POMCs. This health disparity was present regardless of insurance coverage, but was generally more pronounced for public vs. private insured adults with POMCs.
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CR Unknown -, 2020, GLOBAL ACTION PLAN ON PHYSICAL ACTIVITY 2018-2030: MORE ACTIVE PEOPLE FOR A HEALTHIER WORLD, V0, P0
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NR 20
TC 19
Z9 20
U1 0
U2 6
PU KERMAN UNIV MEDICAL SCIENCES
PI KERMAN
PA JAHAD BLVD, KERMAN, 7619813159, IRAN
SN
EI 2322-5939
J9 INT J HEALTH POLICY
JI Int. J. Health Policy Manag.
PD NOV 15
PY 2019
VL 8
IS 11
BP 629
EP 635
DI 10.15171/ijhpm.2019.62
PG 7
WC Health Care Sciences & Services; Health Policy & Services
SC Health Care Sciences & Services
GA JB7MQ
UT WOS:000488746200001
PM 31779288

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PT J
AU Feng, S
Yang, Z
Sun, JN
Zhu, L
Wang, S
Guo, KJ
Chen, XY
Zha, GC
AF Feng, Shuo
Yang, Zhi
Sun, Jian-Ning
Zhu, Liang
Wang, Song
Guo, Kai-Jin
Chen, Xiang-Yang
Zha, Guo-Chun
TI Comparison of the therapeutic effect between the simultaneous and staged unicompartmental knee arthroplasty (UKA) for bilateral knee medial compartment arthritis
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Unicompartmental knee arthroplasty; Simultaneous; Staged; osteoarthritis; Postoperative complications
ID clinical-outcm; replacement; complications
AB BackgroundTo compare the efficacy and safety of simultaneous vs staged unicompartmental knee arthroplasty (UKA) for bilateral unicompartmental osteoarthritis of the knee.MethodsWe performed a retrospective analysis of prospectively collected data on 93 patients with bilateral knee medial compartment arthritis underwent simultaneous UKA (Group A, 39) or staged UKA (Group B, 54 cases) from January 2008 to December 2015. Group A: 6 males and 33 females aged 64.97.7years; Group B: 5 males and 49 females aged 64.26.4years. There were no statistically significant differences in pre-operative age, sex ratio, or body weight index between the groups (P>0.05). Groups were compared in terms of total anesthesia time, volume of drainage, blood transfusion rate, hemoglobin level on post-operative day 3, total post-operative inpatient days, treatment expenses, post-operative therapeutic effect (KSS scores), and complications.Results All patients had follow-up visits post-operatively. The follow-up visit interval was 32-133months and 41.9months on average. Total anesthesia time, postoperative length of hospital stay, and hospitalization expenses in Group A were significantly

less than those of Group B (P<0.05). Hemoglobin levels in Group A were significantly lower than those of Group B at post-op day 3 (P<0.05). However, no significant differences in volume of drainage, the rate of transfusion, complications, and KSS scores were detected between Groups A and B (P>0.05).Conclusions Both simultaneous and staged UKA achieved the desired therapeutic effect in treatment of bilateral knee medial compartment arthritis. However, simultaneous UKA reduced the cost and the postoperative length of hospital stay without increasing post-operative complications.
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FU Jiangsu Provincial Medical Youth Talent [QNRC2016800]; Science and Technology Planning Project of Xuzhou [KC16SL111]
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NR 32
TC 15
Z9 19
U1 1
U2 11
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PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN 1471-2474
EI
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD JUL 27
PY 2019
VL 20
IS
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DI 10.1186/s12891-019-2724-8
PG 7

WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA IM0EC
UT WOS:000477657400005
PM 31351465
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PT J
AU Blaty, T
Krueger, D
Illgen, R
Squire, M
Heiderscheit, B
Binkley, N
Anderson, P
AF Blaty, T.
Krueger, D.
Illgen, R.
Squire, M.
Heiderscheit, B.
Binkley, N.
Anderson, P.
TI DXA evaluation of femoral bone mineral density and cortical width in patients with prior total knee arthroplasty
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Bone mineral density (BMD); Cortical width; Dual energy x-ray absorptiometry (DXA); Total knee arthroplasty (TKA)
ID x-ray absorptiometry; revision total hip; periprosthetic fractures; risk-factors; follow-up; prevalence; epidemiology; osteoporosis; femur; osteoarthritis
AB A Summary Periprosthetic fractures after total knee arthroplasty (TKA) have devastating consequences. Osteoporosis increases periprosthetic fracture risk, but distal femur bone mineral density (BMD) is not measured post-TKA. This study measured distal femur BMD and cortical width; both were lower in the TKA compared to thenon-operated leg. BMD measurement reproducibility was good. Standardized DXA regions of interest are proposed. Introduction Periprosthetic fractures following total knee arthroplasty (TKA) are not rare. We hypothesized that TKA is associated with low BMD, potentially increasing periprosthetic fracture risk. However, distal femur dual energy x-ray (DXA) measurement is virtually never performed after TKA due to lack of standardized approaches. Thus, this study's aims were to develop standard DXA femur regions of interest (ROIs), assess cortical width, and determine measurement reproducibility in TKA patients. Methods Thirty

adults (15 M/15 F) age 59-80 years with unilateral, primary TKA within 2-5 years had femoral DXA scans performed in duplicate using a Lunar iDXA densitometer. In prior work, we established that femur BMD was lowest in the distal metaphysis and highest in mid-shaft. Thus, BMD and cortical width were measured at 15%, 25%, and 60% of the femur length measured from the distal notch. Femur BMD and cortical width were compared between limbs (TKA vs. non-operated side) by paired t test. Results BMD was 3.2-9.9% lower ($p < 0.001$) in the operated femur at all custom ROIs; substantial between individual differences existed with some up to 30% lower. Cortical width was lower ($p < 0.05$) at the 25% ROI on the TKA side. BMD reproducibility was excellent; CV 0.85-1.33%. Conclusions Distal femur BMD can be reproducibly measured using DXA and is similar to 10% lower on the TKA leg. Similarly, medial and lateral cortices are thinner at the 25% ROI. These bone changes likely increase periprosthetic fracture risk. Further work to define and mitigate periprosthetic fracture risk after TKA is needed.
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NR 47
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U1 0
U2 1
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 0937-941X
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J9 OSTEOPOROSIS INT
JI Osteoporosis Int.
PD FEB 15
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WC Endocrinology & Metabolism
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PT J
AU Chianca, V
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TI Interventional therapeutic procedures to treat degenerative and inflammatory musculoskeletal conditions: state of the art
SO RADIOLOGIA MEDICA
LA English
DT Article
DE Interventional radiology; Ultrasound; Musculoskeletal system; Tendinopathy; Osteoarthritis
ID guided percutaneous irrigation; rotator cuff; calcific tendinitis; achilles tendinopathy; magnetic-resonance; septic bursitis; ultrasound; injection; vertebroplasty; osteoporosis
AB Imaging-guided interventional procedures have become increasingly popular in the treatment of several pathologic conditions in the musculoskeletal system. Besides oncological treatments, musculoskeletal procedures can be performed to treat different degenerative or inflammatory conditions. This paper is aimed to review clinical indications and technical aspects of these kinds of procedures. In particular, we revise the general aspects common to most procedures and the different imaging-guided interventions which can be performed around joints, soft tissues, and spine.
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NR 61
TC 23
Z9 24
U1 1
U2 8
PU SPRINGER-VERLAG ITALIA SRL

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PA VIA DECEMBRIO, 28, MILAN, 20137, ITALY
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JI Radiol. Med.
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WC Radiology, Nuclear Medicine & Medical Imaging
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PT J
AU Kayipmaz, S
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AF Kayipmaz, Saadettin
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TI Trabecular structural changes in the mandibular condyle caused by degenerative osteoarthritis: a comparative study by cone-beam computed tomography imaging
SO ORAL RADIOLOGY
LA English
DT Article
DE Cancellous bone; Fractals; Mandibular condyle; Osteoarthritis
ID bone-mineral density; temporomandibular-joint; disorders; pattern; pain; osteonecrosis; osteoporosis
AB ObjectivesTemporomandibular osteoarthritis causes pain and loss of function. In advanced cases, it may also result in destruction of joint cartilage surfaces and bone structure.MethodsThis study was performed to examine the potential changes in the condylar trabecular bone structure in patients with temporomandibular osteoarthritis. Condylar trabecular structures were compared

between 35 healthy patients and 35 patients with temporomandibular osteoarthritis by a box-counting method using fractal dimensional analysis on cone-beam computed tomography images.ResultsThe average fractal dimensions of patients with temporomandibular osteoarthritis and healthy patients were 1.18 and 1.23, respectively. This difference was statistically significant (p0.05).ConclusionsOur results add to the existing preliminary knowledge regarding the osteoporotic changes that occur in the trabecular structure under the subchondral bone, which is normally not seen on radiographic images, as well as the destruction and remodeling that occur on the condyle surface, which is visible on radiographic images.
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NR 29
TC 29
Z9 32
U1 0
U2 9
PU SPRINGER
PI NEW YORK
PA 233 SPRING ST, NEW YORK, NY 10013 USA
SN 0911-6028
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J9 ORAL RADIOL
JI Oral Radiol.
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PT J
AU Diaz-Rodriguez, P
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Landin, Mariana
TI Current Stage of Marine Ceramic Grafts for 3D Bone Tissue Regeneration
SO MARINE DRUGS
LA English
DT Review
DE marine ceramic grafts; calcium phosphate; bone tissue regeneration; osteoinductive properties; structural strength; dissolution rate
ID antler cancellous bone; physicochemical characterization; osteoconductive effectiveness; substitutes; nacre; autograft; defects; matrix; reconstruction; sterilization
AB Bioceramic scaffolds are crucial in tissue engineering for bone regeneration. They usually provide hierarchical porosity, bioactivity, and mechanical support supplying osteoconductive properties and allowing for 3D cell culture. In the case of age-related diseases such as osteoarthritis and osteoporosis, or other bone alterations as alveolar bone resorption or spinal fractures, functional tissue recovery usually requires the use of grafts. These bone grafts or bone void fillers are usually based on porous calcium phosphate grains which, once disposed into the bone defect, act as scaffolds by incorporating, to their own porosity, the intergranular one. Despite their routine use in traumatology and dental applications, specific graft requirements such as osteoinductivity or balanced dissolution rate are still not completely fulfilled. Marine origin bioceramics research opens the possibility to find new sources of bone grafts given the wide diversity of marine materials still largely unexplored. The interest in this field has also been urged by the limitations of synthetic or mammalian-derived grafts already in use and broadly investigated. The present review covers the current stage of major marine origin bioceramic grafts for bone tissue regeneration and their promising properties. Both products already available on the market and those in preclinical phases are included. To understand their clear contribution to the field, the main clinical requirements and

the current available biological-derived ceramic grafts with their advantages and limitations have been collected.
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U2 40
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 1660-3397
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JI Mar. Drugs
PD AUG 15
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VL 17
IS 8
BP
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WC Chemistry, Medicinal; Pharmacology & Pharmacy
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ER

PT J
AU Horii, C
Asai, Y
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TI Differences in prevalence and associated factors between mild and severe vertebral fractures in Japanese men and women: the third survey of the ROAD study
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Vertebral fracture; Prevalence; Low back pain; Walking ability; ROAD study
ID quality-of-life; risk-factors; hong-kong; mortality; osteoporosis; deformity; consequences; level; mros
AB Vertebral fracture (VF) is a common osteoporotic fracture, while its epidemiology varies according to regions and ethnicities, little is known about it in Japan. Using whole-spine radiographs from a population-based cohort study, the Research on Osteoarthritis/Osteoporosis Against Disability study 3rd survey

performed in 2012-2013, we estimated the sex- and age-specific prevalence of VF in the Japanese. Genant's semiquantitative method (SQ) was used to define VF; SQ >= 1 as VF, SQ = 1 as mild VF, SQ >= 2 as severe VF. We also revealed accurate site-specific prevalence, and associated factors with mild and severe VF. The participants were 506 men [mean age 66.3 years, standard deviation (SD):13.0] and 1038 women (mean age 65.3 years, SD: 12.6). The prevalence of VF in participants aged under 40, in their 40s, 50s, 60s, 70s, and >= 80 years was 17.4, 7.9, 18.5, 25.6, 26.3, and 41.5%, respectively, in men, and 2.9%, 2.4%, 7,3, 10.3, 27.1, and 53.0%, respectively, in women. Men had a significantly higher prevalence of mild VF (21.2%) than women (10.0%, $p < 0.001$); whereas, severe VF was significantly more prevalent in women (9.1%) than in men (4.7%, $p = 0.003$). VF was distributed with 2 peaks regarding site; one large peak at the thoracolumbar region, and another at the middle thoracic lesion. Low back pain and decreased walking ability were independently associated with severe VF, but not with mild VF, after adjustment for participant characteristics. Decreased walking ability was associated with multiple VFs in women, but not in men.
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[B23390172]; [B20390182]; [15K15219]; [24659317]; [B23390356]; [C20591774]; [23659580]; [24659666]; [21659349]; [A18689031]; [B26293329]; [B23390357]; [C20591737]; [25670293]
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NR 44
TC 35
Z9 45
U1 0
U2 2
PU SPRINGER JAPAN KK
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AF Karsdal, M. A.
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Bay-Jensen, A. C.
TI Biochemical markers in osteoarthritis with lessons learned from osteoporosis
SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY
LA English
DT Article
DE osteoarthritis; biomarkers; osteoporosis
ID bone-mineral density; oral salmon-calcitonin; healthy postmenopausal women; vertebral fracture risk; ii collagen; synovial-fluid; matrix-metalloproteinase; cartilage degradation; knee osteoarthritis; alendronate treatment
AB Osteoarthritis (OA) is a disease of the whole joint, including synovium, bone and cartilage. OA is a slow degenerative and very heterogeneous disease, with both varying levels of disease activity and progression. Biomarkers are urgently needed to assist drug developers in selecting and developing the projects with the highest chance of success. Biomarkers for enrichment of clinical studies, early efficacy as well as other diagnostic tools are needed. Osteoporosis and OA have many similarities. In osteoporosis an armamentarium of treatments are now available with high clinical efficacy and well-described effects on biomarkers. Possibly, lessons learned from the osteoporosis field in the use of biomarkers may be applied in the OA field, from both technical and scientific perspectives. To help guide the way, the FDA has recently published the BEST guidelines, to facilitate obtaining a common vocabulary to assist biomarker researchers. In the current review, we will review the biomarkers of OA, with emphasis on bone, cartilage and synovial biomarkers, and draw clear perspectives to the use of biomarkers for drug development and clinical practice in the osteoporosis field.
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TI Diffuse idiopathic skeletal hyperostosis is associated with lumbar spinal stenosis requiring surgery
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Diffuse idiopathic skeletal hyperostosis; Lumbar spinal stenosis; General inhabitants; Prevalence; Standing whole-spine radiographs
ID diagnostic support tool; population; prevalence; hypertrophy; disorders; ligament; cohort; adult; pain; dish
AB Factors related to the onset and progression of lumbar spinal stenosis (LSS) have not yet been identified. Diffuse idiopathic skeletal hyperostosis (DISH)

increases mechanical loading on the non-fused lumbar levels and may therefore lead to LSS. This cross-sectional study aimed to identify associations between LSS and DISH. This study included 2363 consecutive patients undergoing surgery for LSS and 787 general inhabitants without symptoms of LSS as participants of the population-based cohort study, Research on Osteoarthritis/Osteoporosis Against Disability. Standing whole-spine radiographs were used to diagnose DISH based on the criteria proposed by Resnick and Niwayama. The prevalence of DISH showed a significant step-wise increase among asymptomatic inhabitants without radiographic LSS, asymptomatic inhabitants with radiographic LSS, and patients with LSS requiring surgery (14.4, 21.1, and 31.7%, respectively; $p<0.001$). The distribution of DISH was similar between the groups, but the lower thoracic and upper-middle lumbar spine regions were more frequently involved in patients with LSS requiring surgery. Multivariate analysis indicated that DISH was an independent associated factor for LSS requiring surgery (adjusted odds ratio 1.65; 95% confidence interval 1.32-2.07) after adjustment for age, sex, body mass index, and diabetes mellitus. Among patients with LSS requiring surgery, a higher occurrence of stenosis at the upper lumbar levels and multi-level stenosis were observed in patients with DISH requiring surgery than in patients without DISH. In conclusion, DISH is independently associated with LSS requiring surgery. The decrease in the lower mobile segments by DISH may increase the onset or severity of LSS.
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TI Characteristics of yoga and meditation users among older Australian women - results from the 45 and up study
SO COMPLEMENTARY THERAPIES IN CLINICAL PRACTICE
LA English
DT Article
DE Chronic illness; Complementary medicine; Meditation; Women's health; Yoga
ID physical-activity; adults; metaanalysis; predictors; depression; outcm; scale; pain
AB Background and purpose: Yoga and meditation are predominantly utilised by healthy well-educated young women, but little is known about utilisation by older chronically ill women. Therefore, the purpose of this study was to investigate the characteristics of yoga and meditation use among middle-to-higher aged Australian women with chronic conditions. Materials and methods: This is a sub-study of the 45 and Up Study including 1925 Australian women aged 53-95 years diagnosed with chronic conditions (asthma, depression, diabetes, osteoarthritis, and osteoporosis). Information on yoga and meditation use frequencies (categories: 'no yoga', 'at least once daily', 'at least once weekly', and 'at least once monthly'), self-perceived effectiveness and communication with

health care providers were assessed via self-report. Logistic regression analyses were conducted to identify independent predictors of yoga and meditation use, using SPSS 24.0. Results: Overall 6.8% and 10.7% of women reported the use of yoga and meditation respectively. Meditation was rarely practiced supervised (11.7%), compared to significant higher rates in yoga (53.2%). Predictors for yoga and meditation use were marital status (married/in relationship > not married/in relationship), higher health related hardiness, and higher education, whereas obesity, and diabetes decreased likelihood of use. While the majority found yoga and meditation helpful for their condition, the use was rarely monitored by or discussed with health care practitioners. Conclusion: This study finds that yoga and meditation are used by middle-to-higher aged Australian women with chronic illnesses. The lack of communication with health care providers is concerning and might hinder co-ordinated and effective health care around chronic illness. Further research is necessary to help understand possible concurrent health care use and thereby help inform safe, effective and coordinate health seeking amongst those with chronic illness.
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TI Glutamine Metabolism Is Essential for Stemness of Bone Marrow Mesenchymal Stem Cells and Bone Homeostasis
SO STEM CELLS INTERNATIONAL
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DT Review
ID amino-acid; parenteral-nutrition; osteogenic differentiation; alpha-ketoglutarate; oral glutamine; stromal cells; osteoclast differentiation; intestinal adaptation; extracellular-matrix; articular-cartilage
AB Skeleton has emerged as an endocrine organ which is both capable of regulating energy metabolism and being a target for it. Glutamine is the most bountiful and flexible amino acid in the body which provides adenosine 5 '-triphosphate (ATP) demands for cells. Emerging evidences support that glutamine which acts as the second metabolic regulator after glucose exerts crucial roles in bone homeostasis at cellular level, including the lineage allocation and proliferation of bone mesenchymal stem cells (BMSCs), the matrix mineralization of osteoblasts, and the biosynthesis in chondrocytes. The integrated mechanism consisting of WNT, mammalian target of rapamycin (mTOR), and reactive oxygen species (ROS) signaling pathway in a glutamine-dependent pattern is responsible to regulate the complex intrinsic biological process, despite more extensive

molecules are deserved to be elucidated in glutamine metabolism further. Indeed, dysfunctional glutamine metabolism enhances the development of degenerative bone diseases, such as osteoporosis and osteoarthritis, and glutamine or glutamine progenitor supplementation can partially restore bone defects which may promote treatment of bone diseases, although the mechanisms are not quite clear. In this review, we will summarize and update the latest research findings and clinical trials on the crucial regulatory roles of glutamine metabolism in BMSCs and BMSC-derived bone cells, also followed with the osteoclasts which are important in bone resorption.

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ID rankl expression; hypoxia; cells; differentiation; il-6; osteoblasts; hif1-alpha; binding; protein; oxygen
AB Osteocytes, entrapped within the mineralized bone matrix, has been found to have numerous functions such as acting as an orchestrator of bone remodeling through regulation of both osteoclast and osteoblast activity and also functioning as an endocrine cell. Due to a specialized morphology and surrounding structure, osteocytes are more tolerant to hypoxia during osteoporosis, fracture, osteoarthritis, and orthodontic-orthognathic combination therapy. Hypoxia-inducible factor-1 alpha (HIF-1 alpha) is one of the master regulators of hypoxia reactions, playing an important role in bone modeling, remodeling, and homeostasis. This study aimed to investigate the pivotal functional role of HIF-1 alpha in osteocytes initiating of bone remodeling under hypoxia. In the present study, the osteoclasts formation induced by RAW264.7 was significantly promoted in conditioned media (CM) from osteocytic MLO-Y4 exposed to hypoxia in vitro. Therefore, hypoxic MLO-Y4 cells simulated by 100 mu mol/L CoCl2 or 2% O-2 stably expressed HIF-1 alpha proteins and upregulated the expression of receptor activator of nuclear factor-kappa B ligand (RANKL) at both the messenger RNA (mRNA) and protein level. Furthermore, with the Knockdown of HIF-1 alpha, the expression of RANKL mRNA and protein decreased after transient transfection. In addition, the phosphorylation of Janus kinase 2 (JAK2) and signal transducer and activator of transcription (STAT3) was also correlated with HIF-1 alpha and RANKL levels under hypoxia. Then AG490, a JAK2 inhibitor, inhibited p-JAK2, p-STAT3 and RANKL expression. It was possible that AG490 disturbed the contact of HIF-1 alpha and RANKL by JAK2/STAT3 pathway, influencing osteoclastogenesis. Our findings suggested that HIF-1 alpha promoted the expression of RANKL by activating JAK2/STAT3 pathway in MLO-Y4 cells, and enhanced osteocyte-mediated osteoclastic differentiation in vitro.
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TC 87
Z9 106
U1 0
U2 68
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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PT J
AU Kasonga, AE
Kruger, MC
Coetzee, M
AF Kasonga, Abe E.
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TI Free fatty acid receptor 4-β-arrestin 2 pathway mediates the effects of different classes of unsaturated fatty acids in osteoclasts and osteoblasts
SO BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR AND CELL BIOLOGY OF LIPIDS
LA English
DT Article
DE beta-Arrestin 2; Free fatty acid receptor 4; Osteoblast; Osteoclast; Unsaturated fatty acids
ID bone-formation; osteoporosis; gpr120; cells; japan
AB Bone is a dynamic tissue that is constantly remodelled by bone resorbing osteoclasts and bone forming osteoblasts, respectively. A breakdown in the remodelling process underlies several bone diseases such as osteoporosis. Unsaturated fatty acids (UFAs) have been shown to have beneficial effects on bone health. However, the mechanism of action of UFAs in bone remains unclear. Free fatty acid receptor 4 (FFAR4) is expressed in bone cells and preferentially binds omega-3 and omega-7 UFAs. Therefore, we sought to determine if FFAR4 influenced the action of different classes of UFAs in bone cells. FFAR4 and potential signalling pathways, beta-arrestin 2 (beta arr2) and G(uq) were silenced in RAW264.7 murine macrophages (pre-osteo-clasts) and MC3T3-E1 murine pre-osteoblasts. Cell differentiation, activation of signalling pathways and expression of regulatory genes were evaluated. The omega-3 UFAs, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), and the omega-7 UFA, palmitoleic acid (PLA), were shown to require the FFAR4/beta arr2 signalling

pathway to inhibit osteoclast differentiation in RAW264.7 murine macrophages. The omega-6 UFA, arachidonic acid, and the omega-9 UFA, oleic acid (OA), were shown to inhibit osteoclast formation but did not use FFAR4. DHA, EPA, PLA and OA enhanced osteoblast signalling through the FFAR4/beta arr2 signalling axis. This study reveals that FFAR4/beta arr2 signalling may mediate the bone protective effects of different classes of UFAs in osteoclasts and osteoblasts.
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NR 38
TC 29
Z9 35
U1 0
U2 29
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 1388-1981
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J9 BBA-MOL CELL BIOL L
JI Biochim. Biophys. Acta Mol. Cell Biol. Lipids
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PT J
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Suarez-Almazor, Maria E.
TI Digital Patient Education and Decision Aids
SO RHEUMATIC DISEASE CLINICS OF NORTH AMERICA
LA English
DT Article
DE Patient education; Decision aids; Digital tools; Multimedia tools; Rheumatic diseases
ID health literacy; conjoint-analysis; rheumatoid-arthritis; information; quality; care; osteoarthritis; osteoporosis; risk; intervention
AB New technologies can do more than just digitize health information; they can support multimedia platforms for patient education and health decision support. Technology can simplify the way health decisions are made by offering quick access to a vast amount of information that can be tailored to specific populations. Digital tools can increase knowledge and assist consumers in comparing health care alternatives. They are well received by patients because of the myriad features that render them visually appealing and entertaining, including audiovisual and interactive elements. To be effective, however, digital tools must be evidence based and developed following quality standards.
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NR 51
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Z9 41
U1 0
U2 8
PU W B SAUNDERS CO-ELSEVIER INC
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JI Rheum. Dis. Clin. North Am.
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PT J
AU Jorgensen, PB
Lamm, M
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Stilling, M
AF Jorgensen, Peter B.
Lamm, Martin

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Stilling, Maiken
TI Equivalent hip stem fixation by Hi-Fatigue G and Palacos R plus G bone cement: a randomized radiostereometric controlled trial of 52 patients with 2 years' follow-up
SO ACTA ORTHOPAEDICA
LA English
DT Article
ID low-viscosity cement; exeter femoral stem; oxford hip; rsa; arthroplasty; migration; replacement; micromotion; model
AB Background and purpose Long-term fixation of cemented femoral stems relies on several factors including cement adhesion and fatigue. Hi-Fatigue is a newer third-generation bone cement with low-viscosity properties at room temperature, good mechanical strength, and stable bone-cement interface in a laboratory testing environment. Palacos bone cement has excellent 10-year survival and is considered gold standard. We compared stem subsidence after fixation with Hi-Fatigue and Palacos bone cements using radiostereometry.Patients and methods In a patient-blinded randomized controlled trial, 52 patients (30 women) at mean age 76 years (71-87) with osteoarthrosis and no osteoporosis received Hi-Fatigue G or Palacos R+G cement fixation of collarless, polished, double-tapered stems (CPT). Tantalum beads were inserted in the periprosthetic bone. Supine stereoradiographs were obtained postoperatively, 3 months, 6 months, 1 year, and 2 years after surgery. Oxford Hip Score (OHS) and VAS pain were recorded preoperatively and 1 and 2 years after surgery. Cement working times and properties were registered.Results At 2 years, mean stem subsidence of 1.12mm (95% CI 0.96-1.29) for Hi-Fatigue and 1.19mm (CI 1.03-1.34) for Palacos was similar. Likewise, stem version was comparable between cement groups. Mean OHS and VAS pain were similar between cement groups.Cement working times were similar between cement groups, but the mean curing time was longer for Hi-Fatigue (13.7min) than for Palacos (11.6min).Interpretation We found similar and generally low migration of CPT femoral stems inserted with Hi-Fatigue and Palacos bone cement until 2 years' follow-up, which indicates a good long-term survival of polished taper femoral stems inserted with both cement types.
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NR 30
TC 2
Z9 3
U1 0
U2 0

PU Medical Journal Sweden AB
PI Uppsala
PA Kungsngsvgen 27St, Uppsala, SWEDEN
SN 1745-3674
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J9 ACTA ORTHOP
JI Acta Orthop.
PD MAY 4
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WC Orthopedics
SC Orthopedics
GA HZ7MT
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PT J
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TI Human Enriched Serum Following Hydrolysed Collagen Absorption Modulates Bone Cell Activity: from Bedside to Bench and Vice Versa
SO NUTRIENTS
LA English
DT Article
DE metabolites; bone; hydrolysed collagen; nutrition; osteoporosis; absorption; collagen peptides
ID postmenopausal women; gene-expression; double-blind; hydroxyproline; peptides; calcium; differentiation; osteoarthritis; tripeptides; metabolism
AB Collagen proteins are crucial components of the bone matrix. Since collagen-derived products are widely used in the food and supplement industry, one may raise the question whether collagen-enriched diets can provide benefits for the skeleton. In this study, we designed an innovative approach to investigate this question taking into account the metabolites that are formed by the digestive tract and appear in the circulation after ingestion of hydrolysed collagen. Blood samples collected in clinical and pre-clinical trials following ingestion and absorption of hydrolysed collagen were processed and applied on bone-related primary cell cultures. This original ex vivo methodology revealed that hydrolysed collagen-enriched serum had a direct impact on the behaviour of cells from both human and mouse origin that was not observed with controls (bovine serum albumin or hydrolysed casein-enriched serum). These ex vivo findings were fully in line with in vivo results obtained from a mouse model of post-menopausal osteoporosis. A significant reduction of bone loss was observed in mice supplemented with hydrolysed collagen compared to a control protein. Both the modulation of osteoblast and osteoclast activity observed upon incubation with human or mouse serum ex vivo and the attenuation of bone loss in vivo, clearly indicates that the benefits of hydrolysed collagen for osteoporosis prevention go beyond the effect of a simple protein supplementation.
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NR 48

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Z9 25
U1 0
U2 27
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 2072-6643
J9 NUTRIENTS
JI Nutrients
PD JUN 15
PY 2019
VL 11
IS 6
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DI 10.3390/nu11061249
PG 17
WC Nutrition & Dietetics
SC Nutrition & Dietetics
GA II1AJ
UT WOS:000474936700055
PM 31159319
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PT J
AU Coimbra, IB
Plapler, PG
de Campos, GC
AF Coimbra, Ibsen Bellini
Plapler, Perola Grinberg
de Campos, Gustavo Constantino
TI Generating evidence and understanding the treatment of osteoarthritis in Brazil: a study through Delphi methodology
SO CLINICS
LA English
DT Article
DE Osteoarthritis; Osteoarthrosis; Surgical Treatment; Drug Therapy; Glucosamine; Chondroitin
ID knee osteoarthritis; rheumatic conditions; european-society; economic-aspects; management; prevalence; arthritis; recommendations; osteoporosis; algorithm
AB OBJECTIVES: This study aimed to provide evidence for understanding how to

treat osteoarthritis (OA) in our country. Therefore, it was necessary to match information and investigations related to the treatment of the disease from the three main types of specialists involved: physiatrists, orthopedists and rheumatologists. METHODS: The authors acted as a scientific advisory committee. From the initial discussions, a structured questionnaire was developed for use with a group of specialists on OA using the Delphi technique. The questionnaire was sent to 21 experts appointed by the authors, and the results obtained were critically analyzed and validated. RESULTS: The prevalence of OA was 33% in Brazil, corresponding to one-third of the individuals in the reference population, which included individuals over 25 years of age. Another significant finding was that most patients did not receive any form of treatment in the early stages of OA. CONCLUSION: The committee pointed to the need for early intervention and that the available medicinal resources can fulfil this important role, as is the case with SYSADOA treatments. Glucosamine-based medicinal products with or without chondroitin could also fulfill this need for early treatment. The other generated evidence and included investigations were then grouped together and are the subject of this publication.
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NR 30
TC 4
Z9 5
U1 0
U2 4
PU HOSPITAL CLINICAS, UNIV SAO PAULO
PI SAO PAULO
PA FAC MEDICINA, UNIV SAO PAULO, SAO PAULO, SP 00000, BRAZIL
SN 1807-5932
EI 1980-5322
J9 CLINICS
JI Clinics
PD JUN 15
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WC Medicine, General & Internal
SC General & Internal Medicine
GA HY4GF
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PT J
AU Bernstein, JJJ
Holt, GB
Bernstein, J
AF Bernstein, John J. J.
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TI Price dispersion of generic medications
SO PLOS ONE
LA English
DT Article
AB Generic pharmaceuticals should have very little price dispersion. Economics' Law of One Price suggests that identical goods, in the absence of trade frictions and under conditions of free competition and price flexibility, should sell for the same price, and the FDA ensures that generics are identical. In this study, we examine whether generic pharmaceuticals indeed have the low price dispersion that theory predicts, and if not, whether the dispersion seen for pharmaceuticals used to treat neuropsychiatric conditions is substantially higher than that of other drugs. Such a difference may offer an explanation for the price dispersion seen: namely, a strategy that takes advantage of buyers' cognitive constraints and impaired ability to comparison shop. We thus assembled a list of generic pharmaceuticals and their prices using www.GoodRx.com, based on a convenience sample of the 5 most popular drugs for 10 common medical conditions listed there. Three neuropsychiatric diagnoses were used: Alzheimer's disease, depression and schizophrenia. Seven other diagnoses served as controls: asthma; diabetes mellitus-type II; high cholesterol; hypertension; osteoarthritis; osteoporosis; and urinary tract infection. For each drug, we identified the highest and lowest prices and calculated the mean, median and coefficient of variation (CV). We further calculated the ratios of the highest price to the median price and of the highest to lowest price. We found that the mean price CV was 43%. For neuropsychiatric drugs and controls, it was 61% and 35%, respectively. The mean high-to-median ratio was3.7 for neuropsychiatric drugs and 1.9 for controls. The mean high-to-low ratio was 5.9 for neuropsychiatric drugs and 2.8 for controls. In short, generic

medications have high price dispersion, despite public availability of prices. Although our study did not examine why this price dispersion is present, the especially large high-to-low price ratio for neuropsychiatric medications suggests a strategy that exploits vulnerable patients.
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NR 5
TC 5
Z9 6
U1 0
U2 5
PU PUBLIC LIBRARY SCIENCE
PI SAN FRANCISCO
PA 1160 BATTERY STREET, STE 100, SAN FRANCISCO, CA 94111 USA
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J9 PLOS ONE
JI PLoS One
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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PT J

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Marumo, Keishi
TI The Regulation of Bone Metabolism and Disorders by Wnt Signaling
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE osteoclast; osteoblast; osteocyte; Wnt; sclerostin; osteoporosis; romosozumab; osteoarthritis; rheumatoid arthritis; skeletal-related events
ID mesenchymal stem-cells; mammary oncogene int-1; sclerostin expression; rheumatoid-arthritis; cortical-bone; postmenopausal women; inhibitory factor-1; osteocyte control; dna methylation; mineral density
AB Wnt, a secreted glycoprotein, has an approximate molecular weight of 40 kDa, and it is a cytokine involved in various biological phenomena including ontogeny, morphogenesis, carcinogenesis, and maintenance of stem cells. The Wnt signaling pathway can be classified into two main pathways: canonical and non-canonical. Of these, the canonical Wnt signaling pathway promotes osteogenesis. Sclerostin produced by osteocytes is an inhibitor of this pathway, thereby inhibiting osteogenesis. Recently, osteoporosis treatment using an anti-sclerostin therapy has been introduced. In this review, the basics of Wnt signaling, its role in bone metabolism and its involvement in skeletal disorders have been covered. Furthermore, the clinical significance and future scopes of Wnt signaling in osteoporosis, osteoarthritis, rheumatoid arthritis and neoplasia are discussed.
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TI Role of MicroRNA-141 in the Aging Musculoskeletal System: A Current Overview
SO MECHANISMS OF AGEING AND DEVELOPMENT
LA English
DT Article
DE MicroRNA-141; MiR-200 family; aging; musculoskeletal
ID oxidative stress; cell proliferation; osteogenic differentiation; regulatory roles; bone; expression; sarcopenia; regeneration; osteoporosis; transporter
AB MicroRNA's are small non-coding RNAs that regulate the expression of genes by targeting the 3' UTR's of mRNA. Studies reveal that miRNAs play a pivotal role in normal musculoskeletal function such as mesenchymal stem cell differentiation, survivability and apoptosis, osteogenesis, and chondrogenesis. Changes in normal miRNA expression have been linked to a number of pathological disease processes. Additionally, with aging, it is noted that there is dysregulation in the normal function of stem cell differentiation, bone formation/degradation, chondrocyte function, and muscle degeneration. Due to the change in expression of miRNA in degenerative musculoskeletal pathology, it is believed that these molecules may be at least partially responsible for cellular dysfunction. A number of miRNAs have already been identified to play a role in osteoarthritis, osteoporosis and sarcopenia. One miRNA that has become of interest recently is miRNA 141. The purpose of this article is to review the current literature available on miRNA 141 and how it could play a role in osteoporosis, osteoarthritis and musculoskeletal pathology overall.
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NR 77
TC 19
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PU ELSEVIER IRELAND LTD
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PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE,

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J9 MECH AGEING DEV
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WC Cell Biology; Geriatrics & Gerontology
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AF Ozden, Fatih
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TI Psychometrical properties of the Turkish translation of the New Knee Society Scoring System
SO ACTA ORTHOPAEDICA ET TRAUMATOLOGICA TURCICA
LA English
DT Article
DE Knee scoring; Reliability; Validity; Knee; Cultural adaptation; Total knee arthroplasty
ID cross-cultural adaptation; osteoarthritis; prevalence; validation; version; arthroplasty; reliability
AB Objective: To translate the New Knee Society Scoring System (KSS) into Turkish and to evaluate the psychometric properties of the translated questionnaire. Methods: This study was conducted on 66 knees of 43 pre-op patients who were scheduled for total knee arthroplasty (TKA) and 50 knees of 26 knee arthroplasty patients at least 6 months postoperatively. KSS was translated and culturally

adapted according to the guidelines of Guillemin and Beaton. Demographic and clinical characteristics of the patients were recorded. Patients completed WOMAC, KOOS and SF-36 surveys along with the Turkish version of the new KSS. After the initial evaluation, patients were asked to refill the new KSS 1 week later. Internal consistency and reliability were tested using Cronbach's alpha coefficient and intraclass correlation coefficient (ICC). Validity was assessed by calculating the Spearman's correlation coefficient between the new KSS and WOMAC, KOOS and SF-36 scores. Results: The mean ages of the pre and post-operative groups were 67.16 +/- 7.85 years and 71.65 +/- 6.95 years respectively. The Cronbach's alpha coefficients of the new KSS calculated for symptoms (0.814), patient satisfaction (0.947), patient expectations (pre-op =1.000, post-op =0.997) and functional activities (0.864) were high. The ICC scores ranged between 0.790 and 0.951. The pain subscore of the new KSS and the pain subscores of the WOMAC ($r = -0.720$; $p < 0.01$), KOOS ($r = 0.550$; $p < 0.01$) and SF-36 ($r = -0.434$; $p < 0.01$) were highly correlated. Emotional role functioning (RH), mental health (MH) and social role functioning (SF) subscores of SF-36 showed no correlation with the all subscores of the new KSS ($p > 0.05$). No floor or ceiling effects in the new KSS scores were detected. Conclusion: It is concluded that the new KSS is a valid and reliable questionnaire which can be used in evaluating the pre and post-operative Turkish speaking TKA patients. (C) 2019 Turkish Association of Orthopaedics and Traumatology. Publishing services by Elsevier B.V.
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10.1007/s11999-013-3149-6
NR 31
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AU Berthelot, JM
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AF Berthelot, J. -M.
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Darrieutort-Lafitte, C.
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Maugars, Y.
TI Pain catastrophising worsens RAPID3 in all rheumatologic conditions
SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY
LA English
DT Article
DE RAPID3; pain catastrophising; rheumatoid arthritis; spondyloarthritis; osteoarthritis; back pain; tendinitis; fibromyalgia; pain; HAQ; osteoporosis
ID index data 3; patient-reported outcm; disease-activity index; assessment questionnaire mdhaq; routine assessment; ankylosing-spondylitis; response criteria;

self-assessment; clinical-trial; activity score
AB Objective To assess RAPID3 in various rheumatologic conditions, and the impact of pain catastrophising on RAPID3. Methods A set of questionnaires, including RAPID3 (0-30) and pain catastrophising score (0-52), was given to all outpatients seen in a one-month period: 518 patients fulfilled the questionnaires, including 127 RA (42% taking biologics), and 135 SpA (58% taking biologics). Results Mean pain catastrophising was 18.5 +/- 12.5, and 19% of patients could be classified as catastrophisers (> 30). Higher RAPID3 scores were observed in the 33 osteoarthritis of lower limbs (16.44 +/- 5.20), 10 fibromyalgia (15.52 +/- 5.53), 47 back-pain (14.88 +/- 5.17), 17 osteoarthritis of upper limbs (13.61 +/- 7.42), and 38 tendinopathies (12.85 +/- 4.38). Lower RAPID3 were observed in the 135 SpA (12.79 +/- 6.03), 127 RA (12.18 +/- 6.30), 27 miscellaneous disorders (9.83 +/- 6.28), 7 entrapment neuropathies (9.81 +/- 4.51), 19 systemic connective tissue disorders (8.26 +/- 7.04) and 58 osteoporosis (7.85 +/- 6.95). Much higher RAPID3 scores were observed in the 19% with high pain catastrophising scores, whatever the conditions, and lower scores in the 15% with disablement benefits. RAPID3 was not associated with age or disease duration, but strongly correlated with daily fatigue, poor sleep, and length of daily pain. Conclusion Thanks to progress made in RA and SpA treatment, higher RAPID3 scores were mostly observed in other rheumatic conditions, but co-morbidities and pain catastrophising might contribute to floor effects when assessing rheumatic disorders with RAPID3, hindering the recognition of low disease activity in some RA of SpA patients.
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NR 39
TC 5
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PU CLINICAL & EXPER RHEUMATOLOGY
PI PISA
PA VIA SANTA MARIA 31, 56126 PISA, ITALY
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WC Rheumatology
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AF Tsai, Meng-Hsiu
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Wang, Jhi-Joung
Huang, Chien-Cheng
TI Long-term mortality in older adults with chronic pain: a nationwide population-based study in Taiwan
SO EUROPEAN GERIATRIC MEDICINE
LA English
DT Article
DE Chronic pain; Long-term; Mortality; Older
ID quality-of-life; low-back-pain; geriatric-patients; risk; prevalence; association; management
AB Purpose This study was conducted to clarify the long-term mortality in the older population with chronic pain (CP), which is still unclear. Methods We identified 17,568 older participants (aged >= 65 years) with CP and an identical number of

comparison cohort without CP matched 1:1 by age and sex between 1996 and 2000 from the Taiwan National Health Insurance Research Database. Causes of CP, underlying comorbidities, living areas, and mortality were collected for analyses. The long-term mortality and the causes of mortality were compared between the two cohorts through follow-up since 2000 until 2015. Results The mean age (+/- standard deviation) was 73.5 +/- 5.7 years, and female participants comprised 55.1% in both cohorts. The most common causes of CP were osteoarthritis (24.2%), spinal disorders (22.4%), peripheral vascular diseases (14.0%), and osteoporosis (9.5%). Older participants with CP had an increased rate of long-term mortality compared to that among their counterparts without CP after adjusting for the underlying comorbidities and the causes of CP (adjusted hazard ratio [AHR]: 1.18; 95% confidence interval [CI] 1.14-1.21). The increased mortality rate was observed even after the follow-up of 6 years (AHR 1.15; 95% CI 1.10-1.20). No significant difference was observed in the causes of mortality between the two cohorts. The most common cause of mortality was malignancy, followed by cardiovascular and cerebrovascular diseases. Conclusions Chronic pain was associated with an increased rate of long-term mortality in the older population. Early detection and intervention for treating CP are suggested for this population.
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TI Nomenclature of Subchondral Nonneoplastic Bone Lesions
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LA English

DT Review
DE nomenclature; nonneoplastic; osteochondral; subchondral bone; white paper
ID edema-like lesions; resonance-imaging score; marrow edema; insufficiency fractures; femoral-head; osteochondritis-dissecans; spontaneous osteonecrosis; transient osteoporosis; rheumatoid-arthritis; destructive osteoarthritis
AB OBJECTIVE. The purpose of this article is to summarize the nomenclature of nonneoplastic conditions affecting subchondral bone through a review of the medical literature and expert opinion of the Society of Skeletal Radiology Subchondral Bone Nomenclature Committee. CONCLUSION. This consensus statement summarizes current understanding of the pathophysiologic characteristics and imaging findings of subchondral nonneoplastic bone lesions and proposes nomenclature to improve effective communication across clinical specialties and help avoid diagnostic errors that could affect patient care.
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TI DXA Measured Distal Femur Bone Mineral Density in Patients After Total Knee Arthroplasty: Method Development and Reproducibility
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DT Article
DE DXA; total knee arthroplasty; bone mineral density
ID x-ray absorptiometry; revision total hip; periprosthetic bone; femoral fractures; risk-factors; follow-up; epidemiology; prevalence; osteoarthritis; osteoporosis
AB Introduction: Total knee arthroplasty (TKA) is increasingly being performed. Distal femur periprosthetic fracture is a potentially catastrophic complication following TKA and existing data document substantial distal femur bone mineral density (BMD) loss following TKA. However, distal femur BMD is virtually never measured clinically as no consensus approach exists. This pilot study's purpose was to define regional BMD variation throughout the femur, suggest standard dual-energy X-ray absorptiometry (DXA) regions of interest (ROIs) and evaluate BMD reproducibility at these ROIs. Methods: Thirty volunteers 2-5 yr post TKA had both entire femurs imaged twice using a Lunar iDXA with subject repositioning between scans; the atypical femur fracture feature of enCORE software was utilized. To define femoral BMD distribution, custom 1 cm ROIs were stacked one atop the other starting at the intercondylar notch and continuing to the base of the lesser trochanter. Femur length was measured with the ruler tool to calculate distance at 5% increments. ROIs encompassing each 5% increment were utilized to measure BMD at each location. Descriptive statistics were used to determine mean BMD at each ROI and reproducibility at the 15%, 25%, 45%, 60%, and 80% ROIs. Results: The 5 and 10% ROIs included prosthetic and/or patella, causing high BMD values. Distal femur BMD was lowest at the 15% ROI and was higher ($p < 0.05$) at each more proximal ROI to 45%, then plateaued from 45% to 75%. BMD reproducibility at these regions was excellent; coefficient of variation (CV) from similar to 1% to 3.5%. As periprosthetic fractures generally occur in the distal femur, we propose measuring femur BMD using ROIs placed at 15% and 25%. A 60% region could also be used as a highly cortical site. Conclusion: Existing DXA capabilities allow distal femur BMD measurement with good reproducibility. Further research using standardized ROIs to assess distal femur BMD loss after TKA, and interventions to

mitigate this loss, is indicated.
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AU Hu, H
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TI miR-26b modulates OA induced BMSC osteogenesis through regulating GSKβ/β-catenin pathway
SO EXPERIMENTAL AND MOLECULAR PATHOLOGY
LA English
DT Article
DE BMSC; miR-26b; GSK3-beta; Osteogenesis; OA; DEX
ID mesenchymal stem-cells; osteoblast differentiation; induced osteoporosis; bone-formation; osteoactivin; dexamethasone; expression; rescues; mirnas
AB Backgrounds: Osteoactivin (OA) is a key regulator promoting bone marrow stromal cells osteogenesis progress, while Dexamethasone (Dex) could inhibit OA induced osteogenesis and lead to osteoporosis. miR-26b increased during BMSC osteogenesis but whether it participates in this progress is enigma. Osteogenesis is under regulation of canonical Wnt signaling pathway which could serve as potential target for miR-26b. It bears therapeutic potential if miR-26b could regulate osteogenesis and antagonize Dex induced Osteoporosis (OP). Methods: BMSC were isolated from bone marrow of rats and induced for osteogenesis by OA administration. We detected miR-26b mRNA level together with osteogenesis related genes or Wnt signal pathway related genes by qRT-PCR. BMSC cells with miR-26b inhibitor or mimics revealed the effect of miR-26b on osteogenesis. The osteogenesis efficiency was detected by Alizarin Red staining and ALP activity. Protein level of canonical Wnt signal pathway and other proteins were detected by Western blot. The interaction between miR-26b and GSK3 beta was detected by dual luciferase reporter assay. Results: We found that miR-26b was increased during OA induced BMSC osteogenesis. Inhibiting miR-26b could lead to osteogenesis inhibition while miR-26b mimics could promote this progress. The key regulator of Wnt signal pathway GSK3 beta is down-regulated when miR-26b was overexpressed, resulting in beta-catenin activation. Since Dex could promote GSK3 beta expression and inhibit Wnt signal, miR-26b could also alleviate Dex

induced osteogenesis inhibition. Conclusion: Our findings indicate that miR-26b promoted BMSC osteogenesis by directly targeting GSK3 beta and activating canonical Wnt signal pathway, suggesting miR-26b might be serve as potential therapeutic candidate of osteoporosis.
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TI Musculoskeletal Factors and Geriatric Syndromes Related to the Absence of Musculoskeletal Degenerative Disease in Elderly People Aged over 70 Years
SO BIOMED RESEARCH INTERNATIONAL
LA English
DT Article
ID quality-of-life; locomotive syndrome; spinal alignment; body-mass; knee; health; osteoarthritis; osteoporosis; association; validation
AB Purpose. To investigate factors with a significant relationship with the absence of musculoskeletal disease (MSD: osteoporosis, knee osteoarthritis (K-OA), and lumbar spondylosis (L-OA)) in elderly people >= 70 years old. Methods. The subjects were 279 people (134 males, 145 females, mean age: 75.2 years) who attended an annual health checkup and were prospectively included in the study.

Osteoporosis was defined as %YAM <= 70%, K-OA as Kellgren-Lawrence grade >= 2, and L-OA as osteophytes of Nathan class >= 3. Subjects were divided into those with (group D) and without (group N) any MSD. Clinical variables including locomotive syndrome (LS), frailty, sarcopenia, and QOL (SF-36) were compared between the groups. Results. There was no significant difference in age or gender between group N (n=54) and group D (n=225). Lower BMI and pain, including neuropathic pain; greater back muscle strength, physical ability, and balance with eyes closed; larger lumbar lordosis, sacral inclination, and lumbar ROM; and smaller spinal inclination were found in group N. The rates of LS and sarcopenia were significantly lower and QOL was significantly higher in group N. Conclusions. This study firstly revealed the significant musculoskeletal factors and geriatric syndromes related to an absence of MSD, which may form the basis of interventions to improve QOL in elderly people >= 70 years old.
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FU Japanese Ministry of Health, Labor, and Welfare [18K09102]
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TI Consequences of bariatric surgery on outcomes in rheumatic diseases
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Review
DE Obesity; Bariatric surgery; Rheumatoid arthritis; Osteoarthritis; Gout; Psoriatic

arthritis; Fibromyalgia; Low back pain; Osteoporosis
ID morbidly obese-patients; quality-of-life; low-back-pain; psoriatic-arthritis; musculoskeletal pain; clinical-features; weight-reduction; risk-factors; bypass; osteoarthritis
AB Obesity is associated with numerous comorbidities including some rheumatic conditions. Through adipose-derived inflammation, obesity has been shown to induce increased initiation, progression, and worse responses on outcomes of rheumatic diseases. Bariatric surgery is being increasingly used thanks to its positive effects on major comorbidities such as type 2 diabetes mellitus and hypertension. Consequently, surgically induced weight and adipose tissue losses might play a role in the course of rheumatic conditions. The present narrative literature review aims to provide rheumatologists with an update on both the positive and negative effects of bariatric surgery on the rheumatic outcomes reported in the literature. Current evidence seems to show improved outcomes in obese populations with rheumatic disorders after bariatric surgery. However, rigorous prospective controlled studies with long follow-up are needed. Bariatric procedures have deleterious effects on bone and are associated with an increased risk of fractures.
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AU Biver, E
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Castronovo, V
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TI Gut microbiota and osteoarthritis management: An expert consensus of the European society for clinical and economic aspects of osteoporosis, osteoarthritis and musculoskeletal diseases (ESCEO)
SO AGEING RESEARCH REVIEWS
LA English
DT Article
DE Osteoarthritis; Gut microbiota; Dysbiosis; Inflammaging; Obesity; Modern diet

ID body-mass index; low-grade inflammation; knee osteoarthritis; chondroitin sulfate; metabolic osteoarthritis; hand osteoarthritis; obese-patients; dietary fiber; cartilage; association
AB The prevalence of osteoarthritis (OA) increases not only because of longer life expectancy but also because of the modern lifestyle, in particular physical inactivity and diets low in fiber and rich in sugar and saturated fats, which promote chronic low-grade inflammation and obesity. Adverse alterations of the gut microbiota (GMB) composition, called microbial dysbiosis, may favor metabolic syndrome and inflammaging, two important components of OA onset and evolution. Considering the burden of OA and the need to define preventive and therapeutic interventions targeting the modifiable components of OA, an expert working group was convened by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) to review the potential contribution of GMB to OA. Such a contribution is supported by observational or dietary intervention studies in animal models of OA and in humans. In addition, several well-recognized risk factors of OA interact with GMB. Lastly, GMB is a critical determinant of drug metabolism and bioavailability and may influence the response to OA medications. Further research targeting GMB or its metabolites is needed to move the field of OA from symptomatic management to individualized interventions targeting its pathogenesis.
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NR 87
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TI Association of blood n-3 fatty acid with bone mass and bone marrow TRAP-5b in the elderly with and without hip fracture
SO OSTEOPOROSIS INTERNATIONAL
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DE Bone mass; Bone resorption; n-3 fatty acid; Osteoporotic fracture

ID adipose-tissue; osteoporotic fracture; mineral density; older-adults; risk; consumption; omega-3-fatty-acids; biomarkers; humans; plasma
AB The SummaryThe plasma n-3 fatty acid level was 26.2% lower in patients with osteoporotic hip fracture than in those with osteoarthritis. In all patients, n-3 fatty acid was positively associated with bone mineral density and inversely associated with tartrate-resistant acid phosphatase-5b level in bone marrow aspirates, reflecting the bone microenvironment.IntroductionDespite the potential beneficial role of n-3 fatty acid (FA) on bone metabolism, the specific mechanisms underlying these effects in humans remain unclear. Here, we assessed whether the plasma n-3 level, as an objective indicator of its status, is associated with osteoporosis-related phenotypes and bone-related markers in human bone marrow (BM) samples.MethodsThis was a case-control and cross-sectional study conducted in a clinical unit. n-3 FA in the blood and bone biochemical markers in the BM aspirates were measured by gas chromatography/mass spectrometry and immunoassay, respectively. BM fluids were collected from 72 patients who underwent hip surgery because of either osteoporotic hip fracture (HF; n=28) or osteoarthritis (n=44).ResultsAfter adjusting for confounders, patients with HF had 26.2% lower plasma n-3 levels than those with osteoarthritis (P=0.006), and each standard deviation increment in plasma n-3 was associated with a multivariate-adjusted odds ratio of 0.40 for osteoporotic HF (P=0.010). In multivariate analyses including all patients, a higher plasma n-3 level was associated with higher bone mass at the lumbar spine (=0.615, P=0.002) and total femur (=0.244, P=0.045). Interestingly, the plasma n-3 level was inversely associated with the tartrate-resistant acid phosphatase-5b level (=-0.633, P=0.023), but not with the bone-specific alkaline phosphatase level, in BM aspirates.ConclusionsThese findings provide clinical evidence that n-3 FA is a potential inhibitor of osteoclastogenesis that favors human bone health.
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TI Management of early-onset hip osteoarthritis in an adolescent patient with osteopetrosis tarda: a case report
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LA English
DT Article
DE adolescent; hip; osteoarthritis; osteopetrosis
ID arthroplasty
AB Osteopetrosis (OP) is a group of rare sclerosing bone dysplasia characterized by increased bone density. The benign autosomal dominant form is the most common type. It typically carries a full life expectancy, despite increased propensity for fractures and other musculoskeletal problems, particularly hip osteoarthritis. In the current literature, the youngest OP patient having hip osteoarthritis is 16 years of

age and treated with total hip arthroplasty. Within the present study, a 16-year-old female patient with early-onset hip osteoarthritis treated with hip joint debridement and femoral head reshaping is presented. The pain relieved and hip joint movements recovered to almost normal range. At the final follow-up at 2 years after the surgery, the patient was still free of pain and ambulating without restriction. Hip joint debridement and femoral shaping may be beneficial in hip osteoarthritis secondary to OP in adolescents, and may delay hip arthroplasty in a young age.
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PU LIPPINCOTT WILLIAMS & WILKINS
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TI FREQUENCY OF DEPRESSION AND ANXIETY SYMPTOMS IN MEXICAN PATIENTS WITH RHEUMATIC DISEASES DETERMINED BY SELF-ADMINISTERED QUESTIONNAIRES ADAPTED TO THE SPANISH LANGUAGE
SO REVISTA DE INVESTIGACION CLINICA-CLINICAL AND TRANSLATIONAL INVESTIGATION
LA English
DT Article
DE Depression; Anxiety; Mental health questionnaires; Rheumatic diseases
ID arthritis; validity; version; cohort
AB Background: The frequency of depression and anxiety symptoms in Spanish-speaking patients suffering from rheumatic conditions is unknown when using self-administered detection tools. Methods: A single-center, cross-sectional survey including 413 patients (341 women) with well-defined rheumatic diseases was conducted. The patient health questionnaire-9 (PHQ-9) and generalized anxiety disorder (GAD)-7 questionnaires were used to detect depression and anxiety symptoms, respectively. Results: A total of 193 patients (46.7%) reported depression symptoms, and increased PHQ-9 scores were more frequently observed in women than in men (23% vs. 13%; p = 0.038), particularly in association with osteoarthritis, fibromyalgia, Sjogren's syndrome, and osteoporosis. From 88 patients (21.3%) with PHQ-9 scores 10 points (moderate-to-severe depression

symptoms), 27 (30.6%) were previously diagnosed to have depression and only four were under antidepressant treatment. Anxiety symptoms were observed in 168 patients (40.6%) and classified as moderate-to-severe by elevated GAD-7 scores in 68 subjects (16.4%). Of them, 12 (17.6%) were previously diagnosed with GAD, but only 4 (5.8%) were under therapy. Conclusions: An unexpected and unusually high frequency of undiagnosed depression and anxiety symptoms was found in rheumatic patients. Self-administered screening tools adapted to the Spanish language are useful and may help clinicians to suspect these conditions.
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TI Determinants, consequences and potential solutions to poor adherence to anti-osteoporosis treatment: results of an expert group meeting organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Osteoporosis Foundation (IOF)
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Adherence; Determinants; Osteoporosis; Persistence; Solutions
ID shared decision-making; medication adherence; fracture risk; postmenopausal women; persistence; care; patient; interventions; bisphosphonates; nonadherence
AB A Summary Many patients at increased risk of fractures do not take their medication appropriately, resulting in a substantial decrease in the benefits of drug therapy. Improving medication adherence is urgently needed but remains laborious, given the numerous and multidimensional reasons for non-adherence, suggesting the need for measurement-guided, multifactorial and individualized solutions. Introduction Poor adherence to medications is a major challenge in the treatment of osteoporosis. This paper aimed to provide an overview of the consequences, determinants and potential solutions to poor adherence and persistence to osteoporosis medication. Methods A working group was organized by the European Society on Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal diseases (ESCEO) to review consequences, determinants and potential solutions to adherence and to make recommendations for practice and further research. A systematic literature review and a face-to-face experts meeting were undertaken. Results Medication non-adherence is associated with increased risk of fractures, leading to a substantial decrease in the clinical and economic benefits of drug therapy. Reasons for non-adherence are numerous and multidimensional for each patient, depending on the interplay of multiple factors, suggesting the need for multifactorial and individualized solutions. Few interventions have been shown to improve adherence or persistence to osteoporosis treatment. Promising actions include patient education with counselling, adherence monitoring with feedback and dose simplification including flexible dosing regimen. Recommendations for practice and further research were also provided. To adequately manage adherence, it is important to (1) understand the problem (initiation, implementation and/or persistence), (2) to measure adherence and (3) to identify the reason of non-adherence and fix it. Conclusion These recommendations are intended for clinicians to manage adherence of their patients and to researchers and policy makers to design, facilitate and appropriately use adherence interventions.

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TI Towards to potential 2-cyano-pyrimidines cathepsin-K inhibitors: An in silico design and screening research based on comprehensive application of quantitative structure-activity relationships, molecular docking and ADMET prediction
SO JOURNAL OF MOLECULAR STRUCTURE
LA English
DT Article
DE QSAR; Docking; Cathepsin K; Molecular fingerprint; Clustering; ADMET prediction
ID qsar models; derivatives; discovery; validation; 3d-qsar; optimization; exploration; solubility; principles; define
AB Cathepsin K (CK) is the only cathepsin showing high expression in osteoclasts. CK is considered to be a drug target in treatment of osteoporosis, rheumatoid arthritis and osteoarthritis. Comprehensive application of quantitative structure-activity relationships (QSAR), molecular docking and absorption, distribution, metabolism, excretion and toxicity (ADMET) prediction was conducted for designing and screening for potential CK inhibitors based on 2-cyano-pyrimidine analogs. For the two-dimensional (2D)-QSAR study, a statistical model of PLS_FCFP was chosen for its best evaluated regression statistic values (r(2) = 0.759, q(2) = 0.637 and r(pred)(2) = 0.699). An equation that implied positive or negative contributions for several molecular descriptors was acquired. For the 3D-QSAR study, based on two methods of generation of molecular poses, three fingerprint-based cluster partitions, and two common substructures, 336 candidate CoMFA and CoMSIA models were generated for evaluation of statistic values. Among them, database Minimize_MDL_subs01 provided superior evaluated models: CoMFA model #41 (r(2) = 0.994, q(2) = 0.746 and r(pred)(2) = 0.8693) and CoMSIA model #42 (r(2) = 0.983, q(2) = 0.753 and r(pred)(2) = 0.8676). Informative clues for molecular design were derived from the created QSAR models and, based on them, an in-house library containing 190 purposefully designed unknown compounds was built for screening for potential CK inhibitors. Based on a combination of activity prediction and calculation of binding affinity, unknown

compound X139 emerged. Detailed molecular docking studies assisted in unveiling of the interactions between unknown compounds and the target protein. The strong pi-pi conjugation and preferably formed hydrogen bonds provided evidence that compound X139 had higher predicted activity. The subsequent study of ADMET prediction suggested acceptable drug-like properties for compound X139. (C) 2019 Elsevier B.V. All rights reserved.
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TI Seno-suppressive molecules as new therapeutic perspectives in rheumatic diseases
SO BIOCHEMICAL PHARMACOLOGY
LA English
DT Review
DE Senescence; Therapies; Osteoarthritis; Osteoporosis; Rheumatology
ID senescent cells; cellular senescence; mitochondrial dysfunction; articular-cartilage; chondrocyte senescence; secretory phenotype; subchondral bone; telomeric loss; autophagy; osteoarthritis
AB Over the past years, through in vitro studies and unique animal models, biologists and clinicians have demonstrated that cellular senescence is at the root of numerous age-related chronic diseases including osteoarthritis and osteoporosis. This non-proliferative cellular syndrome can modify other surrounding tissue-resident cells through the establishment of a deleterious

catabolic and inflammatory microenvironment. Targeting these deleterious cells through local or systemic seno-therapeutic agent delivery in pre-clinical models improves dramatically clinical signs and extends health span. In this review, we will summarize the current knowledge on cellular senescence, list the different strategies for identifying seno-suppressive therapeutic agents and their translations to rheumatic diseases.
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TI CORRELATION OF PRE-OPERATIVE PLANNING TO SURGICAL CORRECTION OF OPENING WEDGE HTO: A RADIOGRAPHIC STUDY UTILIZING A MANUAL MEASUREMENT METHOD
SO JOURNAL OF BIOLOGICAL REGULATORS AND HOMEOSTATIC AGENTS
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DT Article
DE high tibial osteotomy; genu varum; mechanical axis correction; opening wedge
ID high tibial osteotomy; varus deformity; fixation; osteoarthritis; complications; stability; plate; knee
AB High tibial osteotomy (HTO) utilizing a medial opening wedge has become a common and effective surgical technique for treatment of isolated medial compartment knee osteoarthritis secondary to varus malalignment. To reduce the risk of under- or overcorrection, accurate preoperative planning is important. This is a radiographic study to evaluate the reliability of preoperative measurement on full-length weight-bearing X-rays (FLWBXr) compared to post-operative X-rays

after healing. In addition, we calculated if the intraoperative opening wedge performed was consistent with the preoperative calculation and the postoperative correction. Three independent observers measured preoperative and postoperative FLWBXr at three different times. The angle of varus deformity; the angle to correct and the wedge needed to achieve desired alignment: the angle achieved postoperatively, and the postoperative mechanical axis deviation were measured. Intra- and inter-rater reliability showed high values for all the investigated parameters. The discrepancy between the calculated wedge and the wedge actually used in surgery ranged from 1 mm of over-correction to 3 mm of undercorrection, averaging -1.3 mm. The mechanical axis crossed the tibial plateau an average of 53% +/- 12.7. Clustering the data by the plate type statistically significant differences were found for preoperative varus alignment, advocated correction, intraoperative correction and post-op alignment. The Dugdale method can be considered highly reliable. Possible factors affecting the final correction are: surgeon's desire not to overcorrect in young patients and minimal osteoarthritis; measurement errors; variability in the method the FLWBXr is performed. In addition, the under correction could be the result of some collapse with time or the correction could be affected by the fixation system. Further investigation should include complete post-operative evaluation of outcomes and assess the role of these potential factors and their relationship to correction. Level of Evidence: Level III, Retrospective study.
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JI J. Biol. Regul. Homeost. Agents
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WC Endocrinology & Metabolism; Immunology; Medicine, Research & Experimental; Physiology
SC Endocrinology & Metabolism; Immunology; Research & Experimental Medicine; Physiology
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UT WOS:000692695000026
PM 31172931
DA 2026-02-10
ER

PT J
AU Mehta, B
Szymonifka, J
Dey, S
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Grassia, S
Mandl, LA
Bass, AR
Russell, L
Parks, M
Figgie, M
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TI Living in immigrant communities does not impact total knee arthroplasty outcomes: experience from a high-volume center in the United States

SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
ID total joint arthroplasty; total hip; disparity; replacement; health; neighborhoods; projections; limitations; arthritis; born
AB BackgroundCommunity characteristics such as poverty affect total knee arthroplasty (TKA) outcomes. However, it is unknown whether other community factors such as immigrant proportion (IP) also affect outcomes. Our objective was to determine the association of neighborhood IP on preoperative (pre-op) and 2-year postoperative (post-op) Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function after elective TKA.MethodsPatients in a high volume institutional TKA registry between May 2007 and February 2011 were retrospectively analyzed. Demographics, pre-op and 2-year post-op WOMAC pain and function scores, and geocodable addresses were obtained. Patient-level variables were linked to US Census Bureau census tract data. The effect of patient and neighborhood-level factors on WOMAC scores were analyzed using linear mixed effects models.Results3898 TKA patients were analyzed. Pre-op and 2-year post-op WOMAC pain and function scores were between 2.75-4.88 WOMAC points worse in neighborhoods with a high IP (40%) compared to low IP (<10%). In multivariable analyses, these differences were not statistically significant. Women had worse pre-op and 2-year post-op WOMAC scores (all p0.04), but this difference was not influenced by neighborhood IP (all p(interaction) NS).ConclusionsPatients living in high (40%) IP neighborhoods do not have worse pre-op or 2-year post-op pain and function outcomes after TKA compared to those living in low (<10%) IP neighborhoods. Although sex differences favoring males are notable, these differences are not associated with IP. High neighborhood IP do not appear to affect outcomes after TKA.
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NR 33
TC 4
Z9 4

U1 1
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PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 BMC MUSCULOSKEL DIS
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PT J
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TI Is the bone tissue of the femoral neck demineralised in patients with hip fracture?
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English

DT Article
DE Mineralisation; Osteoporosis; Bone metabolism; Hip fracture; Surgical treatment; Hip osteoarthritis; Microstructural trabecular bone
ID eye cataract-surgery; x-ray-microanalysis; older-people; falls; prevention; injury; osteoporosis; risk; malnutrition; supplements
AB The aim of this study is to establish the falsifiability of the "osteoporotic hypothesis" for hip fracture, according to which the bone density and mineral composition of bone tissue in patients with hip fracture is poorer than when no such fracture is present, and that this circumstance is relevant to the occurrence of a fracture. The study population consisted of forty patients treated with arthroplasty. Twenty patients with femoral neck fracture and another twenty with hip osteoarthritis received the same diagnostic protocol and the same antibiotic, anaesthetic, surgical and antithrombotic prophylaxis. Levels of calcium (Ca), phosphorus (P) and vitamin D in blood, amongst other values, were determined, and five samples of bone tissue from the proximal femoral metaphysis were obtained and characterised by optical microscopy and microanalytical analysis. No statistically significant differences were observed between the two groups with respect to the trabecular number, area or thickness, or inter-trabecular distance. However, there were differences in the length of the trabeculae, which was greater in the patients with hip osteoarthritis ($p = 0.002$), but not when the groups were compared by gender. When compared by age, a greater inter-trabecular distance was observed in the patients aged over 75 years ($p = 0.036$) but there were no differences in the remaining parameters. Serum levels of Ca ($p = 0.03$), P ($p < 0.01$) and vitamin D ($p < 0.01$) were lower in the fracture group. In the quantitative microanalytical analysis, no significant differences were observed in bone levels of Ca or P or in the Ca/P index, nor was there any correlation between serum and levels of bone Ca or P (Ca-0.197:$p = 0.314$;P-0.274:$p = 0.158$).Multiple linear regression revealed no correlation between the diagnoses, vitamin D and bone levels of Ca or P. Despite the reduced serum levels of Ca and P in the patients with hip fracture, no correlation was observed with bone levels of Ca and P,which were similar in both groups. There were differences in the organic bone structure, in terms of length and inter-trabecular distance. For patients with osteoporosis, treatment should be aimed at increasing the synthesis of bone trabeculae to reinforce their structure. Nevertheless, no such treatment can prevent falls, and therefore no reduction in hip fractures amongst this population can be assured. (C) 2020 Elsevier Ltd. All rights reserved.
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NR 53
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Z9 3
U1 0
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PU ELSEVIER SCI LTD
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SC General & Internal Medicine; Emergency Medicine; Orthopedics; Surgery
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Voss, Martin
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Ignatius, Anita
Fischer, Verena
TI The Role of Mast Cells in Bone Metabolism and Bone Disorders
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE mast cells; inflammation; bone disorders; osteoporosis; fracture healing
ID growth-factor-beta; necrosis-factor-alpha; human osteoclast formation; antigen-induced arthritis; colony-stimulating factor; kappa-b ligand; rheumatoid-arthritis; systemic mastocytosis; neutrophil recruitment; substance-p
AB Mast cells (MCs) are important sensor and effector cells of the immune system that are involved in many physiological and pathological conditions. Increasing evidence suggests that they also play an important role in bone metabolism and bone disorders. MCs are located in the bone marrow and secrete a wide spectrum of mediators, which can be rapidly released upon activation of mature MCs following their differentiation in mucosal or connective tissues. Many of these mediators can exert osteocatabolic effects by promoting osteoclast formation [e.g., histamine, tumor necrosis factor (TNF), interleukin-6 (IL-6)] and/or by inhibiting osteoblast activity (e.g., IL-1, TNF). By contrast, MCs could potentially act in an osteoprotective manner by stimulating osteoblasts (e.g., transforming growth factor-beta) or reducing osteoclastogenesis (e.g., IL-12, interferon-gamma). Experimental studies investigating MC functions in physiological bone turnover using MC-deficient mouse lines give contradictory results, reporting delayed or

increased bone turnover or no influence depending on the mouse model used. By contrast, the involvement of MCs in various pathological conditions affecting bone is evident. MCs may contribute to the pathogenesis of primary and secondary osteoporosis as well as inflammatory disorders, including rheumatoid arthritis and osteoarthritis, because increased numbers of MCs were found in patients suffering from these diseases. The clinical observations could be largely confirmed in experimental studies using MC-deficient mouse models, which also provide mechanistic insights. MCs also regulate bone healing after fracture by influencing the inflammatory response toward the fracture, vascularization, bone formation, and callus remodeling by osteoclasts. This review summarizes the current view and understanding of the role of MCs on bone in both physiological and pathological conditions.
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TI Notch Signaling in Skeletal Development, Homeostasis and Pathogenesis
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DT Review
DE skeletogenesis; bone; cartilage; fracture repair; osteoporosis; osteoarthritis; osteosarcoma; bone metastasis
ID causes spondylocostal dysostosis; alagille-syndrome; chondrocyte differentiation; osteoclast precursors; intracellular domain; articular-cartilage; missense mutations; synovial joint; mouse model; bone
AB Skeletal development is a complex process which requires the tight regulation of gene activation and suppression in response to local signaling pathways. Among these pathways, Notch signaling is implicated in governing cell fate determination, proliferation, differentiation and apoptosis of skeletal cells-osteoblasts, osteoclasts, osteocytes and chondrocytes. Moreover, human genetic mutations in Notch components emphasize the critical roles of Notch signaling in skeletal development and homeostasis. In this review, we focus on the physiological roles of Notch signaling in skeletogenesis, postnatal bone and cartilage homeostasis and fracture repair. We also discuss the pathological gain- and loss-of-function of Notch signaling in bone and cartilage, resulting in osteosarcoma and age-related degenerative diseases, such as osteoporosis and osteoarthritis. Understanding the physiological and pathological function of Notch signaling in skeletal tissues using animal models and human genetics will provide new insights into disease pathogenesis and offer novel approaches for the treatment of bone/cartilage diseases.
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Z9 85
U1 0
U2 22
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 2218-273X
J9 BIOMOLECULES
JI Biomolecules
PD FEB 15
PY 2020
VL 10
IS 2
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DI 10.3390/biom10020332
PG 18
WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
GA KX8QD
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PT J
AU Swank, KR
Furness, JE
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AF Swank, Katherine R.
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TI Metabolomic Profiling in the Characterization of Degenerative Bone and Joint Diseases
SO METABOLITES
LA English
DT Review
DE metabolomics; arthritis; inflammatory arthropathy; small molecule metabolite synovial fluid; arthritis biomarker
ID human synovial-fluid; rheumatoid-arthritis; knee osteoarthritis; h-1-nmr spectroscopy; metabolites; reveals; signature; subtypes
AB Osteoarthritis and inflammatory arthropathies are a cause of significant morbidity globally. New research elucidating the metabolic derangements associated with a variety of bone and joint disorders implicates various local and systemic metabolites, which further elucidate the underlying molecular mechanisms associated with these destructive disease processes. In osteoarthritis, atty acid metabolism has been implicated in disease development, both locally and systemically. Several series of rheumatoid arthritis patients have demonstrated overlapping trends related to histidine and glyceric acid, while other series showed similar results of increased cholesterol and glutamic acid. Studies comparing osteoarthritis and rheumatoid arthritis reported elevated gluconic acid and glycolytic- and tricarboxylic acid-related substrates in patients with osteoarthritis, while lysosphingolipids and cardiolipins were elevated only in patients with rheumatoid arthritis. Other bone and joint disorders, including osteonecrosis, intervertebral disc degeneration, and osteoporosis, also showed significant alterations in metabolic processes. The identification of the molecular mechanisms of osteoarthritis and inflammatory arthropathies via metabolomics-based workflows may allow for the development of new therapeutic targets to improve the quality of life in these patient populations.
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NR 47
TC 32
Z9 35
U1 2
U2 25
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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J9 METABOLITES
JI Metabolites
PD JUN 15
PY 2020
VL 10
IS 6
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DI 10.3390/metabo10060223
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WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
GA MO5PE
UT WOS:000551576900026
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Sulimani, Riad
TI Diagnosis and management of osteoporosis in postmenopausal women in Gulf Cooperation Council (GCC) countries: consensus statement of the GCC countries' osteoporosis societies under the auspices of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO)
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Osteoporosis; Consensus; Gulf Cooperation Council; Management
ID bone-mineral density; vitamin-d deficiency; practice guidelines; north-africa; middle-east; saudi; fractures; population
AB The Summary A consensus platform is provided by the experts of the Gulf Cooperation Council (GCC) countries' respective osteoporosis societies, on which specific guidelines can be developed further for regional use on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis. Introduction Guidance is provided in a Gulf Cooperation Council (GCC) country setting on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis, which is an adaptation of the European guidance by Kanis et al., jointly published by the International Osteoporosis Foundation and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). The respective osteoporosis societies of the Gulf Cooperation Council (GCC) countries assembled for a unifying consensus

on the diagnosis and management of osteoporosis in postmenopausal women for the region. Methods The Chair for Biomarkers of Chronic Diseases (CBCD) in King Saud University (KSU), Riyadh, Kingdom of Saudi Arabia (KSA), in cooperation with the Saudi Osteoporosis Society (SOS), hosted regional experts and respective leaders from different GCC osteoporosis societies, together with an adviser from the ESCEO. An assembly of experts representing the different osteoporosis societies from Saudi Arabia, the UAE, Bahrain, Oman, and Kuwait gathered on February 15-16, 2019 in Riyadh, KSA for the formulation of a general osteoporosis consensus for the region. Results The following areas were covered: diagnosis of osteoporosis and assessment of fracture risk; general and pharmacological management of osteoporosis; and hip fractures, vitamin D, recommendation on which FRAX tool to follow, and the importance of country-specific FRAX (R) and fracture liaison services for secondary fracture prevention. Conclusions A platform is provided on which specific guidelines can be developed for regional use in GCC.
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NR 43
TC 24
Z9 27
U1 0
U2 11
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 1862-3522
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J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
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DI 10.1007/s11657-020-00778-5
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WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
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PT J
AU Yu, LY
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TI DNA methylation of noncoding RNAs: new insights into osteogenesis and common bone diseases
SO STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE DNA methylation; Noncoding RNAs; Osteogenesis; Bone
ID mesenchymal stem-cells; signaling pathway; osteosarcoma; differentiation; protein; proliferation; demethylation; osteoarthritis; regeneration; pathogenesis
AB Bone diseases such as osteoarthritis, osteoporosis, and bone tumor present a severe public health problem. Osteogenic differentiation is a complex process associated with the differentiation of different cells, which could regulate transcription factors, cytokines, many signaling pathways, noncoding RNAs (ncRNAs), and epigenetic modulation. DNA methylation is a kind of stable epigenetic alterations in CpG islands without DNA sequence changes and is involved in cancer and other diseases, including bone development and homeostasis. ncRNAs can perform their crucial biological functions at the RNA level, and many findings have demonstrated essential functions of ncRNAs in osteogenic differentiation. In this review, we highlight current researches in DNA methylation of two relevant ncRNAs, including microRNAs and long noncoding RNAs, in the initiation and progression of osteogenesis and bone diseases.
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TI Serum concentrations of pesticides including organophosphates, pyrethroids and neonicotinoids in a population with osteoarthritis in Saudi Arabia
SO SCIENCE OF THE TOTAL ENVIRONMENT
LA English
DT Article
DE Organophosphate; Pyrethroid; Neonicotinoid; Metabolite; Biomonitoring
ID urinary concentrations; exposure assessment; dietary exposure; metabolites; insecticides; children; epidemiology; herbicides; health
AB Human exposure to pesticides is widespread and has received much attention in recent years because of its link to adverse health outcomes. Measurement of urinary concentrations of pesticides and their metabolites is often used in the assessment of body burdens of these chemicals. However, pesticides and their metabolites can be present in blood circulatory system, although little is known on serum levels of pesticides. In this study, we aimed to examine the occurrence and profile of four organophosphate (OP), five pyrethroid (PYR) insecticides, two phenoxy acid (PA) herbicides, 14 neonicotinoid (neonic) insecticides and six dialkylphosphate metabolites in serum from 25 individuals diagnosed with osteoarthritis in Jeddah, Saudi Arabia. 2-Isopropyl-4-methyl-6-hydroxypyrimidine (IMPY), 3,5,6-trichloro-2-pyridinol (TCPY), 2,4-dichlorophenoxyacetic acid, 2,4,5-trichlorophenoxyacetic acid, 3-phenoxybenzoic acid, N-desmethyl acetamiprid, dimethylphosphate (DMP) and dimethylthiophosphate (DMTP) were detected in >= 80% of the serum samples analyzed. Metabolites of OPs, DMTP (median concentration: 2.14 ng/mL), DMP (1.04 ng/mL) and TCPY (0.84 ng/mL), collectively accounted for 67-83% of the total serum pesticide concentrations. Serum concentrations of pesticides were similar to or lower than those reported in urine. Our preliminary evidence suggests that serum can be used as a matrix for the assessment of exposure to OPs, PYRs, PAs and neonics. (C) 2020 Elsevier B.V. All rights reserved.
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TI Influence of Extracellular Vesicles Isolated From Osteoblasts of Patients With Cox-Arthrosis and/or Osteoporosis on Metabolism and Osteogenic Differentiation of BMSCs
SO FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY
LA English
DT Article
DE extracellular vesicles; mesenchymal stem cells; osteoblasts; osteoarthritis; osteoporosis; EVs; osteogenic differentiation
ID mesenchymal stem-cells; estrogen deficiency; exosm; osteoarthritis; proliferation; epidemiology; apoptosis; culture; repair; rna
AB Background: Studies with extracellular vesicles (EVs), including exosomes, isolated from mesenchymal stem cells (MSC) indicate benefits for the treatment of musculoskeletal pathologies as osteoarthritis (OA) and osteoporosis (OP). However, little is known about intercellular effects of EVs derived from pathologically altered cells that might influence the outcome by counteracting effects from "healthy" MSC derived EVs. We hypothesize, that EVs isolated from osteoblasts of patients with hip OA (coxarthrosis/CA), osteoporosis (OP), or a combination of both (CA/OP) might negatively affect metabolism and osteogenic differentiation of bone-marrow derived (B)MSCs. Methods: Osteoblasts, isolated from bone explants of CA, OP, and CA/OP patients, were compared regarding growth, viability, and osteogenic differentiation capacity. Structural features of bone explants were analyzed via mu CT. EVs were isolated from supernatant of naive BMSCs and CA, OP, and CA/OP osteoblasts (osteogenic culture for 35 days). BMSC cultures were stimulated with EVs and subsequently, cell metabolism, osteogenic marker gene expression, and osteogenic differentiation were analyzed. Results: Trabecular bone structure was

different between the three groups with lowest number and highest separation in the CA/OP group. Viability and Alizarin red staining increased over culture time in CA/OP osteoblasts whereas growth of osteoblasts was comparable. Alizarin red staining was by trend higher in CA compared to OP osteoblasts after 35 days and ALP activity was higher after 28 and 35 days. Stimulation of BMSC cultures with CA, OP, and CA/OP EVs did not affect proliferation but increased caspase 3/7-activity compared to unstimulated BMSCs. BMSC viability was reduced after stimulation with CA and CA/OP EVs compared to unstimulated BMSCs or stimulation with OP EVs. ALP gene expression and activity were reduced in BMSCs after stimulation with CA, OP, and CA/OP EVs. Stimulation of BMSCs with CA EVs reduced Alizarin Red staining by trend. Conclusion: Stimulation of BMSCs with EVs isolated from CA, OP, and CA/OP osteoblasts had mostly catabolic effects on cell metabolism and osteogenic differentiation irrespective of donor pathology and reflect the impact of tissue microenvironment on cell metabolism. These catabolic effects are important for understanding differences in effects of EVs on target tissues/cells when harnessing them as therapeutic drugs.
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TI Chronic pain and use of analgesics in the elderly: a nationwide population-based study
SO ARCHIVES OF MEDICAL SCIENCE
LA English

DT Article
DE acetaminophen; chronic pain; elderly; geriatric; non-steroidal anti-inflammatory drugs
ID term mortality risk; geriatric-patients; spinal-disorders; management; osteoarthritis; prevalence; arthritis; taiwan; age
AB Introduction: Chronic pain may cause many comorbidities in the elderly; however, nationwide data about this issue remain insufficient. We conducted this study to address the data gap. Material and methods: We identified geriatric participants (>= 65 years) with chronic pain between 2000 and 2013 from the Taiwan National Health Insurance Research Database. The causes of chronic pain and use of analgesics between two sexes and among three age subgroups were compared. Results: A total of 21,018 participants were identified with the mean age (standard deviation) of 72.7 years (5.6) and the female percentage of 50.8%. The prevalence of chronic pain in the elderly was 21.5%, and it was higher in the females than males. The proportions of each age subgroup were 65-74 (66.8%), 75-84 (29.4%), and >= 85 years (3.8%). Common causes of chronic pain were osteoarthritis (21.9%), spinal disorders (19.0%), peripheral vascular diseases (12.4%), and osteoporosis (11.4%). Non-steroidal anti-inflammatory drugs were the most common medication, followed by acetaminophen and opioids. The most commonly used opioid was morphine. The use of opioids increased with age. Conclusions: This study delineated the causes of chronic pain and use of analgesics in a geriatric population, which may help further studies about this issue in the future.
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TI Bisphosphonate Use Is Protective of Radiographic Knee Osteoarthritis Progression Among those With Low Disease Severity and Being Non-Overweight: Data From the Osteoarthritis Initiative
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE ANTIRESORPTIVES; BONE HISTOMORPHOMETRY; FRACTURE RISK ASSESSMENT; OSTEOARTHRITIS; OSTEOPOROSIS
ID bone-marrow lesions; subchondral bone; intraarticular clodronate; hip osteoarthritis; osteoporosis; fracture; association; adherence; symptoms; turnover
AB Antiresorptive medications have been explored for treating knee osteoarthritis (OA); however, little data exist on the effects of today's more potent nitrogen-containing oral bisphosphonates on radiographic disease-progression in patients with varying disease-severity, especially those who are not overweight. The primary objective of this cohort study was to determine if the use of bisphosphonates is protective against 2-year radiographic-progression of knee OA in Osteoarthritis Initiative (OAI) participants, stratified by baseline radiographic disease status. Secondary objectives were to examine effects in non-overweight participants (body mass index [BMI] < 25 kg/m(2)) and cumulative bisphosphonate exposure effects. We identified female OAI participants aged >= 50 years and excluded those missing baseline radiograph readings, bisphosphonate use information, or all clinical questionnaire information at baseline. Participants reporting bisphosphonate use (69% alendronate) were propensity-matched 1:1 to non-bisphosphonate users and followed until first radiographic knee OA progression (1-unit increase in Kellgren and Lawrence [KL] grade) or data were censored (first missed visit or end of 2-year follow-up). Discrete-time logistic regression models estimated hazard ratios (HRs) between bisphosphonate users versus nonusers, with an interaction term for baseline KL grade (KL <2 or KL >= 2). We identified 1977 eligible women (n= 346 bisphosphonate users). Propensity-matched results indicated that bisphosphonate users with KL grade <2 were protected against progression (HR(KL<2)0.53; 95% CI, 0.35 to 0.79), while bisphosphonate use was not associated with radiographic progression in those with KL grade >= 2 (HR(KL >= 2)1.06; 95% CI, 0.83 to 1.35). When restricting analyses to those with BMI <25 kg/m(2), effects were strengthened (HR(KL<2)0.49 [95% CI, 0.26 to 0.92]; HR(KL >= 2)0.69 [95% CI, 0.33 to 1.26]). Duration of bisphosphonate use had no effect on progression, though sample size was limited. Bisphosphonate therapy may be protective against radiographic knee OA progression in early-stage patients, particularly those who are non-overweight, but less so for those with more advanced disease or more weight-bearing joint stress.
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Park, Ki-Soo
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TI Association of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) with Muscle Strength in Community-Dwelling Elderly with Knee Osteoarthritis
SO INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH
LA English
DT Article
DE muscle strength; WOMAC; osteoarthritis
ID body-composition; physical-activity; risk-factor; weakness; pain; incident; healthy; women; life
AB Purpose: The purpose of this study was to evaluate the correlation between muscle strength and knee symptoms (pain, stiffness, and functional limitation) regardless of the presence of radiologic knee osteoarthritis (RKOA) in community-dwelling elderly. Patients and methods: This cross-sectional study used data from the Namgaram-2 cohort. The Namgaram-2 cohort consisted of participants living in three rural communities. Such participants were included for studies on activity limitation due to age-related musculoskeletal disorders including knee osteoarthritis, osteoporosis, and sarcopenia. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), a health assessment tool for patients with arthritis in lower extremities, was used to assess health-related quality of life (HRQOL). Muscle strengths were measured by knee strength (by using the isokinetic dynamometer) and hand grip strength. Results: The WOMAC pain of Kallgren-Lawrence (K/L) grade < 2 was correlated with age, grip strength, nutrition status, and knee extension 180 peak torque. The WOMAC pain of K/L grade <greater than or equal to> 2 was correlated with age, nutrition status, and knee extension 60 peak torque. The WOMAC stiffness of K/L grade < 2 was correlated with having a spouse, nutrition status, and knee extension 60 peak torque. The WOMAC stiffness of K/L grade <greater than or equal to> 2 was correlated with knee extension 60 peak torque. The WOMAC function of K/L grade < 2 was correlated with age, grip strength, osteoporosis, nutrition status, and knee extension 180 peak torque. The WOMAC function of K/L grade <greater than or equal to> 2 was correlated with age, nutrition status, and knee extension 60 peak torque. Conclusion: Muscle strength as measured by grip strength and knee extension was statistically significantly correlated with the WOMAC scores in patients with knee symptoms regardless of whether radiologic signs of knee osteoarthritis were observed.
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U2 6
PU MDPI
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TI Longitudinal changes in bone mineral density and trabecular bone score in Korean adults: a community-based prospective study
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Osteoporosis; Natural history; Bone mineral density; Aging
ID lumbar spine; risk-factors; elderly-men; osteoporosis; age; association; women; tbs; osteoarthritis; population
AB The bone mineral densities (BMDs) of the femoral neck and total hip, and the lumbar spine trabecular bone score (TBS), tended to decrease with age in both men and women, whereas the lumbar spine BMD tended to increase. Lumbar spine BMD is thus inappropriate for evaluating longitudinal changes in bone loss; the lumbar spine TBS is an alternative measure. Purpose Aging is associated with a decrease in bone mass and quality. This community-based prospective cohort study investigated longitudinal changes in bone phenotype in Korean adults. Methods We analyzed data from a prospective community-based cohort study, the Korean Genome and Epidemiology Study. Postmenopausal women and men who underwent dual-energy X-ray absorptiometry at least twice from 2007 to 2014 were included. Longitudinal changes in bone mineral density (BMD) and trabecular bone score (TBS) over 6 years were analyzed by sex, age, and body mass index. Results A total of 1895 subjects were enrolled (men 965; postmenopausal women 929). The femoral neck (FN) BMD, total hip (TH) BMD, and lumbar spine (LS) TBS decreased significantly over time, but the LS BMD increased significantly. In men, the average annual changes were 0.3% in LS BMD ($p < 0.001$), - 0.33% in FN BMD ($p < 0.001$), - 0.26% in TH BMD ($p = 0.001$), and - 0.27% in LS TBS ($p < 0.001$). In women, the average annual changes were 0.27% in LS BMD ($p < 0.001$), - 0.67% in FN BMD ($p < 0.001$), - 0.66% in TH BMD ($p < 0.001$), and - 0.27% in LS TBS ($p < 0.001$). The longitudinal decrease in TH BMD over time was significantly greater in women (versus men) and those who were older (versus younger). Conclusion The

FN and TH BMDs decreased with aging. But, the LS BMD was inappropriate to evaluate longitudinal changes of bone loss. The LS TBS could be alterative.
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NR 27
TC 6
Z9 6
U1 0
U2 2
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JI Arch. Osteoporos.
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TI Arthroscopic ankle fusion only has a limited advantage over the open operation if osseous operation type is the same: a retrospective comparative study
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Arthroscopic ankle fusion; Open ankle fusion; Selection bias; Follow-up; Questionnaire survey
ID avascular necrosis; arthrodesis; expectations; arthritis; osteoarthritis; replacement; fixation; outcm; hindfoot; risk
AB Background A great deal of research suggests that arthroscopic ankle fusion (AAF) has advantages over open ankle fusion (OAF), but these outcomes would be imprecise because of a selection bias. The purpose of this study is to verify which is better for ankle fusion, AAF or OAF. We regrouped the OAF group into two subgroups according to whether the osseous operation type is the same as AAF group. The goal is to minimize the impact of disease severity, thereby reducing selection bias to some extent. Methods We retrospectively analyzed the data of ankle fusion in our hospital between July 2015 and October 2018. Forty-three patients were enrolled and divided into AAF group (n = 17) and OAF group (n = 26). In order to eliminate selection bias, we divided OAF group into complex osseous operation subgroup (COO subgroup) (n = 15) and simple osseous operation subgroup (SOO subgroup) (n = 11). The osseous operation type of SOO subgroup is the same as AAF group. Then, we compared the differences between these groups. All patients were followed up at least 1 year after operation. We analyzed data, including etiology composition, surgical time, intra-op blood loss, reduction of albumin, total hospital stays, union time, fusion situation, complications, radiological examination, functional score, and questionnaire survey. Then we performed statistical analyses. Results We found that the etiological components of AAF group and OAF group were different; the etiological components of AAF group and SOO subgroup were similar. We found that AAF

group has advantages over OAF group and COO subgroup in general. However, except in terms of surgical trauma, hospital stays, and short-term complications occurred, the AAF group has not obvious advantages over SOO subgroup, including intra-op blood loss, fusion condition, postoperative function score, and postoperative patient satisfaction; and AAF group need more surgical time than the SOO subgroup. Conclusions The arthroscopic ankle fusion can bring a good curative effect; however, if the osseous operation type is the same, the arthroscopic ankle fusion only has a limited advantage over the traditional open operation in perioperative soft tissue protection and enhanced recovery after surgery.
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TI Long Noncoding RNAs as Bone Marrow Stem Cell Regulators in Osteoporosis
SO DNA AND CELL BIOLOGY
LA English
DT Article
DE mesenchymal stem cells; epigenetics; noncoding RNA; gene expression; osteoporosis
ID expression; tophat; gene
AB Long noncoding RNAs (lncRNAs) contribute toward regulating gene expression and cell differentiation and may be involved in the pathogenesis of several diseases. The objective of this study was to determine the expression patterns of lncRNAs in bone marrow mesenchymal stem cells (BMSCs) derived from patients with osteoporotic fractures and their relevance to osteogenic function. The BMSCs were isolated from the femoral head of patients with hip fractures (FRX) and controls with osteoarthritis (OA). We found 74 differentially expressed genes between FRX and OA, of which 33 were of the lncRNA type. Among them, 52 genes (20 lncRNAs) were replicated in another independent dataset. The differentially expressed lncRNAs were over-represented among those correlated with differentially expressed protein-coding genes. In addition, the comparison of pre- and post-differentiated paired samples revealed 163 differentially expressed genes, of which 99 were of the lncRNA type. Among them, the overexpression ofLINC00341induced an upregulation of typical osteoblastic genes. In conclusion, the analysis of lncRNA expression in BMSCs shows specific patterns in patients with osteoporotic fractures, as well as changes associated with osteogenic differentiation. The regulation of bone genes through lncRNAs might bring new opportunities for designing bone anabolic therapies in systemic and localized bone disorders.
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TI Association of Tramadol Use With Risk of Hip Fracture
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE COHORT; FRACTURE; TRAMADOL
ID initiated opioid treatment; fall-related injury; trends; osteoporosis; management; recommendations; osteoarthritis; prescription; pharmacology; cohort
AB Several professional organizations have recommended tramadol as one of the first-line or second-line therapies for patients with chronic noncancer pain and its prescription has been increasing rapidly worldwide; however, the safety profile of tramadol, such as risk of fracture, remains unclear. This study aimed to examine the association of tramadol with risk of hip fracture. Among individuals age 50 years or older without a history of hip fracture, cancer, or opioid use disorder in The Health Improvement Network (THIN) database in the United Kingdom general practice (2000-2017), five sequential propensity score-matched cohort studies were assembled, ie, participants who initiated tramadol or those who initiated one of the following medications: codeine (n = 146,956) (another commonly used weak opioid), naproxen (n = 115,109) or ibuprofen (n = 107,438) (commonly used nonselective nonsteroidal anti-inflammatory drugs [NSAIDs]), celecoxib (n = 43,130), or etoricoxib (n = 27,689) (cyclooxygenase-2 inhibitors). The outcome was incident hip fracture over 1 year. After propensity-score matching, the included participants had a mean age of 65.7 years and 56.9% were women. During the 1-year follow-up, 518 hip fracture (3.7/1000 person-years) occurred in the tramadol cohort and 401 (2.9/1000 person-years) occurred in the codeine cohort. Compared with codeine, hazard ratio (HR) of hip fracture for tramadol was 1.28 (95% confidence interval [CI] 1.13 to 1.46). Risk of hip fracture was also higher in the tramadol cohort than in the naproxen (2.9/1000 person-years for tramadol, 1.7/1000 person-years for naproxen; HR = 1.69, 95% CI 1.41 to 2.03), ibuprofen (3.4/1000 person-years for tramadol, 2.0/1000 person-years for ibuprofen; HR = 1.65, 95% CI 1.39 to 1.96), celecoxib (3.4/1000 person-years for tramadol, 1.8/1000 person-years for celecoxib; HR = 1.85, 95% CI 1.40 to 2.44), or etoricoxib (2.9/1000 person-years for tramadol, 1.5/1000 person-years for etoricoxib; HR = 1.96, 95% CI 1.34 to 2.87) cohort. In this population-based cohort study, the initiation of tramadol was associated with a higher risk of hip fracture than initiation of codeine and commonly used NSAIDs, suggesting a need to revisit several guidelines on tramadol use in clinical practice. (c) 2020 American Society for Bone and Mineral Research.
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TI Cycloastragenol prevents age-related bone loss: Evidence in D-galactose-treated and aged rats
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Cycloastragenol; Aging; Osteoporosis; Osteoactivin
ID formation in-vivo; osteoblast differentiation; enhances bone; osteoporosis; metabolism; activation; resorption; toxicity; mutation; disease
AB Background and aims: Aging-induced bone loss is a multifactorial, age-related, and progressive phenomenon among the general population and may further progress to osteoporosis and increase the risk of fractures. Cycloastragenol (CAG), currently the only compound reported that activates human telomerase, is thought to be able to alleviate or delay the symptoms of aging and chronic diseases. Previous research has suggested that CAG may have the potential to alleviate age-related bone loss. However, to date, no research has specifically focused on this aspect. In this study, we aimed to investigate whether CAG could prevent senile osteoporosis, and further reveal its underlying mechanism. Methods: CAG treatment was administrated into two bone loss rat models (D-galactose administration and aging) for 20 weeks and 33 weeks, respectively. Serum biomarkers analyses, bone biomechanical tests, microcomputed tomography assessment, and bone histomorphometry analyses were performed on the bone samples collected at the endpoint, to determine whether CAG could prevent or alleviate age-related bone loss. Proteomic analysis was performed to reveal the

changes in protein profiles of the bones, and western blot was used to further verify the identity of the key proteins. The viability, osteoblastic differentiation, and mineralization of MC3T3-E1 cells were also evaluated after CAG treatment in vitro. Results: The results suggest that CAG treatment improves bone formation, reduces osteoclast number, alleviates the degradation of bone microstructure, and enhances bone biomechanical properties in both n-galactose- and aging-induced bone loss models. CAG treatment promotes viability, osteoblastic differentiation, and mineralization in MC3T3-E1 cells. Proteomic and western blot analyses revealed that CAG treatment increases osteoactivin (OA) expression to alleviate bone loss. Conclusion: The results revealed that CAG alleviates age-related bone loss and improves bone microstructure and biomechanical properties. This may due to CAG-induced increase in OA expression. In addition, the results support preclinical investigations of CAG as a potential therapeutic medicine for the treatment of senile osteoporosis.
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WC Medicine, Research & Experimental; Pharmacology & Pharmacy
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PT J
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Fu, YH
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AF Lei, Jinlai
Fu, Yahui
Zhuang, Yan
Zhang, Kun
TI Sema4D Aggravated LPS-Induced Injury via Activation of the MAPK Signaling Pathway in ATDC5 Chondrocytes

SO BIOMED RESEARCH INTERNATIONAL
LA English
DT Article
ID nf-kappa-b; semaphorin 4d; mouse model; osteoarthritis; expression; cell; pathogenesis; inflammation; suppression; roles
AB Osteoarthritis (OA) is the most common chronic degenerative joint disease, and it remains the main cause of chronic disability in elderly individuals. Sema4D (semaphorin 4D) is involved in the immune system and related to bone injury, osteoporosis, osteoblast differentiation, and rheumatoid arthritis. However, the role of Sema4D in OA remains unclear. Hence, the LPS-stimulated chondrocyte cell injury model was constructed in this study to investigate the role of Sema4D in OA development. The results showed that Sema4D was increased in LPS-treated ATDC5 cells, and the knockdown of Sema4D suppressed the decline of cell viability, the increase of cell apoptosis, and the increase of IL-6, IL-1 beta, and TNF-alpha secretion in ATDC5 cells induced by LPS. Meanwhile, Sema4D overexpression aggravated the cell injury triggered by LPS, and inhibiting Plexin B1 partly abolished the effect of Sema4D overexpression on LPS-induced chondrocyte injury. Furthermore, silencing of Sema4D blocked the activation of the MAPK pathway in LPS-stimulated ATDC5 cells. Enhanced Sema4D promoted the activation of the MAPK pathway in LPS-stimulated ATDC5 cells. What is more, inhibiting the MAPK signaling pathway abolished the promoting effect of Sema4D overexpression on LPS-induced chondrocyte injury. Therefore, our study suggested that the knockdown of Sema4D protects ATDC5 cells against LPS-induced injury through inactivation of the MAPK signaling pathway via interacting with Plexin B1.
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TC 18
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PU HINDAWI LTD
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SC Biotechnology & Applied Microbiology; Research & Experimental Medicine
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TI Differences in subchondral trabecular bone microstructure and finite element analysis-based biomechanical properties between osteoporosis and osteoarthritis
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Article
DE Finite element analysis; Individual trabecular segmentation; Mechanical property; Osteoarthritis; Osteoporosis
ID (its)-based morphological analysis; hip osteoarthritis; cancellous bone; femoral-head; cartilage histopathology; postmenopausal women; biochemical markers; articular-cartilage; elastic-modulus; microarchitecture
AB Background/Objective: The microstructure of the subchondral trabecular bone, including the composition and distribution of plates and rods, has an important influence on the disease progression and mechanical properties of osteoarthritis (OA) and osteoporosis (OP). We aimed to determine whether differences in plates and rods influence the variations in the quantities and qualifies of the subchondral trabecular bone between OA and OP. Materials and methods: Thirty-eight femoral head samples [OA, n = 13; OP, n = 17; normal control (NC), n = 8] were collected from male patients undergoing total hip arthroplasty. They were scanned using microcomputed tomography, and subchondral trabecular structures were analysed using individual trabecular segmentation. Micro-finite element analysis (mu FEA) was applied to assess the mechanical property of the trabecular bone. Cartilage changes were evaluated by using histological assessment. Analysis of variance was used to compare intergroup differences in structural and mechanical properties and cartilage degradation. Pearson analysis was used to evaluate the relationship between the trabecula microstructure and biomechanical properties. Results: Compared with the OP and NC group, there was serious cartilage damage in the OA group. With respect to the microstructure results, the OA group had the highest plate and rod trabecular microstructures including number and junction density among the three groups. For the mechanical properties detected via mu FEA, the OA group had higher stiffness and failure load than did the OP group. Pearson analysis revealed that compared with OP, OA had a higher number of microstructure parameters (e.g., rod bone volume fraction and rod trabecular number) that were positively correlated with its mechanical property. Conclusions: Compared with OP, the OA subchondral bone has both increased plate and rod microarchitecture and has more microstructures positively related with its mechanical property. These differences may help explain the variation in mechanical properties between these bone diseases. The translational potential of this article: Our findings suggested that changes in the plates and rods of the subchondral trabecular bone play a critical role in OA and OP progression and that the improvement of the subchondral trabecular bone may be a promising treatment approach.
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TI Dielectric characterization of diseased human trabecular bones at microwave frequency
SO MEDICAL ENGINEERING & PHYSICS
LA English
DT Article
DE Dielectric properties; Bone volume fraction; Osteoporosis; Osteoarthritis; Open-ended coaxial probe

ID mechanical-property; interrelationships; osteoporosis; density; tissue; systems
AB The objective of this study is to determine whether in vitro dielectric properties of human trabecular bones, can distinguish between osteoporotic and osteoarthritis patients' bone samples. Specifically this study enlightens intra-patient variation of trabecular bone microarchitecture and dielectric properties, inter-disease comparison of bone dielectric properties, and finally establishes the correlation to traditional bone histomorphometry parameter (bone volume fraction) for diseased bone tissue. Bone cores were obtained from osteoporotic and osteoarthritis patients (n = 12). These were scanned using microCT to examine bone volume fraction. An open-ended coaxial probe measurement technique was employed to measure dielectric properties over the 0.5 - 8.5 GHz frequency range. The dielectric properties of osteoarthritis patients are significantly higher than osteoporotic patients; with an increase of 41% and 45% for relative permittivity and conductivity respectively. The dielectric properties within each patient vary significantly, variation in relative permittivity and conductivity was found to be greater than 25% and 1.4% respectively. A weak correlation (r = 0.5) is observed between relative permittivity and bone volume fraction. Osteoporotic and osteoarthritis bones can be differentiated based on difference of dielectric properties. Although these do not correlate strongly to bone volume fraction, it should be noted that bone volume fraction is a poor predictor of fracture risk. The dielectric properties of bones are found to be influenced by mineralization levels of bones. Therefore, dielectric properties of bones may have potential as a diagnostic measure of osteoporosis. (C) 2020 IPEM. Published by Elsevier Ltd. All rights reserved.
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PT J
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TI Peri-prosthetic bone mineral density after simultaneous bilateral total knee arthroplasty under oral bisphosphonate therapy - A comparison between mobile- and fixed-bearing prostheses
SO KNEE
LA English
DT Article
DE Bone mineral density; Total knee arthroplasty; Bisphosphonate; Fixed-bearing; Mobile-bearing
ID prevents periprosthetic loss; follow-up; porous tantalum; japanese patients; trabecular bone; proximal tibia; alendronate; osteoporosis; replacement; component
AB Background: Peri-prosthetic bone mineral density (BMD) decreases after total knee arthroplasty (TKA). We aimed to specifically compare peri-prosthetic BMD changes between mobile- and fixed-bearing prostheses in patients undergoing oral bisphosphonate therapy, hypothesizing that mobile-bearing components would have a favorable effect on postoperative peri-prosthetic BMD. Methods: This prospective cohort study investigated 30 patients who underwent simultaneous bilateral TKA for primary knee osteoarthritis between December 2007 and September 2012. All patients underwent mobile-bearing TKA in one knee and

fixed-bearing TKA in the other and received oral alendronate therapy at a dosage of 35 mg/week. Peri-prosthetic and lumbar spine BMDs were measured using dual X-ray absorptiometry scans, with ped-prosthetic BMD changes being compared between the two prostheses in each patient at six months and one, two, three, and five years post-operation. Results: Clinical results did not significantly differ between two prostheses. Relative change of lumbar spine BMD was significantly greater at five years post-operation than at one year post-operation (p=0.01), and was significantly correlated at five years post-operation with peri-prosthetic BMD in the central femur (r=0.39, p=0.002), posterior femur (r = 0.39, p=0.002), and medial tibia (r = 0.42, p=0.007). Conclusions: There was no difference in peri-prosthetic BMD changes between two prostheses in patients undergoing oral bisphosphonate therapy. Our results suggest that the influence of oral bisphosphonate therapy might offset the influence of prosthetic design. Thus, oral bisphosphonate therapy may be more effective than prosthetic design selection in preventing post-TKA peri-prosthetic BMD loss. (C) 2020 Elsevier B.V. All rights reserved.
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TI Differences between muscle from osteoporotic and osteoarthritic subjects: in vitro study by diffusion-tensor MRI and histological findings
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Osteoporosis; Osteoarthritis; Skeletal muscle; IMCL; DTI
ID marrow fat-content; skeletal-muscle; cancellous bone; sarcopenia; atrophy; women; diagnosis; risk; pain; size
AB Background Osteoarthritis and osteoporosis are strongly coupled with

alterations of muscles quality and fats metabolism. However, there are no studies for investigating possible differences between osteoporotic and osteoarthritic muscles. Understanding muscle-bone and muscle-cartilage interactions would be of high clinical value. Aim Investigate potential microstructural and physiological differences between osteoporotic and osteoarthritic muscles by diffusion Nuclear Magnetic Resonance (NMR) imaging (diffusion MRI) and histological findings. Methods Vastus-lateralis muscles excised from osteoporotic (n = 26, T Score < - 2.5, Kellgren-Lawrence <= 2) and osteoarthritic (n = 26, T Score > - 2.5, Kellgren--Lawrence 3 and 4) age-matched women were investigated by NMR relaxometry, diffusion-tensor imaging (DTI) at 9.4 T, and histological techniques. Intramyocellular (IMCL) and extramyocellular (EMCL) lipid were quantified. The percentage and mean diameters of fibers I and II were evaluated. Relationship between mean diffusivity (MD), fractional anisotropy (FA), the DTI eigenvalues (lambda(1), lambda(2), lambda(3)), histological findings in muscles and clinical data (Kellgren-Lawrence and T score, age, menopausal age, body mass index) were studied. Pairwise comparisons between groups were made using one-way analysis of variance and correlation between variables was assessed with linear correlation analysis (Pearson's r coefficient). Results Osteoporotic muscles showed higher MD, lambda(1,)lambda(2), lambda(3) compared to osteoarthritis ones. This is explainable with a significant higher density of IMCL droplets found inside the osteoarthritic muscles and a large amount of fibrotic tissue and IMCL infiltration between fibers, i.e. in endomysium and perimysium that lead to a more hindered diffusion. Furthermore, histological analysis suggests mitochondrial degeneration as the origin of the greatest amount of IMCL droplets in osteoarthritic muscles. Conclusion This work highlights differences between muscles of osteoporotic and osteoarthritic subjects that can be quantified by NMR DTI investigations.
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TI The role of sphingosine 1-phosphate metabolism in bone and joint pathologies and ectopic calcification
SO BONE
LA English
DT Review
DE Sphingosine 1-phosphate; Sphingosine kinases; Arthritis; Spondyloarthritis; Osteoporosis
ID advanced atherosclerotic lesions; molecular-cloning; functional-characterization; media calcification; oral fingolimod; cancer cells; sphingosine-1-phosphate; kinase; fty720; receptor
AB Sphingolipids display important functions in various pathologies such as cancer, obesity, diabetes, cardiovascular or neurodegenerative diseases. Sphingosine, sphingosine 1-phosphate (SIP), and ceramide are the central molecules of sphingolipid metabolism. Sphingosine kinases 1 and 2 (SKi and SK2) catalyze the conversion of the sphingolipid metabolite sphingosine into S1P. The balance between the levels of SIP and its metabolic precursors ceramide and sphingosine has been considered as a switch that could determine whether a cell proliferates or

dies. This balance, also called "sphingolipid rheostat", is mainly under the control of SKs. Several studies have recently pointed out the contribution of SK/S1P metabolic pathway in skeletal development, mineralization and bone homeostasis. Indeed, SK/S1P metabolism participates in different diseases including rheumatoid arthritis, spondyloarthritis, osteoarthritis, osteoporosis, cancer-derived bone metastasis or calcification disorders as vascular calcification. In this review, we will summarize the most important data regarding the implication of SK/S1P axis in bone and joint diseases and ectopic calcification, and discuss the therapeutic potential of targeting SK/S1P metabolism for the treatment of these pathologies.
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Z9 21
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TI Risk factors for secondary displacement in conservatively treated proximal humeral fractures INTRODUCING TWO NEW RADIOLOGICAL PREDICTORS
SO BONE & JOINT JOURNAL
LA English
DT Article
ID local bone quality; nonoperative treatment; internal-fixation; elderly-patients; open reduction; surgery; classification; epidemiology; arthroplasty
AB Aims Conservative treatment of moderately displaced proximal humeral head fractures yields good clinical results, but secondary fragment displacement may occur. Identification of those fractures at risk of displacement may influence initial decision-making. Methods A total of 163 shoulders in 162 patients with conservatively treated isolated proximal humeral fractures were included. The fractures occurred between January 2015 and May 2018. The mean age of the patients was 69 years (26 to 100) and the mean follow-up was 144 days (42 to 779). The fractures were classified according to Neer. Scores for osteoporosis (Tingart, Deltoid Tuberosity Index (DTI)) and osteoarthritis (OA) of the glenohumeral joint were assessed. Translation of the head on follow-up radiographs of more than 10 mm was defined as displacement. Eccentric head index (EHI) describes the offset of the humeral head centre in relation to the diaphyseal axis. The ratio was estimated on anteroposterior (AP) and Neer views. Medial hinge was considered intact if the medial cortex proximal and distal to the fracture was in line on AP view. Results Secondary fracture displacement occurred in 41 patients (25.2%). Clinical risk factors were alcohol abuse (odds ratio (OR) 6.8; 95% confidence interval (CI) 1.3 to 36; p = 0.025) and previously diagnosed osteoporosis (OR 4.6; 95% CI 0.6 to 34; p = 0.136). Age (OR 1.1; 95% CI 1.0 to 1.1; p = 0.003) and sex (OR 0.9; 95% CI 0.3 to 2.8; p = 0.867) were not independent factors. Radiological risk factors were OA grade 3 (OR 16.4; 95% CI 0.25 to 37.6; p = 0.107) and osteoporosis with the DTI (OR 10; 95% CI 0.8 to 250; p = 0.031) being more predictive than the Tingart score (OR 2.3; 95% CI 0.8 to 4.7; p = 0.041). A high EHI (AP/Neer > 0.4, OR 18.9; 95% CI 2.1 to 30.9/3.0; 95% CI 1.1 to 8.0; p = 0.002/p = 0.033) and a disrupted medial hinge (OR 3.7; 95% CI 1.1 to 12.6; p = 0.039) increased the risk of secondary displacement significantly. Neer classification had no influence. Conclusion During conservative treatment, a quarter of patients showed secondary fracture displacement of at least 10 mm. Patients with alcohol abuse, severe OA, and osteoporosis are at risk. Newly defined EHI and disrupted medial hinge are relevant predictors for secondary displacement.
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AF Faldini, C.
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TI A new ligament-compatible patient-specific 3D-printed implant and instrumentation for total ankle arthroplasty: from biomechanical studies to clinical cases
SO JOURNAL OF ORTHOPAEDICS AND TRAUMATOLOGY
LA English
DT Article
DE Custom-made implant; 3D-printing; Total ankle arthroplasty; Total ankle replacement; PSI; Surgical treatment
ID posttraumatic osteoarthritis; replacement; design; accuracy; rates
AB Background Computer navigation and patient-specific instrumentation for total ankle arthroplasty have still to demonstrate their theoretical ability to improve implant positioning and functional outcomes. The purpose of this paper is to present a new and complete total ankle arthroplasty customization process for severe posttraumatic ankle joint arthritis, consisting of patient-specific 3D-printed implant and instrumentation, starting from a ligament-compatible design. Case presentation The new customization process was proposed in a 57-year-old male patient and involved image analysis, joint modeling, prosthesis design, patient-specific implant and instrumentation development, relevant prototyping, manufacturing, and implantation. Images obtained from a CT scan were processed for a 3D model of the ankle, and the BOX ankle prosthesis (MatOrtho, UK) geometries were customized to best fit the model. Virtual in silico, i.e., at the computer, implantation was performed to optimize positioning of these components. Corresponding patient-specific cutting guides for bone preparation were designed. The obtained models were printed in ABS by additive manufacturing for a final check. Once the planning procedure was approved, the models were sent to final state-of-the-art additive manufacturing (the metal components using cobalt-chromium-molybdenum powders, and the guides using polyamide). The custom-made prosthesis was then implanted using the cutting guides. The design, manufacturing, and implantation procedures were completed successfully and consistently, and final dimensions and location for the implant corresponded with the preoperative plan. Immediate post-op X-rays showed good

implant positioning and alignment. After 4 months, clinical scores and functional abilities were excellent. Gait analysis showed satisfactory joint moment at the ankle complex and muscle activation timing within normality. Conclusions The complete customization process for total ankle arthroplasty provided accurate and reliable implant positioning, with satisfactory short-term clinical outcomes. However, further studies are needed to confirm the potential benefits of this complete customization process.
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NR 29
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U1 0
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TI Incidence rate and risk factors for radiographic hip osteoarthritis in Japanese men and women: a 10-year follow-up of the ROAD study
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Incidence; Progression; Acetabular dysplasia; Cohort study
ID knee osteoarthritis; dysplasia; associations; progression; disability; morphology; joint; hand; pain
AB Objective: To investigate the incidence and progression rate of radiographic hip osteoarthritis (OA) and its risk factors in Japanese men and women using a large-scale population of a nationwide cohort study, Research on Osteoarthritis/osteoporosis Against Disability (ROAD). Methods: From the baseline survey of the ROAD study, 2,975 participants (1,043 men and 1,932 women) aged 23-94 years (mean, 70.2 years) living in urban, mountainous, and coastal communities were followed up with hip radiography at 3, 7, and 10 years (mean follow-up, 7.1 years). Radiographs were scored using the Kellgren/Lawrence (K/L) grading system, and radiographic hip OA was defined as K/L >= 2. The incidence and progression rate of hip OA were examined. Acetabular dysplasia was defined as a central-edge angle <20 degrees. Cox's proportional hazard model was used to assess risk factors for incident and progressive radiographic hip OA. Results: The incidence rate of radiographic hip OA was 5.6/1,000 person-years and 8.4/1,000 person-years in men and women, respectively. The progression rate of hip OA was 2.2/1,000 person-years and 6.0/1,000 person-years in men and women, respectively. The significant risk factors for incident hip OA were age, obesity, and acetabular dysplasia at baseline (hazard risk [HR] 1.05, 95% confidence interval [CI] 1.03-1.08; 1.78, 1.10-2.75; 2.06, 1.30-3.17, respectively). The significant risk factors for progressive hip OA were baseline hip pain and acetabular dysplasia (HR 5.68,

95%CI 1.07-22.61; 14.78, 3.66-56.06, respectively). Conclusion: Continued longitudinal surveys of the ROAD study will contribute to knowledge about and potential prevention of incident and progressive hip OA. (C) 2019 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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NR 21
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Z9 36
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PI London
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AU Veronese, N
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TI Glucosamine sulphate: an umbrella review of health outcomes
SO THERAPEUTIC ADVANCES IN MUSCULOSKELETAL DISEASE
LA English
DT Review
DE glucosamine sulphate; osteoarthritis; umbrella review
ID knee osteoarthritis; systematic reviews; european-society; economic-aspects; chondroitin sulfate; double-blind; progression; osteoporosis; management; efficacy
AB Background and Aims: Glucosamine sulphate (GS) can be used as background therapy in people affected by knee osteoarthritis (OA). Knowledge regarding the efficacy and safety of GS is of importance since its use worldwide is increasing. Therefore, the present study aimed to map and grade the diverse health outcomes associated with GS using an umbrella review approach. Methods: Medline, Cinahl and Embase databases were searched until 1 April 2020. An umbrella review of systematic reviews and meta-analyses of randomized controlled trials (RCTs) was carried out. The evidence from the RCTs was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool. Results: From 140 articles returned, 11 systematic reviews, for a total of 21 outcomes (37 RCTs; 3949 participants; almost all using 1500 mg/day), were included. No systematic reviews/meta-analyses of observational studies were included. Regarding the findings of the meta-analyses, 9/17 outcomes were statistically significant, indicating that GS is more effective than placebo. A high certainty of evidence, as assessed by GRADE, supported the use of GS (versus placebo) in improving the Lequesne Index, joint space width change, joint space width change after 3 years of follow up, joint space narrowing and OA progression. No difference in terms of adverse effects was found between GS and placebo. In systematic reviews, GS was associated with a better glucose profile and a better physical function performance than placebo. Conclusion: GS, when used as a prescription drug (i.e. crystalline glucosamine sulphate) at 1500 mg daily dosage, can positively affect the cartilage structure, reduce pain, improve function and glucose metabolism in people with knee OA, without having a greater incidence of adverse effects than placebo.
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AU Goggin, P
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AF Goggin, Patricia
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TI Development of protocols for the first serial block-face scanning electron microscopy (SBF SEM) studies of bone tissue
SO BONE
LA English
DT Review
DE 3D imaging; Bone; High resolution; Osteocyte; SBF SEM; Serial block-face scanning electron microscopy
ID strain amplification; osteocyte processes; in-situ; contrast; resolution; resins; model; decalcification; reconstruction; environment
AB There is an unmet need for a high-resolution three-dimensional (3D) technique

to simultaneously image osteocytes and the matrix in which these cells reside. In serial block-face scanning electron microscopy (SBF SEM), an ultramicrotome mounted within the vacuum chamber of a microscope repeatedly sections a resin-embedded block of tissue. Backscattered electron scans of the block face provide a stack of high-resolution two-dimensional images, which can be used to visualise and quantify cells and organelles in 3D. High-resolution 3D images of biological tissues from SBF SEM have been exploited considerably to date in the neuroscience field. However, non-brain samples, in particular hard biological tissues, have appeared more challenging to image by SBF SEM due to the difficulties of sectioning and rendering the samples conductive. We have developed and propose protocols for bone tissue preparation using SBF SEM, for imaging simultaneously soft and hard bone tissue components in 3D. We review the state of the art in high-resolution imaging of osteocytes, provide a historical perspective of SBF SEM, and we present first SBF SEM proof-of-concept studies for murine and human tissue. The application of SBF SEM to hard tissues will facilitate qualitative and quantitative 3D studies of tissue microstructure and ultrastructure in bone development, ageing and pathologies such as osteoporosis and osteoarthritis.
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TI The Role of Substance P in the Regulation of Bone and Cartilage Metabolic Activity
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE substance P; Nk-R1 (neurokinin-receptor 1); osteoblasts; osteoclasts; osteoporosis; fracture healing; osteoarthritis
ID gene-related peptide; factor-kappa-b; rheumatoid-arthritis; sensory neurons; synovial-fluid; expression; pain; osteoarthritis; cells; differentiation
AB Substance P (SP) is a neuropeptide that is released from sensory nerve endings and is widely present in nerve fibers. It acts on bones and related tissues by binding to receptors, thereby regulating bone metabolism, cartilage metabolism, and fracture healing. SP has attracted widespread attention as a signaling substance that can be recognized by both the immune system and the nervous system. Previous studies have shown that bone and chondrocytes can synthesize and secrete sensory neuropeptides and express their receptors, and can promote proliferation, differentiation, apoptosis, matrix synthesis, and the degradation of target cells through autocrine/paracrine modes. In this paper, we review the research progress made in this field in recent years in order to provide a reference for further understanding the regulatory mechanism of bone and cartilage physiology and pathological metabolism.

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TI Can knee flexion contracture affect cervical alignment and neck tension? A prospective self-controlled pilot study
SO SPINE JOURNAL
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DT Article
DE Cervical alignment; Compensation mechanism; Flexion-relaxation ratio; Horizontal gaze; Knee flexion contracture; Neck tension; Shear wave elastography; Surface electromyography
ID sagittal spinal alignment; low-back-pain; asymptomatic adults; radiographic data; osseous anatomy; range; motion; osteoarthritis; values
AB BACKGROUND CONTEXT: The coordination of the alignment between the lower extremities and cervical spine helps to achieve balance and horizontal gaze during standing and walking. Malalignment in any segment can disturb the global balance, causing compensation in another segment. Knee flexion contracture (KFC) can cause spine inclination with increased C7 tilt or C7 SVA (sagittal vertical axis). Cervical alignment and the posterior muscles are essential for maintaining the horizontal gaze which is closely related to neck tension (NT). PURPOSE: This study aimed to determine whether KFC can affect cervical alignment and its potential effects on the posterior muscles and NT. DESIGN: A prospective pilot study was carried out in preoperative (pre-op) and postoperative (post-op) phases. PATIENT SAMPLE: This study included 22 consecutive patients with KFC and 12 control subjects in our department who agreed to participate from between August 1, 2018 and February 28, 2019 in our department. OUTCOME MEASURES: Visual analog scale (VAS) and neck disability index (NDI) were used. The sagittal alignment parameters and cervical range of motion (ROM) were measured on radiographic images, and included the C0-C2 lordosis (C0-2L), C2-C7 lordosis (C2-7L), C2 SVA, C7 SVA, T1 slope, thoracic kyphosis, lumbar lordosis (LL), pelvic tilt, sacral slope, and knee flexion angle (KA). Surface electromyography-based flexion-relaxation ratio (FRR) and ultrasound-based shear wave elastography (SWE) were performed. METHODS: The control group was matched for age, sex, and body mass index with the KFC group. Patients in the KFC group underwent arthroscopic surgery to correct knee alignment. Comparisons between pre-op and post-op phases were performed using paired sample t tests, comparisons between KFC and control groups were performed using independent samples t tests. The correlation analysis between the parameters was performed using Spearman analysis. Funding for this study was provided by the National Natural Science Foundation of China (60,000 USD), Beijing Municipal Administration of Hospitals Incubating Program (50,000 USD), and Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support (20,000 USD). There were no conflicts of interest associated with this study. RESULTS: The average follow-up time for this pilot study was 11.4 +/- 1.5 days. Pre-op, the KFC group had higher KA, T1S, C7 SVA, C2 SVA, C0-2L, SWE, VAS, and NDI compared with the control group, but all of these parameters were decreased significantly post-op. The LL, FRR of splenius capitis (FRRsc), and ROM of the KFC group pre-op were lower than the control group, and all of these were increased significantly post-op. There were no differences in pelvic tilt, sacral slope, C2-7 L, or TK between the KFC and control groups, or in FRR of splenius capitis (FRRutr) between pre-op and post-op phases. KA had strong correlations with LL (r=-0.83), which correlated well with C7 SVA

(r=-0.75). C7 SVA correlated strongly with C2 SVA (r=0.79), which also correlated strongly with C0-2 L (r=0.76). C0-2 L correlated well with FRRsc (r=-0.65) and SWEsc (r=0.72), and both of them correlated well with VAS (r=-0.54, r=0.71) and NDI (r=-0.57, r=0.76). ROM correlated well with FRRsc (r=0.71), SWEsc (r=-0.74), VAS (r=-0.66), and NDI (r=-0.66). CONCLUSIONS: KFC may cause spine inclination and craniocervical malalignment, leading to NT and ROM reduction. The results of this pilot study may be helpful in guiding further studies concerning KFC and NT.
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TI Composition and characteristics of trabecular bone in osteoporosis and osteoarthritis
SO BONE
LA English
DT Article
DE Micro-computed tomography; Nuclear magnetic resonance; Femoral head bone fractures; Osteoporosis; Hydroxyapatite; Crystal; Structure
ID synthetic calcium phosphates; age-related-changes; mineral density;

femoral-neck; mechanical-property; cross-polarization; collagen; hip; microarchitecture; fractures
AB Background: Bone strength depends on multiple factors such as bone density, architecture and composition turnover. However, the role these factors play in osteoporotic fractures is not well understood. Purpose: The aim of this study was to analyze trabecular bone architecture, and its crystal and organic composition in humans, by comparing samples taken from patients who had a hip fracture (HF) and individuals with hip osteoarthritis (HOA). Methods: The study included 31 HF patients and 42 cases of HOA who underwent joint replacement surgery between 1/1/2013 and 31/12/2013. Trabecular bone samples were collected from the femoral heads and analyzed using a dual-energy X-ray absorptiometry, micro-CT, and solid-state high-resolution magic-angle-spinning nuclear magnetic resonance (MAS-NMR) spectroscopy. Results: No differences in proton or phosphorus concentration were found between the two groups using H-1 single pulse, P-31 single pulse, P-31 single pulse with proton decoupling NMR spectroscopy, in hydroxyapatite (HA) c-axis or a-axis crystal length. Bone volume fraction (BV/TV), trabecular number (Tb.N), and bone mineral density (BMD) were higher in the HO group than in the HF group [28.6% +/- 10.5 vs 20.3% +/- 6.6 (p = 0.026); 2.58 mm(-1) +/- 1.57 vs 1.5 mm(-1) +/- 0.79 (p = 0.005); and 0.39 g/cm(2) +/- 0.10 vs. 0.28 g/cm(2) +/- 0.05 (p = 0.002), respectively]. The trabecular separation (Tp.Sp) was lower in the HO group 0.42 mm +/- 0.23 compared with the HF group 0.58 mm +/- 0.27 (p = 0.036). In the HO group, BMD was correlated with BV/TV (r = 0.704, p < 0.001), BMC (r = 0.853, p < 0.001), Tb.N (r = 0.653, p < 0.001), Tb.Sp (- 0.561, p < 0.001) and 1 H concentration (- 0.580, p < 0.001) in the HO group. BMD was not correlated with BV/TV, Tb.Sp, Tb.Th, Tb.N, Tb.PF, H-1 concentration or HA crystal size in the HF group. Conclusions: Patients with HO who did not sustain previous hip fractures had a higher femoral head BMD, BV/TV, and Tb.N than HF patients. In HO patients, BMD was positively correlated with the BV/TV and Tb.N and negatively correlated with the femoral head organic content and trabecular separation. Interestingly, these correlations were not found in HF patients with relatively lower bone densities. Therefore, osteoporotic patients with similar low bone densities could have significant microstructural differences. No differences were found between the two groups at a HA crystal level.
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TI Cell Proliferation Stimulation Ability and Osteogenic Activity of Low Molecular Weight Peptides Derived from Bovine Gelatin Hydrolysates
SO JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
LA English
DT Article
DE bioactive peptides; bovine gelatin hydrolysates; cell proliferation stimulation; osteogenic activity; tandem mass spectrometry
ID osteoblast proliferation; alkaline-phosphatase; collagen peptides; bone-development; mc3t3-e1 cells; expression; identification; antioxidant; mechanism; skin
AB It has been recognized that collagen peptides of MW 878 Da (CP1) promote osteoblast proliferation and mineralization. The objective of this study is to identify the peptides responsible for proliferation of osteoblast growth, enhancement of ALP (alkaline phosphatase) activity in osteoblasts and promotion of osteoblast

mineralization. To this end, the CP1 were fractioned by a series of chromatography procedures, and 51 peptides from the fraction possessing the most powerful cell proliferation ability were identified by LC-MS-MS. The peptides, GPAGPSGPAGK and GPPGSPGPR, were validated on a simultaneous basis as possessing enhanced bioactivity-inducing properties. In particular, the ALP activity of the cells treated with these two peptides was almost twice that of the control cells. Hydrogen bonds were formed, and the hydrophobic interactions with the EGFR (epidermal growth factor receptor) might be responsible for the osteoblast proliferation activity. On this basis, the two peptides might be potential lead compounds against osteoporosis and osteoarthritis.
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PT J
AU Hardy, E
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TI Destroy to Rebuild: The Connection Between Bone Tissue Remodeling and Matrix Metalloproteinases
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LA English
DT Review
DE bone; remodeling; metabolism; matrix metalloproteinase; deficiency; underactivity
ID growth-factor-beta; mesenchymal stem-cells; activated protein-c; human osteoarthritic cartilage; sensitive calcium influx; extracellular-matrix; gene-expression; multicentric osteolysis; osteoclast differentiation; in-vitro
AB Bone is a dynamic organ that undergoes constant remodeling, an energetically costly process by which old bone is replaced and localized bone defects are repaired to renew the skeleton over time, thereby maintaining skeletal health. This review provides a general overview of bone's main players (bone lining cells, osteocytes, osteoclasts, reversal cells, and osteoblasts) that participate in bone remodeling. Placing emphasis on the family of extracellular matrix metalloproteinases (MMPs), we describe how: (i) Convergence of multiple protease families (including MMPs and cysteine proteinases) ensures complexity and robustness of the bone remodeling process, (ii) Enzymatic activity of MMPs affects bone physiology at the molecular and cellular levels and (iii) Either overexpression or deficiency/insufficiency of individual MMPs impairs healthy bone remodeling and systemic metabolism. Today, it is generally accepted that proteolytic activity is required for the degradation of bone tissue in osteoarthritis and osteoporosis. However, it is increasingly evident that inactivating mutations in MMP genes can also lead to bone pathology including osteolysis and metabolic abnormalities such as delayed growth. We argue that there remains a need to rethink the role played by proteases in bone physiology and pathology.
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NR 401
TC 67
Z9 75
U1 1
U2 19
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AU Weber, AE
Nakata, H
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TI Return to Sport After Hip Arthroscopy for Femoroacetabular Impingement Syndrome in NCAA Division I Athletes: Experience at a Single Institution
SO ORTHOPAEDIC JOURNAL OF SPORTS MEDICINE
LA English
DT Article
DE femoroacetabular impingement syndrome; surgery; collegiate; sport type; return to sport; endurance
ID radiographic findings; prevalence; outcm
AB Background: The rate of return to sport after surgical treatment of femoroacetabular impingement (FAI) syndrome (FAIS) has been studied in high-level athletes. However, few studies examining this rate have focused exclusively on National Collegiate Athletic Association (NCAA) Division I athletes. Purpose: To evaluate the return-to-sport rate after hip arthroscopy for FAIS and to examine the influence of sport type on the clinical presentation of FAIS in collegiate athletes. Study Design: Case series; Level of evidence, 4. Methods: Included in this study were NCAA Division I student-athletes who underwent hip arthroscopy for FAIS at our institution between 2010 and 2017. Exclusion criteria were history of previous hip pathology, pediatric hip disease, radiographic evidence of osteoarthritis (Tonnis grade >0), prior lower extremity procedure, history of chronic pain, osteoporosis, or history of systemic inflammatory disease. Athletes were categorized into 6 subgroups based on the type of sport (cutting, contact, endurance, impingement, asymmetric/overhead, and flexibility) by using a previously reported classification system. Patient characteristics and preoperative, intraoperative, and return-to-sport variables were compared among sport types. Results: A total of 49 hip arthroscopies for FAIS were performed in 39 collegiate athletes (10 females, 29 males; mean age, 19.5 +/- 1.3 years). A total of 1 (2.6%) cutting athlete, 15 (38.5%) contact athletes, 8 (20.5%) impingement athletes, 6 (15.4%) asymmetric/overhead athletes, and 9 (23.1%) endurance athletes were included in the study. There were no differences among sports groups with respect to the FAI type. Endurance athletes had lower rates of femoral osteochondroplasty (45.5%) and labral debridement (0.0%) (P < .0001). Contact sport athletes had higher rates of labral debridement (50.0%; P < .0001). Patients were evaluated for

return to sport at an average of 1.96 +/- 0.94 years. Overall, the return-to-sport rate was 89.7%. There were no differences in return-to-sport rates based on the sport type except for endurance athletes, who returned at a lower rate (66.6%; P < .001). No differences in return-to-sport rate (P = .411), duration after return (P = .265), or highest attempted level of sport resumed (P = .625) were found between patients who underwent labral repair versus debridement. Conclusion: Collegiate-level athletes who underwent hip arthroscopy for FAIS returned to sport at high and predictable rates, with endurance athletes possibly returning to sport at lower rates than all other sport types. Surgical procedures may be influenced by sport type, but the rate of return to sport between athletes who underwent labral debridement versus labral repair was similar.
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NR 29
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Z9 27
U1 0
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J9 ORTHOP J SPORTS MED
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WC Orthopedics; Sport Sciences
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GA LT1GG
UT WOS:000536822500001
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PT J
AU Wiedemann, A
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Molin, A
Weryha, G
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Guéant, JL
Feillet, F
AF Wiedemann, Arnaud
Renard, Emeline
Molin, Arnaud
Weryha, Georges
Oussalah, Abderrahim
Gueant, Jean-Louis
Feillet, Francois
TI Prolonged 25-OH Vitamin D Deficiency Does Not Impair Bone Mineral Density in Adult Patients With Vitamin D 25-Hydroxylase Deficiency (CYP2R1)
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Rickets; Vitamin D; Bone mass density; Adults
ID d-dependent rickets; 25-hydroxyvitamin d; fractures; risk
AB Vitamin D-dependent rickets type 1B (VDDR1B) is an autosomal semidominant genetic disorder caused by a deficiency in CYP2R1, which encodes vitamin D 25-hydroxylase, an enzyme that plays a crucial role in the conversion of vitamin D to 25-dihydroxyvitamin D-3. VDDR1B is a severe form of rickets that occurs during infancy and which is responsive to 25-OH vitamin D supplementation. We studied three adult patients from a multi-consanguineous family with VDDR1B. They have been diagnosed with pseudo-nutritional rickets and treated during their adolescence with 25-OH vitamin D. These patients stopped their treatments at the end of adolescence and were contacted 14 to 17 years later when VDDR1B diagnosis was carried out in their niece and nephews. These three patients had undetectable 25-OH vitamin D, but normal levels of plasma 1-25(OH)(2) vitamin D. All patients had a hip bone mineral density and a normal vertebral despite osteoarthritis degenerative lesions which may impact BMD evaluation. These findings show that vitamin D supplementation has a questionable effect, if any, for osteoporosis prevention in adulthood in contrast to its crucial importance during infancy and adolescence.
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10.1073/pnas.1315006110
NR 21
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PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 CALCIFIED TISSUE INT
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AU Wang, S
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Liu, Chang
Lyu, Feng-Juan
Zheng, Qiujian
TI The Role of Autophagy and Mitophagy in Bone Metabolic Disorders
SO INTERNATIONAL JOURNAL OF BIOLOGICAL SCIENCES
LA English
DT Review
DE autophagy; mitophagy; bone metabolic disorder; osteoblast; osteoclast
ID pi3k/akt/mtor signaling pathway; coupled estrogen-receptor; peri-implant osteolysis; mesenchymal stem-cells; inflammatory response; oxidative stress; pink1/parkin-mediated mitophagy; mitochondrial dysfunction; osteoclast formation; human chondrocytes
AB Bone metabolic disorders include osteolysis, osteoporosis, osteoarthritis and rheumatoid arthritis. Osteoblasts and osteoclasts are two major types of cells in bone constituting homeostasis. The imbalance between bone formation by osteoblasts and bone resorption by osteoclasts has been shown to have a direct contribution to the onset of these diseases. Recent evidence indicates that autophagy and mitophagy, the selective autophagy of mitochondria, may play a vital role in regulating the proliferation, differentiation and function of osteoblasts and osteoclasts. Several signaling pathways, including PINK1/Parkin, SIRT1, MAPK8/FOXO3, Beclin-1/BECN1, p62/SQSTM1, and mTOR pathways, have been implied in the regulation of autophagy and mitophagy in these cells. Here we review the current progress about the regulation of autophagy and mitophagy in osteoblasts and osteoclasts in these bone metabolic disorders, as well as the molecular signaling activated or deactivated during this process. Together, we hope to draw attention to the role of autophagy and mitophagy in bone metabolic disorders, and their potential as a new target for the treatment of bone metabolic diseases and the requirements of further mechanism studies.
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TI Age-Related Variances in Patients with Tibial Plateau Fractures
SO JOURNAL OF KNEE SURGERY
LA English
DT Article
DE Tibial Plateau Fracture; posttraumatic osteoarthritis; knee replacement; elderly
ID total knee arthroplasty; internal-fixation; open reduction; operative treatment; risk-factors; replacement
AB Tibial plateau fractures account for approximately 8% of fractures in the elderly population. Treatment strategies in the elderly are similar to those for younger patients; however, practitioners must account for the elevated comorbidity burden in this population. To date, few studies have analyzed age-based outcomes in patients with tibial plateau fractures. Therefore, the purpose of this study was to determine age-related variances in demographics, fracture characteristics, mechanism of injury, and complications. A 10-year retrospective review was conducted to identify patients who received treatment for a tibial plateau fracture. There were 351 patients (360 tibial plateau fractures) who were identified and subsequently stratified according to their age at the time of injury. Patients were classified as elderly if they were 65 years of age or older at the time of injury; all other patients were included in the control cohort. These two cohorts were analyzed using bivariate analysis to isolate for age-related variations with respect to risk factors, mechanism of injury, and complications. There were 351 patients (360 tibial plateau fractures) with a median follow-up of 1.84 +/- 2.44 years who

met inclusion criteria. There were a greater proportion of women in the elderly cohort as compared with the younger cohort (60.0 vs. 43.4%, p = 0.06). Elderly patients were significantly more likely to present with diabetes (33.3 vs. 16.1%, p = 0.01) or osteoporosis (14.3 vs. 1.6%, p = 0.001). Younger patients were significantly more likely to require further surgery to address ligament (12.6 vs. 0%, p = 0.008), meniscus (20.9 vs. 7.1%, p = 0.036), or cartilage pathology (13.6 vs. 0%, p = 0.005). There was no difference in the arthroplasty conversion rate (4.8% elderly vs. 7.9% control, p = 0.755). While elderly patients presented with a greater comorbidity burden, they had equivalent or better short-term outcomes when compared with their younger peers when treated with open reduction and internal fixation (ORIF). Despite the recent interest in primary total knee arthroplasty for elderly patients with tibial plateau fractures, the results of this study suggest that elderly patients may respond well when treated with ORIF following a tibial plateau fracture.
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NR 28
TC 23
Z9 25
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TI Bone status and aortic calcifications in chondrocalcinosis patients
SO REVISTA ROMANA DE MEDICINA DE LABORATOR
LA English
DT Article
DE chondrocalcinosis; osteocalcin; osteoprotegerin; beta cross laps; abdominal aortic calcifications
ID crystal deposition disease; vascular calcification; cartilage calcification; arterial calcification; pyrophosphate; association; osteoarthritis; prevalence; menopause; serum
AB Aim: We aimed to examine the association between several circulating bone turnover markers [osteocalcin (OC), osteoprotegerin (OPG). beta-CrossLaps (beta-CTx)], hip and spine bone mineral density (BMD) and abdominal aortic calcification (AAC) in patients with chondrocalcinosis (CC). Methods: Thirty-six patients with CC and thirty-seven controls were consecutively enrolled in this pilot case-control, cross-sectional study. The following parameters were assessed: serum levels of OC, OPG and beta-CTx by enzyme-linked immunosorbent assay (ELISA); hip and spine BMD by dual-energy X-ray absorptiometry and AAC score by lateral radiography. Results: Patients with CC had higher levels of serum bone turnover markers and AAC score than the control group: OC [6.5 (3.5-9.9) vs 4.5 (2.6-7.2) ng/ml; p=0.05]. OPG [(7.7 (6.2-9.4) vs 6.5 (5.5-8.12) pmol/ml; p=0.021, beta-CTx [6078 (5870-6171) vs 5851 (5465-6109) pg/ml; p=0.02] and AAC score (3.6 +/- 6.2 vs 0.5 +/- 2; p=0.006). Conversely, even if statistical significance was not reached, hip and spine BMD was lower in patients with CC. Additionally, we found a positive correlation between OPG and AAC, but also between OPG and osteoporosis in patients with CC. Conclusion: Patients with CC are characterized by higher circulating OC, OPG and beta-CTx. The presence of AAC was more common in patients with CC, being only associated with serum OPG.
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TC 0
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PU UNIV PRESS
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PA UNIV MED FARMACIE TIRGU MURES, DISCIPLINA BIOCHIMIE CLIN, STR GHEORGHE MARINESCU, NR 38, TIRES MURES, 00000, ROMANIA
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TI Knee arthroplasty for acute fractures around the knee
SO EFORT OPEN REVIEWS
LA English
DT Article
DE elderly; fracture; knee; osteoporosis; total knee arthroplasty
ID distal femoral fractures; osteoporotic fractures; revision; replacement; management; femur; hip
AB Results of open reduction and internal fixation for com-plex articular fractures around the knee are poor, particularly in elderly osteoporotic patients. Open reduction and internal fixation may lead to an extended hospital stay and non-weight-bearing period. This may lead to occurrence of complications related to decubitus such as thrombo-embolic events, pneumonia and disorientation. Primary arthroplasty can be a valuable option in a case based and patient-specific approach. It may reduce the number of procedures and allow early full weightbearing, avoiding the above-mentioned complications. There are four main indications: 1) Elderly (osteoporotic) patients with pre-existing (symptomatic) end-stage osteoarthritis. 2) Elderly (osteoporotic) patients with severe articular and metaphyseal destruction. 3) Pathological fractures of the distal femur and/or tibia. 4) Young patients with complete destruction of the distal femur and/or tibia. The principles of knee (revision) arthroplasty should be applied; choice of implant and level of constraint should be considered depending on the type of fracture and involvement of stabilizing ligaments. The aim of treatment is to obtain a stable and functional joint. Long-term data remain scarce in the literature due to limited indications.
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NR 31
TC 13
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TI A Senescence-Centric View of Aging Implications for Longevity and Disease
SO TRENDS IN CELL BIOLOGY
LA English
DT Review
ID inhibiting oxidative stress; cellular senescence; induced osteoporosis; satellite cells; mouse model; stem-cells; cancer; osteoarthritis; atherosclerosis; progression
AB Cellular senescence is a state of stable cell cycle arrest associated with macromolecular alterations and secretion of proinfiammatory cytokines and molecules. From their initial discovery in the 1960s, senescent cells have been hypothesized as potential contributors to the age-associated loss of regenerative potential. Here, we discuss recent evidence that implicates cellular senescence as a central regulatory mechanism of the aging process. We provide a comprehensive overview of age-associated pathologies in which cellular senescence has been implicated. We describe mechanisms by which senescent cells drive aging and diseases, and we discuss updates on exploiting these mechanisms as therapeutic targets. Finally, we critically analyze the use of senotherapeutics and their translation to the clinic, highlighting limitations and suggesting ideas for future applications and developments.
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TI Cathepsin K: The Action in and Beyond Bone
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE Cathepsin K; osteoclast; bone resorption; osteoporosis; osteoarthritis; Cathepsin K inhibitor; cardiovascular diseases; lung fibrosis
ID lysosomal cysteine proteases; rheumatoid-arthritis; postmenopausal osteoporosis; collagenolytic activity; cartilage degeneration; molecular-cloning; expression; deficiency; inhibition; gene
AB Cathepsin K (CatK) is one of the most potent proteases in lysosomal cysteine proteases family, of which main function is to mediate bone resorption. Currently, CatK is among the most attractive targets for anti-osteoporosis drug development. Although many pharmaceutical companies are working on the development of selective inhibitors for CatK, there is no FDA approved drug till now. Odanacatib (ODN) developed by Merck & Co. is the only CatK inhibitor candidate which demonstrated high therapeutic efficacy in patients with postmenopausal osteoporosis in Phase III clinical trials. Unfortunately, the development of ODN was

finally terminated due to the cardio-cerebrovascular adverse effects. Therefore, it arouses concerns on the undesirable CatK inhibition in non-bone sites. It is known that CatK has far-reaching actions throughout various organs besides bone. Many studies have also demonstrated the involvement of CatK in various diseases beyond the musculoskeletal system. This review not only summarized the functional roles of CatK in bone and beyond bone, but also discussed the potential relevance of the CatK action beyond bone to the adverse effects of inhibiting CatK in non-bone sites.
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TI Raloxifene retards cartilage degradation and improves subchondral bone micro-architecture in ovariectomized rats with patella baja-induced - patellofemoral joint osteoarthritis
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article

DE Osteoarthritis; Osteoporosis; Raloxifene; Cartilage; Subchondral bone; Animal models
ID estrogen-receptor modulator; articular-cartilage; model; inflammation; morphology; turnover; knee; pain; transection; association
AB Objective: Abnormal remodeling of subchondral bone (SB) induced by estrogen deficiency has been shown to be involved in osteoarthritis (OA). Raloxifene (RAL) is commonly used to treat postmenopausal osteoporosis (OP). However, little is known about its effects on OA combined with estrogen deficiency. This study was performed to evaluate the efficacy of RAL on patella baja-induced patellofemoral joint OA (PFJOA) in an ovariectomized rat model. Design: Patellar ligament shortening (PLS) and ovariectomy (OVX) were performed simultaneously in 3-month-old female Sprague-Dawley rats, which were treated with RAL (10 mg/kg/day) or vehicle at 72 h postoperatively for 10 weeks. PFJOA was assessed by immunohistochemistry (IHC), real-time polymerase chain reaction (PCR), tartrate-resistant acid phosphatase (TRAP) staining, enzyme-linked immunosorbent assay (ELISA), micro-computed tomography (mu CT), histomorphology and behavioral analyses. Results: X-ray examinations showed that patella baja was successfully established by PLS. Histomorphological analysis revealed that PFJOA was significantly exacerbated by OVX and markedly alleviated by RAL. Moreover, RAL improved cartilage metabolism by decreasing MMP-13, ADAMTS-4, and caspase-3 and increasing Col-II and aggrecan at both the protein and mRNA levels. Furthermore, RAL markedly improved bone mass and SB microarchitecture and reduced osteoclast numbers and the serum osteocalcin and CTX-I levels. Although RAL showed a trend toward reducing pain sensitivity based on mechanical allodynia testing, this result was not statistically significant. Conclusion: These findings demonstrate that RAL treatment retards PFJOA progression in an ovariectomized rat model, suggesting that it may be a potential candidate for amelioration of the progression of PFJOA accompanied by postmenopausal OP. (C) 2019 Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.
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NR 50
TC 23
Z9 25
U1 1
U2 14
PU ELSEVIER SCI LTD
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SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
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PT J
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TI Prevalence of Comorbidities in Individuals Diagnosed and Undiagnosed with Alzheimer's Disease in Leon, Spain and a Proposal for Contingency Procedures to Follow in the Case of Emergencies Involving People with Alzheimer's Disease
SO INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH
LA English
DT Article
DE Alzheimer's disease; comorbidity; older adults; elderly
ID risk; dementia; association
AB Background: Alzheimer's disease (AD) which is the most common type of

dementia is characterized by mental or cognitive disorders. People suffering with this condition find it inherently difficult to communicate and describe symptoms. As a consequence, both detection and treatment of comorbidities associated with Alzheimer's disease are substantially impaired. Equally, action protocols in the case of emergencies must be clearly formulated and stated. Methods: We performed a bibliography search followed by an observational and cross-sectional study involving a thorough review of medical records. A group of AD patients was compared with a control group. Each group consisted of 100 people and were all Leon residents aged >= 65 years. Results: The following comorbidities were found to be associated with AD: cataracts, urinary incontinence, osteoarthritis, hearing loss, osteoporosis, and personality disorders. The most frequent comorbidities in the control group were the following: eye strain, stroke, vertigo, as well as circulatory and respiratory disorders. Comorbidities with a similar incidence in both groups included type 2 diabetes mellitus, glaucoma, depression, obesity, arthritis, and anxiety. We also reviewed emergency procedures employed in the case of an emergency involving an AD patient. Conclusions: Some comorbidities were present in both the AD and control groups, while others were found in the AD group and not in the control group, and vice versa.
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NR 46
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Z9 9
U1 0
U2 2
PU MDPI
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PT J
AU Smith, JK
AF Smith, John Kelly
TI Exercise as an Adjuvant to Cartilage Regeneration Therapy
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE exercise; osteoarthritis; osteoporosis; mesenchymal stem cells; hematopoietic stem cells; stem cell transplantation; chondroblasts; chondrocytes; cytokines
ID mesenchymal stem-cells; autologous chondrocyte implantation; modulates cytokine profile; articular-cartilage; bone-marrow; osteogenic differentiation; moderate exercise; physical-activity; stromal cells; defects
AB This article provides a brief review of the pathophysiology of osteoarthritis and the ontogeny of chondrocytes and details how physical exercise improves the

health of osteoarthritic joints and enhances the potential of autologous chondrocyte implants, matrix-induced autologous chondrocyte implants, and mesenchymal stem cell implants for the successful treatment of damaged articular cartilage and subchondral bone. In response to exercise, articular chondrocytes increase their production of glycosaminoglycans, bone morphogenic proteins, and anti-inflammatory cytokines and decrease their production of proinflammatory cytokines and matrix-degrading metalloproteinases. These changes are associated with improvements in cartilage organization and reductions in cartilage degeneration. Studies in humans indicate that exercise enhances joint recruitment of bone marrow-derived mesenchymal stem cells and upregulates their expression of osteogenic and chondrogenic genes, osteogenic microRNAs, and osteogenic growth factors. Rodent experiments demonstrate that exercise enhances the osteogenic potential of bone marrow-derived mesenchymal stem cells while diminishing their adipogenic potential, and that exercise done after stem cell implantation may benefit stem cell transplant viability. Physical exercise also exerts a beneficial effect on the skeletal system by decreasing immune cell production of osteoclastogenic cytokines interleukin-1 beta, tumor necrosis factor-alpha, and interferon-gamma, while increasing their production of antiosteoclastogenic cytokines interleukin-10 and transforming growth factor-beta. In conclusion, physical exercise done both by bone marrow-derived mesenchymal stem cell donors and recipients and by autologous chondrocyte donor recipients may improve the outcome of osteochondral regeneration therapy and improve skeletal health by downregulating osteoclastogenic cytokine production and upregulating antiosteoclastogenic cytokine production by circulating immune cells.
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NR 67
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U1 3
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PU MDPI
PI BASEL

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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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PT J
AU Kanis, JA
Harvey, NC
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Veronese, N
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TI Algorithm for the management of patients at low, high and very high risk of osteoporotic fractures
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Anabolic agents; Fracture risk assessment; FRAX; Inhibitors of bone resorption; Treatment of osteoporosis
ID trabecular bone score; postmenopausal women; intervention thresholds; hip fracture; older-adults; prevention; exercise; time; bmd; teriparatide
AB Guidance is provided in an international setting on the assessment and specific treatment of postmenopausal women at low, high and very high risk of fragility fractures. Introduction The International Osteoporosis Foundation and European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis published guidance for the diagnosis and management of osteoporosis in 2019.

This manuscript seeks to apply this in an international setting, taking additional account of further categorisation of increased risk of fracture, which may inform choice of therapeutic approach. Methods Clinical perspective and updated literature search. Results The following areas are reviewed: categorisation of fracture risk and general pharmacological management of osteoporosis. Conclusions A platform is provided on which specific guidelines can be developed for national use to characterise fracture risk and direct interventions.
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TI Prevalence and risk factors for bone loss in Southern Chinese with rheumatic diseases
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Rheumatic patients; Bone mineral density; Osteopenia; Osteoporosis
ID body-mass index; serum uric-acid; systemic-sclerosis; mineral density; osteoporosis; women; health; lupus; glucocorticoids; mechanisms
AB Backgroud This study is to explore the prevalence of different stages of bone loss and the potential risk factors in rheumatic patients. Method A cross-sectional study recruits 1398 rheumatic patients and 302 healthy subjects. Demographic data, blood, and bone mineral density (BMD) tests are collected. Risk factors for bone loss in rheumatic patients are analyzed by logistic regression. Results (1) Rheumatic patients are consisted of 40.0% rheumatoid arthritis (RA), 14.7% systemic lupus erythematosus (SLE), 14.2% osteoarthritis (OA), 9.2% ankylosing spondylosis (AS), 7.9% gout, 7.0% primary Sjogren syndrome (pSS), 3.8% systemic sclerosis (SSc), and 3.2% mixed connective tissue disease (MCTD). (2) In male patients aged under 50 and premenopausal female patients, the bone mineral density score of AS (53.9%,P < 0.001) and SLE (39.6%,P = 0.034) patients is lower than the healthy controls (18.2%). (3) Osteopenia and osteoporosis are more prevailing in male patients aged or older than 50 and postmenopausal female patients with RA (P < 0.001), OA (P = 0.02) and SLE (P = 0.011) than healthy counterparts. (4) Those with SLE, RA and AS gain the highest odd ratio of 'score below the expected range for age', osteopenia and osteoporosis, respectively. (5) Age, female, low BMI and hypovitaminosis D are found negatively associated with bone loss. Dyslipidemia and hyperuricemia could be protective factors. Conclusion Young patients with AS and SLE have a significant higher occurrence of bone loss, and older patients with RA, OA and SLE had higher prevalence than healthy counterparts. SLE, RA, SSc and AS were founded significant higher risks to develop into bone loss after adjustment. Age, BMI and gender were commonly-associated with bone loss in all age-stratified rheumatic patients. These findings were not markedly different from those of previous studies.
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TI Osteogenic and Anti-Inflammatory Behavior of Injectable Calcium Phosphate Loaded with Therapeutic Drugs
SO NANOMATERIALS
LA English
DT Article
DE injectable biomaterials; bone tissue regeneration; calcium phosphates; inflammation treatment; drug loaded biomaterials; sol-gel method and in vitro model
ID harpagophytum-procumbens; devils claw; bone; alendronate; differentiation; biomaterials; regeneration; fractures; cells
AB Bone fractures related to musculoskeletal disorders determine long-term disability in older people with a consequent significant economic burden. The recovery of pathologically impaired tissue architecture allows avoiding bone loss-derived consequences such as bone height reduction, deterioration of bone structure, inflamed bone pain, and high mortality for thighbone fractures. Actually, standard therapy for osteoporosis treatment is based on the systemic administration of biphosphonates and anti-inflammatory drugs, which entail several side effects including gastrointestinal (GI) diseases, fever, and articular pain. Hence, the demand of innovative therapeutic approaches for locally treating bone lesions has been increasing in the last few years. In this scenario, the development of injectable materials loaded with therapeutically active agents (i.e., anti-inflammatory drugs, antibiotics, and peptides mimicking growth factors) could be an effective tool to treat bone loss and inflammation related to musculoskeletal

diseases, including osteoporosis and osteoarthritis. According to this challenge, here, we propose three different compositions of injectable calcium phosphates (CaP) as new carrier materials of therapeutic compounds such as bisphosphonates (i.e., alendronate), anti-inflammatory drugs (i.e., diclofenac sodium), and natural molecules (i.e., harpagoside) for the local bone disease treatment. Biological quantitative analyses were performed for screening osteoinductive and anti-inflammatory properties of injectable drug-loaded systems. Meanwhile, cell morphological features were analyzed through scanning electron microscopy and confocal investigations. The results exhibited that the three systems exerted an osteoinductive effect during later phases of osteogenesis. Simultaneously, all compositions showed an anti-inflammatory activity on inflammation in vitro models.
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NR 39
TC 12
Z9 12
U1 1
U2 30
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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J9 NANOMATERIALS-BASEL
JI Nanomaterials
PD SEP 15
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WC Chemistry, Multidisciplinary; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary; Physics, Applied
SC Chemistry; Science & Technology - Other Topics; Materials Science; Physics
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PT J
AU Hu, PL
Du, J
Zhang, S
Wang, T
Li, J
Chen, G
Zhou, GQ
AF Hu, Peilin
Du, Jie
Zhang, Shuai
Wang, Ting
Li, Jun
Chen, Gang
Zhou, Guangqian
TI Oral Administration of Strontium Gluconate Effectively Reduces Articular Cartilage Degeneration Through Enhanced Anabolic Activity of Chondrocytes and Chondrogenetic Differentiation of Mesenchymal Stromal Cells
SO BIOLOGICAL TRACE ELEMENT RESEARCH
LA English
DT Article
DE Osteoarthritis (OA); Cartilage; Strontium gluconate; Chondrogenic differentiation
ID subchondral bone; ranelate; osteoarthritis; osteoporosis; expression; model
AB Osteoarthritis (OA), a common degenerative disease affecting articular cartilage,

is caused by multiple factors, and currently, there are few approaches to effectively delay its progression. This study aimed to evaluate whether a strontium compound (in the form of strontium gluconate, Glu-Sr) could reduce OA pathology severity in osteoarthritic rat models by directly targeting chondrocytes, including catabolic/anabolic activities and/or chondrogenic differentiation. Glu-Sr was administered to OA rats by oral gavage beginning during OA induction and continuing for 8 weeks. Glu-Sr treatment was found to significantly reduce cartilage degeneration and delay OA progression. Further examination showed that collagen II, Sox9, and aggrecan (ACAN) genes were up-regulated whereas IL-1 beta was down-regulated in chondrocytes isolated from Glu-Sr-treated rats. Glu-Sr also antagonized the catabolic effects of IL-1 beta on chondrocytes. Furthermore, Glu-Sr was shown to promote the chondrogenic differentiation of bone marrow mesenchymal stem cells (BMMSCs), possibly through promoting chondrogenic gene expression, including CTGF and FGF1, as revealed by RNA-sequencing (RNA-seq). These results suggest that systemic administration of Glu-Sr may be useful in prophylactic and therapeutic treatment of chronic cartilage degradation through affecting multiple steps from chondrogenic differentiation of progenitors to matrix formation in mature chondrocytes.
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NR 35
TC 9
Z9 9
U1 0
U2 21
PU SPRINGERNATURE
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JI Biol. Trace Elem. Res.
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PG 12
WC Biochemistry & Molecular Biology; Endocrinology & Metabolism
SC Biochemistry & Molecular Biology; Endocrinology & Metabolism
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PT J
AU Florance, J
Hemke, R
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AF Florance, Jonathon
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Bredella, Miriam A.
TI Effects of intra-articular corticosteroid injections on lumbar trabecular density
SO SKELETAL RADIOLOGY
LA English
DT Article
DE Intra-articular corticosteroid injection; Computed tomography (CT); Opportunistic CT; Lumbar spine; Trabecular density
ID bone-mineral density; pituitary-adrenal axis; symptomatic osteoarthritis; postmenopausal women; cartilage loss; osteoporosis; knee; hip; glucocorticoids; recommendations
AB Purpose To determine the effect of intra-articular corticosteroid injections on lumbar spine trabecular density. Materials and methods This retrospective study was IRB-approved and HIPAA-compliant. We identified 50 patients (26 F, 24 M, mean age 69 +/- 14 years) who had undergone at least three medium or large joint corticosteroid injections using insoluble corticosteroids and a subsequent non-contrast abdominal CT within 5 years of the first injection. About 126 age- and sex-matched controls without history of prior corticosteroid use who had undergone non-contrast abdominal CT were identified. Cumulative corticosteroid dose was calculated. Density measurements (HU) of trabecular bone of L1 to L4 were performed, and measurements of L1 were compared to established normative data. Groups were compared using a two-sided paired t-test or a chi-squared test. Linear regression analysis between cumulative corticosteroid dose and trabecular density was performed. Results Patients underwent a mean of 4 corticosteroid injections (range 3 to 11) with a mean cumulative corticosteroid dose of 232 +/- 100 mg triamcinolone equivalent (range 120 mg to 480 mg). There was no significant difference in trabecular density of L1 to L4 between cases and controls, and there was no significant difference in trabecular density at L1 compared to normative data ($p > 0.2$). There was no association between cumulative intra-articular corticosteroid dose and mean lumbar trabecular density ($p > 0.3$). Conclusion Patients who underwent repetitive intra-articular insoluble corticosteroid injections showed no increased risk of bone loss compared to controls. Cumulative intra-articular corticosteroid dose was not associated with lumbar trabecular density.
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Zhang W, 2008, OSTEOARTHR CARTILAGE, V16, P137, DOI 10.1016/j.joca.2007.12.013
NR 40
TC 3
Z9 3
U1 0
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PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 0364-2348
EI 1432-2161
J9 SKELETAL RADIOL
JI Skeletal Radiol.
PD MAY 15
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VL 49
IS 5
BP 787
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DI 10.1007/s00256-019-03362-2
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WC Orthopedics; Radiology, Nuclear Medicine & Medical Imaging
SC Orthopedics; Radiology, Nuclear Medicine & Medical Imaging
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PT J
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Hildebrand, Kevin
Marshall, Deborah A.
TI Systematic review of economic evaluations investigating education, exercise, and dietary weight management to manage hip and knee osteoarthritis: protocol
SO SYSTEMATIC REVIEWS
LA English
DT Review
DE Osteoarthritis; Hip osteoarthritis; Knee osteoarthritis; Education; Patient education; Health education; Exercise; Exercise therapy; Diet; Weight loss; Diet therapy; Cost-effectiveness analysis; Cost-utility analysis; Cost-benefit analysis
ID cost-effectiveness; european-society; consensus; quality; care; transferability; osteoporosis
AB Background: International guidelines recommend education, exercise, and dietary weight management as core treatments to manage osteoarthritis (OA) regardless of disease severity or co-morbidity. Evidence supports the clinical effectiveness of OA management programs, but the cost-effectiveness of core treatments remains unclear. We will systematically review, synthesize, and assess the literature in economic evaluations of core treatments (education, exercise, and dietary weight management) for the management of hip and/or knee OA. Methods: We will search the following elecftronic databases (from inception onwards): MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), National Health Services Economic Evaluation Database, and EconLit. Economic evaluations alongside randomized or nonrandomized clinical trials investigating OA education, exercise, and dietary weight management interventions will be included. Title, abstract, and full text of relevant publications will be screened independently by two reviewers. A content matter expert will resolve any conflicts between two reviewers. Key information from relevant papers will be extracted and tabulated to provide an overview of the published literature. Methodological quality will be evaluated using the Consensus on Health Economic Criteria list. A narrative synthesis without meta-analysis will be conducted. Subgroup analysis will attempt to find trends between research methods, intervention characteristics, and results. Discussion: The findings of this review will evaluate the breadth and quality of economic evaluations conducted alongside clinical trials for core treatments in OA management. Systematic review registration PROSPERO CRD42020155964
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NR 25
TC 2
Z9 3
U1 0
U2 4
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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WC Medicine, General & Internal
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PT J
AU Almeida, M
Kim, HN
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TI Increased marrow adipogenesis does not contribute to age-dependent appendicular bone loss in female mice
SO AGING CELL
LA English
DT Article
DE aging; osteoporosis; osteoblasts; PPARγ rosiglitazone; porosity
ID activated receptor-gamma; ppar-gamma; stem-cells; rosiglitazone; adipocytes; expression; osteoclastogenesis; differentiation; histopathology; osteoarthritis
AB Marrow adipocytes and osteoblasts differentiate from common mesenchymal progenitors in a mutually exclusive manner, and diversion of these progenitors toward adipocytes in old age has been proposed to account for the decline in osteoblasts and the development of involutional osteoporosis. This idea has been supported by evidence that thiazolidinedione (TZD)-induced activation of PPAR gamma, the transcription factor required for adipocyte differentiation, increases marrow fat and causes bone loss. We functionally tested this hypothesis using C57BL/6J mice with conditional deletion of PPAR gamma from early mesenchymal progenitors targeted by the Prx1-Cre transgene. Using a longitudinal littermate-controlled study design, we observed that PPAR gamma is indispensable for TZD-induced increase in marrow adipocytes in 6-month-old male mice, and age-associated increase in marrow adipocytes in 22-month-old female mice. In contrast, PPAR gamma is dispensable for the loss of cortical and trabecular bone caused by TZD or old age. Instead, PPAR gamma restrains age-dependent development of cortical porosity. These findings do not support the long-standing hypothesis that increased marrow adipocyte differentiation contributes to bone loss in old age but reveal a novel role of mesenchymal cell PPAR gamma in the maintenance of cortical integrity.
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TI Senolytic drugs: from discovery to translation
SO JOURNAL OF INTERNAL MEDICINE
LA English
DT Review
DE senolytics; dasatinib; quercetin; fisetin; senescent cell anti-apoptotic pathways; unitary theory of fundamental aging processes
ID cellular senescence; secretory phenotype; in-vivo; aurora kinase; stem-cells; inhibition; p16(ink4a); tissue; age; replication
AB Senolytics are a class of drugs that selectively clear senescent cells (SC). The first senolytic drugs Dasatinib, Quercetin, Fisetin and Navitoclax were discovered using a hypothesis-driven approach. SC accumulate with ageing and at causal sites of multiple chronic disorders, including diseases accounting for the bulk of morbidity, mortality and health expenditures. The most deleterious SC are resistant to apoptosis and have up-regulation of anti-apoptotic pathways which defend SC

against their own inflammatory senescence-associated secretory phenotype (SASP), allowing them to survive, despite killing neighbouring cells. Senolytics transiently disable these SCAPs, causing apoptosis of those SC with a tissue-destructive SASP. Because SC take weeks to reaccumulate, senolytics can be administered intermittently - a 'hit-and-run' approach. In preclinical models, senolytics delay, prevent or alleviate frailty, cancers and cardiovascular, neuropsychiatric, liver, kidney, musculoskeletal, lung, eye, haematological, metabolic and skin disorders as well as complications of organ transplantation, radiation and cancer treatment. As anticipated for agents targeting the fundamental ageing mechanisms that are 'root cause' contributors to multiple disorders, potential uses of senolytics are protean, potentially alleviating over 40 conditions in preclinical studies, opening a new route for treating age-related dysfunction and diseases. Early pilot trials of senolytics suggest they decrease senescent cells, reduce inflammation and alleviate frailty in humans. Clinical trials for diabetes, idiopathic pulmonary fibrosis, Alzheimer's disease, COVID-19, osteoarthritis, osteoporosis, eye diseases and bone marrow transplant and childhood cancer survivors are underway or beginning. Until such studies are done, it is too early for senolytics to be used outside of clinical trials.
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NR 146
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U2 244
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J9 J INTERN MED
JI J. Intern. Med.
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WC Medicine, General & Internal
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PT J
AU Murahashi, Y
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Nagoya, Satoshi
Yamashita, Toshihiko
TI Denosumab prevents periprosthetic bone mineral density loss in the tibial metaphysis in total knee arthroplasty
SO KNEE

LA English
DT Article
DE Periprosthetic bone; Bone mineral density; Osteoporosis; Total knee arthroplasty; Denosumab; Treatment
ID postmenopausal women; vertebral fractures; bisphosphonate use; controlled-trial; early migration; proximal tibia; follow-up; alendronate; discontinuation; bmd
AB Background: Periprosthetic bone quality is one of the most important factors preventing early prosthesis migration and long-term failure. Although denosumab, which binds to the receptor activator of nuclear factor kappa-B ligand (RANKL), has been linked with periprosthetic bone mineral density (BMD), the effectiveness of denosumab against bone loss remains unclear. We hypothesized that denosumab treatment after total knee arthroplasty (TKA) could prevent periprosthetic bone resorption. Methods: In this prospective cohort study. 28 patients with primary knee osteoarthritis were divided into two groups: denosumab (denosumab and vitamin D) and control (vitamin D only) groups. All patients underwent TKA with the same implant model and received medication after surgery. We used dual-energy X-ray absorptiometry to measure periprosthetic BMD after TKA. Results: In the control group, the BMD of the proximal medial tibia decreased drastically at 12 months after TKA (- 19.7%). Denosumab treatment significantly preserved this BMD loss (0.7%). The linear regression analysis revealed that denosumab intervention had the highest significantly positive relationship with BMD. Conclusions: Our results indicate that denosumab treatment significantly reduces periprosthetic BMD loss, even at the early stages after TKA. This therapeutic strategy may facilitate early stable fixation of the prosthesis which, in turn, may help to prevent early implant migration and reduce the need for revision surgery. (C) 2019 Elsevier B.V. All rights reserved.
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NR 31
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Z9 26
U1 1

U2 7
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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J9 KNEE
JI Knee
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WC Orthopedics; Sport Sciences; Surgery
SC Orthopedics; Sport Sciences; Surgery
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PT J
AU Chu, XY
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AF Chu, Xiangyu
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Huang, Xiaojian
Xi, Yang
Ni, Bowei
Zhang, Rui
You, Hongbo
TI Tomatidine suppresses inflammation in primary articular chondrocytes and attenuates cartilage degradation in osteoarthritic rats
SO AGING-US
LA English
DT Article

DE tomatidine; osteoarthritis; interleukin-1 beta; chondrocyte; NF-kappa B
ID nf-kappa-b; tumor-necrosis-factor; matrix degradation; european-society; economic-aspects; expression; pathway; osteoporosis; activation; management
AB In this study, we investigated whether the anti-inflammatory effects of tomatidine alleviate osteoarthritis (OA)-related pathology in primary articular chondrocytes and a rat OA model. STITCH database analysis identified 22 tomatidine-target genes that were enriched in 78 Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. Moreover,39 of the 105 OA-related KEGG pathways were related to tomatidine-target genes. The top two OA-related KEGG pathways with tomatidine-target genes were the MAPK and neutrophin signaling pathways. Pretreating primary chondrocytes with tomatidine suppressed interleukin-1 beta (IL-1 beta)-induced expression of iNOS, COX-2, MMP1, MMP3, MMP13, and ADAMTS-5. Tomatidine also suppressed IL-1 beta-induced degradation of collagen-II and aggrecan proteins by inhibiting NF-kappa B and MAPK signaling. In a rat OA model, histological and immunohistochemical analyses showed significantly less cartilage degeneration in thetibiofemoral joints of rats treated for 12 weeks with tomatidine after OA induction (experimental group) than in untreated OA group rats. However, micro-computed tomography (mu-CT) showed that tomatidine did not affect remodeling of the subchondral bone at the tibial plateau. These data shows that tomatidine suppresses IL-1 beta-induced inflammation in primary chondrocytes by inhibiting the NF-kappa B and MAPK signaling pathways, and protects against cartilage destruction in a rat OA model.
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NR 38
TC 20
Z9 21
U1 1

U2 21
PU IMPACT JOURNALS LLC
PI ORCHARD PARK
PA 6666 E QUAKER ST, STE 1, ORCHARD PARK, NY 14127 USA
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J9 AGING-US
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BP 12799
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WC Cell Biology; Geriatrics & Gerontology
SC Cell Biology; Geriatrics & Gerontology
GA MM0XV
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PT J
AU Fang, X
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Song, LH
Li, J
Duan, H
AF Fang, Xiang
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Yu, Zeping
Liu, Hongyuan
Xiong, Yan
Luo, Yi
Song, Liuhong
Li, Jing
Duan, Hong
TI Tumor-Induced Osteomalacia Caused by a Phosphaturic Mesenchymal Tumor of

the Sole Presenting as a Crippling Illness in a Postmenopausal Woman
SO JOURNAL OF FOOT & ANKLE SURGERY
LA English
DT Article
DE definite diagnosis; fibroblast growth factor 23; fine-needle aspiration biopsy; hypophosphatemia; oncogenic osteomalacia; osteoporosis
ID oncogenic osteomalacia; osteoporosis; diagnosis
AB Tumor-induced osteomalacia, a rare and intriguing paraneoplastic syndrome that is usually caused by a phosphaturic mesenchymal tumor, leads to severe pain and hypophosphatemia. However, during clinical practice, most patients suffer from significant delay of diagnosis and treatment because the symptoms are similar to those of some very common diseases, such as osteoporosis and osteoarthritis. Moreover, physical complaints from postmenopausal women usually exacerbate the possibility of such delays. We describe a case of a postmenopausal woman with crippling bone pain and weakness, who had been diagnosed with a case of simple osteoporosis and osteoarthritis for 3 years, even with fine-needle aspiration biopsy of the offending phosphaturic mesenchymal tumor. After surgical removal of the 2 x 3-cm(2) tumor in her sole, we observed immediate relief of her systemic symptoms, with visual analogue scale improvement from 5 of 10 preoperatively to 2 of 10 5 days after surgery. There were no signs of recurrence during 2-year follow-up. This case highlights the significance of thorough history-taking as a fundamental tool for diagnosis even in the era of advanced technology, and that the awareness of tumor-induced osteomalacia should be raised. Otherwise, such a small localized soft tissue mass would seldom be associated with the severe systemic symptoms. (C) 2020 by the American College of Foot and Ankle Surgeons. All rights reserved.
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PT J
AU Killaars, AR
Walker, CJ
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AF Killaars, Anouk R.
Walker, Cierra J.
Anseth, Kristi S.
TI Nuclear mechanosensing controls MSC osteogenic potential through HDAC epigenetic remodeling
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA
LA English
DT Article
DE hMSCs; epigenetic remodeling; phototunable hydrogels
ID mesenchymal stem-cells; matrix elasticity; gene-expression; stromal cells; differentiation; mechanisms; osteoporosis; organization; acetylation; induction
AB Cells sense mechanical cues from the extracellular matrix to regulate cellular behavior and maintain tissue homeostasis. The nucleus has been implicated as a key mechanosensor and can directly influence chromatin organization, epigenetic modifications, and gene expression. Dysregulation of nuclear mechanosensing has been implicated in several diseases, including bone degeneration. Here, we exploit photostiffening hydrogels to manipulate nuclear mechanosensing in human mesenchymal stem cells (hMSCs) in vitro. Results show that hMSCs respond to matrix stiffening by increasing nuclear tension and causing an increase in histone acetylation via deactivation of histone deacetylases (HDACs). This ultimately induces osteogenic fate commitment. Disrupting nuclear mechanosensing by disconnecting the nucleus from the cytoskeleton up-regulates HDACs and prevents osteogenesis. Resetting HDAC activity back to healthy levels rescues the epigenetic and osteogenic response in hMSCs with pathological nuclear mechanosensing. Notably, bone from patients with osteoarthritis displays similar defective nuclear mechanosensing. Collectively, our results reveal that nuclear mechanosensing controls hMSC osteogenic potential mediated by HDAC epigenetic remodeling and that this cellular mechanism is likely relevant to bone-related diseases.
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TC 93
Z9 108
U1 2
U2 51
PU NATL ACAD SCIENCES
PI WASHINGTON

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J9 P NATL ACAD SCI USA
JI Proc. Natl. Acad. Sci. U. S. A.
PD SEP 1
PY 2020
VL 117
IS 35
BP 21258
EP 21266
DI 10.1073/pnas.2006765117
PG 9
WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
GA NS5SW
UT WOS:000572321800013
PM 32817542
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PT J
AU Camernik, K
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TI Comprehensive analysis of skeletal muscle- and bone-derived mesenchymal stem/stromal cells in patients with osteoarthritis and femoral neck fracture

SO STEM CELL RESEARCH & THERAPY
LA English
DT Article
DE Mesenchymal stem; stromal cells; Skeletal muscle; Trabecular bone; Osteoarthritis; Osteoporosis; Controls; Leptin receptor
ID stem-cells; stromal cells; gene-expression; osteoporosis; obesity; leptin; system; mscs
AB Background Mesenchymal stem/stromal cells (MSCs) can replenish the aged cells of the musculoskeletal system in adult life. Stem cell exhaustion and decrease in their regenerative potential have been suggested to be hallmarks of aging. Here, we investigated whether muscle- and bone-derived MSCs of patients with osteoarthritis and osteoporosis are affected by this exhaustion, compared to healthy donors. Methods Patients with primary osteoarthritis, femoral neck fractures due to osteoporosis, and healthy donors (controls) were included. MSCs were isolated from the skeletal muscle and subchondral bone from each patient and compared using ex vivo and in vitro analyses, including immunophenotyping, colony-forming unit fibroblast assays, growth kinetics, cell senescence, multilineage potential, and MSC marker gene expression profiling. Results Freshly isolated cells from muscle from patients with osteoarthritis showed a lower proportion of CD45/CD19/CD14/CD34-negative cells compared to patients with osteoporosis and healthy donors. Freshly isolated muscle cells from patients with osteoarthritis and osteoporosis also showed higher clonogenicity compared to healthy donors. MSCs from both tissues of osteoarthritis patients showed significantly reduced osteogenesis and MSCs from the bone also reduced adipogenesis. Chondrogenic pellet diameter was reduced in bone-derived MSCs from both patient groups compared to healthy donors. A significant positive correlation was observed between adipogenesis and CD271 expression in muscle-derived MSCs. CD73 was significantly lower in bone-derived MSCs from osteoarthritis patients, compared to osteoporosis patients. Gene expression profiling showed significantly lower expression of MSC marker gene leptin receptor, LEPR, previously identified as the major source of the bone and adipocytes in the adult bone marrow, in bone-derived MSCs from patients with osteoarthritis in comparison with osteoporotic patients and healthy donors. Conclusions Our results show deficient ex vivo and in vitro properties of both skeletal muscle- and bone-derived MSCs in osteoarthritis and osteoporosis patients, compared to healthy donors. In bone-derived MSCs from patients with osteoarthritis, we also identified a lower expression of the leptin receptor, a marker of MSCs that present a major source of MSCs in the adult bone marrow. This suggests that exhaustion of skeletal muscle- and bone-derived MSCs is a hallmark of osteoarthritis and osteoporosis, which defines the need for further clinical trials of stem cell transplantation in these patients.
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NR 42
TC 32
Z9 35
U1 0
U2 12
PU BMC
PI LONDON
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SN
EI 1757-6512
J9 STEM CELL RES THER
JI Stem Cell Res. Ther.
PD APR 3
PY 2020
VL 11
IS 1
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DI 10.1186/s13287-020-01657-z
PG 14
WC Cell & Tissue Engineering; Cell Biology; Medicine, Research & Experimental
SC Cell Biology; Research & Experimental Medicine
GA LA1WN

UT WOS:000523745300004
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PT J
AU Zeng, LY
Yang, SY
Zhang, ZQ
Wang, T
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Wei, XC
AF Zeng, Ling-yuan
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Zhang, Zhi-qiang
Wang, Tao
Wang, Yu-ze
Wei, Xiao-chun
TI Effect of Cholecystectomy on the Occurrence of Knee Osteoarthritis
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE Cholecystectomy; Disease occurrence; KOA; Osteoporosis; Subchondral trabeculae
ID bone-mineral density; laparoscopic cholecystectomy; osteoporosis; population
AB Objective To evaluate the effect of cholecystectomy on the occurrence of knee osteoarthritis (KOA). Methods The present study was a case-control study with a retrospective, cross-sectional, and longitudinal study design. The clinical data for knee osteoarthritis in the Second Hospital of Shanxi Medical University from January 2016 to September 2018 was analyzed. Clinical data, including gender, age, height, weight, smoking, alcohol abuse, prior medical history, and previous surgical history, were recorded. A logistic regression model was used for the univariate and multivariate analysis. Results A total of 1659 patients with KOA (KOA group) and 1195 limb fracture patients (control group) were included in this study. Among the 1659 patients with KOA, 388 patients were male and 1271 were female, while among the 1195 patients in the control group, 638 patients were male and 557 patients were female. The period between cholecystectomy and knee osteoarthritis onset ranged from 0.5 years to 17 years; the average interval time was 8.73 +/- 2.11 years. The age at disease onset was significantly older when compared to the control group, while the body mass index in the KOA group was significantly higher when compared to the control group ($P < 0.05$). There were 97 patients undergoing cholecystectomy in the KOA group and there were 15 patients undergoing cholecystectomy in the control group. The proportion of cholecystectomy in the two groups was statistically significant. After the univariate

analysis, there was a statistically significant difference in distribution between the two groups ($P < 0.05$). The multivariate logistic regression analysis revealed that there was a significant difference in the distribution of these two groups ($P < 0.05$), indicating that cholecystectomy is associated with the occurrence of KOA. Conclusion There is a close relationship between cholecystectomy and KOA. However, the specific mechanism remains unknown and should be further researched.

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NR 22
TC 3
Z9 4
U1 0
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PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 ORTHOP SURG
JI Orthop. Surg.
PD JUN 15
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VL 12
IS 3
BP 756
EP 760
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WC Orthopedics
SC Orthopedics
GA MA1LI
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PT J
AU Kaur, J
Farr, JN
AF Kaur, Japneet
Farr, Joshua N.
TI Cellular senescence in age-related disorders
SO TRANSLATIONAL RESEARCH
LA English
DT Review
ID secretory phenotype; cells; osteoarthritis; clearance; fisetin; tissue; atherosclerosis; inhibition; expression; biomarker
AB Much of the population is now faced with an enormous burden of age-associated chronic diseases. Recent discoveries in geroscience indicate that

healthspan in model organisms such as mice can be manipulated by targeting cellular senescence, a hallmark mechanism of aging, defined as an irreversible proliferative arrest that occurs when cells experience oncogenic or other diverse forms of damage. Senescent cells and their proinflammatory secretome have emerged as contributors to age-related tissue dysfunction and morbidity. Cellular senescence has causal roles in mediating osteoporosis, frailty, cardiovascular diseases, osteoarthritis, pulmonary fibrosis, renal diseases, neurodegenerative diseases, hepatic steatosis, and metabolic dysfunction. Therapeutically targeting senescent cells in mice can prevent, delay, or alleviate each of these conditions. Therefore, senotherapeutic approaches, including senolytics and senomorphics, that either selectively eliminate senescent cells or interfere with their ability to promote tissue dysfunction, are gaining momentum as potential realistic strategies to abrogate human senescence to thereby compress morbidity and extend healthspan.
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NR 84
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Z9 56
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U2 32
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WC Medical Laboratory Technology; Medicine, General & Internal; Medicine, Research & Experimental
SC Medical Laboratory Technology; General & Internal Medicine; Research & Experimental Medicine
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PT J
AU Yang, ZR
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AF Yang, Zirong
Qu, Hangbo
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TI Progranulin Regulates the Differentiation of Bone Marrov Mesenchymal Stem Cells Under Inflammation Through Focal Adhesion Kinase (FAK)/Mitogen-Activated Protein Kinase (MAPK) Pathway
SO JOURNAL OF BIOMATERIALS AND TISSUE ENGINEERING
LA English
DT Article
DE Inflammatory; BMSCs; Proliferation; FAK/MAPK; Osteogenesis
ID cartilage; cancer
AB Osteogenic differentiation of BMSCs is beneficial to the treatment of osteoarthritis. Progranulin (PGRN) is a chondrogenic factor. However, the role of progranulin in the differentiation of BMSCs under inflammation remains unclear. Rat BMSCs were isolated and divided into control group, inflammation group (treated with LPS), and PGRN group (5 and 10 /mu M) followed by analysis of survival rate of BMSCs by MTT assay, Caspase 3 activity, ALP activity, expression of Runx2 and OP by real time PCR, level of MMP-3, TIMP-1, FAK and MAPK by Western blot and IL-6 and IL-10 secretion by ELISA. LPS treatment significantly inhibited BMSCs proliferation, increased Caspase 3 activity, decreased ALP activity, expression of Runx2 and OP, increased IL-6 secretion, decreased IL-10 secretion,

increased MMP-3 expression, decreased expression of TIMP-1, FAK and p-P38 ($P < 0.05$). PGRN treatment on BMSCs under inflammation significantly promoted cell proliferation, decreased Caspase 3 activity, increased ALP activity, expression of Runx2 and OP, decreased IL-6 secretion, increased IL-10 secretion, decreased MMP-3 expression, and increased TIMP-1, FAK and p-P38 expression ($P < 0.05$) with more significant changes in the higher concentration. Under inflammation, BMSCs proliferation was inhibited, apoptosis was increased, and osteogenic differentiation was weakened. PGRN inhibits the proliferation of BMSCs and apoptosis, and promotes osteogenic differentiation by regulating FAK/MAPK pathway.

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PT J
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AF Panach, Layla
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Acebron, Alvaro
Mifsut, Damian
Tarin, Juan J.
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Angel Garcia-Perez, Miguel
TI Comparative transcriptome analysis identifies CARM1 and DNMT3A as genes associated with osteoporosis
SO SCIENTIFIC REPORTS
LA English
DT Article
ID bone-mineral density; insulin-resistance; expression; risk; standardization; metaanalysis; methylation; secretion; tool
AB To identify new candidate genes in osteoporosis, mainly involved in epigenetic mechanisms, we compared whole gene-expression in osteoblasts (OBs) obtained from women undergoing hip replacement surgery due to fragility fracture and severe osteoarthritis. Then, we analyzed the association of several SNPs with BMD in 1028 women. Microarray analysis yielded 2542 differentially expressed transcripts belonging to 1798 annotated genes, of which 45.6% (819) were overexpressed, and 54.4% (979) underexpressed (fold-change between-7.45 and 4.0). Among the most represented pathways indicated by transcriptome analysis were chondrocyte development, positive regulation of bone mineralization, BMP signaling pathway, skeletal system development and Wnt signaling pathway. In the translational stage we genotyped 4 SNPs in DOT1L, HEY2, CARM1 and DNMT3A genes. Raw data analyzed against inheritance patterns showed a statistically significant association between a SNP of DNMT3A and femoral neck-(FN) sBMD and primarily a SNP of CARM1 was correlated with both FN and lumbar spine-(LS) sBMD. Most of these associations remained statistically significant after adjusting for confounders. In analysis with anthropometric and clinical variables, the SNP of CARM1 unexpectedly revealed a close association with BMI (p=0.000082), insulin (p=0.000085), and HOMA-(IR) (p=0.000078). In conclusion, SNPs of the DNMT3A and CARM1 genes are associated with BMD, in the latter case probably owing to a strong correlation with obesity and fasting insulin levels.
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NR 49
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PT J
AU Pignolo, RJ
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AF Pignolo, Robert J.
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TI Fibrodysplasia Ossificans Progressiva (FOP): A Segmental Progeroid Syndrome
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE progeroid syndrome; fibrodysplasia ossificans progressiva; activin A; ACVR1; cell senescence
ID nf-kappa-b; activin-a; cellular senescence; heterotopic ossification; protein; remyelination; cells; follistatin; mortality; skeleton
AB Segmental progeroid syndromes are commonly represented by genetic conditions which recapitulate aspects of physiological aging by similar, disparate, or unknown mechanisms. Fibrodysplasia ossificans progressiva (FOP) is a rare genetic disease caused by mutations in the gene for ACVR1/ALK2 encoding Activin A receptor type I/Activin-like kinase 2, a bone morphogenetic protein (BMP) type I receptor, and results in the formation of extra-skeletal ossification and a constellation of others features, many of which resemble accelerated aging. The median estimated lifespan of individuals with FOP is approximately 56 years of age. Characteristics of precocious aging in FOP include both those that are related to dysregulated BMP signaling as well as those secondary to early immobilization. Progeroid features that may primarily be associated with mutations in ACVR1 include osteoarthritis, hearing loss, alopecia, subcutaneous lipodystrophy, myelination defects, heightened inflammation, menstrual abnormalities, and perhaps nephrolithiasis. Progeroid features that may secondarily be related to immobilization from progressive heterotopic ossification include decreased vital capacity, osteoporosis, fractures, sarcopenia, and predisposition to respiratory infections. Some manifestations of precocious aging may be attributed to both primary and secondary effects of FOP. At the level of lesion formation in FOP, soft tissue injury resulting in hypoxia, cell damage, and inflammation may lead to the accumulation of senescent cells as in aged tissue. Production of Activin A, platelet-derived growth factor, metalloproteinases, interleukin 6, and other inflammatory cytokines as part of the senescence-associated secretory phenotype could conceivably mediate the initial signaling cascade that results in the intense fibroproliferative response as well as the tissue-resident stem cell reprogramming leading up to ectopic endochondral bone formation. Consideration of FOP as a segmental progeroid syndrome offers a unique perspective into potential mechanisms of normal aging and may also provide insight for identification of new

targets for therapeutic interventions in FOP.
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NR 64
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Z9 38
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PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
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PT J
AU Edmonds, EW
Phillips, L
Roocroft, JH

Bastrom, TP
Pennock, AT
Chambers, HG
AF Edmonds, Eric W.
Phillips, Lee
Roocroft, Joanna H.
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Pennock, Andrew T.
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TI Stable childhood osteochondral lesions of the talus: short-term radiographic outcomes suggest risk for early osteoarthritis
SO JOURNAL OF PEDIATRIC ORTHOPAEDICS-PART B
LA English
DT Article
DE osteoarthritis; osteochondritis dissecans; pediatric; talus
ID transchondral fractures; dissecans
AB Recent literature suggests that adults do not necessarily develop osteoarthritis if they have an osteochondral lesion of the talus (OLT). The purpose of this study was to determine if children with OLT are at risk to develop any radiographic evidence of early joint degeneration despite treatment efforts. Fifty-six ankles were identified over 6 years with stable OLT that underwent operative treatment. Preoperatively, each lesion was classified according to Berndt-Hardy for radiographs, Hepple for MRI, and Ferkel and Sgaglione for computed tomography. Radiographs were also evaluated for physeal status, OLT characteristics (location, border, size), and signs of osteoarthritis (Kellgren and Lawrence Scale). Despite incomplete treatment to radiographic resolution, the Kellgren-Lawrence scores still worsened in 23% of the children (pre-op score: mean 0.42 and median 0 versus post-op score: mean 0.69 and median 1). No risk factors (preoperative classification, age, physeal patency) were associated with advancing radiographic evidence of articular degeneration utilizing univariate analysis. However, a classification and regression tree analysis revealed that a patient age of 11.5 years old could be predictive of advancing Kellgren-Lawrence scores with one-third of older children worsening (P = 0.038). Despite active treatment of OLT, the ultimate prognosis is guarded with approximately one out of four children advancing their Kellgren and Lawrence score during treatment. In contrast to the natural history of adult OLT, the short-term advancement of degenerative disease in childhood OLT suggests a potentially different outcome and warrants further investigation into better treatment methods to preserve ankle health in these young patients.
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NR 16
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PI PHILADELPHIA
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AU Dempster, DW
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AF Dempster, David W.
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TI Modeling-Based Bone Formation in the Human Femoral Neck in Subjects Treated With Denosumab
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE ANTIRESORPTIVES; BONE HISTOMORPHOMETRY; BONE MODELING AND REMODELING; OSTEOPOROSIS
ID postmenopausal women; zoledronic acid; hip fracture; osteoporosis; teriparatide; risedronate; alendronate; increase; density; trial
AB Denosumab is associated with continued gains in hip and spine BMD with up to 10 years of treatment in postmenopausal women with osteoporosis. Despite potent inhibition of bone remodeling, findings in nonhuman primates suggest modeling-based bone formation (MBBF) may persist during denosumab treatment.

This study assessed whether MBBF in the femoral neck (FN) is preserved in the context of inhibited remodeling in subjects receiving denosumab. This open-label study enrolled postmenopausal women with osteoporosis who had received two or more doses of denosumab (60 mg subcutaneously every 6 months [Q6M]) per standard of care and were planning elective total hip replacement (THR) owing to osteoarthritis of the hip. Transverse sections of the FN were obtained after THR and analyzed histomorphometrically. MBBF, based on fluorochrome labeling and presence of smooth cement lines, was evaluated in cancellous, endocortical, and periosteal envelopes of the FN. Histomorphometric parameters were used to assess MBBF and remodeling-based bone formation (RBBF) in denosumab-treated subjects (n = 4; mean age = 73.5 years; range, 70 to 78 years) and historical female controls (n = 11; mean age = 67.8 years; range, 62 to 80 years) obtained from the placebo group of a prior study and not treated with denosumab. All analyses were descriptive. All subjects in both groups exhibited MBBF in the periosteal envelope; in cancellous and endocortical envelopes, all denosumab-treated subjects and 81.8% of controls showed evidence of MBBF. Compared with controls, denosumab-treated subjects showed 9.4-fold and 2.0-fold higher mean values of MBBF in cancellous and endocortical envelopes, respectively, whereas RBBF mean values were 5.0-fold and 5.3-fold lower. In the periosteal envelope, MBBF and RBBF rates were similar between subjects and controls. These results demonstrate the occurrence of MBBF in the human FN and suggest that denosumab preserves MBBF while inhibiting remodeling, which may contribute to the observed continued gains in BMD over time after remodeling is maximally inhibited. (c) 2020 The Authors. Journal of Bone and Mineral Research published by American Society for Bone and Mineral Research..
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PT J
AU Khandelwal, S
AF Khandelwal, S.
TI Obesity in midlife: lifestyle and dietary strategies
SO CLIMACTERIC
LA English
DT Article
DE Obesity; menopause; midlife weight gain; lifestyle therapy; dietary strategies; physical activity; behavioral support
ID weight-loss; clinical endocrinologists; american association; practice guidelines; position statement; physical-activity; medical-care; body-weight; health; management
AB As the rate of obesity increases globally, so does the incidence of other non-communicable diseases such as diabetes, cardiovascular disease, cancer, osteoporosis, osteoarthritis, and dementia, which have been referred to as

'adiposity-based chronic disease'. With timely lifestyle modification such as behavioral changes, implementation of a healthy diet, and proper physical activity, many of these diseases can be prevented. Weight gain is one of the major health concerns of midlife. Midlife body changes are the result of aging, menopause, and other influences unique to menopausal women which interfere with adoption of a healthy lifestyle. Reduced metabolism levels lead to low energy levels, which discourage physical activity. In addition, with the onset of bone loss, menopausal women begin to lose muscle mass and gain more fat, resulting in osteopenic sarco-obesity. Adoption of a healthy lifestyle is a first-line option in the treatment for these midlife changes. Lifestyle medicine offers a broad set of network-based interventions, which need to be brought to the forefront in preventing and managing obesity at all stages. This review article focuses on evidence-based lifestyle changes and their benefits for reducing morbidity and mortality related to obesity and its complications prevalent at midlife and beyond.
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TC 34
Z9 40
U1 1
U2 30
PU TAYLOR & FRANCIS LTD
PI ABINGDON
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SN 1369-7137
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J9 CLIMACTERIC
JI Climacteric
PD MAR 3
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WC Obstetrics & Gynecology
SC Obstetrics & Gynecology
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ER

PT J
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AF Major, Kristof
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TI Unknown osteoporosis in older patients admitted to post-acute rehabilitation
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Osteoporosis; Screening or diagnosis or detection; Older patients; Rehabilitation
ID bone-mineral density; vertebral fracture assessment; hip fracture; lumbar spine; instrumental activity; women; risk; diagnosis; men; osteoarthritis
AB Background Osteoporotic fractures are associated with increased morbidity, mortality, and increased health care use. As the number of older adults increases, identifying those at increased risk for osteoporotic fractures has become of utmost importance to providing them with preventive and therapeutic interventions. Aims To determine the prevalence of unknown clinical and densitometric osteoporosis and to investigate the performance of different diagnostic strategies for osteoporosis in elderly patients admitted to rehabilitation. Method This is an observational study. Eligible participants were older adults admitted to rehabilitation in an academic hospital in Switzerland over an 11-month period. Patients with previously unknown osteoporosis underwent dual-energy X-ray absorptiometry (DXA), vertebral fracture assessment (VFA), and history review for past fractures. Results Complete assessment was available for 252 patients. Previously undiagnosed osteoporosis was identified in 62.3% of these patients, a proportion that was higher among women (71.5%) than men (44.8%). DXA proved most sensitive, followed by VFA and history review. Results differed across gender: DXA remained the most sensitive single test among women, but VFA proved most sensitive in men. The best test to combine with history review was DXA in women (detection increasing from 47.5 to 93.2%) and VFA in men (detection increasing

from 35.9 to 84.6%). Conclusions Prevalence of previously unknown osteoporosis appears very high in elderly patients admitted to post-acute rehabilitation. The combination of history review of previous fractures with DXA in women and with VFA in men appears the best two-step strategy to improving detection of osteoporosis in this population.
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NR 41
TC 6
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U2 4
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J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
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WC Geriatrics & Gerontology

SC Geriatrics & Gerontology
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PT J
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AF Gao, Xiaoming
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TI Successful total hip arthroplasty for autosomal dominant osteopetrosis complicated by hip osteoarthritis: A case report and review of the literature
SO EXPERIMENTAL AND THERAPEUTIC MEDICINE
LA English
DT Review
DE total hip arthroplasty (THA); osteopetrosis; osteoarthritis; hip pain; operative difficulties; osteoclast
ID malignant infantile osteopetrosis; stem-cell transplantation; management
AB Osteopetrosis is a rare congenital bone disorder, characterized by systemic osteosclerosis due to a deficiency of or functional defect in osteoclasts. Autosomal dominant osteopetrosis (ADOP) is the most common form with a late onset, a stable condition, relatively few symptoms and a good prognosis. Few studies to date have reported successful total hip arthroplasty (THA) in patients with ADOP and its operative difficulties. We herein describe a case of left hip osteoarthritis in a patient with OP via THA in order to share our experience during the treatment process. The patient was a 52-years-old female with osteopetrosis who was referred to our department due to a history of left hip pain with activity limitation for 20 years. The patient reported no history of fracture or family history. The patient underwent THA in the left hip. At the 6-month, 1- and 2-year follow-up, the components were in a good position and the patient remained asymptomatic and pain-free. Therefore, THA may be a feasible treatment option when patients with ADOP suffer from painful hip osteoarthritis.
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NR 27
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Z9 14
U1 0
U2 6
PU SPANDIDOS PUBL LTD
PI ATHENS
PA POB 18179, ATHENS, 116 10, GREECE
SN 1792-0981
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J9 EXP THER MED
JI Exp. Ther. Med.
PD APR 15
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IS 4
BP 2702
EP 2706
DI 10.3892/etm.2020.8503
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WC Medicine, Research & Experimental
SC Research & Experimental Medicine
GA LA0HB
UT WOS:000523637100038
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PT J
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TI Characteristics of medial condyle sagittal fracture of distal femur involving intercondylar notch in geriatric patients
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article
DE Fragility fracture; Unicondylar fractures; Distal femur
ID unicondylar fractures; fragility fracture
AB Introduction Unicondylar femoral fractures are uncommon injuries, known to occur primarily in young people, with high energy trauma. However, according to our experiences, unicondylar femoral fractures in geriatric patients generally involved the medial femoral condyle, unlike previously reported. In addition, the fractures of medial femoral condyle (FMFC) showed a characteristic fracture pattern. To date, there has been no published article focusing on the FMFC in geriatric patients. Thus, the aim of this study was to determine the characteristics of FMFC in geriatric patients and to present their outcomes. Materials and methods We retrospectively reviewed the medical records of 13 patients over age of 65 who underwent surgery for FMFC (AO-OTA 33B2). Of the 13, 10 patients were treated with Tomofix medial distal femoral plate (MDF) (Synthes GmbH, Switzerland) and additional screws fixation; the other three were treated with screw fixation and cast application. Results The mean age of patients was 76.8 years, and 10 patients were females. The fracture was due to low-energy trauma in all of the cases. Eight patients had medial knee osteoarthritis, and 2 patients were on osteoporosis treatment. A characteristic fracture pattern was observed. The fracture line extended from the lateral aspect of the intercondylar notch to the posteromedial column of the distal femur, with a characteristic medial beak. All fractures belonged to AO classification 33B2.1; there were no cases of AO classification 33B2.2 or 33B2.3. The postoperative joint function was graded according to the Kolmert functional criteria: ten cases were excellent, one case was good, one case was fair, and one case was poor. Conclusion FMFC caused by low-energy trauma in geriatric patients tend to have a characteristic pattern. We believe that anatomic reduction and firm fixation with Tomofix MDF plate and cannulated screw for low-energy trauma FMFC in geriatric patients would yield good outcomes.
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NR 16
TC 2
Z9 4
U1 0
U2 5
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SN 0936-8051
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J9 ARCH ORTHOP TRAUM SU
JI Arch. Orthop. Trauma Surg.
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PT J
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TI How We Manage Bone Marrow Edema-An Interdisciplinary Approach
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE Bone marrow edema (BME); magnetic resonance imaging (MRI); management; diagnosis; treatment
ID mr-imaging findings; osteochondral autograft transplantation; recurrent multifocal osteomyelitis; femoral-head; transient osteoporosis; knee osteoarthritis; nontraumatic osteonecrosis; avascular necrosis; articular defects; surgical options

AB Bone marrow edema (BME) is a descriptive term for a common finding in magnetic resonance imaging (MRI). Although pain is the major symptom, BME differs in terms of its causal mechanisms, underlying disease, as well as treatment and prognosis. This complexity together with the lack of evidence-based guidelines, frequently makes the identification of underlying conditions and its management a major challenge. Unnecessary multiple consultations and delays in diagnosis as well as therapy indicate a need for interdisciplinary clinical recommendations. Therefore, an interdisciplinary task force was set up within our large osteology center consisting of specialists from internal medicine, endocrinology/diabetology, hematology/oncology, orthopedics, pediatrics, physical medicine, radiology, rheumatology, and trauma surgery to develop a consenus paper. After review of literature, review of practical experiences (expert opinion), and determination of consensus findings, an overview and an algorithm were developed with concise summaries of relevant aspects of the respective underlying disease including diagnostic measures, clinical features, differential diagnosis and treatment of BME. Together, our single-center consensus review on the management of BME may help improve the quality of care for these patients.
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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AF Schenk, Pascal
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Beeler, Silvan
Ernstbrunner, Lukas
Meyer, Dominik C.
Gerber, Christian
TI Acromial Fractures Following Reverse Total Shoulder Arthroplasty: A Cohort Controlled Analysis
SO ORTHOPEDICS

LA English
DT Article
ID computed-tomography; glenohumeral joint; hounsfield units; proximal humerus; 4-part fractures; scapula; osteoarthritis; radiographs; prosthesis; angle
AB Fractures of the acromion can develop after reverse total shoulder arthroplasty (RTSA). This study sought to identify risk factors for acromial fracturesin patients with RTSA. A total of 1146 RTSAs were performed at theauthors' institution between 1999 and 2016. In 21 patients (1.8%), the authors identified an acromial fracture during the postoperative course. These patients were compared with a matched cohort of 84 patients who had not developed an acromial fracture postoperatively. As an indicator of changes in pre- to postoperative deltoid loading, the authors created an angle called the "delta angle." There was an elevated risk for acromial fractures with lower lateralization of the humerus from pre- to postoperatively (4.1 +/- 7.1 mm vs 8.4 +/- 6.1 mm; P=.006), lower preoperative anteroposterior acromial slope (117.3 degrees +/- 11.2 degrees vs 121.7 degrees +/- 17.0 degrees; P=.044), and higher glenoid inclination (beta angle, 72.0 degrees +/- 5.5 degrees vs 76.5 degrees +/- 6.8 degrees; P=.005). Pre- topostoperative changes in the beta angle (9.2 degrees +/- 8.0 degrees vs 4.4 degrees +/- 9.4 degrees; P=.022) and the delta angle (29.4 degrees +/- 8.1 degrees vs 19.5 degrees +/- 9.7 degrees; P<.001) were larger in the fracture group. In addition, diagnosed and treated osteoporosis appeared to be a risk factor for acromial fractures (33% vs 13%; P=.047). The delta angle after RTSA seems to correlate with the risk of developing an acromial fracture. Patients with a high glenoid inclination and/or osteoporosis should be informed that they are at risk. Further, surgeons should be aware that lower distalization together with greater medialization of the center of rotation was associated with more acromial fractures in this study.
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TI Underestimation and undertreatment of osteoporosis in patients awaiting primary total knee arthroplasty
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
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DT Article
DE Total knee arthroplasty; Osteoporosis; Prevalence; Treatment
ID bone-mineral density; periprosthetic fractures; osteoarthritis; prevalence; diagnosis; women; classification; korea; risk; hip
AB Introduction Osteoporosis is generally regarded as a risk factor for periprosthetic fracture during or after primary total knee arthroplasty (TKA).

Despite this, little is known about osteoporosis in patients undergoing elective primary TKA Therefore, we sought to investigate the prevalence of osteoporosis and rates of pharmacologic osteoporosis treatment prior to primary TKA. We hypothesized that preoperative osteoporosis is underestimated and undertreated in the primary TKA population. Materials and methods This retrospective study included consecutive 1972 patients scheduled for elective primary TKA at a single tertiary hospital (age, 50-89 years). Charts were reviewed for patient demographics, prior pharmacologic osteoporosis treatment and Knee Society (KS) scoring system and WOMAC score. Dual energy X-ray absorptiometry (DEXA) measurement of the lumbar vertebrae and proximal femur was performed in all patients on the day before surgery. The associations of BMD with age, sex, body mass index (BMI), and clinical outcome were analyzed. Results The prevalence of osteoporosis was 50.0% (53.4% in women and 7.0% in men). Among patients with osteoporosis, only 15.1% (149/986) of patients (15.0% in women and 30.0% in men) had pharmacological osteoporosis treatment prior to primary TKA. Age, sex and WOMAC stiffness showed association with osteoporosis. Sex (odds ratio (OR): 20.83, $p < 0.001$) was the most significant factor associated with osteoporosis. Conclusion Osteoporosis was highly prevalent in patients awaiting TKA, but the rates of diagnosis and pharmacologic osteoporosis treatment were low. Therefore, more attention needs to estimate and treat osteoporosis in patients awaiting primary TKA, especially in female patients.
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SC Orthopedics; Surgery
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PT J
AU Gong, L
Zhang, YY
Yang, N
Qian, HJ
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AF Gong, Long
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TI Raloxifene Prevents Early Periprosthetic Bone Loss for Postmenopausal Women after Uncemented Total Hip Arthroplasty: A Randomized Placebo-Controlled Clinical Trial
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE Bone loss; Postmenopausal osteoporosis; Raloxifene; Total hip arthroplasty (THA)
ID follow-up; mineral density; 2-year rsa; alendronate; pathways; cups; stem; dxa; bmd
AB Objective To examine the results of raloxifene for prevention of periprosthetic bone loss around the femoral stem in patients undergoing total hip arthroplasty (THA). Methods Between January 2015 and May 2017, 240 female patients between 55 and 80 years underwent primary THA and were randomly allocated to receive 60 mg raloxifene hydrochloride per day (treatment group, TG, n = 120) or placebo (control group, CG, n = 120) orally at bedtime using computer-generated randomization sequence generation. Baseline data, the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC), women's quality of life (QoL) score, bone mineral density (BMD) around the prosthesis, and adverse events were compared between the two groups. The measuring range of BMD around the prosthesis was divided into seven regions of interest (ROI). The sample size was calculated to detect a mean difference in BMD of 0.15 g/cm(2)with a standard

deviation (SD) of 0.3. The error was set at 0.05 and the power level at 90% with additional compensation for a possible dropout rate of 20%. Results A total of 240 participants in the study up to 24 months after THA. There were no significant differences in the mean BMD of all the zones between groups before surgery (allP> 0.05). However, there were significant differences in the BMD of Gruen zones 4 and 7 between groups at 6 months postoperatively (bothP< 0.05); there were significant differences in Gruen zones 1, 4, 6, and 7 at 12 months postoperatively (allP< 0.01); there were significant differences in Gruen zones 1, 2, 4, 6, and 7 at 24 months postoperatively (allP< 0.001). Patients taking raloxifene reported higher QoL scores, with better improvement in BMD in all areas except in zones 3 and 5 compared with the control group. There were no significant differences in WOMAC pain (P= 0.4045), WOMAC function (P= 0.4456) and women's QoL scores (P= 0.5983) between groups before surgery. However, WOMAC pain, WOMAC function and women's QoL score in the treatment group were significantly better at all time points (allP< 0.05). Patients in the treatment group showed no increased adverse events, including cardiac events, stroke, venous thromboembolism, and gynecological cancer (allP> 0.05), but did show decreased odds of breast cancer in comparison with those using a placebo (P= 0.0437). Conclusion Raloxifene can help inhibit bone loss around the prosthesis and improve the QoL of postmenopausal women after THA with no increased adverse events, and can even decrease the odds of breast cancer.
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TI The Association of Gait Speed and Frontal Lobe among Various Cognitive Domains: The Korean Frailty and Aging Cohort Study (KFACS)
SO JOURNAL OF NUTRITION HEALTH & AGING
LA English
DT Article
DE Gait; cognitive function; frontal lobe function; elderly
ID walking; decline; impairment; activation; disorders; dementia; people; adults
AB Objective The aim of this study was to determine how gait speed and frontal lobe functionsin community-dwelling older adults in Korea. Design This was a

cross-sectional study. Setting The study used data from the Korean Frailty and Aging Cohort Survey (KFACS), a multi-center longitudinal study addressing 10 centers across urban, rural, and suburban communities in Korea, between 2016 and 2017. Participants A total of 1552 older adults who underwent both gait speed tests and cognitive functions tests during the investigation of the KFACS. Measurements Gait speed was assessed by asking participants to walk from a starting point to a point 4 meters away at a normal gait. Cognitive functions were evaluated using various standardized cognitive functions tests. Results Gait speed was slower when participants were older or less educated The percentage of women, higher BMI, people with lower incomes, singles, smokers, and drinkers was high in the slower gait group. Also, all cognitive function scores were low and depression score was high in the group with slower walking speed. The slower walking speed showed low physical activity score and high prevalence of hypertension, osteoarthritis and osteoporosis. Among the seven cognitive functions (MMSE, memory, TMT, Recall, Recognition, digit span, and Fab), only TMT showed no significant difference between different gait speed groups. The other six cognitive functions showed higher results in the fastest gait speed group (T3), Participants in middle gait speed group (T2) also showed higher results in five of the seven cognitive function scores as well (Memory, Recall, Recognition, digit span, and Fab). Conclusion In this study, we found correlation between the slower gait speeds and the decrease in cognitive function, and especially the frontal lobe dysfunction was most prominent of all cognitive dysfunctions.
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PT J
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TI Sulfurous thermal waters stimulate the osteogenic differentiation of human mesenchymal stromal cells - An in vitro study
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Sulfurous thermal water; Osteogenesis; Hydrogen sulfide; Mesenchymal stromal cells; Mineralization; Complementary medicine
ID hydrogen-sulfide; fluorescent-probes; double-blind; spa therapy; balneotherapy; osteoporosis; inhalations; expression; ions; osteoarthritis
AB Strategies aimed at delaying the onset of bone tissue degeneration and the resulting skeletal fragility are key to decrease the risk of bone fracture correlated to ageing. The therapeutic properties of sulfurous thermal waters (STWs), rich in hydrogen sulfide (H2S), have been claimed for centuries. However, the direct regulation of bone cells by STWs has not been investigated yet. Here we aimed at analyzing the effect of STWs on cultured human mesenchymal stromal cells (hMSCs) derived from bone tissue. Two concentrations of STWs from 2 health spa centers in Italy (here named STW-1 and STW-2) containing, respectively, high and moderate quantities of H2S, were added to the culture media. Cytotoxicity and osteogenic differentiation were evaluated. We provided first evidence that treatment of hMSCs with STWs results in a sharp increase in intracellular H2S content, coherent with the different concentrations of H2S, thereby reveling that STWs-released H2S is internalized by cells. STWs treatment significantly induced osteogenic differentiation of hMSCs. In particular, mineral apposition was increased with a similar pattern by the two STWs, while mRNA expression of osteogenic markers (BSP, OC, RUNX-2, OPN) was differently affected. Only STW-2 induced a significant, dose-dependent increase in these gene expression. These findings support the rationale for the use of STWs as a complementary treatment of bone wasting diseases.
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TI Alterations in DNA methylation profiles in cancellous bone of postmenopausal women with osteoporosis

SO FEBS OPEN BIO
LA English
DT Article
DE differentially methylated genes; DNA methylation profiles; osteoporosis; postmenopausal women; signaling pathways
ID expression profile; fracture; cells; identification; microarray; strength; modulus; density; risk; rna
AB Osteoporosis is characterized by systemic microarchitecture impairment and bone loss, which ultimately lead to fragility fractures. This disease is most common in older people, especially in postmenopausal women. Cancellous bone is affected by osteoporosis earlier than cortical bone, and DNA methylation microarray analysis of the hip cancellous bone of patients with osteoarthritis revealed differential methylation. In view of the important role of cancellous bone in bone development, we examined genome-wide DNA methylation profiles in the cancellous bone from patients with postmenopausal osteoporosis versus healthy postmenopausal women using Illumina 850K methylation microarray analysis. Under a threshold ofP < 0.05, we obtained a total of 8973 differentially methylated genes, such asSOX6,ACE,SYKandTGFB3. Under a threshold ofP 0.2, a total of 17 and 34 key differentially methylated genes were further identified at the promoter region and cytosine- phosphate- guanine (CpG) islands (such asPRKCZ,GNA11andCOL4A1), respectively.PLEKHA2,PLEKHB1,PNPLA7,SCD,MGST3andTSNAXwere the most common differentially methylated genes at both the promoter region and CpG islands. Five important signaling pathways, including the calcium signaling pathway, the cyclic guanosine phospho-protein kinase G (cGMP-PKG) signaling pathway, endocytosis, the Rap1 signaling pathway and the AMPK signaling pathway were identified. Our study may be suitable as a basis for exploring the mechanisms underlying osteoporosis in postmenopausal women.
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FU Scientific Research Project of Sichuan Provincial Health and Family Planning Commission in 2018 of "Application of different guided screw placement techniques in the treatment of senile osteoporotic spinal degeneration" [18PJ472]; Deyang Science and Technology Plan Project in 2019 of "Clinical efficacy of bone filled mesh bag combined with self-curing calcium phosphate artificial bone in the treatment of osteoporotic vertebral compression fracture and finite element analysis of stre [2019SZ046]; Bethune Foundation Scientific Research Project in 2018 of "Clinical effect of bone filled mesh bag on osteoporotic vertebral compression fracture and finite element analysis of stress in adjacent vertebrae" [BK-JS2018002]; Sichuan Provincial Commission of Health and Family Planning/Key

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TI Probing Trace Elements in Human Tissues with Synchrotron Radiation

SO CRYSTALS
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DT Review
DE synchrotron; X-ray fluorescence; X-ray absorption spectroscopy; trace elements; biological tissues; medicine; diseases
ID x-ray-fluorescence; invasive ductal carcinoma; human bone; arsenic microdistribution; absorption spectroscopy; chemical speciation; oxidation-state; iron compounds; breast-cancer; zinc
AB For the past several decades, synchrotron radiation has been extensively used to measure the spatial distribution and chemical affinity of elements found in trace concentrations (<few mu g/g) in animal and human tissues. Intense and highly focused (lateral size of several micrometers) X-ray beams combined with small steps of photon energy tuning (2-3 eV) of synchrotron radiation allowed X-ray fluorescence (XRF) and X-ray absorption spectroscopy (XAS) techniques to nondestructively and simultaneously detect trace elements as well as identify their chemical affinity and speciation in situ, respectively. Although limited by measurement time and radiation damage to the tissue, these techniques are commonly used to obtain two-dimensional and three-dimensional maps of several elements at synchrotron facilities around the world. The spatial distribution and chemistry of the trace elements obtained is then correlated to the targeted anatomical structures and to the biological functions (normal or pathological). For example, synchrotron-based in vitro studies of various human tissues showed significant differences between the normal and pathological distributions of metallic trace elements such as iron, zinc, copper, and lead in relation to human diseases ranging from Parkinson's disease and cancer to osteoporosis and osteoarthritis. Current research effort is aimed at not only measuring the abnormal elemental distributions associated with various diseases, but also indicate or discover possible biological mechanisms that could explain such observations. While a number of studies confirmed and strengthened previous knowledge, others revealed or suggested new possible roles of trace elements or provided a more accurate spatial distribution in relation to the underlying histology. This area of research is at the intersection of several current fundamental and applied scientific inquiries such as metabolomics, medicine, biochemistry, toxicology, food science, health physics, and environmental and public health.
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TI The 2019 Revised Version of Association Research Circulation Osseous Staging System of Osteonecrosis of the Femoral Head
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE staging; hip; osteonecrosis; avascular necrosis; Delphi
ID total hip-arthroplasty; nontraumatic osteonecrosis; rotational osteotomy; avascular necrosis; asymptomatic osteonecrosis; classification-system; natural-history; reproducibility; interobserver; collapse
AB Background: The Association Research Circulation Osseous (ARCO) presents the 2019 revised staging system of osteonecrosis of the femoral head (ONFH) based on the 1994 ARCO classification. Methods: In October 2018, ARCO established a task force to revise the staging system of ONFH. The task force involved 29 experts who used a web-based survey for international collaboration. Content validity ratios for each answer were calculated to identify the levels of agreement. For the rating queries, a consensus was defined when more than 70% of the panel members scored a 4 or 5 rating on a 5-point scale. Results: Response rates were 93.1%-100%, and through the 4-round Delphi study, the 1994 ARCO classification for ONFH was successfully revised. The final consensus resulted in the following 4-staged system: stage I-X-ray is normal, but either magnetic resonance imaging or bone scan is positive; stage II-X-ray is abnormal (subtle signs of osteosclerosis, focal osteoporosis, or cystic change in the femoral head) but without any evidence of subchondral fracture, fracture in the necrotic portion, or flattening of the femoral head; stage III-fracture in the subchondral or necrotic zone as seen on X-ray or

computed tomography scans. This stage is further divided into stage IIIA (early, femoral head depression <= 2 mm) and stage IIIB (late, femoral head depression >2 mm); and stage IV-X-ray evidence of osteoarthritis with accompanying joint space narrowing, acetabular changes, and/or joint destruction. This revised staging system does not incorporate the previous subclassification or quantitation parameters, but the panels agreed on the future development of a separate grading system for predicting disease progression. Conclusion: A staging system has been developed to revise the 1994 ARCO classification for ONFH by an expert panel-based Delphi survey. ARCO approved and recommends this revised system as a universal staging of ONFH. (C) 2019 Published by Elsevier Inc.
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TI PP121 suppresses RANKL-Induced osteoclast formation in vitro and LPS-Induced bone resorption in vivo
SO EXPERIMENTAL CELL RESEARCH
LA English
DT Article
DE PP121; Osteoclasts; RANKL; Bone resorption; Src
ID nf-kappa-b; induced osteolysis; osteoporosis; proliferation; inhibition; expression; tyrosine; cancer; roles
AB Bone resorption, caused by osteoclasts (OCs), is important to bone homeostasis. The abnormalities of bone resorption may induce a series of diseases, including osteoarthritis, osteoporosis and aseptic peri-implant loosening. The latest research developed,a novel tyrosine and phosphoinositide kinase dual inhibitor, named PP121, inhibited Src in anaplastic thyroid carcinoma cell. However, the therapeutic function of PP121 on abnormal bone resorption is still uncertain. In the present study, we showed that PP121 could potently suppress osteoclast differentiation, osteoclast-specific gene expression and bone resorption via suppressing Src/MAPK (ERK and p38)/Akt-mediated NFATc1 induction in vitro. \It was found that PP121 could suppress the formation of osteoclasts from bone marrow macrophages (BMMs) without causing cytotoxicity, inhibit bone resorption and downregulate the mRNA level of osteoclast-specific markers, including calcitonin receptor (CTR), tartrate resistant acid phosphatase (TRAP), cathepsin K (CTSK), matrix metalloproteinase 3 (MMP3), Cellular oncogene fos (C-Fos) and nuclear factor of activated T-cells cytoplasmic 1 (NFATc1). Consistent with in vitro observation, we found that PP121 greatly ameliorated LPS-induced bone resorption. Our results

provide promising evidence of the therapeutic potential of PP121 for osteolytic diseases related to excessive osteoclast-mediated bone resorption.
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TI Efficacy of low-magnitude high-frequency vibration (LMHFV) on musculoskeletal health of participants on wheelchair: a study protocol for a single-blinded randomised controlled study
SO BMJ OPEN
LA English
DT Article
DE musculoskeletal disorders; geriatric medicine; bone diseases
ID whole-body vibration; muscle performance; sitting balance; blood-flow; bone loss; expression; exercise; tests
AB Background Osteoporosis is an age-related disease with progressive loss of bone, leading to fragile bone. It is one of the major health issues in older adults and causes medical, social and economic impacts globally. Patients with osteoporosis have high risk of osteoporotic fractures. Low-magnitude high-frequency vibration (LMHFV) is a non-invasive biophysical intervention providing whole-body mechanical stimulation. Previous studies showed that LMHFV is beneficial to muscle strength, postural control, balancing ability, new bone formation, spinal bone mineral density (BMD) and blood circulation. During the LMHFV treatment, older adults need to stand upright on the platform for 20 min/day. However, some physically weak elderlies with poor musculoskeletal ability cannot stand for a long period. Therefore, the design of vibration platform is modified for the disabled patients to treat at sitting position and the efficacy of LMHFV on this group of elderlies will be verified. It is hypothesised that new design of LMHFV is beneficial to wheelchair users in terms of vertebral BMD, muscle health and musculoskeletal functions. Methods This study is a single-blinded randomised

controlled trial to investigate the effect of LMHFV on vertebral BMD, muscle health, balancing ability and functional ability in wheelchair users (mainly on wheelchair for outdoor activities). Healthy elderlies aged 65 years or above with walking difficulties and using wheelchair are eligible. Exclusion criteria are those: (1) who cannot stand and walk independently, (2) who have vibration treatment before, (3) with malignancy, (4) with acute fractures or severe osteoarthritis, (5) with cardiovascular concern such as with pacemaker in situ, (6) with chronic inflammatory conditions known to affect muscle metabolism such as rheumatoid arthritis and (7) with high frequency of physical activities, such as participants who participated in regular exercise five times a week or more. Recruited participants will be randomised to either LMHFV or control group. Participant assigned to LMHFV group will receive LMHFV (35 Hz, 0.3g (g=gravitational acceleration), 20 min/day, at least three times/week) for 6 months. The primary outcome is BMD at the lumbar spine to be assessed by dual-energy X-ray absorptiometry that is clinically recommended for the diagnosis of osteoporosis. All primary and secondary outcome assessments for all groups will be performed in the investigators' institute at baseline and 6 months post treatment. Discussion This study aims to investigate the effects of LMHFV on wheelchair users. The findings of this study will help to confirm the efficacy of LMHFV on vertebral BMD, muscle health, balancing ability and functional outcomes in wheelchair using elderlies. LMHFV therapy is an intervention strategy that is easy to implement at the community healthcare level or individually at home that has previously been proven to reduce fall risk and muscle strength at the lower limb. The ultimate goal is to improve their bone and muscle quality of wheelchair users, as well as enhancing their quality of life.
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TI Prevalence and Factors Associated with Analgesic Prescribing in Poly-Medicated Elderly Patients
SO DRUGS & AGING
LA English
DT Article
ID drug-metabolism; pain; management; risk; osteoarthritis; polypharmacy; pharmacokinetics; recommendations; frail; falls

AB Background Pain is common in older patients and management guidelines rarely consider the effect of multiple comorbidities and concurrent medications on analgesic selection. Objectives The objectives of this study were to identify the prevalence and pattern of analgesic prescribing and associated factors in older patients with polypharmacy. Methods Older patients (aged >= 75 years) admitted to the Royal Adelaide Hospital between September 2015 and August 2016 and with polypharmacy were included and their comorbidities and medications prescribed at discharge were recorded. Drug Burden Index and Charlson Comorbidity Index were calculated. The number of medications that increased the risk of orthostatic hypotension were recorded. Logistic regression was used to compute the association between analgesic use and participant characteristics, and results were presented as odds ratios and 95% confidence intervals, adjusted for age, sex, Charlson Comorbidity Index, Drug Burden Index and orthostatic hypotension. Results Over 15,000 admissions were identified, of which 1192 patients were included, 824 (69%) of whom were prescribed an analgesic medication. Paracetamol (used by 89% of analgesic users), opioids (34%) and adjuvants (17%) were used more frequently than non-steroidal anti-inflammatory drugs (8%). Analgesic users had a higher Drug Burden Index, were prescribed more medications and were less likely to be male compared with non-users. Charlson Comorbidity Index across the cohort was high (7.3 +/- 1.9) but there was no difference between analgesic users and non-users, but analgesic users were more likely to have a documented diagnosis of osteoarthritis, osteoporosis and falls. Opioid use was associated with the Drug Burden Index, while adjuvant use was associated with orthostatic hypotension. Opioid use was associated with having a diagnosis of osteoporosis and falls. Conclusions In our cohort of poly-medicated elderly patients, prescription of analgesic medications was common, and these patients are likely to have an increased rate of adverse drug reactions and falls compared with those who were not prescribed analgesic medications.
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AF Jiang, Ai
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Song, Chunli
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TI Phenotype changes of subchondral plate osteoblasts based on a rat model of ovariectomy-induced osteoarthritis
SO ANNALS OF TRANSLATIONAL MEDICINE
LA English
DT Article
DE Osteoarthritis (OA); osteoblasts; ovariectomy; phenotype; subchondral bone
ID anterior cruciate ligament; ii collagen degradation; cartilage turnover; bone; differentiation; cells; mineralization; proliferation; osteoporosis; transection
AB Background: Osteoarthritis (OA) is prevalent in postmenopausal women. Subchondral bone in ovariectomized (OVX) rats might play a more important role in cartilage degeneration compared with other types of OA. How subchondral osteoblast changes in OVX rats is still unclear. Understanding of osteoblast changes obtained from OVX subchondral bone might be helpful to clarify pathogenesis of OVX-OA. Methods: Female Sprague-Dawley rats were randomly divided into two groups: Sham (n=20) and OVX (n=20). Serum levels of Alkaline phosphatase (ALP) and C-telopeptide of type I collagen (CTX-I) were measured every one or two weeks. All rats were executed at week 9 post surgery. The weight of rats and the wet weight of uterus were assessed. Micro-computed Tomography (micro-CT) was used to analyze the knee microstructure, and toluidine blue staining was employed to evaluate cartilage erosion. Subchondral osteoblast proliferation ability by cell counting kit-8 assay, osteogenic genes expressions by reverse transcription polymerase chain reaction (RT-PCR), differentiation and mineralization ability by ALP staining and alizarin red staining were evaluated and compared between Sham and OVX. Results: Ovariectomy induced significant increases of serum ALP and CTX-I as early as at week 2. At week 9 after surgery, the body

weight of OVX rats was significantly increased, and uterus weight of OVX rats was remarkably decreased. OVX rats demonstrated significant subchondral bone change and cartilage erosion compared with Sham rats. mRNA levels of early markers of osteogenic differentiation (ALP, type I collagen, Runx2) were enhanced in OVX rats, but the late marker (osteocalcin) was not significantly different. ALP activity of osteoblasts increased, but the mineralization capacity decreased in OVX rats. Conclusions: Subchondral osteoblasts in OVX rats exhibited different proliferation, differentiation and mineralization abilities from normal counterparts.
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TI Specific inhibition of FAK signaling attenuates subchondral bone deterioration and articular cartilage degeneration during osteoarthritis pathogenesis
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Article
DE FAK; H-type vessels; osteoarthritis; subchondral bone; Y15
ID focal adhesion kinase; promotes angiogenesis; vessel formation; knee; cells; osteogenesis; replacement; progression
AB Osteoarthritis (OA), a disease of the entire joint, is characterized by abnormal bone remodeling and coalescent degradation of articular cartilage. We have previously found that elevated levels of H-type vessels in subchondral bone correlate with OA and that focal adhesion kinase (FAK) is critical for H-type vessel formation in osteoporosis. However, the potential role of FAK in OA remains unexplored. Here, we demonstrate that the p-FAK level was dramatically elevated in subchondral bone following anterior cruciate ligament transection (ACLT) in rats. Specific inhibition of FAK signaling with Y15 in subchondral bone resulted in the suppression of subchondral bone deterioration and this effect was mediated by H-type vessel-induced ectopic bone formation. Further, articular cartilage degeneration was also alleviated after Y15 treatment. In vitro, the p-FAK level was significantly elevated in mesenchymal stem cells (MSCs) from vehicle-treated ACLT rats as compared to that in MSCs from sham controls and Y15-treated ACLT rats. Elevated p-FAK level in MSCs promoted vascular endothelial growth factor (VEGF) expression, as demonstrated from the high VEGF level in the blood, subchondral bone, and conditioned medium (CM) of MSCs from vehicle-treated ACLT rats. The CM of MSCs from vehicle-treated ACLT rats might promote the angiogenesis of endothelial cells and the catabolic response of chondrocytes through the FAK-growth factor receptor-bound protein 2-mitogen-activated protein kinase-mediated expression of VEGF. The effect of the CM from MSCs of Y15-treated ACLT rats or that treated with a VEGF-neutralizing antibody on vessel formation and the catabolic response was lowered. Thus, the specific inhibition of FAK signaling may be a promising avenue for the prevention or early treatment of OA.
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TI Efficacy and safety of the first-in-class imidazoline-2 receptor ligand CR4056 in pain from knee osteoarthritis and disease phenotypes: a randomized, double-blind, placebo-controlled phase 2 trial
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article

DE CR4056; Knee osteoarthritis; Imidazoline-2 receptor; Randomized controlled trial; Phenotypes
ID hip osteoarthritis; relevant outcm; european-society; economic-aspects; recommendations; epidemiology; osteoporosis; validation; management; state
AB Objective: CR4056 is a selective imidazoline-2 (I2) receptor ligand with potent analgesic activity in animal pain models. This proof-of-concept study tested CR4056 efficacy and safety in patients with knee osteoarthritis (OA) and different phenotypes. Design: This is a multicenter, randomized, double-blind, placebo-controlled trial. Knee OA patients with moderate to severe pain received CR4056 (women 100 mg bid; men 200 mg bid) or placebo (both genders) for 14 days. The primary outcome was the change in WOMAC pain score (0-100 scale) compared to placebo, analyzed in the intention-to-treat population and pre-defined OA phenotypes. Results: 213 patients were treated with CR4056 (92 women; 52 men) or placebo (69 overall). After 14 days, median WOMAC pain improvements were 10 points on placebo and 14, 20 and 16 in women, men, and pooled CR4056 groups (P = 0.184, 0.030 and 0.070 vs placebo, respectively). Pre-specified subgroup analysis in the metabolic OA phenotype (BMI >= 27.5 kg/m(2), N = 156) showed statistically significant differences in all CR4056-treated groups vs placebo of 12-18 points. Conversely, there were too few patients with a neuropathic or inflammatory phenotype for a meaningful analysis. CR4056 was well tolerated; the most common adverse event was mild headache. Conclusions: Although the primary endpoint was met in males only, this exploratory phase 2 trial shows that CR4056 might be an effective analgesic against knee OA pain, especially in overweight patients representing the metabolic OA phenotype. These findings, along with the broad-spectrum analgesic activity of CR4056 in animal models, warrant further clinical investigation in OA and other pain conditions. Clinical trial
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TI Stress Distributions and Micromovement of Fragment Bone of Pilon Fracture

Treated With External Fixator: A Finite Element Analysis
SO JOURNAL OF FOOT & ANKLE SURGERY
LA English
DT Article
DE external fixator; finite element; micromovement; osteoarthritis; osteoporosis; pilon
ID biomechanical evaluation; internal-fixation; plafond fractures; proximal femur; plate; foot; optimization; simulation; management; ligaments
AB Osteoporosis and osteoarthritis are common pathological problems of the human bone tissue. There are some cases of pilon fractures associated with these 2 pathological conditions. In terms of treatment, for a normal and healthy bone with pilon fracture, the use of the Delta external fixator is a favorable option because it can allow early mobilization for patients and provide stability for the healing process. However, the stability of the external fixator differs when there is low bone stiffness, which has not been previously investigated. Therefore, this study was conducted to determine the stability of the external fixator to treat pilon fracture associated with osteoporosis and osteoarthritis, particularly to differentiate the stress distribution and micromovement of fracture fragment. Three-dimensional finite element models of the ankle and foot bones were reconstructed based on the computed tomography datasets. The bones consisted of 5 metatarsal, 3 cuneiform, and 1 each of cuboid, navicular, calcaneus, talus, fibula, and tibia bones. They were assigned with linear isotropic behavior. The ankle joint consisted of liga-ment and cartilage, and they were assigned with the use of linear links and the Mooney-Rivlin model, respectively. During simulation of the gait cycle, 70 N and 350 N were applied axially to the tibia bone to represent the swing and stance phases, respectively. The metatarsal and calcaneus bones were fixed to prevent any movement of the rigid body. The study found that the greatest von Mises stress value was observed at the pin-bone interface for the osteo-porosis (108 MPa) model, followed by the osteoarthritis (87 MPa) and normal (44 MPa) models, during the stance phase. For micromovement, the osteoporosis model had the largest value at 0.26 mm, followed by the osteoarthritis (0.09 mm) and normal (0.03 mm) models. In conclusion, the greatest magnitudes of stress and micromovement were observed for the osteoporosis bone and extra care should be taken to treat pilon fracture associated with this patho-logical condition. (C) 2019 by the American College of Foot and Ankle Surgeons. All rights reserved.
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TI Impact of Chronic Medical Condition Development on Longitudinal Physical Function from Mid- to Early Late-Life: The Study of Women's Health Across the Nation
SO JOURNALS OF GERONTOLOGY SERIES A-BIOLOGICAL SCIENCES AND MEDICAL SCIENCES
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DT Article
DE Multimorbidities; Physical function; Disablement process
ID change-point model; quality-of-life; cognitive decline; disability; multimorbidity; older; association; comorbidity; population; strength
AB Background: Chronic medical conditions (CMCs) often emerge and accumulate during the transition from mid- to late-life, and the resulting multimorbidity can greatly impact physical function. We assessed the association of CMC presence and incidence on trajectories of physical function from mid- to early late-life in the Study of Women's Health Across the Nation. Methods: Physical function was assessed at eight clinic visits (average 14 years follow-up) using the physical function subscale of the Short Form-36. CMCs included osteoarthritis, diabetes, stroke, hypertension, heart disease, cancer, osteoporosis, and depressive symptomatology, and were considered cumulatively. Repeated-measures Poisson models estimated longitudinal change (expressed as percent difference) in physical function by chronic CMCs. Change-points assessed physical function change coincident with the development of a new condition. Results: Women (N = 2,283) followed from age 50.0 +/- 2.7 to 64.0 +/- 3.7 years; 7.3% had zero CMCs through follow-up, 22.5% (N = 513) had no baseline CMCs but developed >= 1, 22.7% women had >= 1 baseline CMC but never developed another, and 47.6% had >= 1 baseline CMC and developed >= 1 more. Each additional baseline CMC was associated with 4.0% worse baseline physical function and annual decline of 0.20%/year. Women with more baseline CMCs had greater decline in physical function with a new CMC (-1.90% per condition); and annual decline when developing a new condition accelerated by -0.33%/year per condition. Conclusions: Self-reported physical function changes are evident from mid- to early late-life with the development of CMCs. Preventing or delaying CMCs may delay declines in physical function, and these potential pathways to disability warrant further research.
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DT Review
DE aging; cancer; coronary artery disease; diabetes type 2; dyslipidemia; estradiol; hormone therapy; insulin resistance; menopause; midlife transition; metabolic syndrome; steroid and insulin receptors; systemic inflammatory state; visceral adiposity; waist circumference; window of opportunity
ID coronary-heart-disease; postmenopausal hormone-therapy; estrogen plus progestin; body-mass index; breast-cancer; womens health; metabolic syndrome; diabetes-mellitus; insulin-receptor; united-states
AB Heart disease and cancer are the leading causes of death in the United States. In women, the clinical appearance of both entities-coronary heart disease and cancer (breast, endometrium, and ovary)-escalate during the decades of the midlife transition encompassing the menopause. In addition to the impact of aging, during the interval between the age of 40 and 65 years, the pathophysiologic components of metabolic syndrome also emerge and accelerate. These include visceral adiposity (measured as waist circumference), hypertension, diabetes, and dyslipidemia. Osteoporosis, osteoarthritis, sarcopenia, depression, and even cognitive decline and dementia appear, and most, if not all, are considered functionally related. Two clinical reports confirm the interaction linking the emergence of disease: endometrial cancer and metabolic syndrome. One describes the discovery of unsuspected endometrial cancer in a large series of elective hysterectomies performed in aged and metabolically susceptible populations. The other is from the Women's Health Initiative Observational Study, which found a positive interaction between endometrial cancer and metabolic syndrome regardless of the presence or absence of visceral adiposity. Both provide additional statistical support for the long-suspected causal interaction among the parallel but variable occurrence of these common entities-visceral obesity, heart disease, diabetes, cancer, and the prevalence of metabolic syndrome. Therefore, 2 critical clinical questions require analysis and answers: 1: Why do chronic diseases of adulthood-metabolic, cardiovascular, endocrine- and, in women, cancers of the breast and endometrium (tissues and tumors replete with estrogen receptors) emerge and their incidence

trajectories accelerate during the postmenopausal period when little or no endogenous estradiol is available, and yet the therapeutic application of estrogen stimulates their appearance? 2: To what extent should identification of these etiologic driving forces require modification of the gynecologist's responsibilities in the care of our patients in the postreproductive decades of the female life cycle? Part I of this 2-part set of "expert reviews" defines the dimensions, gravity, and interactive synergy of each clinical challenge gynecologists face while caring for their midlife (primarily postmenopausal) patients. It describes the clinically identifiable, potentially treatable, pathogenic mechanisms driving these threats to quality of life and longevity. Part 2 (accepted, American Journal of Obstetrics & Gynecology) identifies 7 objectives of successful clinical care, offers "triage" prioritization targets, and provides feasible opportunities for insertion of primary preventive care initiatives. To implement these goals, a reprogrammed, repurposed office visit is described.YY
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TI Epidemiology of the association between serum 25-hydroxyvitamin D levels and musculoskeletal conditions among elderly individuals: a literature review
SO JOURNAL OF PHYSIOLOGICAL ANTHROPOLOGY
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DT Review
ID bone-mineral density; vitamin-d status; hip fracture risk; d deficiency; physical performance; muscle strength; japanese women; older-adults; falls; population
AB Background Vitamin D deficiency is associated with osteoporosis, fracture, muscle weakness, falls, and osteoarthritis in adults. Elderly individuals are more likely to present with poor musculoskeletal conditions. Recently, several epidemiological studies have assessed the correlation between serum

25-hydroxyvitamin D (25(OH)D) levels and musculoskeletal conditions in elderly individuals. Main text Osteoporosis is a skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Numerous studies have shown a positive association between serum 25(OH)D levels and bone mineral density. Only a few studies have reported an association between serum 25(OH)D levels and quantitative ultrasound (QUS) parameters. Low serum 25(OH)D level may be a risk factor for hip fracture. However, data on the association between vitamin D deficiency and the incidence of non-hip fracture are contrasting. Falls are a major cause of mortality and morbidity in older adults. Several prospective population-based cohort studies have shown that low 25(OH)D levels are associated with an increased risk of falls. Reduced muscle strength and physical performance are risk factors for adverse events, including disability, institutionalization, and mortality. The role of vitamin D in musculoskeletal functionality (muscle weakness and physical performance) among elderly individuals is still controversial. Osteoarthritis (OA) is the most common form of arthritis and is a leading cause of disability among older adults. Data on the association between serum 25(OH)D levels and OA are contrasting. Conclusion Some studies have shown that vitamin D deficiency may be a risk factor for poor musculoskeletal conditions, such as osteoporosis, fracture, muscle weakness, falls, and osteoarthritis in adults. However, other studies did not find an association between serum 25(OH)D levels and musculoskeletal conditions.

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NR 49
TC 12
Z9 18
U1 1
U2 8
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN 1880-6805
EI
J9 J PHYSIOL ANTHROPOL
JI J. Physiol. Anthropol.
PD DEC 26
PY 2020
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IS 1
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DI 10.1186/s40101-020-00249-3
PG 6
WC Physiology
SC Physiology
GA OW6DF
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ER

PT J
AU Black, JE
Terry, AL

Lizotte, DJ
AF Black, Jason E.
Terry, Amanda L.
Lizotte, Daniel J.
TI Development and evaluation of an osteoarthritis risk model for integration into primary care health information technology
SO INTERNATIONAL JOURNAL OF MEDICAL INFORMATICS
LA English
DT Article
DE Prognostic prediction model; Risk; Electronic medical record; Osteoarthritis; CPCSSN
ID clinical-prediction models; knee osteoarthritis; hip; recommendations; surveillance; prevention; imputation; weight; injury; hand
AB Background: We developed and evaluated a prognostic prediction model that estimates osteoarthritis risk for use by patients and practitioners that is designed to be appropriate for integration into primary care health information technology systems. Osteoarthritis, a joint disorder characterized by pain and stiffness, causes significant morbidity among older Canadians. Because our prognostic prediction model for osteoarthritis risk uses data that are readily available in primary care settings, it supports targeting of interventions delivered as part of clinical practice that are aimed at risk reduction. Methods: We used the CPCSSN (Canadian Primary Sentinel Surveillance Network) database, which contains aggregated electronic health information from a cohort of primary care practices, to develop and evaluate a prognostic prediction model to estimate 5-year osteoarthritis risk, addressing contextual challenges of data availability and missingness. We constructed a retrospective cohort of 383,117 eligible primary care patients who were included in the cohort if they had an encounter with their primary care practitioner between 1 January 2009 and 31 December 2010. Patients were excluded if they had a diagnosis of osteoarthritis prior to their first visit in this time period. Incident cases of osteoarthritis were observed. The model was constructed to predict incident osteoarthritis based on age, sex, BMI, previous leg injury, and osteoporosis. Evaluation of the model used internal 10-fold cross-validation; we argue that internal validation is particularly appropriate for a model that is to be integrated into the same context from which the data were derived. Results: The resulting prediction model for 5-year risk of osteoarthritis diagnosis demonstrated state-of-the-art discrimination (estimated AUROC 0.84) and good calibration (assessed visually.) The model relies only on information that is readily available in Canadian primary care settings, and hence is appropriate for integration into Canadian primary care health information technology. Conclusions: If the contextual challenges arising when using primary care electronic medical record data are appropriately addressed, highly discriminative models for osteoarthritis risk may be constructed using only data commonly available in primary care. Because the models are constructed from data in the same setting where the model is to be applied, internal validation provides strong evidence that the

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CR Unknown -, 2009, CLIN PREDICTION MODE, V0, P0, DOI DOI 10.1007/978-0-387-77244-8
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NR 40
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Z9 8
U1 0
U2 6
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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WC Computer Science, Information Systems; Health Care Sciences & Services; Medical Informatics
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ER

PT J
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Khandha, A
Capin, J
Buchanan, TS
Snyder-Mackler, L
AF Wellsandt, Elizabeth
Khandha, Ashutosh
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Buchanan, Thomas S.
Snyder-Mackler, Lynn
TI Operative and nonoperative management of anterior cruciate ligament injury: Differences in gait biomechanics at 5 years
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE ACL; joint contact force; kinematics and kinetics; knee; rehabilitation
ID knee osteoarthritis; deficient knee; reconstruction; individuals; kinematics; patient; asymmetry; predictors; mechanics; walking
AB Gait biomechanics after anterior cruciate ligament (ACL) injury are associated with functional outcomes and the development of posttraumatic knee osteoarthritis. However, biomechanical outcomes between patients treated nonoperatively compared with operatively are not well understood. The primary purpose of this study was to compare knee joint contact forces, angles, and moments during loading response of gait between individuals treated with operative compared with nonoperative management at 5 years after ACL injury. Forty athletes treated operatively and 17 athletes treated nonoperatively completed gait analysis at 5 years after ACL reconstruction or completion of nonoperative rehabilitation. Medial compartment joint contact forces were estimated using a previously validated, patient-specific electromyography-driven musculoskeletal model. Knee joint contact forces, angles, and moments were

compared between the operative and nonoperative group using mixed model 2 x 2 analyses of variance. Peak medial compartment contact forces were larger in the involved limb of the nonoperative group (Op: 2.37 +/- 0.47 BW, Non-Op: 3.03 +/- 0.53 BW; effect size: 1.36). Peak external knee adduction moment was also larger in the involved limb of the nonoperative group (Op: 0.25 +/- 0.08 Nm/kg center dot m, Non-Op: 0.32 +/- 0.09 Nm/kg center dot m; effect size: 0.89). No differences in radiographic tibiofemoral osteoarthritis were present between the operative and nonoperative groups. Overall, participants treated nonoperatively walked with greater measures of medial compartment joint loading than those treated operatively, while sagittal plane group differences were not present. Statement of clinical relevance: The differences in medial knee joint loading at 5 years after operative and nonoperative management of ACL injury may have implications on the development of posttraumatic knee osteoarthritis.
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NR 54
TC 13
Z9 21
U1 1
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PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0736-0266
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J9 J ORTHOP RES
JI J. Orthop. Res.
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WC Orthopedics
SC Orthopedics
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PT J
AU Chen, RH
Yin, H
Dan, Y
Niu, NK
AF Chen, Renhui
Yin, Hui
Dan, Ying
Niu, Ningkui
TI Growth Arrest Specific Gene 6 Affects Osteogenesis of Bone Marrow Mesenchymal Stem Cells in Inflammatory Environment via MAPK/AKT Signaling Pathway
SO JOURNAL OF BIOMATERIALS AND TISSUE ENGINEERING
LA English
DT Article
DE Gas6; Osteoarthritis; MAPK/AKT Signaling Pathway; Oxidative Stress; Inflammatory Factors; BMSCs
ID differentiation; replacement
AB The osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) is beneficial for the treatment of osteoarthritis (OA). Gas6 is a vitamin K-dependent protein and associated with inflammation. Whether Gas6 regulates BMSCs differentiation under inflammatory environment is unknown. Rat BMSCs were isolated and divided into control group and inflammation group (addition of 1 mu g/ml lipopolysaccharide, LPS), and Gas6 group (200 ng/ml Gas6 was added to LPS-stimulated BMSCs cells) followed by analysis of Gas6, Runx2 and OP expression by Real time PCR, ALP activity, ROS content and SOD activity, TNF-alpha and IL-1 beta secretion by ELISA, MAPK/AKT signaling protein expression by Western blot. LPS treatment significantly reduced Gas6 expression, inhibited ALP activity, decreased Runx2 and OP expression, increased ROS content and the secretion of TNF-alpha and IL-1 beta and reduced SOD activity and p-AKT expression compared to control ($P < 0.05$); Gas6 addition to BMSCs in inflammatory environment significantly promoted Gas6 expression and ALP activity, upregulated Runx2 and OP, decreased ROS content and secretion of

TNF-alpha and IL-1 beta, increased SOD activity and p-AKT level ($P < 0.05$). Gas6 expression in BMSCs is reduced in inflammatory environment. Promoting Gas6 expression in BMSCs in inflammatory environment can regulate oxidative stress and MAPK/AKT signaling pathway, inhibit the secretion of TNF-alpha and IL-10, and then promote the osteogenic differentiation of BMSCs.
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CR Ackland DC, 2017, J MECH BEHAV BIOMED, V69, P404, DOI 10.1016/j.jmbbm.2017.01.048
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PA 26650 THE OLD RD, STE 208, VALENCIA, CA 91381-0751 USA
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WC Cell & Tissue Engineering
SC Cell Biology
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ER

PT J
AU Hartley, C
Folland, JP
Kerslake, R
Brooke-Wavell, K
AF Hartley, Chris
Folland, Jonathan P.
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TI High-Impact Exercise Increased Femoral Neck Bone Density With No Adverse Effects on Imaging Markers of Knee Osteoarthritis in Postmenopausal Women
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE DXA; EXERCISE; FRACTURE PREVENTION; OSTEOARTHRITIS; OSTEOPOROSIS

ID t2 relaxation-time; physical-activity; mineral density; articular-cartilage; marrow lesions; older-adults; strength; men; prevalence; barriers
AB High-impact exercise can improve femoral neck bone mass but findings in postmenopausal women have been inconsistent and there may be concern at the effects of high-impact exercise on joint health. We investigated the effects of a high-impact exercise intervention on bone mineral density (BMD), bone mineral content (BMC), and section modulus (Z) as well as imaging biomarkers of osteoarthritis (OA) in healthy postmenopausal women. Forty-two women aged 55 to 70 years who were at least 12 months postmenopausal were recruited. The 6-month intervention consisted of progressive, unilateral, high-impact exercise incorporating multidirectional hops on one randomly assigned exercise leg (EL) for comparison with the contralateral control leg (CL). Dual-energy X-ray absorptiometry (DXA) was used to measure BMD, BMC, and Z of the femoral neck. Magnetic resonance imaging (MRI) of the knee joint was used to analyze the biochemical composition of articular cartilage using T2 relaxometry and to analyze joint pathology associated with OA using semiquantitative analysis. Thirty-five participants (61.7 +/- 4.3 years) completed the intervention with a mean adherence of 76.8% +/- 22.5%. Femoral neck BMD, BMC, and Z all increased in the EL (+0.81%, +0.69%, and +3.18%, respectively) compared to decreases in the CL (-0.57%, -0.71%, and -0.75%: all interaction effects $p < 0.05$). There was a significant increase in mean T2 relaxation times (main effect of time $p = 0.011$) but this did not differ between the EL and CL, indicating no global effect. Semiquantitative analysis showed high prevalence of bone marrow lesions (BML) and cartilage defects, especially in the patellofemoral joint (PFJ), with no indication that the intervention caused pathology progression. In conclusion, a high-impact exercise intervention that requires little time, cost, or specialist equipment improved femoral neck BMD with no negative effects on knee OA imaging biomarkers. Unilateral high-impact exercise is a feasible intervention to reduce hip fracture risk in healthy postmenopausal women. (c) 2019 American Society for Bone and Mineral Research.
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TI Multifaceted Functions and Novel Insight Into the Regulatory Role of RNA N6-Methyladenosine Modification in Musculoskeletal Disorders
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE RNA N-6-methyladenosine; METTL3; FTO; musculoskeletal disorders; epigenetics
ID single-nucleotide-resolution; skeletal-muscle; messenger-rna; dna methylation; rheumatoid-arthritis; demethylase alkbh5; m(6)a rna; fto gene; osteosarcoma; cells
AB RNA modifications have emerged as key regulators of transcript expression in diverse physiological and pathological processes. As one of the most prevalent types of RNA modifications, N-6-methyladenosine (m(6)A) has become the highlight in modulation of various diseases through interfering RNA splicing,

translation, nuclear export, and decay. In many cases, the detailed functions of m(6)A in cellular processes and diseases remain unclear. Notably, recent studies have determined the relationship between m(6)A modification and musculoskeletal disorders containing osteosarcoma, osteoarthritis, rheumatoid arthritis, osteoporosis, etc. Herein, this review comprehensively summarizes the recent advances of m(6)A modification in pathogenesis and progression of musculoskeletal diseases. Specifically, the underlying molecular mechanisms, detection technologies, regulatory functions, clinical implications, and future perspectives of m(6)A in musculoskeletal disorders are discussed, with the aim to provide a novel insight into their association.
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AF Oliveira, Marina C.
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TI Osteoporosis and osteoarthritis are two sides of the same coin paid for obesity
SO NUTRITION
LA English
DT Review

DE Obesity; Osteoarthritis; Osteoporosis; Nutrition; Treatment
ID bone-mineral density; body-mass index; infrapatellar fat pad; necrosis-factor-alpha; knee osteoarthritis; fracture risk; postmenopausal women; synovial-fluid; adipose-tissue; in-vitro
AB Obesity is characterized by adipose tissue expansion and chronic low-grade inflammation. Among the inflammatory mediators related to obesity development are the adipokines. These cytokines are released from fatty tissues and act in an autocrine, paracrine, or endocrine manner. Adipocytes influence the comorbidities of obesity such as osteoporosis (OP) and osteoarthritis (OA). It is still controversial as to whether OP is associated with either a low or high body mass index, but it is quite clear that the latter condition increases the risk for OA development. Bone marrow adipocytes (BMAs) have the same precursors of osteoblasts, which are the primary cells involved in bone formation, and the amount of BMAs appears to be inversely related to bone mineral density. Although adipokines released by these adipocytes influence bone loss progress, their exact role remains controversial. Differently, the infrapatellar fat pad (IPFP) is indicated to protect the function of joint regarding OA. However, there is relatively limited information about the secretion of adipokines and other inflammatory mediators by the IPFP. Despite some inconsistencies, nutritional interventions targeting obesity may also benefit patients with OP and OA. The association among obesity, OP, and OA is quite complex, and many factors need to be explored that are mainly related to the role of adipokines derived locally rather than from visceral and subcutaneous adipose tissue. Also, nutritional intervention may affect fatty tissue mass and secretion of inflammatory mediators that may, at least in part, influence other tissues in the organism such as bone and articular cartilage. The aim of this review was to present the latest knowledge about the interrelationship between obesity and OA or OP and to discuss whether a dietary intervention for obesity will hold promise for patients with OA or OP. (C) 2019 Elsevier Inc. All rights reserved.
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AF Liu, Yang
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TI Effects of Ten-Eleven Translocation 2 on Osteogenic Differentiation of Bone Marrow Mesenchymal Stem Cells in Osteoarthritis by Regulating Extracellular-Signal-Regulated Kinase (ERK) Signaling Pathway
SO JOURNAL OF BIOMATERIALS AND TISSUE ENGINEERING
LA English
DT Article
DE TET2; Inflammation; BMSCs; Osteogenic Differentiation; Adipogenic Differentiation
ID tet2
AB Inflammation affects BMSCs differentiation. TET2 (ten-eleven translocation 2) regulates mammalian genome transcription and promotes development. However, TET2's role in BMSCs osteogenic differentiation in inflammatory environment is unknown. Rat BMSCs were assigned into control group, inflammation group (addition of LPS), TET2 group and TET2 siRNA group, in which TET2 plasmid and TET2 siRNA were transfected into inflammatory BMSCs, respectively followed by analysis of TET2 expression by real-time PCR analysis, cell proliferation by MTT assay, Caspase3 activity, ALP activity, Runx2, OP and FABP4 level by real time PCR, and ERK signaling protein level by Western blot. In inflammatory environment, TET2 expression was significantly decreased, BMSCs proliferation was inhibited, Caspase3 activity was increased along with decreased ALP activity and expression of Runx2 and OP, increased FABP4 level and reduced ERK phosphorylation ($P < 0.05$). TET2 siRNA transfection into inflammatory BMSCs could further significantly aggravate the above changes ($P < 0.05$). Transfection of TET2 plasmid promotes TET2 expression, which can significantly promote BMSCs proliferation, decrease Caspase3 activity, increase ALP activity and Runx2 and OP expression, decrease FABP4 expression and increase ERK phosphorylation ($P < 0.05$). TET2 expression is reduced in BMSCs under inflammation. Up-regulating TET2 in inflammation can inhibit inflammatory factors secretion, regulate BMSCs proliferation, promote their differentiation into osteoblasts, and alleviates osteoarthritis.
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TI Relationship between the AB0 Blood System and Proximal Femoral Fracture Patterns in the Turkish Population
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DT Article
ID association; osteoporosis
AB Objective. AB0 blood groups have shown to be associated with increased risk of several orthopedic disorders such as Achilles tendon rupture and hip osteoarthritis. The objective of this study was to investigate relationships between the AB0 blood system and hip fracture patterns, duration of hospitalization, and amount of blood transfusion. Methods. Data of 308 patients treated due to hip fractures in our hospital between 2017 and 2019 were evaluated. Epicrisis reports and X-rays of the patients included in this study were retrospectively screened, and hip fractures were classified as intracapsular and extracapsular fractures. Patients were divided into A, B, 0, and AB groups according to blood groups. Results. The mean age of the patients was 75.54 +/- 13.5 years. Of all patients, 103 had an intracapsular fracture and 205 had an extracapsular fracture. No statistically significant correlation was found between blood groups and fracture patterns. No statistically significant difference was found between the amounts of transfusion according to the blood groups, and no significant difference between the durations of hospitalizations according to the blood groups. Conclusion. In our study population, we could not find a significant relationship between the AB0 blood

system and fracture patterns. We think that these potential relationships could be explained with further comprehensive studies with larger populations.
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CR Alffram PA, 1964, ACTA ORTHOP SCAN S65, V35, P1, DOI 10.3109/ORT.1964.35.SUPPL-65.01
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AU Wu, JQ
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AF Wu, Jian-Qun
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TI Mechanisms of action of neuropeptide Y on stem cells and its potential applications in orthopaedic disorders
SO WORLD JOURNAL OF STEM CELLS
LA English

DT Review
DE Neuropeptide Y; Bone marrow mesenchymal stem cells; Hematopoietic stem cells; Fracture; Osteoporosis; Osteoarthritis
ID gene-related peptide; induced bone loss; substance-p; osteoblast differentiation; hematopoietic stem; angiogenic factor; induced obesity; stromal cells; regulate bone; nerve-fibers
AB Musculoskeletal disorders are the leading causes of disability and result in reduced quality of life. The neuro-osteogenic network is one of the most promising fields in orthopaedic research. Neuropeptide Y (NPY) system has been reported to be involved in the regulations of bone metabolism and homeostasis, which also provide feedback to the central NPY systemviaNPY receptors. Currently, potential roles of peripheral NPY in bone metabolism remain unclear. Growing evidence suggests that NPY can regulate biological actions of bone marrow mesenchymal stem cells, hematopoietic stem cells, endothelial cells, and chondrocytesviaa local autocrine or paracrine manner by different NPY receptors. The regulative activities of NPY may be achieved through the plasticity of NPY receptors, and interactions among the targeted cells as well. In general, NPY can influence proliferation, apoptosis, differentiation, migration, mobilization, and cytokine secretion of different types of cells, and play crucial roles in the development of bone delayed/non-union, osteoporosis, and osteoarthritis. Further basic research should clarify detailed mechanisms of action of NPY on stem cells, and clinical investigations are also necessary to comprehensively evaluate potential applications of NPY and its receptor-targeted drugs in management of musculoskeletal disorders.
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TI Hyponatremia, Hypokalemia, and Fragility Fractures in Old Patients: More than an Association?
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Hyponatremia; Fracture; Osteoporosis; Sodium; Potassium
ID potassium citrate supplementation; idiopathic hyponatremia; bone; osteoporosis; sodium; vasopressin; fruit; sex
AB Purpose Hyponatremia and hypokalemia are common among elderly and have been associated with osteoporosis, we evaluate the role of these electrolytes as risk for fragility fractures. Methods This study is divided in two parts: one retrospective and one prospective. We retrospectively collected data on urgently admitted patients for femoral fragility fractures (Fx) or for acute myocardial infarction (AMI),

and patients admitted for elective hip/knee replacement surgery for osteoarthrosis (OA). Age, sex, serum sodium, potassium, creatinine, and comorbidities were recorded. We enrolled prospectively in-patients from our unit: age, sex, comorbidities, drugs, and fragility fractures were recorded. Blood electrolytes were measured. Cognitive function, nutrition, muscular strength, and balance were evaluated by standard tests. The mortality rate was recorded with a follow-up after hospital discharge. Results The retrospective study included 2166 subjects: 702 Fx and 1464 controls (907 AMI, 557 OA): the prevalence of hyponatremia was similar in Fx and AMI, whereas it was higher in Fx with respect to OA ($p < 0.001$) as well as hypokalemia ($p < 0.001$). Sodium decrease was associated with higher fracture risk. Among the 284 subjects included in the prospective study, 50 patients were hyponatremic, more likely malnourished, and presented a higher prevalence of fragility fractures ($p = 0.008$). They had a higher mortality after hospital discharge (HR = 1.80, $p = 0.005$), however, this association disappears after correction for confounding variables. Conclusions We suggest that hyponatremia and hypokalemia have to be considered as a marker of poor health more than an independent fracture risk.
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TI An in-depth study of the associations between osteoarthritis- and osteoporosis-related phenotypes at different skeletal locations
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Bone mineral density; Hand; Knee; Osteoarthritis; Osteoporosis; Spine
ID bone-mineral density; radiographic knee osteoarthritis; lumbar disc degeneration; hand osteoarthritis; general-population; fractures; incident; women; risk; classification
AB The relationship between OA and osteoporosis characteristics remains

controversial. This study revealed that age-adjusted hand OA is associated with lower hand/arm BMD levels. Wrist fracture occurrence is associated with increased OA hand scores and low arm BMD. Conversely, age-adjusted knee and spine OA is associated with high spine, hip, and total BMDs. Introduction Osteoarthritis (OA) and osteoporosis are two common musculoskeletal diseases which contribute a high burden of disability, yet assessments of their relationship remains controversial. The aim of this study was to clarify the association between bone mineral densities (BMD) of the hand, arm, spine, hip, and total body, and OA of the hand and knee and lumbar disc degeneration in two different ethnic groups. Methods Radiographic assessments of the hand, knee, and spine were collected and coded for joint space narrowing, osteophytes, and the Kellgren-Lawrence score from Chuvashian (n = 1504) and British (n = 2280) individuals. BMD measurements of standard skeletal sites were estimated by dual X-ray absorptiometry. Age- and familial-adjusted regression analyses were conducted to determine associations. Results Knee OA affection was positively associated with elevated hip, spine, and total body BMD levels ($p < 0.001$). Additionally, disc degeneration phenotypes showed significant positive associations with the hip, spine, and total BMD ($p < 0.001$). However, increased hand OA scores was significantly negatively correlated with arm and hand BMD measurements in males and females in both samples ($p < 0.001$). Additionally, higher hand OA scores were significantly associated with wrist fracture. Conclusions We discovered a clear pattern of association between hand OA and low hand and arm BMD, with increased risk of wrist fracture, as well as reproducing previous associations between knee and spine OA and elevated spine, hip, and total body BMD. It appears that hand OA manifests differently in comparison to hip and knee OA.
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TI Silicon supplementation mitigates salinity stress on Ocimum basilicum L. via improving water balance, ion homeostasis, and antioxidant defense system
SO ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY
LA English
DT Article
DE Antioxidant system; Oxidative impairment; Salinity; Silicon; Sweet basil
ID salt stress; essential oil; osmotic-stress; tolerance; drought; growth; plants; melatonin; responses; photosynthesis
AB Salinity is a key worldwide ecological restriction to sustainable crop production and food security. Various methods were used for inducing salinity tolerance including biotechnological approaches or application of stress tolerance-inducing substances. Silicon supplementation has a decisive role in alleviating of salinity injury, however, the definite mechanisms behind stay scantily understood, and must be examined. The imperative roles of sodium metasilicate (Si, 100 ppm) application methods (foliar spraying at 100 mg/l; soil additive at 100 mg/kg soil; foliar spraying at 100 mg/l plus soil additive at 100 mg/kg soil), in improving growth and essential oil yield, maintaining water status, activating antioxidant system, and keeping ion homeostasis of salt affected-sweet basil (6000 mg NaCl/kg soil) were studied. Salinity induced a notable increase in oxidative biomarkers, coupled with higher osmolyte concentration and osmotic potential (OP) values, as well as increased superoxide dismutase and peroxidase activities. Alternatively, sweet basil growth, essential oil yield, and catalase activity were reduced under salinity. Furthermore, salinity aggravated ion imbalance, decreased photosynthetic pigment and disrupted the plants' water status. Silicon application drastically

increased osmolyte accumulation associated with sustained water status, increased OP, and improved osmotic adjustment (OA) capacity. Additionally, Si application enhanced antioxidant aptitude associated with decreased oxidative biomarkers and improved growth, photosynthetic pigment, and essential oil yield. Greater outcomes were achieved with the foliar spraying method, compared with other application methods. Salinity stress evoked modification in protein assimilation capacity and possibly will withdraw protein biosynthesis and reduce total protein band number; however, Si application may adjust the expression of salinity inducible proteins. Foliar spraying of Si with or without soil additive accelerates the expression of peroxidase isozyme over salinized or control plants. Collectively, Si foliar spraying alleviated salinity-related injuries on sweet basil by maintaining water status, increasing osmolyte assimilation, improving OA, enhancing redox homeostasis, and antioxidant capacity.
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TI Yes-Associated Protein 1: Role and Treatment Prospects in Orthopedic Degenerative Diseases
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
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DT Review
DE yes-associated protein 1; osteoarthritis; osteoporosis; chondrocyte; mesenchymal stem cells
ID mesenchymal stem-cells; hippo signaling pathway; organ size control; articular-cartilage; in-vitro; chondrocyte differentiation; adipogenic differentiation; yap; osteoporosis; taz
AB The Hippo/yes-associated protein 1 signaling pathway is an evolutionarily conserved signaling pathway. This signaling pathway is primarily involved in the regulation of stem cell self-renewal, organ size and tissue regeneration by regulating cell proliferation, differentiation and apoptosis. It plays an important role in embryonic development and tissue organ formation. Yes-associated protein 1 (YAP1) is a key transcription factor in the Hippo signaling pathway and is negatively regulated by this pathway. Changes in YAP1 expression levels affect the occurrence and development of a variety of tumors, but the specific mechanism associated with this phenomenon has not been thoroughly studied. Recently, several studies have described the role of YAP1 in osteoarthritis (OA). Indeed, YAP1 is involved in orthopedic degenerative diseases such as osteoporosis (OP) in addition to OA. In this review, we will summarize the significance of YAP1 in orthopedic degenerative diseases and discuss the potential of the targeted modulation of YAP1 for the treatment of these diseases.
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TI Validation of the Western Ontario and McMaster Universities Arthritis Index Short Form (WOMAC-SF) and Its Relevance to Disability and Frailty
SO YONSEI MEDICAL JOURNAL
LA English
DT Article
DE WOMAC; musculoskeletal disorders; disability; frailty
ID questionnaire length; health; osteoarthritis; adaptation; hip
AB Purpose: This study aimed to evaluate the validity of the Western Ontario and McMaster Universities Arthritis Index Short Form (WOMAC-SF) for the assessment of musculoskeletal disorders. We evaluated whether WOMAC-SF correlated with the World Health Organization Disability Assessment Schedule 12 (WHODAS-12) and Kaigo-Yobo questionnaires for assessing health-outcomes in Korea. Materials and Methods: This cross-sectional study used data from the Namgaram-2 cohort. WOMAC, WOMAC-SF, WHODAS-12, and Kaigo-Yobo questionnaires were administered to patients with musculoskeletal disorders, including radiology-confirmed knee osteoarthritis (RKOA), sarcopenia, and osteoporosis. The

relationships among WOMAC-SF, WHODAS-12, and Kaigo-Yobo scores were analyzed by stepwise multiple regression analysis. Results: WOMAC-SF was associated with the WOMAC questionnaire. The results of confirmatory factor analysis for the hypothesized model with two latent factors, pain and function, provided satisfactory fit indices. WOMAC-SF pain and function were associated with RKOA. Kaigo-Yobo was associated with WOMAC-SF pain (B=0.140, p=0.001) and WOMAC-SF function (B=0.042, p=0.004). WHODAS-12 was associated with WOMAC-SF pain (B=0.679, p=0.003) and WOMAC-SF function (B=0.804, p<0.001). Conclusion: WOMAC-SF was validated for the evaluation of low extremity musculoskeletal disorders and health-related quality of life in a community-based population. Furthermore, we confirmed that WOMAC-SF were reflective of disability and frailty, which affect health outcomes.
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TI Denosumab Prevents Early Periprosthetic Bone Loss After Uncemented Total Hip Arthroplasty: Results from a Randomized Placebo-Controlled Clinical Trial
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE DXA; BIOCHEMICAL MARKERS OF BONE TURNOVER; IMPLANTS; ANTIRESORPTIVES; CLINICAL TRIALS
ID 4-year follow-up; postmenopausal women; vertebral fractures; zoledronic acid; double-blind; total knee; discontinuation; osteoporosis; migration; density
AB Implant loosening is the most common indication for revision surgery after total hip arthroplasty (THA). Although bone resorption around the implants plays a pivotal role in the pathophysiology of loosening, it is unknown whether potent early inhibition of osteoclasts could mitigate this process and thus reduce the need for revision surgery. We performed a randomized, double-blind, placebo-controlled phase 2 trial in 64 patients aged 35 to 65 years with unilateral osteoarthritis of the hip. They underwent surgery with an uncemented THA and were randomized to either two subcutaneous doses of denosumab (n = 32) or placebo (n = 32) given 1 to 3 days and 6 months after surgery. Patients were followed for 24 months. Primary outcome was periprosthetic bone mineral density (BMD) of the hip at 12 months as measured by dual-energy X-ray absorptiometry (DXA). In addition, [F-18] sodium fluoride positron emission tomography/CT (F-PET) was performed in half of the patients for analysis of periprosthetic standardized uptake value (SUV). Analyses were made according to intention-to-treat principles. The trial was registered at ClinicalTrials.gov 2011-001481-18, NCT01630941. Denosumab potently inhibited early periprosthetic

bone loss. After 12 months, BMD in the denosumab group was 32% (95% confidence interval [CI] 22-44) higher in Gruen zone 7 and 11% (95% CI 8-15) higher in zones 1 to 7. After 24 months, the difference in BMD between groups had decreased to 15% (95% CI 4-27) in zone 7 and 4% (95% CI 0-8) in zones 1 to 7. In both groups, SUV increased after surgery, but the increase was less pronounced in the denosumab group. Biochemical markers of bone metabolism decreased in the denosumab group in the first 12 months, but a rebound effect with marker concentrations above baseline was observed after 24 months. Denosumab potently prevents early periprosthetic bone loss after uncemented THA; however, the effect diminishes after discontinuation of treatment. Further research is needed to determine whether this bone loss will prove to be of clinical importance and, if so, whether the positive effect observed in this study could be preserved by either prolonged treatment with denosumab or additional antiresorptive treatment. (c) 2019 American Society for Bone and Mineral Research. (c) 2019 American Society for Bone and Mineral Research.
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TI Communications Between Bone Marrow Macrophages and Bone Cells in Bone Remodeling
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
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DT Review

DE macrophages; intracellular communication; macrophage-derived exosome; bone remodeling; bone diseases
ID tumor-associated macrophages; mesenchymal stem-cells; protein mnsf-beta; osteoblast differentiation; m1 macrophages; tissue-repair; in-vitro; expression; polarization; galectin-3
AB The mammalian skeleton is a metabolically active organ that continuously undergoes bone remodeling, a process of tightly coupled bone resorption and formation throughout life. Recent studies have expanded our knowledge about the interactions between cells within bone marrow in bone remodeling. Macrophages resident in bone (BMMs) can regulate bone metabolism via secreting numbers of cytokines and exosomes. This review summarizes the current understanding of factors, exosomes, and hormones that involved in the communications between BMMs and other bone cells including mensenchymal stem cells, osteoblasts, osteocytes, and so on. We also discuss the role of BMMs and potential therapeutic approaches targeting BMMs in bone remodeling related diseases such as osteoporosis, osteoarthritis, rheumatoid arthritis, and osteosarcoma.
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TI MiR-17-3p inhibits osteoblast differentiation by downregulating Sox6 expression
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ID mesenchymal stem-cells; osteogenic differentiation; target; apoptosis
AB Osteoporosis and osteoarthritis are orthopedic disorders that affect millions of elderly people worldwide; stimulation of bone formation is a potential therapeutic strategy for the treatment of these conditions. As the only bone-forming cells, osteoblasts play a key role in bone reconstruction. The microRNA miR-17-3p is downregulated during osteogenic differentiation of human bone marrow mesenchymal stem cells, but its precise role in this process is unknown. Here, we investigated the role of miR-17-3p in osteoblast differentiation. An in vitro model

of osteogenesis was established by treating MC3T3-E1 murine preosteoblast cells with bone morphogenetic protein 2 (BMP2). The expression of miR-17-3p in BMP2-induced MC3T3-E1 cells was detected by reverse transcription-quantitative PCR, and its effects on cells transfected with miR-17-3p mimic or inhibitor were evaluated by Alizarin Red staining, alkaline phosphatase (ALP) activity assay, and by detection of osteoblast markers including the ALP, collagen type I alpha 1 chain, and osteopontin genes. Bioinformatics analysis was carried out to identify putative target genes of miR-17-3p, and the luciferase reporter assay was used for functional validation. Rescue experiments were performed to determine whether SRY-box transcription factor 6 (Sox6) plays a role in the regulation of osteoblast differentiation by miR-17-3p. We report that miR-17-3p was downregulated upon BMP2-induced osteoblast differentiation in MC3T3-E1 cells, and this was accompanied by decreased differentiation and mineralization, ALP activity, and expression of osteogenesis-related genes. Sox6 was confirmed to be a target gene of miR-17-3p in osteoblasts, and the inhibitory effect of miR-17-3p on osteoblast differentiation was observed to occur via Sox6. These results suggest the existence of a novel mechanism underlying miRNA-mediated regulation of osteogenesis, which has potential implications for the treatment of orthopedic disorders.
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AU Hu, YJ
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TI Defactinib attenuates osteoarthritis by inhibiting positive feedback loop between H-type vessels and MSCs in subchondral bone
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Article
DE Defactinib; FAK; H-type vessels; MSCs; Osteoarthritis; Subchondral bone
ID mesenchymal stem-cells; focal adhesion kinase; knee osteoarthritis; articular-cartilage; angiogenesis; pericytes; origin; osteogenesis; replacement; migration

AB Background: Abnormal bone formation in subchondral bone resulting from uncoupled bone remodeling is considered a central feature in osteoarthritis (OA) pathogenesis. H-type vessels can couple angiogenesis and osteogenesis. We previously revealed that elevated H-type vessels in subchondral bone were correlated with OA and focal adhesion kinase (FAK) in MSCs is critical for H-type vessel formation in osteoporosis. The aim of this study was to explore the correlation between H-type vessels and MSCs in OA pathogenesis through regulation of H-type vessel formation using defactinib (an FAK inhibitor). Methods: In vivo: 3-month-old male C57BL/6J (WT) mice were randomly divided into three groups: sham controls, vehicle-treated ACLT mice, and defactinib-treated ACLT mice (25 mg/kg, intraperitoneally weekly). In vitro: we explored the role of conditioned medium (CM) of MSCs from subchondral bone of different groups on the angiogenesis of endothelial cells (ECs). Flow cytometry, Western blotting, ELISA, real time (RT)-PCR, immunostaining, CT-based microangiography, and bone micro-CT (uCT) were used to detect changes in relative cells and tissues. Results: This study demonstrated that inhibition of H-type vessels with defactinib alleviated OA by inhibiting H-type vessel-linked MSCs in subchondral bone. During OA pathogenesis, H-type vessels and MSCs formed a positive feedback loop contributing to abnormal bone formation in subchondral bone. Elevated H-type vessels provided indispensable MSCs for abnormal bone formation in subchondral bone. Flow cytometry and immunostaining results confirmed that the amount of MSCs in subchondral bone was obviously higher in vehicle-treated ACLT mice than that in sham controls and defactinib-treated ACLT mice. In vitro, p-FAK in MSCs from subchondral bone of vehicle-treated ALCT mice increased significantly relative to other groups. Further, the CM from MSCs of vehicle-treated ACLT mice enhanced angiogenesis of ECs through FAK-Grb2-MAPK-linked VEGF expression. Conclusions: Our results demonstrate that defactinib inhibits OA by suppressing the positive feedback loop between H-type vessels and MSCs in subchondral bone. The translational potential of this article: Our results provide a mechanistic rationale for the use of defactinib as an effective candidate for OA treatment.
C1 [Hu, Yanjun; Wu, Hangtian; Wang, Yutian; Qin, Hanjun; Yao, Zilong; Chen, Peisheng; Xie, Yongheng; Ji, Zhiguo; Yang, Kaifan; Chai, Yu; Zhang, Xianrong; Yu, Bin; Cui, Zhuang] Southern Med Univ, Nanfang Hosp, Dept Orthoped, Guangzhou 510515, Guangdong, Peoples R China.

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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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SC Orthopedics
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AU Hong, JY
Ye, FS
Yu, BJ
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AF Hong, Junyi
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Wang, Wei
TI Identification of the specific microRNAs and competitive endogenous RNA mechanisms in osteoporosis
SO JOURNAL OF INTERNATIONAL MEDICAL RESEARCH
LA English
DT Article
DE Osteoarthritis; Wnt/beta-catenin pathway; competitive endogenous RNA; interleukin-6; microRNA; osteoporosis
ID bone; differentiation; expression; gene; malat1; osteoclastogenesis; proliferation; osteosarcoma; osteoblasts; inhibition
AB Objective: Osteoporosis and osteoarthritis are metabolic skeletal disorders. This study aimed to identify specific networks of competitive endogenous RNA (ceRNA) in osteoporosis that differ from those in osteoarthritis. Methods: The dataset GSE74209 was downloaded from the Gene Expression Omnibus, and differentially expressed microRNAs (DEmiRNAs) in osteoporotic samples and osteoarthritic samples were identified. After predicting target genes and linked long noncoding (lnc)RNAs, ceRNA networks of DEmiRNAs were constructed. The nodes that overlapped between ceRNA networks and the Comparative Toxicogenomics Database were selected as key candidates. Results: Fifteen DEmiRNAs (including 2 downregulated and 13 upregulated miRNAs) were identified in osteoporotic

samples versus osteoarthritic samples; these targeted 161 genes and linked to 60 lncRNAs. The ceRNA network consisted of 6 DEmiRNAs, 63 target genes, and 53 lncRNAs. After searching the Comparative Toxicogenomics Database and mining the literature, 2 lncRNAs (MALAT1andNEAT1), 2 DEmiRNAs (hsa-miR-32-3p, downregulated; andhsa-miR-22-3p, upregulated) and 6 genes (SP1,PTEN,ESR1,ERBB3,CSF1R, andCDK6) that relate to cell death, growth, and differentiation were identified as key candidates separating osteoporosis from osteoarthritis. Conclusions: Two miRNA-ceRNA networks (includingNEAT1/MALAT1-hsa-miR-32-3p-SP1/FZD6andNEAT1/MALAT1-hsa-miR-22-3p-PTEN/ESR1/ERBB3/CSF1R/CDK6) might have crucial and specific roles in osteoporosis.
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AF Cai, G.
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TI The association of subchondral and systemic bone mineral density with osteoarthritis-related joint replacements in older adults
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Bone mineral density; Hip replacement; Knee replacement; Osteoarthritis
ID radiographic knee osteoarthritis; cartilage thickness; compartment; progression; incident; hip; osteoporosis; initiation; criteria; fracture
AB Objective: To describe the association of subchondral and systemic bone mineral density (BMD) with knee and hip replacements (KR and HR, respectively) due to osteoarthritis. Design: 1,095 participants (mean age 63 years, 51% female) were included. At baseline, subchondral BMD of the medial and lateral tibia in three regions of interest (ROI) for the right knee, and systemic BMD of the lumbar spine, femoral neck, total hip and whole-body, were measured using dual-energy X-ray absorptiometry. Subchondral BMD of the hip was not measured. Competing risk regression models were used to estimate sub-distribution hazard ratios (SHRs) of KR/HR per one standard deviation (SD) higher in BMD measures, with adjustment of potential confounders. Results: Over 12.2 years, 79 (7.2%) participants underwent a KR and 56 (5.1%) an HR due to osteoarthritis. For the right side, medial subchondral BMD in ROI-3 was associated with an increased risk of KR (SHR 1.95 per SD; 95% Confidence Interval [CI], 1.57 to 2.43). In contrast, systemic BMD was not associated with the risk of KR, but higher BMD at the lumbar spine (1.42, 1.07 to 1.88) and whole-body (1.29, 1.00 to 1.66) were associated with an increased risk of HR at both sides. Conclusions: Subchondral BMD is positively associated with an increased risk of KR and systemic BMD with an increased risk of HR, suggesting a role of BMD in the progression of osteoarthritis. (C) 2020 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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NR 50
TC 12
Z9 15
U1 0
U2 9

PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
EI 1522-9653
J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
PD APR 15
PY 2020
VL 28
IS 4
BP 438
EP 445
DI 10.1016/j.joca.2020.02.832
PG 8
WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA KX6FP
UT WOS:000521975300006
PM 32119971
DA 2026-02-10
ER

PT J
AU Ren, ZQ
Wang, YF
Ao, GF
Chen, HX
Huang, M
Lai, MX
Zhao, HD
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AF Ren, Z. Q.
Wang, Y. F.
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Chen, H. X.
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Zhao, H. D.
Zhao, R.
TI Overall adjustment acupuncture for postmenopausal osteoporosis (PMOP): a study protocol for a randomized sham-controlled trial
SO TRIALS
LA English

DT Article
DE Osteoporosis; PMOP; Acupuncture; Sham acupuncture; Protocol; Randomised controlled trial
ID chinese herbal medicine; blood-cell count; infertility; association
AB BackgroundOsteoporosis is becoming more prevalent in aging societies worldwide, and the economic burden attributable to osteoporotic fractures is substantial. The medications presently available to treat osteoporosis have side effects. Acupuncture is widely used for treating osteoporotic postmenopausal women because it is non-invasive and has fewer side effects, but the powerful clinical evidence for its efficacy remains insufficient. Our study intends to explore the effect of overall adjustment acupuncture (OA) in the treatment of postmenopausal osteoporosis (PMOP).Methods/designThis study is a randomized, sham-controlled, patient- and assessor-blinded trial and aims to evaluate the effect of OA in women with PMOP. We will recruit 104 women aged 45-70years with a diagnosis of PMOP. Participants will be randomly allocated in a 1:1 ratio to the OA group and the sham acupuncture (SA) group. Both groups will receive real herbal medicine treatment as a basic treatment twice a day for 3 months, the OA group receives real acupuncture treatment and the SA group receives placebo acupuncture treatment (non-penetrating, sham skin-needle therapy, sham cupping). All patients will receive acupuncture treatment twice per week for 3 months. The primary outcome is bone mineral density (BMD) and the secondary outcomes include estradiol (E2), follicle-stimulating hormone (FSH), bone gla protein (BGP), bone alkaline phosphatase (BALP), total antioxidant capacity (TAC), advanced oxidation protein products (AOPP), PPAR gamma, beta -catenin, FoxO3a levels, visual analog pain scale score (VAS), Traditional Chinese medicine (TCM) syndrome scores and quality of daily life score (QOL). Outcome measures will be collected at baseline, middle of the treatment (1.5months), the end of treatment (3months). The present protocol followed the SPIRIT guidelines and fulfills the SPIRIT Checklist.ConclusionThis study will be conducted to compare the efficacy of OA versus SA. This trial should help to evaluate whether OA can effectively prevent and treat PMOP by improving the estrogen levels of postmenopausal women. The mechanism is to improve the imbalance of osteogenic differentiation and lipogenesis of bone-marrow cells under oxidative stress.Trial registrationChinese Clinical Trial Registry, ID: ChiCTR1800017581. Registered on 5 August 2018. URL: http://www.chictr.org.cn.
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NR 30
TC 15
Z9 19
U1 0
U2 26
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1745-6215
J9 TRIALS
JI Trials
PD JUN 3
PY 2020
VL 21
IS 1
BP
EP
DI 10.1186/s13063-020-04435-7
PG 13
WC Medicine, Research & Experimental
SC Research & Experimental Medicine
GA LY1YM
UT WOS:000540317300011
PM 32493411
DA 2026-02-10
ER

PT J
AU Munsch, MA
Safran, MR
Mai, MC
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AF Munsch, Maria A.
Safran, Marc R.
Mai, Matthew C.
Vasileff, W. Kelton
TI Bone marrow lesions: etiology and pathogenesis at the hip
SO JOURNAL OF HIP PRESERVATION SURGERY

LA English
DT Review
ID transient osteoporosis; subchondral cysts; herniation pits; femoral-neck; osteoarthritis; edema; osteonecrosis; density
AB Bone marrow lesions (BML) are painful changes in subchondral bone which can be reliably identified on magnetic resonance imaging and have been identified in patients suffering from hip osteoarthritis (OA) and related conditions. Created via repetitive microdamage at the articular surface and dysregulated subchondral healing, BML have been linked to traumatic, inflammatory, degenerative, metabolic and neoplastic processes. While BML are known to be a common pathology throughout the body, BML at the hip have not been extensively studied in comparison to those at the knee. Due to the hip's unique biomechanical architecture, function and loading, and independent risk factors leading to hip OA, hip BMLs must be independently understood. The identification of BML in the setting of a pre-osteoarthritic condition may provide a target for treatment and prevention of joint degeneration. By continuing to define and refine the relationships between BML, subchondral bone cysts and OA, prevention, diagnosis and treatment of OA could shift, leading to an improved quality of life and increased longevity of individuals' native hips.
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NR 35
TC 5
Z9 6
U1 0
U2 5
PU OXFORD UNIV PRESS
PI OXFORD
PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND

SN 2054-8397
EI
J9 J HIP PRESERV SURG
JI J. Hip Preserv. Surg.
PD AUG 15
PY 2020
VL 7
IS 3
BP 401
EP 409
DI 10.1093/jhps/hnaa056
PG 9
WC Orthopedics
SC Orthopedics
GA TX9BO
UT WOS:000683380500005
PM 33948196
DA 2026-02-10
ER

PT J
AU Zheng, WW
Ding, BB
Li, XL
Liu, DQ
Yokota, H
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AF Zheng, Weiwei
Ding, Beibei
Li, Xinle
Liu, Daquan
Yokota, Hiroki
Zhang, Ping
TI Knee loading repairs osteoporotic osteoarthritis by relieving abnormal remodeling of subchondral bone via Wnt/β-catenin signaling
SO FASEB JOURNAL
LA English
DT Article
DE knee loading; osteoblast; osteoclast; osteoporotic osteoarthritis; Wnt signaling
ID femoral-head; cartilage; histopathology; pathogenesis; expression; model
AB Osteoporotic osteoarthritis (OPOA) is a common bone disease mostly in the elderly, but the relationship between Osteoporotic (OP) and osteoarthritis (OA) is complex. It has been shown that knee loading can mitigate OA symptoms. However, its effects on OPOA remain unclear. In this study, we characterized

pathological linkage of OP to OA, and evaluated the effect of knee loading on OPOA. We employed two mouse models (OA and OPOA), and conducted histology, cytology, and molecular analyses. In the OA and OPOA groups, articular cartilage was degenerated and Osteoarthritis Research Society International score was increased. Subchondral bone underwent abnormal remodeling, the differentiation of bone marrow mesenchymal stem cells (BMSCs) to osteoblasts and chondrocytes was reduced, and migration and adhesion of pre-osteoclasts were enhanced. Compared to the OA group, the pathological changes of OA in the OPOA group were considerably aggravated. After knee loading, however, cartilage degradation was effectively prevented, and the abnormal remodeling of subchondral bone was significantly inhibited. The differentiation of BMSCs was also improved, and the expression of Wnt/beta-catenin was elevated. Collectively, this study demonstrates that osteoporosis aggravates OA symptoms. Knee loading restores OPOA by regulating subchondral bone remodeling, and may provide an effective method for repairing OPOA.
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FU NIAMS NIH HHS [R01 AR052144] Funding Source: Medline
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NR 49
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AU Huang, K
Cai, HL
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AF Huang, Kai
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TI Dehydroepiandrosterone and age-related musculoskeletal diseases: Connections and therapeutic implications
SO AGEING RESEARCH REVIEWS

LA English
DT Review
DE Dehydroepiandrosterone; Osteoporosis; Sarcopenia; Osteoarthritis; Senescence
ID bone-mineral density; sex steroid-hormones; skeletal-muscle; elderly-men; senescent cells; postmenopausal women; physical function; oxidative stress; body-composition; older-adults
AB Musculoskeletal disorders related to ageing are one of the most common causes of mortality and morbidity among elderly individuals worldwide. The typical constitutive components of the musculoskeletal system, including bone, muscle, and joints, gradually undergo a process of tissue loss and degeneration as a result of lifelong mechanical and biological stress, ultimately leading to the onset of a series of age-related musculoskeletal diseases, including osteoporosis (OP), sarcopenia, and osteoarthritis (OA). Dehydroepiandrosterone (DHEA), a precursor of androgen secreted mainly by the adrenal gland, has attracted much attention as a marker for senescence due to its unique age-related changes. This pre-hormone has been publicly regarded as an "antidote for ageing" because of its favourable effect against a wide range of age-related diseases, such as Alzheimer disease, cardiovascular diseases, immunosenescence and skin senescence, though its effect on age-related musculoskeletal diseases has been explored to a lesser extent. In the present review, we summarized the action of DHEA against OP, sarcopenia and OA. Extensive detailed descriptions of the pathogenesis of each of these musculoskeletal disorders are beyond the scope of this review; instead, we aim to highlight the association of changes in DHEA with the processes of OP, sarcopenia and OA. A special focus will also be placed on the overlapping pathogeneses among these three diseases, and the molecular mechanisms underlying the action of DHEA against these diseases are discussed or postulated.
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AU Wong, SK
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TI Berberine and musculoskeletal disorders: The therapeutic potential and underlying molecular mechanisms
SO PHYTOMEDICINE

LA English
DT Review
DE Alkaloid; Bone; Joint; Osteoporosis; Osteoarthritis; Palmatine
ID nf-kappa-b; attenuates osteoclast differentiation; collagen-induced arthritis; mesenchymal stem-cells; wnt/beta-catenin; osteoblast differentiation; chondrocyte apoptosis; rheumatoid-arthritis; rat model; cartilage degeneration
AB Background: Musculoskeletal disorders are a group of disorders that affect the joints, bones, and muscles, causing long-term disability. Berberine, an isoquinoline alkaloid, has been previously established to exhibit beneficial properties in preventing various diseases, including musculoskeletal disorders. Purpose: This review article aims to recapitulate the therapeutic potential of berberine and its mechanism of action in treating musculoskeletal disorders. Methods: A wide range of literature illustrating the effects of berberine in ameliorating musculoskeletal disorders was retrieved from online electronic databases (PubMed and Medline) and reviewed. YResults: Berberine may potentially retard the progression of osteoporosis, osteoarthritis and rheumatoid
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TC 55
Z9 59
U1 1
U2 55
PU ELSEVIER GMBH
PI MUNICH
PA HACKERBRUCKE 6, 80335 MUNICH, GERMANY
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J9 PHYTOMEDICINE
JI Phytomedicine
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WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
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AU Ryan, M
Barnett, L
Rochester, J
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AF Ryan, M.
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TI A new approach to comprehensively evaluate the morphological properties of the human femoral head: example of application to osteoarthritic joint
SO SCIENTIFIC REPORTS
LA English
DT Article
ID subchondral bone; cancellous bone; articular-cartilage; mechanical-property; osteoporosis; microarchitecture; connectivity; osteophytes; tomography; lesions
AB Osteoarthritis affects the morphological properties of the femoral head. The goal of this study was to develop a method to elucidate whether these changes are localised to discrete regions, or if the reported trends in microstructural changes may be identified throughout the subchondral bone of the human femoral head. Whole femoral heads extracted from osteoarthritic (n = 5) and healthy controls (n = 5) underwent microCT imaging 39 mu m voxel size. The subchondral bone plate was virtually isolated to evaluate the plate thickness and plate porosity. The trabecular bone region was divided into 37 volumes of interest spatially distributed in the femoral head, and bone morphometric properties were determined in each region. The study showed how the developed approach can be used to study the heterogeneous properties of the human femoral head affected by a disease such as osteoarthritis. As example, in the superior femoral head osteoarthritic specimens exhibited a more heterogeneous micro-architecture, with trends towards thicker cortical bone plate, higher trabecular connectivity density, higher trabecular bone density and thicker structures, something that could only be observed with the newly developed approach. Bone cysts were mostly confined to the postero-lateral quadrants extending from the subchondral region into the mid trabecular region. Nevertheless, in order to generalise these findings, a larger sample size should be analysed in the future. This novel method allowed a comprehensive evaluation of the heterogeneous micro-architectural properties of the human femoral head, highlighting effects of OA in the superior subchondral cortical and trabecular bone.

Further investigations on different stages of OA would be needed to identify early changes in the bone.
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TC 13
Z9 14
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PU NATURE PORTFOLIO

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WC Multidisciplinary Sciences
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AU Brzeszczynska, J
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AF Brzeszczynska, J.
Brzeszczynski, F.
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Simpson, A. H. R. W.
TI Role of microRNA in muscle regeneration and diseases related to muscle dysfunction in atrophy, cachexia, osteoporosis, and osteoarthritis
SO BONE & JOINT RESEARCH
LA English
DT Article
DE miRNA; Muscle; Atrophy; Regeneration
ID human skeletal-muscle; satellite cell; cancer cachexia; expression; differentiation; inflammation; sarcopenia; mirnas; pax3; proliferation
AB MicroRNAs (miRNAs) are a class of small non-coding RNAs that have emerged as potential predictive, prognostic, and therapeutic biomarkers, relevant to many pathophysiological conditions including limb immobilization, osteoarthritis,

sarcopenia, and cachexia. Impaired musculoskeletal homeostasis leads to distinct muscle atrophies. Understanding miRNA involvement in the molecular mechanisms underpinning conditions such as muscle wasting may be critical to developing new strategies to improve patient management. MicroRNAs are powerful post-transcriptional regulators of gene expression in muscle and, importantly, are also detectable in the circulation. MicroRNAs are established modulators of muscle satellite stem cell activation, proliferation, and differentiation, however, there have been limited human studies that investigate miRNAs in muscle wasting. This narrative review summarizes the current knowledge as to the role of miRNAs in the skeletal muscle differentiation and atrophy, synthesizing the findings of published data.
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NR 72
TC 35
Z9 36
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WC Cell & Tissue Engineering; Orthopedics
SC Cell Biology; Orthopedics
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AU Ziade, N
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TI Prevalence and pattern of comorbidities in chronic rheumatic and musculoskeletal diseases: the COMORD study
SO SCIENTIFIC REPORTS
LA English
DT Article
ID ankylosing-spondylitis; arthritis; cancer; impact; multimorbidity; management; morbidity; mortality; burden; adults
AB Increased risk of comorbidities has been reported in Rheumatic and Musculoskeletal Diseases (RMD). We aimed to evaluate the prevalence and pattern of comorbidities in RMD patients nationwide, to identify multimorbidity clusters and to evaluate the gap between recommendations and real screening. Cross-sectional, multicentric nationwide study. Prevalence of comorbidities was calculated according to six EULAR axes. Latent Class Analysis identified

multimorbidity clusters. Comorbidities' screening was compared to international and local recommendations. In 769 patients (307 RA, 213 OA, 63 SLE, 103 axSpA, and 83 pSA), the most frequent comorbidities were cardiovascular risk factors and diseases (CVRFD) (hypertension 36.5%, hypercholesterolemia 30.7%, obesity 22.7%, smoking 22.1%, diabetes 10.4%, myocardial infarction 6.6%), osteoporosis (20.7%) and depression (18.1%). Three clusters of multimorbidity were identified: OA, RA and axSpA. The most optimal screening was found for CVRF (>=93%) and osteoporosis (53%). For malignancies, mammograms were the most optimally prescribed (56%) followed by pap smears (32%) and colonoscopy (21%). Optimal influenza and pneumococcus vaccination were found in 22% and 17%, respectively. Comorbidities were prevalent in RMD and followed specific multimorbidity patterns. Optimal screening was adequate for CVRFD but suboptimal for malignant neoplasms, osteoporosis, and vaccination. The current study identified health priorities, serving as a framework for the implementation of future comorbidity management standardized programs, led by the rheumatologist and coordinated by specialized health care professionals.
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AU Conesa-Buendía, FM
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Ortega-De Mues, Arantxa
TI Beneficial effects of manually assisted chiropractic adjusting instrument in a rabbit model of osteoarthritis
SO SCIENTIFIC REPORTS
LA English
DT Article
ID extracorporeal shockwave therapy; anterior cruciate ligament; b-ligand rankl; subchondral bone; articular-cartilage; wave therapy; receptor-activator; knee; opg; manipulation
AB Osteoarthritis (OA) is a degenerative disease characterized by injury of all joint tissues. Our previous study showed that in experimental osteoporosis, chiropractic manipulation (CM) exerts protective effects on bone. We here assessed whether CM might ameliorate OA by improving subchondral bone sclerosis, cartilage integrity and synovitis. Male New-Zealand rabbits underwent knee surgery to induce OA by anterior cruciate ligament injury. CM was performed using the chiropractic instrument ActivatorV 3 times/week for 8 weeks as follows: force 2 setting was applied to the tibial tubercle of the rabbit right hind limb (TM-OA),

whereas the corresponding left hind limb received a false manipulation (FM-OA) consisting of ActivatorV firing in the air and slightly touching the tibial tubercle. After sacrifice, subchondral bone integrity was assessed in the tibiae by microCT and histology. Cartilage damage and synovitis were estimated by Mankin's and Krenn's scores, respectively, and histological techniques. Bone mineral density and content in both cortical and trabecular compartments of subchondral bone decreased in OA rabbits compared to controls, but partially reversed in the TM-OA group. Trabecular bone parameters in the latter group also showed a significant improvement compared to FM-OA group. Moreover RANKL, OPG, ALP and TRAP protein expression in subchondral bone significantly decreased in TM-OA rabbits with respect to FM-OA group. CM was associated with lower Mankin's and Krenn's scores and macrophage infiltrate together with a decreased protein expression of pro-inflammatory, fibrotic and angiogenic factors, in TM-OA rabbits with respect to FM-OA. Our results suggest that CM may mitigate OA progression by improving subchondral bone as well as cartilage and synovial membrane status.
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U1 0
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AU Kwak, Y
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Chung, H
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TI Sex-Associated Differences in the Handgrip Strength of Elderly Individuals
SO WESTERN JOURNAL OF NURSING RESEARCH
LA English
DT Article
DE elderly; hand strength; health promotion; sex
ID physical function; grip strength; sarcopenia; decline; capacity; adults
AB This study aimed to identify sex-specific factors associated with handgrip strength in elderly individuals. The analysis cohort comprised 1,197 men and 1,384 women aged >= 65 years. In men, factors associated with low handgrip strength included advanced age; low body mass index; low frequency of performing flexibility exercises; limited self-care ability (which is a measure of the health-related quality of life); and the presence of diabetes, stroke, or osteoporosis (R-2 = 0.285, F = 7.52, p < .001). In women, the factors included advanced age, low body mass index, low frequency of performing muscle strengthening exercises, stress, and osteoarthritis (R-2 = 0.225, F = 4.17, p < .001). Effective health-promoting interventions for elderly individuals require the development of individualized programs that enhance handgrip strength while considering sex-related factors.
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TI NADPH oxidases in bone and cartilage homeostasis and disease: A promising therapeutic target
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Review
DE arthritis; bone; cartilage; NADPH oxidase; Nox4; osteoporosis
ID oxidative stress; ros production; osteoclast differentiation; interferon-gamma; superoxide; expression; chondrocytes; deficiency; inhibition; nox4
AB Reactive oxygen species (ROS) generated by the NADPH oxidase (Nox) enzymes are important short-range signaling molecules. They have been extensively studied in the physiology and pathophysiology of the cardiovascular system, where they have important roles in vascular inflammation, angiogenesis, hypertension, cardiac injury, stroke, and aging. Increasing evidence demonstrates that ROS and Nox enzymes also affect bone homeostasis and osteoporosis, and more recent studies implicate ROS and Nox enzymes in both inflammatory arthritis and osteoarthritis. Mechanistically, this connection may be through the effects of ROS on signal transduction. ROS affect both transforming growth factor-beta/Smad signaling, interleukin-1 beta/nuclear factor-kappa B signaling, and the resulting changes in matrix metalloproteinase expression. The purpose of this review is to describe the role of Nox enzymes in the physiology and pathobiology of bone and joints and to highlight the potential of therapeutically targeting the Nox enzymes.
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TI Association of bone mineral density with the development of knee osteoarthritis in men and women: a cross-sectional study using the fourth and fifth Korea National Health and Nutrition Examination Surveys
SO ARCHIVES OF OSTEOPOROSIS
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DT Article
DE Bone mineral density; Knee osteoarthritis; Sex; Cross-sectional study

ID radiographic osteoarthritis; sexual-dimorphism; femoral-neck; older-adults; elderly-men; hip; osteoporosis; fracture; age; prevalence
AB Bone mineral density (BMD) and osteoarthritis (OA) were correlated but the relationship was varied according to sex. An association between lumbar spine and femur neck BMDs and OA showed a positive relation in women, while lumbar spine and pelvis BMDs in men were associated with OA with a negative relation. Purpose The purpose of this study was to evaluate the association of BMD in various body parts in conjunction with the presence or severity of radiographic knee osteoarthritis (KOA) in relation to sex. Methods This study was a cross-sectional analysis using Korea National Health and Nutrition Examination Surveys. KOA was graded using the Kellgren-Lawrence (KL) grading system. Radiographic KOA was defined as a KL grade 2 or higher. The associations between KOA and BMD in certain body parts (femur, pelvis, lumbar, lower leg, and whole-body) were assessed. BMD was measured using dual-energy X-ray absorptiometry. The BMD of each body part was divided into quartiles and the relationship between KOA and BMD was examined according to sex. Results BMD did not show a significant tendency according to KL grade in either sex. In men, the severity of KL grade have a statistically significant relationship with total femur (R-2=0.303, p<0.05), femur neck (R-2=0.257, p<0.05), lumbar (R-2=0.137, p<0.05), and pelvis BMD (R-2=0.185, p<0.05). In women, total femur (R-2=0.466, p<0.05), lumbar (R-2=0.316, p<0.05), pelvis (R-2=0.343, p<0.05), and lower leg BMD (R-2=0.133, p<0.05) were associated with the severity of KL grade. When the BMD was divided into quartiles, lumbar (p<0.05) and pelvis BMD (p<0.05) in men had statistically significant association with knee OA as BMD decreased. In women, femur neck (p<0.05) and lumbar BMD (p<0.05) were significantly associated with knee OA as BMD increased. Conclusion The relationship between BMD and OA severity varied according to sex. In women, there was a positive association between femur neck and lumbar BMD and OA, while BMD of the lumbar and pelvis in men was negatively correlated with OA.
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TI The Musculoskeletal Knowledge Portal: Making Omics Data Useful to the Broader Scientific Community
SO JOURNAL OF BONE AND MINERAL RESEARCH
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DT Review
DE EPIGENETICS; GENETIC RESEARCH; OSTEOPOROSIS; DISEASES AND DISORDERS OF; RELATED TO BONE; OSTEOARTHRITIS
ID bone-mineral density; genome-wide association; gwas analysis; determinants; heritability; metaanalysis; expression; disease; risk
AB The development of high-throughput genotyping technologies and large biobank collections, complemented with rapid methodological advances in statistical genetics, has enabled hypothesis-free genome-wide association studies (GWAS), which have identified hundreds of genetic variants across many loci associated with musculoskeletal conditions. Similarly, basic scientists have valuable molecular cellular and animal data based on musculoskeletal disease that would be enhanced by being able to determine the human translation of their findings. By integrating these large-scale human genomic musculoskeletal datasets with complementary evidence from model organisms, new and existing genetic loci can be statistically fine-mapped to plausibly causal variants, candidate genes, and biological pathways. Genes and pathways identified using this approach can be further prioritized as drug targets, including side-effect profiling and the potential for new indications. To bring together these big data, and to realize the vision of creating aknowledge portal, the International Federation of Musculoskeletal Research Societies (IFMRS) established a working group to collaborate with scientists from the Broad Institute to create the Musculoskeletal Knowledge Portal (MSK-KP)(). The MSK consolidates omics datasets from humans, cellular experiments, and model organisms into a central repository that can be accessed

by researchers. The vision of the MSK-KP is to enable better understanding of the biological mechanisms underlying musculoskeletal disease and apply this knowledge to identify and develop new disease interventions. (c) 2020 American Society for Bone and Mineral Research (ASBMR).
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NR 52
TC 23
Z9 25
U1 0
U2 5
PU OXFORD UNIV PRESS
PI OXFORD
PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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J9 J BONE MINER RES
JI J. Bone Miner. Res.
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IS 9
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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ER

PT J
AU Casp, AJ
Montgomery, SR
Cancienne, JM
Brockmeier, SF
Werner, BC
AF Casp, Aaron J.
Montgomery, Samuel R., Jr.
Cancienne, Jourdan M.
Brockmeier, Stephen F.
Werner, Brian C.
TI Osteoporosis and Implant-Related Complications After Anatomic and Reverse Total Shoulder Arthroplasty
SO JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
LA English
DT Article
ID proximal humeral fractures; total hip-arthroplasty; osteoarthritis; risk; hemiarthroplasty; epidemiology; outcm; women
AB Introduction:Osteoporosis is a widespread and growing medical condition, with significant orthopaedic implications. However, the effect of osteoporosis on outcomes after total shoulder arthroplasty (TSA) is not well understood. The goal of the present study was to characterize the incidence of osteoporosis in patients undergoing shoulder arthroplasty and to examine whether patients with osteoporosis undergoing anatomic and reverse TSA are at an increased risk of prosthetic-related complications.Methods:Complication rates were calculated for patients with osteoporosis who underwent anatomic and reverse TSA as separate cohorts within 2 years of surgery including loosening/osteolysis, periprosthetic fracture, periprosthetic dislocation, and revision shoulder arthroplasty and compared using a multivariable logistic regression analysis to control for patient demographics and comorbidities during comparisons, including the indication for reverse TSA.Results:The prevalence of an osteoporosis diagnosis at the time of surgery was 14.3% for anatomic TSA patients and 26.2% of reverse TSA patients. Anatomic TSA patients with osteoporosis experienced significantly higher rates of periprosthetic fracture (odds ratio [OR], 1.49; P = 0.017) and revision shoulder arthroplasty (OR, 1.21; P = 0.009) within 2 years of surgery compared with matched controls without osteoporosis. Patients in the reverse TSA group with osteoporosis also had significantly higher rates of periprosthetic fracture (OR, 1.86; P = 0.001) and revision shoulder arthroplasty (OR, 1.42; P = 0.005) within 2 years of surgery compared with matched controls.Discussion:A significant number of patients undergoing both anatomic and reverse TSA have a concurrent diagnosis of osteoporosis. Osteoporosis represents a significant independent risk factor for

periprosthetic fracture and revision shoulder arthroplasty within 2 years of surgery, regardless of the type of implant. Patients with osteoporosis should be counseled on their increased risk of complications after shoulder arthroplasty.
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NR 29
TC 49
Z9 64
U1 0
U2 7
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 1067-151X
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J9 J AM ACAD ORTHOP SUR
JI J. Am. Acad. Orthop. Surg.
PD FEB 1
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WC Orthopedics; Surgery
SC Orthopedics; Surgery
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ER

PT J
AU de Oliveira, RC
de Freitas, LB
Gomes, RR
Cliquet, A
AF de Oliveira, Rafaella Camilo

de Freitas, Laura Bellintani
Gomes, Roberta Rocha
Cliquet Junior, Alberto
TI ORTHOPEDIC RELATED COMORBIDITIES IN SPINAL CORD-INJURED INDIVIDUALS
SO ACTA ORTOPEDICA BRASILEIRA
LA English
DT Review
DE Quadriplegia; Spinal Cord Injuries; Chronic Pain
ID radiographic evaluation; clinical-assessment; strength; shoulder; system
AB Objective: This study aims to review, identify and study the determinations of the main orthopedic aspects in SCI patients. Methods: A total of 80 articles from PUBMED and three theses (MSc. /DSc.) were examined. Results: The results refer to the most essential joints. There is a chronic overload on the shoulder girdle due to the use of the upper limb as a supporting joint. The elbow presents osteoarthritis, subclinical, acute and chronic pain, mainly in quadriplegic patients. In the hand and wrist joints there are cases of paralysis, osteoporosis and osteoarthritis. Hips are the main weight-bearing joints while sitting which leads to a substantial degenerative process of this joint. Lastly, on the knee, feet and ankles, spasticity, contractures, osteoporosis and deformities can arise. Conclusion: Along with the increase in cases and research that analyze the alterations that spinal cord-injured individuals suffer, it is necessary to recognize the orthopedic changes to understand their limits and identify the relevance of the rehabilitation program to improve the muscle performance.
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10.1179/2045772312Y.0000000037
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PU ATHA COMUNICACAO & EDITORA
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J9 ACTA ORTOP BRAS
JI Acta Ortop. Bras.
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WC Orthopedics
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PT J
AU Xie, WC
Li, F
Han, Y
Qin, Y
Wang, Y
Chi, XY
Xiao, J
Li, ZC
AF Xie, Weixin
Li, Fan
Han, Yi
Qin, Yi
Wang, Yuan
Chi, Xiaoying
Xiao, Jie
Li, Zhanchun
TI Neuropeptide Y1 receptor antagonist promotes osteoporosis and microdamage repair and enhances osteogenic differentiation of bone marrow stem cells via cAMP/PKA/CREB pathway
SO AGING-US
LA English
DT Article
DE osteoporosis; neuropeptide Y; bone microstructure; bone mcirodamage; bone marrow stromal cells
ID postmenopausal women; sympathetic activity; cancellous bone; osteoarthritis; osteoblasts; activation; expression; proliferation; metabolism; resorption
AB Osteoporosis is a common metabolic bone disorder in the elderly population. The accumulation of bone microdamage is a critical factor of osteoporotic fracture. Neuropeptide Y (NPY) has been reported to regulated bone metabolism through Y1 receptor (Y1R). In this study the effects and mechanisms of Y1R antagonist on prevention for osteoporosis were characterized. In the clinical experiment, compared with osteoarthritis (OA), osteoporosis (OP) showed significant osteoporotic bone microstructure and accumulation of bone microdamage. NPY and Y1R immunoreactivity in bone were stronger in OP group, and were both correlated with bone volume fraction (BV/TV). In vivo experiment, Y1R antagonist significantly improved osteoporotic microstructure in the ovariectomized (OVX) rats. And Y1R antagonist promoted RUNX2, OPG and inhibit RANKL, MMP9 in bone marrow. In vitro cell culture experiment, NPY inhibited osteogenesis, elevated RANKL/OPG ratio and downregulated the expression of cAMP, p-PKAs and p-CREB in BMSCs, treated with Y1R antagonist or 8-Bromo-cAMP could inhibit the effects

of NPY. Together, Y1R antagonist improved the bone microstructure and reduced bone microdamage in OVX rats. NPY-Y1R could inhibit osteoblast differentiation of BMSCs via cAMP/PKA/CREB pathway. Our findings highlight the regulation of NPY-Y1R in bone metabolism as a potential therapy strategy for the prevention of osteoporosis and osteoporotic fracture.
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FU National Natural Science Foundation of China [81871090, 81400644, 81400904]; Medical-Engineering Joint Fund of Shanghai Jiaotong University [YG2016MS53]; Clinical research and cultivation fund of Renji Hospital [PY2018-III-07]
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NR 51
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U1 2
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WC Cell Biology; Geriatrics & Gerontology
SC Cell Biology; Geriatrics & Gerontology
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PT J
AU Freiberg, Y
Fine, P
Levkovitch, I
Baram, S
AF Freiberg, Yaniv
Fine, Pinchas
Levkovitch, Irit
Baram, Shahar
TI Effects of the origins and stabilization of biosolids and biowastes on their phosphorous composition and extractability
SO WASTE MANAGEMENT
LA English
DT Article
DE Alkaline-treated biosolids; Modified Hedley's fractionation; Manure; Organic amendments; Organic P mineralization
ID waste-water treatment; soil-phosphorus; manure compost; organic wastes; animal manure; fractionation; forms; release; phytoavailability; solubility
AB Phosphorous dissolution and ensuing chemical redistribution of P in organic amendments (OA) were studied by applying a modified Hedley selective fractionation to eight water-extracted and unextracted OAs. Nine 7-day, repeated

extractions were applied using a 60:1 water:dry OA (v:w) ratio at pH 8. Eight OAs were tested including five biosolids, broiler litter, dairy manure compost and municipal solid waste compost. The average PWEP9 (percent water-extractable P following nine water-extraction cycles) for the OAs was 65 +/- 9% and all of the fractions, with almost no exceptions, contributed to that figure. Organic P was depleted by mineralization (in non-stabilized sludges and broiler litter) or dissolution (stabilized composts) or both (in lime-treated biosolids) and that depletion was completed within 1-2 extraction cycles. Only the organic P of the MSWC remained undepleted. Strong linear correlations were observed between the WEP9 values of the OAs (0.8-21 g P kg(-1)) and several more easily determined properties, including total P content (r(2) = 0.84), organic N content (r(2) = 0.82), the sum of Hedley's more easily dissolved SRP (soluble reactive P) and OP (r(2) = 0.95), and the total P and SRP extracted by 16 h of shaking with the bicarbonate reagent (r(2) >= 0.90). These findings indicate that if greater P availability is desired, the stabilization of biosolids and biowastes should be minimized. These insights into the relationships between OA characteristics and P solubility may benefit the use of OAs in agricultural systems and aid assessments of the environmental significance of their use. (C) 2020 Elsevier Ltd. All rights reserved.
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TI Tissue Engineering and Regenerative Medicine Therapies for Cell Senescence in Bone and Cartilage
SO TISSUE ENGINEERING PART B-REVIEWS
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DT Article
DE bone cell senescence; osteoporosis; bone repair; aging
ID mesenchymal stem-cells; sensing receptor antagonist; total shoulder arthroplasty; wide dna methylation; smooth-muscle-cells; knee osteoarthritis; oxidative stress; cancellous bone; mineral density; in-vitro
AB The bone repair and substitute have been developed for decades with the bone defect repair applied successfully in clinical. However, implant complications may occur in more challenging situations, bone cell senescence and osteoporosis (OP). Due to certain microenvironment conditions, including hormonal, nutritional, and aging factors, the bone cell responses are regulated to alteration and end into cell senescence and OP. Thus, the bone tissue regeneration is limited with site morbidity increased, leading to bone graft failure. In such pathological state, bone grafts and substitutes are companied with OP therapies to improve bone tissue engineering and to enhance bone graft healing. Those substitutes with OP therapeutic-based applications have been becoming a growing field of interest in bone repair. Bone grafts, such as scaffolds with antiosteoporotic drugs releasing and implants with surface therapeutic modified, are studied to significantly increase low bone density as well as improve impaired bone regeneration. In this review, we discuss a thorough understanding in bone remodeling process, bone cell senescence, and mechanisms of OA and OP. Based on the understanding, the review concentrates on the treatments to the OP and the bone grafts applied in the bone senescence model and provides a future direction in clinical trial. Impact Statement This review discusses the tissue engineering and regenerative medicine therapies for aging-related bone diseases, which have been highly concerned in

aging society. These therapies can improve the efficacy of bone tissue regeneration, enhance the quality of bone repair, and provide new insights in the field of bone clinical treatments and aging regeneration.
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TI Spinal Osteoarthritis Is Associated With Stature Loss Independently of Incident Vertebral Fracture in Postmenopausal Women
SO SPINE
LA English
DT Article
DE aging; bone mineral density; degenerative joint disease; height loss; incident vertebral fracture; osteoporosis; postmenopausal women; quality of life; spinal osteoarthritis; stature loss
ID historical height loss; older women; mortality; men; accuracy; ratio
AB Study Design. Retrospective observational study from the Nagano Cohort Study. Objective. Clarify the association between spinal osteoarthritis and loss of stature in postmenopausal women. Summary of Background Data. Loss of stature

with aging is known to deteriorate health-related quality of life and has been implicated with increased mortality. Although the association of vertebral fracture with height loss has been well documented, the relationship between stature loss and spinal osteoarthritis remains unclear. Methods. We retrospectively investigated Japanese postmenopausal women recruited from the Nagano Cohort Study. The participants were outpatients at a primary care institute in Nagano prefecture, Japan. A total of 977 postmenopausal patients (mean age: 65.8 yr) completed a minimum of 1 year of follow-up, with an average observation period of 7.6 years. Quartile analysis on the prevalence of spinal osteoarthritis and occurrence of incident fracture was performed based on the rate of stature change per year (Delta cm/yr). Multiple regression analysis was also conducted to identify the determinants of stature change. Results. The lower quartiles of stature change rate (i.e., more rapid stature loss) displayed a significantly higher prevalence of spinal osteoarthritis ($P < 0.001$) and incident vertebral fracture ($P<0.001$). A statistically significant independent negative association for spinal osteoarthritis prevalence with change in stature was revealed by multiple regression analysis after adjusting for confounders including incident vertebral fracture. The partial regression coefficient for spinal osteoarthritis was -0.18 (95% confidence interval -0.33 to -0.03; $P = 0.016$). Conclusion. This study demonstrated an independent association of spinal osteoarthritis with stature loss in postmenopausal women. Adequate understanding of this relationship and appropriate treatment approaches will help improve health-related quality of life in elderly patients.
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TI The role of opioid analgesics in rheumatic disorders: a position paper from the Portuguese Rheumatology Society
SO ACTA REUMATOLOGICA PORTUGUESA
LA English
DT Article
DE Opioids; Musculoskeletal pain; Pain; Rheumatic diseases

ID chronic noncancer pain; low-back-pain; evidence-based recommendations; quality-of-life; eular recommendations; knee osteoarthritis; standing-committee; fibromyalgia pain; task-force; osteoporosis
AB Pain is a common feature of most rheumatic diseases and it is often the main reason for the patient to seek for a clinical appointment. Chronic pain has a major impact on patient's quality of life, being frequently associated with functional incapacity, sleep and mood disorders. This leads to absenteeism and heavy consumption of health resources, both representing huge burdens on national economy. Managing musculoskeletal pain is pivotal but can be challenging. The use of the available pharmaceutical armamentarium should be parsimonious. Opioids are strong analgesic drugs that mostly act through their agonist action on mu-receptors in the central nervous system. Opioid-related side effects are not negligible and are mediated through both central and peripheral opioid receptors. The use of opioids is well established in the treatment of oncologic pain but their role in the management of musculoskeletal pain is still controversial. Inflammatory rheumatic diseases, osteoarthritis, osteoporotic fractures, chronic low back pain and fibromyalgia represent diverse major rheumatic conditions that frequently lead to chronic pain. In order to standardize and optimize management of musculoskeletal chronic pain in these prevalent diseases, the Portuguese Rheumatology Society elaborated this position paper. The objectives were: a) to define the importance of pain assessment and classification; b) to guide patient selection, appropriate choice of opioids, their management, and raise awareness of their adverse effects; c) to review the existent data on possible indications of opioid therapy on rheumatic diseases.
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AF Li, Dan
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TI Clinical Study of Correlation Between Osteoporosis and Osteoarthritis of Knee Joint Using Gold Nanomaterial Contrast Agent
SO JOURNAL OF NANOSCIENCE AND NANOTECHNOLOGY
LA English
DT Article
DE Osteoporosis; Knee Arthritis; Comorbidity; GNP
ID bone-mineral density; subchondral bone; articular-cartilage; hip osteoarthritis; cancellous bone; tissue; men
AB The relationship between osteoporosis (OP) and knee osteoarthritis (OA) was studied using gold nanomaterial (GNP) contrast agent from the imaging and clinical perspectives. Patients were divided into the OA and OP comorbidity group (experimental), OA group (positive control), and OP group (negative control) and evaluated using the Lysholm knee joint score and traditional Chinese medicine syndrome score. Bone density was measured by parallel X-ray examination, magnetic resonance imaging examination, Recht classification, and arthroscopic Outerbridge classification. GNP contrast agents were used in the medical imaging tests. There were significant differences between the various factors compared between the experimental and positive control groups ($P < 0.05$). The correlation analysis of the variables and bone mineral density in all patients showed a positive linear relationship ($P < 0.05$). There was a positive correlation between OP and knee OA. GNP has good clinical value in medical imaging.

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JI J. Nanosci. Nanotechnol.
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WC Chemistry, Multidisciplinary; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary; Physics, Applied; Physics, Condensed Matter
SC Chemistry; Science & Technology - Other Topics; Materials Science; Physics
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PT J
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TI Loading modality and age influence teriparatide-induced bone formation in the human femoral neck
SO BONE
LA English
DT Article
DE Teriparatide; Femoral neck; Clinical study; Mechanical loading; Tension; Compression
ID body-mass index; parathyroid-hormone; postmenopausal women; mineral density; cancellous bone; cortical bone; pth treatment; osteoporosis; denosumab; therapy
AB Teriparatide (TPTD) reduces risk of both vertebral and nonvertebral fracture, but increases bone mineral density (BMD) much more at the spine than the hip. TPTD and mechanical loading may have a synergistic anabolic effect on BMD, which may help explain these site-specific differences. Under normal daily activity, the femoral neck (FN) is under bending, placing one side under tension and the other under compression. We sought to further understand the relationship between mechanical loading and TPTD at the hip by investigating the effect of tensile versus compressive loading on TPTD stimulated bone formation indices in the human FN. Thirty-eight patients receiving total hip replacements for osteoarthritis were randomized to receive placebo (PBO) or TPTD for a mean treatment duration of 6 weeks prior to surgery, and double tetracycline labeling was administered to allow assessment of bone formation. The FN was harvested during surgery and analyzed for dynamic bone formation indices in the compressive and tensile regions of the endocortical and periosteal envelopes. Regression models relating outcome measures to patient characteristics including sex, age, body weight, and FN geometry were also analyzed. Overall, bone formation was higher with TPTD versus placebo on the endocortical surface, but not the periosteal surface. The level of bone formation in both TPTD and placebo groups was greater on the tensile endocortical surface and the compressive periosteal surface. There was a trend toward decreased endocortical eroded surface with TPTD in the compressive but not the tensile region. Patient age and sex explained the greatest variability in endocortical bone formation, and patient body mass and sex explained the greatest variability in periosteal bone formation. Our data represent the first dynamic comparison of teriparatide treatment under two loading modalities in human FN samples. Future work could determine whether specific hip loading intervention could amplify the benefits of teriparatide on the hip in clinical settings.
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TI Zebrafish: A Suitable Tool for the Study of Cell Signaling in Bone
SO CELLS
LA English
DT Review
DE zebrafish; bone; cartilage; osteogenesis imperfecta
ID osteoclast differentiation; expression; osteogenesis; dedifferentiation; osteoblasts; cartilage; genetics; growth; runx2; fate
AB In recent decades, many studies using the zebrafish model organism have been performed. Zebrafish, providing genetic mutants and reporter transgenic lines, enable a great number of studies aiming at the investigation of signaling pathways involved in the osteoarticular system and at the identification of therapeutic tools for bone diseases. In this review, we will discuss studies which demonstrate that many signaling pathways are highly conserved between mammals and teleost and that genes involved in mammalian bone differentiation have orthologs in zebrafish. We will also discuss as human diseases, such asosteogenesis imperfecta, osteoarthritis, osteoporosis and Gaucher disease can be investigated in the zebrafish model.
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WC Cell Biology
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TI Prevalence of osteoporosis and osteopenia diagnosed using quantitative CT in 296 consecutive lumbar fusion patients
SO NEUROSURGICAL FOCUS

LA English
DT Article
DE osteoporosis; osteopenia; quantitative computed tomography; OCT; bone mineral density; disease prevalence; degenerative lumbar disease
ID bone-mineral density; x-ray absorptiometry; postmenopausal women; vertebral fractures; risk-factors; degenerative changes; knee osteoarthritis; computed-tomography; spine surgery; hip
AB OBJECTIVE Osteoporosis is a metabolic bone disease that increases the risk for fragility fractures. Screening and diagnosis can be achieved by measuring bone mineral density (BMD) using quantitative CT tomography (QCT) in the lumbar spine. QCT-derived BMD measurements can be used to diagnose osteopenia or osteoporosis based on American College of Radiology (ACR) thresholds. Many reports exist regarding the disease prevalence in asymptomatic and disease-specific populations; however, osteoporosis/osteopenia prevalence rates in lumbar spine fusion patients without fracture have not been reported. The purpose of this study was to define osteoporosis and osteopenia prevalence in lumbar fusion patients using QCT. METHODS A retrospective review of prospective data was performed. All patients undergoing lumbar fusion surgery who had preoperative fine-cut CT scans were eligible. QCT-derived BMD measurements were performed at L1 and L2. The L1-2 average BMD was used to classify patients as having normal findings, osteopenia, or osteoporosis based on ACR criteria. Disease prevalence was calculated. Subgroup analyses based on age, sex, ethnicity, and history of abnormal BMD were performed. Differences between categorical groups were calculated with Fisher's exact test. RESULTS Overall, 296 consecutive patients (55.4% female) were studied. The mean age was 63 years (range 21-89 years). There were 248 (83.8%) patients with ages >= 50 years. No previous clinical history of abnormal BMD was seen in 212 (71.6%) patients. Osteopenia was present in 129 (43.6%) patients and osteoporosis in 44 (14.9%). There were no prevalence differences between sex or race. Patients >= 50 years of age had a significantly higher frequency of osteopenia/osteoporosis than those who were < 50 years of age. CONCLUSIONS In 296 consecutive patients undergoing lumbar fusion surgery, the prevalence of osteoporosis was 14.9% and that for osteopenia was 43.6% diagnosed by QCT. This is the first report of osteoporosis disease prevalence in lumbar fusion patients without vertebral fragility fractures diagnosed by QCT.
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NR 73
TC 29
Z9 35
U1 0
U2 4
PU AMER ASSOC NEUROLOGICAL SURGEONS
PI ROLLING MEADOWS
PA 5550 MEADOWBROOK DRIVE, ROLLING MEADOWS, IL 60008 USA
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EI
J9 NEUROSURG FOCUS
JI Neurosurg. Focus
PD AUG 15
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IS 2
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DI 10.3171/2020.5.FOCUS20241
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WC Clinical Neurology; Surgery
SC Neurosciences & Neurology; Surgery
GA OA6XW
UT WOS:000577926300005
PM 32738803
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ER

PT J
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TI High bone turnover state under osteoporotic changes induces pain-like behaviors in mild osteoarthritis model mice
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Osteoporosis; Osteoarthritis; High bone turnover; Pain; Bisphosphonate
ID knee pain; marrow lesions; skeletal pain; bisphosphonates; risedronate; mechanisms; markers; p2x2/3; cells; asics
AB Introduction Our previous studies demonstrated that a high bone turnover state under osteoporotic changes decreased the threshold of skeletal pain. Recent studies reported that the incidence of joint pain due to osteoarthritis (OA) in postmenopausal women was higher than that in males even with the same radiographic OA grade. The aim of this study was to evaluate whether a high bone turnover state affects the induction of pain-like behaviors in mild OA model mice. Materials and Methods We established mild OA model mice with accompanying osteoporotic changes by monosodium iodoacetate injection after ovariectomy. We assessed pain-like behaviors by von Frey test and paw-flick test; histological changes in OA joints; the expression of Runx2, Osterix, Osteocalcin, and Rankl; bone micro-architecture by mu CT and measured serum tartrate-resistant acid-phosphatase 5b levels in the model mice. Results Pain-like behaviors in mice with OA and osteoporotic changes were significantly increased in comparison with those in OA mice without osteoporotic changes. The severity of histological OA changes did not differ significantly between the OA mice with and without osteoporotic changes. Bisphosphonate significantly improved pain-like behaviors accompanied with improvement in the high bone turnover state in the OA mice with osteoporosis, while it had no significant effect on pain-like behaviors in the OA mice without osteoporosis. In addition, the improvement was maintained for more than 4 weeks even after the discontinuation of bisphosphonate treatment. Conclusion These results indicated that a high bone turnover state under osteoporotic changes could affect the induction of pain-like behaviors in mild OA model mice.
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NR 36
TC 7
Z9 10
U1 0
U2 3
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J9 J BONE MINER METAB
JI J. Bone Miner. Metab.
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WC Endocrinology & Metabolism; Medicine, Research & Experimental
SC Endocrinology & Metabolism; Research & Experimental Medicine
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TI Labral calcification plays a key role in hip pain and symptoms in femoroacetabular impingement
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Femoroacetabular impingement syndrome; Arthroscopy; Synovial inflammation; Labrum; Calcification
ID nationwide prospective cohort; acetabular labrum; synovial inflammation; cam impingement; risk-factor; osteoarthritis; arthroscopy; deformity; outcm; pathophysiology
AB Background Hip osteoarthritis (HOA) is the most common hip disorder and a major cause of disability in the adult population, with an estimated prevalence of end-stage disease and total hip replacement. Thus, the diagnosis, prevention, and treatment of the early stages of the disease in young adults are crucial to reduce the incidence of end-stage HOA. The purpose of this study was to determine

whether (1) a relationship among the inflammatory status of labrum and synovium collected from patients with femoroacetabular impingement (FAI) would exist; and (2) to investigate the associations among the histopathological features of joint tissues, the pre-operative symptoms and the post-operative outcomes after arthroscopic surgery. Methods Joint tissues from 21 patients undergoing hip arthroscopy for FAI were collected and their histological and immunohistochemical features were correlated with clinical parameters. Results Synovial mononuclear cell infiltration was observed in 25% of FAI patients, inversely correlated with the hip disability and osteoarthritis outcome score (HOOS) pain and function subscales and with the absolute and relative change in total HOOS. All the labral samples showed some pattern of degeneration and 67% of the samples showed calcium deposits. The total labral score was associated with increased CD68 positive cells in the synovium. The presence of labral calcifications, along with the chondral damage worsened the HOOS post-op symptoms (adjusted R-square = 0.76 p = 0.0001). Conclusions Our study reveals a relationship between the histologic labral features, the synovial inflammation, and the cartilage condition at the time of FAI. The presence of labral calcifications, along with the cartilage damage and the synovitis negatively affects the post-operative outcomes in patients with FAI.
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10.1007/s11999-016-4852-x
NR 51
TC 15
Z9 18
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U2 6
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 J ORTHOP SURG RES
JI J. Orthop. Surg. Res.
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PT J
AU Liu, SY
Xu, X
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AF Liu, Shuyu
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Liang, Shujing
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TI The Application of MSCs-Derived Extracellular Vesicles in Bone Disorders: Novel Cell-Free Therapeutic Strategy
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE mesenchymal stem cells; extracellular vesicles; exosomes; osteoarthritis; rheumatoid arthritis; osteoporosis; bone fracture
ID mesenchymal stem-cells; stromal cells; exosome isolation; transferrin receptor; osteoarthritis; microvesicles; transplantation; proliferation; biogenesis; secretion
AB Bone is crucial for supporting the body, protecting other organs, providing minerals, and secreting hormone to regulate other organ's function. Bone disorders result in pain and disability, severely affecting human health, reducing the quality of life and increasing costs to society. With the rapid increase in the aging population worldwide, bone disorders have become one major disease. As a result, efficacious therapies of bone disorders have become the focus of attention worldwide. Mesenchymal stem cells (MSCs) have been widely explored as a new therapeutic method for numerous diseases. Recent evidence suggests that the therapeutic effects of MSCs are mainly mediated by their extracellular vesicles (EV). MSCs-derived extracellular vesicles (MSCs-EV) is indicated as a novel cell-free alternative to cell therapy with MSCs in regenerative medicine. Here, we review the current knowledge of EV and highlight the application studies of MSCs-EV in bone

disorders by focusing on osteoarthritis (OA), rheumatoid arthritis (RA), osteoporosis (OP), and bone fracture. Moreover, we discuss the key issues and perspectives of MSCs-EV as a clinical therapeutic strategy for bone diseases.
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TI The Clinical Potential of Circulating miRNAs as Biomarkers: Present and Future Applications for Diagnosis and Prognosis of Age-Associated Bone Diseases
SO BIOMOLECULES
LA English
DT Review
DE biomarkers; circulating miRNAs; miRNA signature; extra-analytical variability; sensitivity and specificity; osteoporosis; fracture risk; osteoarthritis
ID mesenchymal stem-cells; postmenopausal osteoporosis; adipogenic differentiation; micrornas; cancer; serum; plasma; expression; exercise; women
AB Osteoporosis, related fracture/fragility, and osteoarthritis are age-related pathologies that, over recent years, have seen increasing incidence and prevalence due to population ageing. The diagnostic approaches to these pathologies suffer from limited sensitivity and specificity, also in monitoring the disease progression or treatment. For this reason, new biomarkers are desirable for improving the management of osteoporosis and osteoarthritis patients. The non-coding RNAs, called miRNAs, are key post-transcriptional factors in bone homeostasis, and promising circulating biomarkers for pathological conditions in which to perform a biopsy can be problematic. In fact, miRNAs can easily be detected in biological fluids (i.e., blood, serum, plasma) using methods with elevated sensitivity and specificity (RT-qPCR, microarray, and NGS). However, the analytical phases required for miRNAs' evaluation still present some practical issues that limit their use in clinical practice. This review reveals miRNAs' potential as circulating biomarkers for evaluating predisposition, diagnosis, and prognosis of osteoporosis (postmenopausal or idiopathic), bone fracture/fragility, and osteoarthritis, with a focus on pre-analytical, analytical, and post-analytical protocols used for their validation and thus on their clinical applicability. These evidences may support the definition of early diagnostic tools based on circulating miRNAs for bone diseases and osteoarthritis as well as for monitoring the effects of specific treatments.
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NR 118
TC 45
Z9 48
U1 0
U2 15
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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EI 2218-273X
J9 BIOMOLECULES
JI Biomolecules
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VL 10
IS 4
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DI 10.3390/biom10040589
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WC Biochemistry & Molecular Biology
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GA LW9WG
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PT J
AU Anderson, C
Gapstur, SM
Leach, CR
Smith, TG
Teras, LR
AF Anderson, Chelsea
Gapstur, Susan M.
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TI Medical conditions and physical function deficits among multiple primary cancer survivors
SO JOURNAL OF CANCER SURVIVORSHIP
LA English
DT Article
DE Multiple primary cancers; Cancer survivors; Physical function; Comorbidities
ID mental-health status; quality-of-life; psychological distress; older-adults; prevention; prevalence; behaviors; society; risk
AB Purpose Survivors of multiple primary cancers make up a sizable proportion of all cancer survivors, yet little is known about the health of this population. We examined the prevalence of medical conditions and physical function deficits among multiple primary survivors compared with single primary survivors and individuals without a cancer history. Methods Participants were enrolled in the Cancer Prevention Study (CPS)-II Nutrition Cohort in 1992/1993. Prevalent medical conditions (diabetes, heart conditions, cerebrovascular conditions, emphysema/chronic bronchitis, osteoporosis, osteoarthritis), physical function limitations, use of a cane or walker, balance difficulties, and falls within the past year were assessed on a follow-up survey completed in 2011. We estimated age- and sex-adjusted prevalence ratios (PRs), comparing multiple primary survivors (N = 1003) to single primary survivors (N = 12,849) and participants without cancer (N = 63,578). Results The prevalence of medical conditions did not differ substantially between multiple primary survivors and either comparison group. However, multiple primary survivors were more likely to report severe limitations in physical function than the single primary (PR = 1.48 (95% CI, 1.28-1.71)) and no-cancer (PR = 1.64 (95% CI, 1.42-1.88)) groups. Using a cane or walker and balance difficulties were also significantly more common among multiple primary survivors. Conclusions Despite a similar prevalence of comorbid medical conditions, severe functional limitations were significantly more common among multiple primary survivors than single primary survivors or individuals without cancer. Implications for Cancer Survivors Assessment of functional status and treatment of physical deficits may be an especially critical component of care for older patients with a history of multiple cancer diagnoses.
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NR 25
TC 6
Z9 6
U1 0
U2 5
PU SPRINGER
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SN 1932-2259
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J9 J CANCER SURVIV
JI J. Cancer Surviv.-Res. Pract.
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SC Oncology; Biomedical Social Sciences
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AU Ekeuku, SO
Pang, KL
Chin, KY
AF Ekeuku, Sophia Ogechi
Pang, Kok-Lun
Chin, Kok-Yong
TI Palmatine as an Agent Against Metabolic Syndrome and Its Related Complications: A Review
SO DRUG DESIGN DEVELOPMENT AND THERAPY
LA English
DT Review
DE anti-inflammation; antioxidant; myocardial reperfusion injury; obesity; osteoporosis; osteoarthritis
ID oxidative stress; adipose-tissue; alkaloid palmatine; rhizoma coptidis; p-glycoprotein; bone health; in-vivo; activation; expression; obesity
AB Palmatine is a naturally occurring isoquinoline alkaloid with various pharmacological properties. Given its antioxidant and anti-inflammatory properties, palmatine may be able to impede the effects of metabolic syndrome (MetS) and its related diseases triggered by inflammation and oxidative stress. This review summarises the existing literature about the effects of palmatine supplementation on MetS and its complications. The evidence shows that palmatine could protect against MetS, and cardiovascular diseases, osteoporosis and osteoarthritis, which

might be associated with MetS. These protective effects are mediated by the antioxidant and anti-inflammatory properties of palmatine. Although preclinical experiments have demonstrated the efficacy of palmatine against MetS and its related diseases, no human clinical trials have been performed to validate these effects. This research gap should be bridged to validate the efficacy and safety of palmatine supplementation in protecting humans against MetS and its related diseases.

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AU Blanch-Rubió, J
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TI Influence of anti-osteoporosis treatments on the incidence of COVID-19 in patients with non-inflammatory rheumatic conditions
SO AGING-US
LA English
DT Article
DE denosumab; zoledronate; calcium; vitamin D; anti-resorptive drugs; COVID-19
ID immune-responses; zoledronic acid; mortality; pregabalin; mechanism; diseases; calcium
AB Coronavirus disease 19 (COVID-19) is currently a global pandemic that affects patients with other pathologies. Here, we investigated the influence of treatments for osteoporosis and other non-inflammatory rheumatic conditions, such as osteoarthritis and fibromyalgia, on COVID-19 incidence. To this end, we conducted a cross-sectional study of 2,102 patients being treated at the Rheumatology Service of Hospital del Mar (Barcelona, Spain). In our cohort, COVID-19 cumulative incidence from March 1 to May 3, 2020 was compared to population estimates for the same city. We used Poisson regression models to determine the adjusted relative risk ratios for COVID-19 associated with different treatments and comorbidities. Denosumab, zoledronate and calcium were negatively associated with COVID-19 incidence. Some analgesics, particularly pregabalin and most of the studied antidepressants, were positively associated with COVID-19 incidence, whereas duloxetine presented a negative association. Oral bisphosphonates,

vitamin D, thiazide diuretics, anti-hypertensive drugs and chronic nonsteroidal anti-inflammatory drugs had no effect on COVID-19 incidence in the studied population. Our results provide novel evidence to support the maintenance of the main anti-osteoporosis treatments in COVID-19 patients, which may be of particular relevance to elderly patients affected by the SARS-CoV-2 pandemic.
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TI Soluble Biomarkers of Osteoporosis and Osteoarthritis, from Pathway Mapping to Clinical Trials: An Update
SO CLINICAL INTERVENTIONS IN AGING
LA English
DT Review

DE osteoarthritis; osteoporosis; biomarkers
ID bone turnover markers; oligomeric matrix protein; c-terminal telopeptide; newly developed assay; biochemical markers; knee osteoarthritis; ctx-ii; cartilage degradation; strontium ranelate; mineral density
AB Serum biomarkers of osteoarticular diseases have been in the limelight of current clinical research trends. Laboratory validation of defined and candidate biomarkers for both osteoarthritis and osteoporosis is of key importance for future decisional algorithms in the diagnosis, monitoring, and prognosis of these diseases. The current guidelines recommend the use of collagen degradation remnants, eg, CTX-I and CTX-II, in the complementary diagnosis of both osteoporosis and osteoarthritis. Besides the collagen degradation markers, enzymes that regulate bone and articular metabolism are useful in the clinical evaluation of osteoarticular pathologies. Along these, several other recommended and new nominee molecules have been recently studied. Wnts and Wnt-related molecules have a cardinal role in the bone-joint homeostasis, making them a promising target not only for pharmaceutical modulation, but also to be considered as soluble biomarkers. Sclerostin and dickkopf, two inhibitor molecules of the Wnt/beta-catenin signaling, might have a dual role in the assessment of the clinical manifestations of the osteoarticular unit. In osteoarthritis, besides fragments of collagen type II many pathway-related molecules have been studied and proposed for biomarker validation. The most serious limitation is that a significant proportion of studies lack statistical power due to the reduced number of cases enrolled. Serum biomarkers of bone and joint turnover markers represent an encouraging possibility for the diagnosis and prognosis of osteoarticular diseases, although further studies and laboratory validations should be carried out as to solely rely on them.
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TI The Role of Chronic Inflammatory Bone and Joint Disorders in the Pathogenesis and Progression of Alzheimer's Disease
SO FRONTIERS IN AGING NEUROSCIENCE
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DT Review
DE Alzheimer' s disease; osteoarthritis; osteoporosis; rheumatoid arthritis; inflammation; mesenchymal stem cells
ID mesenchymal stem-cells; platelet-rich plasma; regulates osteogenic differentiation; mild cognitive impairment; vagus nerve-stimulation; necrosis-factor-alpha; rheumatoid-arthritis; knee osteoarthritis; mouse model; systemic inflammation
AB Late-onset Alzheimer's Disease (LOAD) is a devastating neurodegenerative disorder that causes significant cognitive debilitation in tens of millions of patients worldwide. Throughout disease progression, abnormal secretase activity results in the aberrant cleavage and subsequent aggregation of neurotoxic A beta plaques in the cerebral extracellular space and hyperphosphorylation and destabilization of structural tau proteins surrounding neuronal microtubules. Both pathologies ultimately incite the propagation of a disease-associated subset of microglia-the

principle immune cells of the brain-characterized by preferentially pro-inflammatory cytokine secretion and inhibited AD substrate uptake capacity, which further contribute to neuronal degeneration. For decades, chronic neuroinflammation has been identified as one of the cardinal pathophysiological driving features of AD; however, despite a number of works postulating the underlying mechanisms of inflammation-mediated neurodegeneration, its pathogenesis and relation to the inception of cognitive impairment remain obscure. Moreover, the limited clinical success of treatments targeting specific pathological features in the central nervous system (CNS) illustrates the need to investigate alternative, more holistic approaches for ameliorating AD outcomes. Accumulating evidence suggests significant interplay between peripheral immune activity and blood-brain barrier permeability, microglial activation and proliferation, and AD-related cognitive decline. In this work, we review a narrow but significant subset of chronic peripheral inflammatory conditions, describe how these pathologies are associated with the preponderance of neuroinflammation, and posit that we may exploit peripheral immune processes to design interventional, preventative therapies for LOAD. We then provide a comprehensive overview of notable treatment paradigms that have demonstrated considerable merit toward treating these disorders.
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DE Postmenopause; osteoporosis; microRNAs; rats; estrogens
ID subchondral bone; cartilage damage; osteoarthritis; disease; serum; severity; turnover; mirnas; differentiation; homeostasis
AB Postmenopausal osteoporosis (PMOP) is a common disease that seriously threatens human health. Estrogen deficiency plays an essential role in the pathogenesis of PMOP. MicroRNAs (miRNAs) are involved in the development and progression of PMOP. Therefore, identification of miRNAs in PMOP due to estrogen deficiency may contribute to earlier diagnosis and better treatment of this disease. The rat model of PMOP was established by ovariectomy. After one month of treatment, the knee joints were evaluated by microcomputed tomography and histological analysis. The plasma estrogen levels were quantified by enzyme-linked

immunosorbent assays (ELISAs). MiRNA levels were analyzed by high-throughput sequencing and validated using quantitative real-time PCR (qRT-PCR). Two months after ovariectomy, osteoporosis occurred in the subchondral bone of the rats in the PMOP group, while fewer symptoms of osteoporosis occurred in the subchondral bone of the rats with estrogen replacement therapy. Cartilage degeneration was detected in the PMOP group. MiR-29a-3p, miR-93-5p, and miR-486 expression decreased in the PMOP group compared to the control group. After estrogen treatment for one month, the plasma levels of miR-29a-3p, miR-93-5p, and miR-486 recovered to the normal levels. Estrogen eliminated the expression changes in miR-29a-3p, miR-93-5p, and miR-486. The identification of these differentially expressed miRNAs will help elucidate the crucial role of miRNAs in the pathogenesis of PMOP. Our data could lead to the potential utilization of miRNAs in the diagnosis of PMOP and provide a possible therapeutic target for treatment of this disease.
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AF Tantowi, Nur Adeelah Che Ahmad
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TI Comparison of diclofenac with apigenin-glycosides rich Clinacanthus nutans extract for amending inflammation and catabolic protease regulations in osteoporotic-osteoarthritis rat model
SO DARU-JOURNAL OF PHARMACEUTICAL SCIENCES
LA English
DT Article
DE Apigenin-C-glycosides; Anti-inflammatory; Osteoarthritis; Osteoporosis
ID cartilage; osteoclastogenesis; pathogenesis; inhibition; pathway; risk
AB Background Osteoporotic-osteoarthritis is an incapacitating musculoskeletal illness of the aged. Objectives The anti-inflammatory and anti-catabolic actions of Diclofenac were compared with apigenin-C-glycosides rich Clinacanthus nutans (CN) leaf extract in osteoporotic-osteoarthritis rats. Methods Female Sprague Dawley rats were randomized into five groups (n = 6). Four groups were bilateral ovariectomised for osteoporosis development, and osteoarthritis were induced by intra-articular injection of monosodium iodoacetate (MIA) into the right knee joints. The Sham group was sham-operated, received saline injection and deionized

drinking water. The treatment groups were orally given 200 or 400 mg extract/kg body weight or 5 mg diclofenac /kg body weight daily for 28 days. Articular cartilage and bone changes were monitored by gross and histological structures, micro-CT analysis, serum protein biomarkers, and mRNA expressions for inflammation and catabolic protease genes. Results HPLC analysis confirmed that apigenin-C-glycosides (shaftoside, vitexin, and isovitexin) were the major compounds in the extract. The extract significantly and dose-dependently reduced cartilage erosion, bone loss, cartilage catabolic changes, serum osteoporotic-osteoarthritis biomarkers (procollagen-type-II-N-terminal-propeptide PIINP; procollagen-type-I-N-terminal-propeptide PINP; osteocalcin), inflammation (IL-1 beta) and mRNA expressions for nuclear-factor-kappa-beta NF-kappa beta, interleukin-1-beta IL-1 beta, cyclooxygenase-2; and matrix-metalloproteinase-13 MMP13 activities, in osteoporotic-osteoarthritis rats comparable to Diclofenac. Conclusion This study demonstrates that apigenin-C-glycosides at 400 mg CN extract/kg (about 0.2 mg apigenin-equivalent/kg) is comparable to diclofenac in suppressing inflammation and catabolic proteases for osteoporotic-osteoarthritis prevention.
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TI Limited Influence of Comorbidities on Length of Stay after Total Hip Arthroplasty: Experience of Enhanced Recovery after Surgery
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE Enhanced recovery after surgery; Length of stay; predictors; Total hip arthroplasty
ID hospital stay; knee arthroplasty; patient characteristics; joint arthroplasty; united-states; outcm; chinese; replacement; predictors; feasibility
AB Objectives To identify predictors of length of stay (LOS) after total hip arthroplasty (THA) in an enhanced recovery after surgery (ERAS) program and evaluate the safety and cost-efficiency of the ERAS program with reduced LOS for unselected patients in a Chinese population. Methods A total of 311 consecutive, unselected patients undergoing primary THA at a single institution were retrospectively reviewed and divided into two groups: LOS <= 3 and LOS > 3 group. All patients were managed with the same ERAS protocol and went back home after discharge. Multivariate logistic regression analysis was used to determine independent risk factors for LOS > 3. Harris Hip Score at 90-day follow-up, 90-day readmission rate, and hospitalization costs were compared between two groups. Results Multivariate regression analysis identified female gender (odds ratio [OR] = 2.623), living alone (OR = 4.127), and primary osteoarthritis of hip (OR = 3.565) to be correlated with LOS > 3. Preoperative hemoglobin (HB), postoperative HB, drain use, blood transfusion, diabetes, respiratory disease, osteoporosis, number of comorbidities, and CCI score showed no significant influence on LOS after adjusting for other risk factors in the multivariate model. Harris Hip Score and readmission rate at 90-day follow-up showed no significant differences between two groups. Patients in LOS > 3 group had approximately 3948.6 Chinese yuan higher hospital costs. Conclusion Female gender, living alone, and primary osteoarthritis of hip were identified as independent risk factors for prolonged LOS. The experience from our institution suggested aggressive management of comorbidities in the ERAS program can minimize the influence of comorbidities on LOS. The safety, efficiency, and costs-saving benefits of the ERAS program with reduced LOS for unselected patients was confirmed in this study.
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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TI Effect of cadmium on the concentration of essential metals in a human chondrocyte micromass culture
SO JOURNAL OF TRACE ELEMENTS IN MEDICINE AND BIOLOGY
LA English
DT Article
DE Osteoarthritis; Chondrocytes; Cadmium; Essential elements
ID knee-joint; hip-joint; calcium; iron; cartilage; manganese
AB Background: An essential element imbalance in the joint might favor gradual degeneration of the articular cartilage. It has been reported that cadmium (Cd) plays an antagonistic role with regards to the presence of essential elements, such as zinc (Zn), iron (Fe), and manganese (Mn), which may favor the development of

disabling diseases, like osteoarthritis (OA) and osteoporosis. Methods: 3D cultures of human chondrocytes were phenotyped with the Western blot technique and structurally evaluated with histological staining. The samples were exposed to 1, 5, and 10 mu M of CdCl2 for 12 h, with a non-exposed culture as control. The concentration of Cd, Fe, Mn, Zn, chromium (Cr), and nickel (Ni) was quantified through plasma mass spectrometry (ICP-MS). The data were analyzed with a Kruskal Wallis test, a Kendall's Tau test and Spearman's correlation coefficient with the Stata program, version 14. Results: Our results suggest that Cd exposure affects the structure of micromass cultures and plays an antagonistic role on the concentration of essential metals, such as Zn, Ni, Fe, Mn, and Cr. Conclusion: Cd exposure may be a risk factor for developing joint diseases like OA, as it can interfere with cartilage absorption of other essential elements that maintain cartilage homeostasis.
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TI The Roles of FoxO Transcription Factors in Regulation of Bone Cells Function
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES

LA English
DT Review
DE FoxOs; bone cells; antioxidant; osteogenesis; osteoclastogenesis; chondrogenesis; bone diseases
ID oxidative stress; hematopoietic stem; osteoclast differentiation; beta-catenin; chondrocytes; homeostasis; activation; resistance; expression; cancer
AB Forkhead box class O family member proteins (FoxOs) are evolutionarily conserved transcription factors for their highly conserved DNA-binding domain. In mammalian species, all the four FoxO members, FoxO1, FoxO3, FoxO4, and FoxO6, are expressed in different organs. In bone, the first three members are extensively expressed and more studied. Bone development, remodeling, and homeostasis are all regulated bymultiple cell lineages, including osteoprogenitor cells, chondrocytes, osteoblasts, osteocytes, osteoclast progenitors, osteoclasts, and the intercellular signaling among these bone cells. The disordered FoxOs function in these bone cells contribute to osteoarthritis, osteoporosis, or other bone diseases. Here, we review the current literature of FoxOs for their roles in bone cells, focusing on helping researchers to develop new therapeutic approaches and prevent or treat the related bone diseases.
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AF Zhou, Jiaming
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TI Clinical effect of intramuscular calcitonin compared with oral celecoxib in the treatment of knee bone marrow lesions: a retrospective study
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Calcitonin; Celecoxib; Bone marrow lesions; Osteoarthritis
ID salmon-calcitonin; edema syndrome; transient osteoporosis; postmenopausal women; osteoarthritis; pain; cartilage; degradation; progression; metabolism
AB BackgroundBone marrow lesions (BMLs) are a common finding in patients with osteoarthritis (OA), which are predictors of progression and pain related to cartilage damage in OA. The objective of the present research was to compare the short-term clinical effect of intramuscular calcitonin and oral celecoxib in treating knee BMLs.Patients and methodsBetween January 2016 and December 2018, the medical records of patients with knee BMLs treated by intramuscular calcitonin or oral celecoxib were reviewed. Visual analog scale (VAS) and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) were used to assess knee pain and function, respectively. BMLs were assessed by MRI scans and were scored by the modified Whole-Organ MRI Score (WORMS). The safety of these two medications was also evaluated.ResultsA total of 123 eligible patients who received calcitonin treatment (n = 66) or celecoxib treatment (n = 57) were included. All patients were followed up clinically and radiographically for 3months. The VAS and WOMAC scores were lower statistically in calcitonin group than celecoxib group at 4-week and 3-month follow-up. For BMLs, the WORMS scores in the calcitonin group were significantly lower than the celecoxib group. Besides, statistically higher MRI improvement rates were found in the calcitonin group compared with the celecoxib group at 4-week follow-up (21.21% vs. 7.01%; P = 0.039) and 3-month follow-up (37.88% vs. 15.79%; P = 0.006).ConclusionIntramuscular calcitonin 50IU once daily demonstrated a better short-term effect for knee BML patients compared with oral celecoxib 200mg twice per day.
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TI The Emerging Roles of Long Noncoding RNAs in Bone Homeostasis and Their Potential Application in Bone-Related Diseases
SO DNA AND CELL BIOLOGY
LA English
DT Article

DE long noncoding RNAs; bone homeostasis; stem cells; bone-related diseases
ID mesenchymal stem-cells; promotes osteogenic differentiation; osteoblast differentiation; osteosarcoma cells; multiple-myeloma; regulating runx2; poor-prognosis; lncrna malat1; proliferation; metastasis
AB Increasing evidence has announced the emerging roles of long noncoding RNAs (lncRNAs) in modulating bone homeostasis due to their potential regulating effects on bone-related cells' proliferation, migration, differentiation and apoptosis. Thus, lncRNAs have been considered as a promising gene tool to facilitate the bone regeneration process and then to predict and cure bone-related diseases such as osteosarcoma, osteoporosis, and osteoarthritis. In this review, we first enumerated several kinds of dysregulated lncRNAs and concisely summarized their regulating role in bone formation as well as resorption process. The related mechanisms were also discussed, respectively. Then, the positive or negative behavior of these lncRNAs in bone-related diseases was elucidated. This review provides an in-depth sight about the lncRNA's clinical values and limitations, which is conducive to explore new gene targets and further establish new therapeutic strategies for bone-related disease.
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FU National Natural Science Foundation of China [81701027]; National Key Research and Development Program of China [2016YFC1102700]
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TI Network-Based Computational Approach to Identify Delineating Common Cell Pathways Influencing Type 2 Diabetes and Diseases of Bone and Joints
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DT Article
DE T2 diabetes; network-based approach; joint diseases; bone diseases
ID osteoblast differentiation; tyrosine kinase; profiles; mellitus; comorbidity; receptor; database; gene; ucp3
AB Developing type 2 diabetes (T2D) can increase patient risk of developing other common diseases and exacerbate their severity, including diseases that affect bone and joints. Such comorbidity interactions are hard to study in detail by traditional endocrinological methods. Thus, we developed tissue transcript analytical approaches to identify common pathways through which these diseases can interact. We examined RNAseq and microarray transcript datasets from studies of T2D and chronic bone and joint diseases, namely rheumatoid arthritis (RA), osteoarthritis (OA), juvenile idiopathic arthritis (JIA) and low peak bone density, a key osteoporosis (OP) determinant. These datasets contained data from affected individuals and matched controls. Differentially expressed genes (DEGs) for each condition were compared with T2D DEG. Overlapping DEGs (i.e., those common to T2D and a bone or joint condition) were subjected to gene enrichment by pathway analyses and by gene ontology methods, and the results were evaluated by using SNP-disease linkage (dbGaP) and gene-disease association (OMIM) databases that indicate gene involvement in pathologies. By examining gene targets of transcription factors (TFs) and microRNA (miRNAs), we also constructed DEG-TF and DEG-miRNA interactions networks for analysis. We identified strong candidate genes in common pathways, notably including SYK, UCP3, ROR1, PPARG, BUB1, AKT2, ADCY2 and CCR5. The DEG-TF network and DEG-miRNA interactions network analyses revealed a number of TFs (GATA2, FOXC1, USF2, YY1, E2F1, JUN, RELA, CREB1, TFAP2A, NFB1) and miRNAs (mir-335-5p, mir-16-5p, mir-26b-5p, mir-124-3p, mir-218-5p, mir-98-5p, mir-29b-3p, mir-3135b, mir-29c-3p, mir-1-1) that can regulate the identified DEGs at the transcriptional and post-transcriptional levels. Thus this data-driven approach has enabled identification and validation of regulatory factors and cell pathways by which T2D may influence bone and joint conditions, which may suggest new ways to interfere with the pathogenic processes involved.
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ER

PT J
AU Sugano, M
Hagiwara, S
Nakamura, J
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TI Comparison study of bone strength of the proximal femur with and without hip osteoarthritis by computed tomography-based finite element analysis
SO JOURNAL OF BIOMECHANICS
LA English
DT Article
DE Finite element analysis; Bone strength; Proximal femur fracture; Osteoporosis; Hip osteoarthritis
ID femoral fractures; prediction; risk; density; women; qct
AB Proximal femoral fractures are common in elderly osteoporosis patients; however, its prevalence is clinically rare in hip fracture patients with hip osteoarthritis (OA). This study aimed to evaluate bone strength of the proximal femur with or without hip OA and proximal femoral fracture risk using computed tomography (CT)-based finite element analysis (FEA). A retrospective analysis was done on CT data of 20 patients who underwent total hip arthroplasty for unilateral hip OA. Furthermore, the fracture load between OA and contralateral sides was

compared and the association between fracture load and risk factor was analyzed. The fracture load was significantly higher in the OA side than that in the contralateral side (3819.5 +/- 1557.8 N vs. 3224.5 +/- 943.7 N, respectively; P = 0.0405). There was no significant difference in fracture load between OA and the contralateral side in Kellgren-Lawrence (KL)-3 and KL-4 grade, but the KL-4 fracture load tends to be high (P = 0.2461 and P = 0.0527, respectively). Moreover, there was no significant association between fracture load and OA severity or age. The study findings may assist in predicting bone strength and proximal femur fracture risk. The results of this FEA study indicate the bone strength of the proximal femur was affected by the severity of the osteoarthritis. (C) 2020 Elsevier Ltd. All rights reserved.
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AU Nazari-Farsani, S
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AF Nazari-Farsani, Sanaz
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TI Bone Mineral Density and Cortical-Bone Thickness of the Distal Radius Predict Femoral Stem Subsidence in Postmenopausal Women
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE cementless total hip arthroplasty; radiostereometric analysis (RSA); osteoporosis; cortical bone; DXA; pulse-echo ultrasonometry
ID total hip-arthroplasty; cementless; osteoporosis; porosity; rsa; osteoarthritis; fixation; shape; fit
AB Background: The distal radius is an optional site for evaluation of bone quality in postmenopausal women before cementless total hip arthroplasty. We hypothesized that dual-energy X-ray absorptiometry (DXA) and pulse-echo ultrasonometry of the distal radius may help discriminate subjects at high risk of femoral stem subsidence. Methods: A prospective cohort of postmenopausal women with primary hip osteoarthritis underwent total hip arthroplasty with implantation of a parallel-sided femoral stem. Postoperative stem migration was measured using radiostereometric analysis. Preoperatively, subjects had multisite DXA measurement of bone mineral density (BMD) and pulse-echo ultrasonometry of the cortical-bone thickness. The diagnostic abilities of these methods to discriminate <2 mm and >= 2 mm femoral stem subsidence were tested. Results: The accuracy of the distal radius BMD and cortical-bone thickness of the distal radius were moderate (area under the curve, 0.737 and 0.726, respectively) in discriminating between <2 mm and >= 2 mm stem subsidence. Women with low cortical-bone thickness of the radius were more likely (odds ratio = 6.7; P = .002) to develop stem subsidence >= 2 mm. These subjects had lower total hip BMD (P = .007) and reduced thickness of the medial cortex of the proximal femur (P = .048) with lower middle (P < .001) and distal (P = .004) stem-to-canal fill ratios.

Conclusion: Femoral stem stability and resistance to subsidence are sensitive to adequate bone stock and unaltered anatomy. DXA and pulse-echo ultrasonometry of the distal radius may help discriminate postmenopausal women at high risk of stem subsidence. (C) 2020 The Author(s). Published by Elsevier Inc.
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FU Amgen Inc (ISS) [20109714]; Academy of Finland [288607]; Turku University Hospital [13705]; Academy of Finland (AKA) [288607] Funding Source: Academy of Finland (AKA)
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AU Liu, C
He, Y
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He, BR
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AF Liu, Chang
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Kong, Lingbo
TI The Study of Natural Compounds Targeting RANKL Signaling Pathway for the Treatment of Bone Diseases
SO CURRENT DRUG TARGETS
LA English
DT Review
DE RANKL; NF-kappa B; MAPKs; Akt; Ca2+; osteoporosis; osteoarthritis; rheumatoid arthritis; signaling pathways
ID nf-kappa-b; induced osteoclast formation; receptor activator; in-vitro; bisphosphonate use; stewartia-koreana; oxidative stress; gallic acid; differentiation; resorption
AB Millions of people, especially for the aging people, are suffered by bone-loss diseases, such as rheumatoid arthritis (RA) and osteoporosis. Therefore, better understanding the involved mechanisms of bone metabolism is required for further treat on such diseases. Particularly, during the pathological process of bone losing, RANKL as a member of the tumor necrosis factor (TNF) superfamily, could induce osteoclast precursor cells differentiate into mature osteoclast, which grant its essential role in osteolysis. In recent years, with the increased attention paid to the natural compounds discovering studies, the therapeutic application of natural plant-derivatives have been widely recognized. Therefore, our present study aim to summarize the current novel research progressions on RANKL and its downstream signaling pathways in bone cellular differentiation, and provide a further insight for RANKL as the important drug targets in bone loss diseases. Besides that, in our current study, we also aim to briefly introduce the current application of several natural compounds for treating RANKL-mediated osteoclastic activation by modulating the RANKL signaling pathway and their therapeutic effects on the prevention of osteoporosis, osteoarthritis (OA) and RA.
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PA EXECUTIVE STE Y-2, PO BOX 7917, SAIF ZONE, 1200 BR SHARJAH, U ARAB EMIRATES
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J9 CURR DRUG TARGETS
JI Curr. Drug Targets
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WC Pharmacology & Pharmacy
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AU Dechaumet, B
Cleret, D
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Lefai, E
Laroche, N
Lafage-Proust, MH
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Lafage-Proust, Marie-Helene
Vico, Laurence
TI Hypergravity as a gravitational therapy mitigates the effects of knee osteoarthritis on the musculoskeletal system in a murine model
SO PLOS ONE
LA English
DT Article
ID bone-mineral density; hip osteoarthritis; physical-activity; subchondral bone; cancellous bone; muscle; exercise; osteoporosis; metabolism; mechanisms
AB Insights into the effects of osteoarthritis (OA) and physical interventions on the musculoskeletal system are limited. Our goal was to analyze musculoskeletal changes in OA mice and test the efficacy of 8-week exposure to hypergravity, as a replacement of physical activity. 16-week-old male (C57BL/6J) mice allocated to sham control and OA groups not centrifuged (Ctrl 1g and OA 1g, respectively) or centrifuged at 2g acceleration (Ctrl 2g and OA 2g). OA 1g displayed decreased trabecular bone in the proximal tibia metaphysis and increased osteoclastic activity and local TNF alpha gene expression, all entirely prevented by 2g gravitational therapy. However, while cortical bone of tibia midshaft was preserved in OA 1g (vs. ctrl), it is thinner in OA 2g (vs. OA 1g). In the hind limb, OA at 1g increased fibers with lipid droplets by 48% in the tibialis anterior, a fact fully prevented by 2g. In Ctrl, 2g increased soleus, tibialis anterior and gastrocnemius masses. In the soleus of both Ctrl and OA, 2g induced larger fibers and a switch from type-II to type-I

fiber. Catabolic (myostatin and its receptor activin RIIb and visfatine) and anabolic (FNDC5) genes dramatically increased in Ctrl 2g and OA 2g ($p<0.01$ vs 1g). Nevertheless, the overexpression of FNDC5 (and follistatine) was smaller in OA 2g than in Ctrl 2g. Thus, hypergravity in OA mice produced positive effects for trabecular bone and muscle typology, similar to resistance exercises, but negative effects for cortical bone.
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J9 PLOS ONE
JI PLoS One
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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UT WOS:000598626100065
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PT J
AU Barker, K
   Eickmeyer, S
AF Barker, Kim
   Eickmeyer, Sarah
TI Therapeutic Exercise
SO MEDICAL CLINICS OF NORTH AMERICA
LA English
DT Article
DE Exercise; Physical activity; Exercise prescription; Therapeutic exercise
ID physical-activity; american-college; public-health; older-adults; prescription; stability; statement; rehabilitation; osteoarthritis; prevention
AB Physicians often overlook exercise as a treatment or prophylactic measure for many common diseases and ailments. It can be used to treat comorbidities including obesity, cardiovascular disease, chronic obstructive pulmonary disease, diabetes mellitus, osteoporosis, osteoarthritis, cancer, and low back pain. Education

on the general physical activity guidelines as well as easy exercise prescription methods can improve the ability of physicians to prescribe exercise as a therapeutic option. In addition, identifying barriers to compliance with exercise and ways to overcome these barriers is also necessary in order to use therapeutic exercise effectively.
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PU W B SAUNDERS CO-ELSEVIER INC
PI PHILADELPHIA
PA 1600 JOHN F KENNEDY BOULEVARD, STE 1800, PHILADELPHIA, PA 19103-2899 USA
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SC General & Internal Medicine
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AU Diao, MZ
Li, Y
Guan, H
Lu, XZ
Gilbert, BP
AF Diao, Mengzhu
Li, Yi
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Lu, Xinzheng
Gilbert, Benoit P.
TI Influence of horizontal restraints on the behaviour of vertical disproportionate collapse of RC moment frames
SO ENGINEERING FAILURE ANALYSIS
LA English
DT Article
DE RC moment frame structure; Progressive collapse; Horizontal restraints; Static test; Numerical simulation
ID reinforced-concrete frames; progressive collapse; resistance; subject; model; capacity; design
AB Current research studies on progressive collapse of reinforced concrete (RC) moment frames mainly focus on the RC frames with strong horizontal restraints in which collapse only propagates in the vertical direction. Notwithstanding, progressive collapse may propagate in the horizontal direction due to insufficient lateral stiffness and bearing capacity of the real-world structural systems, eventually triggering a wider range of damage associated with a disproportionate collapse. A static collapse test on three asymmetric beam-column substructure specimens with flange slabs was conducted to analyse the effects of different

lateral restraints on the progressive collapse behaviour of RC beam-column specimens. The three specimens, including two one-story and one two-story substructures, are designated as OP, TP and OA, in which OP and OA represent one-story penultimate and antepenult column removal scenarios, respectively, while TP represents a two-story penultimate column removal scenario. Comparing to OP, an extra bay and an extra floor were added in OA and TP, respectively, to create different horizontal restraint scenarios. Experimental results show that under the compressive arch action (CAA), the contribution of the CAA within the beams and slabs in OP and TP was significantly reduced compared to that in OA. Under the catenary action (CA), the collapse resistance of OA was found to develop rapidly to exceed even the peak resistance of CAA, whereas the resistance of OP and TP varied marginally, caused by the continuously released axial force of rebars within the beams and flange slabs. Additionally, the final failure mode of all three specimens demonstrated a compression-bending failure of the edge and penultimate columns. Subsequent to the experiments, a fibre-beam-element-based model was built to analyse the development of the internal forces within the slab-flange beams and columns. In the numerical analyses, the penultimate column in OA was found to damage prior to the edge column, owing to its larger axial force generated from the redistributed force and the additional bending moment. While in TP, the so-called Vierendeel truss action led to an uneven internal force distribution developed within the two floors, causing the failure to propagate from the lower story to the upper story. Finally, design recommendations are provided based on the results obtained from the experimental test and numerical simulation.
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NR 42
TC 45
Z9 49

U1 1
U2 50
PU PERGAMON-ELSEVIER SCIENCE LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND
SN 1350-6307
EI 1873-1961
J9 ENG FAIL ANAL
JI Eng. Fail. Anal.
PD JAN 15
PY 2020
VL 109
IS
BP
EP
DI 10.1016/j.engfailanal.2019.104324
PG 19
WC Engineering, Mechanical; Materials Science, Characterization & Testing
SC Engineering; Materials Science
GA KG3US
UT WOS:000509868200048
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ER

PT J
AU Cho, CH
Min, BW
Lee, KJ
Kim, JY
Kim, DH
AF Cho, Chul-Hyun
Min, Byung-Woo
Lee, Kyung-Jae
Kim, Jun-Young
Kim, Du-Han
TI Rapid Destructive Arthrosis Due to Subchondral Insufficiency Fracture of the Shoulder: Clinical Characteristics, Radiographic Appearances, and Outcomes of Treatment
SO DIAGNOSTICS
LA English
DT Article
DE rapid destructive arthrosis; subchondral fracture; shoulder joint humeral head replacement; osteoarthritis; osteoporosis; shoulder arthroplasty

ID humeral head; arthritis
AB The purpose of our study was the clinical characteristics, radiographic appearance, and outcomes after treatment in patients with rapid destructive arthrosis (RDA) due to subchondral insufficiency fracture (SIF) of the shoulder. Twenty-two cases of RDA of the shoulder were retrospectively reviewed. Clinical outcomes for 15 cases who underwent shoulder arthroplasty were evaluated at an average of 41.4 months. The mean age of patients was 73.7 years (range 50-83 years), and there were 20 women and 2 men. The mean time from onset of symptoms to head collapse was 6.8 months (range 1-12 months). The mean t-score of bone mineral density was -3.1. Nine patients had pseudoparalysis. Based on radiographic appearance, a diversity of types of head destruction with subchondral fracture, bone marrow edema, joint effusion, and synovitis were observed in all cases. In conclusion, RDA due to SIF of the shoulder, presenting with severe short-term pain and functional disability, commonly occurred in elderly women with bone fragility. MRI revealed bone marrow edema, extensive joint effusion, and synovitis as well as a diversity of types of head destruction with subchondral fracture within several months from onset of symptoms.
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NR 19
TC 3
Z9 4
U1 0
U2 1
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
SN
EI 2075-4418
J9 DIAGNOSTICS
JI Diagnostics
PD NOV 15
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IS 11
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DI 10.3390/diagnostics10110885
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WC Medicine, General & Internal
SC General & Internal Medicine
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PT J
AU Al-Sowayan, B
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AF Al-Sowayan, Batla
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TI Preparing the Bone Tissue Regeneration Ground by Exosomes: From Diagnosis to Therapy
SO MOLECULES
LA English
DT Review
DE biomaterials; exosomes; bone regeneration
ID mesenchymal stem-cells; promoting osteoblast proliferation; extracellular vesicles; clinical-significance; prognostic biomarker; improve osteoporosis; delivery; osteoarthritis; doxorubicin; myocardium
AB Bone tissue engineering employs acellular scaffolds or scaffolds, along with cells and growth factors, to provide the mechanical support needed, as well as serve as a delivery vehicle for bioactive molecules to the injury sites. As tissue engineering continues to evolve, it has integrated two emerging fields: stem cells and nanotechnology. A paracrine factor that is found to be responsible for the major regenerative effect in stem cell transplantation is an extracellular vesicle called an 'exosome'. Recent advances in nanotechnology have allowed the 'exosome' to be distinguished from other extracellular vesicles and be polymerized into a well-defined concept. Scientists are now investigating exosome uses in clinical applications. For bone-related diseases, exosomes are being explored as biomarkers for different bone pathologies. They are also being explored as a therapeutic agent where progenitor cell-derived exosomes are used to regenerate damaged bone tissue. In addition, exosomes are being tested as immune modulators for bone tissue inflammation, and finally as a delivery vehicle for therapeutic agents. This review discusses recently published literature on the clinical utilization of exosomes in bone-related applications and the correlated advantages. A particular focus will be placed on the potential utilization of regenerative cell-derived exosomes as a natural biomaterial for tissue regeneration.
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NR 90
TC 24
Z9 25
U1 0
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PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 1420-3049
J9 MOLECULES
JI Molecules
PD SEP 15
PY 2020
VL 25
IS 18
BP
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DI 10.3390/molecules25184205
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
GA OD7SA
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AU Yoon, C
Chang, MJ
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Chang, Moon Jong
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TI Bone Mineral Density Around the Knee Joint: Correlation With Central Bone Mineral Density and Associated Factors
SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE Bone mineral density; dual-energy X-ray absorptiometry; osteoarthritis; osteoporosis
ID x-ray absorptiometry; periprosthetic fractures; tibial component; trabecular bone; osteoarthritis; arthroplasty; osteoporosis; quality; femur; hip
AB Introduction: The aims of this study were to (1) assess the bone mineral density (BMD) around the knee joint, (2) determine the correlation between central and knee BMDs, and (3) investigate the factors associated with BMD around the knee joint in patients with knee osteoarthritis (OA). Methodology: This cross-sectional study included 122 patients who underwent total knee arthroplasty. Central and knee dual-energy X-ray absorptiometry was performed preoperatively. BMD at 6 regions of interest (ROIs) around the knee joint were measured, and their correlations with central BMD were determined using Spearman's correlation analysis. Lower limb alignment, severity of OA, body mass index (BMI), preoperative functional and pain scores were assessed to elucidate the factors associated with knee BMD using linear regression analysis. Results: Around the knee joint, BMD was the lowest at the distal femoral metaphysis and lateral tibial condyle. Knee BMD was significantly correlated with central BMD. However, the correlation coefficients varied by the ROI. Additionally, multivariate analysis revealed different associations with respect to the regions around the knee joint. Varus alignment of the lower limb was associated with increased BMD of the medial condyles and decreased

BMD of lateral condyles. High grade OA was a protective factor; it was associated with increased BMD at the lateral condyles of the femur and tibia. Higher BMI was an independent protective factor in all ROIs around the knee joint except the lateral femoral condyles. Lower functional level was not associated with decreased BMD, whereas a higher pain score was significantly associated with lower BMD at the proximal tibial metaphysis. Conclusions: Knee BMD was significantly correlated with central BMD. However, the correlations varied with the regions around the knee joint probably due to their independent association with the alignment of the lower limb, severity of OA, BMI, and preoperative pain level.
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Welch T, 2016, BULL HOSP JT DIS, V74, P287
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PT J
AU Johanna, I
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AF Johanna, Intemann
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TI Importance of osteocyte-mediated regulation of bone remodelling in inflammatory bone disease
SO SWISS MEDICAL WEEKLY
LA English
DT Review
DE osteocytes; inflammation; bone remodelling; musculoskeletal disorders
ID mesenchymal stem-cells; kappa-b ligand; colony-stimulating factor; staphylococcus-aureus; osteoclast differentiation; receptor activator; international-society; endothelial-cells; solute transport; resorption
AB Although the impact of osteoblast-osteoclast crosstalk in bone remodelling has been intensively studied, the importance of osteocytes, descendants of osteoblasts, in this process has for a long time been neglected. During their embedding phase, osteocytes undergo considerable phenotypic transformation, from a cuboidal, highly metabolically active osteoblast secreting extracellular matrix to a small, stellate, quiescent osteocyte with numerous long dendrites. Osteocytes are encysted in cavities (lacunae) and their dendritic extensions are located in tunnels (canaliculi) forming a remarkable, highly branched, lacunar-canalicular signalling network that spans the entire bone matrix. Osteocytes and their dendrites can communicate directly with each other and through the release of effector proteins such as sclerostin and nuclear factor kappa B ligand (RANKL), influence osteoblast and osteoclast formation. This allows osteocytes embedded within the bone matrix to communicate and coordinate activity of cells on the bone surface to adapt to mechanical needs and hormonal changes. Besides their importance in sustaining physiological bone homeostasis, accumulating evidence suggests that

dysregulated osteocyte function and alterations in the osteocyte lacunar-canalicular network structure are characteristics of skeletal diseases. This review highlights some aspects of osteocyte communication with osteoclasts and mesenchymal stromal cells, the importance of blood vessel-osteocyte interaction and describes central functions of these cells in rheumatoid arthritis, osteoarthritis, osteomyelitis and osteoporosis. Within the last decade new technologies and tools have facilitated the study of osteocyte biology and the search for therapeutic targets to address bone fragility in the near future.
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NR 103
TC 24
Z9 31
U1 0
U2 21
PU SMW supporting association
PI Basel
PA Tragerverein Swiss Medical Weekly, Malzgasse 15, Basel, SWITZERLAND
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AU Akhavan, S
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AF Akhavan, Sam
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TI Bone Marrow Edema, Clinical Significance, and Treatment Options: A Review
SO JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
LA English
DT Review
ID differential-diagnosis; transient osteoporosis; core decompression; vitamin-d; knee; lesions; osteoarthritis; osteonecrosis; subchondroplasty; bisphosphonates
AB Bone marrow edema (BME) is a descriptive term used to describe high-signal intensity changes detected on magnetic resonance fluid-sensitive sequences that could be attributed to a number of underlying pathologies. Regardless of the cause, physiologic remodeling of the subchondral bone can be limited because of ongoing joint forces, increased focalization of stress, and reduced healing capacity of the subchondral bone. BME is a known prognostic factor associated with pain, dysfunction, and progressive cartilage damage. This review summarizes the current known causes of BMEs, theories related to histopathological changes, and current treatment options including novel biologic surgical options.
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NR 40
TC 31
Z9 39
U1 0
U2 11
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JI J. Am. Acad. Orthop. Surg.
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SC Orthopedics; Surgery
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PT J
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Xiao, Lianbo
TI Using electroacupuncture to recover muscle strength in patients with knee osteoarthritis after total knee arthroplasty: a study protocol for a double-blinded, randomized, and placebo-controlled trial
SO TRIALS
LA English
DT Article
DE Electroacupuncture; Knee osteoarthritis; Total knee arthroplasty; Study protocol
ID quadriceps strength; gait speed; pain; acupuncture; stimulation; replacement; reliability; predictor; outcm; 4-meter
AB Background: Total knee arthroplasty (TKA) is a gold standard for patients with terminal term gonarthrosis for reducing pain, correcting deformities, and regaining stability. However, post-TKA muscle strength recovery is often difficult. Although electroacupuncture (EA) enhances lower extremity muscle strength of the lower extremity, there is limited evidence regarding its effect on lower extremity muscle strength in post-TKA patients. Consequently, this trial intends to evaluate the efficacy of post-TKA EA on the recovery of lower extremity muscle strength, specifically, during the early post-TKA period. Methods/design: This is a double-blinded, randomized, and controlled trial. It will be conducted between August 2020 and December 2020. Ninety-four participants with KOA who have undergone unilateral TKA will be randomized into a treatment (EA) group and a control (sham EA) group. The former and latter groups will receive EA and sham EA, respectively, at ST37, ST36, SP10, and SP9 acupoints. The participants will undergo ten treatment sessions over 2 weeks (5 sessions per week). The primary outcomes will include changes in muscle strength and the Hospital for Special Surgery score at the second week from baseline (pre-op 1 day or POD 3). The secondary outcomes will include a 4-m walk test, numerical rating scale score, the Hamilton Anxiety Scale score, and additional analgesia use. Additional outcomes will include the incidence of analgesia-related side effects and the participant satisfaction rate. Participant blinding will also be assessed where they will be asked to guess whether they received EA after the latest intervention. Adverse EA events will be documented and assessed throughout the trial. Discussion: EA is helpful for post-TKA recovery and enhancement of lower limb muscle strength.
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NR 43
TC 3
Z9 5
U1 1
U2 26
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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EI 1745-6215
J9 TRIALS
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PG 9
WC Medicine, Research & Experimental
SC Research & Experimental Medicine
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PT J
AU Chen, GJ
Tang, QM
Yu, SL
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AF Chen, Guangjin
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TI The biological function of BMAL1 in skeleton development and disorders
SO LIFE SCIENCES
LA English
DT Review
DE Circadian clock; BMAL1; Bone development; Cartilage development; Dental development; Bone diseases
ID gene; expression; clocks; rhythm
AB BMAL1 is a core component of the circadian clock loop, which directs the sophisticated circadian expression of clock-controlled genes. Skeletal Bone development is a complex biological process involving intramembranous ossification, endochondral ossification and bone remodeling, as well as specific cells, such as mesenchymal cells, osteoblasts, osteoclasts, chondrocytes, etc. Growing evidences suggest that BMAL1 is indispensable for hard tissue development, including bone, cartilage and teeth. Loss of BMAL1 in animals can inhibit bone and cartilage development, and result in abnormal bone mass. In mesenchymal cells, BMAL1 defect inhibits osteoblastic and chondrocytic differentiation. Inactivation of BMAL1 also can promote the differentiation and formation of os-teoclasts and increase bone resorption. Specifically, preclinical data demonstrate that the abnormity of BMAL1 expression is associated with skeletal disorders such as skeletal mandibular hypoplasia, osteoarthritis, osteo- porosis, etc.

In this review, we systemically describe the impact of BMAL1 in skeletal development and home-ostasis, and devote to searching new therapy strategies for bone disorders.
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NR 20
TC 46
Z9 59
U1 2
U2 59
PU PERGAMON-ELSEVIER SCIENCE LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB,

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WC Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Research & Experimental Medicine; Pharmacology & Pharmacy
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PT J
AU Abdelbadie, A
El-Hennawy, A
Sallam, A
AF Abdelbadie, Ahmed
El-Hennawy, Ayman
Sallam, Asser
TI Primary Total knee Arthroplasty: A Viable Surgical Option for Complex Tibial Plateau Fractures in Elderly
SO JOURNAL OF KNEE SURGERY
LA English
DT Article
DE tibial plateau fracture; osteoarthritis; osteoporosis; total knee arthroplasty; total knee replacement; geriatrics
ID internal-fixation; open reduction; complications; replacement; alignment; management; intramedullary; extramedullary; revision; humerus
AB The optimal treatment of complex tibial plateau fractures in elderly is still controversial. The aim of the study was to retrospectively analyze the clinical and radiological outcomes of primary total knee arthroplasty (TKA) versus open reduction and internal fixation (ORIF) in elderly patients presenting with acute complex tibial plateau fractures. Between June 2011 and December 2015, we have analyzed the clinical outcomes of 22 primary total knee replacements and 21 ORIFs. The mean follow-up was 27 months. The intra- and postoperative complications, as

well as the knee society score (KSS), were our outcome measures. The knee range of motion and the KSS knee and function scores were significantly better in the TKA patients compared with ORIF patients. Early postoperative full weight-bearing was allowed in the TKA patients with lower complications rate. In conclusion, primary TKA utilizing a stemmed tibial component is an effective treatment option for elderly patients with a complex acute fracture of the tibial plateau. This is a Type III therapeutic study.
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NR 48
TC 15
Z9 18
U1 0
U2 2
PU GEORG THIEME VERLAG KG

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PA Oswald-Hesse-Strasse 50, D-70469 STUTTGART, GERMANY
SN 1538-8506
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J9 J KNEE SURG
JI J. Knee Surg.
PD MAY 15
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VL 33
IS 5
BP 496
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PG 8
WC Orthopedics
SC Orthopedics
GA LL9FP
UT WOS:000531859000013
PM 30812042
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PT J
AU Baker, BS
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AF Baker, Breanne S.
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TI Does Blood Flow Restriction Therapy in Patients Older Than Age 50 Result in Muscle Hypertrophy, Increased Strength, or Greater Physical Function? A Systematic Review
SO CLINICAL ORTHOPAEDICS AND RELATED RESEARCH
LA English
DT Review
ID intensity resistance exercise; partial vascular occlusion; low-load; hormone responses; growth-hormone; body-composition; reduction; walking; young; risk
AB Background Blood flow restriction (BFR) is a process of using inflatable cuffs to create vascular occlusion within a limb during exercise. The technique can stimulate muscle hypertrophy and improve physical function; however, most of these studies

have enrolled healthy, young men with a focus on athletic performance. Furthermore, much of the information on BFR comes from studies with small samples sizes, limited follow-up time, and varied research designs resulting in greater design, selection, and sampling bias. Despite these limitations, BFR's popularity is increasing as a clinical rehabilitation tool for aging patients. It is important for practitioners to have a clear understanding of the reported effects of BFR specifically in older adults while simultaneously critically evaluating the available literature before deciding to employ the technique. Questions/purposes (1) Does BFR induce skeletal muscle hypertrophy in adults older than 50 years of age? (2) Does BFR improve muscle strength and/or physical function in adults older than 50 years? Methods Using PubMed, Google Scholar, Web of Science, and Science Direct, we conducted a systematic review of articles using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to assess the reported effects of BFR on skeletal muscle in older adults. Included articles enrolled participants 50 years of age or older and used BFR in conjunction with exercise to study the effects of BFR on musculoskeletal outcomes and functionality. The following search terms were used: "blood flow restriction" OR "KAATSU" OR "ischemic training" AND "clinical" AND "elderly." After duplicates were removed, 1574 articles were reviewed for eligibility, and 30 articles were retained with interventions duration ranging from cross-sectional to 16 weeks. Sample sizes ranged from 6 to 56 participants, and exercise tasks included passive mobilization or electrical stimulation; walking; resistance training using machines, free weights, body weight, or elastic bands; and water-based activities. Furthermore, healthy participants and those with cardiovascular disease, osteoarthritis, osteoporosis, sporadic inclusion body myositis, spinal cord injuries, and current coma patients were studied. Lastly, retained articles were assigned a risk of bias score using aspects of the Risk of Bias in Nonrandomized Studies of Interventions and the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials. Results BFR, in combination with a variety of exercises, was found to result in muscle hypertrophy as measured by muscle cross-sectional area, thickness, volume, mass, or circumference. Effect sizes for BFR's ability to induce muscle hypertrophy were calculated for 16 of the 30 papers and averaged 0.75. BFR was also shown to improve muscle strength and functional performance. Effect sizes were calculated for 21 of the 30 papers averaging 1.15. Conclusions Available evidence suggests BFR may demonstrate utility in aiding rehabilitation efforts in adults older than 50 years of age, especially for inducing muscle hypertrophy, combating muscle atrophy, increasing muscle strength, and improving muscle function. However, most studies in this systematic review were at moderate or high risk of bias; that being so, the findings in this systematic review should be confirmed, ideally using greater sample sizes, randomization of participants, and extended follow-up durations.

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TI Re-appraising the potential of naringin for natural, novel orthopedic biotherapies
SO THERAPEUTIC ADVANCES IN MUSCULOSKELETAL DISEASE
LA English
DT Review
DE diabetes mellitus; naringin; osteoarthritis; osteoclastogenesis; osteomyelitis; osteoporosis
ID bone morphogenetic protein-2; glucocorticoid-induced osteoporosis; pi3k/akt signaling pathway; sulfates cs 4-and-6; chondroitin sulfate; glucosamine sulfate; double-blind; osteogenic differentiation; knee osteoarthritis; oxidative stress
AB Naringin is a naturally occurring flavonoid found in plants of the Citrus genus

that has historically been used in traditional Chinese medical regimens for the treatment of osteoporosis. Naringin modulates signaling through numerous molecular pathways critical to musculoskeletal development, cellular differentiation, and inflammation. Administration of naringin increases in vitro expression of bone morphogenetic proteins (BMPs) and activation of the Wnt/beta-catenin and extracellular signal-related kinase (Erk) pathways, thereby promoting osteoblastic proliferation and differentiation from stem cell precursors for bone formation. Naringin also inhibits osteoclastogenesis by both modifying RANK/RANKL interactions and inducing apoptosis in osteoclasts in vitro. In addition, naringin acts on the estrogen receptor in bone to mimic the native bone-preserving effects of estrogen, with few systemic side effects on other estrogen-sensitive tissues. The efficacy of naringin therapy in reducing the osteolysis characteristic of common musculoskeletal pathologies such as osteoporosis, degenerative joint disease, and osteomyelitis, as well as inflammatory conditions affecting bone such as diabetes mellitus, has been extensively demonstrated in vitro and in animal models. Naringin thus represents a naturally abundant, cost-efficient agent whose potential for use in novel musculoskeletal biotherapies warrants re-visiting and further exploration through human studies. Here, we review the cellular mechanisms of action that have been elucidated regarding the action of naringin on bone resident cells and the bone microenvironment, in vivo evidence of naringin's osteostimulative and chondroprotective properties in the setting of osteolytic bone disease, and current limitations in the development of naringin-containing translational therapies for common musculoskeletal conditions.
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TI Subchondral bone deterioration in femoral heads in patients with osteoarthritis secondary to hip dysplasia: A case-control study
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DT Article
DE Bone remodelling; Hip dysplasia; Microarchitecture; Osteoarthritis; Osteoporosis
ID age-related-changes; developmental dysplasia; articular-cartilage; cancellous bone; trabecular bone; radiographic osteoarthritis; phenotypic characterization; natural-history; sclerotic zones; risk-factor
AB Objectives: Residual hip dysplasia is the most common underlying condition leading to secondary osteoarthritis (OA) of the hip. Subchondral bone alterations in OA secondary to hip dysplasia (HD-OA) are poorly investigated. The aim of the present study was to analyse the microarchitecture, bone remodelling and pathological alterations of subchondral bone in femoral heads from patients with

HD-OA. Methods: Subchondral bone specimens were extracted from both weight-bearing and non-weight-bearing regions of femoral heads from 20 patients with HD-OA and 20 patients with osteoporotic femoral neck fracture, during hip replacement surgery. Micro-CT and histological examination were performed to assess the microarchitecture and histopathological changes. Results: The weight-bearing subchondral bone showed significantly more sclerotic microarchitecture and higher bone remodelling level in HD-OA as compared with osteoporosis. In the non-weight-bearing region, the two diseases shared similar microarchitectural characteristics, but higher bone remodelling level was detected in HD-OA. Distinct regional differences were observed in HD-OA, whereas the two regions exhibited similar characteristics in osteoporosis. In addition, HD-OA displayed more serious pathological alterations, including subchondral bone cyst, metaplastic cartilaginous tissue, bone marrow oedema and fibrous tissue, especially in the weight-bearing region. Conclusions: Osteoarthritic deteriorations of subchondral bone induced by hip dysplasia spread throughout the whole joint, but exhibit region-dependent variations, with the weight-bearing region more seriously affected. Biomechanical stress might exert a pivotal impact on subchondral bone homeostasis in hip dysplasia. The translational potential of this article: The histomorphometric findings in the project indicate an early intervention for the development of hip dysplasia in clinic.
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TI Oleanolic acid exerts inhibitory effects on the late stage of osteoclastogenesis and prevents bone loss in osteoprotegerin knockout mice
SO JOURNAL OF CELLULAR BIOCHEMISTRY
LA English
DT Article
DE oleanolic acid; osteoclastogenesis; osteoprotegerin
ID receptor-activator; differentiation; osteoporosis; cells; mechanisms; expression; ligand; gamma
AB Postmenopausal women undergo rapid bone loss, which caused by the accelerated osteoclastic bone resorption. Receptor activator of nuclear factor kappa-B ligand (RANKL) plays critical and essential roles on varied stages of osteoclastogenesis. Oleanolic acid (OA), a naturally derived small compound, has been found suppress osteoclastogenesis in early stage of bone marrow macrophages (BMMs). However, whether OA also regulates the late stage of osteoclastogenesis remains unclear. Here, the regulatory effect of OA on the late stage of osteoclastogenesis was investigated in vitro using RANKL-pretreated BMMs and in vivo using osteoprotegerin (OPG) knockout mice. Our in vitro studies demonstrate that OA inhibits the late stage of osteoclastogenesis from RANKL-pretreated BMMs. For in vivo animal investigation, OA attenuates the bone loss phenotypes in OPG-knockout mice by decreasing the densities of osteoclast, which are in consistent with the finding with in vitro osteoclastogenesis. Mechanistic investigations found that OA largely inhibit the activity of c-Fos and Nuclear factor of activated T-cells c1 (NFATc1) with RANKL-pretreated BMMs and OPG-knockout mice. Furthermore, OA suppresses the activities of osteoclast genes, such as Tartrate resistant acid phosphatase (TRAP), CathepsinK (Ctsk), and Matrix metalloproteinase 9 (MMP9). Taken together these findings, they have not only defined an inhibitory effect of OA in the late stage of osteoclastogenesis but have also gained new molecular mechanisms underlying the process of osteoclast formation.
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TI Health behaviors in major chronic diseases patients: trends and regional variations analysis, 2008-2017, Korea
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LA English
DT Article
DE Chronic disease; Noncommunicable diseases; Health behavior; Smoking cessation; Alcohol drinking; Walking
ID alcohol-consumption; smoking-cessation; risk-factor; life-style; physical-activity; teachable moment; chronic illness; mental-illness; diagnosis; middle
AB BackgroundImproving the health behaviors of those with chronic diseases such as hypertension and diabetes is important for disease management. Few in-depth studies have been conducted in Korea on the health behaviors of chronic disease patients. This study examined the health behaviors of chronic disease patients over time and compared them with those of the general population.MethodsCross-sectional time-series data obtained from the Korea Community Health Survey from 2008 to 2017 were analyzed. Thirteen diseases were included in this analysis, namely, hypertension, diabetes, dyslipidemia, stroke, myocardial infarction, angina, osteoarthritis, osteoporosis, asthma, allergic rhinitis, atopic dermatitis, cataract, and depression. The current smoking rate, drinking rate, and the walking rate, which are leading health behaviors necessary for preventing chronic diseases, were analyzed by disease type. We compared patients' health behaviors with those of the general population and identified regional variations.ResultsAlthough the current overall smoking rate was seemingly declining, the overall monthly drinking and high-risk drinking rates were increasing. In 2017, patients experiencing depression symptoms had a higher smoking rate than did the general population; hypertension and diabetes patients had a higher risk-drinking rate than did the latter. The general population's walking rate was highest. There were considerable variations by region among chronic disease patients.ConclusionsChronic disease patients displayed worse health behaviors than those of the general population, in some instances. Rather than focusing only on chronic disease patients' medication adherence, strategies must be devised to increase their smoking cessation rate, decrease their drinking rate, and increase their walking rate.
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NR 50
TC 25
Z9 30
U1 2
U2 18
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1471-2458
J9 BMC PUBLIC HEALTH
JI BMC Public Health
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IS 1
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DI 10.1186/s12889-020-09940-7
PG 10
WC Public, Environmental & Occupational Health
SC Public, Environmental & Occupational Health
GA PA7VB
UT WOS:000595837100006
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PT J
AU Chung, KM
Ho, CH
Chen, YC
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Wang, JJ
Huang, CC
AF Chung, Kun-Ming
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Hsu, Chien-Chin
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Wang, Jhi-Joung
Huang, Chien-Cheng
TI Chronic Pain Increases the Risk for Major Adverse Cardiac and Cerebrovascular Events: A Nationwide Population-Based Study in Asia
SO PAIN MEDICINE
LA English
DT Article
DE Asian; Cardiac; Cerebrovascular; Chronic Pain; Death; Mortality
ID chronic widespread pain; prevalence; management; mortality; disease; update
AB Objective. Chronic pain (CP) may increase the risk for major adverse cardiac and cerebrovascular events (MACCEs); however, this issue is still unclear in the Asian population. We conducted this study to delineate it. Design. From the Taiwan National Health Insurance Research Database, we identified 17,614 participants (<65 years) with CP and matched them by age and sex at a 1:2 ratio to participants without CP, who made up the comparison cohort. Several causes of CP and its

underlying comorbidities were also analyzed. Outcome Measure. A comparison of MACCE occurring in the two cohorts was performed via follow-up until 2015. Results. The mean age (SD) was 50.2 (11.5) years and 50.4 (11.7) years in participants with and without CP, respectively. In both cohorts, the percentage of female participants was 55.5%. Common causes of CP were spinal disorders (23.9%), osteoarthritis (12.4%), headaches (11.0%), gout (10.2%), malignancy (6.2%), and osteoporosis (4.5%). After adjusting for hypertension, diabetes, chronic obstructive pulmonary disease, renal diseases, hyperlipidemia, liver diseases, dementia, and depression, participants with CP had a higher risk for MACCE than those without CP (adjusted hazard ratio [AHR] = 1.3, 95% confidence interval [CI] = 1.3 - 1.4). After conducting subgroup analyses, an increased risk was also found for all-cause mortality (AHR = 1.4, 95% CI = 1.1 - 1.8), acute myocardial infarction (AHR = 1.2, 95% CI = 1.0 - 1.4), and stroke (AHR = 1.3, 95% CI = 1.3 - 1.4). Conclusions. CP is associated with increased occurrence of MACCE. Early detection and interventions for CP are suggested.
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NR 28
TC 15
Z9 16
U1 0
U2 2
PU OXFORD UNIV PRESS
PI OXFORD
PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
SN 1526-2375
EI 1526-4637
J9 PAIN MED
JI Pain Med.
PD SEP 15
PY 2020

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IS 9
BP 1985
EP 1990
DI 10.1093/pm/pnaa107
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WC Anesthesiology; Medicine, General & Internal
SC Anesthesiology; General & Internal Medicine
GA OW8QM
UT WOS:000593144400020
PM 32377670
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ER

PT J
AU Albrecht, K
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AF Albrecht, K.
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TI Comorbidity and health care utilisation in persons with Sjogren's syndrome: a claims data analysis
SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY
LA English
DT Article
DE Sjogren's syndrome; health services research; epidemiologic studies; comorbidity
ID epidemiology; prevalence; trends
AB Objective. To capture comorbidity and medication of persons with Sjogren's syndrome (SS) in a population-based cohort in comparison to matched controls. Methods. Individuals with an outpatient diagnosis of M35.0 (ICD-10) in >= 2 quarters of a year or an inpatient diagnosis of M35.0 were identified in a German statutory health insurance fund covering 7.2 million people. Persons in rheumatologic care were grouped by incident or prevalent diagnosis and by co-existing autoimmune disease (sSS) or primary (p)SS and compared to age- and

sex-matched controls regarding comorbidity (ICD-10), medical prescriptions, hospitalisation and inability to work in the previous year. Results. In 2018, 7,283 persons (0.10%) had incident and 54,273 persons (0.75%) prevalent SS diagnosis, and 5,961 (11%) were in rheumatologic care. Of these (90% female, mean age 66 years), 3,457 (58%) had further autoimmune disease (sSS), mostly rheumatoid arthritis (80%) and systemic lupus erythematosus (13%). Compared to controls, frequent comorbid conditions in SS were hypertension (controls: 52%, pSS: 55%, sSS: 63%), osteoarthritis (22%/40%/47%), osteoporosis (10%/26%/38%) and depression (21%/34%/36%). Systemic antirheumatic drugs were prescribed in 31% (pSS) and 66% (sSS) while <5% received topical therapies. Glucocorticoids (8%/34%/59%), NSAIDs (28%/41%/45%), opioids (8%/15%/21%), analgesics (19%/30%/36%) and antidepressants (14%/21%/21%) were frequently prescribed. Compared to controls, hospitalisation (21%/32%/39%) and inability to work in persons <65 years (41%/48%/44%, median days 17/24/30) were more frequent in pSS and sSS than in controls. Conclusion. SS claims diagnosis is associated with substantial comorbidity and frequent prescription of antiinflammatory drugs, analgesics and antidepressants. The individual and societal burden of SS shows that, in addition to effective treatment strategies, intensive attention to comorbidities is important in this disease.
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NR 20
TC 3
Z9 3
U1 0
U2 1
PU CLINICAL & EXPER RHEUMATOLOGY
PI PISA
PA VIA SANTA MARIA 31, 56126 PISA, ITALY
SN 0392-856X
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J9 CLIN EXP RHEUMATOL
JI Clin. Exp. Rheumatol.
PD JUN 15
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VL 38
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BP S78
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DI
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WC Rheumatology
SC Rheumatology
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ER

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AU Sobti, AS
Baryeh, KW
Woolf, R
Chana, R
AF Sobti, Anshul S.
Baryeh, Kwaku W.
Woolf, Rex
Chana, Rishi
TI Autologous matrix-induced chondrogenesis and bone marrow aspirate concentrate compared with microfracture for arthroscopic treatment of femoroacetabular impingement and chondral lesions of the hip: bridging the osteoarthritis gap and facilitating enhanced recovery
SO JOURNAL OF HIP PRESERVATION SURGERY
LA English
DT Article
ID articular-cartilage; defects
AB In an attempt to bridge the osteoarthritis (OA) gap, this study compared biological reconstruction with traditional microfracture (MF) techniques in patients with femoroacetabular impingement and focal cartilage defects. Cohorts of two groups were investigated; age, gender and Tonnis grade matched comparison for outcomes between MF and newer biological reconstruction techniques hip arthroscopy surgery using autologous matrix-induced chondrogenesis and bone marrow aspirate combination. Outcomes investigated were pre-op and post-op mean iHOT-12 scores up to 18 months after surgery with a Kaplan-Meier survivorship analysis. Of 111 patients, 46 patients underwent MF and 65 biological reconstruction hip arthroscopy including cam/pincer osteoplasty and labral repair surgery. Age range was 20-69, mean age 45 years for both groups, Tonnis grading was as follows: Grade 0: 26% versus 30%, Grade 1: 52% versus 47% and Grade 2: 22% versus 23% in MF and biological reconstruction groups, respectively. The mean post-operative iHOT-12 score differences between MF and biological reconstruction were significant at 1-year minimum follow-up (P = 0.01, SD 2.8). Biological reconstruction allowed for an enhanced recovery protocol. The MF group had a 67.4% survivorship for conversion to hip replacement at 18 months (32.6% failure rate for any reason) and biological reconstruction had 100% survivorship at 18 months post-operatively with no failures for any reason. This study provides further support to the evidence base for biological reconstructive techniques as superior to MF in combination with joint preservation arthroscopic surgery, even in the face of focal cartilage defects and offers both surgeons and patients a potential bridging of the OA gap.
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NR 28
TC 11
Z9 12

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PU OXFORD UNIV PRESS
PI OXFORD
PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
SN 2054-8397
EI
J9 J HIP PRESERV SURG
JI J. Hip Preserv. Surg.
PD AUG 15
PY 2020
VL 7
IS 3
BP 503
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DI 10.1093/jhps/hnaa047
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WC Orthopedics
SC Orthopedics
GA TX9BO
UT WOS:000683380500016
PM 33948205
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PT J
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Amling, M.
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TI Skeletal deterioration in COL2A1-related spondyloepiphyseal dysplasia occurs prior to osteoarthritis
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Skeletal dysplasia; Early-onset osteoarthritis; Osteoporosis; Bone turnover; Mouse model
ID high bone mass; col2a1 gene; distal radius; mutation; microstructure; variants; family; growth; mice
AB Objective: Spondyloepiphyseal dysplasia, a combination of progressive arthropathy with variable signs of skeletal dysplasia, can be a result of mutations in the collagen, type II, alpha 1 (COL2A1) gene. However, the bone involvement (e.g., density, microstructure) in this disorder has hitherto not been studied. Design: A 50-year-old female patient and her 8-year-old son with flattening of vertebral bodies and early-onset osteoarthritis were genetically tested using a custom designed gene bone panel including 386 genes. Bone microstructure and turnover were assessed using high-resolution peripheral quantitative computed tomography (HR-pQCT) and serum bone turnover markers, respectively. Furthermore, the bone and cartilage phenotype of male mice heterozygous for the loss-of-function mutation of Col2a1 (Col2a1(+/)(d)) was analyzed compared to wildtype littermates using mu-CT and histomorphometry. Results: We identified a dominant COL2A1 mutation (c.620G > A p.(Gly207Glu)) indicating spondyloepiphyseal dysplasia in the female patient and her son, both being severely affected by skeletal deterioration. Although there was no osteoarthritis detectable at first visit, the son was affected by trabecular osteopenia, which progressed over time. In an iliac crest biopsy obtained from the mother, osteoclast indices were remarkably increased. Col2a1(+/d) mice developed a moderate skeletal phenotype expressed by reduced cortical and trabecular parameters at 4 weeks. Importantly, no articular defects could be observed in the knee joints at 4 weeks, while osteoarthritis was only detectable in 12-week-old mice. Conclusions: Our results indicate that collagen type II deficiency in spondyloepiphyseal dysplasia leads to skeletal deterioration with early-onset in humans and mice that occurs prior to the development of osteoarthritis. (C) 2020 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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NR 41
TC 21
Z9 23
U1 0
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PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
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AU Chu, LY
Liu, XQ
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AF Chu, Linyang
Liu, Xuqiang
He, Zihao
Han, Xuequan
Yan, Mengning
Qu, Xinhua
Li, Xiaofeng
Yu, Zhifeng
TI Articular Cartilage Degradation and Aberrant Subchondral Bone Remodeling in Patients with Osteoarthritis and Osteoporosis
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE BIOMECHANICAL PROPERTIES; BONE REMODELING; CARTILAGE DAMAGE; OSTEOPOROTIC OSTEOARTHRITIS; SUBCHONDRAL MICROSTRUCTURE
ID knee osteoarthritis; bisphosphonate use; trabecular bone; femoral-head; risk; microarchitecture; ovariectomy; progression; inhibition; resorption
AB Osteoarthritis (OA) and osteoporosis (OP) are two skeletal disorders associated with joint structures. Occasionally, OA and OP occur in the same patient. However, the effect of OP changes on OA progression in patients with osteoporotic OA (OP-OA) has not been reported, especially the potential association between subchondral bone and articular cartilage. Thus we investigated the alterations in the microstructure, biomechanical properties, and remodeling of subchondral bone

as well as their association with cartilage damage in the hip joint of patients with OP-OA. Thirty-nine femoral head specimens were obtained from patients who underwent total hip arthroplasty (OA group, n=19; OP-OA group, n=20), and healthy specimens from cadaver donors were used (control group, n=10). The microstructure and biomechanical properties of subchondral bone were evaluated by micro-computed tomography and micro-finite-element analysis. Histology, histomorphometric measurements, and immunohistochemistry were used to assess subchondral bone remodeling and cartilage damage. Linear regression analysis was performed to elucidate the relationship between subchondral bone and articular cartilage. In the subchondral bone of the OP-OA group, compared with that of the OA group, aberrant bone remodeling leads to an inferior microstructure and worsening biomechanical properties, potentially affecting transmission of loading stress from the cartilage to the subchondral bone, and then resulting in accelerated OA progression in patients with OP-OA. The results indicate that changes in subchondral bone could affect OA development and the improvement in subchondral bone with bone-metabolism agents may help mitigate OA progression when OP and OA coexist in the same patients. (c) 2019 American Society for Bone and Mineral Research.
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PU OXFORD UNIV PRESS
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PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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AU Zhang, YP
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Han, Mei
Lai, Bao-Yong
Liang, Shi-Bing
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TI Evidence Base of Clinical Studies on Qi Gong: A Bibliometric Analysis
SO COMPLEMENTARY THERAPIES IN MEDICINE
LA English
DT Article
DE Qigong; Ba Duan Jin; Bibliometric Analysis; Clinical Study; Non-drug therapy
ID quality-of-life; qigong; individuals; exercises; disease; adults; impact
AB Objective: This bibliometric study aimed to systematically and comprehensively summarize the volume, breadth and evidence for clinical research on Qigong. And this bibliometric analysis also can provide the evidence of this field. Design: Bibliometric analysis. Methods: All types of primary and secondary studies on humans were included: systematic reviews, randomized clinical trials, non-randomized controlled clinical studies, case series and case reports. Chinese Biomedical Literature Database, China National Knowledge Infrastructure, Chinese Scientific Journal Database, Chinese Academic Conference Papers Database and Chinese Dissertation Database, PubMed and the Cochrane Library were searched from the date of inception to December 10, 2018. Bibliometric information, such as publication information, disease/condition, Qigong intervention and research

results were extracted and analyzed. Results: A total of 886 clinical studies were identified: including 47 systematic reviews, 705 randomized clinical trials, 116 non-randomized controlled clinical studies, 12 case series and 6 case reports. The studies were conducted in 14 countries. The top 15 diseases/conditions studied were: diabetes, chronic obstructive pulmonary disease, hypertension, stroke, cervical spondylosis, lumbar disc herniation, insomnia, knee osteoarthritis, low back pain, and osteoporosis, Coronary heart disease, breast cancer, periarthritis of shoulder, depression, metabolic syndrome. Of the various Qigong exercises reported in these 886 clinical studies, Ba Duan Jin was the most frequently researched in 492 (55.5%) studies, followed by Health Qigong 107 (12.1%), Dao Yin Shu 85 (9.6%), Wu Qin Xi 67 (7.6%) and Yi Jin Jing 66 (7.4%). The most frequently used comparisons in randomized trials were maintaining normal way of life unchanged 149 (18.1%), the remaining controls included conventional treatment, mainly western medicine, Chinese herbal medicine, acupuncture, health education, psychological therapy, Yoga, Tai Chi and other non-drug therapy. The most frequently reported outcomes were physical function, quality of life, symptoms, pain and mental health indicators. Beneficial results from practicing Qigong were reported in 97% of studies. Conclusions: Qigong research publications have been increasing gradually. Reports on study types, participants, Qigong Intervention, and outcomes are diverse and inconsistent. There is an urgent need to develop a set of reporting standards for various interventions of Qigong. Further trials of high methodological quality with sufficient sample size and real world studies are needed to verify the effects of Qigong in health and disease management.
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NR 33
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U1 17
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PU CHURCHILL LIVINGSTONE
PI EDINBURGH
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Lee, Kang Min
Lee, Seung Woong
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TI Beneficial effects of Vigna angularis extract in osteoporosis and osteoarthritis
SO FOOD SCIENCE & NUTRITION
LA English
DT Article
DE monosodium iodoacetate; osteoarthritis; osteoporosis; ovariectomy; Vigna angularis
ID rankl; inflammation; stat3; model
AB In Asia,Vigna angularis(azuki bean) has been used as a traditional medicine to treat various diseases because of its biological properties. Osteoarthritis (OA) and osteoporosis (OP) are common regenerative bone diseases that are characterized by deterioration of joint and bone structure. In this study, we evaluated the effects ofVigna angularisextract (VAE) on monosodium iodoacetate (MIA)-induced OA and ovariectomy (OVX)-induced OP models. In the MIA-induced OA results, severe OA was alleviated by the administration of VAE. Extensive local damage in the cartilage and hemorrhagic and edematous of surrounding tissues were decreased by VAE treatment. Articular cartilage was almost intact except for a focal mild abrasion, and the surface was glistening, similar to that of the normal joint. In the OVX-induced OP results, bone mineral content (BMC) and bone mineral density (BMD) were recovered by VAE treatment, and it improved the microstructures of bone. These results show that VAE could inhibit OA and OP symptoms.
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NR 31
TC 6
Z9 6
U1 1
U2 6
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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EI
J9 FOOD SCI NUTR
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ER

PT J
AU Karachalios, TS
Koutalos, AA
Komnos, GA
AF Karachalios, Theofilos S.
Koutalos, Antonios A.
Komnos, George A.
TI Total hip arthroplasty in patients with osteoporosis
SO HIP INTERNATIONAL
LA English

DT Review
DE Bone implant interface; osteoporosis; osteoporosis medication; total hip arthroplasty
ID bone-mineral density; (d,l-lactide)-coating increases fixation; local-delivery; femoral stems; periprosthetic fracture; joint arthroplasty; follow-up; bisphosphonate; implants; alendronate
AB There is a high prevalence of osteoporosis in patients undergoing total hip arthroplasty. There are several clinically relevant questions related to the management of such cases: the effect of ageing; the initial osseointegration of implants, especially when cementless THA is used; the effect of medical osteoporosis treatment on bone-implant interface; the incidence of intraoperative and late periprosthetic fractures, and the long-term survival of both cemented and cementless total hip arthroplasty performed for proximal femoral fractures and hip osteoarthritis. A critical review of the literature is presented in an attempt to draw practical conclusions.
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Z9 47
U1 0
U2 17
PU SAGE PUBLICATIONS LTD
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PA 1 OLIVERS YARD, 55 CITY ROAD, LONDON EC1Y 1SP, ENGLAND
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WC Orthopedics
SC Orthopedics
GA MB0SG
UT WOS:000495273500001
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PT J
AU Dincel, YM
Sari, A
Tekin, C
Gunaydin, B
Cetin, MU
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AF Dincel, Yasar Mahsut
Sari, Abdulkadir
Tekin, Cagatay
Gunaydin, Burak
Cetin, Mehmet Umit
Arslan, Yunus Ziya
TI CHANGES IN BONE MINERAL DENSITY AFTER TOTAL KNEE ARTHROPLASTY
SO ACTA ORTOPEDICA BRASILEIRA

LA English
DT Article
DE Bone Density; X-Rays; Absorptiometry; Photon; Osteoarthritis; Knee; Osteoporosis; Arthroplasty; Replacement; Knee
ID proximal femur; follow-up; hip; component; fracture; women; men
AB Objective: We aimed to investigate the change in bone mineral density (BMD) in the first postoperative year in patients that underwent total knee arthroplasty (TKA) due to primary osteoarthritis of the knee. Methods: Preoperative and first postoperative year dual-energy X-ray absorptiometry measurements of 76 patients with knee osteoarthritis, who undergone surgery between 2016 and 2018 due to the recommendation for TKA, were statistically evaluated in the study. Results: Of the 19 patients with a normal BMD in the preoperative period, 73.7% (n = 14) continued to have a normal BMD in the postoperative period. Of the 34 patients with a low BMD (osteopenia) in the preoperative period, 91.2% (n = 31) did not show any change, whereas osteoporosis was observed in two patients (5.9%) in the postoperative period. Of the 23 patients with osteoporosis in the preoperative period, 95.7% (n = 22) did not show any change, whereas osteopenia was observed in one patient (4.3%) in the postoperative period. Both the T and Z scores of the spine (L1-L4) and proximal femur showed a slightly positive trend, however, with an insignificant statistical difference (p >= 0.05). Conclusion: Patients that underwent TKA experienced a statistically insignificant bone gain at the spine and proximal femur twelve months after the surgery.
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NR 20
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Z9 5
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PU ATHA COMUNICACAO & EDITORA
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PA RUA MACHADO BITTENCOURT, 190-40 ANDAR, CONJ 410, SAO PAULO SP, 00000, BRAZIL
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PT J
AU Vestergaard, V
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Schroder, HM
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Pedersen, Alma Becic
Tengberg, Peter Toft
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Schroder, Henrik Morville
TI 20-year trends of distal femoral, patellar, and proximal tibial fractures: a Danish nationwide cohort study of 60,823 patients
SO ACTA ORTHOPAEDICA
LA English
DT Article
ID epidemiology; prevalence
AB Background and purpose - Knee fracture treatment burden remains unknown, impeding proper use of hospital resources. We examined 20-year trends in incidence rates (IRs) and patient-, fracture-, and treatment-related characteristics of knee fracture patients. Patients and methods - This nationwide cohort study of prospectively collected data including patients with distal femoral, patellar, and proximal tibial fractures from the Danish National Patient Registry during 1998-2017, assesses IRs of knee fractures (per 10(5) inhabitants) as well as patient-, fracture-, and treatment-related characteristics of knee fracture patients. Results - During 1998-2017, 60,823 patients (median age 55; 57% female) sustained 74,106 knee fractures. 74% of the study population had a Charlson Comorbidity Index (CCI) of 0 and 18% a CCI of >= 2. 51% were proximal tibial fractures, 31% patellar fractures, and 18% distal femoral fractures. At the time of knee fracture, 20% patients had concomitant near-knee fractures (femur/tibia/fibula shaft/hip/ankle), 13% concomitant fractures (pelvic/spine/thorax/upper extremities), 5% osteoporosis, and 4% primary knee osteoarthritis. Over 1/3 knee fractures were surgically treated and of these 86% were open-reduction internal fixations, 9% external fixations, and 5% knee arthroplasties. The most common surgery type was proximal tibia plating (n = 4,868; 60% female). Knee fracture IR increased 12% to 70, females aged > 51 had the highest knee fracture IR, proximal tibial fracture had the highest knee fracture type IR (32) and surgically treated knee fracture IR increased 35% to 23. Interpretation - Knee fracture IRs, especially of surgically treated knee fractures, are increasing and proximal tibial fracture has the highest knee fracture type IR. Females aged > 51 and patients with comorbidity are associated with knee fracture, proximal tibial fracture, proximal tibial fracture surgery, and posttraumatic knee arthroplasty.
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PT J
AU Myszka, A
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TI Relationships between osteoarthritic changes (osteophytes, porosity, eburnation) based on historical skeletal material
SO ANNALS OF HUMAN BIOLOGY
LA English
DT Article
DE Osteophytes; porosity; eburnation; skeletal populations
ID knee osteoarthritis; subchondral bone; posttraumatic osteoarthritis; marginal osteophytes; older-adults; cartilage; age; pathogenesis; disease; obesity
AB Background: Three main diagnostic types of osteoarthritic changes are

distinguished in clinical and anthropological literature: osteophytes, porosity, and eburnation. The nature of the relationship between these changes and how lesions progress over time is still unclear. Aim: The aim of the present study is the analysis of the relationships between osteophytes, porosity, and eburnation based on skeletal material. Subjects and methods: The analysis employed the skeletal collection from Cedynia (199 individuals) from tenth to fourteenth-century Poland. Marginal osteophytes (OP), porosity (POR), and eburnation (EB) were examined on a shoulder, elbow, wrist, hip, knee, and ankle. Results: Osteophytes and porosity occurred independently of each other. Combinations of osteophytes and porosity (OP + POR) and osteophytes, porosity, and eburnation (OP + POR + EB) were rarely observed. Combinations of osteophytes and eburnation (OP + EB) or porosity and eburnation (POR + EB) were not found. There was a significant correlation between osteophytes and porosity in the scapula, proximal end of the ulna and proximal end of the femur. Osteophytes and eburnation were correlated at the distal end of the ulna. Porosity and eburnation were correlated at the distal end of the radius and distal end of the ulna. When all joints were considered together, all the types of osteoarthritic changes were correlated. However, the relationship between osteophytes and eburnation and between porosity and eburnation was only slightly significant. Osteophytes preceded porosity, but there were a few cases where more developed porosity accompanied less developed osteophytes. Conclusions: The findings indicate that correlations between osteoarthritic changes are weak, albeit statistically significant and further studies of the relationship between changes are necessary.
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TI Traditional uses, processing methods, phytochemistry, pharmacology and quality control of Dipsacus asper Wall. ex CB Clarke: A review
SO JOURNAL OF ETHNOPHARMACOLOGY
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DT Review

DE Dipsacus asper Wall. ex CB Clarke; Triterpenoid; Iridoid; Bone disease
ID akebia-saponin-d; uhplc-ms/ms quantification; asperosaponin vi; cognitive deficits; induced apoptosis; roots; differentiation; constituents; radix; rats
AB Ethnopharmacological relevance: Dipsacus asper Wall. ex C.B. Clarke, a traditional Chinese herbal medicine, has long been used in China for the therapy of bone diseases (e.g. bone fracture, osteoporosis, rheumatic arthritis), traumatic hematoma, uterine bleeding and those caused by the deficiency of liver and kidney. Aim of the study: This work aims to evaluate current research progress on chemical constituents, pharmacological activities, quality control, and pharmacokinetic of Dipsacus asper Wall. ex C.B. Clarke, pinpoint the shortcomings of existing studies, and provide meaningful guidelines for our future investigations. Methods: Extensive database retrieval, such as PubMed, SciFinder and CNKI, was carried out by using keywords such as "Dipsacus asper", "Radix Dipsaci", and "Xuduan". Furthermore, relevant textbooks, patents, reviews, and digital documents were consulted to collate all available scientific literature and to provide a complete science-based survey of the topic. Results: More than 100 compounds have been isolated and identified from Dipsacus asper Wall. ex C.B. Clarke, a substantial proportion of which were reported to be triterpenoids and iridoids. Biological effects such as protective effects against bone fracture, anti-osteoporosis, neuroprotective, cardioprotective, anti-aging and protection of reproductive system activities were also evaluated in vitro and in vivo. Conclusions: Diaphoretic processing resulted in the drop in the content of asperosaponin VI, which was highly associated with bone protective effect of DA. Therefore, diaphoretic processing was not a suitable processing method for DA. Although Dipsacus asper Wall. ex C.B. Clarke was traditionally used for therapy of osteoarthritis, the in-depth study of the underlying mechanism was very rare. Much endeavor had been made on the effect of DA on bone fracture. Notably, high-dose of Dipsacus asper administration may cause adverse impacts in maternal healthy and embryo-fetal development. It's not suitable for further development in those bioactivities, such as anti-inflammatory and free radical scavenging, which are shared in many other plant species. Pharmacological effects of individual component of DA is not equivalent to its traditional usage. Attention should be paid to the traditional effect of extract of DA.
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TI Cartilage and subchondral bone distributions of the distal radius: a 3-dimensional analysis using cadavers
SO OSTEOARTHRITIS AND CARTILAGE
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DT Article
DE Cartilage; Computed tomography (CT); Distal radius; Fracture; Laser scanner; Subchondral bone
ID articular-cartilage; predicting osteoporosis; computed-tomography; thickness; joint; fractures; patterns; surface; weight; osteoabsorptiometry
AB Objective: To quantify the spatial distributions of cartilage and subchondral bone thickness of the distal radius. Design: Using 17 cadaveric wrists, three types of 3-dimensional models were created: a cartilage-bone model, obtained by laser scanning; a bone model, rescanned after dissolving the cartilage; and a subchondral bone model, obtained using computed tomography. By superimposing the bone model onto the cartilage bone and the subchondral bone models, the cartilage and subchondral bone thickness were determined. Measurements along with the spatial distribution were made at fixed anatomic points including the scaphoid and lunate fossa, sigmoid notch and interfossal ridge, and compared at each of these four regions. Results: Cartilage thickness of the interfossal ridge (0.89 +/- 0.23 mm) had a larger average thickness compared to that of the scaphoid fossa (0.70 +/- 0.18 mm; p = 0.004), lunate fossa (0.75 +/-

0.17 mm; p = 0.044) and sigmoid notch (0.64 +/- 0.13 mm; p < 0.001). Subchondral bone was found to be thickest at the scaphoid (2.18 +/- 0.72 mm) and lunate fossae (1.94 +/- 0.93 mm), which were both thicker than that of sigmoid notch (1.63 +/- 1.06 mm: vs scaphoid fossa, p = 0.020) or interfossal ridge (1.54 +/- 0.84 mm: vs scaphoid fossa, p = 0.004; vs lunate fossa, p = 0.048). In the volar-ulnar sub-regions of the scaphoid and lunate fossa, the subchondral bone thickened. Conclusions: Our data can be applied when treating distal radius fractures. Cartilage thickness was less than 1 mm across the articular surface, which may give an insight into threshold for an acceptable range of step-offs. The combined findings of subchondral bone appreciate the importance of the volar-ulnar corner of the distal radius in the volar locking plate fixation. (c) 2020 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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NR 46
TC 6
Z9 6
U1 0
U2 1
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
EI 1522-9653
J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
PD DEC 15
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VL 28
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WC Orthopedics; Rheumatology
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PT J
AU Martins, A
Lazarus, P
Facca, S
Gouzou, S
Meyer, N
Liverneaux, P
AF Martins, Antoine
Lazarus, Priscille
Facca, Sybille
Gouzou, Stephanie
Meyer, Nicolas
Liverneaux, Philippe
TI Isoelastic resurfacing prosthesis for distal radius fractures: Outcomes in 24 cases with at least 2 years' follow-up
SO ORTHOPAEDICS & TRAUMATOLOGY-SURGERY & RESEARCH
LA English
DT Article
DE Unicompartmental isoelastic resurfacing prosthesis; Distal radius fracture; Hemi-prosthesis; Osteoporosis; Elderly; Wrist prosthesis
ID hemiarthroplasty
AB Background: Unicompartmental resurfacing prostheses have been reported to be useful for treating comminuted fractures involving the distal radial joint surface in elderly patients with osteoporosis. However, the data on this method remain scarce and further evaluations are needed. The objective of this study was to evaluate the clinical and radiological outcomes after unicompartmental resurfacing prosthesis implantation in patients with distal radius fractures and at least 2 years' follow-up. Hypothesis: Outcomes with Prosthelast (R) are as good in the mid-term as in the short term. Materials and methods: We studied 24 patients with type C fractures in the AO classification. The Prosthelast (R) prosthesis was implanted in each. Mean age was 78 years (60 to 91). There were 22 females. Three of the fractures were open. The patients were evaluated clinically using a visual analogue scale (VAS) for pain, ranges of motion at the wrist, and grip strength. In addition, functional scores were determined, and radiographs obtained. Results: Mean follow-up was 55.2 months (24-97). Mean tourniquet time was 61.9 minutes (37-126). Mean motion ranges were 39 degrees in flexion, 49 degrees in extension, 74 degrees in pronation, and 68 degrees in supination. The mean VAS pain score was 2.1 (0-7). The mean Quick DASH was 39.8 (9.09-77), the mean PRWE was 42.7 (5-95), and mean grip strength was 38 (25-150). Painful motion limitation of the elbow was noted in a patient treated with total elbow prosthesis. Complex regional

pain syndrome developed in 6 patients, and 5 patients required revision surgery. Asymptomatic perforation of the radial head occurred in 8 patients. No cases of peri-prosthetic osteolysis or osteoarthritis were noted. The prosthesis impinged on the lunate bone in 2 patients and on the scaphoid bone in one patient. Mean ulnar variance was +0.17 mm (-1 to 7.5). Bone remodelling about the prosthesis was noted in all the patients, but 2. Discussion: Our data obtained after a mean follow-up of 55 months indicate that resurfacing prostheses have a role to play in the treatment of comminuted articular fractures in patients with osteoporosis. A long-term study is needed to further evaluate these results. (C) 2020 Elsevier Masson SAS. All rights reserved.
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NR 24
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PT J
AU Zhang, JZ
Zhao, K
Li, JY
Zhu, YB
Zhang, YZ
AF Zhang, Jun-Zhe
Zhao, Kuo
Li, Jun-Yong
Zhu, Yan-Bin
Zhang, Ying-Ze
TI Age-related dynamic deformation of the femoral shaft and associated osteoporotic factors: a retrospective study in Chinese adults
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Ageing; Radiograph; Dynamic deformation; Osteoporosis; Femoral bowing angle (FBA); Femoral cortical index (FCI)
ID cortical bone; hip-fractures; alignment; osteoarthritis; morphology; tissue; knees; plane; femur
AB Dynamic skeletal deformation with ageing showed important signs of degenerative and osteoporotic diseases. We found that both femoral bowing and cortical thickness were correlated with ageing in a Chinese population. Further, femoral cortical index, an osteoporotic indicator, was negatively correlated with femoral bowing angle. Hence, more attention should be paid to these femoral morphological changes to avoid fragility fractures and failed internal fixation. Purpose The purpose of this study was to determine whether morphological parameters of the femoral shaft are in age-related deformation and identify correlations between parameters of femoral cortical thickness and femoral shaft bowing. Methods One hundred twenty patients (mean 50 years, range 18 similar to 104 years) who had received standard long-standing anteroposterior and femoral lateral radiographs from October 2016 to October 2019 were included in this retrospective study. The sagittal femoral bowing angle (sFBA), sagittal femoral cortical index (sFCI), coronal femoral bowing angle (cFBA), and coronal femoral cortical index (cFCI) were measured by two orthopaedists separately. All the participants' demographic data, including age, sex, body laterality, height, and weight, were collected. The Student'sttest, Mann-WhitneyUtest, two-way ANOVA, Pearson correlation, and multiple linear regression were used in the statistical analysis. Results The mean age of the male and female participants was 46.95 +/- 15.25 and 52.22 +/- 15.61 years, respectively. Two-way ANOVA revealed that females had a significantly lower sFCI than males at the right side ($P < 0.05$). There were no significant interactions between sex or body laterality and the sFBA, cFBA, sFCI, and cFCI groups ($P > 0.05$). Pearson correlation revealed that sFCI was

strongly correlated with sFBA (r = - 0.535,P < 0.05) and cFBA (r = - 0.535,P < 0.05). Multiple linear regression analysis demonstrated that both age (beta = 0.304 and 0.308 respectively) and sFCI (beta = - 0.322 and - 0.414 respectively) were two independent predictors associated with sFBA and cFBA respectively. Conclusions The femoral shaft bowing of the Chinese population was positively correlated with ageing, whereas the sagittal femoral cortical thickness negatively correlated with ageing. A high FBA occurred in femoral shafts with a low sFCI, which revealed that femoral shaft bowing was associated with femoral cortical thickness. During femur-related surgery in older patients, more attention should be paid to these femoral morphological changes.
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FU Non-profit Central Research Institute Fund of the Chinese Academy of Medical Sciences [2019PT320001]
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NR 32
TC 6
Z9 7
U1 0
U2 8
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 1862-3522
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J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
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WC Endocrinology & Metabolism; Orthopedics

SC Endocrinology & Metabolism; Orthopedics
GA OB6MH
UT WOS:000578582500002
PM 33026533
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PT J
AU Li, DJ
Yang, CF
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Zhao, F
Chen, ZH
Tian, Y
Dang, K
Jiang, SF
Zhang, WJ
Zhang, G
Qian, AR
AF Li, Dijie
Yang, Chaofei
Yin, Chong
Zhao, Fan
Chen, Zhihao
Tian, Ye
Dang, Kai
Jiang, Shanfeng
Zhang, Wenjuan
Zhang, Ge
Qian, Airong
TI LncRNA, Important Player in Bone Development and Disease
SO ENDOCRINE METABOLIC & IMMUNE DISORDERS-DRUG TARGETS
LA English
DT Review
DE Long noncoding RNA (lncRNA); bone; osteoblast; osteoclast; chondrocyte; osteosarcoma; osteoporosis; osteoarthritis
ID long noncoding rna; mesenchymal stem-cells; extracellular-matrix degradation; promotes osteogenic differentiation; natural antisense transcripts; osteosarcoma cells; up-regulation; osteoblast differentiation; inhibits apoptosis; chondrogenic differentiation
AB Background: Bone is an important tissue and its normal function requires tight coordination of transcriptional networks and signaling pathways, and many of these networks/pathways are dys-regulated in pathological conditions affecting cartilage and bones. Long non-coding RNA (lncRNA) refers to a class of RNAs with

a length of more than 200 nucleotides, lack of protein-coding potential, and exhibiting a wide range of biological functions. Although studies on lcnRNAs are still in their infancy, they have emerged as critical players in bone biology and hone diseases, The functions and exact mechanism of bone-related lncRNAs have not been fully classified yet. Objective: The objective of this article is to summarize the current literature on IncRNAs on the basis of their role in bone biology and diseases, focusing on their emerging molecular mechanism, pathological implications and therapeutic potential. Discussion: A number of IncRNAs have been identified and shown to play important roles in multiple bone cells and bone disease. The function and mechanism of bone-related IncRNA remain to be elucidated. Conclusion: At present, majority of knowledge is limited to cellular levels and less is known on how IncRNAs could potentially control the development and homeostasis of bone. In the present review, we highlight some IncRNAs in the field of bone biology and bone disease. We also delineate some IncRNAs that might have deep impacts on understanding bone diseases and providing new therapeutic strategies to treat these diseases.
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TI Adverse Impact of Heavy Metals on Bone Cells and Bone Metabolism Dependently and Independently through Anemia
SO ADVANCED SCIENCE
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DT Review
DE heavy metals; degenerative bone diseases; anemia; adverse outcome pathways; mode of actions
ID regulated eif2-alpha kinase; iron-deficiency anemia; itai-itai disease; cadmium exposure; mineral density; low-level; intervertebral disc; molecular-mechanisms; protective role; trace-elements
AB Mounting evidence is revealing that heavy metals can incur disordered bone homeostasis, leading to the development of degenerative bone diseases, including osteoporosis, osteoarthritis, degenerative disk disease, and osteomalacia. Meanwhile, heavy metal-induced anemia has been found to be intertwined with degenerative bone diseases. However, the relationship and interplay among these adverse outcomes remain elusive. Thus, it is of importance to shed light on the modes of action (MOAs) and adverse outcome pathways (AOPs) responsible for degenerative bone diseases and anemia under exposure to heavy metals. In the current Review, the epidemiological and experimental findings are recapitulated to interrogate the contributions of heavy metals to degenerative bone disease development which may be attributable dependently and independently to anemia. A few likely mechanisms are postulated for anemia-independent degenerative bone diseases, including dysregulated osteogenesis and osteoblastogenesis, imbalanced bone formation and resorption, and disturbed homeostasis of essential trace elements. By contrast, remodeled bone microarchitecture, inhibited erythropoietin production, and disordered iron homeostasis are speculated to account for anemia-associated degenerative bone disorders upon heavy metal exposure. Together, this Review aims to elaborate available literature to fill in the knowledge gaps in understanding the detrimental effects of heavy metals on bone cells and bone homeostasis through different perspectives.
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TI Telomere length and telomerase activity in osteoporosis and osteoarthritis
SO EXPERIMENTAL AND THERAPEUTIC MEDICINE
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DT Review
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ID mesenchymal stem-cells; bone-mineral density; articular-cartilage; chondrocyte senescence; expression; stress; health; damage; women

AB Osteoarthritis (OA) and osteoporosis (OP) are associated skeletal pathologies and have as a distinct feature the abnormal reconstruction of the subchondral bone. OA and OP have been characterized as age-related diseases and have been associated with telomere shortening and altered telomerase activity (TA). This review discusses the role of telomeres and telomerase in OA and OP pathologies and focuses on the usability of telomere length (TL) and the rate of telomere shortening as potential disease biomarkers. A number of studies have demonstrated that telomere shortening may contribute to OA and OP as an epigenetic factor. Therefore, it has been claimed that the measurement of TL of chondrocytes and/or peripheral blood cells may be an appropriate marker for the evaluation of the progression of these diseases. However, there is a need to be perform further studies with larger cohorts, with the aim of obtaining objective results and a better understanding of the association between TL, inflammation and aging, in order to provide further insight into the pathophysiology of degenerative joint diseases.
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TI Association of Bariatric Surgery With Risk of Fracture in Patients With Severe Obesity
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ID y gastric bypass; bone-mineral density; vertical banded gastroplasty; intentional weight-loss; body-composition; sleeve gastrectomy; vertebral fracture;

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AB Importance Given the complex relationship between body mass index, body composition, and bone density and the correlative nature of the studies that have established the prevailing notion that higher body mass indices may be protective against osteopenia and osteoporosis and, therefore, fracture, the absolute risk of fracture in patients with severe obesity who undergo either Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) compared with those who do not undergo bariatric surgery is unknown. Objective To assess the rates of fractures associated with obesity and compare rates between those who do not undergo bariatric surgery, those who undergo RYGB, and those who undergo SG. Design, Setting, and Participants In this retrospective multicenter cohort study of Medicare Standard Analytic Files derived from Medicare parts A and B records from January 2004 to December 2014, patients classified as eligible for bariatric surgery using the US Centers of Medicare & Medicaid criteria who either did not undergo bariatric surgery or underwent RYGB or SG were exactly matched in a 1:1 fashion based on their age, sex, Elixhauser Comorbidity Index, hypertension, smoking status, nonalcoholic fatty liver disease, hyperlipidemia, type 2 diabetes, osteoporosis, osteoarthritis, and obstructive sleep apnea status. Data were analyzed from November to December 2019. Exposures RYGB or SG. Main Outcomes and Measures The primary outcome measured in this study was the odds of fracture overall based on exposure to bariatric surgery. Secondary outcomes included the odds of type of fracture (humerus, radius or ulna, pelvis, hip, vertebrae, and total fractures) based on exposure to bariatric surgery. Results A total of 49 113 patients were included and were equally made up of 16 371 bariatric surgery-eligible patients who did not undergo weight loss surgery, 16 371 patients who had undergone RYGB, and 16 371 patients who had undergone SG. Each group consisted of an equal number of 4109 men (25.1%) and 12 262 women (74.9%) and had an equal distribution of ages, with 11 780 patients (72.0%) 64 years or younger, 4230 (25.8%) aged 65 to 69 years, 346 (2.1%) aged 70 to 74 years, and 15 (0.1%) aged 75 to 79 years. Patients undergoing RYGB were found to have no significant difference in odds of fractures compared with bariatric surgery-eligible patients who did not undergo surgery. Patients undergoing undergone SG were found to have decreased odds of fractures of the humerus (odds ratio [OR], 0.57; 95% CI, 0.45-0.73), radius or ulna (OR, 0.38; 95% CI, 0.25-0.58), hip (OR, 0.49; 95% CI, 0.33-0.74), pelvis (OR, 0.34; 95% CI, 0.18-0.64), vertebrae (OR, 0.60; 95% CI, 0.48-0.74), or fractures in general (OR, 0.53; 95% CI, 0.46-0.62). Compared with patients undergoing SG, patients undergoing RYGB had a significantly greater risk of total fractures (OR, 1.79; 95% CI, 1.55-2.06) and humeral fractures (OR, 1.60; 95% CI, 1.24-2.07). Conclusions and Relevance In this cohort study, bariatric surgery was associated with a reduced risk of fracture in bariatric surgery-eligible patients. Sleeve gastrectomy might be the best option for weight loss in patients in which fractures could be a concern, as RYGB may be associated with an increased fracture risk compared with SG.
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TC 41
Z9 49
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JI JAMA Netw. Open
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WC Medicine, General & Internal
SC General & Internal Medicine
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UT WOS:000542973600003
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AU Guo, XY
Wei, SJ
Xu, F
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Wang, HS
Ding, R
AF Guo, Xinyu
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Wang, Huasong
Ding, Ran
TI MicroRNA-532-5p is implicated in the regulation of osteoporosis by forkhead box O1 and osteoblast differentiation
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE miR-532-5p; FOXO1; Osteoporosis; Osteogenic differentiation
ID bone metabolism; promotes; expression; foxo1; cells
AB Background MicroRNAs (miRNAs) are critical regulators in osteogenesis and cartilage formation. This study was designed to investigate whether miR-532-5p plays a role in the regulation of osteoporosis. Methods Osteoporotic fractures (OP group, n = 10) or osteoarthritis without osteoporosis (control group, n = 10) were selected as subjects in this study. Quantitative analysis of gene expression was performed by RT-PCR. Western blot was used to determine the expression levels of protein forkhead O1 (FOXO1). Bioinformatics analyses and luciferase reporter assay were used to verify the downstream target of miR-532-5p. Results Compared with the non-osteoporotic controls, miR-532-5p was upregulated in osteoporotic samples, and expression of miR-532-5p was downregulated in the osteogenic C2C12 cell model. Overexpression of miR-532-5p resulted in decreased expression levels of key osteoblast markers, including alkaline phosphatase (ALP), osteocalcin (OC), and collagen type I alpha 1 (COL1A1). The inhibitory results of miR-532-5p were reversed. MiR-532-5p contained a putative FOXO1 binding site. Moreover, miR-532-5p inhibited the expression of FOXO1, and overexpression of FOXO1 inhibited the effect of miR-532-5p on osteoblast markers. Conclusions MiR-532-5p can provide references to osteoporosis by regulating the expression of FOXO1 and osteoblast differentiation. MiR-532-5p might serve as a therapeutic target for osteoporosis.
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NR 39
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Z9 14
U1 0
U2 10
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD MAY 13
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VL 21
IS 1
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA LS3MM
UT WOS:000536292100001
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TI Biomechanical role of posterior cruciate ligament in total knee arthroplasty: A finite element analysis
SO COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE
LA English
DT Article
DE Femoral prosthesis; Total knee arthroplasty; Posterior cruciate ligament; Von Mises stress; Finite element analysis
ID joint; replacement; model; simulation; flexion; kinematics; condylar; bundles; design
AB Background and Objective: The knee joint is a complex structure which is vulnerable to injury due to various types of loadings as a consequence of walking, running, stair climbing, etc. Total knee arthroplasty (TKA) is a widely used and successful orthopedic procedure which during that the posterior cruciate ligament (PCL) can either be retained or substituted. Different surgical techniques suggest retention or sacrifice of the PCL in TKA for the treatment of osteoarthritis which may alter the post-op outcomes. The objective of this study was to evaluate the biomechanical role of PCL after TKA surgery using finite element (FE) modeling. Methods: A three-dimensional (3D) FE model of the prosthetic knee was developed and its validity was compared to available studies in literature. Further, the effect of the retention or removing of the PCL as well as its degradation (i.e. variation in mechanical properties) and angle on knee biomechanics were evaluated during a weight-bearing squatting movement. Results: The validity of the intact model were confirmed. The results revealed higher stresses in the PCL and tibial insert at higher femoral flexion angles. In addition, the effect of variations in the stiffness of the PCL was found to be negligible at lower while considerable at higher femoral flexion angles. The variations in the elevation angle of the PCL from 89 degrees to 83 degrees at the critical femoral angles of 60 degrees and 120 degrees showed the highest von Mises stresses in the tibial insert. Conclusions: The results have implications not only for understanding the stresses in the prosthetic knee model under squat movement but also for providing comprehensive information about the effects of variations in the PCL stiffness and balancing on the induced stresses of the PCL and tibial insert. (C) 2019 Elsevier B.V. All rights reserved.
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J9 COMPUT METH PROG BIO
JI Comput. Meth. Programs Biomed.
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DI 10.1016/j.cmpb.2019.105109
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WC Computer Science, Interdisciplinary Applications; Computer Science, Theory & Methods; Engineering, Biomedical; Medical Informatics
SC Computer Science; Engineering; Medical Informatics
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Chen, Erman
Tang, Lan
Hang, Kai
Ding, Qianhai
Li, Yan
Zhang, Wei
He, Rongxin
TI IGFBP7 acts as a negative regulator of RANKL-induced osteoclastogenesis and oestrogen deficiency-induced bone loss
SO CELL PROLIFERATION
LA English
DT Article
ID in-vitro; differentiation; osteoarthritis; insulin; increases; cells
AB Objectives Insulin-like growth factor-binding protein 7 (IGFBP7) is a low-affinity insulin growth factor (IGF) binder that may play an important role in bone metabolism. We previously reported that IGFBP7 enhanced osteogenic differentiation of bone marrow-derived mesenchymal stem cells (BMSCs) via the Wnt/beta-catenin signalling pathway. In this study, we tried to reveal its function in osteoclast differentiation and osteoporosis. Methods We used both in vitro and in vivo studies to investigate the effects of IGFBP7 on RANKL-induced osteoclastogenesis and osteoporosis, together with the underlying molecular mechanisms of these processes. Results We show that IGFBP7 inhibited receptor activation of nuclear factor-kappa B (NF-kappa B) ligand (RANKL)-induced osteoclastogenesis, F-actin ring formation and bone resorption, which was confirmed by using recombinant IGFBP7 protein, lentivirus and siRNA. The NF-kappa B signalling pathway was inhibited during this process. Moreover, in a mouse ovariectomy-induced osteoporosis model, IGFBP7 treatment attenuated osteoporotic bone loss by inhibiting osteoclast activity. Conclusions Taken together, these findings show that IGFBP7 suppressed osteoclastogenesis in vitro and in vivo and suggest that IGFBP7 is a negative regulator of osteoclastogenesis and plays a protective role in osteoporosis. These novel insights into IGFBP7 may facilitate the development of potential treatment strategies for oestrogen deficiency-induced osteoporosis and other osteoclast-related disorders.
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U1 1
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TI Oxytocin Controls Chondrogenesis and Correlates with Osteoarthritis
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE osteoarthritis; chondrocyte; hMADS cells; oxytocin; clinical OA severity
ID inflammatory disease; adipose-tissue; body-weight; stem-cells; osteoporosis; progression; mechanisms; expression; cartilage; system
AB This study investigated the relationship of oxytocin (OT) to chondrogenesis and osteoarthritis (OA). Human bone marrow and multipotent adipose-derived stem cells were cultured in vitro in the absence or presence of OT and assayed for mRNA transcript expression along with histological and immunohistochemical analyses. To study the effects of OT in OA in vivo, a rat model and a human cohort of 63

men and 19 women with hand OA and healthy controls, respectively, were used. The baseline circulating OT, interleukin-6, leptin, and oestradiol levels were measured, and hand X-ray examinations were performed for each subject. OT induced increased aggrecan, collagen (Col) X, and cartilage oligomeric matrix protein mRNA transcript levels in vitro, and the immunolabelling experiments revealed a normalization of Sox9 and Col II protein expression levels. No histological differences in lesion severity were observed between rat OA groups. In the clinical study, a multivariate analysis adjusted for age, body mass index, and leptin levels revealed a significant association between OA and lower levels of OT (odds ratio = 0.77; p = 0.012). Serum OT levels are reduced in patients with hand OA, and OT showed a stimulatory effect on chondrogenesis. Thus, OT may contribute to the pathophysiology of OA.
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NR 41
TC 11
Z9 15
U1 0
U2 6
PU MDPI
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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AU Wang, N
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He, Hongyi
Yang, Zidan
Yang, Tuo
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TI Selenium and bone health: a protocol for a systematic review and meta-analysis
SO BMJ OPEN
LA English
DT Review
DE bone diseases; public health; orthopaedic & trauma surgery
ID knee osteoarthritis; mineral density; hip fracture; osteoporosis; risk; selenoproteins; management; quality; smoking; women
AB Introduction Bone health affects the ability of human body to stay active, and its degradation can cause considerable morbidity and mortality. The factors related to bone health play an important role in preventing osteoporosis and its adverse consequences. However, the risk factors for osteoporosis have not been fully elucidated. Deficiency in the trace element selenium may be one of the risk factors for the development of osteoporosis. Previous studies have investigated the effects of selenium on osteoporosis; however, the results are inconclusive. Therefore, the present study aimed to systematically examine the existing literature on the associations between dietary or serum selenium and bone mineral density (BMD), osteoporosis or osteoporotic fractures, and to quantify such associations through meta-analysis. Methods and analysis PubMed, Embase and Cochrane Library will be searched using a specified search strategy to identify relevant studies up to October 2019. Both interventional and observational studies in humans will be included. The outcomes will include BMD and the prevalence or incidence of osteoporosis and osteoporotic fractures. For dietary or serum selenium and BMD, osteoporosis or osteoporotic fractures pooled analyses, estimates will be expressed as the mean difference, and the pooled OR, relative risk, HR or beta coefficient, and corresponding 95% CIs. Heterogeneity of the studies and publication bias will be investigated accordingly. To assess the quality and the risk of bias of the included studies, the Newcastle-Ottawa Quality Scale or the Cochrane risk of bias assessment tool will be used where appropriate. Ethics and dissemination Since no

private and confidential patient data will be included in the reporting, approval from an ethics committee is not required. The results will be published in a peer-reviewed journal. The study raises no ethical issues. PROSPERO registration number CRD42019147188.
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PA BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND
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WC Medicine, General & Internal

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TI Use of Tetrahydrocannabinol and Cannabidiol Products in the Perioperative Period Around Primary Unilateral Total Hip and Knee Arthroplasty
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE tetrahydrocannabinol; cannabidiol; opioid epidemic; pain control after arthroplasty; cannabis; arthroplasty
ID preoperative opioid use; medical marijuana; endocannabinoid system; chronic pain; osteoarthritis; revision; legalization; readmission; arthritis; patterns
AB Background: Given the opioid crisis in America, patients are trying alternative medications including tetrahydrocannabinol (THC) and other cannabidiol (CBD) containing products in the perioperative period, especially in states where these products are legal. This study sought to analyze usage rates of CBD/THC products in the perioperative period for primary unilateral total hip and knee arthroplasty (THA/TICS) patients and identify a possible association with post-operative opioid use. Methods: A prospective cohort of primary unilateral THA/TICS patients were enrolled at a single institution. Patients who completed detailed pain journals were retrospectively surveyed for CBD/THC product usage. Pain medications were converted to morphine milligram equivalents (MME). Results: Data from 195 of the 210 patients (92.9% response rate) following primary arthroplasty were analyzed. Overall, 16.4% of arthroplasty-22.6% (n = 19) of WA and 11.7% (n = 13) of THA-patients used CBD/THC products in the perioperative period. There was a

wide variety of usage patterns among those using CBD/THC products. In comparing CBD/THC users and non-users, there was no significant difference in the length of narcotic use, total morphine milligram equivalents taken, narcotic pills taken, average post-op pain scores, the percentage of patients requiring a refill of narcotics, or length of stay. Conclusion: Understanding that CBD/THC usage was not consistent for patients who used these products, 22.6% of TICS and 11.7% of THA patients tried CBD/THC products in the perioperative period. In this small sample, CBD/THC use was not associated with a major effect on narcotic requirements. Further studies on the effects of CBD/THC are needed as these therapies become more widely available. (C) 2020 Elsevier Inc. All rights reserved.
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WC Orthopedics
SC Orthopedics
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PT J
AU Jackson, MJ
AF Jackson, Malcolm J.
TI Mechanistic models to guide redox investigations and interventions in musculoskeletal ageing
SO FREE RADICAL BIOLOGY AND MEDICINE
LA English
DT Review
ID skeletal-muscle fibers; cuzn-superoxide-dismutase; induced oxidative stress; age-related loss; nf-kappa-b; life-span; reactive oxygen; free-radicals; contractile activity; adaptive responses
AB Age is the greatest risk factor for the major chronic musculoskeletal disorders, osteoarthritis, osteoporosis and age-related loss of skeletal muscle mass and function (sarcopenia). Dramatic advances in understanding of the fundamental mechanisms underlying the ageing process are being exploited to understand the causes of these age-related disorders and identify approaches to prevent or treat

these disorders. This review will focus on one of these fundamental mechanisms, redox regulation, and the role of redox changes in age-related loss of skeletal muscle mass and function (sarcopenia). Key to understanding the role of such pathways has been the development and study of experimental models of musculoskeletal ageing that are designed to examine the effect of modification of ROS regulatory enzymes. These have primarily involved genetic deletion of regulatory enzymes for ROS in mice. Many of the models studied show increased oxidative damage in tissues, but no clear relationship with skeletal muscle aging has been seen The exception to this has been mice with disruption of the superoxide dismutases and, in particular, deletion of Cu,ZnSOD (SOD1) localised in the cytosol and mitochondrial intermembrane space. Studies of tissue specific models lacking SOD1 have highlighted the potential role that disrupted redox pathways can play in muscle loss and weakness and have demonstrated the need to study both motor neurons and muscle to understand age-related loss of skeletal muscle. The complex interplay that has been identified between changes in redox homeostasis in the motor neuron and skeletal muscle and their role in premature loss of muscle mass and function illustrates the utility of modifiable models to establish key pathways that may contribute to age-related changes and identify potential logical approaches to intervention.
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WC Biochemistry & Molecular Biology; Endocrinology & Metabolism
SC Biochemistry & Molecular Biology; Endocrinology & Metabolism
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AU Lee, SR
Jeon, H
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Yun, MK
Lim, YJ
Kang, SC
AF Lee, Sung Ryul
Jeon, Hyelin
Kwon, Jeong Eun

Suh, Heeju
Kim, Byung-Hak
Yun, Min-Kyu
Lim, Ye Ji
Kang, Se Chan
TI Anti-osteoporotic effects of Salvia miltiorrhiza Bunge EtOH extract both in ovariectomized and naturally menopausal mouse models
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE Osteoporosis; Menopause; Salvia miltiorrhiza; Bone mineral density; Bone resportipon; Osteoclast differentiation
ID hormone replacement therapy; bone biology; prevention; management; chemistry; estrogen; plasma; cells
AB Ethnopharmacological relevance: Salvia miltiorrhiza is a traditional oriental medicine widely used for preventing and treating disorders of the liver, menstrual, and blood circulation systems. Osteoporosis, loss of bone with age and/or estrogen deficiency, is an important causal factor of fracture. S. miltiorrhiza extract has been used to alleviate dysmenorrhea and painful osteoarthritis. Aim of the study: This study was performed to investigate the anti-osteoporosis activity of the Salvia miltiorrhiza ethanol extract (SME) in osteoporosis-prone conditions: ovariectomized (OVX) and naturally menopaused (NM) ICR mice. Materials and methods: Anti-osteoporotic potentials of SME (50-200 mg/kg) were evaluated based on bone mineral density using microCT analysis, biochemical parameters, and changes in the gene expressions involved in bone resorption. Results: SME ameliorated the loss of trabecular bone both in OVX and NM mice. SME was effective in correcting aberrant levels of RANKL, osteocalcin, and BALP, which are critically involved in bone resorption. In addition, SME suppressed the expression of TRAF6 and NFATc1, which play a role in osteoclast differentiation. Conclusions: SME suppressed the loss of trabecular bone via suppressing bone resorption and osteoclast differentiation both in OVX and NM mice. SME is likely to be developed as a therapeutic agent for osteoporosis.
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JI J. Ethnopharmacol.
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WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
SC Plant Sciences; Pharmacology & Pharmacy; Integrative & Complementary Medicine
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PT J
AU Frysz, M
Gregory, JS
Aspden, RM
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Tobias, JH
AF Frysz, Monika
Gregory, Jennifer S.
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TI The effect of pubertal timing, as reflected by height tempo, on proximal femur

shape: Findings from a population-based study in adolescents
SO BONE
LA English
DT Article
DE ALSPAC; Proximal femur shape; Joint shape; Statistical shape modelling; Pubertal growth
ID bone-mineral density; hip fracture risk; femoral geometry; men; osteoarthritis; prediction; growth; osteoporosis; women; size
AB Objective: To examine the relationship between pubertal timing (using measures of height tempo) and proximal femur shape in a large adolescent cohort. Methods: Hip DXA scans were obtained in offspring from the Avon Longitudinal Study of Parents and Children. To quantify hip morphology, the images were analyzed using Shape software based on a 53-point statistical shape model and independent modes of variation (hip shape mode (HSM) scores) for each image were generated. Height tempo (which corresponds to age at peak height velocity (aPHV)) was estimated from serial height measurements collected between age 5-20 years. Multivariable linear regression was used to examine cross-sectional associations between height tempo and the top ten HSMs at age 14 and 18, adjusting for sex and fat mass index (FMI). Results: Complete outcome and covariate data were available from 3827 and 3507 participants at age 14 and 18 years, respectively. Mean aPHV was 13.5 and 11.8 years for males and females, respectively. At age 14, height tempo was associated with a majority of modes, except for HSM4 and there was strong evidence of interaction by sex. In males, all modes showed evidence of an association with tempo, independent of FMI, with the strongest observed for HSM8 (adjusted beta 0.38 (0.33, 0.43) p = 4.1 x 10(-50)). Compared with males, the associations were generally weaker in females, with the strongest effect observed for HSM8 (adjusted beta 0.10 (0.05, 0.14) p = 1.6 x 10(-5)). The overall effect of later pubertal timing on proximal femur shape in males was a narrower femoral neck and larger superolateral head, whereas in females these changes were hard to discern. When assessed at age 18, there was little relationship between tempo and proximal femur shape in either sex. Conclusion: Our results indicate that significant changes in hip shape occur during puberty, including aspects of shape which may be related to future risk of hip OA and/or fracture. However, puberty timing per se does not appear to exert long lasting effects on proximal femur shape.
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TI Moderate SMFs attenuate bone loss in mice by promoting directional osteogenic differentiation of BMSCs
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DE Bone marrow-derived mesenchymal stem cell; Static magnetic field; Osteoporosis; Osteogenic differentiation; Magnetic therapy
ID static magnetic-fields; mesenchymal stem-cells; pulsed electromagnetic-fields; whole-body exposure; ppar-gamma; marrow; osteoporosis; wnt; microcirculation; osteoarthritis
AB Background Osteoporosis is a common metabolic bone disease without effective treatment. Bone marrow-derived mesenchymal stem cells (BMSCs) have the potential to differentiate into multiple cell types. Increased adipogenic differentiation or reduced osteogenic differentiation of BMSCs might lead to osteoporosis. Whether static magnetic fields (SMFs) might influence the adipo-osteogenic differentiation balance of BMSCs remains unknown. Methods The effects of SMFs on lineage differentiation of BMSCs and development of

osteoporosis were determined by various biochemical (RT-PCR and Western blot), morphological (staining and optical microscopy), and micro-CT assays. Bioinformatics analysis was also used to explore the signaling pathways. Results In this study, we found that SMFs (0.2-0.6 T) inhibited the adipogenic differentiation of BMSCs but promoted their osteoblastic differentiation in an intensity-dependent manner. Whole genomic RNA-seq and bioinformatics analysis revealed that SMF (0.6 T) decreased the PPAR gamma-mediated gene expression but increased the RUNX2-mediated gene transcription in BMSCs. Moreover, SMFs markedly alleviated bone mass loss induced by either dexamethasone or all-trans retinoic acid in mice. Conclusions Taken together, our results suggested that SMF-based magnetotherapy might serve as an adjunctive therapeutic option for patients with osteoporosis.
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TI Hymenialdisine: A Marine Natural Product That Acts on Both Osteoblasts and Osteoclasts and Prevents Estrogen-Dependent Bone Loss in Mice
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DT Article
DE OSTEOCLASTS; OSTEOBLASTS; RANKL; HYMENIALDISINE; MARINE NATURAL COMPOUND
ID inhibits osteoclastogenesis; differentiation; activation; induction; gsk3-beta
AB Excessive osteoclast (OC) activity together with relatively weak osteoblast (OB) function are strongly connected to osteolytic diseases, including osteoporosis, tumor-induced osteolysis, and inflammatory bone erosion. Very few natural products or compounds have been shown to exert therapeutic effects on both OCs and OBs, limiting the potential development of natural compounds for clinical application. Hymenialdisine (HMD) is a marine sponge-derived natural inhibitor of protein kinases with previously reported anti-osteoarthritis and anti-cancer properties. However, the roles of HMD in OCs, OBs, and osteoporosis have not yet been well established. Here, we found that HMD not only suppressed osteoclastogenesis but also promoted OB differentiation. HMD exerted dose-dependent inhibitory effects on RANKL-induced OC formation, bone resorption, and OC-specific gene expression. These strong inhibitory effects were achieved by blocking the NF-kappa B and MAPK signaling pathways, and NFATc1 expression. In addition, HMD potentially stimulated OB differentiation by activating alkaline phosphatase (ALP) and enhancing OB matrix mineralization. We found that HMD can activate the glycogen synthase kinase 3 beta (GSK-3 beta)/beta-catenin/T-cell factor (TCF)/lymphoid enhancer factor (LEF) signaling pathway to upregulate Runx-2 expression, the main transcription factor in this pathway. Increased expression of Runx-2 was also correlated with expression of the OB-specific genes Col1a1 and osteocalcin (Ocn). Furthermore, we also evaluated the therapeutic potential of HMD in a female C57BL/6j mouse model of ovariectomy (OVX)-induced systematic bone loss. HMD showed a remarkable ability to prevent decreases in bone volume (BV/TV) and trabecular thickness (Tb.Th). In summary, HMD exerts notable effects in inhibiting OC-related osteolysis and enhancing OB-induced ossification, suggesting the potential application of HMD in osteoporosis treatment. (c) 2020 American Society for Bone and Mineral Research.
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DI 10.1002/jbmr.4025
EA APR 2020
PG 15
WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA MZ1FZ
UT WOS:000527428600001
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ER

PT J
AU Imagama, S
Ando, K
Kobayashi, K
Seki, T
Hamada, T
Machino, M
Ota, K
Tanaka, S
Morozumi, M
Kanbara, S
Ito, S
Ishiguro, N
Hasegawa, Y
AF Imagama, Shiro
Ando, Kei
Kobayashi, Kazuyoshi
Seki, Taisuke
Hamada, Takashi
Machino, Masaaki
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Tanaka, Satoshi
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Kanbara, Shunsuke
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Ishiguro, Naoki
Hasegawa, Yukiharu
TI Impact of comorbidity rates of lumbar spondylosis, knee osteoarthritis, and osteoporosis on physical QOL and risk factors for poor physical QOL in middle-aged and elderly people

SO MODERN RHEUMATOLOGY
LA English
DT Article
DE Poor quality of life; lumbar spondylosis; knee osteoarthritis; osteoporosis; positive spinal inclination
ID quality-of-life; back extensor strength; locomotive syndrome; spinal alignment; muscle strength; kyphosis; pain
AB Purpose: To examine effects of combined osteoporosis (P), knee osteoarthritis (K-OA), and lumbar spondylosis (L-OA) on quality of life (QOL), and identify risk factors for poor QOL. Methods: 1021 subjects (440 males, 581 females, mean age: 63.4 years) were prospectively included. Osteoporosis (%YAM <= 70%), K-OA (Kellgren-Lawrence grade >= 2), and L-OA (Nathan class >= 3) were defined. Subjects were divided into groups 0 to 3 based on the number of comorbid diseases, and into groups P, K, and L (one disease), PK, PL, and KL (two diseases), and PKL (three diseases). Clinical variables and QOL were compared, and risk factor analysis was conducted. Results: BMI, muscle strength, pain, and spinal inclination significantly increased and physical QOL worsened with more comorbidities. Though age did not differ among disease groups, BMI was significantly higher in groups K and L than in group P. Groups including subjects with L-OA had significantly lower lumbar lordosis and larger spinal inclination. In multivariate logistic regression analysis adjusted for age and gender, group KL, spinal inclination, gait speed, grip strength, and pain were risk factors for poor physical QOL. Conclusion: Increased comorbidity has a negative impact on physical QOL, and six risk factors for poor physical QOL were identified.
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NR 24
TC 12
Z9 18
U1 0
U2 6
PU TAYLOR & FRANCIS LTD
PI ABINGDON
PA 2-4 PARK SQUARE, MILTON PARK, ABINGDON OR14 4RN, OXON, ENGLAND
SN 1439-7595
EI 1439-7609
J9 MOD RHEUMATOL
JI Mod. Rheumatol.
PD MAR 3
PY 2020
VL 30
IS 2
BP 402
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DI 10.1080/14397595.2019.1601839
EA APR 2019
PG 8
WC Rheumatology

SC Rheumatology
GA KR1GZ
UT WOS:000465898600001
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PT J
AU Chen, JB
Tian, YH
Zhang, Q
Ren, DP
Zhang, Q
Yan, X
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Zhang, W
Zhang, TZ
Yuan, X
AF Chen, Junbo
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Wang, Lingzhi
He, Zijing
Zhang, Wei
Zhang, Tianzhen
Yuan, Xiao
TI Novel Insights Into the Role of N6-Methyladenosine RNA Modification in Bone Pathophysiology
SO STEM CELLS AND DEVELOPMENT
LA English
DT Article
DE N6-methyladenosine RNA modification; bone; bone marrow stem cells; methyltransferase-like 3
ID mesenchymal stem-cells; messenger-rna; gene-expression; nuclear-rna; osteogenic differentiation; fat-mass; methylation; marrow; demethylase; protein
AB Thus far, there are more than known 150 modifications to RNA, in which common internal modifications of mRNA include N6-methyladenosine (m6A), N1-methyladenosine, and 5-methylcytosine. Among them, m6A RNA modification is one of the highest abundance modifications in eukaryotes, regulating mechanisms controlling gene expression at the post-transcription level. As an

invertible and dynamic epigenetic marker, m6A base modification influences almost all vital biological processes, cellular components, and molecular functions. Once the m6A modification process is abnormal, a series of diseases-including cancer, neurological diseases, and growth disorders-will be caused. Besides, several base modification activities also have been created by noncoding RNAs (ncRNAs), for instance, microRNAs, and circular RNAs, long ncRNAs, which were dynamically regulated during bone and cartilage pathophysiology processes. Therefore, it has now been clear that dynamic modification on coding RNAs and ncRNAs represents a completely new way to modulate genetic information. In this review, we highlight up-to-date progress and applications of m6A RNA modification in bone and cartilage pathophysiology, and we discuss the pathological roles and underlying molecular mechanism of m6A modifications in osteoarthritis and osteoporosis and osteosarcoma pathogenesis.
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NR 84
TC 25
Z9 27
U1 0
U2 25
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J9 STEM CELLS DEV
JI Stem Cells Dev.
PD JAN 1
PY 2021
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BP 17
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DI 10.1089/scd.2020.0157
EA DEC 2020
PG 12
WC Cell & Tissue Engineering; Hematology; Medicine, Research & Experimental; Transplantation
SC Cell Biology; Hematology; Research & Experimental Medicine; Transplantation
GA SG5PC
UT WOS:000600913400001
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ER

PT J
AU Ji, X
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Chen, J
AF Ji, Xiang
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TI Downregulation of long non-coding RNA PVT1 enhances fracture healing via regulating microRNA-497-5p/HMGA2 axis
SO BIOENGINEERED
LA English
DT Article
DE Fragility fracture; LncRNA pvt1; MiR-497-5p; HFOB1; 19
ID osteoarthritis; regeneration
AB Fragility fracture is a common and serious complication of osteoporosis. Abnormal expression of long non-coding RNAs is closely related to orthopedic diseases and bone metabolism. In the study, the role of lncRNA PVT1 during fracture healing, and the potential mechanism were explained. In the present study, 80 cases with fragility fracture were collected, serum samples were also collected at 7, 14, 21 days after standardized fixation therapy. qRT-PCR was applied for the measurement of mRNA levels. hFOB1.19 cells were recruited for the cell

experiments, and the cell viability and apoptosis were detected. Luciferase reporter gene assay was performed for target gene confirmation. It was found that the level of PVT1 increased gradually, while miR-497-5p showed a downward trend over time in both intra-articular and hand fracture patients, and the changes reached a significant level at 21 day after treatment. In vitro experiments demonstrated that PVT1 knockdown promoted cell proliferation and inhibited cell apoptosis in HFOB1.19 cells. LncRNA PVT1 acts as a competing endogenous RNA (ceRNA) of miR-497-5p, and the influence of PVT1 knockdown on HFOB1.19 cell proliferation and apoptosis was reversed by miR-497-5p inhibition. HMGA2 is the target gene of miR-497-5p. It was concluded that LncRNA PVT1 silencing may enhance fracture healing via mediating miR-497-5p/HMGA2 axis.
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CR Akanno EC, 2018, GENET SEL EVOL, V50, P0, DOI 10.1186/s12711-018-0405-y
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NR 33
TC 9
Z9 10
U1 0
U2 7
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J9 BIOENGINEERED
JI Bioengineered
PD JAN 1
PY 2021
VL 12
IS 1
BP 8125
EP 8134
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WC Biotechnology & Applied Microbiology
SC Biotechnology & Applied Microbiology
GA WJ6BJ
UT WOS:000709128000001
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ER

PT J
AU Yoshikawa, Y
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Takenaga, H
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TI Roles for B[a]P and FICZ in subchondral bone metabolism and experimental temporomandibular joint osteoarthritis via the AhR/Cyp1a1 signaling axis
SO SCIENTIFIC REPORTS
LA English
DT Article
ID aryl-hydrocarbon receptor; hypoxia-inducible factor; arylhydrocarbon receptor; ah receptor; mouse model; dna-binding; tgf-beta; in-vitro; cartilage; differentiation
AB Bone loss due to smoking represents a major risk factor for fractures and bone osteoporosis. Signaling through the aryl hydrocarbon receptor (AhR) and its ligands contributes to both bone homeostasis and inflammatory diseases. It remains unclear whether the same AhR signaling axis affects the temporomandibular joint (TMJ). The aim of this study was to investigate possible mechanisms which mediate bone loss in the TMJ due to smoking. In particular, whether benzo[a]pyrene (B[a]P), a carcinogen of tobacco smoke, induces expression of the AhR target gene, Cyp1a1, in mandibular condyles. Possible functions of an endogenous ligand of FICZ, were also investigated in a TMJ-osteoarthritis (OA) mouse model. B[a]P was administered orally to wild-type and AhR(-/-) mice and bone metabolism was subsequently examined. TMJ-OA was induced in wild-type mice with forceful opening of the mouth. Therapeutic functions of FICZ were detected with mu CT and histology. Exposure to B[a]P accelerated bone loss in the mandibular subchondral bone. This bone loss manifested with osteoclastic bone resorption and upregulated expression of Cyp1a1 in an AhR-dependent manner. In a mouse model of TMJ-OA, FICZ exhibited a dose-dependent rescue of mandibular subchondral bone loss by repressing osteoclast activity. Meanwhile, in vitro, pre-treatment with FICZ reduced RANKL-mediated osteoclastogenesis. B[a]P regulates mandibular subchondral bone metabolism via the Cyp1a1. The AhR ligand, FICZ, can prevent TMJ-OA by regulating osteoclast differentiation.
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TI 3-D microarchitectural properties and rod- and plate-like trabecular morphometric properties of femur head cancellous bones in patients with rheumatoid arthritis, osteoarthritis, and osteoporosis
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Article
DE Rod-and plate-like trabeculae; Microarchitectural properties; Rheumatoid arthritis; Osteoarthritis; Osteoporosis; Mechanical properties

ID femoral-neck; subchondral bone; distal radius; microstructure; tomography; density; quality; decomposition; resorption; disease
AB Objectives: We quantify 3-D microarchitectural properties of femoral head cancellous bones from patients with rheumatoid arthritis (RA, n = 12), osteoarthritis (OA, n = 15), osteoporosis (OP, n = 24), or donor controls (CNT, n = 8); and investigate their rod- and plate-like trabecular morphometric properties of trabecular bone tissues and compare these properties between them. Methods: Femoral heads were harvested during total hip replacement surgeries or collected from donors. Four cubic cancellous bone samples produced from each femoral head were micro-CT scanned to quantify their microarchitectural and rod- and plate-like trabecular properties. The samples were then tested in compression to determine mechanical properties. Results: The microarchitectural properties of femoral head cancellous bone revealed significant differences among the 4 groups, but not between RA and OA. Bone volume fraction was significantly greater in the RA and the OA than in the OP and the CNT. Structure model index was significantly lower in the RA and the OA than in the OP. Number of rods in the RA was significantly greater than in the other 3 groups. Number of plates and plate volume density in the RA and the OA were significantly greater than in the OP and the CNT. Mechanical properties were significantly greater in the RA and the OA than in the OP. The single best determinant for mechanical properties was bone volume fraction. Conclusions: This study demonstrates significant differences in 3-D microarchitectural properties and rod- and plate-like trabecular morphometric properties among patients with RA, OA, or OP. The RA and OA cancellous bones displayed similar patterns of microarchitectural degeneration and pronounced different microarchitectures from the OP. The OP group revealed the weakest cancellous bone strength, while the RA and OA groups exhibited a compensatory effect that maintains bone tissues, and hence mechanical properties. The translational potential of this article: The study enhances the understanding of microarchitectural degeneration of diseased cancellous bone. The OP group had the weakest cancellous bone strength, while the RA and OA groups exhibited a compensatory effect that maintains bone tissues, and hence mechanical properties. These results are particularly important for design and survival of joint prosthesis.
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TI Raloxifene Ameliorates Glucosamine-Induced Insulin Resistance in Ovariectomized Rats
SO BIOMEDICINES
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DT Article
DE apoptosis; endoplasmic reticulum stress; glucosamine; pancreatic beta-cell dysfunction; ovariectomy; raloxifene
ID pancreatic beta-cells; endoplasmic-reticulum stress; parathyroid-hormone 1-34; mesenchymal stem-cells; knee osteoarthritis; postmenopausal women; diabetes-mellitus; oral glucosamine; gene-expression; apoptosis
AB Osteoarthritis (OA) and osteoporosis (OP) are common among older women, especially postmenopausal women. Glucosamine (GlcN) is a common medication for OA, but it may induce insulin resistance and beta-cell dysfunction, especially if ovarian hormones are lacking. Raloxifene (RLX) is a selective estrogen receptor modulator and also an OP drug. Previously, we found that estrogen could improve GlcN-induced insulin resistance in ovariectomized (OVX) rats. Here, we further hypothesized that RLX, similarly to estrogen, can ameliorate GlcN-induced insulin resistance in OVX rats. We used GlcN to induce insulin resistance in OVX rats as a model for evaluating the protective effects of RLX in vivo. We used a pancreatic beta-cell line, MIN-6, to study the mechanisms underlying the effect of RLX in GlcN-induced beta-cell dysfunction in vitro. Increases in fasting plasma glucose, insulin, and homeostasis model assessments of insulin resistance in OVX Sprague Dawley rats treated with GlcN were reversed by RLX treatment (n = 8 in each group). Skeletal muscle GLUT-4 increased, liver PEPCK decreased, pancreatic islet hypertrophy, and beta-cell apoptosis in OVX rats treated with GlcN was ameliorated by RLX. The negative effects of GlcN on insulin secretion and cell viability in MIN-6 cells were related to the upregulation of reticulum (ER) stress-associated proteins (C/EBP homologous protein, phospho-extracellular

signal-regulated kinase, phospho-c-JunN-terminal kinase), the expression of which was reduced by RLX. Pretreatment with estrogen receptor antagonists reversed the protective effects of RLX. GlcN can induce insulin resistance, beta-cell dysfunction, and apoptosis in OVX rats and increase ER stress-related proteins in beta-cells, whereas RLX can reverse these adverse effects. The effects of RLX act mainly through estrogen receptor alpha; therefore, RLX may be a candidate drug for postmenopausal women with OA and OP.
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TI Vitamin D and Rheumatic Diseases: A Review of Clinical Evidence
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DT Review
DE vitamin D; 25-hydroxyvitamin D; 1,25-dihydroxyvitamin D; rheumatic diseases; rheumatology; rheumatoid arthritis; systemic lupus erythematosus; spondyloarthropathies; osteoarthritis; hyperuricemia; gout

ID systemic-lupus-erythematosus; inflammatory-bowel-disease; u-shaped relationship; 1,25-dihydroxyvitamin d-3; d supplementation; d deficiency; knee osteoarthritis; t-cells; double-blind; arthritis
AB Vitamin D plays an important role in maintaining a healthy mineralized skeleton. It is also considered an immunomodulatory agent that regulates innate and adaptive immune systems. The aim of this narrative review is to provide general concepts of vitamin D for the skeletal and immune health, and to summarize the mechanistic, epidemiological, and clinical evidence on the relationship between vitamin D and rheumatic diseases. Multiple observational studies have demonstrated the association between a low level of serum 25-hydroxyvitamin D [25(OH)D] and the presence and severity of several rheumatic diseases, such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), spondyloarthropathies, and osteoarthritis (OA). Nevertheless, the specific benefits of vitamin D supplements for the treatment and prevention of rheumatic diseases are less accepted as the results from randomized clinical trials are inconsistent, although some conceivable benefits of vitamin D for the improvement of disease activity of RA, SLE, and OA have been demonstrated in meta-analyses. It is also possible that some individuals might benefit from vitamin D differently than others, as inter-individual difference in responsiveness to vitamin D supplementation has been observed in genomic studies. Although the optimal level of serum 25(OH)D is still debatable, it is advisable it is advisable that patients with rheumatic diseases should maintain a serum 25(OH)D level of at least 30 ng/mL (75 nmol/L) to prevent osteomalacia, secondary osteoporosis, and fracture, and possibly 40-60 ng/mL (100-150 nmol/L) to achieve maximal benefit from vitamin D for immune health and overall health.
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
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AU Perry, TA
Wang, X
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AF Perry, Thomas A.
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TI Association between current medication use and progression of radiographic knee osteoarthritis: data from the osteoarthritis initiative
SO RHEUMATOLOGY
LA English

DT Article
DE medication; knee osteoarthritis; progression; analgesic
ID joint space width; nonsteroidal antiinflammatory drugs; eular recommendations; global burden; management; disease; hip; replacement; chondrocyte; celecoxib
AB Objective Use of specific medications may accelerate the progression of radiographic knee OA (RKOA). Our aim was to examine the effect of medication use on the progression of RKOA. Methods We used longitudinal data from the Osteoarthritis Initiative (OAI), an observational study of risk factors for knee OA. At baseline, we selected participants with RKOA (Kellgren-Lawrence grade >= 2) and excluded those with a history of knee-related injury/surgery and other musculoskeletal disorders. Current medication use (use/non-use in the previous 30 days) and radiographic medial minimum joint space width (mJSW) data were available at baseline and annually up to 96 months follow-up. We used random effects, panel regression to assess the association between current medication use (non-users as reference group) and change in mJSW. Results Of 2054 eligible participants, 2003 participants with baseline mJSW data were included [55.7% female, mean age 63.3 (s.d. 8.98) years]. Of seven medication classes, at baseline NSAIDs were the most frequently used analgesia (14.7%), anti-histamine (10.4%) use was frequent and the following comorbidity medications were used most frequently: statins (27.4%), anti-hypertensives (up to 15.0%), anti-depressant/anxiolytics/psychotropics (14.0%), osteoporosis-related medication (10.9%) and diabetes-related medication (6.9%). Compared with current non-users, current use of NSAIDs was associated with a loss of mJSW (b = -0.042, 95% CI -0.08, -0.0004). No other associations were observed. Conclusions In current users of NSAIDs, mJSW loss was increased compared with current non-users in participants with RKOA. Clinical trials are required to assess the potential disease-modifying effects of these medications.
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WC Rheumatology
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PT J
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TI Association between hospital surgical volume and complications after total hip arthroplasty in femoral neck fracture: A propensity score-matched cohort study

SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE Total Hip Arthroplasty; Hip Fracture; Femoral neck fracture; Hospital volume; Complication
ID displaced intracapsular fracture; bipolar hemiarthroplasty; independent patients; regression-models; risk-factors; follow-up; mortality; surgeon; replacement; comorbidity
AB Background: For displaced femoral neck fractures (FNF), total hip arthroplasty (THA) or hemiarthroplasty (HA) is preferred rather than fracture fixation. THA for patients with FNF requires skilled operators since patient with FNF likely to have osteoporosis and a higher risk of complications. Several reports suggest that higher hospital surgical volume was associated with a lower risk of complications after THA for osteoarthritis. However, little is known concerning this association with THA for FNF. Herein, we investi-gated the association between THA and complication and the recovery of physical function after THA to optimize the quality of FNF. Methods: A nationwide retrospective cohort study of elderly undergoing THA between April 1, 2011, to March 31, 2018 was performed. The association between hospital surgical volume and complication after THA for FNF was visually described with the restricted cubic spline regression analysis. Then the risk of complications was quantified with propensity score matching analysis based on the cutoff point identified by the restricted cubic spline curve. Primary outcome was secondary revision surgery, and the secondary outcomes included surgical and systemic complications, and the recovery of physical function at hospital discharge. Results: By visualization of the spline curve, we identified 20 cases per year as cutoff point of low hos-pital surgical volume. Following 1,396 patients' propensity score-match analysis (mean age 75.2 [SD] 8.8, female 80.4%), the risk of secondary revision surgery was significantly higher among the low hospital sur-gical volume group (absolute risk difference (RD), 2.44%; p = 0.011). Also, the incidence of blood trans-fusion was higher in the low hospital surgical volume group (RD, 4.01%; p = 0.049). However, there was no significant difference in the recovery of the transferring and walking ability at discharge between high and low hospital surgical volume groups (63.5% vs 62.6%, 58.5% vs 57.5%; p = 0.74, 0.71, respectively). Conclusion: Our research demonstrated that an increase in hospital surgical volume significantly reduced the incidence of secondary revision surgery after a certain inflection point, but not significantly improved short-term physical functions. (c) 2021 Elsevier Ltd. All rights reserved.
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Palmer, Andrew J.
Blizzard, Leigh
van der Mei, Ingrid
TI Change and onset-type differences in the prevalence of comorbidities in people with multiple sclerosis
SO JOURNAL OF NEUROLOGY
LA English
DT Article
DE Multiple sclerosis; Comorbidity; Prevalence; Prevalence ratio; MS onset type
ID quality-of-life; vascular comorbidity; physical-activity; association; disability; diagnosis; risk; hypertension; frequency; disease
AB Background Little is known about the change in prevalence of comorbidities during the disease course of people with multiple sclerosis (MS) and whether the prevalences vary by MS onset type. Objective To calculate the change in prevalence of comorbidities between symptom onset and the time of study, to compare the prevalences of comorbidities with those in the Australian population at the time of study and to examine onset-type differences. Methods Comorbidity data from

1518 participants of the Australian MS Longitudinal Study and Australian population comparator data (2014-2015 National Health Survey) were used. The change in prevalence between time points and prevalence ratios (PR) at the time of study (crude, age and sex adjusted, and stratified by onset type) was calculated. Results Comorbidities were common, and those with the largest increases in prevalence between MS symptom onset and the time of study were depression (+ 26.9%), anxiety (+ 23.1%), hypertension (+ 21.9%), elevated cholesterol (+ 16.3%), osteoarthritis (+ 17.1%), eye diseases (+ 11.6%), osteoporosis (+ 10.9%) and cancer (+ 10.3%). Compared to the general population and after age and sex adjustment, participants had a significantly higher prevalence for 14/19 comorbidities at the time of study. The associations were strongest for anaemia, cancer (both PR > 4.00), anxiety, depression, migraine (all PR > 3.00), psoriasis and epilepsy (both PR > 2.00). No significant differences were seen by onset type. Conclusion Comorbidities are common at MS symptom onset and increase with MS duration. Having MS may thus contribute to accrual of comorbidities. This emphasises the importance of optimal screening for and management of comorbidities in early MS and throughout the disease course.
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CR Unknown -, 2015, NATIONAL HEALTH SURVEY 2014, V0, P0
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TI Subchondral Bone Microarchitectural and Mineral Properties and Expression of Key Degradative Proteinases by Chondrocytes in Human Hip Osteoarthritis
SO BIOMEDICINES
LA English
DT Article
DE cartilage degradation; MMP13; ADAMTS4; subchondral bone remodelling; subchondral bone microarchitecture; tissue mineral density
ID articular-cartilage; knee-joints; ii collagen; degeneration; histopathology; association; inflammation; guidelines; turnover; college
AB Background: The purpose of this study was to investigate the relationship between the expression of key degradative enzymes by chondrocytes and the microarchitectural and mineral properties of subchondral bone across different stages of cartilage degradation in human hip osteoarthritis (OA). Methods: Osteochondral samples at different stages of cartilage degradation were collected from 16 femoral heads with OA. Osteochondral samples with normal cartilage were collected from seven femoral heads with osteoporosis. Microcomputed tomography was used for the investigation of subchondral bone microarchitecture and mineral densities. Immunohistochemistry was used to study the expression and distribution of MMP13 and ADAMTS4 in cartilage. Results: The microarchitecture and mineral properties of the subchondral plate and trabecular bone in OA varied with the severity of the degradation of the overlying cartilage. Chondrocytes expressing MMP13 and ADAMTS4 are mainly located in the upper zone(s) of cartilage regardless of the histopathological grades. The zonal expression of these enzymes in OA (i.e., the percentage of positive cells in the superficial, middle, and deep zones), rather than their overall expression (the percentage of positive cells in the full thickness of the cartilage), exhibited significant variation in relation to the severity of cartilage degradation. The associations between the subchondral bone properties and zonal and overall expression of these enzymes in the cartilage were generally weak or nonsignificant. Conclusions: Phenotypic changes in chondrocytes and remodelling of subchondral bone proceed at different rates throughout the process of cartilage degradation. Biological influences are more important for cartilage degradation at early stages, while biomechanical damage to the compromised tissue may outrun the phenotypic change of chondrocytes and is

critical in the advanced stages.
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TI The role of miR-29 family in disease
SO JOURNAL OF CELLULAR BIOCHEMISTRY
LA English
DT Review
DE cardiorenal disease; immune disease; microRNA; miRNA‐ 29; osteoarthritis; osteoporosis
AB MicroRNAs are small noncoding RNAs that can bind to the target sites in the 3'-untranslated region of messenger RNA to regulate posttranscriptional gene expression. Increasing evidence has identified the miR-29 family, consisting of miR-29a, miR-29b-1, miR-29b-2, and miR-29c, as key regulators of a number of biological processes. Moreover, their abnormal expression contributes to the etiology of numerous diseases. In the current review, we aimed to summarize the differential expression patterns and functional roles of the miR-29 family in the etiology of diseases including osteoarthritis, osteoporosis, cardiorenal, and immune disease. Furthermore, we highlight the therapeutic potential of targeting members of miR-29 family in these diseases. We present miR-29s as promoters of osteoblast differentiation and apoptosis but suppressors of chondrogenic and osteoclast differentiation, fibrosis, and T cell differentiation, with clear avenues for therapeutic manipulation. Further research will be crucial to identify the precise mechanism of miR-29 family in these diseases and their full potential in therapeutics.
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TI Relationship of Bone Mineral Density and Knee Osteoarthritis (Kellgren-Lawrence Grade): Fifth Korea National Health and Nutrition Examination Survey
SO CLINICS IN ORTHOPEDIC SURGERY
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DT Article
DE Osteoarthritis; Osteoporosis; Korea National Health and Nutrition Examination Survey; Kellgren; Lawrence grade
ID osteoporosis; incident; age
AB Background: Osteoarthritis (OA) and osteoporosis (OP) are the 2 most common bone disorders associated with aging. We can simply assume that older patients have a higher incidence of OA and OP with more severity. Although several papers have conducted studies on the relationship between OA and OP, none of them has demonstrated a conclusive link. In this study, we used radiological knee OA and bone mineral density (BMD; T-score of the total hip and lumbar spine) to analyze the incidence of OA and OP in a large population. We aimed to determine the relationship between OA and OP and investigate the associated risk factors. Methods: This cross-sectional study used data extracted from the 2010-2012 Korea National Health and Nutrition Examination Survey. We evaluated a total of 4,250 participants aged >= 50 years who underwent knee radiography and dual-energy X-ray absorptiometry and their laboratory results. The relationship between radiological knee OA and BMD was assessed. The generalized linear model was used to evaluate the relationship between BMD and Kellgren-Lawrence (KL) grade. Results: The higher KL grade was associated with older age, higher body mass index (BMI), female sex, and lower hemoglobin level ($p < 0.001$). No significant

association was found between OA and the following variables: white blood cell, platelet, total cholesterol, vitamin D, alkaline phosphatase, parathyroid hormone, hypertension, diabetes, asthma, dyslipidemia, smoking status, alcohol consumption, and regular exercise ($p > 0.05$). After adjusting for confounding factors (age, BMI, diabetes, hypertension, smoking, and alcohol consumption), the average T-scores of total hip and lumbar spine were the highest in the mild OA group with KL grade 2 (-0.22 +/- 1.08 and -0.89 +/- 1.46, respectively, $p < 0.001$). The average T-scores of the total hip and lumbar spine significantly decreased as OA progressed from moderate (KL grade 3; -0.49 +/- 1.05 and -1.33 +/- 1.38, respectively, $p < 0.001$) to severe (KL grade 4; -0.73 +/- 1.13 and -1.74 +/- 1.75, respectively, $p < 0.001$). T-scores of the moderate-to-severe OA group were significantly lower than those of the non-OA group (KL grades 0 and 1, $p < 0.001$). Conclusions: Compared with the non-OA group, BMD (T-scores of the total hip and lumbar spine) was higher in the mild OA group and lower in the moderate-to-severe OA group.
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TI Associations of LRP5 and MTHFR Gene Variants with Osteoarthritis Prevalence in Elderly Women: A Japanese Cohort Survey Randomly Sampled from a Basic Resident Registry
SO THERAPEUTICS AND CLINICAL RISK MANAGEMENT
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DE genetic variant; LRP5; MTHFR; osteoarthritis; osteoporosis
ID bone-mineral density; polymorphism c677t; smad3 gene; gdf5; lrp5; homocysteine; metaanalysis; fractures; a1330v; risk
AB Objective: Osteoarthritis (OA) is a common and degenerative joint disorder in the elderly. A greater importance of understanding the relationship between genetic factors and OA prevalence has emerged with population aging. We therefore investigated the associations of several bone disease-related genetic variants with the prevalence of OA and osteoporosis in Japanese elderly women from the Obuse study cohort, which was randomly sampled from a basic town resident registry. Methods and Results: In total, 206 female participants (mean +/- standard deviation age: 69.7 +/- 11.0 years) who completed OA, bone mineral density, and genotype assessments were included. The number of patients diagnosed as having knee/hip OA and osteoporosis was 59 (28.6%) and 30 (14.6%), respectively. Fisher's exact testing revealed significant relationships between the minor T allele of LDL receptor related protein 5 (LRP5) rs3736228 and the prevalence of knee/hip OA and osteoporosis. The respective odds ratios (ORs) of the TT genotype for knee/hip OA and osteoporosis were 7.28 (95% confidence interval [CI] 2.22- 28.08) and 5.24 (95% CI 0.95-26.98). An additional subgroup analysis for knee OA revealed that the frequency of the common C allele of methylenetetrahydrofolate reductase (MTHFR) rs1801133 had a statistically significant protective association with the prevalence of knee OA (OR 0.58, 95% CI

0.35-0.97). Conclusion: In sum, the present study demonstrated significant associations of LRP5 rs3736228 and MTHFR rs1801133 with knee/hip OA and osteoporosis prevalences and knee OA prevalence, respectively, in Japanese elderly women. These results will help further the understanding of OA pathogenesis and related genetic risk factors.
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TI Obesity is a risk factor for osteoarthritis progression and spontaneous osteoporosis is a risk for the development of spontaneous osteonecrosis in patients with medial meniscus posterior root tear
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English
DT Article
ID body-mass index; assessment tool; nonoperative treatment; knee; repair; hip
AB Background: Obesity is a representative risk factor for osteoarthritis (OA). The relationship between osteoporosis and executed osteonecrosis has been reported. The primary aim of this study was to determine the influence of obesity and osteoporosis on disease progression in patients with medial meniscus posterior root tear (MMPRT). Methods: We included 41 knees with MMPRT in this study. MMPRT was diagnosed based on the presence of both a meniscus ghost sign and a vertical linear defect on MRI. OA progression and development of osteonecrosis were evaluated using plain radiographs obtained at the initial visit and the final followup. The follow-up period for all knees was 30 +/- 8 (mean +/- standard deviation) months. Patients' physical attributes were assessed at initial visits; these attributes included body mass index (BMI) and the clinical risk for osteoporotic fracture, as determined by the World Health Organization fracture risk assessment tool (FRAX). Patients with a BMI >= 25 kg/m(2) were classified in the obesity group and those with a BMI <25 kg/m(2) in the control group. Patients with a FRAX score of >= 10% were classified in the high FRAX group and those with a FRAX score of <10% in the low FRAX group. Results: OA progression evaluated by Kellgren-Lawrence grading scale was observed in 75% patients in the obesity group (1 grade in 38%, 2 grades in 31%, and 3 grades in 6%) and 58% in the control group (1 grade in 58%). Patients in the obesity group showed significantly greater OA progression. Spontaneous osteonecrosis was observed in no knees at the initial visit and six knees at the final follow-up. All six lesions were observed in the high FRAX group, which was statistically significant. Conclusions: OA progression and development of osteonecrosis were the two representative deterioration patterns in patients with MMPRT. High BMI was related with OA progression, and FRAX score of >= 10% with the development of osteonecrosis. (C) 2020 Published by

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TI 3D assessment of intervertebral disc degeneration in zebrafish identifies changes in bone density that prime disc disease
SO BONE RESEARCH
LA English
DT Article
ID mineral density; osteogenesis imperfecta; genetic-factors; osteoporosis; osterix; osteoarthritis; fractures; image; differentiation; metaanalysis
AB Back pain is a common condition with a high social impact and represents a global health burden. Intervertebral disc disease (IVDD) is one of the major causes of back pain; no therapeutics are currently available to reverse this disease. The impact of bone mineral density (BMD) on IVDD has been controversial, with some studies suggesting osteoporosis as causative for IVDD and others suggesting it as protective for IVDD. Functional studies to evaluate the influence of genetic components of BMD in IVDD could highlight opportunities for drug development and repurposing. By taking a holistic 3D approach, we established an aging zebrafish model for spontaneous IVDD. Increased BMD in aging, detected by automated computational analysis, is caused by bone deformities at the endplates. However, aged zebrafish spines showed changes in bone morphology, microstructure, mineral heterogeneity, and increased fragility that resembled osteoporosis. Elements of the discs recapitulated IVDD symptoms found in humans: the intervertebral ligament (equivalent to the annulus fibrosus) showed disorganized collagen fibers and herniation, while the disc center (nucleus pulposus equivalent) showed dehydration and cellular abnormalities. We manipulated BMD in young zebrafish by mutating sp7 and cathepsin K, leading to low and high BMD, respectively. Remarkably, we detected IVDD in both groups, demonstrating that

low BMD does not protect against IVDD, and we found a strong correlation between high BMD and IVDD. Deep learning was applied to high-resolution synchrotron mu CT image data to analyze osteocyte 3D lacunar distribution and morphology, revealing a role of sp7 in controlling the osteocyte lacunar 3D profile. Our findings suggest potential avenues through which bone quality can be targeted to identify beneficial therapeutics for IVDD.
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TI Biomechanics of the Femoral Head Cartilage and Subchondral Trabecular Bone in Osteoporotic and Osteopenic Fractures
SO ANNALS OF BIOMEDICAL ENGINEERING
LA English
DT Article
DE Osteoporosis; Osteopenia; Articular cartilage; Subchondral trabecular bone; mu-Computed tomography; mu-Finite element method
ID articular-cartilage; cancellous bone; osteoarthritis; neck; microstructure; strength; tissue; damage; model
AB This study aimed to investigate the relationship between the micro structural properties of the subchondral trabecular bone (STB) and the macro mechanical properties of the articular cartilage (AC) in patients with osteoporotic (OP) and osteopenic (OPE) fractures. Sixteen femoral head samples (OP;OPE, n = 8 each) were obtained from female patients who underwent hip hemiarthroplasty. STB and AC specimens were harvested from those heads. Bone specimens were scanned using mu-CT to determine the micro structural properties. In-situ nondestructive compressive tests were performed for the cartilages to obtain elastic properties. The finite element technique was implemented on STB models created from mu-CT data to compute apparent elastic modulus. In addition, dynamic cyclic destructive tests were performed on STB and AC specimens to assess failure cycles. The results demonstrated that STB specimens in OPE group have more interconnected structure and higher cyclic dynamic strength than those in OP group. Furthermore,

bone mineral density, failure cycle, and trabecular number of STB were positively correlated with the cartilage failure cycle, which indicates that STB alteration may affect the macroscopic mechanical properties of AC. The findings suggest that STB loss correlates with a decrease in cartilage strength and that improving of bone quality may prevent cartilage weakness.
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TI Osteoporosis, fracture, osteoarthritis & sarcopenia: A systematic review of circulating microRNA association
SO BONE
LA English
DT Review
DE Aging; Circulating MicroRNA; MicroRNAs; Osteoporosis; Postmenopausal; Osteoarthritis; Systematic review; Sarcopenia
ID inhibits osteoblastic differentiation; mesenchymal stem-cells; postmenopausal osteoporosis; adipogenic differentiation; osteogenic differentiation; normalization strategy; potential biomarkers; mononuclear-cells; disease severity; bone
AB Circulating microRNAs (c-miRs) show promise as biomarkers. This systematic review explores their potential association with age-related fracture/osteoporosis (OP), osteoarthritis (OA) and sarcopenia (SP), as well as crossdisease association. Most overlap occurred between OA and OP, suggesting potentially shared microRNA activity. There was little agreement in results across studies. Few reported receiver operating characteristic analysis (ROC) and many identified significant dysregulation in disease, but direction of effect was commonly conflicting. c-miRs with most evidence for consistency in dysregulation included miR-146a, miR-155 and miR-98 for OA (upregulated). Area under the curve (AUC) for miR-146a biomarker performance was AUC 0.92, p = 0.028. miR125b (AUC 0.76-0.89), miR-100, miR-148a and miR-24 were consistently upregulated in OP. Insufficient evidence exists for c-miRs in SP. Study quality was typically rated intermediate/high risk of bias. Wide study heterogeneity meant meta-analysis was not possible. We provide detailed critique and recommendations for future approaches in c-miR analyses based on this review.
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TC 36
Z9 41
U1 0
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PU ELSEVIER SCIENCE INC
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PA STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA
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SC Endocrinology & Metabolism
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PT J
AU Jing, DD
Wu, W
Deng, XY
Peng, YZ
Yang, WB
Huang, DH
Shao, ZW
Zheng, D
AF Jing, Doudou
Wu, Wei
Deng, Xiangyu
Peng, Yizhong
Yang, Wenbo
Huang, Donghua
Shao, Zengwu
Zheng, Dong
TI FoxO1a mediated cadmium-induced annulus fibrosus cells apoptosis contributes to intervertebral disc degeneration in smoking
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Article
DE annulus fibrosus cells; apoptosis; cadmium; FoxO1a; intervertebral disc degeneration
ID oxidative stress; risk-factors; exposure; cancer; metals; lead
AB Cadmium (Cd), a type of heavy metal that accumulates in the body because of smoking, mediates the toxic effect of smoking in many diseases, such as cardiovascular disease, osteoarthritis, and osteoporosis. However, the toxic effect of

Cd on intervertebral disc tissues have not been reported. In the current study, we demonstrated that Cd induced the apoptosis of annulus fibrosus (AF) cells, which contributed to intervertebral disc degeneration (IVDD). Specifically, Cd induced the nuclear translocation of FoxO1a, which drives AF cells apoptosis through mitochondrial-related pathway. Phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) signal pathway is also involved in this process. The combined use of LY29002, an inhibitor of PI3K, and small interfering RNA-targeting FoxO1a confirmed the relationship between the PI3K/AKT signal pathway and FoxO1a. In summary, present research explores the mechanism behind the contribution of smoking to IVDD and finds a new feasible target for preventing IVDD in smoking.
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NR 32
TC 18
Z9 18
U1 0
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PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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SC Cell Biology; Physiology
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PT J
AU Yeap, SS
Tanavalee, A
Perez, EC
Tan, MP
Reyes, BHM
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TI 2019 revised algorithm for the management of knee osteoarthritis: the Southeast Asian viewpoint
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Knee osteoartrhitis; Patented crystalline glucosamine sulfate; Symptomatic slow-acting drugs for osteoarthritis; Algorithm
ID nonsteroidal antiinflammatory drugs; quality-of-life; crystalline glucosamine sulfate; chondroitin sulfate; double-blind; european-society; economic-aspects; insulin-resistance; oral glucosamine; setting trials
AB Background Since 2014, the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) algorithm for the management of knee osteoarthritis (OA) is available worldwide. Aim Based on

this document, a Southeast Asia Working Group (SEAWG) wished to see how the new ESCEO algorithm developed in 2019 was perceived by Southeast Asian experts and how it was integrated into their clinical practice. Methods A SEAWG was set up between members of the international ESCEO task force and a group of Southeast Asian experts. Results Non-pharmacological management should always be combined with pharmacological management. In step 1, symptomatic slow-acting drugs for osteoarthritis are the main background therapy, for which high-quality evidence is available only for the formulations of patented crystalline glucosamine sulfate and chondroitin sulfate. In step 2, oral NSAIDs are a useful option, considering the cardiovascular/renal/gastrointestinal profiles of the individual patient. Intra-articular hyaluronic acid and corticosteroids are a possible alternative to oral NSAIDs, but limited evidence is available. If steps 1 and 2 do not give adequate relief of symptoms, tramadol can be used, but its safety is debated. In general, the indications of the ESCEO algorithm are important in Southeast Asian countries, but the reimbursement criteria of local health systems are an important aspect for adherence to the ESCEO algorithm. Conclusion This guidance provides evidence-based and easy-to-follow advice on how to establish a treatment algorithm in knee OA, for practical implementation in clinical practice in Southeast Asian countries.
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NR 71
TC 9
Z9 11
U1 0
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PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
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IS 5
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PT J
AU Moss, JJ
Wirth, M
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AF Moss, Joanna J.
Wirth, Martina
Tooze, Sharon A.
Lane, Jon D.
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TI Autophagy coordinates chondrocyte development and early joint formation in zebrafish
SO FASEB JOURNAL

LA English
DT Article
DE Atg13; autophagy; chondrocytes; joints; zebrafish
ID ulk1 complex; noncanonical autophagy; mammalian development; signaling pathways; targeted deletion; cell-death; cartilage; growth; sox9; promotes
AB Autophagy is a catabolic process responsible for the removal of waste and damaged cellular components by lysosomal degradation. It plays a key role in fundamental cell processes, including ER stress mitigation, control of cell metabolism, and cell differentiation and proliferation, all of which are essential for cartilage cell (chondrocyte) development and survival, and for the formation of cartilage. Correspondingly, autophagy dysregulation has been implicated in several skeletal disorders such as osteoarthritis and osteoporosis. To test the requirement for autophagy during skeletal development in zebrafish, we generated an atg13 CRISPR knockout zebrafish line. This line showed a complete loss of atg13 expression, and restricted autophagic activity in vivo. In the absence of autophagy, chondrocyte maturation was accelerated, with chondrocytes exhibiting signs of premature hypertrophy. Focussing on the jaw element, autophagy disruption affected joint articulation causing restricted mouth opening. This gross behavioural phenotype corresponded with a failure to thrive, and death in homozygote atg13 nulls within 17 days. Taken together, our results are consistent with autophagy contributing to the timely regulation of chondrocyte maturation and for extracellular matrix formation.
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TI Bioactive response of PMMA coating obtained by electrospinning on ISO5832-9 and Ti6Al4V biomaterials
SO SURFACE & COATINGS TECHNOLOGY
LA English
DT Article
DE Biometals; Electrospun nanofibers; PMMA; Cytocompatibility; Biofunctionalization
ID surface modification; polymethyl methacrylate; titanium surface; implant surfaces; nanofibers; adhesion; morphology; scaffolds; chemistry; roughness
AB Degenerative diseases, such as osteoarthritis, osteoporosis and accidents can cause hip problems and injuries leading to a necessary hip prosthetic replacement. Acetabular and femoral prosthesis parts, consisting of special alloys of steel and titanium, are fixed to the bones using orthopedic cement based on poly(methyl methacrylate) (PMMA). With aim of improving implant material properties in terms of compatibility with the human body, were evaluated the bioactive responses of ISO 5832-9 steel and Ti6Al4V alloy coated with electrospun PMMA nanofibers. The electrospinning technique is widely used due to the possibility of easily producing fibers within nano or micrometric scale using a low cost, simple experimental apparatus that allows large-scale production. In this work the metallic substrates were submitted to surface pretreatments with sanding alone or in combination with acid etching. After deposition by electrospinning, the surfaces were characterized morphologically, chemically, and for roughness. PMMA fibers were obtained, with nanometric diameter, forming a uniform and homogeneous layer over both metal sample surfaces without appreciable differences in adhesion. The sanded surface, being a one-step process, was chosen for the next step. Fibroblasts

were grown on the sample surfaces, for seven days, to determine biocompatibility. Electrospinning Induced Surface Activation (EISA) was used to incorporate hydroxyl radicals into the PMMA chain to produce hydroxylated PMMA, that was later redissolved and electrospun into nanofibers. Both samples (PMMA and PMMA-OH nanofibers) resulted in good cell adhesion properties. However, a denser cell monolayer was observed on the hydroxyl-terminated sample, indicating better cell-material interaction. Hydroxyl (OH) functionalized molecules can regulate cell behavior acting as a linker capable of reacting with proteins, thus accelerating cell growth, migration, differentiation, synthesis of extracellular matrix components, and tissue morphogenesis. By a simple two-step methodology it was possible to obtain electrospun hydroxyl functionalized bioactive PMMA nanofibers deposited on metallic implant samples with an increased cell response.
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TI Assessment of Wnt pathway selected gene expression levels in peripheral blood mononuclear cells (PBMCs) of postmenopausal patients with low bone mass
SO BOSNIAN JOURNAL OF BASIC MEDICAL SCIENCES
LA English
DT Article
DE Osteoporosis; Wnt pathway; PBMC; expression; BMD; fractures
ID beta-catenin; osteoclast formation; osteoporosis; osteoarthritis; osteocytes; protein; women
AB The purpose of the study was to assess the expression of selected genes of the Wnt pathway: APC, AXIN1, CTNAT1, DKKE, GSK3B, KREMEN1, SFRP1, and WNT1 in peripheral blood mononuclear cells (PBMC) of patients, selected in consideration of

their bone mineral density (BMD), and the occurrence of low-energy fractures. The study involved 45 postmenopausal women, divided into (bur groups, according to BMD and fracture history. Measurements of laboratory parameters and RNA expression in PBMC cells were carried out in material, collected once at the inclusion visit. The densitometric examination was performed on all participants. In the analysis of the relative expression levels (RELs) of the studied genes in the entire population, we observed an overexpression for SFRP1 in 100% of samples and WNT1. In addition, the REL of DKK1, APC and GSK3B genes were slightly elevated versus the calibrator. In contrast, CTNNB1 and AXIM1 presented with a slightly decreased RELs. Analysis did not show any significant differences among the groups in the relative gene expression levels ($p < 0.05$) of particular genes. However, we have observed quite numerous interesting correlations between the expression of the studied genes and BMD, the presence of fractures, and laboratory parameters, both in the whole studied population as well as in selected groups. In conclusion, the high level of CTNNB1 expression maintains normal BMD and/or protects against fractures. It also appears that the changes in expression levels of the Wnt pathway genes in PBMCs reflect the expected changes in bone tissue.
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PU ASSOC BASIC MEDICAL SCI FEDERATION BOSNIA & HERZEGOVINA SARAJEVO
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PT J
AU Giesinger, K
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AF Giesinger, K.
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TI Higher body mass index is associated with larger postoperative improvement in patient-reported outcomes following total knee arthroplasty
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Total knee arthroplasty; Obesity; Patient-reported outcome; EQ-5D; WOMAC Score
ID morbidly obese-patients; quality-of-life; socioeconomic-status; total hip; replacement; pain; osteoarthritis; mortality; womac; age
AB BackgroundTotal knee arthroplasty is known to successfully alleviate pain and improve function in endstage knee osteoarthritis. However, there is some controversy with regard to the influence of obesity on clinical benefits after TKA. The aim of this study was to investigate the impact of body mass index (BMI) on improvement in pain, function and general health status following total knee arthroplasty (TKA).MethodsA single-centre retrospective analysis of primary TKAs

performed between 2006 and 2016 was performed. Data were collected preoperatively and 12-month postoperatively using WOMAC score and EQ-5D. Longitudinal score change was compared across the BMI categories identified by the World Health Organization.ResultsData from 1565 patients [mean age 69.1, 62.2% women] were accessed. Weight distribution was: 21.2% BMI<25.0 kg/m(2), 36.9% BMI 25.0-29.9 kg/m(2), 27.0% BMI 30.0-34.9 kg/m(2), 10.2% BMI 35.0-39.9 kg/m(2), and 4.6% BMI<greater than or equal to>40.0 kg/m(2). All outcome measures improved between preoperative and 12-month follow-up (p<0.001). In pairwise comparisons against normal weight patients, patients with class I-II obesity showed larger improvement on the WOMAC function and total score. For WOMAC pain improvements were larger for all three obesity classes.ConclusionsPost-operative improvement in joint-specific outcomes was larger in obese patients compared to normal weight patients. These findings suggest that obese patients may have the greatest benefits from TKA with regard to function and pain relief one year post-op. Well balanced treatment decisions should fully account for both: Higher benefits in terms of pain relief and function as well as increased potential risks and complications.Trial registrationThis trial has been registered with the ethics committee of Eastern Switzerland (EKOS; Project-ID: EKOS 2020-00,879)

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NR 50
TC 25
Z9 29
U1 1
U2 1
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1471-2474
J9 BMC MUSCULOSKEL DIS
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
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PT J
AU Lee, GW
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AF Lee, Gun-Woo
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Lee, Keun-Bae
TI Comparison of Preoperative Bone Density in Patients With and Without Periprosthetic Osteolysis Following Total Ankle Arthroplasty
SO FOOT & ANKLE INTERNATIONAL
LA English
DT Article
DE total ankle arthroplasty; osteolysis; bone density; ankle osteoarthritis
ID long-term outcm; computed-tomography; replacement; survivorship; osteoporosis; micromotion; joint; intermediate; components; failures
AB Background: Modern total ankle arthroplasty (TAA) prostheses are uncemented press-fit designs whose stability is dependent on bone ingrowth. Preoperative insufficient bone density reduces initial local stability at the bone-implant interface, and we hypothesized that this may play a role in periprosthetic osteolysis. We aimed to investigate the preoperative bone density of the distal tibia and talus and compare these in patients with and without osteolysis. Methods: We enrolled 209 patients (218 ankles) who underwent primary TAA using the HINTEGRA prosthesis. The overall mean follow-up duration was 66 (range, 24-161) months. The patients were allocated into 2 groups according to the presence of periprosthetic osteolysis: the osteolysis group (64 patients, 65 ankles) and nonosteolysis group (145 patients, 153 ankles). Between the 2 groups, we investigated and compared the radiographic outcomes, including the Hounsfield unit (HU) value around the ankle joint and the coronal plane alignment. Results: HU values of the tibia and talus measured at 5 mm from the reference points were higher than those at 10 mm in each group. However, comparing the osteolysis and nonosteolysis groups, we found no significant intergroup difference in HU value at every measured level in the tibia and talus ($P > .05$). Concerning the coronal plane alignment, there were no significant between-group differences in the tibiotalar and talar tilt angles ($P > .05$). Conclusion: Patients with osteolysis showed similar preoperative bone density of the distal tibia and talus compared with patients without osteolysis. Our results suggest that low bone density around the ankle joint may not be associated with increased development of osteolysis.
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PT J
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AF Beaudart, Charlotte
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TI Experts' preferences for sarcopenia outcomes: a discrete-choice experiment from a working group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) in collaboration with the European Union of Geriatric Medicine Society (EUGMS)
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Discrete-choice experiment; Sarcopenia; Outcomes
AB Background and aims To assess experts' preference for sarcopenia outcomes. Methods A discrete-choice experiment was conducted among 37 experts (medical doctors and researchers) from different countries around the world. In the survey, they were repetitively asked to choose which one of two hypothetical patients suffering from sarcopenia deserves the most a treatment. The two hypothetical patients differed in five pre-selected sarcopenia outcomes: quality of life, mobility, domestic activities, fatigue and falls. A mixed logit panel model was used to estimate the relative importance of each attribute. Results All sarcopenia outcomes were shown to be significant, and thus, important for experts. Overall, the most important sarcopenia outcome was falls (27%) followed by domestic activities and mobility (24%), quality of life (15%) and fatigue (10%). Discussion and conclusion Compared to patient's preferences, experts considered falls as a more important outcome of sarcopenia, while the outcomes fatigue and difficulties in domestic activities were considered as less important.
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NR 13
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TI Osteoarthritis: Insights Offered by the Study of Bone Mass Genetics
SO CURRENT OSTEOPOROSIS REPORTS
LA English
DT Review
DE Osteoarthritis; Bone mineral density; High bone mass; Genetics
AB Purpose of Review This paper reviews how bone genetics has contributed to our understanding of the pathogenesis of osteoarthritis. As well as identifying specific genetic mechanisms involved in osteoporosis which also contribute to osteoarthritis, we review whether bone mineral density (BMD) plays a causal role in OA development. Recent Findings We examined whether those genetically predisposed to elevated BMD are at increased risk of developing OA, using our high bone mass (HBM) cohort. HBM individuals were found to have a greater prevalence of OA compared with family controls and greater development of radiographic features of OA over 8 years, with predominantly osteophytic OA. Initial Mendelian randomisation analysis provided additional support for a causal effect of increased BMD on increased OA risk. In contrast, more recent investigation estimates this relationship to be bi-directional. However, both these findings could be explained instead by shared biological pathways. Pathways which contribute to BMD appear to play an important role in OA development, likely reflecting shared common mechanisms as opposed to a causal effect of raised BMD on OA. Studies in HBM individuals suggest this reflects an important role of mechanisms involved in bone formation in OA development; however further work is required to establish whether the same applies to more common forms of OA within the general population.
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TI Association of osteoporosis and varus inclination of the tibial plateau in postmenopausal women with advanced osteoarthritis of the knee
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Osteoporosis; Osteoarthritis of knee; Arthroplasty; Lower extremity varus malalignment; varus inclination of the tibial plateau
AB Background Although varus inclination of the tibial plateau has increasingly been recognized as a major risk factor in the progression of Osteoarthritis of the knee (OA knee), little attention has been placed on the development of the varus inclination of the tibial plateau. Osteoporosis is a disease characterized by low bone mass and may increase the risk of a stress fracture in the proximal tibia. To date, risk factors for varus inclination of the tibial plateau are rarely reported. In this study, we investigated Bone Mineral Density (BMD) as a risk factor of varus inclination of the tibial plateau in postmenopausal women with advanced OA knee. Methods A total of 90 postmenopausal women with varus OA knee who had received a total knee arthroplasty in our department between January 2016 and December 2019 were reviewed. Certain factors may correlate to inclination of the tibial plateau (Medial Tibial Plateau Angle, MTPA), including age, operation side, Kellgren-Lawrence grade of OA knee, BMD, Body Mass Index (BMI), Lateral Distal

Femur Angle (LDFA), lower extremity alignment (Hip-Knee-Ankle angle, HKAA), and history of both spinal compression fracture and hip fracture were collected and analyzed. Results Osteoporosis, lower extremity varus malalignment and age were significantly associated with varus inclination of the tibial plateau (MTPA) (P = 0.15, 0.013 and 0.033 respectively). For patients with a lower extremity varus malalignment (HKAA < 175 degrees), osteoporosis (T-score <= -2.5) was significantly associated with inclination of the tibial plateau. For patients with a normal lower extremity alignment (HKAA >= 175 degrees), no significant association was found between osteoporosis (T-score <= -2.5) and varus inclination of the tibial plateau. Conclusions Osteoporosis, lower extremity varus malalignment and age are major risk factors for inclination of the tibial plateau in postmenopausal women with OA knee. More attention needs to be given to the progression of varus OA knee in postmenopausal women who simultaneously has osteoporosis and lower extremity varus malalignment.
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TI HIV-Positive Patients Are at Increased Risk of Venous Thromboembolism After Total Joint Replacement
SO JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
LA English
DT Article
ID deep-vein thrombosis; perioperative complications; infection increase; natural-history; prophylaxis; osteonecrosis; prevention; hemophilia; aspirin
AB Background: Antiretroviral therapy has improved the life expectancy of HIV patients, leading to an increase in total joint replacement for age-related osteoarthritis. HIV patients are inherently hypercoagulable at baseline. The goal of our study was to compare the incidence of venous thromboembolism (VTE) in HIV patients with HIV-negative controls after total joint replacement. Methods: A multicenter, retrospective cohort study of 110 HIV patients (85 hips and 25 knees) and 240 HIV-negative controls (180 hips and 85 knees) between 2000 and 2018. Prophylactic anticoagulation was used in 98% of patients postoperatively-low-molecular weight heparin (73%), warfarin (19%), aspirin (6%), and clopidogrel (1%). Results: The VTE rate was 3.6% in the HIV-positive group (2.5% total hip arthroplasty [THA] and 8.0% total knee arthroplasty [TKA]) and 0.4% in the control group (0% THA and 1.7% TKA). VTEs occurred at the median (interquartile range) time of 40 days (1 to 52) post-op in the HIV group and 3 days post-op in the one control. Multivariable logistic regression adjusting for sex, smoking, history of VTE, and joint replaced identified HIV as an independent predictor of VTE (odds ratio 10.9, 95% confidence interval 1.1 to 114.0, P = 0.046). All patients with VTE were treated with warfarin (5 to 9 months); two cases were complicated by hemarthrosis and excessive bleeding at the insulin injection site. Conclusion: We observed increased rates of symptomatic VTE in HIV patients after THA (2.5%) and TKA (8%) compared with HIV-negative control patients (0% and 1.7%, respectively). HIV positivity was identified as an independent predictor of perioperative VTE. Our data suggests that HIV patients may be at higher risk for post-op VTE than HIV-negative patients. Surgeons may want to consider the use of more potent anticoagulation (ie, warfarin or novel anticoagulants) for a longer duration in HIV-positive patients. However, further studies are necessary to form evidence-based guidelines regarding this practice.
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U2 3
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
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J9 J AM ACAD ORTHOP SUR
JI J. Am. Acad. Orthop. Surg.
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PT J
AU Tuckermann, J
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TI The endothelium-bone axis in development, homeostasis and bone and joint disease
SO NATURE REVIEWS RHEUMATOLOGY
LA English
DT Review
ID skeletal blood-flow; hematopoietic stem; growth-factor; osteoblast differentiation; vascular niche; angiocrine signals; marrow perfusion; progenitor cells; h vessels; angiogenesis
AB Blood vessels form a versatile transport network that is best known for its critical roles in processes such as tissue oxygenation, metabolism and immune surveillance. The vasculature also provides local, often organ-specific, molecular signals that control the behaviour of other cell types in their vicinity during development, homeostasis and regeneration, and also in disease processes. In the skeletal system, the local vasculature is actively involved in both bone formation and resorption. In addition, blood vessels participate in inflammatory processes and contribute to the pathogenesis of diseases that affect the joints, such as rheumatoid arthritis and osteoarthritis. This Review summarizes the current understanding of the architecture, angiogenic growth and functional properties of the bone vasculature. The effects of ageing and pathological conditions, including arthritis and osteoporosis, are also discussed. Blood vessels perform vital roles in the skeletal system during development and homeostasis, and both participate in and are affected by inflammation. In this Review, the authors highlight the roles of endothelial cells during bone development, homeostasis and disease.
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FU Max Planck Society; European Research Council [AdG 786672]; Leducq Foundation; Deutsche Forschungsgemeinschaft [Tu220/12, Tu220/14-1, Ci 216/2]
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PT J
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TI Low bone mass resulting from impaired estrogen signaling in bone increases severity of load-induced osteoarthritis in female mice
SO BONE
LA English
DT Article
DE Osteoarthritis; Subchondral bone; Estrogen; Preclinical studies
ID subchondral bone; cartilage degradation; knee osteoarthritis; alendronate treatment; osteophyte formation; articular-cartilage; receptor-alpha; rat model; mouse; osteoporosis
AB Objective: Reduced subchondral bone mass and increased remodeling are associated with early stage OA. However, the direct effect of low subchondral bone mass on the risk and severity of OA development is unclear. We sought to determine the role of low bone mass resulting from a bone-specific loss of estrogen signaling in load-induced OA development using female osteoblast-specific estrogen receptor-alpha knockout (pOC-ER alpha KO) mice. Methods: Osteoarthritis was induced by cyclic mechanical loading applied to the left tibia of 26-week-old female pOC-ER alpha KO and littermate control mice at peak loads of 6.5N, 7N, or 9N for 2 weeks. Cartilage damage and thickness, osteophyte development, and joint capsule fibrosis were assessed from histological sections. Subchondral bone morphology was analyzed by microCT. The correlation between OA severity and intrinsic bone parameters was determined. Results: The loss of ER alpha in bone resulted in an osteopenic subchondral bone phenotype, but did not directly affect cartilage health. Following two weeks of cyclic tibial loading to induce OA pathology, pOC-ER alpha KO mice developed more severe cartilage damage, larger osteophytes, and greater joint capsule fibrosis compared to littermate controls. Intrinsic bone parameters negatively correlated with measures of OA severity in loaded limbs. Conclusions: Subchondral bone osteopenia resulting from bone-specific loss of estrogen signaling was associated with increased severity of load-induced OA pathology, suggesting that reduced subchondral bone mass directly exacerbates load-induced OA development. Bone-specific changes associated with estrogen loss may contribute to the increased incidence of OA in post-menopausal women.

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PT J
AU Sindhupakorn, B
Kidkhunthod, P
AF Sindhupakorn, Bura
Kidkhunthod, Pinit
TI Structural investigation in subchondral bone of osteoarthritic knee: Phosphorous K-edge XAS
SO RADIATION PHYSICS AND CHEMISTRY
LA English
DT Article
DE Osteoarthritis; Synchrotron-based X-ray fluorescence; X-ray absorption spectroscopy; XANES; EXAFS
ID mechanical-property; articular-cartilage; model; maintenance; hand; hip
AB The present study reports a structural change of subchondral bone samples

obtained from the patients who suffer from osteoarthritic knee (OA). The structural study was undertaken by comparison between controlled patients aged below 50 years old and OA patients aged over 50 years old. By employing Synchrotron-based X-ray fluorescence (SR-XRF) and X-ray absorption spectroscopy (XAS) techniques including X-ray absorption near edge structure (XANES) and extended X-ray absorption fine structure (EXAFS), the evidence of bone changes in term of Calcium-Phosphorus (Ca-P) contents were revealed. SR-XRF results excited at 2350 eV for P elements were used to clearly identify the amount of phosphorus contents in subchondral bone structure. The result showed the P contents in patients aged above 50 years old (OA) are lower than controlled patients. The depth information obtaining from both XANES and EXAFS results at P K-edge is related to electron transitions and structural modification especially around P ions at different ages. Lower Ca-P proportions which are caused the osteoporosis were obviously found in the elder patients. In addition, the majority amorphous structure of Ca-P is mainly found in all bone samples.
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NR 31
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AU Han, C
Liu, JH
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AF Han, Chang
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TI To Predict the Length of Hospital Stay After Total Knee Arthroplasty in an Orthopedic Center in China: The Use of Machine Learning Algorithms
SO FRONTIERS IN SURGERY
LA English
DT Article
DE machine learning; predictive model; cross-validation; hospital stay; total knee arthroplasty
ID fast-track hip; of-stay; perioperative management; rheumatic conditions; enhanced recovery; united-states; tourniquet; health; replacement; prevalence
AB Background and Objectives: Total knee arthroplasty (TKA) is widely performed to improve mobility and quality of life for symptomatic knee osteoarthritis patients. The accurate prediction of patients' length of hospital stay (LOS) can help clinicians for rehabilitation decision-making and bed assignment planning, which thus makes full use of medical resources. Methods: Clinical characteristics were retrospectively collected from 1,298 patients who received TKA. A total of 36 variables were included to develop predictive models for LOS by multiple machine learning (ML) algorithms. The models were evaluated by the receiver operating characteristic (ROC) curve for predictive performance and decision curve analysis (DCA) for clinical values. A feature selection approach was used to identify optimal predictive factors. Results: The areas under the ROC curve (AUCs) of the nine models ranged from 0.710 to 0.766. All the ML-based models performed better than models using conventional statistical methods in both ROC curves and decision curves. The

random forest classifier (RFC) model with 10 variables introduced was identified as the best predictive model. The feature selection indicated the top five predictors: tourniquet time, distal femoral osteotomy thickness, osteoporosis, tibia component size, and post-operative values of Hb within 24 h. Conclusions: By analyzing clinical characteristics, it is feasible to develop ML-based models for the preoperative prediction of LOS for patients who received TKA, and the RFC model performed the best.
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AU Lakshmanan, DK
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Elangovan, A
Thilagar, S
AF Lakshmanan, Dinesh Kumar
Ravichandran, Guna
Elangovan, Abbirami
Thilagar, Sivasudha
TI Fortification of raw rice and rice flour using Cissus quadrangularis L. (veldt grape) stem powder to overcome osteoporosis and its associated skeletal complication through staple diet
SO JOURNAL OF FOOD BIOCHEMISTRY
LA English
DT Article
DE Cissus quadrangularis; essential minerals; osteoarthritis; osteoporosis; rice fortification
ID bone-mineral density; serum uric-acid; vitamin-d; osteoarthritis; calcium; supplementation; absorption; extract; sodium; rats
AB This study aimed to prepare the fortified rice/flour with Cissus quadrangularis (CQ) stem powder to eliminate nutritional deficiency and improve bone health. Mineral analysis by atomic absorption spectroscopy revealed that the CQ stem has

adequate quantities of calcium, magnesium, and a moderate amount of phosphorous to meet the Recommended Dietary Allowance (RDA). Thus, the rice and flour were fortified with freeze-dried CQ stem powder to improve its nutraceutical contents. The fortification was done using standard vacuum impregnation and blending process. Furthermore, the recuperative activity of prepared fortified rice (CQFR) and flour (CQFF) was tested in chemically induced osteoporosis and osteoarthritis animal models. The efficiency of CQ fortified diet against these complications was confirmed by hematology, radiology, and histopathological analysis. The rat groups fed with CQFF/CQFR diet showed significant improvement from calcium deficiency and its allied physiological damage. Thus, this study confirms that the CQ fortified rice would provide recovery from skeletal complications associated with calcium deficiency through fixing both homeostasis and bio-accessibility of the calcium. Practical applications Micronutrient and mineral deficiency is relatively higher in the regions where rice/rice products are consumed as a staple diet. Dietary intake of calcium and some essential minerals have major influences on bone and joint health. Cissus quadrangularis (CQ) is a familiar herb, conventionally used in India to fix broken bones and strengthen the skeletal system. The Atomic absorption spectroscopy data from this study showed that the CQ stem holds a high amount of calcium and other essential minerals to promote skeletal health. Preparation of fortified rice and flour with CQ stem would be a beneficial source of the essential minerals/ bioactive principles to promote and sustain skeletal health in the underprivileged population. These study data substantiated the practical application of producing the CQ fortified nutraceutical staple diet, especially to the people who are afflicted with morbid skeletal complications.

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TI Chinese Herbal Medicine, Guilu Erxian Glue, as Alternative Medicine for Adverse Side Effects of Chemotherapy in Doxorubicin-Treated Cell and Mouse Models
SO EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE
LA English
DT Article
AB Doxorubicin (DOX), a chemotherapeutic drug, often causes many adverse side effects in patients with cancer, such as weight loss, motor disability, blood circulation defects, myelosuppression, myocardial injury, joint degeneration, and bone loss. The Chinese herbal medicine Guilu Erxian Glue (GEG) has been used in the prevention and treatment of osteoarthritis and osteoporosis for hundreds of years, with considerably fewer side effects. We expected that GEG could serve as a protective and beneficial alternative treatment for DOX-induced adverse side effects. In this study, we evaluated whether GEG can alleviate DOX-induced weight loss, motor disability, abnormal blood circulation, myelosuppression, myocardial injury, joint degeneration, and bone loss by using chemotherapy models of synoviocyte cell line HIG-82 and mice. Moreover, we examined the antioxidant capacity of GEG by using DPPH (1,1-diphenyl-2-picrylhydrazyl) free-radical scavenging. Our results revealed that GEG treatment can significantly enhance DPPH free-radical scavenging and reduce DOX-induced cytotoxicity in synoviocyte HIG-82 cells. In addition, GEG treatment for 2 weeks can significantly relieve weight loss, enhance exhaustive exercise capacity, improve blood circulation, alleviate myocardial oxidative stress and inflammation, and strengthen the tibias of DOX-treated mice. Thus, we suggest that GEG treatment can be a protective and alternative therapy for alleviating chemotherapy-related side effects such as weight loss, motor disability, blood circulation defects, and bone loss.
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TI 2021 revised algorithm for the management of knee osteoarthritis-the Chinese viewpoint
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DE Knee osteoartrhitis; Patented crystalline glucosamine sulfate; Symptomatic slow-acting drugs for osteoarthritis; Algorithm; China
ID nonsteroidal antiinflammatory drugs; quality-of-life; crystalline glucosamine

sulfate; chondroitin sulfate; double-blind; european-society; economic-aspects; insulin-resistance; oral glucosamine; setting trials
AB Aim The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) algorithm for the management of knee osteoarthritis (OA) is available worldwide from 2014, but in 2019 an update was published. Based on this algorithm, a Working Group (WG), including ESCEO members and Chinese experts, wished to see how the new ESCEO algorithm was perceived by Chinese experts in knee OA and how it was integrated into their clinical practice. Methods A WG was held between members of the international ESCEO task force and a group of Chinese experts. Results Non-pharmacological approach should be combined with pharmacological interventions. In step 1, symptomatic slow-acting drugs for osteoarthritis (SYSADOA) are the most important background drugs. Evidence, supported by high-quality research, is available only for crystalline glucosamine sulfate (pCGS) and chondroitin sulfate. Topical NSAIDs could be used as an additional option. In step 2, oral NSAIDs could be useful, but cardiovascular/renal/gastrointestinal profiles of the patients should be considered. Intra-articular hyaluronic acid and corticosteroids are alternative to oral NSAIDs, but the evidence is still limited. If steps 1 and 2 are not sufficient, weak opioids could be used. Overall, the conclusions of the ESCEO algorithm are accepted in China for products available in this country. The WG suggests the importance of economic studies, specifically made in China. Conclusion This work provides evidence-based advice to establish a treatment algorithm in knee OA, for practical implementation in clinical practice in China.
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TI Applications of Artificial Intelligence in Musculoskeletal Imaging: From the

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LA English
DT Article
DE musculoskeletal imaging; artificial intelligence; deep learning; machine learning; neural networks; appropriate utilization; image interpretation; image acquisition
AB Artificial intelligence (AI) will transform every step in the imaging value chain, including interpretive and noninterpretive components. Radiologists should familiarize themselves with AI developments to become leaders in their clinical implementation. This article explores the impact of AI through the entire imaging cycle of musculoskeletal radiology, from the placement of the requisition to the generation of the report, with an added Canadian perspective. Noninterpretive tasks which may be assisted by AI include the ordering of appropriate imaging tests, automatic exam protocoling, optimized scheduling, shorter magnetic resonance imaging acquisition time, computed tomography imaging with reduced artifact and radiation dose, and new methods of generation and utilization of radiology reports. Applications of AI for image interpretation consist of the determination of bone age, body composition measurements, screening for osteoporosis, identification of fractures, evaluation of segmental spine pathology, detection and temporal monitoring of osseous metastases, diagnosis of primary bone and soft tissue tumors, and grading of osteoarthritis.
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CR Acar E, 2019, BRIT J RADIOL, V92, P0, DOI 10.1259/bjr.20190286
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TI Nanotechnology application in drug delivery to osteoarthritis (OA), rheumatoid arthritis (RA), and osteoporosis (OSP)
SO JOURNAL OF DRUG DELIVERY SCIENCE AND TECHNOLOGY
LA English
DT Review
DE Nanotechnology; Drug delivery; Osteoarthritis (OA); Rheumatoid arthritis (RA); Osteoporosis (OSP)
ID collagen-induced arthritis; mesenchymal stem-cells; cartilage degeneration; transdermal delivery; hyaluronic-acid; nanoparticles; methotrexate; bone; efficacy; systems
AB Nanoparticles (NPs) show great promise as tools for designing formulations capable of meeting the challenge of targeted and non-targeted drug delivery to bone and cartilage tissue. NPs can also be employed to deliver regenerative materials, growth factors, and genes to bone and cartilage. Furthermore, the application of nanomaterials in tissue engineering has permitted scaffold preparation for delivery of growth factors, genes, and other agents required for bone and cartilage regeneration. The application of nanotechnology to different areas of medicine such as cancer therapy, drug delivery, nano-biosensing, and tissue engineering has recently generated a notable impact on diagnostics and treatments. Orthopedic applications of nanotechnology include drug delivery, surface modification of implants and prosthesis, tissue engineering for bone and cartilage regeneration, and novel diagnostics. Osteoarthritis (OA), rheumatoid arthritis (RA), and osteoporosis (OSP) are the three most common chronic orthopedic diseases. In this review, we discuss the application of nanotechnology in the diagnosis and treatment of OA, RA, and OSP. We also evaluate the limitations associated with existing treatments, as well as those related to drug delivery to orthopedic tissues.
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TI Spatiotemporally controlled calcitonin delivery: Long-term and targeted therapy of skeletal diseases
SO JOURNAL OF CONTROLLED RELEASE
LA English
DT Article
DE Calcitonin; Long-term delivery; Targeted delivery; Bone; Osteoclast; Osteoblasts; Skeletal diseases
ID oral salmon-calcitonin; in-vivo; postmenopausal women; double-blind; bone loss; biomedical applications; recombinant calcitonin; drug-delivery; nasal spray; back-pain
AB Bone is a connective tissue that support the entire body and protect the internal organs. However, there are great challenges on curing intractable skeletal diseases such as hypercalcemia, osteoporosis and osteoarthritis. To address these issues, calcitonin (CT) therapy is an effective treatment alternative to regulate calcium metabolism and suppress inflammation response, which are closely related to skeletal diseases. Traditional calcitonin formulation requires frequent administration due to the low bioavailability resulting from the short half-life and abundant calcitonin receptors distributed through the whole body. Therefore, long-term and targeted calcitonin delivery systems (LCDS and TCDS) have been widely explored as the popular strategies to overcome the intrinsic limitations of calcitonin and improve the functions of calcium management and inflammation inhibition in recent years. In this review, we first explain the physiological effects of calcitonin on bone remodeling: (i) inhibitory effects on osteoclasts and (ii)

facilitated effects on osteoblasts. Then we summarized four strategies for spatiotemporally controlled delivery of calcitonin: micro-/nanomedicine (e.g. inorganic micro-/nanomedicine, polymeric micro-/nanomedicine and supramolecular assemblies), hydrogels (especially thermosensitive hydrogels), prodrug (PEGylation and targeting design) and hybrid biomaterials. Subsequently, we discussed the application of LCDS and TCDS in treating hypercalcemia, osteoporosis, and arthritis. Understanding and analyzing these advanced calcitonin delivery applications are essential for future development of calcitonin therapies toward skeletal diseases with superior efficacy in clinic.
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TI Amelioration of bone fragility by pulsed electromagnetic fields in type 2 diabetic KK-Ay mice involving Wnt/β-catenin signaling
SO AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM
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DT Article
DE bone deterioration; osteocytes; pulsed electromagnetic fields; type 2 diabetes mellitus; Wnt/beta-catenin signaling
ID biological tissue; double-blind; mellitus; mass; sclerostin; fractures; strength; microarchitecture; risk; osteoarthritis
AB Type 2 diabetes mellitus (T2DM) results in compromised bone microstructure and quality, and subsequently increased risks of fractures. However, it still lacks safe and effective approaches resisting T2DM bone fragility. Pulsed electromagnetic fields (PEMFs) exposure has proven to be effective in accelerating fracture healing and attenuating osteopenia/osteoporosis induced by estrogen deficiency. Nevertheless, whether and how PEMFs resist T2DM-associated bone deterioration remain not fully identified. The KK-Ay mouse was used as the T2DM model. We found that PEMF stimulation with 2 h/day for 8wk remarkably improved trabecular bone microarchitecture, decreased cortical bone porosity, and promoted trabecular and cortical bone material properties in KK-Ay mice. PEMF stimulated bone formation in KK- Ay mice, as evidenced by increased serum levels of bone formation (osteocalcin and P1NP), enhanced bone formation rate, and increased osteoblast number. PEMF significantly suppressed osteocytic apoptosis and sclerostin expression in KK-Ay mice. PEMF exerted beneficial effects on osteoblast- and osteocyte-related gene expression in the skeleton of KK-Ay mice. Nevertheless, PEMF exerted no effect on serum biomarkers of bone resorption (TRAcP5b and CTX-1), osteoclast number, or osteoclast-specific gene expression (TRAP and cathepsin K). PEMF upregulated gene expression of canonical Wnt ligands (including Wnt1, Wnt3a, and Wnt10b), but not noncanonical Wnt5a. PEMF also upregulated skeletal protein expression of downstream p-GSK-3b and b-catenin in KK-Ay mice. Moreover, PEMF-induced improvement in bone microstructure, mechanical strength, and bone formation in KK-Ay mice was abolished after intragastric administration with the Wnt antagonist ETC-159. Together, our results suggest that PEMF can improve bone microarchitecture and quality by enhancing the biological activities of osteoblasts and osteocytes, which are associated with the activation of the Wnt/b-catenin signaling pathway. PEMF might become an

effective countermeasure against T2DMinduced bone deterioration. NEW & NOTEWORTHY PEMF improved trabecular bone microarchitecture and suppressed cortical bone porosity in T2DM KKAy mice. It attenuated T2DM-induced detrimental consequence on trabecular and cortical bone material properties. PEMF resisted bone deterioration in KK-Ay mice by enhancing osteoblast-mediated bone formation. PEMF also significantly suppressed osteocytic apoptosis and sclerostin expression in KK-Ay mice. The therapeutic potential of PEMF on T2DM-induced bone deterioration was associated with the activation of Wnt/beta-catenin signaling.
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PT J
AU Albrecht, K
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AF Albrecht, Katinka
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TI Comorbidity and healthcare utilisation in persons with incident systemic lupus erythematosus followed for 3 years after diagnosis: analysis of a claims data cohort
SO LUPUS SCIENCE & MEDICINE
LA English
DT Article
DE lupus erythematosus; systemic; health services research; outcome assessment; health care
AB Objective To analyse comorbidity and healthcare utilisation in individuals with SLE. Methods A cohort of individuals with incident SLE diagnosis in 2016 were investigated using claims data from a German statutory health insurance fund. Concomitant diagnoses, medical prescriptions, hospitalisation and sick leave were analysed in the year prior to diagnosis and during a 3-year follow-up in comparison with age-matched and sex-matched controls (1) without autoimmune diseases and (2) with incident diabetes mellitus. Sensitivity analyses were performed excluding cases with additional autoimmune diagnoses and without prescription of antimalarials. Results Among 571 individuals with SLE, hypertension (48%), depression (30%), hyperlipidaemia (25%), osteoarthritis (25%) and osteoporosis (20%) were the most frequent comorbidities in 2016. Cerebrovascular disease was documented in 9.6%. The number of drugs (mean 9.6, increment +6.2), hospitalisation (40%, increment +27%) and days on sick leave (median 46 days, increment +27 days) increased significantly in the first year with SLE diagnosis. Individuals with SLE were more frequently hospitalised and had more medications compared with both control groups (all $p<0.001$). The increase in comorbidity diagnoses was low in controls without autoimmune diseases, while controls with diabetes showed a more pronounced increase in cardiovascular risk factors, but less in osteoporosis and cerebrovascular disease. Sensitivity analyses showed comparable results. Conclusion Comorbidities are frequently detected at the time of diagnosis of SLE. High numbers of drug prescriptions and hospitalisation following SLE diagnosis reflect the comprehensive disease burden. The comparison with incident diabetes shows that differences with controls without autoimmune disease are overestimated by detection bias.
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AU Papageorgiou, M
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TI Interactions of the microbiome with pharmacological and non-pharmacological approaches for the management of ageing-related musculoskeletal diseases
SO THERAPEUTIC ADVANCES IN MUSCULOSKELETAL DISEASE
LA English
DT Review
DE ageing; bone health; microbiome; osteoarthritis; osteoporosis; prebiotics; probiotics; sarcopenia
ID bone-mineral density; whey-protein supplementation; proton pump inhibitors; gut microbiota; calcium-absorption; double-blind; vitamin-d; postmenopausal women; chondroitin sulfate; muscle mass
AB Despite major progress in the understanding of the pathophysiology and therapeutic options for common ageing-related musculoskeletal conditions (i.e. osteoporosis and associated fractures, sarcopenia and osteoarthritis), there is still a considerable proportion of patients who respond sub optimally to available

treatments or experience adverse effects. Emerging microbiome research suggests that perturbations in microbial composition, functional and metabolic capacity (i.e. dysbiosis) are associated with intestinal and extra-intestinal disorders including musculoskeletal diseases. Besides its contributions to disease pathogenesis, the role of the microbiome is further extended to shaping individuals' responses to disease therapeutics (i.e. pharmacomicrobiomics). In this review, we focus on the reciprocal interactions between the microbiome and therapeutics for osteoporosis, sarcopenia and osteoarthritis. Specifically, we identify the effects of therapeutics on microbiome's configurations, functions and metabolic output, intestinal integrity and immune function, but also the effects of the microbiome on the metabolism of these therapeutics, which in turn, may influence their bioavailability, efficacy and side-effect profile contributing to variable treatment responses in clinical practice. We further discuss emerging strategies for microbiota manipulation as preventive or therapeutic (alone or complementary to available treatments) approaches for improving outcomes of musculoskeletal health and disease.
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TI S-Equol Protects Chondrocytes against Sodium Nitroprusside-Caused Matrix Loss and Apoptosis through Activating PI3K/Akt Pathway
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE osteoarthritis (OA); S-equol; chondrocyte; PI3K; Akt pathway
ID nitric-oxide; articular chondrocyte; reactive oxygen; expression; osteoarthritis; estrogen; receptor; 17-beta-estradiol; death; knee
AB Osteoarthritis (OA) is a common chronic disease with increasing prevalence in societies with more aging populations, therefore, it is causing more concern. S-Equol, a kind of isoflavones, was reported to be bioavailable and beneficial to humans in many aspects, such as improving menopausal symptoms, osteoporosis and prevention of cardiovascular disease. This study investigated the effects of S-Equol on OA progress in which rat primary chondrocytes were treated with

sodium nitroprusside (SNP) to mimic OA progress with or without the co-addition of S-Equol for the evaluation of S-Equol's efficacy on OA. Results showed treatment of 0.8 mM SNP caused cell death, and increased oxidative stress (NO and H2O2), apoptosis, and proteoglycan loss. Furthermore, the expressions of MMPs of MMP-2, MMP-3, MMP-9, and MMP-13 and p53 were increased. The addition of 30 mu M S-Equol could lessen those caused by SNP. Moreover, S-Equol activates the PI3K/Akt pathway, which is an upstream regulation of p53 and NO production and is associated with apoptosis and matrix degradation. As a pretreatment of phosphoinositide (3)-kinases (PI3K) inhibitor, all S-Equol protective functions against SNP decrease or disappear. In conclusion, through PI3K/Akt activation, S-Equol can protect chondrocytes against SNP-induced matrix degradation and apoptosis, which are commonly found in OA, suggesting S-Equol is a potential for OA prevention.
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TI Cholesterol-induced toxicity: An integrated view of the role of cholesterol in multiple diseases
SO CELL METABOLISM
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DT Review
ID nonalcoholic fatty liver; blood-brain-barrier; density-lipoprotein cholesterol;

coronary-heart-disease; crown-like structures; bone-mineral density; dietary-cholesterol; lipid-accumulation; diabetic mice; united-states
AB High levels of cholesterol are generally considered to be associated with atherosclerosis. In the past two decades, however, a number of studies have shown that excess cholesterol accumulation in various tissues and organs plays a critical role in the pathogenesis of multiple diseases. Here, we summarize the effects of excess cholesterol on disease pathogenesis, including liver diseases, diabetes, chronic kidney disease, Alzheimer's disease, osteoporosis, osteoarthritis, pituitary-thyroid axis dysfunction, immune disorders, and COVID-19, while proposing that excess cholesterol-induced toxicity is ubiquitous. We believe this concept will help broaden the appreciation of the toxic effect of excess cholesterol, and thus potentially expand the therapeutic use of cholesterol-lowering medications.
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TI Ferulic acid attenuates osteoporosis induced by glucocorticoid through regulating the GSK-3β/Lrp-5/ERK signalling pathways
SO PHYSIOLOGY INTERNATIONAL
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DT Article
DE ferulic acid; osteoporosis; glucocorticoids; osteoblast; oxidative injury
ID oxidative stress; osteoblastic differentiation; osteoclast differentiation; ovariectomized rats; opg/rankl ratio; mc3t3-e1 cells; bone mass; expression; mineralization; osteoprotegerin
AB Objective: To evaluate in-vivo and in-vitro effects of ferulic acid (FA) on glucocorticoid-induced osteoarthritis (GIO) to establish its possible underlying mechanisms. Methods: The effects of FA on cell proliferation, cell viability (MTT assay), ALP activity, and mineralization assay, and oxidative stress markers (ROS, SOD, GSH LDH and MDA levels) were investigated by MC3T3-E1 cell line. Wistar rats received standard saline (control group) or dexamethasone (GC, 2 mg-1 kg) or DEX+FA (50 and 100 mg-1 kg) orally for 8 weeks. Bone density, micro-architecture, bio-mechanics, bone turnover markers and histo-morphology were determined. The expression of OPG, RANKL, osteogenic markers, and other signalling proteins was assessed employing quantitative RT-PCR and Western blotting. Results: The findings indicated the elevation of ALP mRNA expressions, osteogenic markers (Runx-2, OSX, Col-I, and OSN), and the b-Catenin, Lrp-5 and GSK-3b protein expressions. FA showed the potential to increase MC3T3-E1 cell differentiation, proliferation, and mineralization. FA increased oxidative stress markers (SOD, MDA, and GSH) while decreasing ROS levels and lactate dehydrogenase release in GIO rats. The OPG/RANKL mRNA expression ratio was increased by FA, followed by improved GSK-3b and ERK phosphorylation with enhanced mRNA expressions of Lrp-5 and b-catenin. Conclusion: These findings showed that FA improved osteoblasts proliferation with oxidative stress suppression by controlling the Lrp-5/GSK-3b/ERK pathway in GIO, demonstrating the potential pathways involved in the mechanism of actions of FA in GIO therapy.
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TI WNT5B in Physiology and Disease
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE WNT5B; WNT signaling; development; cancer; WNT5A
ID epithelial-mesenchymal transition; squamous-cell carcinoma; f-box protein; signaling pathway; colon-cancer; stem-cells; expression patterns; growth-factor; beta-catenin; bone-growth
AB WNT5B, a member of the WNT family of proteins that is closely related to WNT5A, is required for cell migration, cell proliferation, or cell differentiation in many cell types. WNT5B signals through the non-canonical beta-catenin-independent signaling pathway and often functions as an antagonist of canonical WNT signaling. Although WNT5B has a high amino acid identity with WNT5A and is often assumed to have similar activities, WNT5B often exhibits unique expression patterns and functions. Here, we describe the distinct effects and mechanisms of WNT5B on development, bone, adipose tissue, cardiac tissue, the nervous system, the mammary gland, the lung and hematopoietic cells, compared to WNT5A. We also highlight aberrances in non-canonical WNT5B signaling contributing to diseases such as osteoarthritis, osteoporosis, obesity, type 2 diabetes mellitus, neuropathology, and chronic diseases associated with aging, as well as various cancers.
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TI Ficus deltoidea promotes bone formation in streptozotocin-induced diabetic rats
SO PHARMACEUTICAL BIOLOGY
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DE Diabetes; osteoporosis; bone histomorphometry; micro-CT; insulin; antioxidant; osteocalcin; BALP; DPD; fatty acids
ID alkaline-phosphatase; mineral density; osteoarthritis; metabolism; osteoporosis; osteocalcin; resorption; turnover; mellitus; increase
AB Context: Diabetes mellitus increases the risk of bone diseases including osteoporosis and osteoarthritis. We have previously demonstrated that Ficus deltoidea Jack (Moraceae) is capable of reducing hyperglycaemia. However, whether F. deltoidea could protect against diabetic osteoporosis remains to be determined. Objective: The study examines the effect of F. deltoidea on bone histomorphometric parameters, oxidative stress, and turnover markers in diabetic rats. Materials and methods: Streptozotocin (STZ)-induced diabetic Sprague-Dawley rats (n = 6 animals per group) received one of the following treatments via gavage for 8 weeks: saline (diabetic control), metformin (1000 mg/kg bwt), and methanol leaves extract of F. deltoidea (1000 mg/kg bwt). A group of healthy rats served as normal control. The femoral bones were excised and scanned ex vivo using micro-computed tomography (micro-CT) for histomorphometric analysis. The serum levels of insulin, oxidative stress, and bone turnover markers were determined by ELISA assays. Results: Treatment of diabetic rats with F. deltoidea could significantly increase bone mineral density (BMD) (from 526.98 +/- 11.87 to 637.74 +/- 3.90). Higher levels of insulin (2.41 +/- 0.08 vs. 1.58 +/- 0.16), osteocalcin (155.66 +/- 4.11 vs. 14.35 +/- 0.97), and total bone n-3 PUFA (2.34 +/- 0.47 vs. 1.44 +/- 0.18) in parallel with the presence of chondrocyte hypertrophy were also observed following F. deltoidea treatment compared to diabetic control. Conclusions: F. deltoidea could prevent diabetic osteoporosis by enhancing osteogenesis and inhibiting bone oxidative stress. These findings

support the potential use of F. deltoidea for osteoporosis therapy in diabetes.
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TI Molecular Interactions between Dietary Lipids and Bone Tissue during Aging
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DE dietary lipids; hallmarks of aging; oxidative stress; saturated fat diet
ID high-fat diet; gamma-linolenic acid; nf-kappa-b; parathyroid-hormone levels; marrow stromal-cells; age-related-changes; forkhead-box-o; mineral density; postmenopausal women; induced obesity
AB Age-related bone disorders such as osteoporosis or osteoarthritis are a major public health problem due to the functional disability for millions of people worldwide. Furthermore, fractures are associated with a higher degree of morbidity and mortality in the long term, which generates greater financial and health costs. As the world population becomes older, the incidence of this type of disease increases and this effect seems notably greater in those countries that present a more westernized lifestyle. Thus, increased efforts are directed toward reducing risks that need to focus not only on the prevention of bone diseases, but also on the treatment of persons already afflicted. Evidence is accumulating that dietary lipids play an important role in bone health which results relevant to develop

effective interventions for prevent bone diseases or alterations, especially in the elderly segment of the population. This review focuses on evidence about the effects of dietary lipids on bone health and describes possible mechanisms to explain how lipids act on bone metabolism during aging. Little work, however, has been accomplished in humans, so this is a challenge for future research.
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TI Lateral Trochanteric Pain Following Primary Total Hip Arthroplasty: Incidence and Success of Nonoperative Treatment
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE lateral trochanteric pain; trochanteric bursitis; total hip arthroplasty; corticosteroid injection; surgical approach
ID corticosteroid injection; surgical approach; osteoarthritis; complications; replacement; posterior; bursitis
AB Background: Our study aimed at quantifying the overall incidence of lateral trochanteric pain (LTP) following total hip arthroplasty (THA) and risk based on surgical approach. The success of conservative treatment and potential risk factors for failure of conservative treatment were evaluated. Methods: This is a retrospective review of patients who underwent primary THA between 2010 and 2019 and had a postoperative diagnosis of ipsilateral LTP. Chart review revealed patient demographics/comorbidities, preoperative diagnosis, surgical approach, femoral components, and nonoperative treatment modalities. Radiographic analysis was performed to measure leg length discrepancy, femoral offset, and

femoral head lateralization. Results: The incidence of LTP following primary THA was 1.70% (573/33,761) with an average time to diagnosis of 27.3 months. The direct anterior approach demonstrated the highest risk and the direct lateral demonstrated the lowest risk for LTP (P < .001). Also, 82.4% (472/573) were diagnosed greater than 6 months postoperatively (P < .001). Of 573 patients, 95 (16.6%) were treated with physical therapy, home exercises, or oral medications with a success rate of 96.8% (92/95). Remaining 478 (83.4%) were treated with corticosteroid injection (CSI). And 89.5% (428/478) of the CSI cohort demonstrated clinical improvement with 3 or less CSIs. Risk factors for failure of conservative treatment were depression (P = .034), kidney disease (P = .040), and osteoporosis (P = .007). Conclusion: Postoperative LTP after THA is rare with an incidence of 1.70%. The direct anterior approach presented higher risk of LTP. Non-CSI modalities and CSIs were both successful treatment options. In patients with depression, kidney disease, and osteoporosis, conservative treatment may be less efficacious. (C) 2020 Elsevier Inc. All rights reserved.
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TI Update on the ESCEO recommendation for the conduct of clinical trials for drugs aiming at the treatment of sarcopenia in older adults

SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Clinical trial; Sarcopenia; Guidelines; Recommendations; Drug registration; Treatment
ID quality-of-life; patient-reported outcm; physical performance; muscle mass; nutritional-status; body-composition; dietary-protein; grip strength; working group; gait speed

AB Background In 2016, an expert working group was convened under the auspices of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and formulated consensus recommendations for the conduct of clinical trials for drugs to prevent or treat sarcopenia. Aims The objective of the current paper is to provide a 2020 update of the previous recommendations in accordance with the evidence that has become available since our original recommendations. Methods This paper is based on literature reviews performed by members of the ESCEO working group and followed up with face to face meetings organized for the whole group to make amendments and discuss further recommendations. Results The randomized placebo-controlled double-blind parallel-arm drug clinical trials should be the design of choice for both phase II and III trials. Treatment and follow-up should run at least 6 months

for phase II and 12 months for phase III trials. Overall physical activity, nutrition, co-prescriptions and comorbidity should be recorded. Participants in these trials should be at least 70-years-old and present with a combination of low muscle strength and low physical performance. Severely malnourished individuals, as well as bedridden patients, patients with extremely limited mobility or individuals with physical limitations clearly attributable to the direct effect of a specific disease, should be excluded. Multiple outcomes are proposed for phase II trials, including, as example, physical performance, muscle strength and mass, muscle metabolism and muscle-bone interaction. For phase III trials, we recommend a co-primary endpoint of a measure of functional performance and a Patient Reported Outcome Measure. Conclusion The working group has formulated consensus recommendations on specific aspects of trial design, and in doing so hopes to contribute to an improvement of the methodological robustness and comparability of clinical trials. Standardization of designs and outcomes would advance the field by allowing better comparison across studies, including performing individual patient-data meta-analyses, and different pro-myogenic therapies.

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NR 83
TC 58
Z9 67
U1 0
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PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
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PT J
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AF Serra Aguado, Claudio Ivan
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TI Effects of Oral Hyaluronic Acid Administration in Dogs Following Tibial Tuberosity Advancement Surgery for Cranial Cruciate Ligament Injury
SO ANIMALS
LA English
DT Article
DE hyaluronic acid; synovial fluid; paraoxonase-1; osteoarthritis; canine; cranial cruciate ligament
ID nitric-oxide; synovial-fluid; intraarticular hyaluronan; joint osteoarthritis; stifle joint; knee; serum; inflammation; cytokines; synoviocytes
AB Simple Summary Hyaluronic acid injections into the stifle are often used for managing osteoarthritis in dogs. Giving hyaluronic acid orally would be easier, but to date we do not have enough information regarding its effects when administered by this route. For this reason, in this study we evaluated the effects of oral administration of hyaluronic acid in dogs with cranial cruciate ligament rupture after surgical resolution. Dogs were divided into two groups that received either oral hyaluronic acid or a placebo. We measured changes in several biomarkers of osteoarthritis before surgery, and at ten weeks after surgery. Results showed significant improvements in some of these biomarkers, namely synovial fluid levels of hyaluronic acid and paraoxonase-1. These changes indicate that post-op oral administration of hyaluronic acid may be effective for the management of stifle osteoarthritis in the dog. Hyaluronic acid (HA) intraarticular injection is used in the management of osteoarthritis in veterinary medicine. However, HA oral administration is less common given the scarce currently available scientific evidence. This study was aimed at evaluating the effects of oral HA administration on synovial fluid concentrations of several selected biomarkers in dogs with cranial cruciate ligament (CCL) injury operated on using the tibial tuberosity advancement (TTA) technique. Fifty-five dogs were included in this prospective, randomized, double-blind, clinical study; they were randomly assigned to receive either a placebo (group A; n = 25) or HA (group B; n = 30) orally for 10 weeks. Synovial

fluid samples were obtained before surgery, and at 10 weeks postoperatively to measure concentrations of HA, haptoglobin, nitric oxide, and paraoxonase-1. After 10 weeks, group HA showed a significant increase in HA concentration ($p = 0.0016$) and a significant decrease in PON-1 concentration ($p = 0.011$) compared to baseline. In conclusion, post-op oral HA administration in canine patients with CCL injury leads to improvements in osteoarthritis biomarkers, namely higher synovial fluid HA concentrations and reduced synovial fluid paraoxonase-1 concentrations. These findings support the bioavailability of orally-administered HA and its usefulness in improving biomarkers of osteoarthritis.
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NR 51
TC 7
Z9 7
U1 1
U2 18
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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J9 ANIMALS-BASEL
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WC Agriculture, Dairy & Animal Science; Veterinary Sciences; Zoology
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TI Mobile health technologies for the management of rheumatic diseases: a systematic review of online stores in Brazil
SO CLINICAL RHEUMATOLOGY
LA English
DT Review
DE Chronic disease; Fibromyalgia; mHealth; Mobile health technology; Osteoporosis; Rheumatology; Spondylarthritis
ID patient-reported outcm; self-management; osteoporosis; prevalence; adherence
AB Rheumatic diseases are serious conditions with a low uptake of conservative treatments. Mobile health (mHealth) applications (apps) offer potential to assist the self-management of rheumatic diseases. Our goal was to perform a systematic review of available mHealth apps for rheumatic diseases in Brazil. We focused on the most prevalent rheumatic diseases: osteoarthritis, rheumatoid arthritis, fibromyalgia, systemic lupus erythematosus, osteoporosis, and axial spondylarthritis. Google Play Store and AppStore in Brazil were queried by two independent reviewers on September 2020, and the quality of eligible mHealth apps was assessed using the Mobile App Rating Scale (MARS). Of the 3173 mHealth apps found, five were eligible for inclusion. Two for fibromyalgia and two for axial spondylarthritis offered exercise, educational content, and tools to track patient-reported symptoms; and one for osteoporosis offered educational content and tracking tools only. The included apps scored moderately on the MARS quality scale, with a mean score (SD) of 3.1 (0.7) on a 0-5 scale. Most apps scored poorly based on credibility, user interface and experience, and engagement. There is growing interest in the development of mHealth technologies to support rheumatic diseases patients. Although the majority of the included apps came from non-profit organizations, they are still of poor quality and limited functionality. This study is a call for to the development of new user-centered mHealth apps that can empower rheumatic diseases patients in Brazil, especially in the area of osteoarthritis, rheumatoid arthritis, and lupus, since no apps were found.
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NR 60
TC 16
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PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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JI Clin. Rheumatol.

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PT J
AU Fang, L
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Ge, Qinwen
Shi, Zhenyu
Kong, Liya
Zhang, Peng
Xu, Rui
Zou, Zhen
Wang, Pinger
Jin, Hongting
Tong, Peijian
TI Defining disease progression in Chinese mainland people: Association between bone mineral density and knee osteoarthritis

SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Article
DE Age; Body mass index; Bone mineral density; Osteoarthritis; Speed of sound
ID quantitative ultrasound; older-adults; cartilage; risk; osteoporosis; prevalence; collagen; hip
AB Objective: To evaluate change in bone mineral density (BMD) during development of knee osteoarthritis (OA) in elderly Chinese community residents. Further, to monitor disease progression by recording speed of sound (SOS), one parameter of BMD provided by quantitative ultrasound measurement. Methods: A total of 4173 community residents of the Chinese mainland were organized to complete questionnaires and relevant measurements, including anthropometry, radiology and quantitative ultrasound (QUS). SOS measurements of the distal radius were acquired using QUS measurements. The Kellgren-Lawrence (KL) grade of knee OA was evaluated by two experienced radiographers using X-rays. Finally, a general linear models analysis was performed to determine potential relationships. Further, the area under the receiver operating characteristic curve (ROC AUC) was applied to assess the distinction model. Results: The SOS score in the OA group was significantly lower than that in the control group ($p < 0.001$). However, after adjustment for age and body mass index (BMI), no significant difference was observed in the male population ($p = 0.841$), while a significantly lower SOS score presented in knee OA participants in the female population ($p = 0.033$). A turning point in SOS scores, from increasing to decreasing trends, occurred around KL grade 2; the SOS score gradually increased with progression in participants from KL grades 0 to 2, whereas the SOS score presented a significant decrease in participants with KL grades 3 and 4. The AUC for the model to distinguish OA progression was 0.891. Conclusion: There was a non-linear and stage-specific association between SOS score and knee OA, which presented a positive relationship in early stages, but a negative relationship in advanced stages. A decline of SOS score in knee OA patients in early stages should alert clinicians to the possibility of disease progression. The Translational potential of this article: In the present study, the relationship between OA and BMD had established by SOS. The results suggested that close monitoring of SOS in elderly Chinese communities residents with knee OA could alert disease progression involvement by an easily accessible method, and help early referral to orthopedist consultation for further examination and treatment.
C1 [Fang, Liang; Xia, Chenjie; Xu, Huihui; Ge, Qinwen; Shi, Zhenyu; Kong, Liya; Zhang, Peng; Xu, Rui; Zou, Zhen; Wang, Pinger; Jin, Hongting; Tong, Peijian] Zhejiang Chinese Med Univ, Coll Clin Med 1, Hangzhou, Zhejiang, Peoples R China.
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TC 15
Z9 17

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U2 14
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 2214-031X
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J9 J ORTHOP TRANSL
JI J. Orthop. Transl.
PD JAN 15
PY 2021
VL 26
IS
BP 39
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DI 10.1016/j.jot.2020.07.006
PG 6
WC Orthopedics
SC Orthopedics
GA PM9TR
UT WOS:000604132600005
PM 33437621
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PT J
AU Campos, DM
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TI Effects of aquatic physical exercise on neuropsychological factors in older people: A systematic review
SO ARCHIVES OF GERONTOLOGY AND GERIATRICS
LA English
DT Review
DE Exercise therapy; Hydrotherapy; Cognition; Mental health; Aged

ID adults; therapy; program; women; osteoarthritis; hydrotherapy; dementia; strength; quality
AB Background:. There is a lack of standardized protocols and clinical trials for older adults involving neuropsychological factors in the literature. Furthermore, no systematic review has been published investigating this theme. Purpose:. The purpose of this systematic review was to analyze the effects of aquatic physical exercise on neuropsychological factors in older adults. Methods:. A systematic review (CRD42020176899) was conducted, using articles from Pubmed, Web of Science, Scopus, Cochrane Library, Science Direct and Medline published until March 2020 (without limit of previous year). Eligibility criteria for selecting studies were: clinical trials; samples with a mean age of 65 years old and over; articles involving aquatic physical exercise; and presenting neuropsychological outcomes (behavior, cognition, psychological, mental health). Results and discussion:. The search yielded 801 records and 16 studies were included, totaling: 1707 older adults, with a mean age of 71.3 years old (range of mean ages in the studies: 65.3 to 88.4 years old) and a predominance of women. Aquatic physical exercise showed positive results in the mental component of quality of life, fear of falling, mood, anxiety and internal health locus of control in healthy sedentary older adults. Only one study out of 5 carried out with older adults with osteoarthritis showed improvements in psychological well-being after aquatic intervention. Older women with osteopenia or osteoporosis showed improvements in the mental component of quality of life. Studies on dementia showed a significant improvement in behavioral and psychological symptoms after aquatic intervention and no effect on depressive symptoms. Conclusion:. Based on the results of this systematic review, aquatic physical exercise has positive effects on quality of life, fear of falling, cognitive functions, mood, anxiety and internal health locus of control in sedentary community-dwelling older people. It can be a great resource for carrying out physical activities in this population.
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NR 29
TC 14
Z9 23
U1 6

U2 26
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
SN 0167-4943
EI 1872-6976
J9 ARCH GERONTOL GERIAT
JI Arch. Gerontol. Geriatr.
PD SEP-OCT 15
PY 2021
VL 96
IS
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DI 10.1016/j.archger.2021.104435
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA UU2OO
UT WOS:000698640900004
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ER

PT J
AU Park, H
   Park, CY
AF Park, Hansaem
   Park, Clara Yongjoo
TI Risk of Osteoarthritis is Positively Associated with Vitamin D Status, but Not Bone Mineral Density, in Older Adults in the United States
SO JOURNAL OF THE AMERICAN COLLEGE OF NUTRITION
LA English
DT Article
DE Vitamin D; osteoarthritis; bone mineral density; NHANES
ID knee osteoarthritis; d supplementation; radiographic osteoarthritis; general-population; cartilage volume; elderly-women; progression; prevalence; calcium; expression
AB Objective We examined the risk of osteoarthritis (OA) according to vitamin D status and bone mineral density (BMD) using a cross-sectional nationally representative database. Methods National Health and Nutrition Examination Survey (NHANES) data from 2007 to 2010 were used to assess the relationship

between OA and vitamin D status in adults aged >= 40 years (n = 2934). NHANES data from 2005 to 2010 and 2013 to 2014 were analyzed to investigate the association between OA and BMD (n = 5949). Vitamin D status was categorized as serum 25-hydroxyvitamin D (25OHD) <20 ng/mL or >= 20 ng/mL. Bone health was classified according to T-score (normal, osteopenia, or osteoporosis) and BMD tertile. Risk of OA was assessed using logistic regression and adjusted for covariates. Results Participants with serum 25OHD <20 ng/mL had a 37% lower risk of OA (95% confidence interval (CI) [0.39-0.99], P = 0.046). When stratified by sex, the odds ratio for OA in men with lower vitamin D status was 0.35 (95% CI [0.15-0.81], P = 0.02). No association was found in women. The risk for OA did not differ according to BMD tertile or T-score classification. Conclusions The risk of OA is lower in older men with 25OHD less than 20 ng/mL but not in older women. Bone mineral density is not associated with OA risk in older adults in the United States.
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CR Unknown -, 2019, NHANES QUESTIONNAIRES, V0, P0
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Unknown -, 2018, BMI CLASSIFICATION, V0, P0
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NR 57
TC 3
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U1 0
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PU ROUTLEDGE JOURNALS, TAYLOR & FRANCIS LTD
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PA 2-4 PARK SQUARE, MILTON PARK, ABINGDON OX14 4RN, OXON, ENGLAND
SN 0731-5724
EI 1541-1087
J9 J AM COLL NUTR
JI J. Am. Coll. Nutr.
PD AUG 6
PY 2021
VL 40
IS 6
BP 562
EP 570
DI 10.1080/07315724.2020.1787907
EA MAY 2021
PG 9
WC Nutrition & Dietetics
SC Nutrition & Dietetics
GA UC8QY
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PT J
AU Skibicki, HE
Ponzio, DY
Brustein, JA
Post, ZD
Ong, AC
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AF Skibicki, H. E.
Ponzio, D. Y.
Brustein, J. A.
Post, Z. D.
Ong, A. C.
Orozco, F. R.
TI A cautionary case: osteoporotic femur fracture after robotic-assisted total knee arthroplasty
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Denosumab; Osteoporosis; Periprosthetic fracture; Robotics; Robotic-assisted total knee arthroplasty; Total knee replacement
ID denosumab
AB Osteoporosis is a disease of low bone mass which leads to an increased risk of fracture. The prevalence of osteoporosis is greatest amongst postmenopausal women who also form a large portion of patients with osteoarthritis presenting for total knee arthroplasty. We present a case of a 77-year-old female with knee osteoarthritis and osteoporosis on denosumab who underwent robotic-assisted total knee arthroplasty. Postoperatively, she suffered an atraumatic midshaft femur fracture at the pin site associated with the use of intraoperative robotic technology. This is a unique complication related to the use of robotics which requires additional skeletal fixation versus standard arthroplasty surgical technique. We recommend caution and further study regarding the use of robotics in total knee arthroplasty in the setting of osteoporosis and denosumab use.
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NR 27
TC 5
Z9 6
U1 0
U2 9
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA WG1DP
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PT J
AU Hao, Y
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Yu, GH
Liu, ZM
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AF Hao, Ying
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Wang, Chungguo
Qu, Sihao
Li, Li
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Zhao, Zhen
Fan, Pengcheng
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TI Quantitative proteomics reveal the protective effects of EDS against osteoarthritis via attenuating inflammation and modulating immune response
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE Epimedium brevicornu Maxim; Dioscorea nipponica Makino; Salvia miltiorrhiza Bunge; Osteoarthritis; Quantitative proteomics
ID induced osteoporosis; expression; arthritis; herb; cryptotanshinone; differentiation; quantification; identification; inhibition; flavonoids
AB Ethnopharmacological relevance: Epimedium brevicornu Maxim, Dioscorea nipponica Makino, and Salvia miltiorrhiza Bunge formula (EDS) are three traditional Chinese medicines commonly combined and used to treat osteoarthritis (OA). However, the mechanism of its therapeutic effect on OA is still unclear. Aim of the study: The aim of this study was to investigate the potential anti osteoarthritis mechanism of EDS in the treatment of OA rats' model by quantitative proteomics. Materials and methods: A papain-induced rat OA model was established, and then EDS was intragastrically administered for 28 days. A label-free quantification proteomics was performed to evaluate the holistic efficacy of EDS against OA and identify the possible protein profiles mechanisms. The expression levels of critical changed proteins were validated by RT-qPCR and Western blotting. The effects of EDS were then assessed by evaluating pathologic changes in the affected knee joint and measuring pressure pain threshold, acoustic reflex threshold, angle of joint curvature. Results: Proteomics analysis showed that 62 proteins were significantly upregulated and 208 proteins were downregulated in OA group compared to control group. The changed proteins were involved in activation of humoral immunity response, complement cascade activation, leukocyte mediated immunity, acute inflammatory response, endocytosis regulation, and proteolysis regulation. The EDS treatment partially restored the protein profile changes. The protective effects of EDS on pathologic changes in OA rats' knee joint and pain threshold assessment were consisted with the proteomics results. Conclusions: The results suggest that EDS exerted synergistic therapeutic efficacies to against OA through suppressing inflammation, modulating the immune system, relieving joint pain, and attenuating cartilage degradation.
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TC 17
Z9 19
U1 1
U2 63
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
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UT WOS:000625359600006
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PT J
AU Li, YF
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Sharif, M
AF Li, Yunfei
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Blom, Ashley
Sharif, Mohammed
TI Subchondral bone microarchitecture and mineral density in human osteoarthritis and osteoporosis: A regional and compartmental analysis
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE cartilage degeneration; mineral density; osteoarthritis; osteoporosis; subchondral bone
ID cancellous bone; articular-cartilage; femoral-head; tissue mineralization;

mechanical-property; trabecular bone; cortical bone; knee-joints; microstructure; histopathology
AB Osteoarthritis (OA) and osteoporosis (OP) are historically considered to be inversely correlated but there may be an overlap between the pathophysiology of the two diseases. This study aimed to investigate the subchondral bone microarchitecture and matrix mineralization, and the association between them in OA and OP in relation to the degree of cartilage degeneration. Fifty-six osteochondral plugs were collected from 16 OA femoral heads. They were graded on a regional basis according to the stages of cartilage degeneration, as evaluated by a new macroscopic and a modified microscopic grading system. Twenty-one plugs were collected from seven femoral heads with OP. Plugs were scanned by microcomputed tomography and the microarchitectural and mineral properties were obtained for both subchondral plate and trabecular bone. Microarchitecture and material and apparent densities of subchondral bone in OP were similar to regions with early cartilage degeneration but different from regions with advanced cartilage degradation in OA femoral heads. Subchondral trabecular bone was more mineralized than subchondral plate in both OP and OA, and this compartmental difference varied by severity of cartilage degradation. Furthermore, the relationship among trabecular bone volume fraction, tissue mineral density, and apparent bone density was similar in OP and different stages of OA. Subchondral bone microarchitecture and mineral properties in OP are different from OA in a regionalized manner in relation to stages of cartilage degeneration. Both regional and compartmental differences at structural, material, and cellular levels need to be studied to understand the transition of OA subchondral bone from being osteoporotic to sclerotic.
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Z9 36
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PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0736-0266
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J9 J ORTHOP RES
JI J. Orthop. Res.
PD DEC 15
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WC Orthopedics
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PT J
AU Pertusa, C
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AF Pertusa, Clara
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TI Serum microRNAs in osteoporotic fracture and osteoarthritis: a genetic and functional study
SO SCIENTIFIC REPORTS
LA English
DT Article
ID circulating micrornas; mirna signatures; differentiation; standardization; expression; density; plasma; tissue
AB The rising incidence of bone pathologies such as osteoporosis and osteoarthritis is negatively affecting the functional status of millions of patients

worldwide. The genetic component of these multifactorial pathologies is far from being fully understood, but in recent years several epigenetic mechanisms involved in the pathophysiology of these bone diseases have been identified. The aim of the present study was to compare the serum expression of four miRNAs in women with hip fragility fracture (OF group), osteoarthritis requiring hip replacement (OA group) and control women (Ctrl group). Serum expression of miR-497-5p, miR-155-5p, miR-423-5p and miR-365-3p was determined in a sample of 23 OA women, 25 OF women and 52 Ctrl women. Data shown that women with bone pathologies have higher expression of miR-497 and miR-423 and lower expression of miR-155 and miR-365 than control subjects. Most importantly, miR-497 was identified as an excellent discriminator between OA group and control group (AUC: 0.89, $p < 0.000$) and acceptable in distinguishing from the OF group (AUC: 0.76, $p = 0.002$). Our data suggest that circulating miR-497 may represent a significant biomarker of OA, a promising finding that could contribute towards future early-stage diagnosis of this disease. Further studies are required to establish the role of miR-155, miR-423 and miR-365 in bone pathologies.
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TI Edema-like marrow signal intensity: a narrative review with a pictorial essay
SO SKELETAL RADIOLOGY
LA English
DT Review
DE Edema-like marrow signal intensity; MRI; Rheumatoid arthritis; SIFK; AVN
ID early rheumatoid-arthritis; bone-marrow; subchondral bone; insufficiency fractures; differential-diagnosis; migratory osteoporosis; transient osteoporosis; avascular necrosis; mri; knee
AB The term edema-like marrow signal intensity (ELMSI) represents a general term describing an area of abnormal signal intensity at MRI. Its appearance includes absence of clear margins and the possibility of exceeding well-defined anatomical borders (for example, physeal scars). We can define "ELMSI with unknown cause" an entity where the characteristic MR appearance is associated with the absence of specific signs of an underlying condition. However, it is more often an important finding indicating the presence of an underlying disease, and we describe this case as "ELMSI with known cause." It presents a dynamic behavior and its evolution can largely vary. It initially corresponds to an acute inflammatory response with edema, before being variably replaced by more permanent marrow remodeling changes such as fibrosis or myxomatous connective tissue that can occur over time. It is important to study ELMSI variations over time in order to evaluate the activity state and therapeutic response of an inflammatory chronic joint disease, the resolution of a trauma, and the severity of an osteoarthritis. We propose a narrative review of the literature dealing with various subjects about this challenging topic that is imaging, temporal evolution, etiology, differential diagnoses, and possible organization, together with a pictorial essay.
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TI Human osteoclasts/osteoblasts 3D dynamic co-culture system to study the beneficial effects of glucosamine on bone microenvironment
SO INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE
LA English
DT Article
DE glucosamine; bone tissue; bone cells; 3D culture system; osteoarthritis
AB Glucosamine (GlcN) functions as a building block of the cartilage matrix, and its multifaceted roles in promoting joint health have been extensively investigated. However, the role of GlcN in osteogenesis and bone tissue is poorly understood,

mainly due to the lack of adequate experimental models. As a result, the benefit of GlcN application in bone disorders remains controversial. In order to further elucidate the pharmacological relevance and potential therapeutic/nutraceutic efficacy of GlcN, the effect of GlcN treatment was investigated in human primary osteoclasts (hOCs) and osteoblasts (hOBs) that were cultured with two-dimensional (2D) traditional methods or co-cultured in a 3D dynamic system more closely resembling the in vivo bone microenvironment. Under these conditions, osteoclastogenesis was supported by hOBs and sizeable self-assembling aggregates were obtained. The differentiated hOCs were evaluated using tartrate-resistant acid phosphatase assays and osteogenic differentiation was monitored by analyzing mineral matrix deposition via Alizarin Red staining, with expression of specific osteogenic markers determined via reverse transcription-quantitative PCR. It was found that crystalline GlcN sulfate was effective in decreasing osteoclastic cell differentiation and function. hOCs isolated from patients with OA were more sensitive compared with those from healthy donors. Additionally, GlcN exhibited anabolic effects on hOCs both in 2D conventional cell culture and in hOC/hOB 3D dynamic co-culture. The present study demonstrated for the first time the effectiveness of a 3D dynamic co-culture system for characterizing the spectrum of action of GlcN on the bone microenvironment, which may pave the way for more fully determining the potential applications of a compound such as GlcN, which is positioned between pharmaceuticals and nutraceuticals. Based on the present findings, it is hypothesized that GlcN may have potential benefits in the treatment of osteopenic diseases such as osteoporosis, as well as in bone maintenance.
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TI Management of Rheumatic Diseases During the COVID-19 Pandemic: A National Veterans Affairs Survey of Rheumatologists
SO ARTHRITIS CARE & RESEARCH
LA English
DT Article

ID telemedicine; satisfaction; patient
AB Objective To assess the experience, views, and opinions of rheumatology providers at Veterans Affairs (VA) facilities about rheumatic disease health care issues during the COVID-19 pandemic. Methods We performed an anonymized cross-sectional survey, conducted from April 16 to May 18, 2020, of VA rheumatology providers. We assessed provider perspectives on COVID-19 issues and resilience. Results Of the 153 eligible VA rheumatologists, 103 (67%) completed the survey. A significant proportion of providers reported a >= 50% increase related to COVID-19 in visits by telephone (53%), video-based VA video connect (VVC; 44%), and clinical video telehealth with a facilitator (29%). A majority of the responders were somewhat or very comfortable with technology for providing health care to established patients during the COVID-19 pandemic using telephone (87%), VVC (64%), and in-person visits (54%). A smaller proportion were comfortable with technology providing health care to new patients. At least 65% of rheumatologists considered telephone visits appropriate for established patients with gout, osteoporosis, polymyalgia rheumatica, stable rheumatoid arthritis, stable spondyloarthritis, or osteoarthritis; 32% reported a rheumatology medication shortage. Adjusted for age, sex, and ethnicity, high provider resilience was associated with significantly higher odds ratios (ORs) of comfort with technology for telephone (OR 3.1 [95% confidence interval (95% CI) 1.1-9.7]) and VVC visits for new patients (OR 4.7 [95% CI 1.4-15.7]). Conclusion A better understanding of COVID-19 rheumatic disease health care issues using a health-system approach can better inform providers, improve provider satisfaction, and have positive effects on the care of veterans with rheumatic disease.
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TI Periostin: An Emerging Molecule With a Potential Role in Spinal Degenerative Diseases
SO FRONTIERS IN MEDICINE
LA English
DT Review
DE periostin; osteoarthritis; extracellular matrix; spinal degeneration; signaling pathways
ID intervertebral disc degeneration; nucleus pulposus cells; extracellular-matrix; tnf-alpha; periodontal-ligament; bone-formation; cathepsin k; rat model; collagen fibrillogenesis; matricellular proteins
AB Periostin, an extracellular matrix protein, is widely expressed in a variety of tissues and cells. It has many biological functions and is related to many diseases: for example, it promotes cell proliferation and differentiation in osteoblasts, which are closely related to osteoporosis, and mediates cell senescence and apoptosis in chondrocytes, which are involved in osteoarthritis. Furthermore, it also plays an

important role in mediating inflammation and reconstruction during bronchial asthma, as well as in promoting bone development, reconstruction, repair, and strength. Therefore, periostin has been explored as a potential biomarker for various diseases. Recently, periostin has also been found to be expressed in intervertebral disc cells as a component of the intervertebral extracellular matrix, and to play a crucial role in the maintenance and degeneration of intervertebral discs. This article reviews the biological role of periostin in bone marrow-derived mesenchymal stem cells, osteoblasts, osteoclasts, chondrocytes, and annulus fibrosus and nucleus pulposus cells, which are closely related to spinal degenerative diseases. The study of its pathophysiological effects is of great significance for the diagnosis and treatment of spinal degeneration, although additional studies are needed.</p>
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TI Cadmium toxicity: A role in bone cell function and teeth development
SO SCIENCE OF THE TOTAL ENVIRONMENT
LA English
DT Article
DE Cadmium; BMSC; Osteoblast; Osteoclast; Chondrocyte; Osteocyte; Teeth
ID mesenchymal stem-cells; osteoblast-like cells; induced apoptosis; osteoclast differentiation; raw264.7 cells; messenger-rna; exposure; osteoporosis; tissue; sclerostin
AB Cadmium (Cd) is a widespread environmental contaminant that causes severe bone metabolism disease, such as osteoporosis, osteoarthritis, and osteomalacia. The present review aimed to explore the molecular mechanisms of Cd-induced bone injury starting from bone cell function and teeth development Cd inhibits the differentiation of bone marrow mesenchymal stem cells (BMSCs) into osteoblasts, and directly causes BMSC apoptosis. In the case of osteoporosis, Cd mainly affects the activation of osteoclasts and promotes bone resorption. Cd-induces osteoblast injury and oxidative stress, which causes DNA damage, mitochondria! dysfunction, and endoplasmic reticulum stress, resulting in apoptosis. In addition, the

development of osteoarthritis (OA) might be related to Cd-induced chondrocyte damage. The high expression of metallothionein (MT) might reduce Cd toxicity toward osteocytes. The toxicity of Cd toward teeth mainly focuses on enamel development and dental caries. Understanding the effect of Cd on bone cell function and teeth development could contribute to revealing the mechanisms of Cd-induced bone damage. This review explores Cd-induced bone disease from cellular and molecular levels, and provides new directions for removing this heavy metal from the environment. (C) 2021 Elsevier B.V. All rights reserved.
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TI Medical overuse of therapies and diagnostics in rheumatology
SO CLINICAL RHEUMATOLOGY
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DT Article
DE Osteoarthritis; Overtesting; Overtreatment; Rheumatoid arthritis
AB Medical overuse leads to a burden on healthcare costs and potentially is harmful to patients. We wanted to address medical overuse in musculoskeletal disease and rheumatology. We performed a systemic literature review from PubMed and Embase to study medical overuse. On the initial screen, 1499 studies were identified, 839 of them were related to medical overuse. Out of these, 52 were related to overuse in musculoskeletal diseases. Finally, 20 articles were chosen for this systemic review that reported overuse in rheumatology. The article identifies issues with overtesting, including the use of dual-energy X-ray absorptiometry to screen for osteoporosis in women younger than 65 years old and the use of magnetic resonance imaging to evaluate for osteoarthritis. Studies related to

overtreatment reported over-prescription of vitamin D supplements resulting in vitamin D toxicity and increased risk of inappropriate prescriptions in patients with osteoarthritis and rheumatoid arthritis. Overtreating osteoporosis was reported after industry-sponsored education. Articles describing methods to reduce overuse included a study showing the reduction of unnecessary dual-energy X-ray absorptiometry scans after the introduction of the Choosing Wisely Campaign. Our findings suggest that there is some evidence that overtesting and overtreatment may be present in the field of rheumatology. This review aims to highlight this and help rheumatologists to be aware of overuse practices and provide appropriate evidence-based healthcare.
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TI The Gut Microbiome: a New Frontier in Musculoskeletal Research
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ID vitamin-d-receptor; bone-mineral density; immune-system; double-blind; intestinal microbiota; postmenopausal women; health; mass; exercise; supplementation
AB Purpose of the review The human gut harbors a complex community of microbes that influence many processes regulating musculoskeletal development and homeostasis. This review gives an update on the current knowledge surrounding the impact of the gut microbiota on musculoskeletal health, with an emphasis on research conducted over the last three years. Recent findings The gut microbiota and their metabolites are associated with sarcopenia, osteoporosis,

osteoarthritis, and rheumatoid arthritis. The field is moving fast from describing simple correlations to pursue establishing causation through clinical trials. The gut microbiota and their microbial-synthesized metabolites hold promise for offering new potential alternatives for the prevention and treatment of musculoskeletal diseases given its malleability and response to environmental stimuli.
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TI Local delivery systems of morphogens/biomolecules in orthopedic surgical challenges
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DT Article
DE Biomaterials; Local drug delivery; Antibiotics; Anticancerous drugs; Anti osteoarthric drugs; Bone disorders
ID bone morphogenetic protein-2; in-vivo release; fibroblast growth factor-2; mesenchymal stem-cells; mesoporous silica nanoparticles; sequential bmp-2/bmp-7 delivery; resistant staphylococcus-aureus; loaded chitosan nanoparticles; cytoplasmic drug-delivery; glycolic acid plga
AB Musculoskeletal disorders and bone deficiencies have been established among the most important human health conditions that exist today. Because of the numerous and complex functions of bone, there are many disorders, such as osteoarthritis, rheumatoid arthritis, osteoporosis and bone cancer that arise with time. Conventional therapy alone does not always yield satisfactory results and the treatment protocol is difficult, time consuming and expensive. Systemic therapy has the disadvantages of the need for long-term treatment due to being unable to create a high local concentration and the resultant risk of toxicity in addition to problems of drug transport and cost. As a result, intensive research activity on targeted local delivery of drugs/growth factors has been initiated. Local drug delivery is potentially an advantage over standard oral/intravenous therapy/other

modalities. In the present review, we have highlighted various drugs/growth factors/molecules and their potential local delivery systems for effective management of bone disorders.
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TI Structured clinical examinations in labor: rekindling the craft of obstetrics

SO JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
LA English
DT Article
DE Clinical examination; intrapartum ultrasound; labor; position; station
ID fetal head position; transvaginal digital examination; transabdominal ultrasound assessment; randomized controlled-trial; transperineal ultrasound; instrumental delivery; vaginal examination; 2nd-stage; sonography; morbidity
AB Objectives: Exact knowledge of fetal station and position is of paramount importance for reliable surveillance of labor progress and a prerequisite for safe operative vaginal procedures. Detailed clinical assessments are thoroughly described in old textbooks, but almost forgotten in contemporary obstetrics. Ultrasound is suggested as an objective diagnostic tool in active labor. Several publications have demonstrated a low correlation between ultrasound and clinical assessment of fetal head station and position, but the methods of clinical assessment in these studies are poorly described. We wanted to explore if a quality clinical assessment could perform better than clinical assessment in previous publications, by analyzing the correlation between a structured method of clinical assessment and intrapartum ultrasound. Methods: In all, 100 laboring women with cervical dilatation >= 7 cm were included in a prospective cohort study at Oslo University Hospital-Ulleval from October to December 2016. The study design was cross-sectional. Clinical examinations were performed by one special educated consultant (JKI), and transabdominal and transperineal ultrasound clips were recorded and examined by a blinded expert in intrapartum ultrasound (TME). Fetal position was classified as a clock face with 12 units (hourly divisions) and thereafter categorized as occiput anterior (OA), left occiput transverse (LOT), occiput posterior (OP), and right occiput transverse (ROT) positions. Fetal station was categorized clinically from -5 to +5 and measured with ultrasound as angle of progression (AoP) and head-perineum distance (HPD). AoP is the angle between a longitudinal line through the symphysis and a tangent to the head contour. HPD is the shortest distance between the fetal skull and the perineum. Results: Eight women were excluded due to strong contractions between clinical assessments and ultrasound measurements, fetal distress, or incomplete examinations. Fetal position assessed with ultrasound and clinical examination agreed exactly in 48/92 (52%) of cases, within one unit (hour) in 87/92 (95%) of cases and within two units in 90/92 (98%) of cases. It differed by three units in one case and by five units in one case. The agreement categorized into OA, LOT, OP, and ROT was good (Cohen's kappa 0.72; 95% CI 0.61-0.84). For station, the agreement was very good for both HPD (Pearson correlation coefficient r = 0.86; 95% CI 0.80-0.91) and AoP (r = 0.77; 95% CI to 0.67-0.84). The correlation between HPD and AoP was good (r = 0.76; 95% CI 0.65-0.84). Conclusion: We found very good correlations between structured clinical assessments and ultrasound examinations, suggesting that an objective quality in clinical examinations is possible to achieve. More focus on clinical skills training may improve accuracy for clinicians.
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NR 27
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TI Novel Insights Into the Multifaceted Functions of RNA n6-Methyladenosine Modification in Degenerative Musculoskeletal Diseases
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE N6-methyladenosine; degenerative musculoskeletal diseases; osteoarthritis; osteoporosis; sarcopenia; degenerative spinal disorders
ID body-mass index; messenger-rna; nucleotide-sequences; knee osteoarthritis; structural basis; nuclear-rna; m(6)a rna; binding; n6-methyladenosine; osteoporosis
AB N-6-methyladenosine (m(6)A) is an important modification of eukaryotic mRNA. Since the first discovery of the corresponding demethylase and the subsequent identification of m(6)A as a dynamic modification, the function and mechanism of m(6)A in mammalian gene regulation have been extensively investigated. "Writer", "eraser" and "reader" proteins are key proteins involved in the dynamic regulation of m(6)A modifications, through the anchoring, removal, and interpretation of m(6)A modifications, respectively. Remarkably, such dynamic modifications can regulate the progression of many diseases by affecting RNA splicing, translation, export and degradation. Emerging evidence has identified the relationship between m(6)A modifications and degenerative musculoskeletal diseases, such as osteoarthritis, osteoporosis, sarcopenia and degenerative spinal disorders. Here, we have comprehensively summarized the evidence of the pathogenesis of m(6)A modifications in degenerative musculoskeletal diseases. Moreover, the potential molecular mechanisms, regulatory functions and clinical implications of m(6)A modifications are thoroughly discussed. Our review may provide potential prospects for addressing key issues in further studies.
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TI Endotypes of primary osteoarthritis identified by plasma metabolomics analysis
SO RHEUMATOLOGY
LA English
DT Article
DE osteoarthritis; endotypes; butyrylcarnitine; arginine; lysophosphatidylcholine
ID synovial-fluid; l-arginine; lysophosphatidylcholine; classification; cells; ratio
AB Objective. To identify endotypes of osteoarthritis (OA) by a metabolomics analysis. Methods. Study participants included hip/knee OA patients and controls. Fasting plasma samples were metabolomically profiled. Common factor analysis and K-means clustering were applied to the metabolomics data to identify the endotypes of OA patients. Logistic regression was utilized to identify the most significant metabolites contributing to the endotypes. Clinical and epidemiological factors were examined in relation to the identified OA endotypes. Results. Six hundred and fifteen primary OA patients and 237 controls were included. Among the 186 metabolites measured, 162 passed the quality control analysis. The 615 OA patients were classified in three clusters (A, 66; B, 200; and C, 349). Patients in cluster A had a significantly higher concentration of butyrylcarnitine (C4) than other clusters and controls (all $P < 0.0002$). Elevated C4 is thought to be related to muscle

weakness and wasting. Patients in cluster B had a significantly lower arginine concentration than other clusters and controls (all P < 7.98 x 10(-11)). Cluster C patients had a significantly lower concentration of lysophosphatidylcholine (with palmitic acid), which is a pro-inflammatory bioactive compound, than other clusters and controls (P < 3 .7 9 x 10(-6)). Further, cluster A had a higher BMI and prevalence of diabetes than other clusters (all P <= 0.0009), and also a higher prevalence of coronary heart disease than cluster C (P = 0 .04) . Cluster B had a higher prevalence of coronary heart disease than cluster C (P = 0 .003) whereas cluster C had a higher prevalence of osteoporosis (P = 0 .009). Conclusion. Our data suggest three possible clinically actionable endotypes in primary OA: muscle weakness, arginine deficit and low inflammatory OA.
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NR 50
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Z9 40
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PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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J9 RHEUMATOLOGY
JI RHEUMATOLOGY
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WC Rheumatology
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Fu, CY
Wang, L
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Liang, ZJ
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AF Peng, Lihong
Fu, Chenying
Wang, Lu
Zhang, Qing
Liang, Zejun
He, Chengqi
Wei, Quan
TI The Effect of Pulsed Electromagnetic Fields on Angiogenesis
SO BIOELECTROMAGNETICS
LA English
DT Review
DE pulsed electromagnetic field (PEMF); angiogenesis; endothelial cells; growth factor
AB A pulsed electromagnetic field (PEMF) has been used to treat inflammation-based diseases such as osteoporosis, neurological injury, and osteoarthritis. Numerous animal experiments and in vitro studies have shown that PEMF may affect angiogenesis. For ischemic diseases, in theory, blood flow may be richer by increasing the number of blood vessels which supply blood to ischemic tissue. PEMF plays a role in enhancing angiogenesis, and their clinical application may go far beyond the current scope. In this review, we analyzed and summarized the effects and possible mechanisms of PEMF on angiogenesis. Most studies have shown that PEMF with specific parameters can promote angiogenesis, which is manifested by an increased vascular growth rate and increased capillary density. The potential mechanisms consist of promoting vascular endothelial cell proliferation, migration, and tube formation, and increasing the expression level of vascular endothelial growth factor (VEGF), fibroblast growth factor 2 (FGF2), angiopoietin-2 (Ang-2), and other angiogenic growth factors. Additionally, PEMF has an impact on the activation of voltage-gated calcium channels (VGCC). Bioelectromagnetics. (c) 2021 Bioelectromagnetics Society.
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TC 37
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PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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WC Biology; Biophysics
SC Life Sciences & Biomedicine - Other Topics; Biophysics
GA RG7CB
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AU Zheng, ZR
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AF Zheng, Zhirong
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TI Thoracolumbar flexion dysfunction and thoracolumbar compression fracture in postmenopausal women: a single-center retrospective study
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Thoracolumbar flexion dysfunction; Vertebral fracture; Osteoporosis; Postmenopausal women; Quantitative computed tomography
ID community-dwelling women; quality-of-life; vertebral fracture; disc space; osteoporotic fractures; risk; kyphosis; spine; biomechanics; degeneration
AB Objective To investigate whether thoracolumbar flexion dysfunctions increase the risk of thoracolumbar compression fractures in postmenopausal women. Methods The records of postmenopausal women with thoracolumbar vertebral compression fractures and without vertebral compression fractures were surveyed. Demographic data, clinical data, and quantitative computed tomography (QCT) findings were compared between the groups. Chi-squared tests, unpaired t-tests, Spearman, and Mann-Whitney U were used to assess the group characteristics and proportions. The relationship between the risk of fracture and the difference of Cobb's angle of thoracolumbar segment (DCTL) was evaluated by logistic regression. DCTL was calculated by subtracting thoracolumbar Cobb's angles (TLCobb's) from thoracolumbar hyperflexion Cobb's angles (TLHCobb's). Quantitative computed tomography (QCT) values and spinal osteoarthritis (OA) of postmenopausal women in the two groups were compared. Results 102 of 312 were enrolled to the study group of postmenopausal women with the fracture, and 210 of 312 were enrolled to the control group of postmenopausal women without the fracture. There were significant differences in QCT values and spinal OA including disc narrowing (DSN) and osteophytes (OPH) between the two groups ($p < 0.001$ for all four). The risk of thoracolumbar compression fractures in the postmenopausal women with DCTL <= 8.7 degrees was 9.95 times higher (95% CI 5.31-18.64) than that with > 8.7 degrees after adjusting for age, BMI, and QCT values. Conclusion Low DCTL may be a risk factor of thoracolumbar compression fractures in postmenopausal women, and a DCTL <= 8.7 degrees can be a threshold value of thoracolumbar compression fractures.
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FU National Natural Science Foundation of China [81972128]; Medical big data and artificial intelligence of Chinese PLA General Hospital Foundation [2019MBD-022]
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AU Kato, M
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AF Kato, Michitaka
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TI Calcaneal insufficiency fractures following ipsilateral total knee arthroplasty
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE Total knee arthroplasty; Calcaneal stress fracture; Calcaneal insufficiency fracture; Osteoporosis; Complication
ID stress-fracture; hindfoot alignment; femoral-neck; risk; deformity; ankle; pain
AB Introduction: Only a few reports have described calcaneal insufficiency fractures (IFs) following total knee arthroplasty (TKA). Herein, we describe nine cases of calcaneal IFs following ipsilateral TKA. The purpose of this study was to investigate the incidence of calcaneal fractures following TKA and determine the characteristics of patients with IFs. Patients and methods: We retrospectively investigated cases of calcaneal IF that occurred following TKA. We collected and analyzed radiographic and magnetic resonance imaging (MRI) findings as well as patient demographic data. We compared the demographic data, bone mineral density (BMD), and preoperative hip-knee-ankle angle (HKA) between cases with a calcaneal fracture following TKA and 100 cases without a fracture following TKA. Results: We performed a total of 1548 knee arthroplasties at our clinic from 2011 to 2020. Nine calcaneal IFs in eight patients were diagnosed following ipsilateral TKA. All patients were women with varus knee osteoarthritis (mean age, 71.8 years). The average change in the alignment angle was 14.7 degrees +/- 5.4 degrees. In eight cases, dysfunction was observed in the opposite lower limb. The postoperative onset of hindfoot pain started at an average of 5.6 months. In seven patients, calcaneal fractures occurred idiopathically, but in one patient, two fractures occurred after long-distance walking. No abnormal findings on a calcaneus radiograph were seen for six fractures. MRI demonstrated a definite fracture line and bone marrow

edema in all patients. All patients, except one with type 2 diabetes mellitus (T2DM), had osteoporosis. Fractures healed without complications in eight patients; however, the calcaneal anterior facet fracture became displaced and caused a flat foot in one case. The calcaneal IF rate was 0.58% among all cases. Besides one case with T2DM, significant differences were observed in preoperative HKA and BMD between cases with a calcaneal fracture following TKA and those without a fracture. Conclusions: A change in the load on the calcaneus due to changes in the alignment of the lower extremities after TKA may cause calcaneal IFs. Orthopedic surgeons should be aware of the possible occurrence of calcaneal IFs following TKA, especially in women with osteoporosis and severe varus knee. (c) 2021 Elsevier Ltd. All rights reserved.
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AU Visconti, VV
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TI DNA Methylation Signatures of Bone Metabolism in Osteoporosis and Osteoarthritis Aging-Related Diseases: An Updated Review
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE epigenetics; DNA methylation; bone metabolism; osteoporosis; osteoarthritis; aging-related diseases
ID cartilage
AB DNA methylation is one of the most studied epigenetic mechanisms that play a pivotal role in regulating gene expression. The epigenetic component is strongly involved in aging-bone diseases, such as osteoporosis and osteoarthritis. Both are complex multi-factorial late-onset disorders that represent a globally widespread health problem, highlighting a crucial point of investigations in many scientific studies. In recent years, new findings on the role of DNA methylation in the pathogenesis of aging-bone diseases have emerged. The aim of this systematic review is to update knowledge in the field of DNA methylation associated with osteoporosis and osteoarthritis, focusing on the specific tissues involved in both pathological conditions.

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NR 96
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Z9 45
U1 0
U2 24
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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AF Arthur, Agnieszka
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TI Eph-Ephrin Signaling Mediates Cross-Talk Within the Bone Microenvironment
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE bone marrow microenvironment; bone marrow mesenchymal stem cells; osteogenic differentiation; hematopoietic stem cells; osteoimmunology; vasculature; musculoskeletal pathology; Eph-ephrin communication
AB Skeletal integrity is maintained through the tightly regulated bone remodeling process that occurs continuously throughout postnatal life to replace old bone and to repair skeletal damage. This is maintained primarily through complex interactions between bone resorbing osteoclasts and bone forming osteoblasts. Other elements within the bone microenvironment, including stromal, osteogenic, hematopoietic, endothelial and neural cells, also contribute to maintaining skeletal integrity. Disruption of the dynamic interactions between these diverse cellular systems can lead to poor bone health and an increased susceptibility to skeletal diseases including osteopenia, osteoporosis, osteoarthritis, osteomalacia, and major fractures. Recent reports have implicated a direct role for the Eph tyrosine kinase receptors and their ephrin ligands during bone development, homeostasis and skeletal repair. These membrane-bound molecules mediate contact-dependent signaling through both the Eph receptors, termed forward signaling, and through the ephrin ligands, referred to as reverse signaling. This review will focus on Eph/ephrin cross-talk as mediators of hematopoietic and stromal cell communication, and how these interactions contribute to blood/ bone marrow function and skeletal integrity during normal steady state or pathological conditions.
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FU National health and Medical Council Australian project [APP1142954]
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AF White, R.
Krueger, D.
De Guio, F.
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Binkley, N.
TI An Exploratory Study of the Texture Research Investigational Platform (TRIP) to Evaluate Bone Texture Score of Distal Femur DXA Scans - A TBS-Based Approach
SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE Knee arthroplasty; DXA; TBS; TRIP
ID total knee arthroplasty; periprosthetic femoral fractures; mineral density changes; follow-up; total hip; prevalence; classification; osteoarthritis; osteoporosis; replacement
AB Poor bone status is associated with increased complications following orthopedic surgery. Therefore, assessing site-specific skeletal status prior to or after

orthopedic surgery to optimize outcomes is appealing. The trabecular bone score (TBS) approach, a surrogate for microarchitecture, was adapted to the Texture Research Investigational Platform (TRIP), which allows assessment of many skeletal sites imaged by various modalities. TRIP generates a bone texture score (TBS ORTHO), which could potentially guide surgical decision-making and offer insight into postsurgical fracture risk. As distal femur bone loss occurs following total knee arthroplasty (TKA), we hypothesized that TBS ORTHO after TKA would identify poorer texture in the operated femur compared to the nonoperated. We evaluated 30 subjects (15 M/15 F) with unilateral TKA 2-5 yr previously, mean age 67.9 yr and body mass index 30 kg/m(2). Using a Lunar iDXA, lumbar spine and entire femur scans were obtained, the latter using the atypical femur fracture feature. Distal femur bone mineral density (BMD) and TBS ORTHO were obtained using manual regions of interest (ROI) at 15% and 25% of leg length from the intercondylar notch. TBS ORTHO was determined using distal femur DICOM images and TRIP v1.0 (Medimaps, France). Differences in operated vs nonoperated femur were evaluated by paired t test. As previously reported, operated leg BMD was approx 10% lower at 15% and 25% ROIs. Similarly, TBS ORTHO values in the operated leg were approx 5% lower ($p < 0.05$) at these same ROIs. Distal femur TBS ORTHO and BMD were largely unrelated. TBS ORTHO reproducibility at these ROIs was approx 3.5%. In conclusion, this pilot study documents the feasibility of reproducibly obtaining distal femur TBS ORTHO values. Lower values were observed in the surgical leg, consistent with the bone loss that follows TKA. Further work is indicated to refine TRIP use and evaluate whether such data provides guidance for surgical decision-making and improves periprosthetic fracture prediction.
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TI The use of bone turnover markers for monitoring the treatment of osteoporosis in postmenopausal females undergoing total knee arthroplasty: a prospective randomized study
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Bone turnover markers; Postmenopausal osteoporosis; Total knee arthroplasty; Monitoring treatment; Osteoarthritis
AB BackgroundOsteoporosis (OP) and osteoarthritis (OA) commonly coexist in postmenopausal females. The decrease in bone density and increase in bone

resorption in postmenopausal females with OP may consequently affect the surgical outcome of total knee arthroplasty (TKA). However, clinicians often ignore monitoring the treatment of OP in the perioperative management of TKA. Bone turnover marker (BTM) can timely and accurately reflect bone metabolism to monitor the treatment of OP. The purpose of this study was to investigate the effect of BTM monitoring to guide the treatment of OP in postmenopausal females undergoing TKA.MethodsPostmenopausal females with OP who underwent primary unilateral TKA were randomly divided into two groups (monitoring group and control group), given oral medication (alendronate, calcitriol, and calcium), and followed for 1 year. In the monitoring group, serum BTMs (C-telopeptide of type I collagen (CTX-I), N-terminal propeptide of type I procollagen (PINP), and 25(OH)D) were assessed preoperatively and repeated postoperatively; alendronate was withdrawn when CTX-I and PINP reached the reference interval; and calcitriol and calcium were withdrawn when 25(OH)D reached the reference interval. In the control group, oral medication was implemented for a uniform duration of 3 months. During the 1-year follow-up, the mean maximum total point motion (MTPM) of the tibial component, bone mineral density (BMD), visual analog scale (VAS) score, range of motion, and Oxford Knee Score (OKS) score were obtained.ResultsIn the monitoring group, BTM monitoring prolonged the medication duration, but did not cause more adverse reactions than in the control group. The mean MTPM values at 6 m and 12 m in the monitoring group were lower than those in the control group, and the BMD at 12 m in the monitoring group was significantly higher than that in the control group. Patients in the monitoring group had lower VAS scores at 6 m and higher OKS scores at 6 m and 12 m than those in the control group.ConclusionIn postmenopausal females with osteoporosis undergoing primary TKA, the application of BTM monitoring to guide the treatment of osteoporosis can enhance bone density, maintain prosthesis stability, and improve surgical outcome.Trial registrationChiCTR ChiCTR-INR-17010495. Registered on 22 January 2017
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TI Circular RNAs in osteoporosis: expression, functions and roles
SO CELL DEATH DISCOVERY

LA English
DT Review
ID postmenopausal osteoporosis; osteoclast differentiation; stem-cells; bone; osteogenesis; promotes
AB Osteoporosis, which is caused by an imbalance in osteoblasts and osteoclasts, is a global age-related metabolic disease. Osteoblasts induce osteocyte and bone matrix formation, while osteoclasts play an important role in bone resorption. Maintaining a balance between osteoblast formation and osteoclastic absorption is crucial for bone remodeling. Circular RNAs (circRNAs), which are characterized by closed-loop structures, are a class of novel endogenous transcripts with limited protein-coding abilities. Accumulating evidence indicates that circRNAs play important roles in various bone diseases, such as osteosarcoma, osteoarthritis, osteonecrosis, and osteoporosis. Recent studies have shown that circRNAs regulate osteoblast and osteoclast differentiation and may be potential biomarkers for osteoporosis. In the current review, we summarize the expression, function, and working mechanisms of circRNAs involved in osteoblasts, osteoclast differentiation, and osteoporosis.
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NR 59
TC 13
Z9 18
U1 0
U2 14
PU SPRINGERNATURE
PI LONDON
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SN
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JI Cell Death Discov.
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IS 1
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WC Cell Biology
SC Cell Biology
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PT J
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TI Effects of a dynamic combined training on impulse response for middle-aged and elderly patients with osteoporosis and knee osteoarthritis: a randomized control trial
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Dynamic combined training; Musculoskeletal conditions; Maximal voluntary contraction (MVC); Rate of force development (RFD)
ID hydraulic-resistance exercise; force development; muscle strength; older women; sarcopenia; fitness; adults; adaptation; prevalence; osteopenia
AB Dynamic combined training is a crucial component in treating musculoskeletal conditions to increase muscle strength and improve functional ability. This randomized control trial aimed to examine the effect of dynamic combined training on muscle strength and contractile rate of force development (RFD) in patients with osteoporosis (OP) and knee osteoarthritis (KOA). 58 participants with OP or KOA were randomly assigned to a control group (CG) (CGOP, n = 12; CGKOA, n = 15) or training group (TG) (TGOP, n = 14; TGKOA, n = 17). The training group participated in a 12-week, three-days-per-week supervised program consisting of stretching and warm-up exercises (10 min), hydraulic resistance training (40 min), and cool-down and relaxation exercises (10 min). All participants were evaluated at baseline and post-training. The maximal voluntary contraction (MVC) and contractile RFD at 0-200 ms increased significantly in middle-aged and older patients with OP. As for KOA, the dynamic combined training program was effective in improving the muscle strength. The maximal voluntary contraction (MVC) and contractile RFD at 0-200 ms increased significantly (by 29.22%, P = .000 and 27.25%, P = .019, respectively) in middle-aged and older patients with OP. In the KOA group, MVC and contractile RFD improved but did not reach statistical significance. The dynamic combined training program is effective for health promotion in older adults with OP or KOA.
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NR 48
TC 6
Z9 11
U1 0
U2 30
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SN 1594-0667
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J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
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EA FEB 2020
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
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PT J
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TI An assessment of intervention thresholds for very high fracture risk applied to the NOGG guidelines A report for the National Osteoporosis Guideline Group (NOGG)
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Anabolic treatments; Assessment guidelines; High risk; Intervention thresholds; Very high risk
ID postmenopausal women; teriparatide; management; frax; prevention; romosozumab; alendronate; efficacy
AB The National Osteoporosis Guideline Group (NOGG) has developed intervention thresholds based on FRAX (R) to characterise patients at high and very high risk of fracture. Introduction Guidelines for the assessment of fracture risk have begun to categorise patients eligible for treatment into high and very high risk of fracture to inform choice of therapeutic approach. The aim of the present study was to develop intervention thresholds based on the hybrid assessment model of NOGG. Methods We examined the impact of intervention thresholds in a simulated cross-sectional cohort of women age 50 years or more from the UK with the distribution of baseline characteristics based on that in the FRAX cohorts. The prevalence of very high risk using the hybrid model was compared with age-dependent thresholds used by the International Osteoporosis Foundation and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (IOF/ESCEO). The appropriateness of thresholds was tested based on the populations treated with anabolic agents. Results With an upper intervention threshold using the IOF/ESCEO criteria, 56% of women age 50 years or more would be characterised at very high risk. This compares with 36% using the IOF/ESCEO criteria and an age-specific intervention threshold over all ages. With an upper intervention threshold of 1.6 times the pre-existing intervention threshold, 10% of women age 50 years or more would be characterised at very high risk. The data from phase 3 studies indicate that most trial participants exposed to romosozumab or teriparatide would fall into the very high-risk category. Conclusions Proposals for FRAX-based criteria for very high risk for the NOGG hybrid model categorise a small proportion of women age 50 years or more (10%) in this highest risk stratum. The level of risk identified was comparable to that of women enrolled in trials of anabolic agents.
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NR 31
TC 53
Z9 60
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PU SPRINGER LONDON LTD
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SN 0937-941X
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J9 OSTEOPOROSIS INT
JI Osteoporosis Int.
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IS 10
BP 1951
EP 1960
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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TI Impact of Exposure to Ambient Fine Particulate Matter Pollution on Adults with Knee Osteoarthritis
SO INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH
LA English
DT Article
DE knee osteoarthritis; fine particulate matter; air pollution; outpatients; time-series; China
ID air-pollution; global burden; prevalence; hip; disease; time; osteoporosis; cytokines; china; older
AB The impact of exposure to fine particulate matter (PM2.5) on the incidence of knee osteoarthritis is unclear, especially in Beijing which is a highly polluted city. We conducted a time-series study to examine the correlation between PM2.5 exposure and outpatient visits for knee osteoarthritis in Beijing. Changes (in percentage) in the number of outpatient visits corresponding to every 10-mu g/m(3) increase in the PM2.5 concentration were determined using a generalized additive quasi-Poisson model. There were records of 9,797,446 outpatient visits for knee osteoarthritis in the study period from 1 January 2010 to 31 December 2017. The daily concentration of PM2.5 was 86.8 (74.3) mu g/m(3) over this period. A 10-mu g/m(3) increase in PM2.5 concentrations on lag days 0-3 was associated with a 1.41% (95% confidence interval: 1.40-1.41%) increase in outpatient visits for knee osteoarthritis. Females and patients aged above 65 years were more sensitive to the adverse effects of PM2.5 exposure. The present findings demonstrate that

short-term exposure to PM2.5 resulted in an increase in the number of outpatient visits for knee osteoarthritis in Beijing. The findings shed light on the effects of air pollution on knee osteoarthritis and could guide risk-mitigating strategies in cities such as Beijing.
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AF Zhuang, Chenyang
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Tian, Bo
Lin, Hong
TI Jintiange Capsules Ameliorate Osteoarthritis by Modulating Subchondral Bone Remodeling and Protecting Cartilage Against Degradation
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE Jintiange capsule; osteoarthritis; subchondral bone; cartilage; osteoclast; chondrocyte
ID traditional chinese medicine; articular-cartilage; osteoporosis; epidemiology;

degeneration; pathogenesis; mechanism
AB Osteoarthritis (OA) is the most prevalent joint disease worldwide, making it a major cause of pain and disability. Identified as a chronic and progressive disease, effective treatment at the early stages of OA has become critical to its management. Jintiange (Jtg) capsules are a traditional Chinese medicine produced from multiple organic components of various animal bones and routinely used to treat osteoporosis in China. However, the effect of Jtg on subchondral bone and cartilage degeneration in OA remains unknown. The purpose of the present study was to investigate the biomolecular role and underlying mechanisms of Jtg in OA progression. Herein, we found that Jtg inhibited receptor activator of nuclear factor-kappa B ligand (RANKL)-induced osteoclast formation and it functions through the NF-kappa B signaling pathway. Jtg also inhibited chondrocyte apoptosis via reducing the reactive oxygen species concentration in these cells. Moreover, in vivo evaluation revealed that Jtg significantly attenuates subchondral bone remodeling and cartilage destruction in anterior cruciate ligament transection (ACLT) mouse models. Taken together, our data demonstrate that Jtg inhibits osteoclast differentiation in subchondral bone and chondrocyte apoptosis in cartilage, supporting its potential therapeutic value for treating OA.
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AF Shah, A.
Wu, F.
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TI The association between incident vertebral deformities, health-related quality of life and functional impairment: a 10.7-year cohort study
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Osteoporosis; Physical function; Quality of life; Vertebral fracture; Vertebral morphometry
ID postmenopausal women; back-pain; assessment questionnaire; fractures; osteoporosis; prevalent; men; impact; osteoarthritis; reliability
AB We aimed to describe longitudinal changes in health-related quality of life (HRQoL) measures associated with incident vertebral deformities (VDs) over 10.7

years. Incident VDs are associated with clinically significant functional impairment in men, and reduction in overall HRQoL in older women. Increasing severity and number of incident VDs are associated with clinically meaningful functional impairment in men, but not women. Introduction To describe associations between incident VD and changes in HRQoL and functional ability in older adults over 10.7 years. Methods Participants (n = 780) underwent whole-body dual-energy X-ray absorptiometry (DXA) scans at baseline, 2.5, 5.1 and 10.7 years later. VD was defined as >= 25% reduction in anterior height relative to posterior height of vertebrae from T4 to L4. An incident VD was defined as a new VD at any follow-up visit. Assessment of Quality of Life (AQoL-4D) questionnaire and Health Assessment Questionnaire-Disability Index (HAQ-DI) were used to assess HRQoL and functional impairment. Changes in AQoL and HAQ-DI associated with incident VD were analysed using multilevel mixed-effects linear regression. Log binomial regression was used to examine clinically relevant changes and effects of severity and number of VD. Results The incidence of VD was 37% over 10.7 years. In women, incident VDs were associated with annual reduction in AQoL utility score (beta = -0.005, 95% CI -0.008 to -0.002). Men had increased risk of clinically significant reduction in HAQ-DI (IRR = 1.76, 95% CI 1.07-2.89). Men had increased risk of clinically important functional impairment with increasing severity (IRR 1.76, 95% CI 1.04-2.95 for mild vs IRR 1.98, 95% CI 1.13-3.47 for moderate to severe VD) as well as number of incident VD (IRR 1.85, 95% CI 1.17-2.93 for one vs IRR 1.88, 95% CI 0.94-3.78 for >= 2 VDs). Such associations were not observed in women. Conclusions Incident VDs are associated with clinically significant functional impairment in men, and reduction in overall HRQoL in older women. Increasing severity and number of incident VDs are associated with clinically meaningful functional impairment in men, but not women.
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NR 37
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PT J
AU Zhang, YH
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Zhang, WF
AF Zhang, Yuhan
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Zhang, Weifen
TI Berberine for bone regeneration: Therapeutic potential and molecular mechanisms

SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE Berberine; Bone regeneration; Traditional Chinese medicine; Drug delivery; Cellular mechanism
ID attenuates osteoclast differentiation; resorption in-vitro; nf-kappa-b; osteoblast differentiation; kampo formulas; iliac crest; stem-cells; tissue; rankl; graft
AB Ethnopharmacological relevance: Berberine is a quaternary ammonium isoquinoline alkaloid, mainly extracted from plants berberaceae, papaveraceae, ranunculaceae and rutaceae such as coptis chinensis Franch, Phellodendron chinense, and berberis pruinosa. The plants are extensively used in traditional medicine for treating infection, diabetes, arrhythmia, tumor, osteoporosis et al. Pharmacological studies showed berberine has effects of antiinflammation, anti-tumor, lower blood lipid, lower blood glucose, anti-osteoporosis, anti-osteoarthritis et al. Aim of the study: This review aims to summarize the application of natural herbs that contain berberine, the further use and development of berberine, the effects as well as mechanism of berberine on osteoblasts and osteoclasts, the recent advances of in vivo studies, in order to provide a scientific basis for its traditional uses and to prospect of the potential applications of berberine in clinics. Method: The research was achieved by retrieving from the online electronic database, including PubMed, Web of Science, Google Scholar and China national knowledge infrastructure (CNKI). Patents, doctoral dissertations and master dissertations are also searched. Results: Berberine has a long history of medicinal use to treat various diseases including bone disease in China. Recent studies have defined its function in promoting bone regeneration and great potential in developing new drugs. But the systemic mechanism of berberine on bone regeneration still needs more research to clarify. Conclusion: This review has systematically summarized the application, pharmacological effects, mechanism as well as in vivo studies of berberine and herbs which contain berberine. Berberine has a definite effect in promoting the proliferation and differentiation of osteoblasts as well as inhibiting the production of osteoclasts to promote bone regeneration. However, the present studies about the system mechanisms and pharmacological activity of berberine were incomplete. Applying berberine for new drug development remains an exciting and promising alternative to bone regeneration engineering, with broad potential for therapeutic and clinical practice.
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TI Prospective midterm results of a new convertible glenoid component in anatomic shoulder arthroplasty: a cohort study
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
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DT Article
DE Shoulder arthroplasty; Cementless glenoid; Convertible glenoid; Midterm results
ID follow-up; polyethylene; osteoarthritis; replacement; prosthesis; conversion; survival; system; bone; stem
AB Purpose The purpose of our study was to evaluate the clinical and radiological results of a new anatomic convertible cementless glenoid component. Methods Forty-eight patients with a mean age of 67.3 years were clinically and radiologically followed-up with a mean of 49 months. Indications for glenoid replacement were A2 glenoid wear in 21.7%, B1 glenoid wear in 28.3%, B2 glenoid wear in 28.3%, B3 glenoid wear in 13%, D glenoid wear in 2.2%, and glenoid component loosening in 6.5%. Results The Constant-Murley score improved significantly ($p < 0.0001$) from

50% pre-OP to 103% post-OP. Patients with a B3 glenoid type according to Walch achieved a significant (p = 0.044) lower Constant-Murley Sscore post-OP compared to patients with a B1 glenoid type (88% vs 106%). The mean subluxation index changed significantly (p < 0.0001) from 0.54 pre-OP to 0.46 post-OP. At the metal-back bone interface an incomplete radiolucent line < 1 mm was observed in two cases (4.2%) and an incomplete radiolucent line < 2 mm was observed in another two cases (4.2%). PE dissociation occurred in two cases. No glenoid loosening was observed. The implant related revision rate was 4.2% (2 cases). All components (n = 612.5%) requiring conversion to reverse were converted without any further complications or loosening. Conclusion Good functional results can be achieved in cases with a B1 and a B2 glenoid after anatomic shoulder arthroplasty using the described metal back glenoid. A conversion from an anatomic to a reverse glenoid component were possible in all cases without any further complications. Conversion of the anatomic glenoid component to a reverse system alleviates revision surgery.
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TI The risk of revision following total hip arthroplasty in patients with inflammatory bowel disease, a registry based study
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DT Article
ID bone-mineral density; knee arthroplasty; corticosteroid use; natural-history;

crohns-disease; microbiome; health; osteoporosis; metabolism; fractures
AB Inflammatory bowel disease (IBD) is characterized by chronic inflammation of the intestinal tract and is associated with decreased bone mineral density. IBD patients are at higher risk of osteopenia, osteoporosis and fracture compared to non-IBD patients. The impact of IBD on the performance of orthopedic implants has not been well studied. We hypothesized that a history of IBD at the time of primary total hip arthroplasty (THA) would increase the risk of subsequent failure as assessed by revision surgery. A retrospective implant survival analysis was completed using the Swedish Hip Arthroplasty Registry and the Sweden National Patient Register. A total of 150,073 patients undergoing THA for osteoarthritis within an 18-year period were included in the study. THA patients with (n = 2,604) and without (n = 147,469) a history of IBD at the time of THA were compared with primary revision as the main endpoint and adjusted using sex, age category and comorbidity (Elixhauser scores) as covariates. We found that patients with a history of IBD had a relatively higher risk of revision surgery for septic causes while the non-IBD patients had a relatively higher risk of revision for aseptic causes (p = 0.004). Our findings suggest there may be an association between gut health and THA performance.
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NR 74
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Z9 12
U1 0
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J9 PLOS ONE
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TI An oligopeptide/aptamer-conjugated dendrimer-based nanocarrier for dual-targeting delivery to bone
SO JOURNAL OF MATERIALS CHEMISTRY B
LA English
DT Article
AB Bone targeting is one of the most potentially valuable therapeutic methods for medically treating bone diseases, such as osteoarthritis, osteoporosis, nonunion bone defects, bone cancer, and myeloma-related bone disease, but its efficacy remains a challenge due to unfavorable bone biodistribution, off-target effects, and the lack of cell specificity. To address these problems, we synthesized a new dual-targeting nanocarrier for delivery to bone by covalently modifying the G4.0 PAMAM dendrimer with the C11 peptide and the CH6 aptamer (CH6-PAMAM-C11). The molecular structure was confirmed using H-1-NMR and FT-IR spectroscopy. CLSM results showed that the novel nanocarrier could successfully accumulate in the targeted cells, mineralized areas and tissues. DLS and TEM demonstrated that CH6-PAMAM-C11 was approximately 40-50 nm in diameter. In vitro targeting experiments confirmed that the C11 ligand had a high affinity for HAP, while the CH6 aptamer had a high affinity for osteoblasts. The in vivo biodistribution analysis showed that CH6-PAMAM-C11 could rapidly accumulate in bone within 4 h and 12 h and then deliver drugs to sites of osteoblast activity. The components of CH6-PAMAM-C11 were well excreted via the kidneys. The accumulation of many more CH6-PAMAM-C11 dual-targeting nanocarriers than single-targeting nanocarriers was observed in the periosteal layer of the rat skull, along with aggregation at sites of osteoblast activity. All of these results indicate that CH6-PAMAM-C11 may be a promising nanocarrier for the delivery of drugs to bone, particularly for the treatment of osteoporosis, and our research strategy may serve as a reference for research in targeted drug, small molecule drug and nucleic acid delivery.
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TC 35
Z9 38
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PI CAMBRIDGE

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WC Materials Science, Biomaterials
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AU Nowell, WB
Gavigan, K
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AF Nowell, W. Benjamin
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TI Which patient-reported outcomes do rheumatology patients find important to track digitally? A real-world longitudinal study in ArthritisPower
SO ARTHRITIS RESEARCH & THERAPY

LA English
DT Article
DE Patient-reported outcomes; Real-world evidence; Rheumatoid arthritis
ID inadequate response; baricitinib; fatigue; flare; set
AB Background Patient-reported outcomes (PROs) are increasingly used to track symptoms and to assess disease activity, quality of life, and treatment effectiveness. It is therefore important to understand which PROs patients with rheumatic and musculoskeletal disease consider most important to track for disease management. Methods Adult US patients within the ArthritisPower registry with ankylosing spondylitis, fibromyalgia syndrome, osteoarthritis, osteoporosis, psoriatic arthritis, rheumatoid arthritis, and systemic lupus erythematosus were invited to select between 3 and 10 PRO symptom measures they felt were important to digitally track for their condition via the ArthritisPower app. Over the next 3 months, participants (pts) were given the option to continue tracking their previously selected measures or to remove/add measures at 3 subsequent monthly time points (month [m] 1, m2, m3). At m3, pts prioritized up to 5 measures. Measures were rank-ordered, summed, and weighted based on pts rating to produce a summary score for each PRO measure. Results Among pts who completed initial selection of PRO assessments at baseline (N = 253), 140 pts confirmed or changed PRO selections across m1-3 within the specified monthly time window (28 days +/- 7). PROs ranked as most important for tracking were PROMIS Fatigue, Physical Function, Pain Intensity, Pain Interference, Duration of Morning Joint Stiffness, and Sleep Disturbance. Patient's preferences regarding the importance of these PROs were stable over time. Conclusion The symptoms that rheumatology patients prioritized for longitudinal tracking using a smartphone app were fatigue, physical function, pain, and morning joint stiffness.
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JI Arthritis Res. Ther.
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WC Rheumatology
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TI Design options for high-speed OA-based fully differential buffers able to drive large loads
SO MICROELECTRONICS JOURNAL
LA English
DT Article
DE Fully differential voltage buffer; Class-AB voltage buffer; Differential to single-ended converter; Common-mode feedback; Current re-use; Unbalanced load
ID op-amp; gain; amplifier
AB This paper presents several options for the design of OA-based highly linear fully differential voltage buffers able to drive heavy loads at frequencies in the tens of MHz range. The buffer is first implemented by using a telescopic OA with

enlarged voltage swing; two circuits for controlling the common mode level of the output voltage are proposed. Next, two implementations based on the folded cascode transconductor with a Monticelli-type complementary source-followers second stage are presented. One of them uses complementary source followers embedded into the Monticelli gain stage, in order to lower the buffer output impedance. The proposed circuits have been implemented in a standard 0.35 mu m CMOS technology as design options for a voltage buffer required by a downhole sensor used in geological surveys. There, they have to drive a standard one-OA difference amplifier which presents heavy, unbalanced loads to their positive and negative outputs, respectively 1.5 k52 and 50052. Simulation results validate the designs, demonstrating that all four circuits meet the requirements: they handle sine voltages with amplitudes up to 2VPPDIFF at frequencies up to 100 MHz, with THD values better than 0.4% for signals in the tens of MHz range, achieving CMRR and PSRR values above 40 dB at 100 MHz, while consuming between 5.3 mA and 8.3 mA from a 3.3V supply.
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TI Bone Microvasculature: Stimulus for Tissue Function and Regeneration
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DT Article
DE bone vasculature; angiogenesis; osteogenesis; tissue engineering; diseases; growth factors; stem cells
ID mesenchymal stem-cells; endothelial growth-factor; term-follow-up; bb rhpdgf-bb; femoral-head; progenitor cells; sonic hedgehog; avascular necrosis; osteoblast differentiation; osteogenic differentiation
AB Bone is a highly vascularized organ, providing structural support to the body, and its development, regeneration, and remodeling depend on the microvascular homeostasis. Loss or impairment of vascular function can develop diseases, such as large bone defects, avascular necrosis, osteoporosis, osteoarthritis, and osteopetrosis. In this review, we summarize how vasculature controls bone development and homeostasis in normal and disease cases. A better understanding of this process will facilitate the development of novel disease treatments that promote bone regeneration and remodeling. Specifically, approaches based on tissue engineering components, such as stem cells and growth factors, have demonstrated the capacity to induce bone microvasculature regeneration and mineralization. This knowledge will have relevant clinical implications for the treatment of bone disorders by developing novel pharmaceutical approaches and bone grafts. Finally, the tissue engineering approaches incorporating vascular components may widely be applied to treat other organ diseases by enhancing their regeneration capacity. Impact statement Bone vasculature is imperative in the process of bone development, regeneration, and remodeling. Alterations or disruption of the bone vasculature leads to loss of bone homeostasis and the development of bone diseases. In this study, we review the role of vasculature on bone diseases and how vascular tissue engineering strategies, with a detailed emphasis on the role of stem cells and growth factors, will contribute to bone therapeutics.
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TI Insight into the roles of melatonin in bone tissue and bone-related diseases (Review)
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DT Review
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ID gingival crevicular fluid; periodontal-disease; stem-cells; osteoblastic

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AB Bone-related diseases comprise a large group of common diseases, including fractures, osteoporosis and osteoarthritis (OA), which affect a large number of individuals, particularly the elderly. The progressive destruction and loss of alveolar bone caused by periodontitis is a specific type of bone loss, which has a high incidence and markedly reduces the quality of life of patients. With the existing methods of prevention and treatment, the incidence and mortality of bone-related diseases are still gradually increasing, creating a significant financial burden to societies worldwide. To prevent the occurrence of bone-related diseases, delay their progression or reverse the injuries they cause, new alternative or complementary treatments need to be developed. Melatonin exerts numerous physiological effects, including inducing anti-inflammatory and antioxidative functions, resetting circadian rhythms and promoting wound healing and tissue regeneration. Melatonin also participates in the health management of bone and cartilage. In the present review, the potential roles of melatonin in the pathogenesis and progression of bone injury, osteoporosis, OA and periodontitis are summarized. Furthermore, the high efficiency and diversity of the physiological regulatory effects of melatonin are highlighted and the potential benefits of the use of melatonin for the clinical prevention and treatment of bone-related diseases are discussed.
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NR 164
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Z9 58
U1 3
U2 45
PU SPANDIDOS PUBL LTD
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PA POB 18179, ATHENS, 116 10, GREECE

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J9 INT J MOL MED
JI Int. J. Mol. Med.
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DI 10.3892/ijmm.2021.4915
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WC Medicine, Research & Experimental
SC Research & Experimental Medicine
GA RA0JM
UT WOS:000631105600001
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PT J
AU Kato, H
Koga, M
Kinoshita, Y
Taniguchi, Y
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TI Incidence of Complications in 25 Adult Patients With X-linked Hypophosphatemia
SO JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM
LA English
DT Article

DE X-linked hypophosphatemia; fibroblast growth factor 23; ossification of posterior longitudinal ligament; enthesopathy; osteophyte
ID posterior longitudinal ligament; computed-tomography; ossification; nephrocalcinosis; histomorphometry; prevalence; rickets; hearing; fgf-23
AB Context: Adults with X-linked hypophosphatemia (XLH) present complications other than osteomalacia. Objective: To describe the incidence and severity of comorbidities in adults with XLH. Methods: This observational retrospective study included a total of 25 adults with XLH with thorough investigations, including spinal computed tomography scans, x-rays of hip/knee joints and Achilles tendons, abdominal ultrasounds, and audiograms.The index of ossification of the anterior/posterior longitudinal ligament and yellow ligament (OA/OP/OY index) and the sum of OA/OP/OY index (OS index) were utilized to evaluate the severity of spinal ligament ossification. The Kellgren-Lawrence (KL) classification was adopted to evaluate the severity of the hip/knee osteophytes. Results: The participants consisted of 13 male patients and 12 female patients from 21 families, with a median age of 43 (range, 18-72) years. In all, 20 patients (80%) showed spinal ligament ossification. The median OA/OP/OY/OS indices were 2 (0-22), 0 (0-15), 6 (0-13), and 12 (0-41), respectively. Hip/knee osteophytes were reported in 24 (96%) and 17 cases (68%). The median KL grade was 3 in the hip joint and 2 in the knee joint, and 18 cases (72%) developed enthesopathy in the Achilles tendon. Nephrocalcinosis and hearing impairment were observed in 18 (72%) and 8 (32%) cases. Conclusion: This study revealed a high prevalence and severity of ectopic ossification and disclosed the incidence of nephrocalcinosis and hearing impairment in adults with XLH. In cases with severe spinal ligament ossification or noticeable osteophytes around the hip/ knee joints, undiagnosed XLH should be considered as a possible underlying condition.
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TC 33
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PU ENDOCRINE SOC
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JI J. Clin. Endocrinol. Metab.
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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PT J
AU Zeng, PM
Fu, Y
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Wu, YY
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Qin, A
Kong, XQ
AF Zeng, Pingmei
Fu, Yao

Pang, Yichuan
He, Tian
Wu, Yuanyuan
Tang, Ruikang
Qin, An
Kong, Xueqian
TI Solid-State Nuclear Magnetic Resonance Identifies Abnormal Calcium Phosphate Formation in Diseased Bones
SO ACS BIOMATERIALS SCIENCE & ENGINEERING
LA English
DT Article
DE bone; solid-state NMR; calcium phosphate; osteoclasts; osteoporosis; osteopetrosis; osteoarthritis
AB The crystallites of calcium phosphate (CaP) in bones consist of hydroxyl apatite (HA) and amorphous calcium phosphate (ACP). These nanoscale structures of CaP are sculptured by biological bone formation and resorption processes and are one of the crucial factors that determine the overall strength of the constructs. We used one- and two-dimensional H-1-P-31 solid-state nuclear magnetic resonance (SSNMR) to investigate the nanoscopic structural changes of CaP. Two quantitative measurables are deduced based on the heterogeneous linewidth of P-31 signal and the ratio of ACP to HA, which characterize the mineral crystallinity and the relative proportion of ACP, respectively. We analyzed bones from different murine models of osteopetrosis and osteoporosis and from human samples with osteoporosis and osteoarthritis. It shows that the ACP content increases notably in osteopetrotic bones that are characterized by defective osteoclastic resorption, whereas the overall crystallinity increases in osteoporotic bones that are marked by overactive osteoclastic resorption. Similar pathological characteristics are observed for the sclerotic bones of late-stage osteoarthritis, as compared to those of the osteopetrotic bones. These findings suggest that osteoclast-related bone diseases not only alter the bone density macroscopically but also lead to abnormal formation of CaP crystallites. The quantitative measurement by SSNMR provides a unique perspective on the pathology of bone diseases at the nanoscopic level.
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TC 7
Z9 8
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U2 41
PU AMER CHEMICAL SOC
PI WASHINGTON
PA 1155 16TH ST, NW, WASHINGTON, DC 20036 USA
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WC Materials Science, Biomaterials
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PT J
AU Beckers, G
Mazy, D
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AF Beckers, Gautier
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TI Knee mega-prosthesis in the management of complex knee fracture of the elderly : a case series and review of the literature
SO ACTA ORTHOPAEDICA BELGICA
LA English
DT Review
DE distal femur fracture; knee mega-prosthesis; elderly; osteoporosis
ID distal femoral fractures; femur; arthroplasty; replacement
AB The management of complicated distal femur fractures (DFF) of the elderly continues to pose a challenge. Knee mega-prosthesis are mostly used for Total knee arthroplasty revision and tumor resection surgery but they can be used for the treatment of complex knee fractures. The purpose of the present study is to examine the short-to midterm outcomes of their use for complex DFF of the elderly. We retrospectively identified 4 patients with DFF AO33C3 on osteoporotic bone treated by total knee arthroplasty from September 2015 to October 2019. The average age at the time of the surgery was 79,5 years (range, 69 to 95 years). All patients were females and underwent a total knee replacement by one senior surgeon, with the OSSTM Orthopaedic Salvage System (Zimmer Biomet, Warsaw, Indiana, USA). Outcome measures included clinical outcome scores, radiological analyses, reoperation rate and complications. At an average follow-up of 2,3 years (range, 0,6 to 4,2 years), the average Western Ontario and McMaster Universities

Osteoarthritis index (WOMAC) was 17,25 (range, 7 to 37), the average Oxford knee score was 35,25 (range, 25 to 41) and the average pain Numerical Rating Scale (NRS) was 0,5 (range, 0 to 1). 3 Patients had postoperative anemia but no implant related complications has been reported. Complex DFF of the elderly treated with mega knee arthroplasty exhibit good clinical outcomes scores. The patients should be selected carefully as the complication rate found in the literature remains high.
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NR 17
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PU ACTA MEDICA BELGICA
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UT WOS:000697000400020
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AU Zaharia, OP
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TI Reduced Muscle Strength Is Associated With Insulin Resistance in Type 2 Diabetes Patients With Osteoarthritis
SO JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM
LA English
DT Article
DE type 2 diabetes; osteoarthritis; insulin secretion; muscle strength; insulin sensitivity
ID beta-cell function; rheumatoid-arthritis; knee osteoarthritis; oxidative stress; osteoporosis; biomarkers; signatures; fractures; mellitus; inflammation
AB Context: Type 2 diabetes is associated with a greater risk for musculoskeletal disorders, yet its impact on joint function remains unclear. Objective: We hypothesized that patients with type 2 diabetes and osteoarthritis would exhibit musculoskeletal impairment, which would associate with insulin resistance and distinct microRNA profiles. Methods: Participants of the German Diabetes Study with type 2 diabetes (T2D, n = 39) or normal glucose tolerance (CON, n = 27), both with (+OA) or without osteoarthritis (-OA) underwent intravenous glucose tolerance and hyperinsulinemic-euglycemic clamp tests. Musculoskeletal function was assessed by isometric knee extension strength (KES), grip strength, range of motion (ROM), and balance skills, while neural function was measured by nerve conductance velocity (NCV). Arthritis-related symptoms were quantified using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire, serum arthritis-related microRNA using quantitative polymerase chain reaction. Results: Insulin sensitivity was lower in T2D+OA vs T2D-OA (4.4 +/- 2.0 vs 5.7 +/- 3.0 mg* kg(-1)*min(-1)) and in CON+OA vs CON-OA (8.1 +/- 2.0 vs 12.0 +/- 2.6 mg*kg(-1),*min(-1), both P <.05). In T2D+OA, KES and ROM were 60% and 22% lower than in CON+OA, respectively (both P <.05). Insulin sensitivity correlated positively with KES (r = 0.41, P <.05) among T2D, and negatively with symptom severity in CON and T2D (r = -0.60 and r = -0.46, respectively, P <.05). CON+OA and T2D+OA had inferior balance skills than CON-OA, whereas NCV was

comparable in T2D+OA and T2D-OA. Expression of arthritis-related microRNAs was upregulated in T2D compared to CON, but downregulated in CON+OA compared to CON-OA (P <.05), and did not differ between T2D+OA and T2D-OA. Conclusion: Musculoskeletal impairment and osteoarthritis-related symptoms are associated with insulin resistance. Type 2 diabetes can mask changes in arthritis-related microRNA profiles.
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TI Musculoskeletal complications associated with pathological iron toxicity and its molecular mechanisms
SO BIOCHEMICAL SOCIETY TRANSACTIONS
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DT Review
ID transferrin receptor 2; hereditary hemochromatosis; oxidative stress; physiological implications; heme oxygenase-1; mouse model; bound iron; cell-death; bone mass; metabolism
AB Iron is fundamental for several biological functions, but when in excess can lead to the development of toxic events. Some tissues and cells are more susceptible than others, but systemic iron levels can be controlled by treating patients with iron-chelating molecules and phlebotomy. An early diagnostic can be decisive to limit the progression of musculoskeletal complications like osteoarthritis and osteoporosis because of iron toxicity. In iron-related osteoarthritis, aggravation can be associated to a few events that can contribute to joints articular cartilage exposure to high iron concentrations, which can promote articular degeneration with very little chance of tissue regeneration. In contrast, bone metabolism is much more dynamic than cartilage, but progressive iron accumulation and ageing can be decisive factors for bone health. The iron overload associated with hereditary diseases like hemochromatosis, hemophilias, thalassemias and other hereditary anaemias increase the negative impact of iron toxicity in joints and bone, as well as in life quality, even when iron levels can be controlled. The molecular mechanisms by which iron can compromise cartilage and bone have been illusive and only in the last 20 years studies have started to shed some light into the molecular mechanisms associated with iron toxicity. Ferroptosis and the regulation of intracellular iron levels is instrumental in the balance between detoxification and induced cell death. In addition, these complications are accompanied with multiple susceptibility factors that can aggravate iron toxicity and should be identified. Therefore, understanding tissues microenvironment and cell communication is fundamental to contextualize iron toxicity.
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WC Biochemistry & Molecular Biology
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AU Zhang, C
Zhuang, ZK
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Li, KD
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Wei, QS
AF Zhang, Cheng
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TI Osteoporosis is associated with varus deformity in postmenopausal women with knee osteoarthritis: a cross-sectional study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Knee osteoarthritis; Varus deformity; Bone mineral density; Limb alignment Osteoporosis
ID bone-mineral density; alignment; population; college; oa
AB Background: Varus deformity of the knee is a common pathological characteristic in knee osteoarthritis (KOA), and not enough attention has been given to the relationship between knee varus deformity and the state of systemic bone mass. The purpose of this study was to evaluate the potential relationship between bone mineral density (BMD) and varus deformity in postmenopausal women with KOA. Methods: A total of 202 postmenopausal women with KOA(KL grade >= 2)in our department from January 2018 to June 2020 were reviewed in this cross-sectional study. The hip-knee-ankle angle of the lower extremity (HKA), medial distal femoral angle (MDFA), medial proximal tibial angle (MPTA), and the angle of the joint line (JLCA) were measured in all patients. According to the HKA Angle, these participants were divided into the varus deformity group (HKA < 175.3 degrees) and the normal limb alignment group (175.3 degrees <= HKA <= 180.3 degrees). The BMD of the lumbar (L1-L4), left femoral neck, and left hip were measured by dual-energy X-ray absorptiometry in all patients. The difference in BMD between the knee varus deformity group and the normal limb alignment group was compared, and the relationship between the different angles of limb

alignment and the BMD values at different sites was evaluated. Results: There were 144 cases (71.3 %) in the varus deformity group and 58 cases (28.7 %) in the normal limb alignment group. BMD at different joint sites within the knee varus deformity group was lower than of the normal limb alignment group, and the prevalence of osteoporosis was higher. After adjusting for confounding factors such as age, BMI, pain duration, and affected side, binary logistic regression showed that osteoporosis was an independent risk factor for varus deformity of KOA, and multiple linear regression showed that the BMD of spine, femoral neck, and hip was significantly associated with varus deformity of KOA. Pearson correlation analysis showed that BMD of the lumbar spine (L1-L4), left femoral neck and left hip joint were positively correlated with the HKA, but negatively correlated with JLCA. MPTA was positively correlated with the left femoral neck and left hip joint BMD, but not correlated with lumbar bone density. Furthermore, in the normal limb alignment group, the HKA was only negatively correlated with JLCA, but not significantly correlated with MDFA and MPTA. In the varus deformity group, the HKA was not only negatively correlated with JLCA but also positively correlated with MDFA and MPTA. Conclusions: Osteoporosis should be a major risk factor for varus deformity in postmenopausal women with KOA. The progression of varus deformity of the knee should be concerned in postmenopausal women who simultaneously has KOA and osteoporosis.
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NR 38
TC 16
Z9 18
U1 0
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PU BMC
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SN
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JI BMC Musculoskelet. Disord.
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DI 10.1186/s12891-021-04580-3
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TI Reduced serum levels of anti-Mullerian hormone is a putative biomarker of early knee osteoarthritis in middle-aged females at menopausal transition
SO SCIENTIFIC REPORTS
LA English
DT Article
ID bone-mineral density; prevalence; osteoporosis; cartilage; association; population; synovitis; arthritis; target; women
AB A recent epidemiological study revealed that the highest prevalence of early knee osteoarthritis (OA) was observed in females aged >= 50 years. The major causal factor of early knee OA was sex. Despite the relevance of estrogen in evaluating chondral and bone metabolism in OA, it is not easily clinically monitored because irregular menstrual cycles induce unstable female hormone patterns during menopausal transitions. Anti-Mullerian hormone (AMH) has been found to be a new stable biomarker to predict menopause. This study aimed to investigate the association between menopausal transition and early knee OA by using serum biomarkers, with special focus on AMH. A total of 518 female volunteers who participated in the Iwaki cohort study were enrolled and divided into pre-menopause and post-menopause groups. Weight-bearing anterior-posterior knee radiographs were classified by Kellgren-Lawrence (KL) grade, and grade >= 2 was defined as radiographic knee OA. In participants with KL grades 0 and 1, early knee OA was defined by Luyten's criteria. AMH, luteinizing hormone, follicle-stimulating hormone, estradiol (pg/ml), prolactin, and testosterone were measured on the female hormones. Bone mineral density at a distal radius was measured. The predictive power of female hormones for early knee OA was estimated by ROC analysis (comparison of area under curve, AUC) and regression analysis. Fifty-two participants (10.0%) were diagnosed with early knee OA and 204 (39.4%) with radiographic knee OA. In 393 (75.9%) females, menopause began.

From the ROC analysis in pre-menopausal females, cutoff value of AMH for detecting early knee OA was 0.08 ng/ml (area under curve (AUC), 0.712; 95% CI, 0.527-0.897; p value, 0.025; odds ratio, 8.28). AUCs of other female hormones did not reach the level of AMH (range, 0.513 of prolactine to 0.636 of estradiol). Logistic regression analysis focusing on AMH reduction at menopausal transition showed that the related AMH below 0.08 ng/ml was significantly related to the presence of early knee OA (p=0.035; odds ratio, 5.55). Reduced serum levels of AMH in middle-aged females were correlated with the presence of early knee OA, which might be a useful serum biomarker.
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TC 7
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U1 1
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PU NATURE PORTFOLIO
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PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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WC Multidisciplinary Sciences
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TI Prevalence and Risk Factors of Osteoporosis in Chinese Postmenopausal Women Awaiting Total Knee Arthroplasty
SO CLINICAL INTERVENTIONS IN AGING
LA English
DT Article
DE osteoporosis; postmenopausal women; total knee arthroplasty; Chinese; bone mineral density
ID bone-mineral density; osteoarthritis; hip; population; diagnosis; severity; spine; men
AB Background: Total knee arthroplasty (TKA) complications associated with low bone quality are challenging for orthopaedic surgeons to treat, but little is known about bone quality in Chinese postmenopausal women awaiting TKA. This study investigated the incidence of osteoporosis (OP) and explored the preoperative risk factors for OP in this population. Methods: We retrospectively reviewed the data of Chinese postmenopausal women who were indicated for TKA between May 2017 and June 2020. The bone mineral density (BMD) of the hip and lumbar spine and multiple preoperative parameters were collected and analyzed. Binary logistic regression analysis was performed to identify independent risk factors for OP in this population. Results: A total of 204 postmenopausal women with advanced knee OA were included in the study (age: 69.7 +/- 8.5 years; body mass index [BMI]: 25.5 +/- 4.0 kg/m2). The OP prevalence among all participants was 59.8%, and the patients aged 60-80 years had a significantly lower BMD than did the age/ethnicity-adjusted population. An age >= 60 years, a BMI<25, and the presence of a varus knee deformity were independent risk factors for preoperative OP in the postmenopausal women awaiting TKA. Conclusion: The prevalence of OP in Chinese postmenopausal women awaiting TKA is higher than that in the age/ethnicity-adjusted normal population. An age >= 60 years, a BMI<25, and the presence of a varus knee deformity are independent risk factors that can be used to predict preoperative OP in this population.
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Z9 20
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TI Three-Dimensional Quantification of Bone Mineral Density in the Distal Femur and Proximal Tibia Based on Computed Tomography: In Vitro Evaluation of an Extended Standardization Method
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE bone mineral density; knee; registration; osteoarthritis; osteoporosis; quantitative computed tomography; computational anatomy
ID cartilage thickness; computational anatomy; knee osteoarthritis; hip fracture; osteoporosis; reproducibility; registration; validation; mri; oa
AB While alterations in bone mineral density (BMD) are of interest in a number of musculoskeletal conditions affecting the knee, their analysis is limited by a lack of tools able to take full advantage of modern imaging modalities. This study introduced a new method, combining computed tomography (CT) and computational anatomy algorithms, to produce standardized three-dimensional BMD quantification in the distal femur and proximal tibia. The method was evaluated on ten cadaveric knees CT-scanned twice and processed following three different experimental settings to assess the influence of different scans and operators. The median reliability (intraclass correlation coefficient (ICC)) ranged from 0.96 to 0.99 and the median reproducibility (precision error (RMSSD)) ranged

from 3.97 to 10.75 mg/cc for the different experimental settings. In conclusion, this paper presented a method to standardize three-dimensional knee BMD with excellent reliability and adequate reproducibility to be used in research and clinical applications. The perspectives offered by this novel method are further reinforced by the fact it relies on conventional CT scan of the knee. The standardization method introduced in this work is not limited to BMD and could be adapted to quantify other bone parameters in three dimension based on CT images or images acquired using different modalities.
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NR 55
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U1 0
U2 5
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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TI Machine-learning, MRI bone shape and important clinical outcomes in osteoarthritis: data from the Osteoarthritis Initiative
SO ANNALS OF THE RHEUMATIC DISEASES
LA English
DT Article
ID knee osteoarthritis; cartilage; area; pain
AB Objectives Osteoarthritis (OA) structural status is imperfectly classified using radiographic assessment. Statistical shape modelling (SSM), a form of machine-learning, provides precise quantification of a characteristic 3D OA bone shape. We aimed to determine the benefits of this novel measure of OA status for assessing risks of clinically important outcomes. Methods The study used 4796 individuals from the Osteoarthritis Initiative cohort. SSM-derived femur bone shape (B-score) was measured from all 9433 baseline knee MRIs. We examined the relationship between B-score, radiographic Kellgren-Lawrence grade (KLG) and current and future pain and function as well as total knee replacement (TKR) up to 8 years. Results B-score repeatability supported 40 discrete grades. KLG and B-score were both associated with risk of current and future pain, functional limitation and TKR; logistic regression curves were similar. However, each KLG included a wide range of B-scores. For example, for KLG3, risk of pain was 34.4 (95% CI 31.7 to 37.0)%, but B-scores within KLG3 knees ranged from 0 to 6; for B-score 0, risk was 17.0 (16.1 to 17.9)% while for B-score 6, it was 52.1 (48.8 to 55.4)%. For TKR, KLG3 risk was 15.3 (13.3 to 17.3)%; while B-score 0 had negligible risk, B-score 6 risk was 35.6 (31.8 to 39.6)%. Age, sex and body mass index had negligible effects on association between B-score and symptoms. Conclusions

B-score provides reader-independent quantification using a single time-point, providing unambiguous OA status with defined clinical risks across the whole range of disease including pre-radiographic OA. B-score heralds a step-change in OA stratification for interventions and improved personalised assessment, analogous to the T-score in osteoporosis.
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Z9 98
U1 0
U2 24
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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PT J
AU Zhang, SQ
Xie, DH
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AF Zhang, Shuqin
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TI Mesenchymal stem cells plus bone repair materials as a therapeutic strategy for abnormal bone metabolism: Evidence of clinical efficacy and mechanisms of action implied
SO PHARMACOLOGICAL RESEARCH
LA English
DT Review
DE Bone metabolism; Mesenchymal stem cells; Bone tissue engineering; Biomaterials
ID quality-of-life; postmenopausal women; breast-cancer; the-art; scaffolds; osteosarcoma; cartilage; osteoporosis; fractures; differentiation
AB The regeneration process of human bones is very complicated, the management and treatment of bone damage caused by diseases are the main problems faced by clinicians worldwide. It is known that cell-based stem cell therapy together with biomaterials is a fast-developing method of tissue regeneration. This review focuses on the different types and main characteristics of scaffolds and stem cells suitable for bone regeneration, and aims to provide a state-of-the-art description of the current treatment of common bone metabolism related diseases such as osteoarthritis, osteoporosis and osteosarcoma and the strategies based on stem cell biological scaffolds used in bone tissue engineering. This method may provide a new treatment option for the treatment of common bone metabolism-related diseases that cannot be cured by ordinary and routine applications. Three databases (PubMed, CNKI and Web of Science) search terms used to write this review are: "arthritis", "osteoporosis", "osteosarcoma", "bone tissue engineering", "mesenchymal stem cells", "materials", "bioactive scaffolds" and their combinations, and the most relevant studies are selected. As a conclusion, it needs to be emphasized that despite the encouraging results, further development is needed due to the need for more in-depth research, standardization of stem cell manufacturing processes, large-scale development of clinical methods for bone tissue engineering, and market regulatory approval.

Although the research and application of tissue regeneration technology and stem cells are still in their infancy, the application prospect is broad and it is expected to solve the current clinical problems.
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TI Recent Advances in Osteoclast Biological Behavior

SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE osteoclast; origin; differentiation; apoptosis; functions; intercellular interactions
ID common lymphoid progenitors; estrogen-receptor-alpha; dendritic cell transdifferentiation; rankl-induced osteoclastogenesis; osteoblast lineage cells; sex steroid deficiency; mesenchymal stem-cells; bone-formation; in-vitro; inhibits osteoclastogenesis
AB With the progress of the aging population, bone-related diseases such as osteoporosis and osteoarthritis have become urgent problems. Recent studies have demonstrated the importance of osteoclasts in bone homeostasis, implying these will be an important mediator in the treatment of bone-related diseases. Up to now, several reviews have been performed on part of osteoclast biological behaviors such as differentiation, function, or apoptosis. However, few reviews have shown the complete osteoclast biology and research advances in recent years. Therefore, in this review, we focus on the origin, differentiation, apoptosis, behavior changes and coupling signals with osteoblasts, providing a simple but comprehensive overview of osteoclasts for subsequent studies.
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TI Cross-modality imaging of bisphosphonate-treated murine jawbones
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DT Article
ID shock-wave treatment; medication-related osteonecrosis; cell-proliferation; therapy; bone; jaws; mechanisms; laser; zinc

AB In this proof-of-principle study, we established and implemented a cross-modality imaging (CMI) pipeline to characterize and compare bisphosphonate (BIS)-treated jawbones of Sprague-Dawley rats after tooth extraction after physical therapies (photobiomodulation and extracorporeal shockwave therapy (PBMT and ESWT)). We showcase the feasibility of such a CMI approach and its compatibility across imaging modalities to probe the same region of interest (ROI) of the same jawbone. Jawbones were imaged in toto in 3D using micro-Computed Tomography to identify ROIs for subsequent sequential 2D analysis using well-established technologies such as Atomic Force Microscopy and Scanning Electron Microscopy, and recent imaging approaches in biomedical settings, such as micro-X-Ray Fluorescence Spectroscopy. By combining these four modalities, multiscale information on the morphology, topography, mechanical stiffness (Young's modulus), and calcium, zinc and phosphorus concentrations of the bone was collected. Based on the CMI pipeline, we characterized and compared the jawbones of a previously published clinically relevant rat model of BIS-related osteonecrosis of the jawbone (BRONJ) before and after treatment with BISs, PBMT and ESWT. While we did not find that physical therapies altered the mechanical and elemental jawbone parameters with significance (probably due to the small sample size of only up to 5 samples per group), both ESWT and PBMT reduced pore thicknesses and bone-to-enamel distances significantly compared to the controls. Although focused on BIS-treated jawbones, the established CMI platform can be beneficial in the study of bone-related diseases in general (such as osteoarthritis or -porosis) to acquire complementary hallmarks and better characterize disease status and alleviation potentials.
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NR 59
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TI The long pentraxin PTX3: a novel serum marker to improve the prediction of osteoporosis and osteoarthritis bone-related phenotypes
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English

DT Article
DE PTX3; Biomarker; Osteoporosis; Osteoarthritis; Bone-related phenotypes; Inflammation
ID innate immunity; inflammation; activation; expression; rankl
AB Background The long pentraxin PTX3 is generating great interest given the recent discovery of its involvement in bone metabolism. This study investigates the role of circulating PTX3 as a marker of bone-related phenotypes in patients with osteoporosis (OP) and osteoarthritis (OA). Methods Serum PTX3 levels were determined using an enzyme-linked immunosorbent assay (ELISA) in a total of OP (n=32), OA (n=19) patients and healthy controls (CTR; n=25). ROC curve analysis was carried out to evaluate the potential of PTX3 for the diagnosis of bone-related phenotypes. In addition, the association between PTX3 serum levels and biochemical markers was estimated by Spearman correlation analysis. Results Serum analysis reveals a statistically significant increase of PTX3 levels in OP and OA patients, compared to CTR subjects (**** $p < 0.0001$, **** $p < 0.0001$). ROC curve of PTX3 levels exhibits an excellent sensitivity and specificity for OP and OA diseases (**** $p < 0.0001$ and **** $p < 0.0001$, respectively). Moreover, serum PTX3 levels are positively associated with ALP ($r = -0.5257$, $p = 0.0083$) and PTH levels ($r = 0.4704$, $p = 0.0203$) in OP patients. Conclusions These results confirm the pivotal role of PTX3 in bone metabolism and suggest its potential use as a predictor of OP and OA bone-related phenotypes.
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TI Bone mineral density assessment by DXA in rheumatic patients with end-stage osteoarthritis undergoing total joint arthroplasty
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Rheumatoid arthritis; Arthroplasty; DXA; Bone mineral density
AB Background: Patients with rheumatic diseases have a high risk for joint destruction and secondary osteoarthritis (OA) as well as low bone mineral density

(BMD, i.e., osteoporosis). While several factors may lead to low BMD in these patients, the value of BMD measurements in rheumatic patients with end-stage OA scheduled for total joint arthroplasty is unknown. Methods: In this retrospective cross-sectional study of 50 adults with secondary OA due to rheumatic diseases, we evaluated dual energy X-ray absorptiometry (DXA) measurements of both hips and the spine performed within 3 months prior to arthroplasty (n=25 total hip arthroplasty, THA; n=25 total knee arthroplasty, TKA). We analyzed various demographic and disease-specific characteristics and their effect on DXA results by using group comparisons and multivariate linear regression models. Results: Although patients undergoing TKA were younger (63.214.2 vs. 71.0 +/- 10.8yr., p=0.035), osteoporosis was observed more frequently in patients scheduled for TKA than THA (32% vs. 12%). Osteopenia was detected in 13/25 patients (52%) in both the THA and TKA cohort. In the THA cohort, female sex, lower BMI and prednisolone use were associated with lower T-score in the hip. In TKA patients, higher OA grade determined by Kellgren-Lawrence score was associated with lower T-score in the hip of the affected side. Conclusions: Osteoporosis is present in a considerable frequency of rheumatic patients with end-stage OA, and THA and TKA patients show distinct frequencies and risk factors of low BMD. Our findings point to a potential value of DXA regarding preoperative evaluation of bone status.
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TI Osteocyte transcriptome mapping identifies a molecular landscape controlling skeletal homeostasis and susceptibility to skeletal disease
SO NATURE COMMUNICATIONS
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DT Article
ID genome-wide; r/bioconductor package; sclerostin antibody; differential gene; image-analysis; bone-formation; sost gene; r package; in-vitro; osteoblast
AB Osteocytes are master regulators of the skeleton. We mapped the transcriptome of osteocytes from different skeletal sites, across age and sexes in mice to reveal genes and molecular programs that control this complex cellular-network. We define an osteocyte transcriptome signature of 1239 genes that distinguishes osteocytes from other cells. 77% have no previously known role in the skeleton and are enriched for genes regulating neuronal network formation, suggesting this programme is important in osteocyte communication. We evaluated 19 skeletal parameters in 733 knockout mouse lines and reveal 26 osteocyte transcriptome signature genes that control bone structure and function. We showed osteocyte transcriptome signature genes are enriched for human orthologs that cause monogenic skeletal disorders (P=2.4x10(-22)) and are associated with the polygenic diseases osteoporosis (P=1.8x10(-13)) and osteoarthritis (P=1.6x10(-7)). Thus, we reveal the molecular landscape that regulates osteocyte network formation and function and establish the importance of osteocytes in human skeletal disease. Osteocytes are the master regulatory cells within the skeleton. Here, the authors map the transcriptome of osteocytes from diverse skeletal sites, ages and between sexes and identify an osteocyte transcriptome signature associated with rare skeletal disorders and common complex skeletal diseases.
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AU Martinato, M
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AF Martinato, Matteo
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TI Usability and Accuracy of a Smartwatch for the Assessment of Physical Activity in the Elderly Population: Observational Study
SO JMIR MHEALTH AND UHEALTH
LA English
DT Article
DE wearable devices; elderly; physical activity; smartwatches
ID activity trackers; intraclass correlations; older-adults; validity; walking; technology; pedometers; monitors; health
AB Background: Regular physical activity (PA) contributes to the primary and

secondary prevention of several chronic diseases and reduces the risk of premature death. Physical inactivity is a modifiable risk factor for cardiovascular disease and a variety of chronic disorders such as diabetes, obesity, hypertension, bone and joint diseases (eg, osteoporosis and osteoarthritis), depression, and colon and breast cancer. Population aging and the related increase in chronic diseases have a major impact on the health care systems of most Western countries and will produce an even more significant effect in the future. Monitoring PA is a valuable method of determining whether people are performing enough PA so as to prevent chronic diseases or are showing early symptoms of those diseases. Objective: The aim of this study was to estimate the accuracy of wearable devices in quantifying the PA of elderly people in a real-life setting. Methods: Participants aged 70 to 90 years with the ability to walk safely without any walking aid for at least 300 meters, who had no walking disabilities or episodes of falling while walking in the last 12 months, were asked to walk 150 meters at their preferred pace wearing a v & iacute;voactive HR device (Garmin Ltd) and actual steps were monitored and tallied by a researcher using a hand-tally counter to assess the performance of the device at a natural speed. A Bland-Altman plot was used to analyze the difference between manually counted steps and wearable device-measured steps. The intraclass correlation coefficient (ICC) was computed (with a 95% confidence interval) between step measurements. The generalized linear mixed-model (GLMM) ICCs were estimated, providing a random effect term (random intercept) for the individual measurements (gold standard and device). Both adjusted and conditional ICCs were computed for the GLMM models considering separately the effect of age, sex, BMI, and obesity. Analyses were performed using R software (R Foundation for Statistical Computing) with the rms package. Results: A total of 23 females and 26 males were enrolled in the study. The median age of the participants was 75 years. The Bland-Altman plot revealed that, excluding one observation, all differences across measurements were in the confidence bounds, demonstrating the substantial agreement between the step count measurements. The results were confirmed by an ICC equal to .98 (.96-.99), demonstrating excellent agreement between the two sets of measurements. Conclusions: The level of accuracy of wearable devices in quantifying the PA of elderly people in a real-life setting that was found in this study supports the idea of considering wrist-wearable nonmedical devices (widely available in nonspecialized stores) as reliable tools. Both health care professionals and informal caregivers could monitor the level of PA of their patients.
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TI Remote Patient Monitoring with Wearable Sensors Following Knee Arthroplasty
SO SENSORS
LA English
DT Article
DE knee arthroplasty; wearable sensor; inertial measurement unit (IMU); PROMs; remote monitoring; telemedicine
ID osteoarthritis outcome score; total hip; mechanical alignment; replacement; rehabilitation; questionnaire; discharge; injury
AB (Background) Inertial Measurement Units (IMUs) provide a low-cost, portable solution to obtain functional measures similar to those captured with three-dimensional gait analysis, including spatiotemporal gait characteristics. The primary aim of this study was to determine the feasibility of a remote patient monitoring (RPM) workflow using ankle-worn IMUs measuring impact load, limb impact load asymmetry and knee range of motion in combination with patient-reported outcome measures. (Methods) A pilot cohort of 14 patients undergoing primary knee arthroplasty for osteoarthritis was prospectively enrolled. RPM in the community was performed weekly from 2 up to 6 weeks post-operatively using wearable IMUs. The following data were collected using IMUs: mobility (Bone Stimulus and cumulative impact load), impact load asymmetry and maximum knee flexion angle. In addition, scores from the Oxford Knee Score (OKS), EuroQol Five-dimension (EQ-5D) with EuroQol visual analogue scale (EQ-VAS) and 6 Minute Walk Test were collected. (Results) On average, the Bone Stimulus and cumulative impact load improved 52% ($p = 0.002$) and 371% ($p = 0.035$), compared to Post-Op Week 2. The impact load asymmetry value trended ($p = 0.372$) towards equal impact loading between the operative and non-operative limb. The mean maximum flexion angle achieved was 99.25 degrees at Post-Operative Week 6, but this was not significantly different from pre-operative

measurements (p = 0.1563). There were significant improvements in the mean EQ-5D (0.20; p = 0.047) and OKS (10.86; p < 0.001) scores both by 6 weeks after surgery, compared to pre-operative scores. (Conclusions) This pilot study demonstrates the feasibility of a reliable and low-maintenance workflow system to remotely monitor post-operative progress in knee arthroplasty patients. Preliminary data indicate IMU outputs relating to mobility, impact load asymmetry and range of motion can be obtained using commercially available IMU sensors. Further studies are required to directly correlate the IMU sensor outputs with patient outcomes to establish clinical significance.
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SC Chemistry; Engineering; Instruments & Instrumentation
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TI Prevalence of and risk factors for hallux rigidus: a cross-sectional study in Japan
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Hallux rigidus; Cohort study; Epidemiology
ID radiographic osteoarthritis; foot; osteoporosis; knee
AB Background Hallux rigidus (HR) is a common osteoarthritis of the first metatarsophalangeal joint. However, the epidemiology and risk factors of this pathology have yet to be clarified. Methods We have been conducting cohort studies among individuals over 50 years old every 2 years since 1997. This study analyzed data from the 7th to 10th checkups in 2009, 2011, 2013, and 2015. We investigated the prevalence of HR and its risk factors in a total of 604 individuals (mean age, 67.1 +/- 6.4 years; 208 men, 396 women). Radiographic HR was defined as Hattrup and Johnson classification grade 1 or higher. Knee osteoarthritis (KOA) was scored according to the Kellgren-Lawrence grading system. Radiographic KOA was defined as grade 2 or higher. Cases with a hallux valgus (HV) angle of 20 degrees or higher were defined as showing HV. Statistical analyses were performed using the Kruskal-Wallis test, Fisher's exact test, logistic regression modeling, and the Cochran-Armitage trend test. All p-values presented are two-sided and values of $p < .05$ were considered statistically significant. Results The prevalence of HR was 26.7% (161/604). Rates of grade 0, 1, 2, and 3 HR according to the Hattrup and Johnson classification were 73.3% (443/604), 16.4% (99/604), 8.0% (48/604), and 2.3% (14/604), respectively. Overall ratio of symptomatic HR was 8.1%. Univariate analysis revealed KOA, gout attack (GA), and HV as significantly associated with HR. The same factors were confirmed as independent risk factors for HR in multivariate analysis. All parameters were significantly associated with HR. Odds ratios of KOA, HV, and GA for HR were 1.73, 3.98, and 3.86, respectively. The presence or absence of KOA was significantly associated with severity of HR. Conclusions This study revealed that the prevalence of HR in the elderly (>= 50 years) was 26.7%. KOA, HV, and GA were independent risk factors for HR. KOA was associated with severity of HR.
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NR 30
TC 19
Z9 23
U1 0
U2 2
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD SEP 13
PY 2021
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DI 10.1186/s12891-021-04666-y
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
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UT WOS:000698365000001
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PT J
AU Miyamoto, K
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TI A Metabolomic Profile Predictive of New Osteoporosis or Sarcopenia Development
SO METABOLITES
LA English
DT Article
DE osteoporosis; sarcopenia; metabolome; cohort study; the Research on Osteoarthritis; Osteoporosis Against Disability (ROAD)
ID bone-mineral density; skeletal-muscle; amino-acids; mass; women; irisin; association; fractures; consensus; risk
AB The increasing number of patients with osteoporosis and sarcopenia is a global concern among countries with progressively aging societies. The high medical costs of treating those patients suggest that prevention rather than treatment is preferable. We enrolled 729 subjects who attended both the second and third surveys of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study. Blood samples were collected from subjects at the second survey, and then a comprehensive metabolomic analysis was performed. It was found that 35 had newly developed osteoporosis at the third survey performed four years later, and 39 were newly diagnosed with sarcopenia at the third survey. In the second survey, we found that serum Gly levels were significantly higher even after adjustment for age, sex, and BMI in subjects with newly developed osteoporosis relative to those who remained osteoporosis-negative during the four-year follow-up. We also show that serum taurine levels were significantly lower at the second survey, even after adjustment for age, sex, and BMI in subjects with newly developed sarcopenia during the four-year follow-up compared with those not diagnosed with sarcopenia at the second or third surveys. Though our sample size and odds ratios were small, increased Gly and decreased taurine levels were found to be predictive of new development of osteoporosis and sarcopenia, respectively, within four years.
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FU JOA-Subsidized Science Project Research [2020-3]; Yamagata prefectural government; city of Tsuruoka
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NR 47
TC 25
Z9 29
U1 0

U2 14
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 2218-1989
J9 METABOLITES
JI Metabolites
PD MAY 15
PY 2021
VL 11
IS 5
BP
EP
DI 10.3390/metabo11050278
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WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
GA SH7AP
UT WOS:000654286900001
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PT J
AU Hiyama, Y
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AF Hiyama, Yoshinori
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TI Quantitative Ultrasound of the Heel in Women With Knee Osteoarthritis
SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE Fracture risk; knee osteoarthritis; physical activity; quantitative ultrasound
ID bone-mineral density; elderly-men; fracture; risk; association; age; osteoporosis; pain; hip; management
AB The prevalence of multiple falls is higher in older women, and knee pain is associated with multiple falls in women; thus, it is important to detect individuals at risk of fractures among women with knee osteoarthritis. We aimed to clarify the association between knee osteoarthritis and the quantitative ultrasound (QUS)

parameter, and investigate the clinical relevance of the QUS parameter with osteoarthritis-related characteristics in women with knee osteoarthritis. This was a cross-sectional study. We recruited 101 women with knee osteoarthritis at a local orthopedic hospital and 102 healthy individuals from the community. Heel QUS measurements were performed using the QUS device, measuring the stiffness index. We also assessed knee pain, quadriceps strength, and physical activity in women with knee osteoarthritis. We fitted a multiple regression model to estimate the association between knee osteoarthritis and the stiffness index. We also fitted 3 multiple regression models to investigate the clinical relevance of the QUS parameter with osteoarthritis-related characteristics in women with knee osteoarthritis. Compared with the control group, individuals with grade 2 osteoarthritis did not demonstrate a significant difference in stiffness index ($p = 0.68$); however, those with grade 3 osteoarthritis ($p < 0.001$) and 4 ($p < 0.001$) showed a lower stiffness index than that of the control group. Additionally, although the QUS parameter did not show an association with knee pain score ($p = 0.70$) or quadriceps strength ($p = 0.11$), we found a significant association between the QUS parameter and physical activity ($p = 0.003$). Our results demonstrate that women with moderate or severe knee osteoarthritis showed lower QUS parameters compared to healthy women, and the QUS parameter was associated with physical activity in women with knee osteoarthritis.
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NR 32
TC 3
Z9 3
U1 0
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PU ELSEVIER SCIENCE INC
PI NEW YORK
PA STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA
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JI J. Clin. Densitom.
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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PT J
AU Lawrence, EA
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TI Exposure to hypergravity during zebrafish development alters cartilage material properties and strain distribution
SO BONE & JOINT RESEARCH
LA English
DT Article
DE Zebrafish; Musculoskeletal; Gravity; Finite element analysis; Extracellular matrix
ID articular-cartilage; simulated microgravity; physical exercise; relaxation-times; skeletal; knee; chondrocytes; osteoarthritis; muscle; degeneration
AB Aims Vertebrates have adapted to life on Earth and its constant gravitational field, which exerts load on the body and influences the structure and function of tissues. While the effects of microgravity on muscle and bone homeostasis are well

described, with sarcopenia and osteoporosis observed in astronauts returning from space, the effects of shorter exposures to increased gravitational fields are less well characterized. We aimed to test how hypergravity affects early cartilage and skeletal development in a zebrafish model. Methods We exposed zebrafish to 3 g and 6 g hypergravity from three to five days post-fertilization, when key events in jaw cartilage morphogenesis occur. Following this exposure, we performed immunostaining along with a range of histological stains and transmission electron microscopy (TEM) to examine cartilage morphology and structure, atomic force microscopy (AFM) and nanoindentation experiments to investigate the cartilage material properties, and finite element modelling to map the pattern of strain and stress in the skeletal rudiments. Results We did not observe changes to larval growth, or morphology of cartilage or muscle. However, we observed altered mechanical properties of jaw cartilages, and in these regions we saw changes to chondrocyte morphology and extracellular matrix (ECM) composition. These areas also correspond to places where strain and stress distribution are predicted to be most different following hypergravity exposure. Conclusion Our results suggest that altered mechanical loading, through hypergravity exposure, affects chondrocyte maturation and ECM components, ultimately leading to changes to cartilage structure and function.
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TI Musculoskeletal morbidity following spinal cord injury: A longitudinal cohort study of privately-insured beneficiaries
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DE Spinal cord injury; Osteoporosis; Osteoarthritis; Sarcopenia; Musculoskeletal
ID secondary health conditions; quality-of-life; shoulder pain; risk-factors; rehabilitation; osteoporosis; contractures; people; impact; bone
AB Background: People living with spinal cord injuries (SCIs) experience motor, sensory and autonomic impairments that cause musculoskeletal disorders following the injury and that progress throughout lifetime. The range and severity of issues are largely dependent on level and completeness of the injury and preserved function. Objective: High risk of developing musculoskeletal morbidities among individuals after sustaining a traumatic SCI is well known in the clinical setting, however, there is a severe lack of evidence in literature. The objective of this study was to compare the incidence of and adjusted hazards for musculoskeletal morbidities among adults with and without SCIs. Methods: Privately-insured beneficiaries were included if they had an ICD-9-CM diagnostic code for SCI (n = 9081). Adults without SCI were also included (n = 1,474,232). Incidence estimates of common musculoskeletal morbidities (e.g., osteoporosis, sarcopenia, osteoarthritis, fractures, etc.) were compared at 5-years of enrollment. Survival models were used to quantify unadjusted and adjusted hazard ratios for incident musculoskeletal morbidities. Results: Adults living with traumatic SCIs had a higher incidence of any musculoskeletal morbidities (82.4% vs. 47.5%) as compared to adults without SCI, and differences were to a clinically meaningful extent. Survival models demonstrated that adults with SCI had a greater fully-adjusted hazard for any musculoskeletal morbidity (Hazard Ratio [HR]: 2.41; 95%CI: 2.30, 2.52), and all musculoskeletal disorders, and ranged from HR: 1.26

(1.14, 1.39) for rheumatoid arthritis to HR: 7.02 (6.58, 7.49) for pathologic fracture. Conclusions: Adults with SCIs have a significantly higher incidence of and risk for common musculoskeletal morbidities, as compared to adults without SCIs. Efforts are needed to facilitate the development of improved clinical screening algorithms and early interventions to reduce risk of musculoskeletal disease onset/progression in this higher risk population.
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TI Risk Factors for Recurrence of Benign Paroxysmal Positional Vertigo. A Clinical Review
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Review
DE BPPV; BPPV recurrence; risk factors
ID term-follow-up; bone-mineral density; vitamin-d; oxidative stress; osteoporosis; association; disorders; migraine; features; otoconia
AB Benign paroxysmal positional vertigo (BPPV) is one of the most common peripheral vestibular dysfunctions encountered in clinical practice. Although the treatment of BPPV is relatively successful, many patients develop recurrence after treatment. Our purpose is to evaluate the mean recurrence rate and risk factors of BPPV after treatment. A review of the literature on the risk factors of BPPV recurrence was performed. A thorough search was conducted using electronic databases, namely Pubmed, CINAHL, Academic Search Complete and Scopus for studies published from 2000 to 2020. Thirty studies were included in this review

with 13,358 participants. The recurrence rate of BPPV ranged from 13.7% to 48% for studies with follow-up < 1 year, and from 13.3% to 65% for studies with follow-up & GE;2 years. Pathophysiologic mechanisms and implication of each of the following risk factors in the recurrence of BPPV were described: advanced age, female gender, Meniere's disease, trauma, osteopenia or osteoporosis, vitamin D deficiency, diabetes mellitus, hypertension, hyperlipidemia, cardiovascular disease, migraine, bilateral/multicanal BPPV, cervical osteoarthrosis and sleep disorders. Patients with hyperlipidemia and hypertension had the highest recurrence rates of BPPV, 67.80% and 55.89%, respectively, indicating that vascular comorbidities increase the risk of BPPV recurrence. In addition, more than half of patients (53.48%) with diabetes mellitus and BPPV experienced recurrence of BPPV. Knowledge and awareness of risk factors for recurrence of BPPV are essential for the assessment and long-term prognosis of patients. Identification of these relapse risk factors may enhance the ability of clinicians to accurately counsel patients regarding BPPV and associated comorbidities.
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TC 50
Z9 61
U1 6
U2 21
PU MDPI
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PT J
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TI Characterization of Products from the Aqueous-Phase Photochemical Oxidation of Benzene-Diols
SO ATMOSPHERE
LA English
DT Article
DE benzene-diols; oxidative potential; light absorption; secondary organic aerosol

ID secondary organic aerosol; triplet excited-state; brown carbon; phenolic-compounds; mass-spectrometry; source apportionment; air-pollution; wood smoke; emissions; chemistry
AB Chemical processing in atmospheric aqueous phases, including cloud and fog drops, might be significant in reconciling the gap between observed and modeled secondary organic aerosol (SOA) properties. In this work, we conducted a relatively comprehensive investigation of the reaction products generated from the aqueous-phase photochemical oxidation of three benzene-diols (resorcinol, hydroquinone, and methoxyhydroquinone) by hydroxyl radical (center dot OH), triplet excited state (C-3*) 3,4-dimethoxybenzaldehyde (3,4-DMB), and direct photolysis without any added oxidants. The results show that OH-initiated photo-degradation is the fastest of all the reaction systems. For the optical properties, the aqueous oxidation products generated under different reaction conditions all exhibited photo-enhancement upon illumination by simulated sunlight, and the light absorption was wavelength dependent on and increased as a function of the reaction time. The oxygen-to-carbon (O/C) ratio of the products also gradually increased against the irradiation time, indicating the persistent formation of highly oxygenated low-volatility products throughout the aging process. More importantly, aqueous-phase products from photochemical oxidation had an increased oxidative potential (OP) compared with its precursor, indicating they may more adversely impact health. The findings in this work highlight the importance of aqueous-phase photochemical oxidation, with implications for aqueous SOA formation and impacts on both the chemical properties and health effects of OA.
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NR 64
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Z9 7
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U2 61
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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JI Atmosphere
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WC Environmental Sciences; Meteorology & Atmospheric Sciences
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AU Oskarsson, T
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TI Skeletal adverse events in childhood cancer survivors: An Adult Life after Childhood Cancer in Scandinavia cohort study
SO INTERNATIONAL JOURNAL OF CANCER
LA English
DT Article
DE ALiCCS; childhood cancer; late effects; skeletal adverse events; survivorship
ID acute lymphoblastic-leukemia; bone-mineral density; long-term survivors; pediatric-patients; young-adults; risk-factors; osteonecrosis; children; fractures; lymphoma
AB The dynamic growth of the skeleton during childhood and adolescence renders it vulnerable to adverse effects of cancer treatment. The lifetime risk and patterns of skeletal morbidity have not been described in a population-based cohort of childhood cancer survivors. A cohort of 26 334 1-year cancer survivors diagnosed before 20 years of age was identified from the national cancer registries of Denmark, Finland, Iceland and Sweden as well as a cohort of 127 531 age- and sex-matched comparison subjects randomly selected from the national population registries in each country. The two cohorts were linked with data from the national hospital registries and the observed numbers of first-time hospital admissions for adverse skeletal outcomes among childhood cancer survivors were compared to the expected numbers derived from the comparison cohort. In total, 1987 childhood cancer survivors had at least one hospital admission with a skeletal adverse event as discharge diagnosis, yielding a rate ratio (RR) of 1.35 (95% confidence interval, 1.29-1.42). Among the survivors, we observed an increased risk for osteonecrosis with a RR of 25.9 (15.0-44.5), osteoporosis, RR 4.53 (3.28-6.27), fractures, RR 1.27 (1.20-1.34), osteochondropathies, RR 1.57 (1.28-1.92) and osteoarthrosis, RR 1.48 (1.28-1.72). The hospitalization risk for any skeletal adverse event was higher among survivors up to the age of 60 years, but the lifetime pattern was different for each type of skeletal adverse event. Understanding the different lifetime patterns and identification of high-risk groups is crucial for developing strategies to optimize skeletal health in childhood cancer survivors.
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NR 53
TC 8
Z9 12
U1 0
U2 5
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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Xiao, Ye
Huang, Yan
Liu, Ya
Luo, Xiang-Hang
TI The role of autophagy in bone homeostasis
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Review
DE autophagy; bone homeostasis; osteoblast; osteoclast; osteoporosis
ID mesenchymal stem-cells; rapamycin reduces severity; osteogenic differentiation; knee osteoarthritis; signaling pathway; gene-expression; osteoblast; osteoporosis; activation; mechanisms
AB Autophagy is an evolutionarily conserved intracellular process and is considered one of the main catabolism pathways. In the process of autophagy, cells are digested nonselectively or selectively to recover nutrients and energy, so it is regarded as an antiaging process. In addition to the essential role of autophagy in cellular homeostasis, autophagy is a stress response mechanism for cell survival. Here, we review recent literature describing the pathway of autophagy and its role in different bone cell types, including osteoblasts, osteoclasts, and osteocytes. Also discussed is the mechanism of autophagy in bone diseases associated with bone homeostasis, including osteoporosis and Paget's disease. Finally, we discuss the application of autophagy regulators in bone diseases. This review aims to introduce autophagy, summarize the understanding of its relevance in bone physiology, and discuss its role and therapeutic potential in the pathogenesis of bone diseases such

as osteoporosis.
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DT Article
DE Multimorbidity; Clustering; Correspondence analysis; Long term conditions
ID health-care; patterns; impact
AB Background: Globally, there is increasing research on clusters of multimorbidity, but few studies have investigated multimorbidity in urban contexts characterised by a young, multi-ethnic, deprived populations. This study identified clusters of associative multimorbidity in an urban setting. Methods: This is a population-based retrospective cross-sectional study using electronic health records of all adults aged 18 years and over, registered between April 2005 to May 2020 in general practices in one inner London borough. Multiple correspondence analysis and cluster analysis was used to identify groups of multimorbidity from 32 long-term conditions (LTCs). Results: The population included 41 general practices with 826,936 patients registered between 2005 and 2020, with mean age 40 (SD15.6) years. The prevalence of multimorbidity was 21% (n = 174,881), with the median number of conditions being three and increasing with age. Analysis identified five consistent LTC clusters: 1) anxiety and depression (Ratio of within- to between-sum of squares (WSS/BSS <0.01 to <0.01); 2) heart failure, atrial fibrillation, chronic kidney disease (CKD), chronic heart disease (CHD), stroke/transient ischaemic attack (TIA), peripheral arterial disease (PAD), dementia and osteoporosis (WSS/BSS 0.09 to 0.12); 3) osteoarthritis, cancer, chronic pain, hypertension and diabetes (0.05 to 0.06); 4) chronic liver disease and viral hepatitis (WSS/BSS 0.02 to 0.03); 5) substance dependency, alcohol dependency and HIV (WSS/BSS 0.37 to 0.55). Interpretation: Mental health problems, pain, and at-risk behaviours leading to cardiovascular diseases are the important clusters identified in this young, urban population. (C) 2021 The Author(s). Published by Elsevier Ltd.

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TI Sulforaphane protects against oxidative stress-induced apoptosis via activating SIRT1 in mouse osteoarthritis
SO MOLECULAR MEDICINE REPORTS
LA English
DT Article
DE osteoarthritis; sulforaphane; chondrocyte; inflammation; sirtuin 1
ID inhibiting apoptosis; in-vitro; cartilage; expression; reticulum; injury; model
AB Osteoarthritis (OA), the most common form of human joint disease, is characterized by progressive degeneration of the articular cartilage, synovitis and subchondral osteoporosis. Chondrocyte apoptosis is the primary pathogenic mechanism of OA and is considered to be a potential therapeutic target. Sulforaphane (SFN), a dietary isothiocyanate obtained from cruciferous vegetables, has been reported to exert an anti-apoptotic effect by activating sirtuin 1 (SIRT1). To the best of our knowledge, however, the effects of SFN on apoptotic responses in OA have not been reported. In the present study, SFN was shown to significantly inhibit chondrocyte apoptosis while enhancing expression levels of SIRT1 in a H2O2-induced OA mouse model. The anti-apoptotic effect of SFN was reversed by SIRT1 small interfering RNA, implying that SIRT1 exerted a protective role against the effect of SFN on chondrocytes. The expression levels of C/EBP homologous protein, 78-kDa glucose regulated protein, Bax, Bcl-2 and cleaved caspase 3 were found to be downregulated in SFN-treated mice. Furthermore, SFN ameliorated cartilage degradation in the OA mouse model. These findings indicate that SFN exerted an anti-apoptotic effect on chondrocytes and ameliorated OA in vivo by activating the SIRT1 signaling pathway.
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AU Stock, M
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TI Vitamin K-Dependent Proteins in Skeletal Development and Disease
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE vitamin K; vitamin K-dependent proteins; osteocalcin; matrix Gla protein; Ucma; GRP
ID matrix gla-protein; gamma-carboxyglutamic acid; bone-mineral density; serum undercarboxylated osteocalcin; receptor tyrosine kinase; rich protein; osteoblast differentiation; osteoarthritic cartilage; oral anticoagulants; knee osteoarthritis
AB Vitamin K and Vitamin K-dependent proteins (VKDPs) are best known for their pivotal role in blood coagulation. Of the 14 VKPDs identified in humans to date, 6 play also important roles in skeletal biology and disease. Thus, osteocalcin, also termed bone Gla-protein, is the most abundant non-collagenous protein in bone. Matrix Gla protein and Ucma/GRP on the other hand are highly abundant in cartilage. Furthermore, periostin, protein S, and growth arrest specific 6 protein (GAS 6) are expressed in skeletal tissues. The roles for these VKDPs are diverse but include the control of calcification and turnover of bone and cartilage. Vitamin K plays an important role in osteoporosis and serum osteocalcin levels are recognized as a promising marker for osteoporosis. On the other hand, matrix Gla

protein and Ucma/GRP are associated with osteoarthritis. This review focuses on the roles of these three VKDPs, osteocalcin, matrix Gla protein and Ucma/GRP, in skeletal development and disease but will also summarize the roles the other skeletal VKDPs (periostin, protein S and GAS6) in skeletal biology.
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NR 113
TC 36
Z9 39
U1 1
U2 30
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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J9 INT J MOL SCI
JI Int. J. Mol. Sci.
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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PT J
AU Sapino, S
Chindamo, G
Chirio, D
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Peira, E
Riganti, C
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AF Sapino, Simona
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Manzoli, Maela
Peira, Elena
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TI Calcium Phosphate-Coated Lipid Nanoparticles as a Potential Tool in Bone Diseases Therapy
SO NANOMATERIALS
LA English
DT Article
DE lipid nanoparticles; calcium phosphate coating; bone diseases; human osteosarcoma cells; cellular uptake
ID delivery; carriers
AB The treatment of bone diseases (including osteoporosis, osteoarthritis, and bone cancer) often results in reduced efficiency and/or adverse reactions due to the fact that it is not specifically targeted to the site of action. The employment of a suitable carrier should increase drug location to the site of bone disease. The purpose of this study is to prepare and characterize lipid nanoparticles (NPs) coated with calcium phosphate (CaP-NPs). A coating method, to date used only to obtain liposomes covered with CaP, is herein partially-modified to prepare CaP-coated lipid NPs. An extensive physico-chemical characterization was achieved by employing several techniques (DLS, SEM and TEM, and both combined with EDS, XRD, and FTIR) that confirmed the feasibility of the developed coating method. Preliminary uptake studies on human osteosarcoma cells (U-2OS) were performed by entrapping, as a lipid probe, Sudan Red III in NPs. The obtained data provided evidence that CaP-NPs showed higher cell accumulation than uncoated

NPs. This result may have important implications for the development of drug loaded CaP-NPs to be tested in vitro with a view of planning future treatment of bone diseases, and indicate that CaP-NPs are potential vehicles for selective drug delivery to bone tissue.
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NR 25
TC 15
Z9 16
U1 0
U2 23
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
SN
EI 2079-4991
J9 NANOMATERIALS-BASEL
JI Nanomaterials
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DI 10.3390/nano11112983
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WC Chemistry, Multidisciplinary; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary; Physics, Applied
SC Chemistry; Science & Technology - Other Topics; Materials Science; Physics
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Weigend, Annett
Weigend, Steffen
TI Identification and Functional Annotation of Genes Related to Bone Stability in Laying Hens Using Random Forests
SO GENES
LA English
DT Article
DE bone mineral density; bone breaking strength; gene set enrichment analysis; osteoporosis; Random Forests; single nucleotide polymorphism; skeletal integrity
ID genome-wide association; quantitative trait loci; single nucleotide polymorphism; egg-production; mineral density; body-composition; chicken; osteoporosis; osteoarthritis; calcitonin
AB Skeletal disorders, including fractures and osteoporosis, in laying hens cause major welfare and economic problems. Although genetics have been shown to play a key role in bone integrity, little is yet known about the underlying genetic architecture of the traits. This study aimed to identify genes associated with bone breaking strength and bone mineral density of the tibiotarsus and the humerus in laying hens. Potentially informative single nucleotide polymorphisms (SNP) were identified using Random Forests classification. We then searched for genes known to be related to bone stability in close proximity to the SNPs and identified 16 potential candidates. Some of them had human orthologues. Based on our findings, we can support the assumption that multiple genes determine bone strength, with each of them having a rather small effect, as illustrated by our SNP effect estimates. Furthermore, the enrichment analysis showed that some of these candidates are involved in metabolic pathways critical for bone integrity. In conclusion, the identified candidates represent genes that may play a role in the bone integrity of chickens. Although further studies are needed to determine causality, the genes reported here are promising in terms of alleviating bone disorders in laying hens.
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NR 94
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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WC Genetics & Heredity
SC Genetics & Heredity
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AF Zhuang, Chenyang
Wang, Zixiang
Chen, Weisin
Tian, Bo
Li, Juan
Lin, Hong
TI Osteoporosis and Endplate Damage Correlation Using a Combined Approach of Hounsfield Unit Values and Total Endplate Scores: A Retrospective Cross-Sectional Study
SO CLINICAL INTERVENTIONS IN AGING
LA English
DT Article
DE degenerative disc diseases; bone mineral density; computed tomography; magnetic resonance imaging
ID bone-mineral density; intervertebral disc degeneration; cartilage; osteoarthritis; association; disease; fusion

AB Purpose: Osteoporosis and endplate damage, two primary orthopedic disorders that have adverse effects on the quality of life of older adults, may have some previously unknown relationship. The purpose of this study was to determine the potential association between osteoporosis and endplate damage with two specific imaging scoring systems and analyze the underlying mechanisms. Patients and Methods: A cross-sectional study including 156 patients with degenerative disc disease (DDD) who visited our department in 2018 was performed. Data including age, sex, body mass index, Hounsfield unit (HU) values utilizing computed tomography (CT), and total endplate scores (TEPSs) using magnetic resonance imaging (MRI) of all patients were retrospectively collected and analyzed. The average HU value and TEPS of L1-L4 were used to represent the degrees of bone mineral density (BMD) and endplate damage, respectively. Patients with an HU value < 110 were defined as having osteoporosis and placed in the low-BMD group; otherwise, they were placed in the normal-BMD group. Multivariate logistic regression models were used to determine the independent factors of endplate damage. Results: The TEPSs in the low-BMD group were significantly higher (6.4 +/- 1.6 vs 5.0 +/- 0.9, p < 0.001) overall and in every segment of L1-L4 (p < 0.01). A significant negative correlation was found between TEPS and HU values (p < 0.001). The HU value (odds ratio [OR] 0.221; 95% confidence interval [CI], 0.148-0.295, p < 0.001), age (OR 0.047; 95% CI, 0.029-0.224, p < 0.001), and BMD (OR 3.796; 95% CI, 2.11-7.382, p < 0.05) were independent factors influencing endplate damage. Conclusion: A significantly positive correlation was observed between osteoporosis and endplate damage, indicating the requirement for a more comprehensive therapeutic regimen for treating patients with DDD complicated with osteoporosis.
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TI Anterior Cruciate Ligament Reconstruction versus Nonoperative Treatment: Better Function and Less Secondary Meniscectomies But No Difference in Knee Osteoarthritis-A Meta-Analysis
SO CARTILAGE
LA English

DT Article
DE anterior cruciate ligament; ACL reconstruction; conservative treatment; osteoarthritis; radiologic evaluation
ID quality-of-life; nonsurgical treatment; cartilage injury; high prevalence; soccer players; rupture; classification; epidemiology; individuals; lesions
AB Objectives The impact of anterior cruciate ligament (ACL) reconstruction on knee osteoarthritis (OA) is still unclear. The aim of the current meta-analysis was to compare surgical treatment versus nonoperative management of ACL tears to assess the impact of these approaches on knee OA development at a 5 and 10 years of follow-up. Design A meta-analysis was performed after a systematic literature search (May 2021) was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. Both randomized and nonrandomized comparative studies with more than 5 years of follow-up were selected. Influence of the treatment was assessed in terms of knee OA development, subjective and objective clinical results, activity level, and risk of further surgeries. Risk of bias and quality of evidence were assessed following the Cochrane guidelines. Results Twelve studies matched the inclusion criteria, for a total of 1,004 patients. Level of evidence was rated low to very low. No difference was documented in terms of knee OA development, Tegner score, subjective International Knee Documentation Committee (IKDC), and Lysholm scores. A significant difference favoring the surgical treatment in comparison with a nonsurgical approach was observed in terms of objective IKDC score ($P = 0.03$) and risk of secondary meniscectomy ($P < 0.0001$). The level of evidence was considered very low for subjective IKDC, low for knee OA development, objective IKDC, number of secondary meniscectomies, and Lysholm score, and moderate for post-op Tegner score. Conclusions The meta-analysis did not support an advantage of ACL reconstruction in terms of OA prevention in comparison with a nonoperative treatment. Moreover, no differences were reported for subjective results and activity level at 5 and 10 years of follow-up. On the contrary, patients who underwent surgical treatment of their ACL tear presented important clinical findings in terms of better objective knee function and a lower rate of secondary meniscectomies when compared with conservatively managed patents. Protocol Registration: CRD420191156483 (PROSPERO)
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TI Nanotechnological approach and bio-inspired materials to face degenerative diseases in aging
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Biomimetic materials; Osteoarthritis; Osteoporosis; Cell therapy; Bioresorbable nanoparticles; Regenerative medicine
ID autologous chondrocyte implantation; calcium-phosphate cements; attributable activity limitation; doctor-diagnosed arthritis; osteochondral regeneration; electromagnetic-fields; mechanical-property; cardiac dysfunction; periodontal-disease; tissue regeneration
AB The aging of the world population is increasingly claimed as an alarming situation, since an ever-raising number of persons in advanced age but still physically active is expected to suffer from invalidating and degenerative diseases. The impairment of the endogenous healing potential provoked by the aging requires the development of more effective and personalized therapies, based on new biomaterials and devices able to direct the cell fate to stimulate and sustain the regrowth of damaged or diseased tissues. To obtain satisfactory results, also in cases where the cell senescence, typical of the elderly, makes the regeneration process harder and longer, the new solutions have to possess excellent ability to mimic the physiological extracellular environment and thus exert biomimetic stimuli on stem cells. To this purpose, the "biomimetic concept" is today recognized as elective to fabricate bioactive and bioresorbable devices such as hybrid osteochondral scaffolds and bioactive bone cements closely resembling the natural hard tissues and with enhanced regenerative ability. The review will illustrate some recent results related to these new biomimetic materials developed for application in different districts of the musculoskeletal system, namely bony,

osteochondral and periodontal regions, and the spine. Further, it will be shown how new bioactive and superparamagnetic calcium phosphate nanoparticles can give enhanced results in cardiac regeneration and cancer therapy. Since tissue regeneration will be a major demand in the incoming decades, the high potential of biomimetic materials and devices is promising to significantly increase the healing rate and improve the clinical outcomes even in aged patients.
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Comprehensive Review
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DT Review
DE flavonoids; linarin; chemotaxonomy; phytochemistry; bioactivities
ID flos-chrysanthemi-indici; nf-kappa-b; cirsium-japonicum; in-vitro; liquid-chromatography; simultaneous quantification; inflammatory response; chemical-constituents; inhibitory-activity; cytokine production
AB Many flavonoids, as eminent phenolic compounds, have been commercialized and consumed as dietary supplements due to their incredible human health benefits. In the present study, a bioactive flavone glycoside linarin (LN) was designated to comprehensively overview its phytochemical and biological properties. LN has been characterized abundantly in the Cirsium, Micromeria, and Buddleja species belonging to Asteraceae, Lamiaceae, and Scrophulariaceae families, respectively. Biological assessments exhibited promising activities of LN, particularly, the remedial effects on central nervous system (CNS) disorders, whereas the remarkable sleep enhancing and sedative effects as well as AChE (acetylcholinesterase) inhibitory activity were highlighted. Of note, LN has indicated promising anti osteoblast proliferation and differentiation, thus a bone formation effect. Further biological and pharmacological assessments of LN and its optimized semi-synthetic derivatives, specifically its therapeutic characteristics on osteoarthritis and osteoporosis, might lead to uncovering potential drug candidates.
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TI Senolytics and senomorphics: Natural and synthetic therapeutics in the treatment of aging and chronic diseases
SO FREE RADICAL BIOLOGY AND MEDICINE
LA English
DT Review
DE Senolytics; Senomorphics; Cellular senescence; Natural compounds; Aging; Age-related diseases; Senescence-associated secretory phenotype (SASP)
ID extends life-span; senescence-like phenotype; mesenchymal stem-cells; dna-damage response; cellular senescence; secretory phenotype; oxidative stress; human fibroblasts; bcl-2 family; transcription factor
AB Cellular senescence is a heterogeneous process guided by genetic, epigenetic and environmental factors, characterizing many types of somatic cells. It has been suggested as an aging hallmark that is believed to contribute to aging and chronic diseases. Senescent cells (SC) exhibit a specific senescence-associated secretory phenotype (SASP), mainly characterized by the production of proinflammatory and matrix-degrading molecules. When SC accumulate, a chronic, systemic, low-grade inflammation, known as inflammaging, is induced. In turn, this chronic immune system activation results in reduced SC clearance thus establishing a vicious circle that fuels inflammaging. SC accumulation represents a causal factor for various age-related pathologies. Targeting of several aging hallmarks has been suggested as a strategy to ameliorate healthspan and possibly lifespan. Consequently, SC and SASP are viewed as potential therapeutic targets either through the selective killing of SC or the selective SASP blockage, through natural or synthetic compounds. These compounds are members of a family of agents called senotherapeutics divided into senolytics and senomorphics. Few of them are already in clinical trials, possibly representing a future treatment of age-related pathologies including diseases such as atherosclerosis, osteoarthritis, osteoporosis, cancer, diabetes, neurodegenerative diseases such as Alzheimer's disease, cardiovascular diseases, hepatic steatosis, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis and age-related macular degeneration. In this review, we present the already identified senolytics and senomorphics focusing on their redox-sensitive properties. We describe the studies that revealed their effects on cellular senescence and enabled their nomination as novel anti-aging agents. We refer to the senolytics that are already in clinical trials and we present various adverse effects exhibited by senotherapeutics so far. Finally, we discuss aspects of the senotherapeutics that need improvement and we suggest the design of future senotherapeutics to target specific redox-regulated signaling pathways implicated either in the regulation of SASP or in the elimination of SC.
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TI Subchondral Trabecular Microstructure and Articular Cartilage Damage Variations Between Osteoarthritis and Osteoporotic Osteoarthritis: A Cross-sectional Cohort Study
SO FRONTIERS IN MEDICINE
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DT Article
DE individual trabeculae segmentation; osteoarthritis; osteoporotic osteoarthritis; cartilage damage; subchondral trabecular boned
ID morphological analyses; element analysis; cancellous bone; finite-element; knee; plate; microarchitecture; hip; bisphosphonates; progression
AB Osteoporotic osteoarthritis (OP-OA) is a specific type of OA. In this study, we aimed to assess the subchondral plate and rod microstructural differences between OA and OP-OA patients by using an individual trabeculae segmentation (ITS) system and to analyze the relationships between subchondral microstructures and cartilage damage in OA and OP-OA patients. Overall, 31 femoral heads were included in this study, which included 11 samples with OA and 13 samples with OP-OA; the normal control (NC) group contained 7 healthy femoral heads. ITS was performed to segment the subchondral trabecular bone into plate and rod trabeculae based on microcomputed tomography (micro-CT) images. We compared the plate and rod trabeculae of the subchondral trabecular bone between OA and OP-OA patients. The Osteoarthritis Research Society International (OARSI) score was employed to evaluate cartilage damage based on histological observations. Pearson's correlation coefficient and linear regression analysis were applied to analyze the relationships between subchondral microstructures and articular cartilage damage. Results showed that several microstructural parameters, including bone volume fraction (BV/TV), plate bone volume fraction (pBV/TV), rod bone volume fraction (rBV/TV), plate trabecular number (pTb.N), rod trabecular number (rTb.N), junction density between rod and plate (R-P Junc.D), and junction density between plate and plate (P-P Junc.D), were significantly decreased in patients with OP-OA compared with those in patients with OA ($p < 0.05$). Histological observations indicated that cartilage damage was more serious in patients with OP-OA than that in patients with OA ($p < 0.05$). Moreover, BV/TV, pBV/TV, pTb.N, and pTb.Th were significantly related to the OARSI score in both OA and OP-OA patients. These results indicated that there were differences in the subchondral rod and plate trabeculae between OA and OP-OA patients. Subchondral decreased plate trabeculae (pBV/TV, pTb.N, and pTb.Th) might account for cartilage damage in the progression of OP-OA. This study provided

new insights to research OA when it is combined with OP.
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DE Knee Osteoarthritis; Osteoporosis Research; Retrospective Research; Treatment Methods
AB With the rapid development of population aging, the incidence rate of osteoarthritis and osteoporosis is increasing. There is currently a controversy regarding the relationship between knee osteoarthritis and osteoporosis. Therefore, it is of practical significance to study the relationship between knee osteoarthritis and osteoporosis on the basis of analyzing medical records. A

retrospective study of medical records collected 2110 hospitalized patients with knee osteoarthritis, the first patient diagnosed in the hospital. According to the relevant inclusion and exclusion criteria, 1772 medical records were excluded, including 338 medical records. Information on the patient's name and gender, age, course of disease, medication, clinical symptoms and treatment methods were collected. According to the presence or absence of anti-osteoporosis drug combination therapy, the patients were divided into two groups. Group A was treated with anti-osteoporosis drugs in the basic treatment of knee osteoarthritis. The basic treatment of knee osteoarthritis in group B. The symptoms of the two groups were scored, HSS and VAS scores were evaluated and analyzed before and after hospitalization, and the therapeutic effects of the two groups were compared. From this, we can see that group A is better than group B after treatment ($P < 0.05$).
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TI Cellular senescence in musculoskeletal homeostasis, diseases, and regeneration
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ID oncogene-induced senescence; age-related-changes; synovial lining macrophages; secretory phenotype; metabolic syndrome; posttraumatic osteoarthritis; replicative senescence; therapeutic target; possible mechanism; sarcopenia facts
AB Emerging insights into cellular senescence highlight the relevance of senescence in musculoskeletal disorders, which represent the leading global cause of disability. Cellular senescence was initially described by Hayflick et al. in 1961 as an irreversible nondividing state in in vitro cell culture studies. We now know that

cellular senescence can occur in vivo in response to various stressors as a heterogeneous and tissue-specific cell state with a secretome phenotype acquired after the initial growth arrest. In the past two decades, compelling evidence from preclinical models and human data show an accumulation of senescent cells in many components of the musculoskeletal system. Cellular senescence is therefore a defining feature of age-related musculoskeletal disorders, and targeted elimination of these cells has emerged recently as a promising therapeutic approach to ameliorate tissue damage and promote repair and regeneration of the skeleton and skeletal muscles. In this review, we summarize evidence of the role of senescent cells in the maintenance of bone homeostasis during childhood and their contribution to the pathogenesis of chronic musculoskeletal disorders, including osteoporosis, osteoarthritis, and sarcopenia. We highlight the diversity of the senescent cells in the microenvironment of bone, joint, and skeletal muscle tissue, as well as the mechanisms by which these senescent cells are involved in musculoskeletal diseases. In addition, we discuss how identifying and targeting senescent cells might positively affect pathologic progression and musculoskeletal system regeneration.
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NR 198
TC 106
Z9 119
U1 2
U2 49
PU SPRINGERNATURE
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON, N1 9XW, ENGLAND
SN 2095-4700
EI 2095-6231
J9 BONE RES
JI Bone Res.
PD SEP 10
PY 2021
VL 9
IS 1
BP
EP
DI 10.1038/s41413-021-00164-y
PG 12
WC Cell & Tissue Engineering
SC Cell Biology
GA UO7GY
UT WOS:000694862700001
PM 34508069
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ER

PT J
AU von Vopelius, E
Oheim, R
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Rolvien, T
Beil, FT
AF von Vopelius, E.
Oheim, R.
Amling, M.
Rolvien, T.
Beil, F. T.

TI Skeletal characterization in a patient with Hajdu-Cheney syndrome undergoing total knee arthroplasty
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Hajdu-Cheney syndrome; Histomorphometry; NOTCH2; Osteoarthritis; Osteoporosis; Total knee arthroplasty
AB Hajdu-Cheney syndrome (HCS) is a rare genetic connective tissue disorder caused by gain-of-function mutations in the NOTCH2 gene. We report a 38-year-old male HCS patient with a history of multiple pathologic fractures, poor bone stock under intermittent antiresorptive therapy, and secondary osteoarthritis (OA) of the knee, in which we successfully performed total knee arthroplasty (TKA). Next to a detailed skeletal assessment including laboratory bone metabolism markers, dual energy X-ray absorptiometry (DXA), and high-resolution peripheral quantitative computed tomography (HR-pQCT), undecalcified histologic and histomorphometric analysis was performed on intraoperatively obtained tibial cut sections. This multiscale assessment revealed a severe, combined trabecular-cortical microarchitectural deterioration, increased bone turnover indices, and advanced cartilage degeneration, thus demonstrating the crucial role of Notch2 in skeletal and cartilage homeostasis, which is in line with the findings of previous mouse models.
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NR 21
TC 2
Z9 2
U1 2
U2 3
PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
SN 0937-941X
EI 1433-2965
J9 OSTEOPOROSIS INT
JI Osteoporosis Int.
PD SEP 15
PY 2021
VL 32
IS 9
BP 1899
EP 1904
DI 10.1007/s00198-021-05914-6
EA MAR 2021
PG 6
WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA UF3AG
UT WOS:000630617400001

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PT J
AU Kim, YJ
Kim, BR
Kim, SR
Nam, KW
Lee, SY
Choi, JH
Kim, WB
Kim, BS
AF Kim, Youn Ji
Kim, Bo Ryun
Kim, Sang Rim
Nam, Kwang Woo
Lee, So Young
Choi, Jun Hwan
Kim, Won Bin
Kim, Beom Su
TI Influence of Comorbidities on Short-Term Functional Outcomes After Unilateral Total Knee Arthroplasty
SO AMERICAN JOURNAL OF PHYSICAL MEDICINE & REHABILITATION
LA English
DT Article
DE Comorbidity; Arthroplasty; Replacement; Knee; Osteoarthritis; Rehabilitation
ID osteoarthritis; reliability; epidemiology; validation; diagnosis; recovery; hip
AB Objective The aim of the study was to determine the effect of comorbidities on physical function and quality of life of patients at 3 mos after total knee arthroplasty. Design Data from 140 patients who underwent a primary unilateral total knee arthroplasty were examined retrospectively. Comorbidities were osteoporosis, presarcopenia, degenerative spine disease, diabetes, and hypertension. All patients completed the following: range of motion, stair climbing test, 6-min walk test, Timed Up and Go Test, peak torque of the knee extensor and flexor, instrumental gait analysis, Western Ontario McMaster Universities Osteoarthritis Index, and EuroQoL five-dimension questionnaire. Results Univariate analyses revealed that osteoporosis led to a significantly longer time to complete the stair climbing test-ascent, stair climbing test-descent, and Timed Up and Go Test and to lower scores for the 6-min walk test and peak torque of the knee extensor. Patients with degenerative spine disease showed significant negative scores for knee extension range of motion. Diabetes showed a negative correlation with peak torque of the knee extensor and knee flexion range of motion, as well as a higher Western Ontario McMaster Universities Osteoarthritis Index-stiffness

score. Multivariable linear regression analysis showed that Western Ontario McMaster Universities Osteoarthritis Index-stiffness remained independently associated with diabetes. Six-minute walk test, Timed Up and Go Test, stair climbing test-ascent, and peak torque of the knee extensors showed a significant association with osteoporosis. Conclusions Comorbidities, particularly osteoporosis and diabetes, affect short-term functional outcomes 3 mos after total knee arthroplasty.
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NR 30
TC 6
Z9 6
U1 1
U2 4
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0894-9115
EI 1537-7385
J9 AM J PHYS MED REHAB
JI Am. J. Phys. Med. Rehabil.
PD NOV 15
PY 2021
VL 100
IS 11
BP 1062
EP 1069
DI 10.1097/PHM.0000000000001702
PG 8
WC Rehabilitation; Sport Sciences
SC Rehabilitation; Sport Sciences
GA 5Q8MS
UT WOS:000874079700019
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PT J
AU Ghafouri-Fard, S
Bahroudi, Z
Shoorei, H
Abak, A
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AF Ghafouri-Fard, Soudeh
Bahroudi, Zahra
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Abak, Atefe
Ahin, Maliheh
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TI microRNA-140: A miRNA with diverse roles in human diseases
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Review
DE miR-140; Carcinogenesis; Osteoarthritis; Atherosclerosis; Ischemia; Diabetes
ID epithelial-mesenchymal transition; affects chondrocyte proliferation; promotes cell-proliferation; colorectal-cancer; mir-140-5p; carcinoma; invasion; progression; apoptosis; expression
AB MicroRNA-140 (miR-140) has been shown to be associated with the pathogenesis of a wide range of pathologies including osteoarthritis, osteoporosis, renal fibrosis, ischemic conditions, and most importantly neoplasia. This miRNA has been shown to be down-regulated in a diversity of cancers namely breast cancer, gastrointestinal cancers, lung cancer, and prostate cancer. miR-140 has a lot of immune-related targets. Moreover, several miR140 targets regulate cell proliferation, cell cycle transition, and apoptosis. This miRNA has been shown to be sponged by a number of lncRNAs and circ-RNAs. miR-140 has essential roles in the determination of the sensitivity of neoplastic cells to chemotherapeutic agents such as temozolomide, doxorubicin, and cisplatin. Besides, expression quantities of miR-140 in cancer tissues can be used for the prediction of clinical outcomes of patients with neoplasia. In the present paper, we describe the impact of miR-140 in neoplastic and non-neoplastic disorders.
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PT J
AU Elashry, MI
Baulig, N
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AF Elashry, Mohamed I.
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TI Combined macromolecule biomaterials together with fluid shear stress promote the osteogenic differentiation capacity of equine adipose-derived mesenchymal stem cells
SO STEM CELL RESEARCH & THERAPY
LA English
DT Article
DE Stem cells; Osteogenic differentiation; Biomaterials; Fluid shear stress
AB BackgroundCombination of mesenchymal stem cells (MSCs) and biomaterials is

a rapidly growing approach in regenerative medicine particularly for chronic degenerative disorders including osteoarthritis and osteoporosis. The present study examined the effect of biomaterial scaffolds on equine adipose-derived MSC morphology, viability, adherence, migration, and osteogenic differentiation.MethodsMSCs were cultivated in conjunction with collagen CultiSpher-S Microcarrier (MC), nanocomposite xerogels B30 and combined B30 with strontium (B30Str) biomaterials in osteogenic differentiation medium either under static or mechanical fluid shear stress (FSS) culture conditions. The data were generated by histological means, live cell imaging, cell viability, adherence and migration assays, semi-quantification of alkaline phosphatase (ALP) activity, and quantification of the osteogenic markers runt-related transcription factor 2 (Runx2) and alkaline phosphatase (ALP) expression.ResultsThe data revealed that combined mechanical FSS with MC but not B30 enhanced MSC viability and promoted their migration. Combined osteogenic medium with MC, B30, and B30Str increased ALP activity compared to cultivation in basal medium. Osteogenic induction with MC, B30, and B30Str resulted in diffused matrix mineralization. The combined osteogenic induction with biomaterials under mechanical FSS increased Runx2 protein expression either in comparison to those cells cultivated in BM or those cells induced under static culture. Runx2 and ALP expression was upregulated following combined osteogenic differentiation together with B30 and B30Str regardless of static or FSS culture.ConclusionsTaken together, the data revealed that FSS in conjunction with biomaterials promoted osteogenic differentiation of MSCs. This combination may be considered as a marked improvement for clinical applications to cure bone defects.

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SC Cell Biology; Research & Experimental Medicine
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Gao, LJ
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Li, Qin
TI Network Pharmacology-Based Analysis on the Action Mechanism of Oleanolic Acid to Alleviate Osteoporosis
SO ACS OMEGA
LA English
DT Article
ID bone; osteoclastogenesis; apoptosis; gene; induction; exerts; tp53
AB Oleanolic acid (OA) is a triterpenoid commonly found in plants and has shown extensive pharmaceutical activities. This study aimed to investigate the underlying mechanism of antiosteoporosis (OP) action of OA by utilizing the network pharmacology approach and molecular docking methods. First, the targets of OA were identified using the GeneCards, Stitch, and Swisstarget databases, and the targets related to OP were mined using the NCBI, Genecards, and DisGeNet databases. The overlapped targets of OA and OP were regarded as candidate targets, and the String database was used to obtain the protein- protein interactions among the targets. Then, Gene Ontology (GO) functional enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) metabolic pathway enrichment pathways of the candidate targets were performed using the DAVID database. In addition, the top 16 targets in the protein interaction network were used for molecular docking. Finally, an animal model constructed using 6-galactose-induced oxidative stress and a low-calcium diet with accelerated bone loss was used to verify the in vivo effects of OA on osteoporotic mice. A total of 42 candidate targets for OA to treat OP were obtained. According to the protein-protein interaction network, MAPK1 showed the highest connectivity with other proteins. Additionally, GO analysis identified the top 20 biological processes, 9 cellular components, and top 20 molecular functions. Moreover, the candidate targets were mainly involved in 13 signaling pathways such as TNF signaling pathway, insulin resistance, MAPK signaling pathway, apoptosis, and PI3K-Akt signaling pathways. Furthermore, molecular docking revealed that OA has a high degree of connections with 16 key proteins. In addition, the anti-OP effects of OA are further validated through the in vivo model. Altogether, our study elucidated the candidate targets for OA to alleviate OP, explored the protein-protein interactions and related signaling pathways of the targets, and validated the anti-OP effects of OA. It could provide a better understanding of the action mechanism in OA to treat OP.
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TI Age-related alterations and senescence of mesenchymal stromal cells: Implications for regenerative treatments of bones and joints

SO MECHANISMS OF AGEING AND DEVELOPMENT
LA English
DT Article
DE Mesenchymal stromal cells; Aging; Senescence; Osteoarthritis; Osteoporosis
ID human articular-cartilage; stem-cells; cellular senescence; osteogenic differentiation; extracellular vesicles; knee osteoarthritis; adipose-tissue; gremlin 1; in-vitro; marrow
AB The most common clinical manifestations of age-related musculoskeletal degeneration are osteoarthritis and osteoporosis, and these represent an enormous burden on modern society. Mesenchymal stromal cells (MSCs) have pivotal roles in musculoskeletal tissue development. In adult organisms, MSCs retain their ability to regenerate tissues following bone fractures, articular cartilage injuries, and other traumatic injuries of connective tissue. However, their remarkable regenerative ability appears to be impaired through aging, and in particular in age-related diseases of bones and joints. Here, we review age-related alterations of MSCs in musculoskeletal tissues, and address the underlying mechanisms of aging and senescence of MSCs. Furthermore, we focus on the properties of MSCs in osteoarthritis and osteoporosis, and how their changes contribute to onset and progression of these disorders. Finally, we consider current treatments that exploit the enormous potential of MSCs for tissue regeneration, as well as for innovative cell-free extracellular-vesicle-based and anti-aging treatment approaches.
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TI Potential modulatory mechanisms of action by long-chain polyunsaturated fatty acids on bone cell and chondrocyte metabolism
SO PROGRESS IN LIPID RESEARCH
LA English
DT Review
DE Long-chain polyunsaturated fatty acids; Osteoclasts; Osteoblasts; Chondrocytes; Prostaglandins; PPAR ligands
ID mesenchymal stem-cells; growth-factor-i; factor binding protein-3; ppar-gamma; osteoblastic differentiation; cartilage degeneration; osteoclast formation; articular-cartilage; receptor activator; nitric-oxide
AB Long-chain polyunsaturated fatty acids (LCPUFAs) and their metabolites are considered essential factors to support bone and joint health. The n-6 PUFAs suppress the osteoblasts differentiation via increasing peroxisome proliferator-activated receptor gamma (PPAR gamma) expression and promoting adipogenesis while n-3 PUFAs promote osteoblastogenesis by down-regulating PPAR gamma and enhancing osteoblastic activity. Arachidonic acid (AA) and its metabolite prostaglandin E2 (PGE2) are key regulators of osteoclast differentiation via induction of the receptor activator of nuclear factor kappa-B ligand (RANKL) pathway. Marine-derived n-3 LCPUFAs have been shown to inhibit osteoclastogenesis by decreasing the osteoprotegerin (OPG)/RANKL signalling pathway mediated by a reduction of pro-inflammatory PGE2 derived from AA. Omega-3 PUFAs reduce the expression of cartilage degrading enzyme matrix metalloproteinase-13 (MMP-13) and a disintegrin and metalloprotease with thrombospondin motifs-5 (ADAMTS-5) protein, oxidative stress and thereby apoptosis via nuclear factor kappabetta (NF-k beta) and inducible nitric oxide synthase (iNOS) pathways. In this review, a diverse range of important effects of LCPUFAs on bone cells and chondrocyte was highlighted through different mechanisms of action established by cell cultures and animal studies. This review allows a better understanding of the possible role of LCPUFAs in bone and

chondrocyte metabolism as potential therapeutics in combating the pathological complications such as osteoporosis and osteoarthritis.
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NR 87
TC 89
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U1 4
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TI Associations between dietary patterns and osteoporosis-related outcomes in older adults: a longitudinal study
SO EUROPEAN JOURNAL OF CLINICAL NUTRITION
LA English
DT Article
ID bone-mineral density; fracture risk; life-style; quality; women; mortality; cohort; mass; men
AB Background/Objectives To describe the associations of baseline dietary pattern scores with falls risk, bone mineral density (BMD), and incident fractures measured over 10 years in older adults. Subjects/Methods Dietary patterns were identified using exploratory factor analysis. Femoral neck (FN), hip, and lumbar spine (LS) BMD were measured using dual-energy X-ray absorptiometry, falls risk z-score using the Physiological Profile Assessment, and incident fractures by self-report.

Linear mixed-effects models and log-binomial regression were used to estimate associations between baseline dietary pattern z-scores and outcomes. Results Of 1098 participants at baseline, 567 were retained over 10 years. Four dietary patterns were derived: fruit and vegetable (FV), animal protein (AP), snack, and Western. FV pattern reduced falls risk at baseline by beta = 0.05-0.08/SD and the annual decreases of FN and hip BMD were less for higher Western or AP pattern scores in all populations and women. The annual increase in LS of the entire population was greater with higher scores of FV, AP, and Western patterns (all beta = 0.001 g/cm(2)/year/SD, $p < 0.05$). Higher scores of FV and snack were associated with a higher risk of LS BMD increasing over 10 years ($p < 0.05$ for all, except snack pattern in men) and incident fracture was not associated with any dietary pattern in the overall cohort and both men and women separately. Conclusions An FV dietary pattern may be beneficial for reducing falls risk. The associations of dietary patterns and BMD are modest in magnitude and did not translate into an improved fracture risk. Associations between diet and LS BMD may reflect osteoarthritis rather than osteoporosis.

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TI Adverse Local Tissue Reactions are Common in Asymptomatic Individuals After Hip Resurfacing Arthroplasty: Interim Report from a Prospective Longitudinal Study
SO CLINICAL ORTHOPAEDICS AND RELATED RESEARCH
LA English
DT Article
ID metal-ion levels; head-neck taper; follow-up; pseudotumors; corrosion; knee; association; replacement; prevalence; prostheses
AB Background The evaluation of the natural history prevalence of adverse local tissue reactions (ALTRs) using MRI has focused only on metal-on-metal (MoM) bearing surfaces without comparison to nonMoM bearing surfaces. Questions/purposes To determine (1) the longitudinal changes and differences in blood metal ion levels in patients with hip resurfacing arthroplasty (HRA), ceramic-on-ceramic (CoC) THA, and metal-on-polyethylene (MoP) THA compared with those undergoing ceramic-on-polyethylene (CoP) THA; (2) how the longitudinal change of synovial reaction classification in patients with HRA, CoC THA, and MoP THA compares with those undergoing CoP THA, and whether there is an association between the presence of an ALTR or metallosis on MRI with corresponding patient-reported outcomes, or the presence of capsular dehiscence; and (3) differences in blood metal ion levels between patients undergoing HRA with an ALTR or metallosis on MRI and those with HRA without these conditions. Methods Between March 2014 and February 2019, 22,723 patients underwent primary HRA and THA at one center. Patients received an HRA based on their desired athletic level after surgery and the presence of normal acetabular and proximal femoral bone morphology without osteopenia or osteoporosis. Two percent (342 of 22,723) of patients were contacted to participate, and 71% (243 of 342 hips in 206 patients) were enrolled for analysis at baseline. The patients underwent arthroplasty for degenerative joint disease, and 25 patients withdrew over the course of the study. We included patients who were more than 1 year postarthroplasty. All participants had an MRI examination and blood serum ion testing and completed a Hip Disability and Osteoarthritis Outcome Score survey annually for four years (baseline, year 1, year 2, year 3). Morphologic and susceptibility-reduced MR images were evaluated by a single radiologist not involved in the care of patients for the presence and classification of synovitis (Gwet AC1: 0.65 to 0.97), synovial thickness, and volume (coefficient of repeatability: 1.8 cm(3)). Linear mixed-effects models were used to compare the mean synovial thickness, synovial volume, and Hip Disability and Osteoarthritis Outcome Score subscales between bearing surfaces at each timepoint and within each bearing surface over time. Marginal Cox proportional hazards models were used to compare the time to and the risk of developing ALTR only, metallosis only, and ALTR or metallosis between bearing surfaces. All models were adjusted for age, sex, BMI, and length of implantation based on known confounders for hip arthroplasty. Adjustment for multiple comparisons was performed using the Dunnett-Hsu method. Results Patients with unilateral HRA had higher cobalt and

chromium serum ion levels (baseline: 1.8 +/- 0.8 ppb, year 1: 2.0 +/- 1.5 ppb, year 2: 2.1 +/- 1.2 ppb, year 3: 1.6 +/- 0.7 ppb) than those with unilateral CoP bearings (baseline: 0.0 +/- 0.1 ppb, year 1: 0.1 +/- 0.3 ppb, year 2: 0.0 +/- 0.2 ppb, year 3: 0.0 +/- 0.0 ppb) at all timepoints ($p < 0.001$ for each time point). More patients who received an HRA developed ALTR or metallosis on MRI than did patients with CoP bearings (hazard ratio 4.8 [95% confidence interval 1.2 to 18.4]; $p = 0.02$). There was no association between the longitudinal change of synovial reaction to ALTR or metallosis on MRI with patient-reported outcomes. In addition, there was no association between the presence of dehiscence at baseline and the subsequent development of ALTR or metallosis, as seen on MRI. There were elevated cobalt (4.7 +/- 3. 5 ppb) and chromium (4.7 +/- 2.6 ppb) serum levels in patients with unilateral HRA who had an ALTR or metallosis present on MRI at year 1 compared with patients without an ALTR or metallosis on MRI (cobalt: 1.8 +/- 1.0 ppb, mean difference 4.7 ppb [95% CI 3.3 to 6.0]; $p < 0.001$; chromium: 2.3 +/- 0.5 ppb, mean difference 3.6 ppb [95% CI 2.2 to 5.0]; $p < 0.001$) as well as for chromium at year 3 (3.9 +/- 2.4 ppb versus 2.2 +/- 1.1 ppb, mean difference 1.3 ppb [95% CI 0.3 to 2.4]; $p = 0.01$). Conclusion We found a higher proportion of ALTR or metallosis on MRI in patients with HRA compared with patients with CoP, even when patient self-assessed symptomatology of those with an ALTR or metallosis on MRI was not different than the absence of these features. MRI detected ALTRs in high-function patients, emphasizing that an annual clinical assessment dependent on survey or blood ion testing alone may not detect soft tissue complications. The results of this study are in line with prior consensus recommendations of using MRI as part of a routine follow-up protocol for this patient population.
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J9 CLIN ORTHOP RELAT R
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TI Global Public Interests and Dynamic Trends in Osteoporosis From 2004 to 2019: Infodemiology Study
SO JOURNAL OF MEDICAL INTERNET RESEARCH
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DT Article
DE global public interest; Google trends; osteoporosis; seasonality; trends; infodemiology; information seeking; web-based information
ID health information; aboriginal women; bone-density; people; epidemiology; seasonality; insights; google; risk
AB Background: With the prolonging of human life expectancy and subsequent population aging, osteoporosis (OP) has become an important public health issue. Objective: This study aimed to understand the global public search interests and dynamic trends in "osteoporosis" using the data derived from Google Trends. Methods: An online search was performed using the term "osteoporosis" in Google Trends from January 1, 2004, to December 31, 2019, under the category "Health." Cosinor analysis was used to test the seasonality of relative search volume (RSV) for "osteoporosis." An analysis was conducted to investigate the public search topic rising in RSV for "osteoporosis." Results: There was a descending trend of global RSV for "osteoporosis" from January 2004 to December 2014, and a slowly increasing trend from January 2015 to December 2019. Cosinor analysis showed significant seasonal variations in global RSV for "osteoporosis" (P=.01), with a peak in March and a trough in September. In addition, similar decreasing trends of RSV for "osteoporosis" were found in Australia, New Zealand, Ireland, and Canada from January 2004 to December 2019. Cosinor test revealed significant seasonal variations in RSV for "osteoporosis" in Australia, New Zealand, Canada, Ireland, UK,

and USA (all P<.001). Furthermore, public search rising topics related to "osteoporosis" included denosumab, fracture risk assessment tool, bone density, osteopenia, osteoarthritis, and risk factor. Conclusions: Our study provided evidence about the public search interest and dynamic trends in OP using web-based data, which would be helpful for public health and policy making.
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TI Current advances and novel research on minimal invasive techniques for musculoskeletal disorders
SO DM DISEASE-A-MONTH
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DT Article
ID myofascial trigger points; tension-type headache; intratissue percutaneous electrolysis; electrical nerve-stimulation; heart-rate-variability; knee adduction moment; mechanical neck pain; low-back-pain; referred pain; adverse events
AB The present review summarized the current advances and novel research on minimal invasive techniques for musculoskeletal disorders. Different invasive approaches were proposed in the physical therapy field for the management of musculoskeletal disorders, such as ultrasound-guided percutaneous needle electrolysis, dry needling, acupuncture and other invasive therapy techniques, discussing about their worldwide status, safety and interventional ultrasound imaging. Indeed, dry needling may be one of the most useful and studies invasive physical therapy applications in musculoskeletal disorders of different body regions, such as back, upper limb, shoulder, arm, hand, pelvis, lower limb, neck, head, or temporomandibular joint, and multiple soreness location disorders, such as fibromyalgia. In addition, the assessment and treatment by acupuncture or electro-acupuncture was considered and detailed for different conditions such as plantar fasciitis, osteoarthritis, spasticity, myofascial pain syndrome, osteoporosis and rheumatoid arthritis. As an increasing technique in physical therapy, the use of

ultrasound guided percutaneous needle electrolysis was discussed in injuries of the musculoskeletal system and entrapment neuropathies. Also, ultrasound-guided percutaneous neuromodulation was established as a rising technique combined with ultrasound evaluation of the peripheral nerve system with different clinical applications which need further studies to detail their effectiveness in different musculoskeletal conditions. Thus, invasive physical therapy may be considered as a promising approach with different novel applications in several musculoskeletal disorders and a rising use in the physiotherapy field. (c) 2021 Elsevier Inc. All rights reserved.
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TI Risk factors of ankle osteoarthritis in the treatment of critical bone defects using ilizarov technique
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Bone defect; Bone transport; Ilizarov technique; Joint; Osteoarthritis
ID posttraumatic osteoarthritis; external fixation; arthrodesis; complications; fractures; fusion; reconstruction; osteomyelitis
AB BackgroundDistraction osteogenesis using the Ilizarov external circular fixator has been applied in lower limb reconstructive surgery widely. The increasing ankle osteoarthritis (OA) progression and severity are often associated with the period of external fixator and the greater relative instability of the ankle joint, but few studies have quantified risk factors directly during this technique.MethodsThe study was conducted on 236 patients who underwent bone transport surgery for tibias using the Ilizarov external circular fixator from 2008 to 2018. The cumulative incidence of ankle OA diagnoses in patients after the Ilizarov technique treatment was calculated and stratified by risk factors from preoperative and postoperative management. After the data were significant through the Mann-Whitney U test analyzed, odds ratios were calculated using logistic regression to describe factors associated with the OA diagnosis including gender, age, BMI, location of bone defect, diabetes, hypertension, osteoporosis, the history of metal allergy and glucocorticoid intake, the American Orthopaedic Foot & Ankle Society (AOFAS) ankle-HF scale scores, defect size (DS), the type of bone transport, the bone union time, external fixator time (EFT), and external fixator index (EFI).ResultsThere were 199 males and 37 females with a mean age of 47 years (range 28-59 years). Out of 236 patients, 49 had an additional treatment for ankle OA after the Ilizarov technique treatment of bone defects (average follow-up time 2.1 years, range 1.6-4.2 years). The incidence of postoperative ankle OA was 20.8%, with 19 patients classified as K&L grade 3 and seven patients as grade 4. The top five risk factors included double-level bone transport (OR3.79, P=0.005), EFI>50days/cm (OR3.17, P=0.015), age>45years (OR2.29, P=0.032), osteoporosis (OR1.58, P<0.001), BMI>25 (OR1.34, P<0.001). Male, BMI>25, diabetes, osteoporosis, and AOFAS ankle-HF scale scores are the independent risk factors.ConclusionsIlizarov external circular fixator is a safe and effective method of treatment for critical bone defects. The double level bone transport, EFI>50days/cm, age>45years, osteoporosis, BMI>25

are the top five relevant risk factors of ankle OA. The probability of developing ankle OA among patients having three or more risk factors is 50-70%.
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TI Crosstalk between Bone and Nerves within Bone
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DE bioactive factors; bone metabolism; crosstalk; nerve growth; peripheral nerves
ID gene-related peptide; mesenchymal stem-cells; peripheral nervous-system; osteoblast-like cells; growth-factor-beta; substance-p; heterotopic ossification; rat model; acetylcholine-receptors; adrenergic-receptor
AB For the past two decades, the function of intrabony nerves on bone has been a subject of intense research, while the function of bone on intrabony nerves is still hidden in the corner. In the present review, the possible crosstalk between bone and intrabony peripheral nerves will be comprehensively analyzed. Peripheral nerves participate in bone development and repair via a host of signals generated through the secretion of neurotransmitters, neuropeptides, axon guidance factors and neurotrophins, with additional contribution from nerve-resident cells. In return, bone contributes to this microenvironmental rendezvous by housing the nerves within its internal milieu to provide mechanical support and a protective shelf. A large ensemble of chemical, mechanical, and electrical cues works in harmony with

bone marrow stromal cells in the regulation of intrabony nerves. The crosstalk between bone and nerves is not limited to the physiological state, but also involved in various bone diseases including osteoporosis, osteoarthritis, heterotopic ossification, psychological stress-related bone abnormalities, and bone related tumors. This crosstalk may be harnessed in the design of tissue engineering scaffolds for repair of bone defects or be targeted for treatment of diseases related to bone and peripheral nerves.
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TI MicroRNA-21: An Emerging Player in Bone Diseases
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE miRNAs; miR-21; osteoblasts; osteoclasts; bone diseases
ID mesenchymal stem-cells; promotes osteogenic differentiation; induced osteonecrosis; postmenopausal women; signaling pathway; rankl/opg ratio; mineral density; down-regulation; mir-21; expression
AB MicroRNAs (MiRNAs) are small endogenous non-coding RNAs that bind to the 3 '-untranslated region of target genes and promote their degradation or inhibit translation, thereby regulating gene expression. MiRNAs are ubiquitous in biology and are involved in many biological processes, playing an important role in a variety of physiological and pathological processes. MiRNA-21 (miR-21) is one of them. In recent years, miR-21 has received a lot of attention from researchers as an emerging player in orthopedic diseases. MiR-21 is closely associated with the occurrence, development, treatment, and prevention of orthopedic diseases through a variety of mechanisms. This review summarizes its effects on osteoblasts, osteoclasts and their relationship with osteoporosis, fracture, osteoarthritis (OA), osteonecrosis, providing a new way of thinking for the diagnosis, treatment and prevention of these bone diseases.
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NR 83
TC 22
Z9 27
U1 0
U2 23
PU FRONTIERS MEDIA SA
PI LAUSANNE
PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
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EI 1663-9812
J9 FRONT PHARMACOL
JI Front. Pharmacol.
PD SEP 7
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VL 12
IS
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DI 10.3389/fphar.2021.722804
PG 11
WC Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
GA US4MI
UT WOS:000697405100001
PM 34557095
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PT J
AU Otsuka, Y
Iidaka, T
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TI Dietary Intake of Vitamin E and Fats Associated with Sarcopenia in Community-Dwelling Older Japanese People: A Cross-Sectional Study from the Fifth Survey of the ROAD Study
SO NUTRIENTS
LA English
DT Article
DE sarcopenia; ROAD study; dietary intake; vitamin E; fats
ID skeletal-muscle mass; asian working group; protein-synthesis; consensus; women; antioxidant; leucine; decline; index; frailty
AB Dietary habits are of considerable interest as a modifiable factor for the maintenance of muscle health, especially sarcopenia. The present study aimed to investigate the association between dietary intake and sarcopenia prevalence in community-dwelling Japanese subjects. This cross-sectional study was conducted using data from the fifth survey of the Research on Osteoarthritis/Osteoporosis against Disability (ROAD) study, and 1345 participants (437 men and 908 women) aged >= 60 years were included in the analysis. Sarcopenia was determined by the definition of the Asian Working Group for Sarcopenia established in 2014, and dietary intake was assessed with the brief-type self-administered diet history questionnaire. Overall, 77 subjects (5.7%) were identified as having sarcopenia,

5.0% of men and 6.1% of women. Multiple logistic regression analysis showed that the odds ratios of sarcopenia for the dietary intake of vitamin E (alpha-tocopherol, 0.14 (CI 0.04-0.49), beta-tocopherol (0.24, CI 0.07-0.78), gamma-tocopherol (0.28, CI 0.09-0.87), and fats (fat 0.27, CI 0.08-0.96; monounsaturated fatty acids, 0.22, CI 0.07-0.72, polyunsaturated fatty acids, 0.28, CI 0.09-0.89) at the highest quantile were significantly lower compared with those at the lowest quantile. Therefore, higher dietary intakes of vitamin E and fats would be associated with a lower prevalence of sarcopenia.
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FU Ministry of Health, Labour and Welfare [19FA1401, 19FA0701, 19FA1901]; JSPS KAKENHI [19H03895, 18K18447, JP19K19454]; Japan Agency for Medical Research and Development [17dk0110028h0001, 17gk0210007h0003]; Mitsui Sumitomo Insurance Welfare Foundation; Japan Dairy Association; Nakatomi Foundation; Japan Osteoporosis Foundation; Grants-in-Aid for Scientific Research [18K18447, 19H03895] Funding Source: KAKEN
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NR 54
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U2 18
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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J9 NUTRIENTS
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PD MAY 15
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PG 12
WC Nutrition & Dietetics

SC Nutrition & Dietetics
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PT J
AU Marchese, P
Young, R
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Afoullouss, S
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AF Marchese, Pietro
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Allcock, A. Louise
Barry, Frank
Murphy, J. Mary
TI Deep-Sea Coral Garden Invertebrates and Their Associated Fungi Are Genetic Resources for Chronic Disease Drug Discovery
SO MARINE DRUGS
LA English
DT Article
DE High-throughput screening; hMSC; anti-inflammatory; regenerative medicine; marine fungi; natural products; osteoarthritis; osteoporosis
ID mesenchymal stem-cells; osteogenic differentiation; bone-marrow; in-vitro; chondrogenic differentiation; expression; calcification; cartilage
AB Chronic diseases characterized by bone and cartilage loss are associated with a reduced ability of progenitor cells to regenerate new tissues in an inflammatory environment. A promising strategy to treat such diseases is based on tissue repair mediated by human mesenchymal stem cells (hMSCs), but therapeutic outcomes are hindered by the absence of small molecules to efficiently modulate cell behaviour. Here, we applied a high-throughput drug screening technology to bioprospect a large library of extracts from Irish deep-sea organisms to induce hMSC differentiation toward musculoskeletal lineages and reduce inflammation of activated macrophages. The library included extracts from deep-sea corals, sponges and filamentous fungi representing a novel source of compounds for the targeted bioactivity. A validated hit rate of 3.4% was recorded from the

invertebrate library, with cold water sea pens (octocoral order Pennatulacea), such as Kophobelemnon sp. and Anthoptilum sp., showing the most promising results in influencing stem cell differentiation toward osteogenic and chondrogenic lineages. Extracts obtained from deep-sea fungi showed no effects on stem cell differentiation, but a 6.8% hit rate in reducing the inflammation of activated macrophages. Our results demonstrate the potential of deep-sea organisms to synthetize pro-differentiation and immunomodulatory compounds that may represent potential drug development candidates to treat chronic musculoskeletal diseases.
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NR 47
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Z9 12
U1 2
U2 18
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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J9 MAR DRUGS
JI Mar. Drugs
PD JUL 15
PY 2021
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IS 7
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DI 10.3390/md19070390
PG 18
WC Chemistry, Medicinal; Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
GA TO0AK
UT WOS:000676586100001
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PT J
AU Qu, ZH
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Yan, SG

AF Qu, Zihao
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Hong, Jianqiao
Wang, Wei
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Jiang, Guangyao
Yan, Shigui
TI Causal relationship of serum nutritional factors with osteoarthritis: a Mendelian randomization study
SO RHEUMATOLOGY
LA English
DT Article
DE nutritional factor; OA; Mendelian randomization
ID genome-wide association; knee osteoarthritis; vitamin-e; selenium; risk; osteoporosis; metaanalysis; prevalence; retinol; health
AB Objectives. OA is the most common form of arthritis worldwide and has a major impact on the quality of life among the older population. This study aimed at determining the potential causal effects of several serum nutritional factors on OA. Methods. A total of seven serum nutritional factors were identified from genome-wide association studies. Summary statistics for OA were obtained from UK Biobank (194153 for women and 166 988 for men) and a large genome-wide association studies meta-analysis based on the European population (455 221, 393 873 and 403 124 for overall, hip and knee OA, respectively). Two-sample Mendelian randomization approach was used to estimate the causal association between the selected nutritional factors and the risk of OA. Results. The Mendelian randomization analyses suggested that serum calcium levels were inversely associated with overall OA (95% CI, 0.595, 0.850), hip OA (95% CI, 0.352, 0.799) and knee OA (95% CI, 0.461, 0.901). Serum retinol levels were also inversely associated with hip OA (95% CI, 0.257, 0.778). Moreover, sex-specific associations were observed between serum calcium levels (95% CI, 0.936, 0.998), iron levels (95% CI, 1.000, 1.012), selenium levels (95% CI, 0.923, 0.999) and OA in women. Conclusion. In this study, an inverse causal association between serum calcium levels and OA was established. Serum retinol levels were inversely associated with hip OA. In addition, we provide evidence for the causal effect of serum calcium, iron and selenium on the risk of OA in women.
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TC 39
Z9 42
U1 0
U2 15
PU OXFORD UNIV PRESS
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PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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TI Identification and characterization of two consistent osteoarthritis subtypes by transcriptome and clinical data integration
SO RHEUMATOLOGY
LA English
DT Article
DE osteoarthritis; cluster analyses; subtypes; RNA sequencing
ID knee; proliferation
AB Objective. To identify OA subtypes based on cartilage transcriptomic data in cartilage tissue and characterize their underlying pathophysiological processes and/or clinically relevant characteristics. Methods. This study includes n = 66

primary OA patients (41 knees and 25 hips), who underwent a joint replacement surgery, from which macroscopically unaffected (preserved, n = 56) and lesioned (n = 45) OA articular cartilage were collected [Research Arthritis and Articular Cartilage (RAAK) study]. Unsupervised hierarchical clustering analysis on preserved cartilage transcriptome followed by clinical data integration was performed. Protein-protein interaction (PPI) followed by pathway enrichment analysis were done for genes significant differentially expressed between subgroups with interactions in the PPI network. Results. Analysis of preserved samples (n = 56) resulted in two OA subtypes with n = 41 (cluster A) and n = 15 (cluster B) patients. The transcriptomic profile of cluster B cartilage, relative to cluster A (DE-AB genes) showed among others a pronounced upregulation of multiple genes involved in chemokine pathways. Nevertheless, upon investigating the OA pathophysiology in cluster B patients as reflected by differentially expressed genes between preserved and lesioned OA cartilage (DE-OA-B genes), the chemokine genes were significantly downregulated with OA pathophysiology. Upon integrating radiographic OA data, we showed that the OA phenotype among cluster B patients, relative to cluster A, may be characterized by higher joint space narrowing (JSN) scores and low osteophyte (OP) scores. Conclusion. Based on whole-transcriptome profiling, we identified two robust OA subtypes characterized by unique OA, pathophysiological processes in cartilage as well as a clinical phenotype. We advocate that further characterization, confirmation and clinical data integration is a prerequisite to allow for development of treatments towards personalized care with concurrently more effective treatment response.
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TI Microstructural and Strength Changes in Trabecular Bone in Elderly Patients with Type 2 Diabetes Mellitus
SO DIAGNOSTICS
LA English
DT Article
DE trauma; fracture; hip; diagnostic; imaging; osteoporosis; type 2 diabetes mellitus
AB Type 2 diabetes mellitus (T2DM) is one of the most common chronic diseases worldwide and it is associated with an increased risk of osteoporosis and fragility fractures. Our aim is to analyze the effect of T2DM on bone quality. This is a case-control study. The studied population consisted of 140 patients: 54 subjects with hip fracture (OP) without T2DM, 36 patients with hip fracture and T2DM (OP-T2DM), 28 patients with osteoarthritis (OA) without T2DM, and 22 patients with OA and T2DM (OA-T2DM). Bone markers, bone mineral density, FRAX score, microstructural, and bone material strength from femoral heads were assessed. The group with hip fracture presented lower BMD values than OA ($p < 0.05$). The OP, OP-T2DM, and OA-T2DM groups showed a decrease in bone volume fraction (BV/TV), in trabecular number (Tb.N), and in trabecular thickness (Tb.Th), while an increase was presented in the structural model index (SMI) and trabecular bone pattern factor (Tb.Pf), The groups OP, OP-T2DM, and OA-T2DM also presented lower values than those in group OA regarding the biomechanical parameters in the form of Young's modulus or elastic modulus, toughness, ultimate stress, ultimate load, extrinsic stiffness, and work to failure ($p < 0.05$). Our results show the negative effect of type 2 diabetes mellitus on trabecular bone structure and mechanical properties.
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U2 6
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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EI 2075-4418
J9 DIAGNOSTICS
JI Diagnostics
PD MAR 15
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DI 10.3390/diagnostics11030577
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SC General & Internal Medicine
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PT J
AU Zhu, ZX
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AF Zhu, Zhongxin
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TI Correlation of osteoarthritis or rheumatoid arthritis with bone mineral density in adults aged 20-59 years
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Osteoarthritis; Degenerative arthritis; Rheumatoid arthritis; Bone health; NHANES
ID radiographic knee osteoarthritis; osteoporosis; women; hip; fracture; risk; bmd; association; prevalence; validation
AB BackgroundIt is reported that osteoporosis commonly occurs among patients with rheumatoid arthritis (RA), whereas the association between osteoporosis and osteoarthritis (OA) remains controversial. Our aim in this study was to investigate the association between BMD, as a marker of osteoporosis, and OA and RA among adults 20-59 years of age, using a population-based sample from the National Health and Nutrition Examination Survey (NHANES).MethodsOur analysis was based on the NHANES data collected between 2011 and 2018. Data regarding arthritis status and the type of arthritis (OA or RA) were obtained from questionnaires. Lumbar BMD was measured by dual-energy X-ray absorptiometry. The association between OA, RA, and lumbar BMD was evaluated using logistic regression models. Subgroup analyses, stratified by gender and race, were performed. The association between duration of arthritis and lumbar BMD was also investigated.ResultsA total of 11,094 adults were included in our study. Compared to the non-arthritis group, participants with OA had a higher lumbar BMD (beta = 0.023, 95% CI 0.011-0.035), with no significant association between lumbar BMD and RA (beta = 0.014, 95% CI - 0.003 to 0.031). On subgroup analyses stratified by gender, males with OA had a higher lumbar BMD compared to those without OA (beta = 0.047, 95% CI 0.028-0.066). In females, OA was not associated with lumbar BMD (beta = 0.007, 95% CI - 0.008 to 0.021). There was no association between lumbar BMD and RA in both males (beta = 0.023, 95% CI - 0.003 to 0.048) and females (beta = 0.008, 95% CI - 0.015 to 0.031). Duration of arthritis was not associated with lumbar BMD for both OA (beta = - 0.0001, 95% CI - 0.0017 to 0.0015) and RA (beta = 0.0006, 95% CI - 0.0012 to 0.0025).ConclusionsLumbar BMD was associated with OA but not with RA. While a higher lumbar BMD was associated with OA in males, but not in females. Our findings may improve our understanding between OA, RA, and bone health.
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PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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JI J. Orthop. Surg. Res.
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WC Orthopedics
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PT J
AU Ariosa-Morejon, Y
Santos, A
Fischer, R
Davis, S
Charles, P
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AF Ariosa-Morejon, Yoanna
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TI Age-dependent changes in protein incorporation into collagen-rich tissues of mice by in vivo pulsed SILAC labelling
SO ELIFE
LA English
DT Article
DE Age; protein dynamics; proteomics; SILAC; matrisome; collagen-rich tissues; Mouse
ID human articular-cartilage; growth-factor 2; computational platform; extracellular-matrix; aspartic-acid; mouse; skin; osteoarthritis; accumulation; turnover
AB Collagen-rich tissues have poor reparative capacity that predisposes to common age-related disorders such as osteoporosis and osteoarthritis. We used in vivo pulsed SILAC labelling to quantify new protein incorporation into cartilage, bone, and skin of mice across the healthy life course. We report dynamic turnover of the matrisome, the proteins of the extracellular matrix, in bone and cartilage during skeletal maturation, which was markedly reduced after skeletal maturity. Comparing young adult with older adult mice, new protein incorporation was reduced in all tissues. STRING clustering revealed changes in epigenetic modulators across all tissues, a decline in chondroprotective growth factors such as FGF2 and TGF beta in cartilage, and clusters indicating mitochondrial dysregulation and reduced collagen synthesis in bone. Several pathways were implicated in age-related disease. Fewer changes were observed for skin. This methodology provides dynamic protein data at a tissue level, uncovering age-related molecular changes that may predispose to disease.
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FU Daphne Jackson Trust; Versus Arthritis Centre for Osteoarthritis Pathogenesis [20205, 21621]; Wellcome Trust [106995/Z/15/Z] Funding Source: researchfish
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WC Biology
SC Life Sciences & Biomedicine - Other Topics
GA WA8BR
UT WOS:000703109300001
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PT J
AU Nazari-Farsani, S
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AF Nazari-Farsani, Sanaz

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TI Contributing factors to the initial femoral stem migration in cementless total hip arthroplasty of postmenopausal women
SO JOURNAL OF BIOMECHANICS
LA English
DT Article
DE Hip arthroplasty; Radiostereometric analysis; Postmenopausal osteoporosis; Gait analysis; Walking activity
ID radiostereometric analysis; cortical porosity; early subsidence; distal radius; wedge stem; rsa; stability; fill; osteoporosis; denosumab
AB In cementless total hip arthroplasty (THA), femoral stems rely on the initial press-fit fixation against cortical bone to achieve osseointegration. Decreased bone mineral density (BMD) in postmenopausal women poses natural difficulties in achieving axial and rotational femoral stem stability. The present study examined contributing demographic, surgery-related and postoperative factors in determining the magnitude of early stem migration prior to osseointegration. A prospective cohort of 65 postmenopausal women with hip osteoarthritis (Dorr type A or B femur anatomy) underwent THA with implantation of an uncemented parallel-sided femoral component. Postoperative femoral stem translation and rotation were measured using model-based radiostereometric analysis. Based on analysis of covariance, which controlled for outliers and randomized antiresorptive treatment with denosumab or placebo, none of the analyzed demographics (including BMI) and surgery-related variables (including the stem-to-canal fil ratio) was associated with stem subsidence. Stem subsidence (mean 1.8 mm, 95% CI 1.2 to 2.4) occurred even in women with normal hip BMD. Total hip BMD and postoperative walking activity (measured three months after surgery) were significantly associated with stem rotation, and height acted as a confounding factor. The effect of walking activity on stem rotation was significant at 5 months ($p = 0.0083$) and at 11 months ($p = 0.0117$). This observation confirms the previous results of instrumented hip prostheses on torsional moments affecting stems during daily activities. High-resolution imaging modalities of local bone quality are needed to explore reasons for RSA-measurable stem subsidence even in women with normal hip BMD. (c) 2021 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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NR 53
TC 13
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U2 4
PU ELSEVIER SCI LTD
PI London
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PT J
AU Villatoro-Villar, M
   Kwoh, CK
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TI Bisphosphonates, Bone and Joint Pain
SO CURRENT OSTEOPOROSIS REPORTS
LA English
DT Review
DE Bisphosphonates; Anti-resorptive therapy; Osteoarthritis; Pain
ID knee osteoarthritis; marrow lesions; articular-cartilage; subchondral bone; lining cells; risedronate; alendronate; clodronate; arthritis; symptoms
AB Purpose of Review Bisphosphonates (BPs) have an established role in a number of diseases including osteoporosis, but the role of BPs for treating symptomatic conditions other than bone metastases is less clear. We review recent data on the efficacy of BPs in the treatment of symptomatic bone and joint pain with osteoarthritis (OA) as an example. Recent Findings Although controversial, BPs have been reported to improve pain ratings, imaging features, and inflammatory markers in patients with arthritis, more specifically OA. It is possible that their effects in periarticular bone strongly influence the complex inflammatory process within the joints. Recent data also suggests that they can potentially impact synovial and synoviocytes and macrophages. Although more studies are needed to define their contribution in clinical practice, increasing evidence suggests they hold an important function, especially in conditions with periarticular bone involvement such as OA. Although BPs are indicated primarily for prevention and treatment of osteoporosis, they can also have potential effects on the inflammatory process of other conditions, including OA. Improvements in pain scale ratings, periarticular findings through imaging, and inflammatory response suggest their potential extra-osteoporotic properties.
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PI NEW YORK
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AU Easwaran, K
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AF Easwaran, Kobena
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TI Effectiveness of Tai Chi for health promotion for adults with health conditions: a scoping review of Meta-analyses
SO DISABILITY AND REHABILITATION
LA English
DT Review
DE Tai Ji; PubMed; health promotion; adults; meta-analysis
ID quality-of-life; obstructive pulmonary-disease; chronic heart-failure; cancer-patients; challenges inherent; pain conditions; ji quan; qigong; balance; exercise
AB Purpose: To complete a scoping review of meta-analyses summarizing evidence of the effectiveness of Tai Chi for adults with health conditions. Materials and Methods: Meta-analyses were retrieved from Medline, Embase, AMED, CINAHL, SPORTDiscus, PsychINFO, Web of Science, PubMed Health and the Cochrane Library from database inception to early September 2018. Multistage deduplication and screening processes identified full-length, unique, peer-reviewed meta-analyses. Two people independently appraised 42 meta-analyses based on the GRADE system and organized results into 3 appendices subsequently collated into heterogeneous, statistically significant, and statistically insignificant tables. Results: "High" and "moderate" quality evidence indicates that Tai Chi can significantly benefit adults with health conditions including cancers, chronic obstructive pulmonary disease, coronary heart disease, depression, heart failure, hypertension, low back pain, osteoarthritis, osteoporosis, Parkinson's Disease and stroke. Outcomes included significant improvements in activities of daily living, balance, exercise capacity, gait, mastery, mental health, mobility, motor function, participation in daily life, physical function, quality of life, range of motion, and strength; with reductions in blood pressure, body mass index, depression, disability, dyspnea, falls, fatigue, pain, stiffness, and waist circumference. Conclusions: Healthcare providers now have information to advise clients with health conditions on the effectiveness of Tai Chi for overall health promotion.
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NR 73
TC 29
Z9 33
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AU Liu, Y
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TI Zoledronic Acid for Periprosthetic Bone Mineral Density Changes in Patients With Osteoporosis After Hip Arthroplasty-An Updated Meta-Analysis of Six Randomized Controlled Trials
SO FRONTIERS IN MEDICINE
LA English
DT Article
DE zoledronic acid; total hip arthroplasty; osteoporosis; systematic review; meta-analysis; randomized controlled trial
ID follow-up; double-blind; women; bisphosphonates; osteoarthritis; prevention;

fractures; prognosis; infusion; stem
AB Introduction: Periprosthetic bone mineral density (BMD) loss following total hip arthroplasty (THA) may threaten the survival of the implant, especially in patients with osteoporosis. Zoledronic acid (ZA) is the representative of the third generation of bisphosphonates, which were effective in reducing bone loss in conditions associated with accelerated bone turnover. The aim of this study was to evaluate the efficacy and safety of ZA in patients with osteoporosis after THA.Methods: Randomized controlled trials (RCTs) associated with ZA and THA were searched from the MEDLINE, PubMed, EMBASE, Wanfang database, and the Web of Science (August 2021). Other methods, such as hand search and email request were also tried. The methodological quality was assessed by the Risk of Bias (RoB) 2.0. Relevant data were abstracted from the included RCTs and authors were contacted when necessary.Results: In this study, six RCTs involving a total of 307 patients were finally included and analyzed. The pooled data demonstrated that significantly less periprosthetic BMD loss in Gruen zone seven had occurred in the ZA-treated patients than in the control patients at 3 months (mean difference [MD] = 4.03%; 95% CI: 0.29-7.76%; P = 0.03), 6 months (MD = 7.04%; 95% CI: 2.12-11.96%; P = 0.005), and 12 months (MD = 7.12%; 95% CI: 0.33-13.92%; P = 0.04). The Harris Hip Score (HHS) was also significantly increased in ZA group at 6 and 12 months after operation (P = 0.03 and P = 0.02, respectively). Influenza-like symptom was found related to the usage of ZA [relative risk (RR) = 7.03, P < 0.0001].Conclusion: A meta-analysis of six RCTs suggested that ZA was beneficial in maintaining the periprosthetic BMD in patients with osteoporosis at 6 and 12 months after THA. In addition, the HHS was significantly improved in patients treated with ZA. However, the short length of follow-up of the available studies resulted in the lack of analyses regarding the survival of implants including the rate of aseptic loosing, periprosthetic fracture, and revision. It still needs to be determined in research with longer follow-up period.
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NR 40
TC 12
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AU Li, H
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TI Role of Exosomal Non-Coding RNAs in Bone-Related Diseases
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE bone-related diseases; exosomes; non-coding RNAs; osteoporosis; osteoarthritis
ID mesenchymal stem-cells; in-vitro; regulates osteoclastogenesis; osteogenic differentiation; chondrocyte proliferation; mediated delivery; signaling circuit; messenger-rnas; micro-rnas; osteoporosis
AB Bone-related diseases seriously affect the lives of patients and carry a heavy economic burden on society. Treatment methods cannot meet the diverse clinical needs of affected patients. Exosomes participate in the occurrence and development of many diseases through intercellular communication, including bone-related diseases. Studies have shown that exosomes can take-up and "package" non-coding RNAs and "deliver" them to recipient cells, thereby regulating the function of recipient cells. The exosomal non-coding RNAs secreted by osteoblasts, osteoclasts, chondrocytes, and other cells are involved in the regulation of bone-related diseases by inhibiting osteoclasts, enhancing chondrocyte activity and promoting angiogenesis. Here, we summarize the role and therapeutic potential of exosomal non-coding RNAs in the bone-related diseases osteoporosis, osteoarthritis, and bone-fracture healing, and discuss the clinical application of exosomes in patients with bone-related diseases.
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TI High prevalence and undertreatment of osteoporosis in elderly patients undergoing total hip arthroplasty
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LA English
DT Article
DE Arthroplasty; Bone mineral density; DXA; Osteoarthritis; Osteoporosis
ID periprosthetic bone loss; vitamin-d deficiency; joint arthroplasty; bisphosphonate use; osteoarthritis; replacement; women; risk; epidemiology; fracture
AB We detected a high prevalence of low bone mineral density assessed by DXA in 268 elderly patients with end-stage osteoarthritis scheduled for total hip arthroplasty (18% osteoporosis, 41% osteopenia). Therefore, and due to the identified concomitant undertreatment, routine DXA measurements should be considered in elderly patients prior to surgery. Introduction Bone quality represents a decisive factor for osseointegration, durability, and complications of an implanted prosthesis. Although the risk of osteoporosis increases with age and the assessment of bone mineral density (BMD) prior to total hip arthroplasty (THA) is recommended in elderly patients, a systematic, unbiased analysis of such patients is not available in the literature. Methods In this retrospective study, we examined 268 elderly patients (age >= 70 years) who underwent dual-energy X-ray absorptiometry (DXA) within 3 months prior to primary THA. Demographics, medical history, radiographic OA grade, and stem fixation method (i.e., cemented or cementless) were obtained. Results In total, 153 (57%) cemented and 115 (43%)

cementless stem fixations during THA were performed. Forty-nine patients (18%) were diagnosed with osteoporosis (T-score <=-2.5), 110 patients (41%) with osteopenia (T-score <=-1.0), and 109 patients (41%) with normal BMD (T-score >-1.0). Importantly, 36/49 patients (73%) with osteoporosis were not diagnosed before, resulting in a relevant undertreatment. Female sex and low body mass index (BMI) were the main factors negatively influencing the bone mineral density (BMD). Conclusions Due to a high incidence of undiagnosed and untreated osteoporosis in elderly patients with potential effects on the success of osseointegration as well as other clinical outcomes, DXA measurements should be included in the clinical routine for these patients prior to THA.
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NR 34
TC 53
Z9 58
U1 0
U2 10
PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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JI Osteoporosis Int.
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SC Endocrinology & Metabolism
GA UC8MV

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PT J
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TI miR-21-5p targets SKP2 to reduce osteoclastogenesis in a mouse model of osteoporosis
SO JOURNAL OF BIOLOGICAL CHEMISTRY
LA English
DT Article
ID rankl-induced osteoclast; differentiation; estrogen
AB Osteoporosis results from an imbalance between bone formation and bone resorption. Traditional drugs for treating osteoporosis are associated with serious side effects, and thus, new treatment methods are required. This study investigated the role of differentially expressed microRNAs during osteoclast differentiation and osteoclast activity during osteoarthritis as well as the associated underlying mechanisms. We used a microarray to screen microRNAs that decreased in the process of osteoclast differentiation and verified miR-21-5p to decrease significantly using RT-qPCR. In follow-up experiments, we found that miR-21-5p targets SKP2 to regulate osteoclast differentiation. In vivo, ovariectomized mice were used to simulate perimenopausal osteoporosis induced by estrogen

deficiency, and miR-21-5p treatment inhibited bone resorption and maintained bone cortex and trabecular structure. These results suggest that miR-21-5p is a new therapeutic target for osteoporosis.
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TC 29
Z9 32
U1 1
U2 14
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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JI J. Biol. Chem.
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WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
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PT J

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Tian, SQ
AF Zhang, Chi
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Sun, Kang
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Tian, Shaoqi
TI Effects of Melatonin on Osteogenic Differentiation of Bone Marrow Mesenchymal Stem Cells in Inflammatory Environment by Regulating Mammalian Target of Rapamycin/Phosphatidylinositol 3-Kinase/Protein Kinase B Signaling
SO JOURNAL OF BIOMATERIALS AND TISSUE ENGINEERING
LA English
DT Article
DE Melatonin; Osteoarthritis; mTOR/PI3K/AKT Signaling Pathway; Oxidative Stress; Inflammatory Factors
ID osteoarthritis; degeneration; replacement; cartilage; joint; risk; knee; hip
AB Human bone marrow mesenchymal stem cells (BMSCs) differentiation into special cell types is affected by inflammation. Melatonin has various effects such as anti-oxidation and immune regulation. However, melatonin's effect on BMSCs osteogenic differentiation during inflammation has not been elucidated. Rat BMSCs were isolated and assigned into control group, inflammation group (1 mu g/ml lipopolysaccharide, LPS) and melatonin group (100 mu M melatonin was added to LPS-stimulated BMSCs cells) followed by analysis of BMSCs proliferation by MTT assay, Caspase 3 and ALP activity, expression of Runx2 and OP by Real time PCR, ROS content and SOD activity, TNF-alpha and IL-1 beta secretion by ELISA and mTOR/PI3K/AKT signaling protein level by Western blot. LPS action on BMSCs significantly inhibits BMSCs proliferation, promotes Caspase 3 activity, inhibits ALP activity, decreases Runx2 and OP expression and SOD activity, increases ROS content and TNF-alpha and IL-1 beta secretion as well as reduced mTOR and p-PI3K level ($P < 0.05$). Melatonin addition significantly reversed the above changes ($P < 0.05$). Melatonin can regulate oxidative stress, inhibit inflammation, and promote BMSCs proliferation and osteogenic differentiation in inflammatory environment by activating mTOR/PI3K/AKT signaling pathway.
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NR 26
TC 0
Z9 0
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WC Cell & Tissue Engineering
SC Cell Biology
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PT J
AU Langer, RD
AF Langer, R. D.
TI The role of medications in successful aging
SO CLIMACTERIC
LA English
DT Review
DE Menopause; disability-adjusted life year; primary prevention; menopausal hormone therapy; aging; medications; chronic diseases; women’ s health
ID hormone-replacement therapy; estrogen plus progestin; healthy postmenopausal women; coronary-heart-disease; breast-cancer risk; venous thromboembolism; cardiovascular-disease; depressive symptoms; primary prevention; equine estrogen
AB Successful aging includes good health and low levels of disability. To that end, primary prevention is far better than managing subsequent organ damage. When medication is needed to prevent or manage disease, the preferred choice should be associated with the greatest benefits and fewest adverse effects. Cardiovascular diseases are the leading cause of morbidity and mortality in postmenopausal women worldwide. Considering disease-adjusted life years, other leading causes are chronic obstructive pulmonary disease, diabetes mellitus, dementias, hearing loss, cancers of the breast, lung and bowel, osteoporosis, fractures and falls, depression, osteoarthritis, refractive errors of the eye and non-diabetic chronic kidney disease. This review explores the global prevalence of these diseases in women aged 50 years and older, and medications commonly used for them, and contrasts the effects of menopausal hormone therapy (MHT) with others. When initiated early, there is good evidence for MHT benefit in all-cause mortality and primary prevention of cardiovascular disease, diabetes and osteoporosis; fair

evidence for benefit in dementias, depression and osteoarthritis; limited evidence for benefit in chronic obstructive pulmonary disease, hearing loss, non-diabetic chronic kidney disease and colorectal cancer; null effects on lung cancer and refractive errors; and varied effects on breast cancer and stroke. Relative benefits and adverse effects of other medications warrant consideration.
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TI LncRNAs as a new regulator of chronic musculoskeletal disorder
SO CELL PROLIFERATION
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DT Review
DE arthropathy; chronic musculoskeletal disorder; long non-coding RNA; rachiopathy; osteopathy
ID long noncoding rna; mesenchymal stem-cells; intervertebral disc degeneration; nucleus pulposus cells; chondrocyte apoptosis; satellite cells; osteoarthritis; proliferation; bone; growth
AB Objectives In recent years, long non-coding RNAs (lncRNAs) have been found to play a role in the occurrence, progression and prognosis of chronic musculoskeletal disorders. Design and methods Literature exploring on PubMed was conducted using the combination of keywords 'LncRNA' and each of the following: 'osteoarthritis', 'rheumatoid arthritis', 'osteoporosis', 'osteogenesis', 'osteoclastogenesis', 'gout arthritis', 'Kashin-Beck disease', 'ankylosing spondylitis', 'cervical spondylotic myelopathy', 'intervertebral disc degeneration', 'human muscle disease' and 'muscle hypertrophy and atrophy'. For each disorder, we focused on the publications in the last five years (5/1/2016-2021/5/1, except for Kashin-Beck disease). Finally, we excluded publications that had been reported in reviews of various musculoskeletal disorders during the last three years. Here, we summarized the progress of research on the role of lncRNA in multiple pathological processes during musculoskeletal disorders. Results LncRNAs play a crucial role in regulating downstream gene expression and maintaining function and homeostasis of cells, especially in chondrocytes, synovial cells, osteoblasts, osteoclasts and skeletal muscle cells. Conclusions Understanding the mechanisms of lncRNAs in musculoskeletal disorders may provide promising strategies for clinical practice.
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TI Influences of the IL-6 cytokine family on bone structure and function
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ID leukemia-inhibitory factor; ciliary neurotrophic factor; cardiotrophin-like cytokine; kappa-b ligand; induced sweating syndrome; soluble interleukin-6 receptors; alkaline-phosphatase activity; rheumatoid-arthritis patients; human articular chondrocytes; inflammatory-bowel-disease
AB The IL-6 family of cytokines comprises a large group of cytokines that all act via the formation of a signaling complex that includes the glycoprotein 130 (gp130) receptor. Despite this, many of these cytokines have unique roles that regulate the activity of bone forming osteoblasts, bone resorbing osteoclasts, bone-resident osteocytes, and cartilage cells (chondrocytes). These include specific functions in craniofacial development, longitudinal bone growth, and the maintenance of trabecular and cortical bone structure, and have been implicated in musculoskeletal pathologies such as craniosynostosis, osteoporosis, rheumatoid arthritis, osteoarthritis, and heterotopic ossifications. This review will work systematically through each member of this family and provide an overview and an update on the expression patterns and functions of each of these cytokines in the skeleton, as well as their negative feedback pathways, particularly suppressor of cytokine signaling 3 (SOCS3). The specific cytokines described are interleukin 6 (IL-6), interleukin 11 (IL-11), oncostatin M (OSM), leukemia inhibitory factor (LIF), cardiotrophin 1 (CT-1), ciliary neurotrophic factor (CNTF), cardiotrophin-like cytokine factor 1 (CLCF1), neuropoietin, humanin and interleukin 27 (IL-27).
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TI The Effect of Individual Musculoskeletal Conditions on Depression: Updated Insights From an Irish Longitudinal Study on Aging
SO FRONTIERS IN MEDICINE
LA English
DT Article
DE depression; late-life depression; musculoskeletal conditions; arthritis; pain
ID activity restriction; life; disease; health; risk; osteoporosis; fracture; design; burden; women
AB Few longitudinal studies have systematically investigated whether or how individual musculoskeletal conditions (IMCs) convey risks for negative psychological health outcomes, and approaches to assess such risk in the older population are lacking. In this Irish nationally representative longitudinal prospective study of 6,715 individuals aged 50 and above, machine learning algorithms and various models, including mediation models, were employed to elaborate the underlying mechanisms of IMCs leading to depression and to develop an IMC-induced negative psychological risk (IMCPR) classification approach. Resultantly, arthritis [odds ratio (95% confidence interval): 2.233 (1.700-2.927)], osteoporosis [1.681 (1.133-2.421)], and musculoskeletal chronic pain [MCP, 2.404 (1.838-3.151)] were found to increase the risk of depression after 2 years, while fracture and joint replacement did not. Interestingly, mediation models further demonstrated that arthritis per se did not increase the risk of depression; such risk was augmented only when arthritis-induced restrictions of activities (ARA) existed [proportion of mediation: 316.3% (ARA of usual), 213.3% (ARA of social and leisure), and 251.3% (ARA of sleep)]. The random forest algorithm attested that osteoarthritis, not rheumatoid arthritis, contributed the most to depressive symptoms. Moreover, bone mineral density was negatively associated with depressive symptoms. Systemic pain contributed the most to the increased risk of depression, followed by back, knee, hip, and foot pain (mean Gini-Index: 3.778, 2.442, 1.980, 1.438, and 0.879, respectively). Based on the aforementioned findings, the IMCPR classification approach was developed using an interpretable machine learning model, which stratifies participants into three grades. Among the IMCPR grades, patients with a grade of "severe" had higher odds of depression than those with a "mild" [odds ratio (95% confidence interval): 4.055 (2.907-5.498)] or "moderate" [3.584 (2.101-5.883)] grade. Females with a "severe" grade had higher odds of depression by 334.0% relative to those with a "mild" grade, while males had a relative risk of 258.4%. In conclusion, the present data provide systematic insights into the IMC-induced depression risk and updated the related clinical knowledge. Furthermore, the IMCPR classification approach could be used as an effective tool to evaluate this risk.
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Liu, Wen Shan
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TI Long-term functional outcomes of diffuse pigmented villonodular synovitis of knee The role of adjuvant radiotherapy
SO MEDICINE
LA English
DT Article
DE functional outcome; pigmented villonodular synovitis; radiotherapy; synovectomy
ID external-beam radiotherapy; arthroscopic synovectomy; postoperative treatment; recurrence
AB Diffuse pigmented villonodular synovitis (PVNS) of knee is a rare benign disease that has a destructive clinical course. Synovectomy and adjuvant radiotherapy (RT) have been reported as treatment options but literatures reporting functional outcomes were sparse. This study aimed to evaluate the long-term functional outcomes and disease control among treatment modalities through the 22 years of experience. A single-center database was searched for patients who received synovectomy of knee with the pathologic diagnosis of PVNS. General data, treatment modalities, and recurrent status were retrospectively collected from medical records. Functional outcomes were evaluated by Western Ontario and McMaster Universities Osteoarthritis Index through phone interviews by an independent orthopedist. From January 1995 to December 2017, 24 patients with diffuse PVNS of knee were identified, including 19 receiving open synovectomy (OP) and 5 undergoing arthroscopic surgery. Adjuvant RT was performed on 14 patients with a median dose of 35 Gy (range 20-40 Gy). After median follow up of 6 years, recurrences were recorded in 10 cases. The recurrence rate was significantly lower in the OP + RT group than the OP group (8.3% vs 57.1%, P = .038). Among those with preserved knee joints, there was no significant difference in the Western Ontario and McMaster Universities Osteoarthritis Index score and stiffness score between patients in the OP + RT and OP groups. For patients with diffuse PVNS of knee, the addition of moderate-dose adjuvant RT following OP provided excellent local control while maintaining good joint function with limited treatment-related morbidity. Our study emphasized the importance of moderate dose RT in diffuse PVNS of knee joint.
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TI Abductor muscle strengthening in THA patients operated with minimally-invasive anterolateral approach for developmental hip dysplasia
SO HIP INTERNATIONAL
LA English
DT Article
DE Developmental hip dysplasia; gluteal muscle weakness; outcome; rehabilitation; total hip replacement
AB Objective: In developmental hip dysplasia (DDH) patients, the chronic dislocation of the femoral head with respect to the true acetabulum determines muscle contracture and atrophy, particularly of the abductor muscles, and leads to secondary osteoarthritis (OA) with severe motor dysfunction, pain and disability. The correct positioning when a total hip replacement (THR) is performed is fundamental to the recovery of gait function. Also, inadequate rehabilitation of the

abductor muscles for pelvic stabilisation can be responsible for residual dysfunction. Consensus on a programme for abductor muscle strengthening in these patients is not currently available. The aim of this study was to evaluate the effectiveness of a specific program of exercises for strengthening the abductor muscles in these patients. Methods: A multicentre, prospective, randomised clinical trial was carried out in an outpatient rehabilitation setting on 103 patients given THR for DDH through a minimally-invasive anterolateral approach. Patients were randomly divided into a Study Group, including 46 patients, and a Control Group, including 57 patients. All patients underwent standard early postoperative rehabilitation. In addition, the Study Group were given an extra 2-week rehabilitation once full weight-bearing on the operated limb was allowed, aimed at strengthening the abductor muscles. All patients were evaluated preoperatively, and at about 3 and 6 months postoperatively. Clinical measures (lower limb-length differences, hip range of motion, abductor muscle strength), and functional measures (WOMAC, HHS, 10mt WT, SF-12) were taken. Results: Hip range of motion and functional outcome measures showed a progressive improvement at follow ups in both groups, significantly higher in the Study Group. In particular, abductor strength at 6 months post-op improved by 92.5% with respect to 35.7% in the Control Group. Conclusion: In addition to standard rehabilitation, a rehabilitation programme for strengthening the gluteal muscles in DDH patients who underwent THR determined an increase in muscle strength that improved functional performance and patient satisfaction.
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AU Wang, Q
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Chen, Lidong
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Jiang, Xiaowei
Shen, Yingchao
TI MicroRNA-15a-5p plays a role in osteogenic MC3T3-E1 cells differentiation by targeting PDCD4 (programmed cell death 4) via Wnt/β-catenin dependent signaling pathway
SO BIOENGINEERED
LA English
DT Article

DE miR-15a-5p; osteoporosis; programmed cell death 4 (PDCD4); Wnt/beta-catenin pathway
ID mesenchymal stem-cells; osteoblast differentiation; proliferation; cancer; osteoarthritis; expression; fractures
AB Osteoporosis is defined as a bone condition characterized by bone mass reduction, bone micro-architectural and quality deterioration, leading to compromised strength and increased chances of fracture. Evidence have shown an essential role of microRNAs (miRNAs) in various osteogenic differentiation processes. However, the function of miR-15a-5p in the differentiation of osteogenic cells and possible mechanisms remains unclear. The present study explored the expression of miR-15a-5p in human osteoporosis specimens and during the osteogenic differentiation of MC3T3-E1 cells. Functions of miR-15a-5p were determined using miR-15a-5p mimics and inhibitors. Luciferase assay was used to verify the binding of miR-15a-5p and PDCD4 3MODIFIER LETTER PRIMEUTR. Alizarin Red Staining (ARS) and Alkaline phosphatase (ALP) activity were used to determine the miR-15a-5p role in osteogenic differentiation. Finally, Wnt pathway inhibitor was used to determine the miR-15a-5p/PDCD4/Wnt signaling pathway in regulating osteogenic differentiation. We found miR-15a-5p expression was increased in human osteoporosis specimens and during differentiation of MC3T3-E1 cells. PDCD4 was also identified as a target of miR-15a-5p and was found to be involved in osteogenic differentiation. Further, miR-15a-5p mimics attenuated the effects of PDCD4 overexpression. Finally, use of XAV939 (Wnt pathway inhibitor) downregulated osteogenic differentiation in miR-15a5p/PDCD4/Wnt-dependent signaling pathway. In conclusion, miR-15a-5p induced differentiation of osteoblasts and mineralization by modulating osteoblast differentiation factors, mainly OSX, ALP, OCN, and RUNX2, by inhibiting PDCD4 and Wnt signaling pathways. This study provides a modality for the future use of miR-15a-5p in the treatment and prevention of osteoporosis.
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AU Bei, HP
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TI Bone-a-Petite: Engineering Exosomes towards Bone, Osteochondral, and Cartilage Repair
SO SMALL
LA English
DT Review
DE exosome; extracellular vesicles; osteochondral repair; tissue engineering
ID mesenchymal stem-cells; induced osteonecrosis; femoral-head; pathways; osteoarthritis; angiogenesis; apoptosis; delivery; roles; rats
AB Recovery from bone, osteochondral, and cartilage injuries/diseases has been burdensome owing to the damaged vasculature of large defects and/or avascular nature of cartilage leading to a lack of nutrients and supplying cells. However, traditional means of treatment such as microfractures and cell-based therapy only display limited efficacy due to the inability to ensure cell survival and potential aggravation of surrounding tissues. Exosomes have recently emerged as a powerful tool for this tissue repair with its complex content of transcription factors, proteins, and targeting ligands, as well as its unique ability to home in on target cells thanks to its phospholipidic nature. They are engineered to serve specialized applications including enhancing repair, anti-inflammation, regulating homeostasis, etc. via means of physical, chemical, and biological modulations in its deriving cell culture

environments. This review focuses on the engineering means to functionalize exosomes for bone, osteochondral, and cartilage regeneration, with an emphasis on conditions such as osteoarthritis, osteoporosis, and osteonecrosis. Finally, future implications for exosome development will be given alongside its potential combination with other strategies to improve its therapeutic efficacy in the osteochondral niche.
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J9 SMALL
JI Small
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WC Chemistry, Multidisciplinary; Chemistry, Physical; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary; Physics, Applied; Physics,

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AF Chen, Liyuan
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TI Effect of Integrin-Linked Kinase on Osteogenesis of Bone Marrow Mesenchymal Stem Cells in Inflammatory Environment via Regulating Mitogen Activated Protein Kinase/Protein Kinase B Signaling Pathway
SO JOURNAL OF BIOMATERIALS AND TISSUE ENGINEERING
LA English
DT Article
DE ILK; Osteoarthritis; MAPK/AKT Signaling Pathway; Inflammatory Factors; BMSCs
ID risk; differentiation; osteoarthritis; cartilage; knee; hip
AB Osteoarthritis (OA) pathogenesis involves inflammation, age, weight and other factors. Integrin-linked kinase (ILK) regulates cell apoptosis, metastasis, and growth. However, whether ILK affects bone formation of bone marrow mesenchymal stem cells in an inflammatory environment has not been elucidated. Rat BMSCs were isolated and assigned into control group, inflammation group (lipopolysaccharide was added to cells); and si-ILK group (ILK siRNA was transfected into the inflammation group BMSCs) followed by analysis of cell proliferation by MTT assay, expression of ILK, Runx2 and OP by real time PCR, ALP activity, TNF-alpha and IL-6 secretion by ELISA and MAPK/AKT signaling protein expression by western blot. Compared to control, ILK in BMSCs cells in inflammatory environment was significantly upregulated, resulting in inhibition of cell proliferation, decreased ALP

activity, reduced expression of osteogenic genes Runx2 and OP, increased secretion of TNF-alpha and IL-6, and downregulated p-AKT ($P < 0.05$); transfection of ILK siRNA downregulated ILK in inflammatory environment BMSCs, which significantly increased BMSCs cell proliferation, increased ALP activity and expression of Runx2 and OP, decreased TNF-alpha and IL-6 secretion and increased p-AKT expression ($P < 0.05$). ILK expression is increased in BMSCs in an inflammatory environment. Down-regulation of ILK in BMSCs cells in an inflammatory environment can regulate MAPK/AKT signaling, inhibit inflammatory factors secretion, thereby promoting BMSCs proliferation and osteogenesis differentiation.

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AU Li, NN
Cornelissen, D
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Si, L
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Cornelissen, Dennis
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TI An Updated Systematic Review of Cost-Effectiveness Analyses of Drugs for Osteoporosis
SO PHARMACOECONOMICS
LA English
DT Review
ID postmenopausal osteoporosis; oral bisphosphonates; economic evaluations; vertebral fractures; zoledronic acid; denosumab; women; alendronate; prevention; discontinuation
AB Background Considering the heavy economic burden of osteoporotic fractures, the limits of healthcare resources, and the recent availability of new anti-osteoporosis drugs, there is continuing interest in economic evaluation studies of osteoporosis management strategies. Objectives This study aims to (1) systematically review recent economic evaluations of drugs for osteoporosis and (2) to apply an osteoporosis-specific guideline to critically appraise them. Methods A literature search was undertaken using PubMed, EMBASE, National Health Service Economic Evaluation database, and the Cost-Effectiveness Analysis Registry to identify original articles containing economic evaluations of anti-osteoporosis drugs, published between 1 July, 2013 and 31 December, 2019. A recent European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases-International Osteoporosis Foundation (ESCEO-IOF) guideline for the conduct and reporting of economic evaluations in osteoporosis was used to assess the quality of included articles. Results The database search

retrieved 3860 records, of which 27 studies fulfilled the inclusion criteria. These studies were conducted in 15 countries; 12 active drugs were assessed, including various traditional pharmacological treatments such as bisphosphonates, raloxifene, strontium ranelate, denosumab, and teriparatide, and new agents such as abaloparatide, romosozumab, and gastro-resistant risedronate. Eight out of 12 studies that compared traditional oral bisphosphonates to other active interventions (denosumab, zoledronic acid, gastro-resistant risedronate, and teriparatide) suggested that the other active agents were generally cost-effective or dominant. Additionally, the cost-effectiveness of sequential therapy has recently been assessed and indications are that it can lead to extra health benefits (larger gains in quality-adjusted life-year). The key drivers of cost effectiveness included baseline fracture risk, drug effect on the risk of fractures, drug cost, and medication adherence/persistence. The current average score for quality assessment was 17 out of 25 (range 2-15); room for improvement was observed for most studies, which could potentially be explained by the fact that most studies were published prior to the osteoporosis-specific guideline. Greater adherence to guideline recommendations was expected for future studies. The quality of reporting was also suboptimal, especially with regard to treatment side effects, treatment effect after discontinuation, and medication adherence. Conclusions This updated review provides an overview of recently published cost-effectiveness analyses. In comparison with a previous review, recent economic evaluations of anti-osteoporosis drugs were conducted in more countries and included more active drugs and sequential therapy as interventions/comparators. The updated economic evidence could help decision makers prioritize health interventions and the unmet/unreported quality issues indicated by the osteoporosis-specific guideline could be useful in improving the transparency, quality, and comparability of future economic evaluations in osteoporosis.
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TI Development of chemiluminescence method based on serum type I collagen hydroxyl terminal peptide β special sequence (β-CTX)
SO SCANDINAVIAN JOURNAL OF CLINICAL & LABORATORY INVESTIGATION
LA English
DT Article
DE Type I collagen; type I collagen hydroxyl terminal peptide beta specific sequence; chemiluminescence immunoassay; osteoporosis; osteoarthritis; degenerative bone disease
ID hip fracture; assay; age
AB The objective of this work is to develop and verify the analytical performance of a chemiluminescence immunoassay for the specific sequence beta-carboxy-terminal cross-linking telopeptide of type I collagen (beta-CTX) in human serum. Two specific monoclonal antibodies (mAb-8A03 and mAb-3D12) with high affinity for beta-CTX were selected, and, under optimized conditions, a chemiluminescence immunoassay method (CLIA) for beta-CTX was established. The CLIA of beta-CTX detected beta-CTX in a wide range of 2.0-6000 ng/L. The recovery rate in serum is 95-105%, the specificity is high, and the cross-reaction rate with common easily interfering substances is low (not more than 0.01%). The CLIA correlates well with Roche electrochemiluminescence immunoassay (ECLIA), with a correlation coefficient of 0.9551, which fully meets the requirements of clinical analysis. The developed beta-CTX CLIA kit has high sensitivity and good stability. It has the same performance as the commercial Roche ECLIA kit and can be applied clinically.
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TI Promising diagnostic and therapeutic circRNAs for skeletal and chondral disorders
SO INTERNATIONAL JOURNAL OF BIOLOGICAL SCIENCES
LA English
DT Review
DE Circular RNAs; skeletal and chondral disorders; regulatory mechanism; biomarker; therapeutic target
ID promoting osteoblast proliferation; extracellular-matrix degradation; blood mononuclear-cells; rna expression profiles; circular rnas; osteoarthritis chondrocyte; improve osteoporosis; apoptosis; translation; progression
AB Circular RNAs (circRNAs) belong to a highly conserved subtype of non-coding RNAs, produced by the back-splicing of specific regions of pre-mRNA. CircRNAs have wide-ranging effects on eukaryotic physiology and pathology by acting as transcription regulators, miRNA sponges, protein sponges, and templates for translation. Skeletal and chondral disorders are the leading causes of pain and disability, especially for elders, affecting hundreds of millions of people worldwide. Plenty of evidence have shown that circRNAs are dysregulated and play vital roles in the occurrence and progression of skeletal and chondral disorders. Herein, we systematically summarize the emerging roles and underlying molecular mechanisms of hub circRNAs in the pathogenesis of several representative skeletal and chondral disorders. Our findings may provide further insight into the mechanistic details of the role of circRNA in bone or cartilage metabolism, and highlight the promising application of circRNAs in serving as potential diagnostic or therapeutic targets for the prevention and treatment of skeletal and chondral disorders.
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AU Hernandez, CJ
AF Hernandez, Christopher J.
TI Musculoskeletal microbiology: The microbiome in orthopaedic biomechanics
SO CURRENT OPINION IN BIOMEDICAL ENGINEERING
LA English
DT Article
DE Microbiome; Biomechanics; Osteoporosis; Osteoarthritis
ID gut microbiota; arthroplasty; growth
AB Orthopaedic biomechanics and bioengineering is a founding discipline of biomedical engineering that focuses on the effects of mechanical stress and strain on musculoskeletal tissues during growth, function and repair. In the past decade, the gut microbiome has emerged as a contributor to disease processes throughout the body but only recently has been shown to influence orthopaedic biomechanics. Here I review emergent findings showing that the gut microbiome can regulate important aspects of the musculoskeletal system including growth and development, tissue failure and disease and orthopaedic surgery. These early findings suggest that the microbiome may help answer questions in orthopaedic biomechanics that are not well addressed by current interventions and highlight the promise of the emerging field of "Musculoskeletal Microbiology".
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TI Evaluation of Orthopedic Problems in Relation with Vitamin D3 at Clinical Settings of Hyderabad, Pakistan
SO LATIN AMERICAN JOURNAL OF PHARMACY
LA English
DT Article
DE hyperparathyroidism; osteoarthritis; osteoporosis
ID d deficiency; bone health; osteoporosis; sunlight; outcm; risk
AB Vitamin-D deficiency increases the occurrence of fractures and osteoporosis. The study aims to evaluate the different orthopedic complications and contributing factors by deficient of vitamin D. A descriptive, cross-sectional study was conducted for a period of 6 months (October 2019-March 2020), at different clinical settings of Hyderabad, Sindh, Pakistan. Three hundred patients were included via random sampling technique, and data was collected on a structured proforma. Later on, data was analyzed by SPSS version 21. From total patients, female patients were 37.0% and 63.0% male, while 31-40 years of age having 23.0% patients. Further 57.7% of the patients had positive medications history and 12.7% were negative medication history. Majority of the patients were admitted in orthopedic ward due to fracture (self-fall fracture) i.e., 46.7% patients. In current study, 300 patients had received 1554 drugs prescribed drugs in orthopedic patients i.e., analgesics 29.3% and its p value are 0.033. The results showed that mostly patients i.e., 47.66% (n = 137) take daily sunlight (<= 10 min) followed by 25.67% of the patients take daily sunlight (20 min) and 27.6% take more than 30 minutes. 20.33% (n = 61) patients were observed with lack of knowledge about orthopedic problem (p value are 0.001), 79.6% (n = 239) stated the cost of medication is expensive to afford. Vitamin D insufficiency can be direct to a thrashing of bone compactness, which can be contributed to osteoporosis and fractures. All reasons that relate to orthopedic problems and vitamin D deficiencies area of skin exposed and duration of sunlight exposure strongly correlated with vitamin D levels.
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WC Pharmacology & Pharmacy
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AU He, P
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AF He, Pei
Cao, Rong-Rong
Deng, Fei-Yan
Lei, Shu-Feng
TI Identification of Potential Pleiotropic Genes for Immune and Skeletal Dis-eases Using Multivariate MetaCCA Analysis
SO CURRENT GENOMICS
LA English
DT Article
DE GWAS; metaCCA; VEGAS2; pleiotropic gene; immune diseases; skeletal diseases
ID rheumatoid-arthritis; psoriatic-arthritis; osteoporosis; association; ccr6
AB Background: Immune and skeletal systems physiologically and pathologically

interact with each other. The immune and skeletal diseases may share potential pleiotropic genetics factors, but the shared specific genes are largely unknown. Objective: This study aimed to investigate the overlapping genetic factors between multiple diseases (including rheumatoid arthritis (RA), psoriasis, osteoporosis, osteoarthritis, sarcopenia and fracture). Methods: The canonical correlation analysis (metaCCA) approach was used to identify the shared genes for six diseases by integrating genome-wide association study (GWAS)-derived summary statistics. Versatile Gene-based Association Study (VEGAS2) method was further applied to refine and validate the putative pleiotropic genes identified by metaCCA. Results: About 157 ($p<8.19E-6$), 319 ($p<3.90E-6$) and 77 ($p<9.72E-6$) potential pleiotropic genes were identified shared by two immune disease, four skeletal diseases, and all of the six diseases, respectively. The top three significant putative pleiotropic genes shared by both immune and skeletal diseases, including HLA-B, TSBP1 and TSBP1-AS1 ($p<E-300$) were located in the major histocompatibility complex (MHC) region. Nineteen of 77 putative pleiotropic genes identified by metaCCA analysis were associated with at least one disease in the VEGAS2 analysis. Specifically, majority (18) of these 19 putative validated pleiotropic genes were associated with RA. Conclusion: The metaCCA method identified some pleiotropic genes shared by the immune and skeletal diseases. These findings help to improve our understanding of the shared genetic mechanisms and signaling pathways underlying immune and skeletal diseases.
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PA EXECUTIVE STE Y-2, PO BOX 7917, SAIF ZONE, 1200 BR SHARJAH, U ARAB EMIRATES
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WC Biochemistry & Molecular Biology; Genetics & Heredity
SC Biochemistry & Molecular Biology; Genetics & Heredity
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AU Zhang, QY
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AF Zhang, Qingyu
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TI Dynamics of Transcription Factors in Three Early Phases of Osteogenic, Adipogenic, and Chondrogenic Differentiation Determining the Fate of Bone Marrow Mesenchymal Stem Cells in Rats
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Article
DE bone marrow mesenchymal stem cells (BMSCs); high-throughput sequencing; osteogenic differentiation; chondrogenic differentiation; transcription factors; adipogenic differentiation
ID identification; expression; growth; sox9; beta
AB The imbalance of osteogenic, adipogenic, and chondrogenic differentiation in bone marrow mesenchymal stem cells (BMSCs) occurred in multiple age-related degenerative diseases such as osteoporosis and osteoarthritis. In order to improve our understanding and control of multi-directional differentiation of BMSCs in rats, using high-throughput sequencing, we identified key gene regulatory events in the early stages of lineage commitment. Data analysis revealed two transcription factors (TFs, Tsc22d3, and Epas1) with elevated expression throughout the initiation of differentiation (3 h), lineage acquisition (12 h), and early lineage progression (72 h) of three-directional differentiation. For osteogenic differentiation, 792, 1,042, and 638 differentially expressed genes including 48, 59, and 34 TFs were identified at three time points, respectively. Moreover, the functional analysis demonstrated that 4, 12, and 5 TFs were only differentially expressed during osteogenic differentiation at 3, 12, and 72 h, respectively, and not during other two-directional differentiation. Hopx showed enhanced expression throughout three early phases during the osteogenic differentiation but no significant change in other two-directional differentiation. A similar pattern of Gbx2 expression occurred in chondrogenic differentiation. Thus, Hopx and other early responder TFs may control the osteogenic cell fate of BMSCs and participate in the development of osteoporosis. Gbx2 and other early responder TFs should be considered in mechanistic models that clarify cartilage-anabolic changes in the clinical

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AU Cellini, M
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TI Vertebral Fractures Associated with Spinal Sagittal Imbalance and Quality of Life in Acromegaly: A Radiographic Study with EOS 2D/3D Technology
SO NEUROENDOCRINOLOGY
LA English
DT Article
DE Acromegaly; Fractures; Osteoporosis; Kyphosis; Spine imbalance
ID bone-mineral density; clinical-practice; postmenopausal women; thoracic kyphosis; society; prevalence; validation; men; osteoarthritis; osteoporosis
AB Introduction: Acromegaly is commonly complicated by arthropathy and skeletal fragility with high risk of vertebral fractures (VFs). Objective: This study aimed to assess whether VFs may be associated with sagittal spine deformities, arthropathy, impaired quality of life (QoL), pain, and disability. Methods: Thirty-eight patients with acromegaly (median age: 55 years, 20 males) and 38 matched control subjects were evaluated by a low-dose sagittal and coronal planes, X-ray imaging system (EOS (R)-2D/3D) for morphometric VFs, radiological signs of spine arthropathy, and

spine deformities (Cobb thoracic index >= 40 degrees, pelvic incidence minus lumbar lordosis >= 10 degrees, pelvic tilt >20 degrees, and sagittal vertical axis >= 4 cm) determining sagittal spine imbalance. Acromegalic patients were also evaluated by questionnaires for QoL (Acromegaly QoL Questionnaire [AcroQoL] and Short Form-36 [SF-36]) and pain and disability (Western Ontario and McMaster University [WOMAC]). Results: Acromegalic patients showed higher prevalence of thoracic hyperkyphosis (i.e., Cobb thoracic index >= 40 degrees; p = 0.04) and pelvic tilt >20 degrees (p = 0.02) than control subjects. VFs were found in 34.2% of acromegalic patients (p = 0.003 vs. control subjects), in relationship with higher prevalence of hyperkyphosis (p = 0.03), pelvic tilt >20 degrees (p = 0.04), sagittal vertical axis >= 4 cm (p = 0.03), and moderate/severe subchondral degeneration (p = 0.01). Moreover, patients with VFs had lower AcroQoL general health (p = 0.007) and SF-36 general health (p = 0.002) scores and higher WOMAC pain (p = 0.003) and global (p = 0.009) scores than patients who did not fracture. Conclusions: In acromegaly, VFs may be associated with spine deformities and sagittal imbalance, spine arthropathy, impaired QoL, and disability.
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NR 63
TC 23
Z9 23
U1 0
U2 2
PU KARGER
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WC Endocrinology & Metabolism; Neurosciences
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TI Association of vitamin D, BMD and knee osteoarthritis in postmenopausal women
SO JOURNAL OF MUSCULOSKELETAL & NEURONAL INTERACTIONS
LA English
DT Article
DE Bone Mineral Density; Hypovitaminosis D; Osteoarthritis; Osteoporosis; Vitamin D
ID bone-mineral density; serum 25-hydroxyvitamin d; radiographic osteoarthritis; femoral-neck; hip; osteoporosis; replacement; cartilage; falls; risk
AB Objectives: The aim of this study was to analyze the association of knee OA with bone mineral density (BMD) and vitamin D serum levels in postmenopausal women. Methods: A cross-sectional study including 240 postmenopausal women with knee OA was conducted. Demographic data were recorded along with balance and functionality scores. Knee OA severity was assessed by the radiological Kellgren & Lawrence scale. BMD and T-scores were calculated in hips and lumbar spine. Serum levels of vitamin D were also measured. Results: High BMI ($p<0.005$), high number of children ($p=0.022$) and family history of hip fracture ($p=0.011$) are significantly associated with knee OA severity. Lumbar spine OP is negatively associated with knee OA ($p<0.005$). A significant difference was detected between vitamin D deficiency and severe knee OA. adjusted for BMD [OR (95%CI): 3.1 (1.6-6.1), $p=0.001$]. BMD does not affect the relationship of vitamin D levels in relation to OA and vitamin D levels do not affect the relationship of BMD with OA. Conclusions: Low BMD has a protective role against knee OA while vitamin D deficiency contributes significantly to knee OA severity. However, the association

between OA and OP is not affected by vitamin D deficiency and the association of OA and vitamin D serum levels is not affected by BMD.
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NR 54
TC 9
Z9 9
U1 1
U2 4
PU JMNI
PI NAFPLION
PA 7 SPILIADOU SQ, NAFPLION, 21 100, GREECE
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J9 J MUSCULOSKEL NEURON
JI J. Musculoskelet. Neuronal Interact.
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SC Neurosciences & Neurology; Physiology
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PT J
AU Date, K
Sakagami, H
Yura, K
AF Date, Kimie
Sakagami, Hiromi
Yura, Kei
TI Regulatory properties of vitronectin and its glycosylation in collagen fibril

formation and collagen-degrading enzyme cathepsin K activity
SO SCIENTIFIC REPORTS
LA English
DT Article
ID n-linked oligosaccharides; i collagen; binding; protein; inhibitor; adhesion; porcine; domain; liver; osteoporosis
AB Vitronectin (VN) is a glycoprotein found in extracellular matrix and blood. Collagen, a major extracellular matrix component in mammals, is degraded by cathepsin K (CatK), which is essential for bone resorption under acidic conditions. The relationship between VN and cathepsins has been unclear. We discovered that VN promoted collagen fibril formation and inhibited CatK activity, and observed its activation in vitro. VN accelerated collagen fibril formation at neutral pH. Collagen fibers formed with VN were in close contact with each other and appeared as scattered flat masses in scanning electron microscopy images. VN formed collagen fibers with high acid solubility and significantly inhibited CatK; the IC50 was 8.1-16.6 nM and competitive, almost the same as those of human and porcine VNs. VN inhibited the autoprocessing of inactive pro-CatK from active CatK. DeN-glycosylation of VN attenuated the inhibitory effects of CatK and its autoprocessing by VN, but had little effect on acid solubilization of collagen and VN degradation via CatK. CatK inhibition is an attractive treatment approach for osteoporosis and osteoarthritis. These findings suggest that glycosylated VN is a potential biological candidate for CatK inhibition and may help to understand the molecular mechanisms of tissue re-modeling.
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FU JSPS KAKENHI [JP 19K16072]; Lotte Shigemitsu Prize; Ito Science Foundation
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NR 68
TC 13

Z9 14
U1 0
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PU NATURE PORTFOLIO
PI BERLIN
PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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AU Sun, KQ
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AF Sun, Kaiqiang
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Huan, Le

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TI Gamabufotalin Inhibits Osteoclastgenesis and Counteracts Estrogen-Deficient Bone Loss in Mice by Suppressing RANKL-Induced NF-κB and ERK/MAPK Pathways
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE gamabufotalin; OVX model; osteoporosis; osteoclast; ERK; MAPK; receptor activator of nuclear factor kappa-B ligand; TRAF6
AB Osteolytic bone disease is a condition of imbalanced bone homeostasis, characterized mainly by excessive bone-resorptive activity, which could predispose these populations, such as the old and postmenopausal women, to developing high risk of skeletal fragility and fracture. The nature of bone homeostasis is the coordination between the osteoblasts (OBs) and osteoclasts (OCs). Abnormal activation of osteoclasts (OCs) could compromise the bone homeostasis, constantly followed by a clutch of osteolytic diseases, including postmenopausal osteoporosis, osteoarthritis, and rheumatoid arthritis. Thus, it is imperatively urgent to explore effective medical interventions for patients. The traditional Chinese medicine (TCM) gamabufotalin (CS-6) is a newly identified natural product from Chansu and has been utilized for oncologic therapies owing to its good clinical efficacy with less adverse events. Previous study suggested that CS-6 could be a novel anti-osteoporotic agent. Nevertheless, whether CS-6 suppresses RANK-(receptor activator of nuclear factor-kappa B ligand)/TRAF6 (TNF receptor-associated factor 6)-mediated downstream signaling activation in OCs, as well as the effects of CS-6 on OC differentiation in vivo, remains elusive. Therefore, in this present study, we aimed to explore the biological effects of CS-6 on osteoclastogenesis and RANKL-induced activation of related signaling pathways, and further to examine the potential therapeutic application in estrogen-deficient bone loss in the mice model. The results of in vitro experiment showed that CS-6 can inhibit RANKL-induced OC formation and the ability of bone resorption in a dose-dependent manner at both the early and late stages of osteoclastogenesis. The gene expression of OC-related key genes such as tartrate-resistant acid phosphatase (TRAP), CTSK, DC-STAMP, MMP9, and beta 3 integrin was evidently reduced. In addition, CS-6 could mitigate the systemic estrogen-dependent bone loss and pro-inframammary cytokines in mice in vivo. The molecular mechanism analysis suggested that CS-6 can suppress RANKL/TRAF6-induced early activation of NF-kappa B and ERK/MAPK signaling pathways, which consequently suppressed the transcription activity of c-Fos and NFATc1. Taken together, this present study provided ample evidence that CS-6 has the promise to become a therapeutic candidate in treating osteolytic conditions mediated by elevated OC formation and bone resorption.
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FU National Natural Science Foundation of China [81871828, 81802218, 81702141]
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NR 57
TC 23
Z9 28
U1 0
U2 10
PU FRONTIERS MEDIA SA
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PT J
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Lemaitre, JM
AF Pichard, Lydiane
Brondello, Jean-Marc
Becker, Fabienne
Desprat, Romain
De Ceuninck, Frederic
Pastoureau, Philippe
Noel, Daniele
Jorgensen, Christianf
Lemaitre, Jean-Marc
TI Establishment of a collection of human pluripotent stem cell lines (iPSC) from mesenchymal stem cells (MSC) from three healthy elderly donors
SO STEM CELL RESEARCH
LA English
DT Article
AB The study of molecular mechanism driving osteoarticular diseases like osteoarthritis or osteoporosis is impaired by the low accessibility to mesenchymal

stem cells (MSC) from healthy donors (HD) for differential multi-omics analysis. Advances in cell reprogramming have, however, provided both a new source of human cells for laboratory research and a strategy to erase epigenetic marks involved in cell identity and the development of diseases. To unravel the pathological signatures on the MSC at the origin of cellular drifts during the formation of bone and cartilage, we previously developed iPSC from MSC of osteoarthritis donors. Here we present the derivation of three iPSCs from healthy age matched donors to model the disease and further identify (epi)genomic signatures of the pathology.
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NR 4
TC 1
Z9 1
U1 1
U2 4
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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JI Stem Cell Res.
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WC Cell & Tissue Engineering; Biotechnology & Applied Microbiology; Cell Biology
SC Cell Biology; Biotechnology & Applied Microbiology
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UT WOS:000663437900004
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ER

PT J
AU Xian, YS
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AF Xian, Yansi
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Xiao, Yu
Lian, Haoyu
Xu, Jiake
Zhao, Jinmin
Liu, Qian
Song, Fangming
TI Oroxylin A reduces osteoclast formation and bone resorption via suppressing RANKL-induced ROS and NFATc1 activation
SO BIOCHEMICAL PHARMACOLOGY
LA English
DT Article
DE Oroxylin A; Osteoclast; ROS; NFATc1
ID osteoporosis; osteolysis
AB Excessive bone erosion by osteoclasts is associated with osteoporosis,

rheumatoid arthritis, and periprosthetic osteolysis. Targeting osteoclasts may serve as an effective treatment for osteolytic diseases. Although drugs are currently available for the treatment of these diseases, exploring potential anti-osteoclast natural compounds with safe and effective treatment remains needed. Oroxylin A (OA), a natural flavonoid isolated from the root of Scutellaria baicalensis Georgi, has numerous beneficial pharmacological characteristics, including antiinflammatory and antioxidant activity. However, its effects and mechanisms on osteoclast formation and bone resorption have not yet been clarified. Our research showed that OA attenuated the formation and function of osteoclast induced by RANKL in a time-and concentration-dependent manner without any cytotoxicity. Mechanistically, OA suppressed intracellular reactive oxygen species (ROS) levels through the Nrf2-mediated antioxidant response. Moreover, OA inhibited the activity of NFATc1, the master transcriptional regulator of RANKLinduced osteoclastogenesis. OA exhibited protective effects in mouse models of post-ovariectomy (OVX)-and lipopolysaccharide (LPS)-induced bone loss, in accordance with its in vitro anti-osteoclastogenic effect. Collectively, our findings highlight the potential of OA as a pharmacological agent for the prevention of osteoclastmediated osteolytic diseases.
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NR 54
TC 71
Z9 77
U1 1
U2 23
PU PERGAMON-ELSEVIER SCIENCE LTD
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JI Biochem. Pharmacol.
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WC Pharmacology & Pharmacy
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AU Wang, C
Shu, X
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AF Wang, Chao
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Yuan, Yue
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TI Seasonal Variation and Global Public Interest in the Internet Searches for Osteoporosis
SO BIOMED RESEARCH INTERNATIONAL
LA English
DT Article
ID bone-mineral density; physical-activity; vitamin-d; health information; management; cortisol; women; time; epidemiology; hypocalcemia
AB Background. To ascertain the seasonal pattern and global public interest in osteoporosis by evaluating search term popularity changes of the disease over a decade. Methods. We applied Google Trends to retrieve search popularity scores for the term "osteoporosis" between January 01, 2004, and December 31, 2019. Cosinor analyses were conducted to examine the seasonality of osteoporosis, and analysis on osteoporosis-related topics including hot topics and rising-related topics was also performed. Results. The cosinor analyses demonstrated a statistically significant seasonal variation in relative search volume of the "osteoporosis" in the world ($p = 0.0083$), USA ($p < 0.001$), UK ($p < 0.001$), Canada ($p < 0.001$), Ireland ($p < 0.001$), Australia ($p <0.001$), and New Zealand ($p <0.001$), with a peak in the late winter months and trough in the summer months. The peaks in late winter and valley in summer presented an approximately 6-month difference between hemispheres. The top 11 rising topics were denosumab, FRAX, hypocalcaemia, zoledronic acid, ibandronic acid, osteomyelitis, osteopenia, osteoarthritis, bone, calcium, and bone density. Conclusions. Google search query volumes related to osteoporosis follow strong seasonal patterns with late winter peaks and summer troughs. Further studies aimed at elucidating the possible mechanisms behind seasonality in osteoporosis are needed. Moreover, Internet

data including the top rising topics may alert physicians to strengthen the propaganda of osteoporosis timely, so as to further promote the development of public health interventions.
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NR 57
TC 2
Z9 4
U1 0
U2 3
PU HINDAWI LTD
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PA ADAM HOUSE, 3RD FLR, 1 FITZROY SQ, LONDON, W1T 5HF, ENGLAND
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JI Biomed Res. Int.
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WC Biotechnology & Applied Microbiology; Medicine, Research & Experimental
SC Biotechnology & Applied Microbiology; Research & Experimental Medicine
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PT J
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Dewadas, HD
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Lim, Yang Mooi
TI Effect of Traditional Chinese Medicine on Musculoskeletal Symptoms in Breast Cancer: A Systematic Review and Meta-Analysis
SO JOURNAL OF PAIN AND SYMPTOM MANAGEMENT
LA English
DT Review
DE Traditional Chinese Medicine (TCM); breast cancer; aromatase inhibitor-associated musculoskeletal symptoms (AIMSS); systematic review; meta-analysis
ID postmenopausal women; osteoarthritis index; tamoxifen therapy; randomized-trial; western-ontario; short-form; brief pain; osteoporosis; reliability; acupuncture
AB Context. Traditional Chinese Medicine (TCM) has been widely used as a complementary medical treatment for arthralgia and other types of pain. The available literature on the effectiveness of TCM on breast cancer patients with musculoskeletal symptoms reports controversial results. Objectives. The objective of this review is to assess the effectiveness of TCM as a treatment option for musculoskeletal symptoms in patients with breast cancer who were treated with aromatase inhibitors (AIs). Methods. A comprehensive literature search was conducted using PubMed, the Cochrane Library, SAGE journals, Scopus, EMBASE, Web of Science, Medline, Cumulated Index to Nursing and Allied Health Literature (CINAHL), Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), Wanfang, and Chinese Medical Journal Database (CMJ) from May 2020 to November 2020. The literature review included randomized controlled trials (RCTs) of TCM for AI-related musculoskeletal symptoms. Results. Four RCTs incorporating TCM were assessed by meta-analysis and reported favorable effects in reducing worst pain score (n = 284, mean difference [MD]: 2.31; 95% CI, 1.74 to 2.88; P < 0.00001). Three trials showed favorable effects of TCM in reducing pain interference (n = 211, MD: 2.62; 95% CI, 1.29 to 3.94; P= 0.0001), while two trials reported no significant effects of TCM on stiffness (n = 147, MD: 1.21; 95% CI, -0.39 to 2.82; P= 0.14). The meta-analysis of three trials also found no significant effect of TCM on bone mineral density (n = 214, MD, -0.01; 95% CI, -0.07 to 0.05; P= 0.71). The physical aspect of quality of life was significantly increased in breast cancer patients after TCM treatment (n = 220, MD, 5.13; 95% CI, 2.04 to 8.22; P = 0.001). In addition, three RCTs reported minimal TCM-related adverse events. Conclusion. The results suggest that TCM could be an effective treatment in relieving pain especially worst pain and pain interference as well as improving quality of life caused by AI-related musculoskeletal symptoms. However, further investigation of the molecular pathway involved and in-depth safety profile are needed. J Pain Symptom Manage 2021;62:159e173. (c) 2020 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.
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Z9 17
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J9 J PAIN SYMPTOM MANAG
JI J. Pain Symptom Manage.
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SC Health Care Sciences & Services; General & Internal Medicine; Neurosciences & Neurology
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UT WOS:000664736200021
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PT J

AU MacKay, JW
Watkins, L
Gold, G
Kogan, F
AF MacKay, J. W.
Watkins, L.
Gold, G.
Kogan, F.
TI [18F]NaF PET-MRI provides direct in-vivo evidence of the association between bone metabolic activity and adjacent synovitis in knee osteoarthritis: a cross-sectional study
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Synovitis; Subchondral bone; Magnetic resonance imaging; Positron emission tomography; Osteoarthritis
ID lining macrophages; contrast; pain; scintigraphy; progression; volume; ion
AB Objective: Synovitis is hypothesized to play a role in the development and growth of osteophytes. Our objectives were to use hybrid positron emission tomography-magnetic resonance imaging (PET-MRI) to (1) determine whether synovitis adjacent to peripheral bone subregions with increased metabolic activity is greater than adjacent to regions without increased metabolic activity and (2) assess the association between subregional bone metabolic activity and adjacent synovitis. Design: We recruited 11 participants (22 knees) with a diagnosis of OA in at least one knee. Simultaneous bilateral knee PET-MRI was performed. We quantified bone metabolic activity using the radiotracer [18F] sodium fluoride ([18F]NaF) with calculation of maximum standardized uptake values (SUVmax). Synovitis was quantified using dynamic contrast-enhanced MRI with calculation of Ktrans. Bone subregions were coded as osteophyte (OP), focal increased [18F]NaF uptake without osteophyte (FIU), or normal (no osteophyte or FIU). We used robust linear mixed effects models to assess differences in adjacent Ktrans between different subregion types and to assess association between Ktrans and adjacent SUVmax. Results: 94 OPs were detected (59 MOAKS grade 1, 30 grade 2, 5 grade 3), along with 28 FIU and 18 normal subregions. Ktrans was higher adjacent to FIU (adjusted mean [95% CI] = 0.06 [0.03,0.09]) and OPs (0.08 [0.05,0.11]) when compared to normal bone subregions (0.03 [0.00,0.09]). PET SUVmax was positively associated with adjacent Ktrans (b[95% CI] = 0.018 [0.008,0.027]). Conclusions: Synovitis is more intense adjacent to peripheral bone regions with increased metabolic activity than those without, although there is some overlap. Subregional bone metabolic activity is positively associated with intensity of adjacent synovitis.
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NR 39
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Z9 33
U1 0
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PI London
PA 125 London Wall, London, ENGLAND
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AU Ping, SH
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Zhang, L
AF Ping, Shao-Hua
Tian, Fa-Ming
Liu, Hao
Sun, Qi
Shao, Li-Tao
Lian, Qiang-Qiang
Zhang, Liu
TI Raloxifene inhibits the overexpression of TGF-β1 in cartilage and regulates the metabolism of subchondral bone in rats with osteoporotic osteoarthritis
SO BOSNIAN JOURNAL OF BASIC MEDICAL SCIENCES
LA English
DT Article
DE Osteoporosis; osteoarthritis; raloxifene; TGF-beta 1; cartilage; subchondral bone
ID growth-factor-beta; cruciate ligament transection; tgf-beta; articular-cartilage; model; degeneration; collagen; knee; chondrocytes; combination
AB Overexpression of transforming growth factor-beta 1 (TGF-beta 1) and subchondral bone remodeling play key roles in osteoarthritis (OA). Raloxifene (RAL) reduces the serum level of TGF-beta 1 in postmenopausal women. However, the effect of RAL on TGF-beta 1 expression in articular cartilage remains unclear. Therefore, we aimed to investigate the protective effect of RAL against osteoporotic OA mediated by TGF-beta 1 expression in the cartilage and the metabolism of subchondral bone. Osteoporotic OA was induced by a combination of anterior cruciate ligament transection (ACLT) and ovariectomy (OVX). Rats were divided into five groups (n = 12): the sham, ACLT, OVX, ACLT + OVX, and RAL groups (ACLT + OVX + RAL, 6.25 mg/kg/day for 12 weeks). Assessment was performed by histomorphology, microcomputed tomography (micro-CT),

immunohistochemistry, and tartrate-resistant acid phosphatase (TRAP) staining. Extreme cartilage degeneration was detected in the ACLT + OVX group. The histomorphological scores, levels of TGF-beta 1, and its related catabolic enzymes and osteoclasts numbers in the ACLT + OVX group were higher than those in other groups ($p < 0.05$). Furthermore, the structure model index (SMI) and trabecular spacing (Tb.Sp) were decreased ($p < 0.05$), while the bone mineral density (BMD), bone volume fraction (BV/TV), and trabecular number (Tb.N) were increased after treatment with RAL compared with the corresponding parameters in the ACLT + OVX group ($p < 0.05$). Our findings demonstrated that RAL at clinical doses retards the development of osteoporotic OA associated with the inhibition of TGF-beta 1 overexpression in the cartilage and regulation of subchondral bone metabolism. These results suggest an expansion of the clinical indications for RAL to include the prevention and treatment of postmenopausal OA.
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Z9 18
U1 4
U2 11
PU ASSOC BASIC MEDICAL SCI FEDERATION BOSNIA & HERZEGOVINA SARAJEVO
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PT J
AU Wang, W
Wang, B
AF Wang, Wei
Wang, Bo
TI Isofraxidin Inhibits Receptor Activator of Nuclear Factor-κB Ligand-Induced Osteoclastogenesis in Bone Marrow-Derived Macrophages Isolated from Sprague-Dawley Rats by Regulating NF-κB/NFATc1 and Akt/NFATc1 Signaling Pathways
SO CELL TRANSPLANTATION

LA English
DT Article
DE osteoporosis; isofraxidin; osteoclast formation; RANKL; NFATc1
AB Osteoporosis is a common bone disease that is characterized by decreased bone mass and fragility fractures. Isofraxidin is a hydroxy coumarin with several biological and pharmacological activities including an anti-osteoarthritis effect. However, the role of isofraxidin in osteoporosis has not yet been investigated. In the present study, we used receptor activator of nuclear factor-kappa B ligand (RANKL) to induce osteoclast formation in primary bone marrow macrophages (BMMs). Our results showed that RANKL treatment significantly increased tartrate-resistant acid phosphatase (TRAP) activity, as well as the expression of osteoclastogenesis-related markers including MMP-9, c-Src, and cathepsin K at both mRNA and protein levels; however, these effects were inhibited by isofraxidin in BMMs. In addition, luciferase reporter assay demonstrated that isofraxidin treatment suppressed the RANKL-induced an increase in nuclear factor of activated T-cells cytoplasmic 1 (NFATc1) transcriptional activity. Besides, the decreased expression level of I kappa B alpha and increased levels of p-p65, p-I kappa B alpha, and p-Akt in RANKL-induced BMMs were attenuated by isofraxidin. Moreover, NFATc1 overexpression rescued the anti-osteoclastogenic effect of isofraxidin with increased expression levels of MMP-9, c-Src, and cathepsin K. Taken together, these findings indicated that isofraxidin inhibited RANKL-induced osteoclast formation in BMMs via inhibiting the activation of NF-kappa B/NFATc1 and Akt/NFATc1 signaling pathways. Thus, isofraxidin might be a therapeutic agent for the treatment of osteoporosis.
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NR 34
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Z9 7
U1 1
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PU SAGE PUBLICATIONS INC
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J9 CELL TRANSPLANT
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WC Cell & Tissue Engineering; Medicine, Research & Experimental; Transplantation
SC Cell Biology; Research & Experimental Medicine; Transplantation
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PT J
AU Najdi, H
Mouarbes, D
Karnib, S
Dimassi, A
AF Najdi, Hassan
Mouarbes, Danny
Karnib, Soha
Dimassi, Ahmad
TI Periacetabular triple osteotomy by single anterior approach for children under 6-years-old with severe acetabular deficiency: prevention of retroversion and anterior impingement
SO JOURNAL OF PEDIATRIC ORTHOPAEDICS-PART B
LA English
DT Article
DE hip dysplasia; pelvic osteotomy; periacetabular triple osteotomy; reorientation maneuver; salter osteotomy
ID computed-tomography analysis; congenital dislocation; innominate osteotomy; pelvic osteotomy; developmental dysplasia; hip-dysplasia; osteoarthritis; acetabuloplasty; subluxation; salter
AB The aim of this study was to perform periacetabular triple osteotomy (PATO) in children under 6-years-old with severe acetabular deficiency aiming to obtain important correction and avoid excessive pressure on epiphysis, anterior overcorrection and acetabular retroversion. This is a retrospective study of 29 PATO using single anterior approach in 24 patients under 6-years-old with dysplasia of the hip. Clinical examination and radiographic evaluation were done pre-op, post-op and at last follow-up. Computed tomography (CT) scan was obtained, comparing operated hip to contro-lateral normal hip. Clinical examination of the

operated hip, at the last follow-up, showed a normal range of motion with nonsignificant difference when compared to normal hip. All hips were classified as Wicart A, and all activities were allowed. Radiographically, X-ray revealed improvement of all parameters postoperatively, with nonsignificant change compared to the last follow-up. CT-2D axial analysis demonstrated the absence of acetabular retroversion with good anterior and posterior coverage. CT-3D imaging comparing the anterior acetabular inclination, anterolateral and posterolateral inclination angles of operated hip and normal hip showed comparable results. Patients less than 6 years with severe acetabular deficiency could benefit from PATO. Performing osteotomies close to joint gave important acetabular fragment freedom, allowing an important correction. Appropriate manoeuver of reorientation avoided anterior overcorrection and acetabular retroversion, responsible for early pain and osteoarthritis. Age should not be the only criteria to choose the type of osteotomy. Level of evidence: level IV.

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NR 35
TC 1
Z9 1
U1 0
U2 1
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
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JI J. Pediatr. Orthop.-Part B
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PT J
AU Holzapfel, BM
Rak, D
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AF Holzapfel, Boris Michael
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Thaler, Martin
Rudert, Maximilian
TI Short stem hip arthroplasty via the minimally invasive direct anterior approach
SO OPERATIVE ORTHOPADIE UND TRAUMATOLOGIE
LA English
DT Article
DE Osteoarthritis, primary/secondary; DAA; Minimally invasive; Neck-preserving; Hip arthroplasty
ID revision; nerve
AB Objective: Tissue-sparing, minimally invasive hip arthroplasty via the direct anterior approach (DAA) using a partially neck-preserving, calcar-guided short stem. Indications: Primary and secondary osteoarthritis of the hip due to developmental dysplasia, femoroacetabular impingement, femoral head necrosis or trauma sequelae. Contraindications: Severe osteoporosis, active infection, American Society of Anesthesiologists (ASA) > III, large metaphyseal bone defects, severe metaphyseal deformities, Dorr type C femur. Surgical technique: Supine position on a standard operating table without extension device. Classic DAA skin incision or bikini incision distal to the inguinal fold. Blunt dissection entering the Hueter interval. Capsulotomy with capsule preservation or partial capsulectomy.

Intraoperatively, it is crucial to adhere to the preoperatively planned angle and height of the femoral neck osteotomy. During femoral head removal and acetabular preparation, care must be taken to avoid iatrogenic damage to the remaining neck. After cup positioning, femoral access is achieved by release of superior capsular structures. During opening of the medullary canal and broaching, femoral torsion and axis have to be taken into account for correct rotational and axial alignment. Femoral broaches are inserted in an ascending series of sizes until the last broach is firmly lodged and is in direct contact with the antero-medial femoral neck cortex. Fluoroscopic control in two planes to check for femoral anatomic and overall offset and assess whether the implant is adequately seated with cortical support at the calcar, the distal lateral and the dorsal cortex. Implantation of the definitive implants, local infiltration analgesia and wound closure. Results: Between 1/2011 and 12/2016 60 patients (24 female, 36 male; mean age 44 years) were treated with a partially neck-preserving short stem via the described approach. Seven patients underwent a bi-lateral procedure. Thus, 67 procedures were analysed in this retrospective cohort study. Mean follow-up was 70 months (range 28-93). The median Harris Hip Score was 48 (range 11-88) preoperatively and 98 (range 80-100) postoperatively. Conclusion: The minimally invasive implantation of a partially neck-preserving stem via DAA provides a safe technique with good to excellent clinical results in the mid-term.

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NR 30
TC 7
Z9 10
U1 0
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PU URBAN & VOGEL
PI MUNICH
PA NEUMARKTER STRASSE 43, D-81673 MUNICH, GERMANY
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JI Oper. Orthopade Traumatol.
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PT J
AU Wolff, L
Strathmann, EA
Müller, I
Mählich, D
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Niehoff, A
Wirth, B
AF Wolff, Lisa
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Niehoff, Anja
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TI Plastin 3 in health and disease: a matter of balance
SO CELLULAR AND MOLECULAR LIFE SCIENCES
LA English
DT Review
DE Cutaneous T-cell lymphomas; Colorectal cancer; Osteoclasts; Amyotrophic lateral sclerosis; Ataxia
ID spinal muscular-atrophy; epithelial-mesenchymal transition; early-onset osteoporosis; colon-cancer recurrence; filament cross-linking; x-linked osteoporosis; t-plastin; gene-expression; aberrant expression; actin cytoskeleton
AB For a long time, PLS3 (plastin 3, also known as T-plastin or fimbrin) has been

considered a rather inconspicuous protein, involved in F-actin-binding and -bundling. However, in recent years, a plethora of discoveries have turned PLS3 into a highly interesting protein involved in many cellular processes, signaling pathways, and diseases. PLS3 is localized on the X-chromosome, but shows sex-specific, inter-individual and tissue-specific expression variability pointing towards skewed X-inactivation. PLS3 is expressed in all solid tissues but usually not in hematopoietic cells. When escaping X-inactivation, PLS3 triggers a plethora of different types of cancers. Elevated PLS3 levels are considered a prognostic biomarker for cancer and refractory response to therapies. When it is knocked out or mutated in humans and mice, it causes osteoporosis with bone fractures; it is the only protein involved in actin dynamics responsible for osteoporosis. Instead, when PLS3 is upregulated, it acts as a highly protective SMN-independent modifier in spinal muscular atrophy (SMA). Here, it seems to counteract reduced F-actin levels by restoring impaired endocytosis and disturbed calcium homeostasis caused by reduced SMN levels. In contrast, an upregulation of PLS3 on wild-type level might cause osteoarthritis. This emphasizes that the amount of PLS3 in our cells must be precisely balanced; both too much and too little can be detrimental.
Actin-dynamics, regulated by PLS3 among others, are crucial in a lot of cellular processes including endocytosis, cell migration, axonal growth, neurotransmission, translation, and others. Also, PLS3 levels influence the infection with different bacteria, mycosis, and other pathogens.
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TI Effect of compression fracture on trabecular bone score at lumbar spine
SO OSTEOPOROSIS INTERNATIONAL
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DT Article
DE Bone mineral density; Compression fracture; Dual-energy X-ray absorptiometry; Osteoporosis; Trabecular bone scores
ID predicts osteoporotic fractures; mineral density; tbs; diagnosis; men; consensus; severity; quality; women; dxa
AB Bone mineral density (BMD) may be increased due to vertebral compression fractures (VCF). Our study showed trabecular bone scores (TBS) was less affected than BMD by fractured vertebrae. The TBS of most compression fractures, including old and recent VCF with mild or moderate deformity and old VCF with severe deformity, could still be used in predicting fracture risk. Introduction Trabecular bone score (TBS), a noninvasive tool estimating bone microarchitecture, provides complementary information to lumbar spine bone mineral density (BMD). Lumbar spine BMD might be increased due to both degenerative disease and vertebral compression fractures (VCF). Lumbar spine TBS has been confirmed not influenced by osteoarthrosis, but the effects of VCF are still not been well evaluated. This study aimed to investigate whether lumbar spine TBS was affected by fractured vertebrae. Methods We studied postmenopausal women and men above 50 years

old who underwent DXA between January 1, 2017, and May 31, 2019. By calculating the difference of BMD and TBS between L1 and the mean of L2-3, the study compared the difference of values between the control group and fracture group to determine the effects of fractured vertebrae on BMD and TBS. Results A total of 377 participants were enrolled with 202 in the control group (157 females; age: 68.06 +/- 6.47 years) and 175 in the fracture group (147 females; age: 71.71 +/- 9.44 years). The mean BMD of the L1 vertebrae in the fracture group was significantly higher than that in the control group ($p < 0.0001$). There was no significant difference between the mean differences of TBS between L1 and the means of L2-3 vertebrae in the control group and the most compression fractures, including old and recent VCF with mild or moderate deformity and old VCF with severe deformity. Conclusion Lumbar spine TBS, unlike BMD, is less affected by fractured vertebrae. The TBS of most compression fractures, including old and recent VCF with mild or moderate deformity and old VCF with severe deformity, could still be used in predicting fracture risk.
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TI Prevalence and Risk Factors Associated with Low Back Pain in the Saudi Adult Community: A Cross-Sectional Study
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LA English
DT Article
DE low back pain; prevalence; community; risk factors
ID global burden; osteoarthritis; knee; epidemiology; hypertension; arthritis; disease
AB Worldwide, low back pain is common and linked with many risk factors. There is a lack of studies in the Saudi Arabian community on low back pain prevalence and risk factors. Therefore, the present research will investigate the prevalence of low back pain in the middle-aged and elderly community population and examine the risk factors contributing to low back pain in Saudi Arabia. The present paper is a cross-sectional study of the community living in Riyadh and the surrounding areas in Saudi Arabia. Data were collected between October 2019 and April 2020 via trained research assistants. A total of 276 participants were included in the analysis. The prevalence of low back pain was 27.9% (n = 77) among the participants included in this study. All participants reported low back pain severity with a mean

of 4.35 +/- 2.19 on the pain rating scale. Older age, arthritis, hypertension, anemia, osteoporosis, and a history of fractures were all associated with having LBP. Low back pain is highly prevalent in the Saudi community adult population living in Riyadh and its surrounding areas. More than a fourth of the sample reported experiencing back pain. The study outlines several modifiable risk factors (BMI, education, employment status, marital status, and smoking status) and unmodifiable risk factors (arthritis, hypertension, anemia, osteoporosis, and a history of fractures) associated with low back pain in the study sample.
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NR 51

TC 23
Z9 24
U1 1
U2 15
PU MDPI
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WC Environmental Sciences; Public, Environmental & Occupational Health
SC Environmental Sciences & Ecology; Public, Environmental & Occupational Health
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PT J
AU Hernandez, CJ
AF Hernandez, Christopher J.
TI Musculoskeletal microbiology: The utility of the microbiome in orthopedics
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE infection; microbiome; osteoarthritis; osteoporosis
ID gut microbiome; intestinal microbiota; bone; transplantation; arthroplasty; infections
AB The past 15 years have witnessed a renaissance in the study of the microbes that colonize the human body. The vast majority of the human microbiome resides within the gut. Alterations to the gut microbiome have been associated with the pathogenesis and progression of wide-ranging diseases throughout the body-including atherosclerosis, depression, and obesity. Our understanding of the effects of the gut microbiome on the musculoskeletal system remains in its infancy,

but preclinical work has demonstrated an effect of the gut microbiome on the success of orthopedic surgical procedures, osteoporosis, osteoarthritis, and muscle mass. In this perspective I review preclinical findings demonstrating that an impaired presurgical gut microbiome can increase the likelihood of developing periprosthetic joint infection and how alterations in the gut microbiome can reduce bone strength by impairing bone tissue material properties. In addition to discussing these examples, I review the hypothesis that many chronic non-communicable diseases have become more prevalent in modern industrialized societies as a result of changes in the composition of the gut microbiome resulting from changes in environment/lifestyle (diet, sanitation, antibiotic use). The most burdensome musculoskeletal disorders are chronic and non-communicable and may therefore be related to generational shifts in the composition of the gut microbiome, a possibility I illustrate by reviewing changes in the prevalence of osteoarthritis over the last century. Microbiome-based therapeutics are potentially innocuous, inexpensive, and have the potential to be effective with only occasional use, making them attractive for addressing the needs of chronic and/or slowly progressing musculoskeletal disorders.
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Z9 14
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AU Zhang, Y
Zhang, C
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AF Zhang, Yan
Zhang, Cheng
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Wang, Muyao
TI Bone-Adipose Tissue Crosstalk: Role of Adipose Tissue Derived Extracellular Vesicles in Bone Diseases
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Review
DE adipose tissue; bone remodeling; extracellular vesicles; obesity; osteoporosis
ID marrow adipose; stem-cells; circulating micrornas; adipocytes; exosm; inflammation; adipokines; pathway; obesity; fat
AB Bone is a metabolically active organ that undergoes constant remodeling throughout life. A failure of this process leads to pathological destructive bone diseases such as osteoporosis, rheumatoid arthritis, and osteoarthritis. Studies of the interplay between adipose tissue and bone system, have revealed that adipose tissue disorders (e.g. obesity) strongly influence the development of bone diseases. Adipokines secreted by adipose tissue play important roles in the crosstalk between bone and adipose tissue. Recently, extracellular vesicles (EVs) have been identified as a novel method of communication between different organs and have attracted increased attention in the field of bone remodeling process. Adipokines carried by EVs are known to play pivotal roles in bone remodeling processes

including osteogenesis and osteoclastogenesis. In this review, we highlighted the role of adipose tissue derived EVs (EVs-AT) in the context of bone remodeling events and focused on the characteristics of EVs-AT and their components in the regulation of bone diseases. Moreover, we introduced the intriguing therapeutic application of EVs-AT in different pathological destructive bone diseases and proposed future directions for research on EVs-AT in bone diseases.
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TI H2S Donor and Bone Metabolism
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE bone metabolism; mechanisms; diseases; hydrogen sulfide; donor
ID hydrogen-sulfide donor; nf-kappa-b; diabetes-mellitus; in-vitro; physiology; oxidation; molecule; insights; synthase; receptor
AB Hydrogen sulfide (H2S) has been recognized as the third gasotransmitter, following nitric oxide and carbon monoxide, and it exerts important biological effects in the body. Growing evidence has shown that H2S is involved in many physiological processes in the body. In recent years, much research has been carried out on the role of H2S in bone metabolism. Bone metabolic diseases have been linked to abnormal endogenous H2S functions and metabolism. It has been found that H2S plays an important role in the regulation of bone diseases such as osteoporosis and osteoarthritis. Regulation of H2S on bone metabolism has many interacting signaling pathways at the molecular level, which play an important role in bone formation and absorption. H2S releasing agents (donors) have achieved significant effects in the treatment of metabolic bone diseases such as osteoporosis and osteoarthritis. In addition, H2S donors and related drugs have been widely used as research tools in basic biomedical research and may be explored as potential therapeutic agents in the future. Donors are used to study the mechanism and function of H2S as they release H2S through different mechanisms. Although H2S releasers have biological activity, their function can be inconsistent. Additionally, donors have different H2S release capabilities, which could lead to different effects. Side effects may form with the formation of H2S; however, it is unclear whether these side effects affect the biological effects of H2S. Therefore, it is necessary to study H2S donors in detail. In this review, we summarize the current information about H2S donors related to bone metabolism diseases and discuss some mechanisms and biological applications.
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NR 71
TC 33
Z9 34
U1 2
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PU FRONTIERS MEDIA SA
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TI Methylsulfonylmethane Increases the Alveolar Bone Density of Mandibles in Aging Female Mice
SO FRONTIERS IN PHYSIOLOGY

LA English
DT Article
DE osteoblasts; aging mice; bone formation; osteoclasts; methylsulfonylmethane
ID stem-cells; estrogen deficiency; periodontal-disease; double-blind; differentiation; osteoporosis; inflammation; jaw; osteoblastogenesis; osteoarthritis
AB Methylsulfonylmethane (MSM) is a naturally occurring anti-inflammatory compound that effectively treats multiple degenerative diseases such as osteoarthritis and acute pancreatitis. Our previous studies have demonstrated the ability of MSM to differentiate stem cells from human exfoliated deciduous (SHED) teeth into osteoblast-like cells. This study examined the systemic effect of MSM in 36-week-old aging C57BL/6 female mice in vivo by injecting MSM for 13 weeks. Serum analyses showed an increase in expression levels of bone formation markers [osteocalcin (OCN) and procollagen type 1 intact N-terminal propeptide (P1NP)] and a reduction in bone resorption markers [tartrate-resistant acid phosphatase (TRAP) and C-terminal telopeptide of type I collag (CTX-I)] in MSM-injected animals. Micro-computed tomographic images demonstrated an increase in trabecular bone density in mandibles. The trabecular bone density tended to be higher in the femur, although the increase was not significantly different between the MSM- and phosphate-buffered saline (PBS)-injected mice. In mandibles, an increase in bone density with a corresponding decrease in the marrow cavity was observed in the MSM-injected mice. Furthermore, immunohistochemical analyses of the mandibles for the osteoblast-specific marker - OCN, and the mesenchymal stem cell-specific marker - CD105 showed a significant increase and decrease in OCN and CD105 positive cells, respectively. Areas of bone loss were observed in the inter-radicular region of mandibles in control mice. However, this loss was considerably decreased due to stimulation of bone formation in response to MSM injection. In conclusion, our study has demonstrated the ability of MSM to induce osteoblast formation and function in vivo, resulting in increased bone formation in the mandible. Hence, the application of MSM and stem cells of interest may be the right combination in alveolar bone regeneration under periodontal or other related diseases that demonstrate bone loss.</p>
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TI Associated Factors of Sarcopenia in Community-Dwelling Older Adults: A Systematic Review and Meta-Analysis
SO NUTRIENTS
LA English
DT Article
DE older adults; sarcopenia; associated factors; community; systematic review; meta-analysis
ID skeletal-muscle mass; asian working group; risk-factors; physical-activity; chinese men; prevalence; people; health; osteoporosis; impairment
AB (1) Background: To review the associated factors of sarcopenia in community-dwelling older adults. (2) Methods: PubMed, Embase, Web of Science, and four Chinese electronic databases were searched for observational studies that reported the associated factors of sarcopenia from inception to August 2021. Two researchers independently selected the literature, evaluated their quality, and extracted relevant data. The pooled odds ratio (OR) and its 95% confidence interval (CI) were calculated for each associated factors of sarcopenia using random-effects/fixed-effects models. Publication bias was assessed using funnel plot and the Eggers test. We performed statistical analysis using Stata 15.0 software. (3) Results: A total of 68 studies comprising 98,502 cases were included. Sociodemographic associated factors of sarcopenia among community-dwelling older adults included age (OR = 1.12, 95% CI: 1.10-1.13), marital status (singled, divorced, or widowed) (OR = 1.57, 95% CI: 1.08-2.28), disability for activities of daily living (ADL) (OR = 1.49, 95% CI: 1.15-1.92), and underweight (OR = 3.78, 95% CI: 2.55-5.60). Behavioral associated factors included smoking (OR = 1.20, 95% CI: 1.10-1.21), physical inactivity (OR = 1.73, 95% CI: 1.48-2.01), malnutrition/malnutrition risk (OR = 2.99, 95% CI: 2.40-3.72), long (OR = 2.30, 95% CI: 1.37-3.86) and short (OR = 3.32, 95% CI: 1.86-5.93) sleeping time, and living alone (OR = 1.55, 95% CI: 1.00-2.40). Disease-related associated factors included diabetes (OR = 1.40, 95% CI: 1.18-1.66), cognitive impairment (OR = 1.62, 95% CI: 1.05-2.51), heart diseases (OR = 1.14, 95% CI: 1.00-1.30), respiratory diseases (OR = 1.22, 95% CI: 1.09-1.36), osteopenia/osteoporosis (OR = 2.73, 95% CI: 1.63-4.57), osteoarthritis (OR = 1.33, 95% CI: 1.23-1.44), depression (OR = 1.46, 95% CI: 1.17-1.83), falls (OR = 1.28, 95% CI: 1.14-1.44), anorexia (OR = 1.50, 95% CI: 1.14-1.96), and anemia (OR = 1.39, 95% CI: 1.06-1.82). However, it remained unknown whether gender (female: OR = 1.10, 95% CI: 0.80-1.51; male: OR = 1.50, 95% CI: 0.96-2.34), overweight/obesity (OR = 0.27, 95% CI: 0.17-0.44), drinking (OR = 0.92, 95% CI: 0.84-1.01), hypertension (OR = 0.98, 95% CI: 0.84-1.14), hyperlipidemia (OR = 1.14, 95% CI: 0.89-1.47), stroke (OR = 1.70, 95% CI: 0.69-4.17), cancer (OR = 0.88, 95% CI: 0.85-0.92), pain (OR = 1.08, 95% CI: 0.98-1.20), liver disease (OR = 0.88, 95% CI: 0.85-0.91), and kidney disease (OR = 2.52, 95% CI: 0.19-33.30) were associated with sarcopenia. (4) Conclusions: There are many sociodemographic, behavioral, and disease-related associated factors of sarcopenia in community-dwelling older adults. Our view provides evidence for the early identification of high-risk individuals and the development of relevant

interventions to prevent sarcopenia in community-dwelling older adults.
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TI Osteoblast role in the pathogenesis of rheumatoid arthritis
SO MOLECULAR BIOLOGY REPORTS
LA English
DT Review
DE Osteoblasts; Rheumatoid arthritis; RANKL; RANK; Bone loss; Cytokines
AB In the pathogenesis of several rheumatic diseases, such as rheumatoid arthritis, spondyloarthritis, osteoarthritis, osteoporosis, alterations in osteoblast growth,

differentiation and activity play a role. In particular, in rheumatoid arthritis bone homeostasis is perturbed: in addition to stimulating the pathologic bone resorption process performed by osteoclasts in course of rheumatoid arthritis, proinflammatory cytokines (such as Tumor Necrosis factor-alpha, Interleukin-1) can also inhibit osteoblast differentiation and function, resulting in net bone loss. Mouse models of rheumatoid arthritis showed that complete resolution of inflammation (with maximal reduction in the expression of pro-inflammatory factors) is crucial for bone healing, performed by osteoblasts activity. In fact, abnormal activity of factors and systems involved in osteoblast function in these patients has been described. A better understanding of the pathogenic mechanisms involved in osteoblast dysregulation could contribute to explain the generalized and focal articular bone loss found in rheumatoid arthritis. Nevertheless, these aspects have not been frequently and directly evaluated in studies. This review article is focused on analysis of the current knowledge about the role of osteoblast dysregulation occurring in rheumatoid arthritis: a better knowledge of these mechanisms could contribute to the realization of new therapeutic strategies.
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TI Apelin/APJ system: A novel therapeutic target for locomotor system diseases
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DT Article
DE Apelin; APJ system; Locomotor system; Metabolism; Osteoarthritis; Osteoporosis
ID endoplasmic-reticulum stress; activated protein-kinase; mesenchymal stem-cells; fatty-acid oxidation; skeletal-muscle; insulin-resistance; endogenous ligand; aerobic exercise; receptor; apj
AB Apelin is an endogenous ligand of G protein-coupled receptor APJ. Apelin/APJ system is widely expressed in abundant tissues, especially bone, joint and muscle tissue. This review focus on the effects of apelin/APJ system on locomotor system. An increasing number of evidence suggests that apelin/APJ system plays a crucial role in many physiological and pathological processes of locomotor system. Physiologically, apelin/APJ system promotes bone formation, muscle metabolism and skeletal muscle production. Pathologically, apelin/APJ system exacerbates osteoarthritis pathogenesis, whereas it alleviates osteoporosis. Besides, the level of apelin expression is regulated by different training modes, including continuous aerobic exercise, high-intensity interval training and resistance exercises. More importantly, exercise-induced apelin may be a potent pharmacological agent for the treatment of diseases and the regulation of physiological processes. Considering the pleiotropic effects of apelin on locomotor system, apelin/APJ system may be an important therapeutic target for locomotor system diseases.
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TI Deciphering Myostatin's Regulatory, Metabolic, and Developmental Influence in Skeletal Diseases
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DT Review
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ID muscle-bone interactions; activin-a; osteogenesis imperfecta; diabetes-mellitus; beta superfamily; mineral density; mouse model; mass; mice; expression
AB Current research findings in humans and other mammalian and non-mammalian species support the potent regulatory role of myostatin in the morphology and function of muscle as well as cellular differentiation and metabolism, with real-life implications in agricultural meat production and human disease. Myostatin null mice (mstn(-/-)) exhibit skeletal muscle fiber hyperplasia and hypertrophy whereas myostatin deficiency in larger mammals like sheep and pigs engender muscle fiber hyperplasia. Myostatin's impact extends beyond muscles, with alterations in myostatin present in the pathophysiology of myocardial infarctions, inflammation, insulin resistance, diabetes, aging, cancer cachexia, and musculoskeletal disease. In this review, we explore myostatin's role in skeletal integrity and bone cell biology either due to direct biochemical signaling or indirect mechanisms of mechanotransduction. In vitro, myostatin inhibits

osteoblast differentiation and stimulates osteoclast activity in a dose-dependent manner. Mice deficient in myostatin also have decreased osteoclast numbers, increased cortical thickness, cortical tissue mineral density in the tibia, and increased vertebral bone mineral density. Further, we explore the implications of these biochemical and biomechanical influences of myostatin signaling in the pathophysiology of human disorders that involve musculoskeletal degeneration. The pharmacological inhibition of myostatin directly or via decoy receptors has revealed improvements in muscle and bone properties in mouse models of osteogenesis imperfecta, osteoporosis, osteoarthritis, Duchenne muscular dystrophy, and diabetes. However, recent disappointing clinical trial outcomes of induced myostatin inhibition in diseases with significant neuromuscular wasting and atrophy reiterate complexity and further need for exploration of the translational application of myostatin inhibition in humans.
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TI Investigation of the Effect of Bone Mineral Density on the Postoperative Outcome of Ankle Fractures in Elderly Patients
SO FOOT & ANKLE INTERNATIONAL
LA English
DT Article
DE aged; bone density; treatment outcome; absorptiometry

ID internal-fixation; open reduction; epidemiology; women; scale; osteoarthritis; men; age
AB Background: The association between ankle fractures in elderly patients and low bone mineral density (BMD) has recently been recognized, but the effect of BMD on the postoperative outcome of these fractures is unknown. The aim of this study was to investigate the effect of BMD on the postoperative outcome of ankle fractures in elderly patients to evaluate the need for BMD screening. Methods: We retrospectively reviewed 48 patients aged 65 years or older who had ankle fractures and underwent dual-energy x-ray absorptiometry to assess BMD after surgical treatment of the fracture. Postoperative outcomes were assessed using the Olerud-Molander Ankle Score (OMAS), visual analog scale (VAS) score for pain, Kellgren and Lawrence (K&L) grading scale score, and quality of fracture reduction. The correlation between the BMD and the outcome measures at 12 months after surgery was analyzed using the Pearson correlation coefficient. Results: The mean absolute value of BMD was 0.6 +/- 0.1 g/cm(2) (T-score, -1.5 +/- 1.2) at the femoral neck and 0.8 +/- 0.2 g/cm(2) (T-score, -1.2 +/- 1.5) at the lumbar spine. Osteoporosis was present in 33% of female patients and in 11% of male patients. At 12 months after surgery, the OMAS was 70 +/- 17 and the VAS score for pain was 18 +/- 17. Of the patients, 20, 21, 5, 1, and 1 had K&L grades of 0, 1, 2, 3, and 4, respectively. None of the clinical and radiographic outcome measures were correlated with the BMD values of the patients. Conclusion: The postoperative outcome of the ankle fractures in elderly patients at 12 months after surgery showed no correlation with femoral neck or lumbar spine BMD at the time of fracture.
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TI Tai Chi for health and well-being: A bibliometric analysis of published clinical studies between 2010 and 2020
SO COMPLEMENTARY THERAPIES IN MEDICINE
LA English
DT Article
DE Tai Chi; Physical therapy; Exercise; Mind-body therapies; Complementary therapies
ID trials
AB The objective of this bibliometric review was to identify the volume, breadth, and characteristics of clinical studies evaluating Tai Chi published between January 2010 and January 2020. Five English and four Chinese language databases were searched. Following independent screening, 1018 eligible publications representing 987 studies were identified, which was a three-fold increase from the previous decade. Most common were randomized controlled trials (548/987, 55.5 %), followed by systematic reviews (157/987, 15.9 %), nonrandomized controlled clinical studies (152/987, 15.4 %), case series (127/987, 12.9 %) and case reports (3/987, 0.3 %) that were conducted in China (730/987, 74.0 %), followed by the United States of America (123/ 987, 12.5 %) and South Korea (20/987, 2.0 %). Study participants were mostly in the adult (55.2 %) and/or older adult (72.0 %) age groups. The top ten diseases/conditions were hypertension, chronic obstructive pulmonary disease, diabetes, knee osteoarthritis, heart failure, depression, osteoporosis/osteopenia, breast cancer, coronary heart disease and insomnia. A quarter of the studies enrolled healthy participants to evaluate the effects of Tai Chi on health promotion/preservation, balance/falls, and physiological/biomechanical outcomes. Yang style Tai Chi was the most popular, followed by Chen and Sun

style. Tai Chi was mostly commonly delivered faceto-face by a Tai Chi instructor in group settings for 60 min, three times a week, for 12 weeks. Most studies (93.8 %) reported at least one outcome in favor of Tai Chi. Adverse events were underreported (7.2 %). Over half fell short of expected intervention reporting standards, signalling the need for Tai Chi extensions to existing guidelines.
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PT J
AU García-López, S
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AF Garcia-Lopez, Sofia
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TI Patient self-reported functioning by pain severity and usual analgesic treatment among older adults with osteoarthritis: analysis of the 2017 Spanish National Health Survey
SO EUROPEAN GERIATRIC MEDICINE
LA English
DT Article
DE Osteoarthritis; Functioning; Treated; Untreated; Pain; Dependency
ID epidemiology; osteoporosis; limitations; prevalence; outcm; frailty
AB Purpose Osteoarthritis (OA) pain is among the leading causes of disability worldwide in older people. Since its prevalence is growing in aging, a significant burden for society is expected. This work ascertained whether level of disability in self-reported functioning differs by pain severity and usual analgesic treatment among older OA patients in Spain. Methods The Spanish-National-Health-Survey, a large, nationally representative, cross-sectional general health survey including 23,089 persons, was analyzed. Patients aged 65 + years with a self-reported physician OA diagnosis were classified according to severity of pain (no/mild, moderate or severe pain) and treated or untreated with analgesia. Assessment of function included basic and instrumental activities-of-daily-living (BADL, IADL), mental, social, and cognitive functions, scored on a 0% (no limitation) to 100% (complete limitation) standardized metric. Caregiver need for BADL and IADL was also recorded. Results A total of 3526 patients were analyzed (women 73.3%; age 77.4 [SD: 7.5]). Adjusted functioning scores showed significant association with pain severity, and for BADL, IADL and social function. Patients with severe pain and treated with analgesia had higher limitation scores, ranging on average between 31.5% on BADL, 34.1% on IADL, 45.0% on mental, 42.2% on social, and 23.4% in cognitive domain. The proportions of patients needing a caregiver for BADL (43.4%) and IADL (56.2%) were also the highest in patients with severe pain and treated with analgesia. Conclusions Regardless of usual utilization of analgesics, the severity of pain seemed to be the major determinant of functional impairment, and

caregiving need, in all domains of functioning in older OA patients in Spain. Existing treatment strategies are analgesics based and do not meet patient needs for adequate pain management.
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TI Correlation and responsiveness of global health, upper extremity-specific, and shoulder-specific functional outcome measures following reverse total shoulder arthroplasty for proximal humerus fracture

SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Proximal humerus fracture; Reverse total shoulder arthroplasty; Functional outcome; Correlation; Responsiveness; Floor effect; Ceiling effect
ID western ontario osteoarthritis; cross-cultural adaptation; american shoulder; response burden; version; score; validation; quickdash; dash
AB Purpose Reverse total shoulder arthroplasty (rTSA) is effective and increasingly utilized for the management of proximal humerus fracture (PHF). However, the optimal patient-reported outcome metrics (PROMs) for the evaluation of patient outcomes after this surgery are unclear. We investigated the correlation among global, upper extremity-specific, and shoulder-specific PROMs in patients undergoing rTSA for PHF as well as the responsiveness of these PROMs as assessed by floor and ceiling effects. We hypothesized that patients' post-operative outcome would be best reflected by a combination of these metrics. Methods Thirty patients with a history of rTSA for ipsilateral PHF filled out the following outcomes questionnaires at a minimum of 3 years post-op: EQ-5D, EQ-5D VAS, PROMIS physical function, DASH, SSV, SPADI, and ASES. Correlation between metrics was assessed using the Spearman correlation coefficient. Responsiveness was assessed by comparing the proportion of patients reaching floor or ceiling values using McNemar's test. Results Global health metrics (EQ-5D and PROMIS physical function) were strongly correlated with the upper extremity-specific metric (DASH). Shoulder-specific outcomes (SPADI, ASES, and ASES) were moderately correlated with both the global metrics and DASH. There was no significant difference between PROMs with regards to floor and ceiling effects. Conclusions The DASH score has been shown to be valid and responsive for shoulder interventions, and our data demonstrate that it correlates strongly with overall quality of life. Shoulder-specific metrics are valid and responsive for shoulder interventions but correlate less with global quality of life. An optimal PROM strategy in rTSA for PHF might involve both DASH and a shoulder-specific score. Based on our assessment of floor and ceiling effects, none of these metrics should be excluded for poor responsiveness.
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TI Osteo-modulatory dietary proteins and peptides: A concise review
SO JOURNAL OF FOOD BIOCHEMISTRY
LA English
DT Review
DE bioactive peptides; dietary proteins; functional foods; nutraceuticals; osteo-modulatory peptides
ID gadus-macrocephalus bone; calcium-binding peptide; bioactive peptides; mbp supplementation; controlled-trial; mineral density; whey-protein; milk; differentiation; osteoporosis
AB The integrity of the bone is dependent on the strict balance between osteoclastogenesis and osteoblastogenesis, and any imbalance results in bone diseases. Dietary proteins (DP) have been shown to promote osteogenesis while inhibiting bone resorption in cultured osteoblasts, and in animal models of bone diseases such as ovariectomy, 1 alpha,25-dihydroxy-vitamin D3 (VD3), and prostaglandin E2 (PGE2)-induced bone resorption. Hydrolysis of some of these DPs with osteo-modulatory properties has been shown to generate hydrolysates with bioactive peptides that exhibit higher osteo-modulatory properties in comparison to intact (parent) proteins. The higher bioactivity of the isolated peptides and protein hydrolysates compared to intact proteins indicates that the osteo-modulatory properties are dependent on the degree of exposure of the functional groups of amino acid residues involved in target interaction. This review provides an overview of the preparation of DP and select peptides with osteo-modulatory properties, and summarizes the potential underlying mechanisms of action through which the bioactive peptides help maintain bone health. Practical applications Bone diseases such as osteoporosis (OP), osteoarthritis (OA), bone cancer (BC), and others have negative impacts on the quality of life, especially in older women after menopause. Current drugs used in treating many bone diseases such as bisphosphonates, anabolic steroids, and selective estrogen receptor modulators have been limited by worrisome adverse effects such as organ toxicity, increased risk of cancer, and cardiovascular abnormalities, and gastrointestinal discomfort. There is growing scientific evidence that certain multifunctional dietary proteins and bioactive peptides may positively modulate bone health by modifying risk factors for bone diseases including inflammation, oxidative stress, hyperlipidemia, and hyperglycemia.
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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AF Morttinen-Vallius, Heidi
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TI Factors associated with daily opioid use among aged home care clients: a cross-sectional analysis of Resident Assessment Instrument data
SO EUROPEAN GERIATRIC MEDICINE
LA English
DT Article
DE Aged; Cognitive impairment; Home care; Opioids; Resident Assessment Instrument
ID community-dwelling persons; minimum data set; older-adults; analgesic use; pain; dementia; depression; scale; osteoarthritis; population
AB Key summary pointsAim To examine which client characteristics and other factors, including possible adverse effects, identified in the Resident Assessment Instrument-Home Care (RAI-HC) are associated with daily opioid use among aged home care clients. Findings After adjustment for pain-related diseases, disabilities, depressive symptoms and the estimated severity of pain, daily opioid use was associated with osteoporosis, cancer within previous 5 years and greater disabilities in Instrumental Activities of Daily Living, and cognitive impairment was associated with less frequent opioid use. Constipation was the only adverse effect identified in the RAI-HC associated with daily opioid use. Message The pain of home care clients with cognitive impairment may not be treated optimally, whereas there might be prolonged opioid use without a sufficient evaluation of current pain among clients with osteoporosis, cancer within previous 5 years and disabilities in Instrumental Activities of Daily Living. Purpose To examine which client characteristics and other factors, including possible adverse effects, identified in the Resident Assessment Instrument-Home Care (RAI-HC) are associated with daily opioid use among aged home care clients. Methods The study sample comprised 2584 home care clients aged >= 65 years, of which 282 persons used opioids daily. Clients using opioids less than once daily were excluded. The cross-sectional data were gathered from each client's first assessment with the RAI-HC during 2014. Multivariable logistic regression was used to study associations of daily opioid use with the clients' characteristics and symptoms. Results Cognitive impairment was associated with less frequent opioid use after adjusting for pain-related diseases, disabilities and depressive symptoms (OR 0.43, 95% CI 0.32-0.58). The association

was not explained by the estimated severity of pain. Osteoporosis, cancer within previous 5 years and greater disabilities in Instrumental Activities of Daily Living (IADL) were associated with daily opioid use regardless of the estimated severity of pain. Depressive symptoms and Parkinson's disease were associated with daily opioid use only among clients with cognitive impairment, and disabilities in Activities of Daily Living, cancer, arthritis, fractures and pressure ulcers only among clients without cognitive impairment. Constipation was the only adverse effect associated with daily opioid use. Conclusion The pain of home care clients with cognitive impairment may not be treated optimally, whereas there might be prolonged opioid use without a sufficient evaluation of current pain among clients with osteoporosis, cancer within previous 5 years and disabilities in IADLs.
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TI Chinese herbal medicine Xianling Gubao capsule for knee osteoarthritis A protocol for systematic review and meta-analysis
SO MEDICINE
LA English
DT Review
DE knee osteoarthritis; protocol; systematic review; Xianling Gubao capsule
AB Background: Knee osteoarthritis (KOA) is the most prevalent degenerative joint disease among populations over 60 years old, and is the most common cause of musculoskeletal pain and disability worldwide. Xianling Gubao capsule (XLGBC), a Chinese patent medicine, is widely used for treatment of osteoporosis. Meanwhile, according to the theory of homotherapy for heteropathy, XLGBC is increasingly applied in the clinical practice of KOA. However, no systematic review has found that XLGBC is as effective in treatment of KOA as it is in treatment of osteoporosis. Therefore, we will conduct a systematic review of XLGBC in KOA treatments. Methods: All randomized controlled trials assessing the validity of XLGBC therapy

for KOA will be retrieved from the following seven databases, including the Cochrane Library, PubMed, EMBASE, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, Wan Fang Database, and Chinese Scientific Journal Database. The primary outcome measures are the visual analogue scale pain score, and a comprehensive evaluation including the Western Ontario and McMaster Universities Arthritis Index scores, Lysholm scores, and Bristol scores. And the secondary outcome measures include cure rate and adverse events. The procedure such as retrieval and selection of literature, data extraction, evaluation of risk of bias, and assessment of reporting bias will be executed by 2 reviewers independently. The data synthesis for meta-analysis will be conducted by Review Manager 5.4 software. Results: A high-quality evidence of XLGBC for the treatment of KOA will be generated from the aspects of safety and efficacy. Conclusion: This systematic review will provide evidence to help us confirm the clinical efficacy of XLGBC in the treatment of KOA. OSF Registration number: Registration DOI 10.17605/OSF.IO/QD5SY.
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NR 17
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PU LIPPINCOTT WILLIAMS & WILKINS
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PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
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TI Are 3D-printed Models of Tibial Plateau Fractures a Useful Addition to Understanding Fractures for Junior Surgeons?
SO CLINICAL ORTHOPAEDICS AND RELATED RESEARCH
LA English
DT Article
ID classification; epidemiology; fixation; outcm
AB Background Tibial plateau fractures are often complex, and they can be challenging to treat. Classifying fractures is often part of the treatment process, but intra- and interobserver reliability of fracture classification systems often is inadequate to the task, and classifications that lack reliability can mislead providers and result in harm to patients. Three-dimensionally (3D)-printed models might help in this regard, but whether that is the case for the classification of tibial plateau fractures, and whether the utility of such models might vary by the experience of the individual classifying the fractures, is unknown. Questions/purposes (1) Does the overall interobserver agreement improve when fractures are classified with 3D-printed models compared with conventional radiology? (2) Does interobserver agreement vary among attending and consultant trauma surgeons, senior surgical residents, and junior surgical residents? (3) Do surgeons' and surgical residents' confidence and accuracy improve when tibial plateau fractures are classified with an additional 3D model compared with conventional radiology? Methods Between 2012 and 2020, 113 patients with tibial plateau fractures were treated at a Level 1 trauma center. Forty-four patients were excluded based on the presence of bone diseases (such as osteoporosis) and the absence of a CT scan. To increase the chance to detect an improvement or deterioration and to prevent observers from losing focus during the classification, we decided to include 40 patients with tibial plateau fractures. Nine trauma surgeons, eight senior surgical residents, and eight junior surgical residents-none of whom underwent any study-specific pretraining-classified these fractures according to three often-used classification systems (Schatzker, OA/OTA, and the Luo three-column concept), with and without 3D-printed models, and they indicated their overall confidence on a 10-point Likert scale, with 0 meaning not confident at all and 10 absolutely certainty. To set the gold standard, a panel of three experienced trauma surgeons who had special expertise in knee surgery and 10 years to 25 years of experience in practice also classified the fractures until consensus was reached. The Fleiss kappa was used to determine interobserver agreement for fracture classification. Differences in confidence in assessing fractures with and without the 3D-printed model were compared using a paired t-test. Accuracy was calculated by comparing the participants' observations with the gold standard. Results The overall interobserver agreement improved minimally for fracture classification according to two of three classification systems (Schatzker: kappa(conv) = 0.514 versus kappa(3Dprint) =

0.539; p = 0.005; AO/OTA:kappa(conv) = 0.359 versus kappa(3Dprint) = 0.372; p = 0.03). However, none of the classification systems, even when used by our most experienced group of trauma surgeons, achieved more than moderate interobserver agreement, meaning that a large proportion of fractures were misclassified by at least one observer. Overall, there was no improvement in self-assessed confidence in classifying fractures or accuracy with 3D-printed models; confidence was high (about 7 points on a 10-point scale) as rated by all observers, despite moderate or worse accuracy and interobserver agreement Conclusion Although 3D-printed models minimally improved the overall interobserver agreement for two of three classification systems, none of the classification systems achieved more than moderate interobserver agreement. This suggests that even with 3D-printed models, many fractures would be misclassified, which could result in misleading communication, inaccurate prognostic assessments, unclear research, and incorrect treatment choices. Therefore, we cannot recommend the use of 3D-printed models in practice and research for classification of tibial plateau fractures.
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NR 22
TC 17
Z9 18
U1 0
U2 15
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0009-921X
EI 1528-1132
J9 CLIN ORTHOP RELAT R
JI Clin. Orthop. Rel. Res.
PD JUN 15
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VL 480
IS 6
BP 1170
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WC Orthopedics; Surgery
SC Orthopedics; Surgery
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PT J
AU Kim, SM
Kim, YC
Kim, KT
Ha, KY
Luo, Q
Li, X
Park, J
AF Kim, Sung-Min
Kim, Yong-Chan
Kim, Ki-Tack
Ha, Kee-Yong
Luo, Qiang
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Park, JunBum
TI Surgical sequence in anterior column realignment with posterior osteotomy is important for degree of adult spinal deformity correction: advantages and indications for posterior to anterior sequence
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Adult spinal deformity; Posterior osteotomy; Anterior column realignment; Surgical sequence
ID pedicle subtraction osteotomy; interbody fusion; sagittal alignment; cage subsidence; complications; osteoarthritis; parameters; balance; degeneration; reliability
AB Background We hypothesized that posterior osteotomy prior to ACR (Anterior column realignment) through P-A-P surgical sequence would permit a greater correction for deformity corrective surgery than the traditional A-P sequence without posterior osteotomy. This study aimed to determine the impact of the P-A-P sequence on the restoration of lumbar lordosis (LL) compared to the A-P sequence in deformity corrective surgery for adult spinal deformity (ASD) patients and to identify the characteristics of patients who require this sequence. Methods Between 2017 and 2019, 260 ASD patients who had undergone combined corrective surgery were reviewed retrospectively. This study included 178 patients who underwent posterior osteotomy before the ACR (P-A group) and 82 patients who underwent the A-P sequence (A-P group). Sagittal spinopelvic parameters were determined from pre- and postoperative whole-spine radiographs and compared between the groups. To find better indications for the P-A-P sequence,

we conducted additional analysis on postoperative outcomes of patients in the A-P group. Results The P-A group showed a significantly higher change in LL (53.7 degrees vs. 44.3 degrees, p < 0.001), C7 sagittal vertical axis (C7 SVA: 197.4 mm vs. 146.1 mm, p = 0.021), segmental lordosis (SL) L2/3 (16.2 degrees vs. 14.4 degrees, p = 0.043), SL L3/4 (16.2 degrees vs. 13.8 degrees, p = 0.004), and SL L4/5 (15.1 degrees vs. 11.3 degrees, p = 0.001) compared to the A-P group. At the final follow-up, pelvic incidence (PI) minus LL mismatch (PI - LL mismatch) was significantly higher in the A-P group (13.4 degrees vs. 2.9 degrees, p < 0.001). Stepwise logistic regression analysis showed that age >= 75 years (odds ratio [OR] = 2.151; 95% confidence interval [CI], 1.414-3.272; p < 0.001), severe osteoporosis (OR = 2.824; 95% CI, 1.481-5.381; p = 0.002), rigid lumbar curve with dynamic changes in LL < 10 degrees (OR = 5.150; 95% CI, 2.296-11.548; p < 0.001), and severe facet joint osteoarthritis (OR = 4.513; 95% CI, 1.958-10.402; p < 0.001) were independent risk factors for PI - LL mismatch >= 10 degrees after A-P surgery. Conclusion P-A-P sequence for deformity corrective surgery in ASD offers greater LL correction than the A-P sequence. Indications for the procedure include patients aged >= 75 years, severe osteoporosis, rigid lumbar curve with dynamic change in LL < 10 degrees, or more than four facet joints of Pathria grade 3 in the lumbar region.
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NR 60
TC 4
Z9 5
U1 0
U2 1
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD NOV 22
PY 2022
VL 23
IS 1
BP
EP
DI 10.1186/s12891-022-05915-4
PG 13
WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA 6J7AG
UT WOS:000886972800004
PM 36419151
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ER

PT J
AU Zhang, X
Cai, GQ

Jones, G
Laslett, LL
AF Zhang, Xu
Cai, Guoqi
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TI Intravenous bisphosphonates do not improve knee pain or bone marrow lesions in people with knee osteoarthritis: a meta-analysis
SO RHEUMATOLOGY
LA English
DT Review
DE bisphosphonates; knee; osteoarthritis; pain; trial; meta-analysis
ID zoledronic acid; double-blind; alendronate; symptoms; burden; osteoporosis; risedronate; risk
AB Objective To summarize effects of intravenous bisphosphonates (IVBP) in patients with symptomatic knee OA and bone marrow lesions (BMLs), using a meta-analysis of randomized controlled trials (RCTs). Methods Literature databases were searched for placebo-controlled RCTs of IVBPs for knee OA from inception, and included validated pain and function scales, BML size and incidence of adverse events. Efficacy was compared using standardized mean differences (SMD) and risk ratios (RR) with fixed-effect or random-effects models. Methodological quality was assessed using the Cochrane risk of bias tool, heterogeneity was assessed by I-2 statistics. Results We included 428 patients in four RCTs of 2-24 months duration; most patients (84%) received zoledronic acid (ZA). Risk of bias was low-moderate. IVBP had large effect sizes on pain within 3 months [SMD = -2.33 (95% CI: -3.02, -1.65)] mainly driven by neridronate (resulting in substantial heterogeneity, I-2 = 92%) with no effect for ZA alone. Differences in knee function were statistically significant at 3 months [SMD = -0.22 (-0.43, -0.01), I-2 = 0.2%]. Effect sizes for pain did not reach statistical significance at any other time point. IVBPs improved a semi-quantitative measure of BML size within 6 months [SMD = -0.52 (-0.89, -0.14), I-2 = 0%] but not at 12 months or two years. Adverse events [RR = 1.19 (1.00, 1.41) I-2 = 52%], occurred more frequently with IVBP. Conclusion ZA has no effect on knee pain, possibly a short-term effect on BML size and higher rates of adverse events. Neridronate may improve pain in the short term, but this is based on a single trial.
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Woolf AD, 2003, B WORLD HEALTH ORGAN, V81, P646
NR 30
TC 19
Z9 21
U1 0
U2 8
PU OXFORD UNIV PRESS
PI OXFORD
PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
SN 1462-0324
EI 1462-0332
J9 RHEUMATOLOGY
JI RHEUMATOLOGY
PD MAY 30
PY 2022
VL 61
IS 6
BP 2235
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WC Rheumatology
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PT J
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TI Musculoskeletal manifestations in a Portuguese cohort of 235 inflammatory bowel disease patients
SO ARP RHEUMATOLOGY
LA English
DT Article
DE Inflammatory bowel disease; Rheumatic manifestations
ID society classification criteria; peripheral spondyloarthritis; prevalence
AB Background: Musculoskeletal symptoms represent the most common extraintestinal manifestations of inflammatory bowel disease (IBD) and a major cause of impaired quality of life in these patients. Spondyloarthritis (SpA) is classically associated with IBD, but other rheumatic manifestations may occur. Objective: To characterize musculoskeletal symptoms and rheumatic diseases in an IBD cohort. Methods: Retrospective monocentric descriptive study including all the patients with IBD consecutively referred from Gastroenterology to the Reumatology Department (from January of 2013 to April of 2021) in a Portuguese tertiary university hospital. Demographic and clinical data were collected and musculoskeletal symptoms and rheumatic diseases diagnosed in the Rheumatology outpatient center were registered. Results: A total of 235 patients were included: 177 (75.3%) with Crohn ' s disease (CD) and 58 (24.7%) with ulcerative colitis. Musculoskeletal symptoms were observed in 142 (60.4%) patients and 105 (44.7%) had some rheumatic condition. Regarding spondyloarthritis, 46 (19.6%) patients fulfilled ASAS (Assessment of SpondyloArthritis international Society) criteria for axial SpA and 5 (2.1%) for peripheral SpA. Osteoarthritis (n=70, 29.8%) and osteoporosis (n=33, 14%) were the most frequent non-inflammatory rheumatic conditions observed, mostly previously undiagnosed. No significant differences were observed between CD and UC. Conclusion: Rheumatic conditions are frequent in IBD patients and are not limited to SpA features. They remain mostly undiagnosed and the collaboration between gastroenterologists and rheumatologists is important for their best management.
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CR Al-Jarallah K, 2013, INT J RHEUM DIS, V16, P134, DOI 10.1111/j.1756-185X.2012.01811.x
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PT J
AU Wang, YQ
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Chen, Silong
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TI Long Non-Coding RNA GAS5 in Age-Related Diseases
SO CURRENT MEDICINAL CHEMISTRY
LA English
DT Review
DE lncRNAs; GAS5; age-related diseases; atherosclerosis; type 2 diabetes mellitus; cancer
ID lncrna gas5; cell carcinoma; apoptosis; expression; osteoarthritis; polarization; osteoporosis; chondrocytes; inflammation; resistance
AB Aging refers to a natural process and a universal phenomenon in all cells,

tissues, organs, and the whole organism. Long non-coding RNAs (lncRNAs) are non-coding RNAs with a length of 200 nucleotides. LncRNA growth arrest-specific 5 (lncRNA GAS5) is often down-regulated in cancer. The accumulation of lncRNA GAS5 has been found to be able to inhibit cancer growth, invasion, and metastasis while enhancing the sensitivity of cells to chemotherapy drugs. LncRNA GAS5 can be a signaling protein, which is specifically transcribed under different triggering conditions. Subsequently, it is involved in signal transmission in numerous pathways as a signal node. LncRNA GAS5, with a close relationship to multiple miRNAs, was suggested to be involved in the signaling pathway under three action modes (i.e., signal, bait, and guidance). LncRNA GAS5 was found to be involved in different age-related diseases (e.g., rheumatoid arthritis, type 2 diabetes, atherosclerosis, osteoarthritis, osteoporosis, multiple sclerosis, cancer, etc.). This study mainly summarized the regulatory effect exerted by lncRNA GAS5 on age-related diseases.

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PA EXECUTIVE STE Y-2, PO BOX 7917, SAIF ZONE, 1200 BR SHARJAH, U ARAB EMIRATES
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WC Biochemistry & Molecular Biology; Chemistry, Medicinal; Pharmacology & Pharmacy
SC Biochemistry & Molecular Biology; Pharmacology & Pharmacy
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PT J
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TI Association between acetabular dysplasia and sagittal spino-pelvic alignment in a population-based cohort in Japan
SO SCIENTIFIC REPORTS
LA English
DT Article
ID spinopelvic alignment; hip; osteoarthritis
AB The relationship between acetabular dysplasia and spino-pelvic alignment remains unclear. The aim of this study was to clarify the association between acetabular dysplasia and spino-pelvic alignment, based on a large-scale population-based cohort in Japan. From the third survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study, 1,481 participants (491 men and 990 women; mean age, 65.3 years) were analyzed. Center-edge (CE) angle and spino-pelvic parameters (lumbar lordosis, LL; sacral slope, SS; pelvic tilt, PT; pelvic incidence, PI) were measured radiographically. Acetabular dysplasia was defined as a CE angle < 20 degrees, and associations between acetabular dysplasia and spino-pelvic parameters were assessed. The group with acetabular dysplasia had significantly higher age, higher percentage of female, higher SS and higher PI than the group without acetabular dysplasia in a univariate analysis. On the other hand, acetabular dysplasia was not significantly associated with spino-pelvic parameters in a multiple logistic regression analysis that include age, sex, SS and PI as explanatory variables; however, PI demonstrated a positive odds ratio (odds ratio, 1.02; 95% CI 1.00-1.04). In conclusion, acetabular dysplasia was not significantly associated with spino-pelvic parameters, but higher PI may be an associated factor for acetabular dysplasia.
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NR 20
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PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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TI Subchondral insufficiency fracture of the knee: review of current concepts and radiological differential diagnoses
SO JAPANESE JOURNAL OF RADIOLOGY
LA English
DT Review
DE Subchondral insufficiency fracture; Spontaneous osteonecrosis of the knee; Subchondral plate; Meniscal root tear
ID bone-marrow edema; juvenile osteochondritis-dissecans; medial femoral condyle; spontaneous osteonecrosis; parathyroid-hormone; transient osteoporosis; hip osteoarthritis; symptomatic knee; mineral density; posterior root
AB Subchondral insufficiency fracture of the knee (SIFK) is a common cause of knee joint pain in older adults. SIFK is a type of stress fracture that occurs when repetitive and excessive stress is applied to the subchondral bone. If the fracture does not heal, the lesion develops into osteonecrosis and results in osteochondral collapse, requiring surgical management. Because of these clinical features, SIFK was initially termed "spontaneous osteonecrosis of the knee (SONK)" in the pre-MRI era. SONK is now categorized as an advanced SIFK lesion in the spectrum of this disease, and some authors believe the term "SONK" is a misnomer. MRI plays a significant role in the early diagnosis of SIFK. A subchondral T2 hypointense line of the affected condyle with extended bone marrow edema-like signal intensity are characteristic findings on MRI. The large lesion size and the presence of osteochondral collapse on imaging are associated with an increased risk of osteoarthritis. However, bone marrow edema-like signal intensity and osteochondral collapse alone are not specific to SIFK, and other osteochondral lesions, including avascular necrosis, osteochondral dissecans, and osteoarthritis should be considered. Chondral lesions and meniscal abnormalities, including posterior root tears, are also found in many patients with SIFK, and they are considered to be related to the development of SIFK. We review the clinical and imaging findings, including the anatomy and terminology history of SIFK, as well as its differential diagnoses. Radiologists should be familiar with these imaging features and clinical presentations for appropriate management.
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TI A Novel Osteoporosis Screening Protocol to Identify Orthopedic Surgery Patients for Preoperative Bone Health Optimization
SO GERIATRIC ORTHOPAEDIC SURGERY & REHABILITATION
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DE osteoporosis; bone health screening; bone health optimization; bone mineral density; adult reconstructive surgery; metabolic bone disorders; fragility fractures; spine surgery
ID total hip-arthroplasty; periprosthetic fractures epidemiology; total joint arthroplasty; mineral density; bisphosphonates; mortality; osteoarthritis; prevalence; women
AB Introduction: Osteoporosis is highly prevalent in elective orthopedic surgery. While preoperative bone health optimization decreases osteoporosis-related complications, there is an unmet need to establish who may benefit from preoperative dual-energy x-ray absorptiometry (DXA). This study assesses a novel, simple screening protocol to identify orthopedic surgical patients for preoperative DXA. Materials/Methods: This retrospective cohort study included 628 patients undergoing total knee, hip, or shoulder arthroplasty or thoracolumbar spine fusion.

Inclusion criteria were >= 40 years undergoing primary elective surgery. Screening criteria defining who should obtain DXA due to high osteoporosis risk included: female A.5, male >= 70 fracture history when >= 50 years, or FRAX major osteoporotic fracture risk (without bone mineral density [BMD]-adjustments) >= 8.4%. Osteoporosis was defined by World Health Organization criteria [T-score <= -2.5], clinical National Osteoporosis Foundation (NOF) criteria [T-score <= -2.5, elevated BMD-adjusted FRAX risk, or prior hip/spine fracture], and modified clinical criteria [NOF criteria simplified to include any non-traumatic prior fracture and FRAX without BMD]. Results: The study included 100 TKAs, 100 THAs, 251 TSAs, and 177 spine fusions, average age 65.6 +/- 9.8. DXA was available for 209 patients. Screening criteria recommending DXA was met by 362 patients. For those with DXA, screening sensitivity was .96 (CI: .78 to .99) and specificity was .19 (CI: .14 to .25) for identifying T-score osteoporosis. Similar sensitivity of .99 (CI: .91 to .99) and specificity of .61 (CI: .56 to .66) were found for modified clinical osteoporosis. For modified clinical osteoporosis, 192 patients with osteoporosis met criteria (true pos.), 1 patient with osteoporosis did not meet criteria (false neg.), 170 patients without osteoporosis met criteria (false pos.), and 265 patients without osteoporosis did not meet criteria (true neg.). Discussion/Conclusion: A simple screening protocol identifies orthopedic surgical candidates at risk of T-score or clinical osteoporosis for preoperative DXA with high sensitivity.
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TI Impact of Cadmium Mediated by Tobacco Use in Musculoskeletal Diseases
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DT Article
DE Tobacco use; Cadmium; Osteoarthritis; Osteoporosis; Rheumatoid arthritis; Oxidative stress
ID scalp hair samples; rheumatoid-arthritis; cigarette-smoking; chronic exposure; toxic metals; knee; lead; association; mechanism; level
AB Tobacco use has a negative impact on health due to its relationship with the development of high-mortality diseases, such as pulmonary cancer. However, the effect of cadmium (Cd), present in tobacco smoke, on the development of joint diseases has been scarcely studied. The objective of this review is to discuss the evidence regarding the mechanisms by which Cd exposure, through tobacco smoke, may lead to the development of osteoarthritis (OA), osteoporosis (OP), and rheumatoid arthritis (RA). There's evidence suggesting a string association between moderate to severe OA development and tobacco use, and that a higher blood concentration of Cd can trigger oxidative stress (OS) and inflammation, favoring cartilage loss. At the bone level, the Cd that is inhaled through tobacco smoke affects bone mineral density, resulting in OP mediated by a decrease in the antioxidant enzymes, which favors the bone resorption process. In RA, tobacco use promotes the citrullination process through Cd exposure, as well as an increase in OS and inflammation. Understanding how tobacco use can increase the damage at the articular level mediated by a toxic metal, i.e., Cd, is important. Finally, proposing prevention, control, and treatment strategies for frequently disabling diseases, such as OA, OP, and RA to reduce its prevalence in the population.
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AU Salo, S
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TI Association between severe lumbar disc degeneration and self-reported occupational physical loading
SO JOURNAL OF OCCUPATIONAL HEALTH
LA English
DT Article
DE intervertebral disc degeneration; lumbosacral region; occupational exposure;

postmenopause; spine; women's health
ID low-back-pain; resonance-imaging changes; risk-factors; spine; osteoarthritis; epidemiology; mri
AB Objectives Occupational physical loading has been reported to be associated with intervertebral disc degeneration. However, previous literature reports inconsistent results for different vertebral levels. The aim of our study was to investigate the association between lumbar disc degeneration (LDD) at different vertebral levels and the self-reported physical loading of occupation. Methods The study population consisted of 1,022 postmenopausal women and was based on the prospective Kuopio Osteoporosis Risk Factor and Prevention (OSTPRE) study cohort. The severity of LDD was graded from T2-weighted MRI images using the five-grade Pfirrmann classification. Five intervertebral levels (L1-L2 to L5-S1) were studied (total 5110 discs). The self-rated occupational physical loading contained four groups: sedentary, light, moderate, and heavy. Results The heavy occupational physical loading group had higher odds for severe LDD at the L5-S1 vertebral level (OR 1.86, 95% CI: 1.19-2.92, p = .006) in comparison with the sedentary work group. A clear trend of increasing disc degeneration with heavier occupational loading was also observed at the L5-S1 level. Age, smoking, and higher body mass index (BMI) were associated with more severe LDD. Leisure-time physical activity at the age of 11-17 years was associated with less severe LDD. Controlling for confounding factors did not alter the results. Conclusions There appears to be an association between occupational physical loading and severe disc degeneration at the lower lumbar spine in postmenopausal women. Individuals in occupations with heavy physical loading may have an increased risk for work-related disability due to more severe disc degeneration.
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TI Activation and Function of NLRP3 Inflammasome in Bone and Joint-Related Diseases
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
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DT Review
DE interleukin-1; inflammasome; NLRP3; caspase-1; rheumatoid arthritis; osteoarthritis; gout; osteoporosis; periodontal disease; aging; bone and joint diseases
ID collagen-induced arthritis; rheumatoid-arthritis; nalp3 inflammasome; aggregatibacter-actinomycetemcomitans; osteoclast differentiation; aim2 inflammasome; gouty-arthritis; tnf-alpha; k+ efflux; interleukin-1

AB Inflammation is a pivotal response to a variety of stimuli, and inflammatory molecules such as cytokines have central roles in the pathogenesis of various diseases, including bone and joint diseases. Proinflammatory cytokines are mainly produced by immune cells and mediate inflammatory and innate immune responses. Additionally, proinflammatory cytokines accelerate bone resorption and cartilage destruction, resulting in the destruction of bone and joint tissues. Thus, proinflammatory cytokines are involved in regulating the pathogenesis of bone and joint diseases. Interleukin (IL)-1 is a representative inflammatory cytokine that strongly promotes bone and cartilage destruction, and elucidating the regulation of IL-1 will advance our understanding of the onset and progression of bone and joint diseases. IL-1 has two isoforms, IL-1 alpha and IL-1 beta. Both isoforms signal through the same IL-1 receptor type 1, but the activation mechanisms are completely different. In particular, IL-1 beta is tightly regulated by protein complexes termed inflammasomes. Recent research using innovative technologies has led to a series of discoveries about inflammasomes. This review highlights the current understanding of the activation and function of the NLRP3 (NOD-like receptor family, pyrin domain-containing 3) inflammasome in bone and joint diseases.
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FU JSPS [JP19H03824, JP22H03261]; Takeda Science Foundation
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TI Physically active primary care doctors are more likely to offer exercise counselling to patients with cardiovascular diseases: a cross-sectional study
SO BMC PRIMARY CARE
LA English
DT Article
DE Physical activity; Primary care doctors; Counselling; Chronic disease; Cardiovascular diseases
ID medical-students; health-promotion; activity habits; physicians; behaviors; attitudes; women
AB Background Regular physical activity had been shown to reduce morbidity and mortality from chronic diseases such as cardiovascular diseases, hypertension, type 2 diabetes mellitus, dyslipidaemia, obesity/metabolic syndrome, osteoarthritis, osteoporosis, bronchial asthma and chronic obstructive pulmonary disease. Research had shown that physically active doctors were more likely to offer exercise counselling to patients. However, few studies looked into this association with counselling practices to patients with specific chronic diseases. This study aims to determine the association between physical activity levels of primary care doctors (PCDs) in Malaysian private practice with physical activity counselling to patients with chronic diseases. Methodology A cross-sectional study involving PCDs in private practice in 3 states was done. Participants were recruited from

members of the Malaysian Academy of Family Physicians and attendees of a conference. A self-administered questionnaire obtained information on sociodemography, initiation of exercise counselling to patients with chronic diseases as well as physical activity levels using the International Physical Activity Questionnaire (IPAQ). Results The response rate was 32.3% (272/842). 47.1% of the respondents were post-graduate holders. 50% of participants had a moderate level of physical activity and 24.3% a high level. Most respondents answered 'always' or 'often' for initiation of exercise counselling to patients with cardiovascular diseases (59.9%), hypertension (72.8%), type 2 diabetes mellitus (78.6%), obesity/metabolic syndrome (86.4%), dyslipidaemia (81.6%), osteoarthritis/osteoporosis (41.9%) and bronchial asthma/COPD (29.5%). PCDs being physically active and non-smokers were associated with a higher initiation of exercise counselling to patients with cardiovascular diseases. Doctors with post-graduate degrees were more likely to offer exercise counselling to hypertensive patients. Conclusion The association between PCDs' physical activity levels and their physical activity counselling varies between different types of chronic diseases. Primary care doctors with higher physical activity levels were more likely to initiate physical activity counselling in patients with cardiovascular disease during chronic disease follow up visits.
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TI Emerging Potential Therapeutic Targets of Ferroptosis in Skeletal Diseases
SO OXIDATIVE MEDICINE AND CELLULAR LONGEVITY
LA English
DT Review
ID hydroperoxide glutathione-peroxidase; dependent cell-death; spinal-cord-injury; rheumatoid-arthritis; lipid-peroxidation; iron; activation; protects; deficiency; metabolism
AB Ferroptosis is a new programmed cell death characterized by the accumulation of lipid peroxidation mediated by iron and inflammation. Since the transcentury realization of ferroptosis as an iron-dependent modality of nonapoptotic cell death in 2012, there has been growing interest in the function of ferroptosis and its relationship to clinical diseases. Recent studies have shown that ferroptosis is associated with multiple diseases, including degenerative diseases, ischemia

reperfusion injury, cardiovascular disease, and cancer. Cell death induced by ferroptosis has also been related to several skeletal diseases, such as inflammatory arthritis, osteoporosis, and osteoarthritis. Research on ferroptosis can clarify the pathogenesis of skeletal diseases and provide a novel therapeutic target for its treatment. In this review, we summarize current information about the molecular mechanism of ferroptosis and describe its emerging role and therapeutic potential in skeletal diseases.
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TI Regenerating zebrafish scales express a subset of evolutionary conserved genes involved in human skeletal disease
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DE Bone; Collagen; Osteoblast; Musculoskeletal disease; Zebrafish; Scales; Transcriptomics; Extracellular matrix; Ossification
ID osteoporosis-like phenotype; teleost fish; targeted disruption; collagen fibrils; bone metabolism; elasmoid scales; osteopontin; model; mineralization; osteoarthritis
AB Background Scales are mineralised exoskeletal structures that are part of the dermal skeleton. Scales have been mostly lost during evolution of terrestrial vertebrates whilst bony fish have retained a mineralised dermal skeleton in the form of fin rays and scales. Each scale is a mineralised collagen plate that is decorated with both matrix-building and resorbing cells. When removed, an ontogenetic scale is quickly replaced following differentiation of the scale pocket-lining cells that regenerate a scale. Processes promoting de novo matrix formation and mineralisation initiated during scale regeneration are poorly understood. Therefore, we performed transcriptomic analysis to determine gene networks and their pathways involved in dermal scale regeneration. Results We defined the transcriptomic profiles of ontogenetic and regenerating scales of zebrafish and identified 604 differentially expressed genes (DEGs). These were enriched for extracellular matrix, ossification, and cell adhesion pathways, but not in enamel or dentin formation processes indicating that scales are reminiscent to bone. Hypergeometric tests involving monogenetic skeletal disorders showed that DEGs were strongly enriched for human orthologues that are mutated in low bone mass and abnormal bone mineralisation diseases ($P < 2x\ 10(-3)$). The DEGs were also enriched for human orthologues associated with polygenetic skeletal traits, including height ($P < 6x\ 10(-4)$), and estimated bone mineral density (eBMD, $P < 2x\ 10(-5)$). Zebrafish mutants of two human orthologues that were robustly associated with height (COL11A2, $P=6x\ 10(-24)$) or eBMD (SPP1, $P=6x\ 10(-20)$) showed both exo- and endo- skeletal abnormalities as predicted by our genetic association analyses; col11a2(Y228X/Y228X) mutants showed exoskeletal and endoskeletal features consistent with abnormal growth, whereas spp1(P160X/P160X) mutants predominantly showed mineralisation defects. Conclusion We show that scales have a strong osteogenic expression profile comparable to other elements of the dermal skeleton, enriched in genes that favour collagen matrix growth. Despite the many differences between scale and endoskeletal developmental processes, we also show that zebrafish scales express an evolutionarily conserved sub-population

of genes that are relevant to human skeletal disease.
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DE Angelica gigas; In Vivo Bioactivities; Pyranocoumarins; Decursin; Decursinol; Review
ID induced memory impairment; nf-kappa-b/rel; decursinol angelate; korean angelica; active compound; ethanol extract; nakai extract; brain-injury; activation; scopolamine
AB Angelica gigas Nakai (AGN) root is a medicinal herbal widely used in traditional medicine in Korea. AGN root ethanolic extract dietary supplements are marketed in

the United States for memory health and pain management. We comprehensively reviewed the anticancer, analgesic, pro-memory and other bio-activities of AGN extract and its signature phytochemicals decursin, decursinol angelate, and decursinol a decade ago in 2012 and updated their anticancer activities in 2015. In the last decade, significant progress has been made for understanding the pharmacokinetics (PK) and metabolism of these compounds in animal models and single dose human PK studies have been published by us and others. In addition to increased knowledge of the known bioactivities, new bioactivities with potential novel health benefits have been reported in animal models of cerebral ischemia/stroke, anxiety, sleep disorder, epilepsy, inflammatory bowel disease, sepsis, metabolic disorders, osteoporosis, osteoarthritis, and even male infertility. Herein, we will update PK and metabolism of pyranocoumarins, review in vivo bioactivities from animal models and human studies, and critically appraise the relevant active compounds, the cellular and molecular pharmacodynamic targets, and pertinent mechanisms of action. Knowledge gaps include whether human pyranocoumarin PK metrics are AGN dose dependent and subjected to metabolic ceiling, or metabolic adaptation after repeated use. Critical clinical translation challenges include sourcing of AGN extracts, product consistency and quality control, and AGN dose optimization for different health conditions and disease indications. Future research directions are articulated to fill knowledge gaps and address these challenges.
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TI Osteogenic capacity of mesenchymal stem cells from patients with osteoporotic hip fractures in vivo
SO CONNECTIVE TISSUE RESEARCH
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DT Article
DE Bone formation; osteoblasts; mesenchymal stem cells; cell senescence; bone nodules; in vivo
AB Purpose: Human mesenchymal stem cells (MSCs) have the ability to differentiate into bone-forming osteoblasts. The aim of this study was to elucidate if MSCs from patients with OP show a senescent phenotype and explore their bone-forming ability in vivo. Materials and methods: MSCs from patients with OP and controls with osteoarthritis (OA) were implanted into the subcutaneous tissue of immunodeficient mice for histological analysis and expression of human genes by RT-PCR. The expression of senescence-associated phenotype (SASP) genes, as well as p16, p21, and galactosidase, was studied in cultures of MSCs. Results: In vivo bone formation was evaluated in 103 implants (47 OP, 56 OA). New bone was observed in 45% of the implants with OP cells and 46% of those with OA cells ($p = 0.99$). The expression of several bone-related genes (collagen, osteocalcin, alkaline phosphatase, sialoprotein) was also similar in both groups. There were no differences between groups in SASP gene expression, p16, and p21 expression, or in senescence-associated galactosidase activity. Conclusion. Senescence markers

and the osteogenic capacity in vivo of MSCs from patients with OP are not inferior to that of cells from controls of similar age with OA. This supports the interest of future studies to evaluate the potential use of autologous MSCs from OP patients in bone regeneration procedures.
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TI Patterns of the physical, cognitive, and mental health status of older individuals in a real-life primary care setting and differences in coping styles
SO FRONTIERS IN MEDICINE
LA English
DT Article
DE complex patients; clusters; physical; cognitive and mental health status; comorbidities; copying styles; primary care setting
ID frailty; impairment; adults; risk; resilience; disease; multimorbidity; validity; scale; recommendations
AB BackgroundPhysical frailty and cognitive decline are two major consequences of aging and are often in older individuals, especially in those with multimorbidity. These two disorders are known to usually coexist with each other, increasing the risk of each disorder for poor health outcomes. Mental health disorders, anxiety and depression, are common in older people with multimorbidity, in particular those with functional or sensory deficits, and frailty. PurposeThe aim of this study was to show how physical frailty, cognitive impairments and mental disorders, cluster in the real life setting of older primary care (PC) patients, and how these clusters relate to age, comorbidities, stressful events, and coping strategies. Knowing that, could improve risk stratification of older individuals and guide the action plans. MethodsParticipants were older individuals (>= 60, N = 263), attenders of PC, independent of care of others, and not suffering from dementia. For screening participants on physical frailty, cognitive impairment, and mental disorders, we used Fried's phenotype model, the Mini-Mental State Examination (MMSE), the Geriatric Anxiety Scale (GAS), and the Geriatric Depression Scale (GDS). For testing participants on coping styles, we used the 14-scale Brief-Coping with Problems Experienced (Brief-COPE) questionnaire. To identify clusters, we used the algorithm fuzzy k-means. To further describe the clusters, we examined differences in age, gender, number of chronic diseases and medications prescribed, some diagnoses of chronic diseases, the number of life events, body mass index, renal function, expressed as the glomerular filtration rate, and coping styles. ResultsThe most appropriate cluster solution was the one with three clusters, that were termed as: functional (FUN; N = 139), with predominant frailty or dysfunctional (DFUN; N = 81), and with predominant cognitive impairments or cognitively impaired (COG-IMP; N = 43). Participants in two pathologic clusters, DFUN and COG-IMP, were in average older and had more somatic diseases, compared to participants in cluster FUN. Significant differences between the clusters were found in diagnoses of osteoporosis, osteoarthritis, anxiety/depression, cerebrovascular disease, and periphery artery disease. Participants in cluster FUN expressed mostly positive reframing coping style. Participants in two pathological clusters were represented

with negative coping strategies. Religion and self-blame were coping mechanisms specific only for cluster DFUN; self-distraction only for cluster COG-IMP; and these two latter clusters shared the mechanisms of behavioral disengagement and denial. ConclusionThe research approach presented in this study may help PC providers in risk stratification of older individuals and in getting insights into behavioral and coping strategies of patients with similar comorbidity patterns and functional disorders, which may guide them in preparing prevention and care plans. By providing some insights into the common mechanisms and pathways of clustering frailty, cognitive impairments and mental disorders, this research approach is useful for creating new hypotheses and in accelerating geriatric research.
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TI Autophagy: An important target for natural products in the treatment of bone metabolic diseases
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE autophagy; natural products; bone metabolism; osteoporosis; rheumatoid

arthritis; osteoarthritis; fracture nonunion/delayed union
ID chaperone-mediated autophagy; mesenchymal stem-cells; nf-kappa-b; oxidative stress; rheumatoid-arthritis; activating autophagy; mitochondrial dysfunction; induced apoptosis; osteogenic differentiation; stromal cells
AB Bone homeostasis depends on a precise dynamic balance between bone resorption and bone formation, involving a series of complex and highly regulated steps. Any imbalance in this process can cause disturbances in bone metabolism and lead to the development of many associated bone diseases. Autophagy, one of the fundamental pathways for the degradation and recycling of proteins and organelles, is a fundamental process that regulates cellular and organismal homeostasis. Importantly, basic levels of autophagy are present in all types of bone-associated cells. Due to the cyclic nature of autophagy and the ongoing bone metabolism processes, autophagy is considered a new participant in bone maintenance. Novel therapeutic targets have emerged as a result of new mechanisms, and bone metabolism can be controlled by interfering with autophagy by focusing on certain regulatory molecules in autophagy. In parallel, several studies have reported that various natural products exhibit a good potential to mediate autophagy for the treatment of metabolic bone diseases. Therefore, we briefly described the process of autophagy, emphasizing its function in different cell types involved in bone development and metabolism (including bone marrow mesenchymal stem cells, osteoblasts, osteocytes, chondrocytes, and osteoclasts), and also summarized research advances in natural product-mediated autophagy for the treatment of metabolic bone disease caused by dysfunction of these cells (including osteoporosis, rheumatoid joints, osteoarthritis, fracture nonunion/delayed union). The objective of the study was to identify the function that autophagy serves in metabolic bone disease and the effects, potential, and challenges of natural products for the treatment of these diseases by targeting autophagy.
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TI Impact of Icariin and its derivatives on inflammatory diseases and relevant signaling pathways
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Review
DE Icariin; Inflammatory diseases; MAPK; NF-kappa B; GR; Nrf2
ID modulating hpa function; glucocorticoid-receptor; parkinsons-disease; reperfusion injury; mapk pathways; inhibition; stress; activation; involvement; model
AB Herba Epimedii is a famous herb collected from China and Korea. It has been used for impotency, osteoporosis, and amnestic treatment for thousands of years. Icariin, a typical flavonoid compound isolated from Herba Epimedii, was reported as a potential anti-inflammatory drug. Icariside and icaritin are the two metabolites of icariin. Icariin and its metabolites have been used to treat a wide range of inflammatory diseases, such as atherosclerosis, Alzheimer's disease, depression, osteoarthritis, and asthma. They exert powerful suppression of proinflammatory signaling, such as NF-kappa B and MAPKs. More importantly, they can upregulate anti-inflammatory signaling, such as GR and Nrf2. In this study, we review the therapeutic effects and mechanisms of icariin and its metabolites in inflammatory diseases and provide novel insights into these potential anti-inflammatory drugs.
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AU Li, X
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AF Li, Xiang
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TI Overall adjustment acupuncture improves osteoporosis and exerts an endocrine-modulating effect in ovariectomized rats
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Article
DE overall adjustment acupuncture; postmenopausal osteoporosis; estradiol; hypothalamus-pituitary-adrenal axis; ovariectomy
ID aromatase; bone; estrogen; androgens; aromatization; expression; women
AB BackgroundAcupuncture is a widely practiced, convenient, and safe treatment modality within complementary and integrative medicine. Increasing studies have revealed the efficacy of acupuncture for the treatment of osteoporosis in both human and non-human subjects. The aim of the present study was to assess the improvement of osteoporosis after overall adjustment acupuncture (OA) as well as its endocrine-modulating effect in an ovariectomized rat model. MethodsIn total, 32 female Sprague-Dawley (SD) rats were randomly divided into the sham, model, ovariectomy+estrogen (OVX+E), and OVX+OA (OVX+A) groups with eight rats in each group. The postmenopausal osteoporosis (PMOP) rat model was induced by bilateral ovariectomy. At 12 weeks after surgery, rats in the OVX+E group received estradiol (0.2 mg/kg/i.g./qod) for 12 weeks, and rats in the OVX+A group were treated with acupuncture at Zusanli (ST36), Shenshu (BL23), and Dazhu (BL11) points (qod) for 12 weeks. At the end of the treatment, all rats were sacrificed, and the body weight, uterus index, bone mineral density (BMD), bone mineral content (BMC), bone trabeculae structural parameters, femoral biomechanical properties, femoral histomorphology, and several hormone levels were examined. ResultsIn OVX rats, OA abrogated the body weight gain and improved osteoporosis in terms of BMD, BMC, bone trabeculae structural parameters, bone strength, and bone tissue histomorphology. Moreover, OA modulated the serum levels of estradiol, corticotropin releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and corticosterone (CORT). ConclusionsOA improves osteoporosis and exerts an endocrine-modulating effect in ovariectomized rats.
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NR 57
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Z9 18
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J9 FRONT ENDOCRINOL
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SC Endocrinology & Metabolism
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AU Lin, L
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AF Lin, Liu
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TI Causal relationship between osteoporosis and osteoarthritis: A two-sample Mendelian randomized study
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Article
DE osteoporosis; osteoarthritis; Mendelian randomization; genetics; causal relationship
ID high bone mass; increased prevalence; articular-cartilage; hip osteoarthritis; subchondral bone; mineral density; knee; men; epidemiology; risk
AB IntroductionAt present, clinical studies have confirmed that osteoporosis (OP) has an inverse relationship with osteoarthritis (OA), but it has not been proven from the point of view of genetics, so our study hopes to clarify the potential effect of OP on OA at the level of gene prediction through two-sample Mendelian randomization (MR) analysis. MethodsA two-sample MR was adopted to research the causal relationship of OP with OA (including total OA, knee OA and hip OA). All data come from a public shared database. Such traditional methods as simple and weighted models, inverse variance weighted, weighted median, and Mendelian Randomization (MR-Egger) regression were employed to assess the causal effect of

OP on OA. We used the Pleiotrophy RESidual Sum and Outlier (MR-PRESSO) method and MR-Egger method to study sensitivity. The leave-one-out test is used to determine the influence of outliers. The heterogeneity was calculated by using Cochran Q statistics and MR-Egger regression in the inverse variance-weighted (IVW) method. P > 0.05 indicates that there is a large heterogeneity. MR-Robust Adjustment Profile Score (RAPS) is stable to both systematic and specific multiplicity, so we used MR-RAPS as a supplementary method to verify the results of IVW. ResultsAccording to the results of IVW, we found that there was a causal relationship between OP and total OA, and OP reduced the incidence of total OA (beta=-0.285, OR=0.751, P value< 0.016). The MR estimation of the causal effect of OP on knee OA suggested that the genetic prediction of OP was negatively correlated with knee osteoarthritis (KOA) (IVW: beta=-6.11, OR=0.002, P value< 0.016). The IVW results suggested that OP was causally related to hip OA, and OP had a protective effect on hip OA (beta=-5.48, OR=4.15e-3, P value= 3.99e-3). Except for heterogeneity in the analysis of OP and knee OA, there was no horizontal pleiotropy or heterogeneity in the other analyses. ConclusionWe explored the causal relationship between OP and OA through a two-sample MR analysis and found that OP can reduce the incidence of OA (including knee OA and hip OA).
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Lian, Qiangqiang
Wang, Yudan
Hou, Xiaoli
Tian, Faming
TI Parathyroid Hormone (1-34) Attenuates Cartilage Degradation and Preserves Subchondral Bone Micro-architecture in Rats with Patella Baja-Induced-Patellofemoral Joint Osteoarthritis
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE PTH1-34; Patella femoral osteoarthritis; Patella baja; Animal model
ID total knee arthroplasty; progression; prevalence; association; morphology;

pth(1-34)
AB Several studies have revealed that PTH1-34 may possess the potential for treating osteoarthritis (OA) and osteoporosis. However, no study has yet determined whether PTH1-34 can be used for the treatment of patella baja-induced patellofemoral joint OA (PFJOA). Thus, this study sought to assess the efficacy of PTH1-34 for the treatment of PFJOA in a rat model. Patella baja was induced in 3-month-old female Sprague-Dawley (SD) rats by patellar ligament shortening (PLS), after which the rats were randomly divided into three groups (n = 12): Sham, PLS, and PTH group (PTH + PLS, PTH1-34, 30 mu g/kg/d, 5 days per week for 10 weeks). Thereafter, radiographic imaging, macroscopic and microscopic analyses, immunohistochemistry, and microcomputed tomography (CT) analysis were performed. The appearance of PLS-induced PFJOA promoted obvious changes in the patellar position and structure in the PLS group, which were characterized by cartilage degeneration, subchondral bone microstructure deterioration, patella baja, and increasing patella length. However, these negative characteristics were markedly ameliorated by PTH1-34, which not only inhibited cartilage catabolism by decreasing MMP-13 and ADAMTS-4 but also enhanced anabolism by increasing Col-II and Aggrecan. Furthermore, the micro-CT results showed a marked improvement in subchondral bone microarchitecture. The findings presented herein demonstrated that early treatment with PTH1-34 could improve cartilage metabolism and subchondral bone health in this PFJOA model.
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TI "Osteomicrobiology": The Nexus Between Bone and Bugs
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ID chain fatty-acids; segmented filamentous bacteria; regulatory t-cells; gut microbiota; peripheral-blood; double-blind; th17 cells; intestinal microbiota; th17/treg cells; immune-system
AB A growing body of scientific evidence supports the notion that gut microbiota

plays a key role in the regulation of various physiological and pathological processes related to human health. Recent findings have now established that gut microbiota also contributes to the regulation of bone homeostasis. Studies on animal models have unraveled various underlying mechanisms responsible for gut microbiota-mediated bone regulation. Normal gut microbiota is thus required for the maintenance of bone homeostasis. However, dysbiosis of gut microbiota communities is reported to be associated with several bone-related ailments such as osteoporosis, rheumatoid arthritis, osteoarthritis, and periodontitis. Dietary interventions in the form of probiotics, prebiotics, synbiotics, and postbiotics have been reported in restoring the dysbiotic gut microbiota composition and thus could provide various health benefits to the host including bone health. These dietary interventions prevent bone loss through several mechanisms and thus could act as potential therapies for the treatment of bone pathologies. In the present review, we summarize the current knowledge of how gut microbiota and its derived microbial compounds are associated with bone metabolism and their roles in ameliorating bone health. In addition to this, we also highlight the role of various dietary supplements like probiotics, prebiotics, synbiotics, and postbiotics as promising microbiota targeted interventions with the clinical application for leveraging treatment modalities in various inflammatory bone pathologies.
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TI Safety and efficacy of probiotic supplementation in 8 types of inflammatory arthritis: A systematic review and meta-analysis of 34 randomized controlled trials
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE inflammatory bowel disease arthritis; juvenile idiopathic arthritis; osteoarthritis; osteoporosis and osteopenia; spondyloarthritis; probiotics
ID juvenile idiopathic arthritis; enthesitis-related arthritis; collagen-induced arthritis; rheumatoid-arthritis; double-blind; gut microbiota; synbiotic supplementation; knee osteoarthritis; chondroitin sulfate; oxidative stress
AB ObjectiveTo evaluate Safety and efficacy of probiotic supplementation in inflammatory arthritis.MethodsThe literature on the treatment of inflammatory arthritis with probiotics has been collected in databases such as CNKI, Pubmed, Cochrane library, Embase, etc. The search time is for them to build the database

until May 2022. The included literatures are randomized controlled trials (RCTs) of probiotics in the treatment of hyperuricemia and gout. The Cochrane risk assessment tool was used for quality evaluation, and the Rev Man5.3 software was used for meta-analysis.ResultsA total of 37 records were finally included, involving 34 RCTs and 8 types of autoimmune disease (Hyperuricemia and gout, Inflammatory bowel disease arthritis, juvenile idiopathic arthritis [JIA], Osteoarthritis [OA], Osteoporosis and Osteopenia, Psoriasis, rheumatoid arthritis (RA), Spondyloarthritis). RA involved 10 RCTs (632 participants) whose results showed that probiotic intervention reduced CRP. Psoriasis involved 4 RCTs (214 participants) whose results showed that probiotic intervention could reduce PASI scores. Spondyloarthritis involved 2 RCTs (197 participants) whose results showed that probiotic intervention improved symptoms in patients. Osteoporosis and Ostepenia involving 10 RCTs (1156 participants) showed that probiotic intervention improved bone mineral density in patients. Hyperuricemia and gout involving 4 RCTs (294 participants) showed that probiotic intervention improved serum uric acid in patients. OA involving 1 RCTs (433 participants) showed that probiotic intervention improved symptoms in patients. JIA involving 2 RCTs (72 participants) showed that probiotic intervention improved symptoms in patients. Inflammatory bowel disease arthritis involving 1 RCTs (120 participants) showed that probiotic intervention improved symptoms in patients. All of the above RCTs showed that probiotics did not increase the incidence of adverse events. Conclusion: Probiotic supplements may improve Hyperuricemia and gout, Inflammatory bowel disease arthritis, JIA, OA, Osteoporosis and Osteopenia, Psoriasis, RA, Spondyloarthritis. However, more randomized controlled trials are needed in the future to determine the efficacy and optimal dosing design of probiotics.Systematic Review Registrationhttps://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021286425, identifier CRD42021286425.

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DE Danio rerio; zebrafish; transgenic lines; bone matrix; probiotics; mineralization; BMP inhibitors; bone growth
ID skeletal mineralization; retinoic acid; nitric-oxide; pathway; regeneration; osteogenesis; microbiota; cyp26b1; density; medaka
AB Zebrafish larvae, especially gene-specific mutants and transgenic lines, are increasingly used to study vertebrate skeletal development and human pathologies such as osteoporosis, osteopetrosis and osteoarthritis. Probiotics have been recognized in recent years as a prophylactic treatment for various bone health issues in humans. Here, we present two new zebrafish transgenic lines containing the coding sequences for fluorescent proteins inserted into the endogenous genes for sp7 and col10a1a with larvae displaying fluorescence in developing osteoblasts and the bone extracellular matrix (mineralized or non-mineralized), respectively. Furthermore, we use these transgenic lines to show that exposure to two different probiotics, Bacillus subtilis and Lactococcus lactis, leads to an increase in osteoblast formation and bone matrix growth and mineralization. Gene expression analysis revealed the effect of the probiotics, particularly Bacillus subtilis, in modulating several skeletal development genes, such as runx2, sp7, spp1 and col10a1a, further supporting their ability to improve bone health. Bacillus subtilis was the more potent probiotic able to significantly reverse the inhibition of bone matrix formation when larvae were exposed to a BMP inhibitor (LDN212854).
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TI Chrysin Protects Against Titanium Particle-Induced Osteolysis by Attenuating Osteoclast Formation and Function by Inhibiting NF-κB and MAPK Signaling
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE osteoclast; chrysin; osteolysis; NF-?B; MAPK
ID rankl-induced osteoclastogenesis; receptor activator; bone-resorption; nuclear-factor; differentiation; cells; nfatc1
AB Bone homeostasis only exists when the physical function of osteoblast and osteoclast stays in the balance between bone formation and resorption. Bone resorption occurs when the two processes are uncoupled, shifting the balance in favour of bone resorption. Excessive activation of osteoclasts leads to a range of osteolytic bone diseases including osteoporosis, aseptic prosthesis loosening, rheumatoid arthritis, and osteoarthritis. Receptor activator of nuclear factor kappa-B ligand (RANKL) and its downstream signaling pathways are recognized as key mediators that drive the formation and activation of osteoclastic function. Hence, osteoclast formation and/or its function remain as dominant targets for research and development of agents reaching the treatment towards osteolytic diseases. Chrysin (CHR) is a flavonoid with a wide range of anti-inflammatory and anti-tumor effects. However, its effect on osteoclasts remains unknown. In this

study, we found the effects of CHR on inhibiting osteoclast differentiation which were assessed in terms of the number and size of TRAcP positive multinucleated osteoclasts (OCs). Further, the inhibitory effects of CHR on bone resorption and osteoclast fusion of pre-OC were assessed by hydroxyapatite resorption pit assay and F-actin belts staining; respectively. Western blotting analysis of RANKL-induced signaling pathways and immunofluorescence analysis for p65 nuclear translocation in response to RANKL-induced osteoclasts were used to analyze the mechanism of action of CHR affecting osteoclasts. Lastly, the murine calvarial osteolysis model revealed that CHR could protect against particle-induced bone destruction in vivo. Collectively, our data strongly suggested that CHR with its promising anti-tumor effects would also be a potential therapeutic agent for osteolytic diseases.
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TI Components of the Endocannabinoid System and Effects of Cannabinoids Against Bone Diseases: A Mini-Review
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE cannabinoids; bone loss; osteoporosis; osteoarthritis; bone tumor; bone fractures
ID receptor agonists; in-vitro; constituent; cb2; involvement; expression; growth; cells; mass; osteoarthritis
AB Background: The endocannabinoid system (ECS) is involved in multiple physiological processes, including appetite regulation, pain perception, motor function development, and immune response regulation. Cannabinoids have been approved for the clinical treatment of nausea and vomiting caused by cytostatic therapy or cancer chemotherapy, loss of appetite in HIV/AIDS-associated cachexia, refractory spasms induced by multiple sclerosis, chronic pain, and urinary incontinence.Methods: Check out the research on ECS and bone diseases in the past 20 years.Results: Many studies have demonstrated that endocannabinoids (eCBs) and cannabinoid receptors (CBRs) are expressed in bone and synovial tissues, playing important roles in bone metabolism. Preclinical studies using cannabis-based therapies in animal models have shown that cannabinoids (CBs) can alleviate the development of osteoarthritis (OA), prevent osteoporosis (OP), reduce cancer-induced osteolytic destruction, and improve fracture healing, highlighting the therapeutic potential of CBs for human bone diseases.Conclusions: The present review summarizes various components of the ECS in bone diseases and their potential as a therapeutic target.
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WC Pharmacology & Pharmacy
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TI Circulating methylation level of HTR2A is associated with inflammation and disease activity in rheumatoid arthritis
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Article
DE rheumatoid arthritis; circulating methylation level; HTR2A; inflammation; disease activity
ID serotonin receptor 2a; upstream enhancer; dna methylation; gene htr2a; schizophrenia; comorbidity; foxp3
AB ObjectivesHTR2A is previously identified as a susceptibility gene for rheumatoid arthritis (RA). In this study, we performed the association analysis between DNA methylation of HTR2A with RA within peripheral blood samples. MethodsWe enrolled peripheral blood samples from 235 patients with RA, 30 osteoarthritis (OA) patients, and 30 healthy controls. The DNA methylation levels of about 218 bp from chr13: 46898190 to chr13: 46897973 (GRCh38/hg38) around HTR2A cg15692052 from patients were analyzed by targeted methylation sequencing. ResultsWe measured methylation status for 7 CpGs in the promoter region of HTR2A and obseved overall methylation status are signficantly increased in RA compared with normal inviduals (FDR= 9.05 x 10(-5)). The average cg15692052 methylation levels (methylation score) showed a positive correlation with CRP (r=0.15, P=0.023). Compared with the OA group or HC group, the proportion of haplotypes CCCCCCC (FDR=0.02 and 2.81 x 10(-6)) is signficantly increased while TTTTTCC (FDR =0.01) and TTTTTTT(FDR =6.92 x 10(-3)) are significantly decreased in RA. We find methylation haplotypes combining with RF and CCP could signficantly enhance the performance of the diagnosing RA and its comorbidities (hypertension, interstitial lung disease, and osteoporosis), especially in interstitial lung disease. ConclusionsIn our study, we found signficant hypermethylation of promoter region of HTR2A which indicates the potential clinical diagnostic role in rheumatoid arthritis.

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TI Research hotspots and emerging trends of deep learning applications in orthopedics: A bibliometric and visualized study
SO FRONTIERS IN PUBLIC HEALTH
LA English
DT Article
DE orthopedics; deep learning; bibliometric analysis; research trends; Citespace
ID artificial-intelligence; classification; par
AB BackgroundAs a research hotspot, deep learning has been continuously combined with various research fields in medicine. Recently, there is a growing amount of deep learning-based researches in orthopedics. This bibliometric analysis aimed to identify the hotspots of deep learning applications in orthopedics in recent years and infer future research trends. MethodsWe screened global publication on deep learning applications in orthopedics by accessing the Web of Science Core Collection. The articles and reviews were collected without language and time restrictions. Citespace was applied to conduct the bibliometric analysis of the publications. ResultsA total of 822 articles and reviews were finally retrieved. The analysis showed that the application of deep learning in orthopedics has great prospects for development based on the annual publications. The most prolific country is the USA, followed by China. University of California San Francisco, and Skeletal Radiology are the most prolific institution and journal, respectively. LeCun Y is the most frequently cited author, and Nature has the highest impact factor in the cited journals. The current hot keywords are convolutional neural network, classification, segmentation, diagnosis, image, fracture, and osteoarthritis. The burst keywords are risk factor, identification, localization, and surgery. The timeline viewer showed two recent research directions for bone tumors and osteoporosis. ConclusionPublications on deep learning applications in orthopedics have increased in recent years, with the USA being the most prolific. The current research mainly focused on classifying, diagnosing and risk predicting in osteoarthritis and fractures from medical images. Future research directions may put emphasis on reducing intraoperative risk, predicting the occurrence of postoperative complications, screening for osteoporosis, and identification and classification of bone tumors from conventional imaging.
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TI Osteoarthritis of the knee- biochemical aspect of applied therapies: a review
SO BOSNIAN JOURNAL OF BASIC MEDICAL SCIENCES
LA English
DT Review
DE Knee osteoarthritis; prostaglandin; nonsteroidal anti-inflammatory drugs; symptomatic slow-acting drugs for OA; corticosteroids; bisphosphonates
ID glucosamine sulfate; chondroitin sulfate; european-society; economic-aspects; management; safety; drugs; hip; bisphosphonates; acetaminophen
AB The most prevalent form of arthritis is osteoarthritis (OA) of the knee, which is characterized by a degeneration of articular cartilage resulting in the development of osteophytes, or bone spurs. Main goals of OA treatment are to reduce pain, slow the disease progression, and improve joint function and the quality of life. The purpose of this study was to verify all the therapies recommended by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) from the biochemical point of view. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the synthesis of eicosanoids, whereas paracetamol prevents the production of prostaglandin (PG) by interacting with peroxidase (PDX) site of the prostaglandin H2 synthase complex. Tramadol is an opioid that has a dual

mechanism of action: It binds to the p-opioid receptor and it inhibits serotonin and adrenaline. Corticosteroids, which are also prescribed for OA pain, inhibit the activity of phospholipase A2 and block the synthesis of arachidonate-derived eicosanoids. Symptomatic slow-acting drugs for osteoarthritis (SYSADOA) are drugs that are well tolerated by patients and help to restore proteoglycan matrix of the cartilage. These drugs include compounds that naturally build articular cartilage:The articular cartilage, as well as the bone located around the cartilage, is destroyed as osteoarthritis progresses. Thus, bisphosphonates, commonly used in the treatment of osteoporosis, were evaluated as potential therapy. However, there is no official recommendation for their use in therapy. The aim of the study was to analyze the biochemical mechanisms of principal drugs used for the treatment of knee OA. Therefore, a narrative review summarizing the current knowledge regarding the applied therapies was prepared.
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NR 75
TC 16
Z9 20
U1 2
U2 11
PU ASSOC BASIC MEDICAL SCI FEDERATION BOSNIA & HERZEGOVINA SARAJEVO
PI CEKALUSA
PA UNIV SARAJEVO, MEDICAL FAC, CEKALUSA, SARAJEVO 90, BOSNIA & HERCEG
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JI Bosnian J. Basic Med. Sci.
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PT J
AU Tkacz, R
Larysz, D
Przybylski, R
Tkacz, M
Safranow, K
Tarnowski, M
AF Tkacz, Rafal
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Przybylski, Rafal
Tkacz, Marta
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TI Short-Term Functional Outcomes of Short Femoral Neck Stems Are the Same as

Those of Conventional Stems in Primary Total Hip Arthroplasty
SO INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH
LA English
DT Article
DE osteoarthritis; total hip arthroplasty; hip implant; short stem
ID metaanalysis; risk
AB (1) Background: In this study, two types of implants were compared-a conventional hip stem and a femoral neck prosthesis. (2) Methods: The femoral neck prosthesis study group included 21 patients, while the conventional hip stem control group was 40 patients. The first examination was the pre-op check, while the next ones were performed 6 weeks, 1 year, and 3 years after surgery. The Harris Hip Score (HHS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Hip Score (OHS), University of California at Los Angeles Activity Score (UCLA), and Visual Analog Scale EQ (VAS EQ) forms were completed at each clinical study visit. (3) Results: The HHS in the femoral neck prosthesis group and the conventional hip stem group 6 weeks after surgery was 68.8 +/- 16.47 and 67.6 +/- 8.92, respectively, and 1 year after surgery, this was 93 +/- 5.58 vs. 90.6 +/- 5.17, respectively. The OHS of the femoral neck prosthesis group was 34.8 points after 6 weeks, 45.5 points after 1 year, and 43.9 points after 3 years. The respective values in the conventional hip stem group were 35.5, 41.55, and 42.13 points. The WOMAC values for the femoral neck prosthesis group were 70.6, 92.7, and 86 points, respectively, while for the conventional hip stem group, they were 74, 88.1, and 86.1 points. The UCLA scores recorded in the conventional hip stem group ranged from 3.15 to 5.05 points, but a higher mean value of 5.33 points was obtained in the femoral neck prosthesis group. VAS EQ was equal to 84 points three years after the operation. (4) Conclusions: The study showed no significant differences in the functional scores of both groups, and the new type of cervical femoral stem could be the first choice in younger patients.
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NR 21
TC 1
Z9 1
U1 0
U2 0
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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PT J
AU Citla-Sridhar, D
Sidonio, RF
Ahuja, SP
AF Citla-Sridhar, Divyaswathi
Sidonio, Robert F., Jr.
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TI Bone health in haemophilia carriers and persons with von Willebrand disease: A large database analysis
SO HAEMOPHILIA
LA English
DT Article
DE bone health; fractures; haemophilia carriers; osteoarthritis; osteoporosis; risk factors; von Willebrand disease
ID mineral density; risk-factors; prevalence; osteoporosis; children; patient; death; males
AB Introduction: Persons with haemophilia(PWH) have been shown to have low bone mineral density likely the result of prolonged immobility, recurrent hemarthrosis, decreased weight bearing, lower physical activity level and obesity. Bone health has been poorly characterized in haemophilia carriers (HC) and persons with von Willebrand disease (PWvWD). Aim: To estimate the prevalence of osteoporosis, osteoarthritis and bone fractures in HC and PWvWD and identify risk factors for poor bone health. Methods: This is a retrospective study using a population level, commercial database - Explorys (IBM Watson Health, Cleveland, USA). We compared prevalence rates of osteoporosis, osteoarthritis and fractures among cases (HC or PWvWD) and controls (general population without an underlying bleeding disorder) from 1999 to 2020. Prevalence of common risk factors for poor bone health were compared among cases and controls. Results: Among 72,917,850 active persons in the database, we identified 940 women with the diagnosis of HC and 19,580 PWvWD. Among HC and PWvWD, prevalence of osteoporosis, osteoarthritis and fractures were significantly higher in cases, when compared to controls. In HC, the prevalence of vitamin D deficiency, obesity, hypothyroidism, smoking, diabetes mellitus, hypocalcaemia, corticosteroid use, malignancy, renal failure and Nonsteroidal anti-inflammatory drugs (NSAID) use

were significantly higher among the cases. In PWvWD, the prevalence of risk factors was significantly higher in cases when compared to controls. Conclusion: The prevalence of osteoporosis, osteoarthritis and fractures is significantly higher among HC and PWvWD. This data highlights the importance of screening patients for risk factors for poor bone health and provide education to prevent these complications.
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NR 43
TC 12
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U1 0
U2 2
PU WILEY
PI HOBOKEN

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SN 1351-8216
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J9 HAEMOPHILIA
JI Haemophilia
PD JUL 15
PY 2022
VL 28
IS 4
BP 671
EP 678
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WC Hematology
SC Hematology
GA 2V1ME
UT WOS:000781741900001
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PT J
AU Huang, XY
Lan, YH
Shen, JH
Chen, Z
Xie, ZJ
AF Huang, Xiaoyuan
Lan, Yanhua
Shen, Jiahui
Chen, Zhuo
Xie, Zhijian
TI Extracellular Vesicles in Bone Homeostasis: Emerging Mediators of Osteoimmune Interactions and Promising Therapeutic Targets
SO INTERNATIONAL JOURNAL OF BIOLOGICAL SCIENCES
LA English
DT Review
DE Extracellular vesicle; Exosome; Osteoimmune interaction; Bone disease
ID mesenchymal stem-cells; outer-membrane vesicles; osteogenic differentiation; polarization; osteoclast; exosm; microvesicles; communication; osteoporosis; macrophages
AB An imbalance in bone homeostasis results in bone loss and poor healing in bone diseases and trauma. Osteoimmune interactions, as a key contributor to bone

homeostasis, depend on the crosstalk between mesenchymal stem cell-osteoblast (MSC-OB) and monocyte-macrophage (MC-M??) lineages. Currently, extracellular vesicles (EVs) are considered to be involved in cell-to-cell communication and represent a novel avenue to enhance our understanding of bone homeostasis and to develop novel diagnostic and therapeutic options. In this comprehensive review, we aim to present recent advances in the study of the effect of MC-M??-derived EVs on osteogenesis and the regulatory effects of MSC-OB-derived EVs on the differentiation, recruitment and efferocytosis of M??. Furthermore, we discuss the role of EVs as crucial mediators of the communication between these cell lineages involved in the development of common bone diseases, with a focus on osteoporosis, osteoarthritis, bone fracture, and periodontal disease. Together, this review focuses on the apparent discrepancies in current research findings and future directions for translating fundamental insights into clinically relevant EV-based therapies for improving bone health.
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PT J
AU Snodgrass, JJ
AF Snodgrass, J. Josh
TI Minimally invasive biomarkers in human population biology research, part 2: An introduction to the special issue
SO AMERICAN JOURNAL OF HUMAN BIOLOGY
LA English
DT Article
ID life-history; yakut sakha; health; stress
AB Over the past several decades, biomarkers have become indispensable tools in human biology, allowing researchers to investigate biocultural and evolutionary questions and to generate basic data on health and well-being. Human biologists are central players in biomarker methods development, pioneering the creation of

"field friendly," minimally invasively collected biomarker approaches, as well as leading the innovative use of biomarkers, most notably to map the complex pathways from social and environmental conditions to altered physiology to health effects. This special issue, Part 2 of a collection focused on minimally invasively collected biomarkers, is comprised of nine papers that jointly contribute to driving the science of biomarker methods development and application. This compilation of papers engages with topics such as biological normalcy, ecoimmunology, and the ethics of working with vulnerable and underserved populations. It also focuses attention on research areas at present not emphasized in human biology such as bone turnover markers as a window onto osteoporosis and osteoarthritis and the use of cancer-related biomarkers in population screening and epidemiology. Taken together, these papers help draw the roadmap for future biomarker work, emphasizing: (1) the need for systematic and transparent approaches to assay validation, with open access publication; (2) simultaneous measurement of multiple biomarkers and expanded use of instrument platforms that increase the range of physiological, genomics, and omics markers available to researchers; and, (3) increased attention to ethics and researcher responsibilities, encouraging a mindset that recognizes our obligation to provide benefits to individuals and communities and to help redress past abuses.
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TI A review of musculoskeletal adaptations in individuals following major lower-limb amputation
SO JOURNAL OF MUSCULOSKELETAL & NEURONAL INTERACTIONS
LA English
DT Review
DE Anatomy; Limb Loss; Physiology; Remodeling; Symmetry
ID bone-mineral density; thigh muscle atrophy; walking ability; knee-joint; amputees; prevalence; gait; osteoarthritis; osteoporosis; association
AB Structural musculoskeletal adaptations following amputation, such as bone mineral density (BMD) or muscle architecture, are often overlooked despite their established contributions to gait rehabilitation and the development of adverse secondary physical conditions. The purpose of this review is to provide a summary of the existing literature investigating musculoskeletal adaptations in individuals with major lower-limb amputations to inform clinical practice and provide directions for future research. Google Scholar, PubMed, and Scopus were searched for original peer-reviewed studies that included individuals with transtibial or transfemoral amputations. Summary data of twenty-seven articles indicated reduced BMD and increased muscle atrophy in amputees compared to controls, and in the amputated limb compared to intact and control limbs. Specifically, BMD was reduced in T-scores and Z-scores, femoral neck, and proximal tibia. Muscle atrophy was evidenced by decreased thigh cross-sectional area, decreased quadriceps thickness, and increased amounts of thigh fat. Overall, amputees have impaired musculoskeletal health. Future studies should include dysvascular etiologies to address their effects on musculoskeletal health and functional mobility. Moreover, clinicians can use these findings to screen increased risks of adverse sequelae such as fractures, osteopenia/porosis, and muscular atrophy, as well as target specific rehabilitation exercises to reduce these risks.
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NR 62
TC 23
Z9 31
U1 0
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PU JMNI
PI NAFPLION
PA 7 SPILIADOU SQ, NAFPLION, 21 100, GREECE
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J9 J MUSCULOSKEL NEURON
JI J. Musculoskelet. Neuronal Interact.
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BP 269
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DI
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WC Neurosciences; Physiology
SC Neurosciences & Neurology; Physiology
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PT J
AU Peruri, A
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Kayal, Gabriella
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Ellis, Reilly
Wynne, Taylor
Fritz, Virginia
Simmons, Zachary
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TI Pineal Gland from the Cell Culture to Animal Models: A Review
SO LIFE-BASEL
LA English
DT Review
DE melatonin; regeneration; neurodegenerative process; cell culture; animal models
ID nerve; axons; regeneration; injury; brain; rats
AB This review demonstrates current literature on pineal gland physiology, pathology, and animal model experiments to concisely explore future needs in research development with respect to pineal gland function and neuro-regenerative properties. The pineal gland plays an integral role in sleep and recovery by promoting physiologic circadian rhythms via production and release of melatonin. Yet, the current literature shows that the pineal gland has neuroprotective effects that modulate both peripheral and central nerve injuries through several direct and indirect mechanisms, such as angiogenesis and induction of growth factors and anti-inflammatory mediators. Animal models have also shown correlations between pineal gland function and metabolic homeostasis. Studies have shown that a functional pineal gland is essential in preventing and slowing the progression of certain diseases such as diabetes, osteoporosis, vertebral osteoarthritis, and neurodegenerative processes. Lastly, the array of cell culturing methods and animal models that can be used to further develop the

study of pineal gland function and nervous system injury were reviewed.
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NR 58
TC 2
Z9 4
U1 0
U2 6
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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EI 2075-1729
J9 LIFE-BASEL
JI Life-Basel
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IS 7
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WC Biology; Microbiology
SC Life Sciences & Biomedicine - Other Topics; Microbiology
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PT J
AU Ajami, S
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Pitsillides, AA
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TI Spatial links between subchondral bone architectural features and cartilage degeneration in osteoarthritic joints
SO SCIENTIFIC REPORTS
LA English
DT Article
ID age-related-changes; femoral-head; hip osteoarthritis; mineral density; trabecular bone; proximal femur; osteoporosis; microstructure; heterogeneity; association
AB Early diagnosis of osteoarthritis (OA), before the onset of irreversible changes is crucial for understanding the disease process and identifying potential disease-modifying treatments from the earliest stage. OA is a whole joint disease and affects both cartilage and the underlying subchondral bone. However, spatial relationships between cartilage lesion severity (CLS) and microstructural changes in subchondral plate and trabecular bone remain elusive. Herein, we collected femoral heads from hip arthroplasty for primary osteoarthritis (n = 7) and femoral neck fracture (n = 6; non-OA controls) cases. Samples were regionally assessed for cartilage lesions by visual inspection using Outerbridge classification and entire femoral heads were micro-CT scanned. Scans of each femoral head were divided into 4 quadrants followed by morphometric analysis of subchondral plate and trabecular bone in each quadrant. Principal component analysis (PCA), a data reduction method, was employed to assess differences between OA and non-OA samples, and spatial relationship between CLS and subchondral bone changes. Mapping of the trabecular bone microstructure in OA patients with low CLS revealed trabecular organisation resembling non-OA patients, whereas clear differences were identifiable in subchondral plate architecture. The OA-related changes in subchondral plate architecture were summarised in the first principle component (PC1) which correlated with CLS in all quadrants, whilst by comparison such associations in trabecular bone were most prominent in the higher weight-bearing regions of the femoral head. Greater articular cartilage deterioration in OA was regionally-linked with lower BV/TV, TMD and thickness, and greater BS/BV and porosity in the subchondral plate; and with thinner, less separated trabeculae with greater TMD and BS/BV in the trabecular bone. Our findings suggest that impairment of subchondral bone microstructure in early stage of OA is more readily discernible in the cortical plate and that morphological characterisation of the femoral head bone microstructure may allow for earlier OA diagnosis and monitoring of progression.
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FU European Commission via H2020-MSCARISE programme [734156]; Innovate UK via Newton Fund [102872]; Rosetrees Trust [A1184]; Engineering and Physical Science Research Council (EPSRC) via DTP Case Programme [EP/T517793/1]; Innovate UK [102872] Funding Source: UKRI
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PU NATURE PORTFOLIO
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PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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PT J
AU Walter, N
   Lowenberg, DW
   Kurtz, SM
   Alt, V
   Lau, EC
   Rupp, M
AF Walter, Nike
   Lowenberg, David W.
   Kurtz, Steven M.
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   Lau, Edmund C.
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TI Revision Rates and Associated Risk Factors after Shoulder Arthroplasty
SO JOURNAL OF CLINICAL MEDICINE
LA English

DT Article
DE proximal humerus fracture; shoulder arthroplasty; revision risk factors; osteoarthritis; rotator cuff injury
ID proximal humeral fractures; registry research; surgery; complications; database; outcm; trends
AB This study aims at answering the following questions (1) How high is the revision rate after osteoarthritis-, and rotator cuff-related compared to proximal humerus fracture (PHF)-related shoulder arthroplasty? (2) What are the associated risk factors for a revision after shoulder arthroplasty? Shoulder arthroplasty procedures occurring between 1 January 2009 and 31 December 2019 were identified from the Medicare database. First, revision rates for PHF patients and age- and sex-matched non-fracture patients, grouped into osteoarthritis-related and rotator cuff-related arthroplasty, were compared. Second, revision rates between total shoulder arthroplasty and hemiarthroplasty after PHF were compared. Semiparametric Cox regression was applied, incorporating 23 demographic, clinical, and socioeconomic covariates, to investigate risk factors for revision surgery. Between the considered time period from 2009 through 2019, a total number of 47,979 PHFs was identified. A shoulder arthroplasty procedure was performed in n = 2639 (5.5%, 95%CI: 4.8-6.1) of the cases. The five-year survivorship of the implant was 96.3 (95%CI: 93.8-97.9) after hemiarthroplasty and 96.1% (05%CI: 94.2-97.3) after total shoulder arthroplasty. To compare the revision rates, n = 14,775 patients with osteoarthritis and n = 4268 patients with rotator cuff arthropathy, who received a shoulder arthroplasty, served as a non-fracture control group. Patients receiving a rotator cuff-related arthroplasty were more likely to require a revision compared to patients treated for osteoarthritis (HR: 1.27, 95%CI: 1.04-1.44, p = 0.018). Identified significant risk factors for revision surgery after shoulder arthroplasty included age <= 75 years, male sex, and osteoporosis. High implant survival was found for hemiarthroplasty and total shoulder arthroplasty for the treatment of PHF in elderly patients. The risk of revision surgery was elevated in patients receiving a rotator cuff-related arthroplasty as well as in patients with osteoporosis, male patients and patients older than 75 years.
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NR 35
TC 12
Z9 19
U1 0
U2 4
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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J9 J CLIN MED
JI J. Clin. Med.
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WC Medicine, General & Internal
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PT J
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Korthagen, NM
Weinans, H
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Rios, Jaqueline L.
van Valkengoed, Devin R.
Korthagen, Nicoline M.
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TI Sprague Dawley Rats Show More Severe Bone Loss, Osteophytosis and Inflammation Compared to Wistar Han Rats in a High-Fat, High-Sucrose Diet Model of Joint Damage
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE animal models; osteoarthritis; osteoporosis; obesity
ID synovial lining macrophages; osteoarthritis; glucose
AB In animal models, joint degeneration observed in response to obesogenic diet varies in nature and severity. In this study, we compare joint damage in Sprague Dawley and Wistar-Han rats in response to a high-fat, high-sucrose (HFS) diet groove model of osteoarthritis (OA). Wistar Han (n = 5) and Sprague Dawley (n = 5) rats were fed an HFS diet for 24 weeks. OA was induced 12 weeks after the diet onset by groove surgery in the right knee joint. The left knee served as a control. Outcomes were OARSI histopathology scoring, bone changes by mu CT imaging, local (synovial and fat pad) and systemic (blood cytokine) inflammation markers. In both rat strains, the HFS diet resulted in a similar change in metabolic parameters, but only Sprague Dawley rats showed a large, osteoporosis-like decrease in trabecular bone volume. Osteophyte count and local joint inflammation were higher in Sprague Dawley rats. In contrast, cartilage degeneration and systemic inflammatory marker levels were similar between the rat strains. The difference in bone volume loss, osteophytosis and local inflammation suggest that both rat strains show a different joint damage phenotype and could, therefore, potentially represent different OA phenotypes observed in humans.
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NR 29
TC 14
Z9 17

U1 0
U2 5
PU MDPI
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SC Biochemistry & Molecular Biology; Chemistry
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AF Kawai, T.
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TI Bisphosphonate use is associated with a decreased joint narrowing rate in the non-arthritic hip

SO BONE & JOINT RESEARCH
LA English
DT Article
DE Hip osteoarthritis; Bisphosphonate; Osteoporosis; Joint space narrowing; Knee arthroplasty; Joint cartilage
ID vitamin-d supplementation; knee osteoarthritis; subchondral bone; articular-cartilage; space; progression; cells; age; metaanalysis; risedronate
AB Aims The preventive effects of bisphosphonates on articular cartilage in non-arthritic joints are unclear. This study aimed to investigate the effects of oral bisphosphonates on the rate of joint space narrowing in the non-arthritic hip. Methods We retrospectively reviewed standing whole-leg radiographs from patients who underwent knee arthroplasties from 2012 to 2020 at our institute. Patients with previous hip surgery, Kellgren-Lawrence grade >= II hip osteoarthritis, hip dysplasia, or rheumatoid arthritis were excluded. The rate of hip joint space narrowing was measured in 398 patients (796 hips), and the effects of the use of bisphosphonates were examined using the multivariate regression model and the propensity score matching (1:2) model. Results A total of 45 of 398 (11.3%) eligible patients were taking an oral bisphosphonate at the time of knee surgery, with a mean age of 75.8 years (SD 6.2) in bisphosphonate users and 75.7 years (SD 6.8) in non-users. The mean joint space narrowing rate was 0.04 mm/year (SD 0.11) in bisphosphonate users and 0.12 mm/year (SD 0.25) in non-users ($p < 0.001$). In the multivariate model, age (standardized coefficient = 0.0867, $p = 0.016$) and the use of a bisphosphonate (standardized coefficient = -0.182, $p < 0.001$) were associated with the joint space narrowing rate. After successfully matching 43 bisphosphonate users and 86 non-users, the joint narrowing rate was smaller in bisphosphonate users ($p < 0.001$). Conclusion The use of bisphosphonates is associated with decreased joint degeneration in non-arthritic hips after knee arthroplasty. Bisphosphonates slow joint degeneration, thus maintaining the thickness of joint cartilage in the normal joint or during the early phase of osteoarthritis.
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NR 38
TC 5
Z9 5
U1 0
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PU BRITISH EDITORIAL SOC BONE & JOINT SURGERY
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PA 22 BUCKINGHAM STREET, LONDON WC2N 6ET, ENGLAND
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J9 BONE JOINT RES
JI Bone Jt. Res.
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WC Cell & Tissue Engineering; Orthopedics
SC Cell Biology; Orthopedics
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PT J
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TI Epidemiology of locomotive syndrome using updated clinical decision limits: 6-year follow-ups of the ROAD study
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Locomotive syndrome; Prevalence; Incidence; ROAD study; Disability
ID care insurance system; certified need; osteoarthritis/osteoporosis; association
AB Introduction Locomotive syndrome (LOCOMO) is defined by the Japanese Orthopaedic Association (JOA) as a condition requiring nursing care due to a decline in mobility resulting from musculoskeletal disorders. In 2020, the JOA announced the new definition of LOCOMO stage 3 and revision of clinical decision limits in stages of LOCOMO. However, there are few reports on the epidemiological indices of LOCOMO. This prospective cohort study aimed to investigate the prevalence, incidence, and association of poor prognosis with LOCOMO stages. Materials and methods The third survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study was conducted during 2012-2013, examining a population-based cohort of 1575 participants (513 men and 1062 women, mean age 65.6 years). Three LOCOMO risk tests were performed, and patients were classified into LOCOMO stages 0, 1, 2, and 3. They were followed up for 6 years, and identical examination of LOCOMO was performed in 3- and 6-year follow-ups. Data on patients' prognoses, including disability and death, were collected. Results The prevalence of LOCOMO stages 1, 2, and 3 was 41.3, 14.9, and 11.6%, respectively. The incidence of LOCOMO stages 1, 2, and 3 were 83.7, 23.0, and 18.6 per 1000 person-years, respectively. Compared with LOCOMO stage 0, logistic regression analysis showed that LOCOMO stage 3 significantly increased the risk of disability and mortality. In addition, each value of LOCOMO risk tests for LOCOMO stage 3 increased the risk of poor prognosis. Conclusion LOCOMO stage 3 is a sensitive indicator of future disability and mortality.

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NR 19
TC 35
Z9 37
U1 1
U2 6
PU SPRINGER JAPAN KK
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J9 J BONE MINER METAB
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WC Endocrinology & Metabolism; Medicine, Research & Experimental
SC Endocrinology & Metabolism; Research & Experimental Medicine
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Shuler, Franklin D.
TI Targeting the Gut Microbiome for Inflammation and Pain Management in Orthopedic Conditions
SO ORTHOPEDICS
LA English
DT Review
ID randomized double-blind; intestinal calcium-absorption; lactobacillus-casei-shirota; necrosis-factor-alpha; bone-mineral density; rheumatoid-arthritis; short-chain; postmenopausal women; knee osteoarthritis; perna-canaliculus
AB The human gut microbiome can be altered with probiotics, prebiotics, synbiotics, and anti-inflammatory foods and spices as part of an evidence-based strategy that targets inflammation and pain in common orthopedic conditions. Implementing these strategies avoids adverse effects associated with nonsteroidal anti-inflammatory drugs and minimizes the potential for opioid use. This review focuses exclusively on human trials studying the effects of gut microbiome alterations to address pain and inflammatory markers in common orthopedic conditions: osteoarthritis, rheumatoid arthritis, fractures/osteoporosis, and bone pain associated with chemotherapy. Individualized supplementation strategies can be further explored with the information in this review.
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NR 73
TC 8
Z9 10
U1 0
U2 5
PU SLACK INC
PI THOROFARE
PA 6900 GROVE RD, THOROFARE, NJ 08086 USA
SN 0147-7447
EI 1938-2367
J9 ORTHOPEDICS
JI Orthopedics
PD SEP-OCT 15
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BP E226
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PG 13
WC Orthopedics
SC Orthopedics
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UT WOS:001124810800001
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AU Huang, LT
Su, W
Wu, ZQ
Zheng, LD
Lv, C
AF Huang, Lintuo
Su, Wei
Wu, Ziqian
Zheng, Lidan
Lv, Chen
TI Glucosamine suppresses oxidative stress and induces protective autophagy in

osteoblasts by blocking the ROS/Akt/mTOR signaling pathway
SO CELL BIOLOGY INTERNATIONAL
LA English
DT Article
DE autophagy; Glucosamine; Osteoblast; ROS; Akt; mTOR signaling pathway
ID induced apoptosis; inhibition; activation; damage
AB Oxidative stress is the crucial pathogenic factor in osteoporosis. Cell autophagy, a major form of self-digestion, plays critical functions in different forms of stress by devouring harmful cytosolic proteins or organelles for the renewal of organelles and to maintain cellular homeostasis. Glucosamine (GlcN) has been widely utilized in treatments for patients with osteoarthritis-related joint pain. It has potential antioxidant effects and its pharmacological effect in osteoblasts remains unclear. The present study aimed to investigate whether autophagy participates in the protective effects of GlcN in osteoblasts under oxidative stress and the possible mechanism. First of all, MC3T3-E1 cells were treated with hydrogen peroxide (H2O2) to induce oxidative stress, as assessed by viability assays, apoptosis, the intracellular reactive oxygen species production. GlcN was capable of inducing autophagy and protected osteoblasts from those cytotoxic effects. Moreover, it significantly attenuated H2O2-induced oxidative stress as measured by malondialdehyde, glutathione, nitrite, and superoxide dismutase levels. Importantly, the autophagy level increased in osteoblasts treated with GlcN as represented by an increase in both Beclin1 expression and the LC3 II/I ratio. Immunofluorescence analysis of autophagosomes also confirmed the above results. In addition, GlcN decreased the mammalian target of rapamycin (mTOR) and protein kinase B (Akt). However, the Akt activator (SC79) suppressed the autophagy level induced by GlcN in osteoblasts. Consequently, the antioxidant effects of GlcN were mediated, at least in part, by enhancing autophagy through the Akt/mTOR pathway. These results suggested that GlcN might be a promising candidate for osteoporosis treatment.
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NR 31
TC 16
Z9 17

U1 1
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PU WILEY
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J9 CELL BIOL INT
JI Cell Biol. Int.
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BP 829
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WC Cell Biology
SC Cell Biology
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TI How osteogenic is dexamethasone?-effect of the corticosteroid on the osteogenesis, extracellular matrix, and secretion of osteoclastogenic factors of jaw periosteum-derived mesenchymal stem/stromal cells

SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Article
DE dexamethasone; osteogenic differentiation; mesenchymal stem/stromal cells; periosteum; osteoclast; extracellular matrix
ID stem-cells; bone-resorption; differentiation; mechanisms; expansion; apoptosis; gamma
AB Dexamethasone (dexa) is commonly used to stimulate osteogenic differentiation of mesenchymal stem/stromal cells (MSCs) in vitro. However, it is paradoxical that glucocorticoids (GCs) such as dexa lead to bone loss and increased fracture risk in patients undergoing glucocorticoid therapy, causing glucocorticoid-induced osteoporosis (GIOP). In a recent publication, we demonstrated that osteogenic differentiation of progenitor cells isolated from jaw periosteal tissue (JPCs) does not depend on dexa, if the medium is supplemented with human platelet lysate (hPL) instead of fetal bovine serum (FBS). This allows the in vitro conditions to be much closer to the natural situation in vivo and enables us to compare osteogenic differentiation with and without dexa. In the present study, we demonstrate that the absence of dexa did not reduce mineralization capacity, but instead slightly improved the osteogenic differentiation of jaw periosteal cells. On the other hand, we show that dexa supplementation strongly alters the gene expression, extracellular matrix (ECM), and cellular communication of jaw periosteal cells. The secretome of periosteal cells previously treated with an osteogenic medium with and without dexa was used to investigate the changes in paracrine secretion caused by dexa. Dexa altered the secretion of several cytokines by jaw periosteal cells and strongly induced osteoclast differentiation of peripheral blood mononuclear cells (PBMCs). This study demonstrates how dexa supplementation can influence the outcome of in vitro studies and highlights a possible role of periosteal cells in the pathogenesis of glucocorticoid-induced osteoporosis. The methods used here can serve as a model for studying bone formation, fracture healing, and various pathological conditions such as (glucocorticoid-induced) osteoporosis, osteoarthritis, bone cancer, and others, in which the interactions of osteoblasts with surrounding cells play a key role.
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NR 42
TC 7
Z9 7
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U2 7
PU FRONTIERS MEDIA SA
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JI Front. Cell. Dev. Biol.
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WC Cell Biology; Developmental Biology
SC Cell Biology; Developmental Biology
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PT J
AU Liu, AF
Chen, JX
Zhang, JT
Zhang, C
Zhou, QX

Niu, PY
Yuan, Y
AF Liu, Aifeng
Chen, Jixin
Zhang, Juntao
Zhang, Chao
Zhou, Qinxin
Niu, Puyu
Yuan, Ye
TI Intra-Articular Injection of Umbilical Cord Mesenchymal Stem Cells Loaded With Graphene Oxide Granular Lubrication Ameliorates Inflammatory Responses and Osteoporosis of the Subchondral Bone in Rabbits of Modified Papain-Induced Osteoarthritis
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Article
DE graphene oxide; umbilical cord mesenchymal stem cells; knee osteoarthritis; cartilage repair; osteoporosis
ID cartilage degeneration; articular-cartilage; pathogenesis; scaffolds; acid
AB AimThis study is to investigate the effects of umbilical cord mesenchymal stem cells (UCMSCs) loaded with the graphene oxide (GO) granular lubrication on ameliorating inflammatory responses and osteoporosis of the subchondral bone in knee osteoarthritis (KOA) animal models. MethodsThe KOA animal models were established using modified papain joint injection. 24 male New Zealand rabbits were classified into the blank control group, GO group, UCMSCs group, and GO + UCMSCs group, respectively. The concentration in serum and articular fluid nitric oxide (NO), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), type II collagen (COL-II), and glycosaminoglycan (GAG) was detected using ELISA, followed by the dissection of femoral condyles and staining of HE and Micro-CT for observation via the microscope. ResultsGO granular lubrication and UCMSCs repaired the KOA animal models. NO, IL-6, TNF-alpha, GAG, and COL-II showed optimal improvement performance in the GO + UCMSCs group, with statistical significance in contrast to the blank group ($P < 0.01$). Whereas, there was a great difference in levels of inflammatory factors in serum and joint fluid. Micro-CT scan results revealed the greatest efficacy of the GO + UCMSCs group in improving joint surface damage and subchondral bone osteoporosis. HE staining pathology for femoral condyles revealed that the cartilage repair effect in GO + UCMSCs, UCMSCs, GO, and blank groups were graded down. ConclusionUCMSCs loaded with graphene oxide granular lubrication can promote the secretion of chondrocytes, reduce the level of joint inflammation, ameliorate osteoporosis of the subchondral bone, and facilitate cartilage repair.
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NR 65
TC 12
Z9 14
U1 3
U2 39
PU FRONTIERS MEDIA SA
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA YS3MM
UT WOS:000750584400001
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PT J
AU Yang, ZL
Hu, SH
Zhang, YW
AF Yang, Ziliang
Hu, Sihui

Zhang, Yongwei
TI Effect of methoxy-polyethylene glycol-polylactic acid-bone protective protein nano micelle complex on osteoprotegerin and bone mineral density in osteoporotic rats
SO MATERIALS EXPRESS
LA English
DT Article
DE PEG-PLL-OPG; Osteoporosis; OPG; Bone Density
ID rankl/rank/opg
AB This study assessed the effect of nanomicelle complex Methoxy-polyethylene glycol Polylactic acid bone protective protein on OPG and bone mineral density in osteoporotic rats. 35 rats were assigned into group A, B, C, D and E. Except for group A, Osteoarthritis (OA) rat models were established in all other groups. After modeling, group C, D and E were injected with PEG+ OPG plasmid, PLL+ OPG plasmid and PEG-PLL+ plasmid at 40 mg/kg dose of nanoparticles into mice via tail vein. The other groups were injected with an equal volume of NaCl solution to observe the bone density and OPG level. The bone trabeculae in the femoral tissues of group A were mostly plate-shaped and dense and uniform. Group B bones were sparse without new bone, while the trabecular bone in group C increased, the gap among trabecular bones decreased. The number of trabecular bones increased in group D, and new bone trabecula from group E increased, and arrangement was neat. Bone mineral density (BMD) and BMc levels in the femoral tissue from rats in group B decreased relative to group A ($P < 0.05$), and the levels of BMD and BMc in the femoral tissue from rats in group C increased ($P < 0.05$). BMD and BMc from mouse femur tissue were lower than group E ($P < 0.05$). Moreover, Group B had a lower maximum load than group A ($P < 0.05$) and group E was higher than group D ($P < 0.05$). The femoral tissue structure of rats in group A was complete and bone matrix was arranged well without cavities. The number of bone cells in group B was reduced, while the bone matrix was disorderly distributed, and bones were fractured and more cavities were formed. Compared with group B, groups C, and D, and E had increased bone cells number and reduced bone matrix disorder improvement voids. Immunohistochemistry showed that, OPG increased in group B, and RANKL decreased ($P < 0.05$), which was different from group A ($P < 0.05$). OPG protein and mRNA from C, D and E groups decreased, and RANKL levels increased ($P < 0.05$). PEG-PLL-OPG (PPO) significantly improved OP rat bone mineral density via regulation of BMD, BMc and biomechanical indicators, and the mechanism is related to increased OPG expression and reduced RANKL activity.
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PT J
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TI A randomized, parallel control and multicenter clinical trial of evidence-based traditional Chinese medicine massage treatment VS External Diclofenac Diethylamine Emulgel for the treatment of knee osteoarthritis
SO TRIALS
LA English
DT Article
DE Clinical effect; Safety evaluation; Evidence-based traditional Chinese medicine massage; External Diclofenac Diethylamine Emulgel; Knee Osteoarthritis; Magnetic resonance imaging; Multi-center; Clinical trial
ID european-society; economic-aspects; management; osteoporosis; guidelines; algorithm; efficacy; ligament; safety
AB Background: Both massage and topically administered NSAIDs are safe and effective treatments for knee osteoarthritis (KOA); however, different massage technique sects in China caused assessment difficulties for the treatment of KOA. In order to standardize the massage techniques and procedures, we organized multi-disciplinary experts in China to acquire an evidence-based traditional Chinese medicine massage treatment of knee osteoarthritis. The purposes of this study will be to provide clinicians a complementary and alternative therapy for patients and to evaluate the efficacy and safety of evidence-based traditional Chinese medicine massage treatment of KOA compared to External Diclofenac Diethylamine Emulgel. Methods and design: A randomized controlled trial in which 300 participants diagnosed with KOA will be recruited and randomly allocated to either the experimental group or the control group in a ratio of 2:1. Two hundred participants will receive evidence-based traditional Chinese medicine massage 2 sessions per week for 10 weeks as the experimental group, and 100 participants will receive External Diclofenac Diethylamine Emulgel 3-4 times per day for 10 weeks as the control group. The patients in the two groups will receive follow-up at two time points at 5 weeks and 10 weeks from the beginning of treatment, respectively. The MRI scans and X-ray will be performed at baseline and at the end of the intervention. The primary outcome will be the changes in the Western Ontario and McMaster Osteoarthritis Index (WOMAC). Secondary outcomes will be measured by the PRO scale for knee osteoarthritis based on the concept of traditional Chinese medicine (Chinese scale for knee osteoarthritis (CSKO)), X-ray evaluation, and MRI scan evaluation. The data of WOMAC and CSKO will be analyzed at the baseline, 5 weeks, and 10 weeks from the beginning of treatment. The data from MRI scans and X-rays will be analyzed at baseline and at the end of the intervention. The significance level sets as 5%. The safety of interventions will be

evaluated after each treatment session. Discussion: This study will provide clinicians with much-needed knowledge for the treatment of KOA through a controlled trial.
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NR 24
TC 3
Z9 4
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U2 18
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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PT J
AU Alrashed, MM
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Ahmad, M
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AF Alrashed, May Mohammed
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Xu, Yaozeng
TI miRNA Let-7a-5p targets RNA KCNQ1OT1 and Participates in Osteoblast Differentiation to Improve the Development of Osteoporosis
SO BIOCHEMICAL GENETICS
LA English
DT Article
DE Osteoporosis; miR-497-5p; RNA KCNQ1OT1; Osteogenic differentiation
ID akt3
AB It is known that miRNA mediates the formation of osteogenesis, but the mechanism by which miRNA let-7a-5p regulates osteogenesis in osteoporosis (OP) is not yet understood. This paper aims to probe into the regulatory mechanism of miRNA let-7a-5p in the development of OP. Fresh femoral trabecular bones of patients with osteoporotic fracture (OP group, n = 25) and non-OP osteoarthritis (Non-OP group, n = 23) who underwent hip replacement in our hospital from December 2016 to December 2019 were collected. The expression and protein levels of miRNA let-7a-5p and V-AKT murine thymoma viral oncogene homolog 3 (RNA KCNQ1OT1) were detected. C2C12 cells were purchased and osteogenic differentiation model was constructed by BMP2 induction. After miRNA let-7a-5p up-regulation or down-regulation by transfection of corresponding mimics and inhibitors, the impacts of miRNA let-7a-5p and RNA KCNQ1OT1 on osteogenic differentiation-related factors (OC, ALP, COL1A1) in C2C12 cells were analyzed. The determination of targeting correlation of miRNA let-7a-5p with RNA KCNQ1OT1 was performed by dual-luciferase reporter (DLR). In OP samples, miRNA let-7a-5p was notably declined while RNA KCNQ1OT1 were remarkably up-regulated. MiRNA let-7a-5p reduced in C2C12 cells as BMP2 treatment proceeded. MiRNA let-7a-5p up-regulation or RNA KCNQ1OT1 down-regulation increased OC, ALP, COL1A1 levels and ALP activity. RNA KCNQ1OT1 was directly targeted to miR-497-5p. RNA KCNQ1OT1 up-regulation weakened the promoting effect of miRNA let-7a-5p up-regulation on osteoblast differentiation. MiRNA let-7a-5p up-regulation can target to reduce RNA KCNQ1OT1 and promote osteoblast differentiation, thereby improving the development of osteoporosis.
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TC 8
Z9 9
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WC Biochemistry & Molecular Biology; Genetics & Heredity
SC Biochemistry & Molecular Biology; Genetics & Heredity
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PT J
AU Williams, PT
AF Williams, Paul T.
TI Quantile-Dependent Expressivity of Serum Interleukin-6 Concentrations as a Possible Explanation of Gene-Disease Interactions, Gene-Environment Interactions, and Pharmacogenetic Effects
SO INFLAMMATION
LA English
DT Article
DE interleukin-6; heritability; gene-environment interaction; pharmacogenetics; inflammation
ID c-reactive protein; single-nucleotide polymorphism; promoter polymorphism; inflammatory markers; plasma-levels; g/c polymorphism; cytokine levels; il-6 levels; tnf-alpha; il6 gene
AB Interleukin 6 (IL-6) is a moderately heritable pleiotropic cytokine whose

elevated concentrations in coronary artery disease, peripheral arterial disease, pulmonary arterial hypertension, Eales' disease, Sjogren's syndrome, osteoarthritis, adenocarcinoma, neuroblastoma, polymyalgia rheumatica, pulmonary tuberculosis, and enterovirus 71 infection, and following coronary artery bypass graft show larger genetic effects than in unaffected low IL-6 controls. We hypothesize that genetic effects may depend upon whether average IL-6 concentrations are high or low, i.e., quantile-dependent expressivity. Quantile-specific offspring-parent (beta(OP)) and full-sib regression slopes (beta(FS)) were estimated by applying quantile regression to the age- and sex-adjusted serum IL-6 concentrations in families surveyed in the Framingham Heart Study. Quantile-specific heritabilities were calculated as h(2) = 2 beta(OP) / (1 + r(spouse)) and h(2) = {(1 + 8r(spouse)beta(FS))(0.5) -1} / (2r(spouse))). Heritability (h(2) +/- SE) of IL-6 concentrations increased from 0.01 +/- 0.01 at the 10th percentile (NS), 0.02 +/- 0.01 at the 25th (P = 0.009), 0.03 +/- 0.01 at the 50th (P = 0.007), 0.04 +/- 0.02 at the 75th (P = 0.004), and 0.13 +/- 0.05 at the 90th percentile (P = 0.03), or 0.0005 +/- 0.0002 for each 1% increase in the offspring's phenotype distribution (P-linear trend = 0.02) when estimated from beta(OP) and from 0.02 +/- 0.02 at the 10th (NS), 0.02 +/- 0.02 at the 25th (NS), 0.06 +/- 0.02 at the 50th (P = 0.01), 0.12 +/- 0.04 at the 75th (P = 0.001), and 0.30 +/- 0.03 at the 90th percentile (P < 10(-16)), or 0.0015 +/- 0.0007 for each 1% increase in the sibling phenotype distribution (P-linear trend = 0.02) when estimated from beta(FS). Thus the heritability of serum IL-6 concentrations is quantile dependent, which may contribute in part to the larger genetic effect size reported for diseases and environmental conditions that elevate IL-6 concentrations vis-a-vis unaffected controls.
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NR 66
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PT J
AU Gardner, JE
Williams, CW
Bowers, RL
AF Gardner, James E.
Williams, Christopher W.
Bowers, Robert L.
TI Subchondral versus intra-articular orthobiologic injections for the treatment of knee osteoarthritis: a review
SO REGENERATIVE MEDICINE
LA English
DT Review
DE adipose; intra-articular; intraosseous; mesenchymal stromal cells; orthobiologics; osteoarthritis; platelet-rich plasma; subchondral bone marrow concentrate
ID platelet-rich plasma; bone-marrow concentrate; stromal cells; double-blind; adipose-tissue; stem-cells; osteoporosis; progression; placebo; cysts
AB Recent perspectives suggest that osteoarthritis (OA) is a disease involving not only the articular cartilage but also the osteochondral unit, including the synovium, supportive cartilage and subchondral bone. Current conservative treatments for OA are symptomatic and do not prevent progression or reverse the disease process. Compelling data show that intra-articular orthobiologic injections, such as platelet-rich plasma and mesenchymal stromal cells, are effective in providing relief of OA symptoms. However, recent data suggest that injections of orthobiologics into the subchondral bone may be superior to intra-articular injections for the management of OA. This review highlights the rationale and current evidence for intra-articular and subchondral bone injections of orthobiologics for the treatment of OA.
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Zhen GH, 2013, NAT MED, V19, P704, DOI 10.1038/nm.3143
NR 68
TC 5
Z9 5
U1 1
U2 18
PU FUTURE MEDICINE LTD
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PT J
AU Akiyama, S
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AF Akiyama, Shoshi
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Chazono, Masaaki
Matsuoka, Tatsuki
Saito, Mitsuru
TI Factors affecting spine-femur discordance in the percentage of young adult mean on dual-energy X-ray absorptiometry in the elderly population: a retrospective study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Spine-femur discordance; Young adult mean; Dual-energy X-ray absorptiometry; Osteoporosis; Lumbar spine; Bone mineral density
ID bone-mineral density; abdominal aortic calcification; skeletal hyperostosis dish; lumbar spine; hip; osteoarthritis; prevalence; risk; osteoporosis; impact
AB Background Several retrospective studies have reported spine-femur discordance in bone mineral density (BMD) values. However, the average age of individuals in these studies was the mid-50s, which is younger than the typical age of individuals requiring treatment for primary osteoporosis. Therefore, we aimed to investigate factors associated with discordance in the percentage of young adult mean (YAM) between the lumbar spine and femoral neck in the elderly population. Methods We evaluated 4549 dual-energy X-ray absorptiometry (DXA) measurements obtained from 2161 patients (269 men and 1892 women) between January 2014 and December 2017 at our hospital. For individuals with more than one eligible set of measurements, the first record was used. We investigated each patient's age, sex, body mass index, current smoking status, alcohol consumption, use of steroids, presence of diabetes mellitus, and presence of rheumatoid arthritis. Results The mean age of the patients was 76.4 +/- 8.9 years. Older age ($p < 0.001$), male sex ($p < 0.001$), and diabetes mellitus ($p = 0.007$) were significantly associated with spine-femur discordance in the percentage of YAM. Conclusion The frequency and magnitude of spine-femur discordance in the percentage of YAM from DXA scans increased with age. Notably, more than 77.4% of patients in their 90s had spine-femur discordance > 10% of YAM. Furthermore, the frequency of spine-femur discordance was higher in men and in patients with diabetes mellitus, suggesting that the percentage of YAM at the lumbar spine may not be reliable for diagnosis of osteoporosis in patients with these factors.
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NR 32
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Z9 5
U1 0
U2 2
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD JAN 21
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IS 1
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DI 10.1186/s12891-022-05015-3
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA YK7OG
UT WOS:000745397200002
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PT J
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TI Risk of Comorbidities Following Physician-Diagnosed Knee or Hip Osteoarthritis: A Register-Based Cohort Study
SO ARTHRITIS CARE & RESEARCH
LA English
DT Article
ID global burden; epidemiology; population; disease; inflammation; association; fractures; arthritis; symptoms; obesity
AB Objective. To estimate the risk of developing comorbidities in patients after physician-diagnosed knee or hip osteoarthritis (OA). Methods. This was a cohort study using Swedish longitudinal health care register data; we studied residents in the Skane region age >= 35 years on January 1, 2010 who were free from diagnosed hip or knee OA (n = 548,681). We then identified subjects with at least 1 new diagnosis of knee or hip OA (incident OA) between 2010 and 2017 (n = 50,942 considered exposed). Subjects without diagnosed OA were considered unexposed. From January 2010 both unexposed and exposed subjects were observed for the occurrence of 18 different predefined comorbidities until either relocation outside of the region, death, occurrence of the comorbidity, or December 2017, whichever came first. We calculated unadjusted hazard ratios (HRs) and adjusted HRs of comorbidities using Cox models with knee and hip OA as time-varying exposures. Results. Subjects with incident knee or hip OA had 7% to 60% higher adjusted HRs (range 1.07-1.60) of depression, cardiovascular diseases, back pain, and osteoporosis than individuals without an OA diagnosis. An increased risk of diabetes mellitus was found only for knee OA (adjusted HR 1.19 [95% confidence interval 1.13-1.26]). For the rest of the diagnoses, we found either no increased risk or estimates with wide confidence intervals, excluding clear interpretations of the direction or size of effects. Conclusion. Incident physician-diagnosed knee and hip OA is associated with an increased risk of depression, cardiovascular diseases, back pain, osteoporosis, and diabetes mellitus. However, the latter was only found for knee OA.
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NR 42
TC 31
Z9 39
U1 0
U2 2
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PI HOBOKEN
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J9 ARTHRIT CARE RES
JI Arthritis Care Res.
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TI Reduced Awareness for Osteoporosis in Hip Fracture Patients Compared to Elderly Patients Undergoing Elective Hip Replacement
SO MEDICINA-LITHUANIA
LA English
DT Article
DE awareness; osteoporosis; proximal femur fracture; hip replacement; fracture liaison service
ID mortality; epidemiology; probability
AB Background: Osteoporotic fractures are associated with a loss of quality of life, but only few patients receive an appropriate therapy. Therefore, the present study aims to investigate the awareness of musculoskeletal patients to participate in osteoporosis assessment and to evaluate whether there are significant differences between acute care patients treated for major fractures of the hip compared to elective patients treated for hip joint replacement.; Methods: From May 2015 to December 2016 patients who were undergoing surgical treatment for proximal femur fracture or total hip replacement due to osteoarthritis and were at risk for an underlying osteoporosis (female > 60 and male > 70 years) were included in the study and asked to complete a questionnaire assessing the awareness for an underlying osteoporosis. ASA Score, FRAX Score, and demographic information

have also been examined. Results: In total 268 patients (female = 194 (72.0%)/male = 74 (28%)), mean age 77.7 years (+/- 7.7) undergoing hip surgery were included. Of these, 118 were treated for fracture-related etiology and 150 underwent total hip arthroplasty in an elective care setting. Patients were interviewed about their need for osteoporosis examination during hospitalization. Overall, 76 of 150 patients receiving elective care (50.7%) considered that an examination was necessary, whereas in proximal femur fracture patients the awareness was lower, and the disease osteoporosis was assessed as threatening by significantly fewer newly fractured patients. By comparison, patients undergoing trauma surgery had a considerably greater risk of developing another osteoporotic fracture than patients undergoing elective surgery determined by the FRAX (R) Score ($p <= 0.001$).; Conclusions: The patients' motivation to endure additional osteoporosis diagnostic testing is notoriously low and needs to be increased. Patients who underwent acute care surgery for a fragility proximal femur fracture, although acutely affected by the potential consequences of underlying osteoporosis, showed lower awareness than the elective comparison population that was also on average 6.1 years younger. Although elective patients were younger and at a lower risk, they seemed to be much more willing to undergo further osteoporosis assessment. In order to better identify and care for patients at risk, interventions such as effective screening, early initiation of osteoporosis therapy in the inpatient setting and a fracture liaison service are important measures.
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NR 26
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J9 MEDICINA-LITHUANIA
JI Med. Lith.
PD NOV 15
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VL 58
IS 11
BP
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WC Medicine, General & Internal
SC General & Internal Medicine

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PT J
AU Zhang, L
Lin, Y
Zhang, XN
Shan, C
AF Zhang, Liang
Lin, Yi
Zhang, Xiannan
Shan, Chen
TI Research progress of exosomes in orthopedics
SO FRONTIERS IN GENETICS
LA English
DT Review
DE exosomes; bone marrow mesenchymal stem cell; bone remodeling; spinal cord injury; osteoarthritis; bone tumor
ID mesenchymal stem-cells; femoral-head; chondrocyte proliferation; osteogenic differentiation; induced osteonecrosis; promote angiogenesis; apoptosis; osteoblasts; osteocyte; migration
AB Exosomes are nano-extracellular vesicles secreted by a variety of cells. They are composed of a double-layer membrane that can transport a variety of proteins, coding and non-coding genes, and bioactive substances. Exosomes participate in information transmission between cells and regulate processes such as cell proliferation, migration, angiogenesis, and phenotypic transformation. They have broad prospects in the occurrence, development, and treatment of many diseases including orthopedics. Exosomes derived from different types of bone cells such as mesenchymal stem cells, osteoblasts, osteoclasts, and their precursors are recognized to play pivotal roles in bone remodeling processes including osteogenesis, osteoclastogenesis, and angiogenesis. This articlesummarizes the characteristics of exosomes and their research progress in bone remodeling, bone tumors, vascular skeletal muscle injury, spinal cord injury, degenerative disc diseases, cartilage degeneration, osteoarthritis, necrosis of the femoral head, and osteoporosis.
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TI The crucial mechanism and therapeutic implication of RNA methylation in bone pathophysiology
SO AGEING RESEARCH REVIEWS
LA English
DT Review
DE RNA methylation; N6-methyladenosine; Epigenetic modulation; Physiology of bone; Pathological bone diseases
ID 25s ribosomal-rna; mesenchymal stem-cells; messenger-rna; osteogenic

differentiation; nuclear-rna; n-6-methyladenosine modification; osteoblast differentiation; m(6)a methyltransferase; base modification; adipose-tissue
AB Methylation is the most common posttranscriptional modification in cellular RNAs, which has been reported to modulate the alteration of RNA structure for initiating relevant functions such as nuclear translocation and RNA degradation. Recent studies found that RNA methylation especially N6-methyladenosine (m6A) regulates the dynamic balance of bone matrix and forms a complicated network in bone metabolism. The modulation disorder of RNA methylation contributes to several pathological bone diseases including osteoporosis (OP), osteoarthritis (OA), rheumatoid arthritis (RA), and so on. In the review, we will discuss advanced technologies for detecting RNA methylation, summarize RNA methylation-related biological impacts on regulating bone homeostasis and pathological bone diseases. In addition, we focus on the promising roles of RNA methylation in early diagnosis and therapeutic implications for bone-related diseases. Then, we aim to establish a theoretical basis for further investigation in this meaningful field.
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TI Artemisinin relieves osteoarthritis by activating mitochondrial autophagy through reducing TNFSF11 expression and inhibiting PI3K/AKT/mTOR signaling in cartilage

SO CELLULAR & MOLECULAR BIOLOGY LETTERS
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DT Article
DE Artemisinin; PI3K; AKT signaling pathway; Autophagy; TNFSF11; Mitochondria; Osteoarthritis
ID in-vitro; suppressing osteoclastogenesis; pathway; rankl; chondrocytes; osteoporosis; artesunate; apoptosis; interleukin-1-beta; proliferation
AB Osteoarthritis (OA) is a widespread chronic degenerative joint disease characterized by the degeneration of articular cartilage or inflamed joints. Our findings indicated that treatment with artemisinin (AT) downregulates the protein levels of MMP3, MMP13, and ADAMTS5, which are cartilage degradation-related proteins in OA, and inhibits the expression of inflammatory factors in interleukin-1 beta (IL-1 beta)-stimulated chondrocytes. However, the mechanism of the role of AT in OA remains unclear. Here, we performed gene sequencing and bioinformatics analysis in control, OA, and OA + AT groups to demonstrate that several mRNA candidates were enriched in the PI3K/AKT/mTOR signaling pathway, and TNFSF11 was significantly downregulated after AT treatment. TNFSF11 was downregulated in the OA + AT group, whereas it was upregulated in rat OA tissues and OA chondrocytes. Therefore, we confirmed that TNFSF11 was the target gene of AT. In addition, our study revealed that AT relieved cartilage degradation and defection by activating mitochondrial autophagy via inhibiting the PI3K/AKT/mTOR signaling pathway in IL-1 beta-induced chondrocytes. Furthermore, an OA model was established in rats with medial meniscus destabilization. Injecting AT into the knee joints of OA rat alleviated surgical resection-induced cartilage destruction. Thus, these findings revealed that AT relieves OA by activating mitochondrial autophagy by reducing TNFSF11 expression and inhibiting PI3K/AKT/mTOR signaling.
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TI Incidence and risk factors associated with hospital-acquired pressure ulcers following total hip arthroplasty: A retrospective nationwide inpatient sample database study
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DT Article
DE Arthroplasty; Database; Hip; Pressure ulcer; Replacement
ID cardiac-surgery; frailty; care
AB Aim: To examine the incidence and risk factors associated with hospital-acquired pressure ulcers (HAPUs) following total hip arthroplasty (THA) using a large-scale national database.Material and methods: A retrospective database analysis was performed based on Nationwide Inpatient Sample (NIS) from 2005 to 2014. Patients who underwent THA were included. Patient demographics, hospital characteristics, length of stay (LOS), total charges during hospitalization, in-hospital mortality, preoperative comorbidities, and perioperative complications were assessed.Results: The general incidence of HAPUs after THA was 0.05%, with a fluctuating trend annually. Patients suffered from HAPUs were older, less likely through elective admission, more likely in large hospital, more usage of Medicare, and less possibly paying via Private insurance. Additionally, the occurrence of HAPUs was associated with more preoperative comorbidities, longer LOS, extra total charges, and higher in-hospital mortality. Risk factors associated with HAPUs

included advanced age (>= 75 years), large hospital, multiple comorbidities (n >= 3), diabetes with chronic complications, drug abuse, liver disease, fluid and electrolyte disorders, metastatic cancer, peripheral vascular disorders, psychoses, chronic renal failure, peptic ulcer disease, and weight loss. Besides, HAPUs were associated with inflammatory arthritis and femoral neck fracture (compared with primary/ secondary osteoarthritis), frailty/senility, osteoporosis, acute renal failure, pneumonia, postoperative delirium, urinary tract infection, deep vein thrombosis, sepsis/septicemia, wound dehiscence/non-healing surgical wound, periprosthetic joint infection, and mechanical prosthesis-related complications. Conclusion: It is beneficial to study the risk factors associated with HAPUs after THA to ensure the preventive management and optimize outcomes although a low incidence was identified.
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TI A concise review on implications of silver nanoparticles in bone tissue engineering
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ID mesenchymal stem-cells; in-vitro; cellular uptake; coated megaprostheses; osteogenic differentiation; ag nanoparticles; stromal cells; antibacterial; titanium; staphylococcus
AB Skeletal disorders represent a variety of degenerative diseases that affect bone and cartilage homeostasis. The regenerative capacity of bone is affected in osteoporosis, osteoarthritis, rheumatoid arthritis, bone fractures, congenital defects, and bone cancers. There is no viable, non-invasive treatment option and bone regeneration requires surgical intervention with the implantation of bone grafts. Incorporating nanoparticles in bone grafts have improved fracture healing by providing fine structures for bone tissue engineering. It is currently a revo-lutionary finding in the field of regenerative medicine. Silver nanoparticles

(AgNPs) have garnered particular attention due to their well-known anti-microbial and potential osteoinductive properties. In addition, AgNPs have been demonstrated to regulate the proliferation and differentiation of mesenchymal stem cells (MSCs) involved in bone regeneration. Furthermore, AgNPs have shown toxicity towards cancer cells derived from bone. In the last decade, there have been multiple studies focusing on the effect of nanoparticles on the proliferation and/or differentiation of MSCs and bone cancer cells; however, the specific studies with AgNPs are limited. Although the reported investigations show promising in vitro and in vivo potential of AgNPs for application in bone regeneration, more studies are required to ensure their implications in bone tissue engineering. This review aims to highlight the current advances related to the production of AgNPs and their effect on MSCs and bone cancer cells, which will potentiate their possible implications in orthopedics. Moreover, this review article evaluates the future of AgNPs in bone tissue engineering.
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TI Relationship between Gut Microbiota and Bone Health
SO MINI-REVIEWS IN MEDICINAL CHEMISTRY
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DT Review
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ID helveticus-fermented milk; menopausal hormone-therapy; ankylosing-spondylitis; inflammatory disease; postmenopausal women; mineral absorption; future-directions; intestinal flora; secretory iga; serum-levels
AB Gut Microbiota (GM) are microorganisms that live in the host gastrointestinal tract, and their abundance varies throughout the host's life. With the development of sequencing technology, the role of GM in various diseases has been increasingly elucidated. Unlike earlier studies on orthopedic diseases, this review elucidates the correlation between GM health and bone health and discusses the potential mechanism of GM effects on host metabolism, inflammation, and ability to induce or aggravate some common orthopedic diseases, such as osteoarthritis, osteoporosis, rheumatoid arthritis, etc. Finally, the prospective methods of GM

manipulation and evaluation of potential GM-targeting strategies in the diagnosis and treatment of orthopedic diseases are reviewed.
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TI Donor age effects on in vitro chondrogenic and osteogenic differentiation performance of equine bone marrow- and adipose tissue-derived mesenchymal stromal cells
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DT Article
DE Horse; Donor age; Aging; Mesenchymal stromal cells; Cartilage; Bone
ID umbilical-cord blood; stem-cells; osteoarthritis; culture; pcr; osteoporosis; senescence; expression; capacity; horses
AB Background Bone marrow (BM)- and adipose tissue (AT)-derived mesenchymal stromal cells (MSCs) have shown potential as cell-based therapies for cartilage and bone injuries and are used increasingly in human and veterinary practice to facilitate the treatment of orthopedic conditions. However, human and rodent studies have documented a sharp decline in chondrogenic and osteogenic differentiation potential with increasing donor age, which may be problematic for the important demographic of older orthopedic patients. The aim of this study was to identify the effect of donor age on the chondrogenic and osteogenic differentiation performance of equine BM- and AT-MSCs in vitro. BM- and AT-MSCs and dermal fibroblasts (biological negative control) were harvested from horses in five different age groups (n = 4, N = 60); newborn (0 days), yearling (15-17 months), adult (5-8 years), middle-aged (12-18 years), and geriatric (>= 22 years). Chondrogenic differentiation performance was assessed quantitatively by measuring pellet size, matrix proteoglycan levels, and gene expression of articular cartilage biomarkers. Osteogenic differentiation performance was assessed quantitatively by measuring alkaline phosphatase activity, calcium deposition, and gene expression of bone biomarkers. Results Chondrogenic and osteogenic differentiation performance of equine BM- and AT-MSCs declined with increasing donor age. BM-MSCs had a higher chondrogenic differentiation performance. AT-MSCs showed minimal chondrogenic differentiation performance in all age groups. For osteogenesis, alkaline phosphatase activity was also higher in BM-MSCs, but BM-MSCs calcium deposition was affected by donor age earlier than AT-MSCs. Chondrogenic and osteogenic differentiation performance of BM-MSCs exhibited a decline as early as between the newborn and yearling samples. Steady state levels of mRNA encoding growth factors, chondrogenic, and osteogenic biomarkers were lower with increasing donor age in both MSC types. Conclusions The data showed that chondrogenic and osteogenic differentiation performance of equine BM-MSCs declined already in yearlings, and that AT-MSCs showed minimal chondrogenic potential, but were affected later by donor age with regards to osteogenesis (calcium deposition). The results highlight the importance of donor age considerations and MSC selection for cell-based treatment of orthopedic injuries and will help inform clinicians on when to implement or potentially

cryopreserve cells. Moreover, the study provides molecular targets affected by donor age.
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AU Londzin, P
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TI Lack of berberine effect on bone mechanical properties in rats with experimentally induced diabetes
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Berberine; Diabetes; Osteoporosis; Rats; Skeletal system
ID nf-kappa-b; osteoclast differentiation; cartilage degeneration; animal-models; cells; osteoporosis; pathophysiology; osteoarthritis; proliferation; chondrocytes
AB Multidirectional health-promoting activities of some plant-derived substances make them candidates for drugs used in diabetes and its complications such as osteoporosis. Berberine is a compound for which both antidiabetic and antiosteoporotic effects have been documented. The aim of the study was to investigate the effects of berberine on the skeletal disorders induced by experimental type 1 diabetes in rats. The experiments were performed on 3-month-old female rats, divided into three groups: I - healthy control rats, II - diabetic control rats, III - diabetic rats receiving berberine. Diabetes was induced by a single streptozotocin injection. Berberine administration (50 mg/kg/day p.o.) started two weeks later and lasted four weeks. Serum bone turnover markers and other biochemical parameters, bone mass and mineralization, histomorphometric parameters and mechanical properties were studied. Diabetes induced strong disorders of bone turnover, bone microarchitecture, and strength of cancellous bone. Berberine counteracted the effect of diabetes on the bone formation marker (osteocalcin) concentration, the growth plate, and some parameters of cancellous

bone microarchitecture, but did not improve bone mineralization and bone mechanical properties in the diabetic rats. The lack of effect of berberine on bone quality does not support its use in the prevention of diabetes-induced bone damage.
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TI Systemic iron reduction via an iron deficient diet decreases the severity of knee cartilage lesions in the Dunkin-Hartley guinea pig model of osteoarthritis
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Iron; Aging; Knee; Guinea pig
ID bone-mineral density; serum ferritin levels; rheumatoid-arthritis; articular-cartilage; subchondral bone; overload; tissue; osteoporosis; association; stores
AB Objective: Iron accumulation is emerging as a player in aging-related disorders due to its propensity for generating reactive oxygen species (ROS). Studies investigating the role of iron in the pathogenesis of primary osteoarthritis (OA) are limited. We designed a proof-of-principle study to determine the effect of systemic iron deficiency, via an iron deficient diet, on knee OA in an animal model.Methods:

Twelve-week-old male Hartley guinea pigs received the standard diet (n = 6) or a diet devoid of iron (n = 6) for 19-weeks. Iron levels were determined in the serum, liver, and articular cartilage. Knees were collected to assess structural changes related to OA (microcomputed tomography, histopa-thology). Immunohistochemistry was performed to evaluate the presence and distribution of a disintegrin and metalloproteinase with thrombospondin motifs 4 (ADAMTS4) and ROS-driven 4-hydroxynonenal (4-HNE)-induced protein adducts. Transcript expression was also assessed.Results: Relative to control animals, an iron deficient diet reduced the concentration of this mineral in serum, liver, and articular cartilage. Iron deficient animals had lower histologic OA scores; decreased subchondral bone mineral density was also noted. This reduction in knee joint pathology was accom-panied by a decrease in: ADAMTS4 in synovium; and 4-HNE protein adducts from lipid peroxidation in both the menisci and articular cartilage of iron deficient animals. Expression of iron-related genes in these tissues was also altered in treated animals.Conclusions: Results from this study suggest that systemic iron levels may play a role in knee OA pathogenesis, with a short-term deficit in dietary iron reducing the severity of knee cartilage lesions. (c) 2022 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
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NR 50
TC 8
Z9 9
U1 1
U2 7
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
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WC Orthopedics; Rheumatology
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AU Wang, Z
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AF Wang, Zhe
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TI Effects of urolithin A on osteoclast differentiation induced by receptor activator of nuclear factor-κB ligand via bone morphogenic protein 2
SO BIOENGINEERED
LA English
DT Article
DE RAW264; 7 cells; osteoclast; urolithin A; RANKL; BMP2; transcriptome sequencing
ID stimulates osteoblastic differentiation; rankl-induced osteoclast; osteogenic differentiation; raw264.7 cells; dc-stamp; osteoporosis; apoptosis; phosphatase; erk1/2; model
AB Urolithin A (UA) is an intestinal microbial metabolite derived from ellagitannins and a promising agent for treating osteoarthritis. However, its effects on osteoporosis are unclear. This study explored the effects of urolithin A (UA) on receptor activator of nuclear factor-kappa B ligand (RANKL)-induced osteoclasts and its underlying molecular mechanisms. RANKL treatment significantly increased tartrate-resistant acid phosphatase (TRACP) or osteoclast marker levels ($P < 0.05$), while adding UA decreased the RANKL-induced levels ($P < 0.05$) in RAW264.7 cells. Total RNA isolated from RANKL- or RANKL + UA-treated cells was sequenced, and the obtained transcriptome dataset revealed 2,399 differentially expressed genes. They were enriched in multiple pathways involved in rheumatoid arthritis, ERK1 and ERK2 cascade, regulation of inflammatory response, ECM-receptor interactions, and TNF signaling. Scanning electron microscopy showed that RANKL promoted bone resorption pits in bone biopsy specimens, whereas UA inhibited their formation. When bone morphogenic protein 2 (BMP2) was shRNA-silenced, the bone

resorption pits were restored. Moreover, while RANKL significantly enhanced the levels of p-ERK2/ERK2, p-p38/p38, p-Akt1/Akt1, p-ERK1/ERK1, and osteoclast-related proteins ($P < 0.05$), UA reduced them. BMP2 silencing also reversed the UA inhibitory effect. Thus, UA represses the RANKL-induced osteoclast differentiation of RAW264.7 cells by regulating Akt1, p38, and ERK1/2 signaling, and BMP2 likely reverses the UA inhibitory effect via these pathways. We propose BMP2 as a potential drug target for treating bone metabolic diseases, such as osteoporosis.
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NR 59
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PU TAYLOR & FRANCIS INC
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TI Regulatory of miRNAs in tri-lineage differentiation of C3H10T1/2
SO STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE Adipogenic differentiation; Chondrogenic differentiation; 2; MicroRNA; Osteogenic differentiation
ID mesenchymal stem-cells; bone morphogenetic protein-2; osteogenic differentiation; chondrogenic differentiation; adipose-tissue; adipocyte differentiation; signaling pathway; gene-expression; rna; adipogenesis
AB MicroRNAs (miRNAs) are non-coding single-stranded RNA molecules encoded by endogenous genes, which play a vital role in cell generation, metabolism, apoptosis and stem cell differentiation. C3H10T1/2, a mesenchymal cell extracted from mouse embryos, is capable of osteogenic differentiation, adipogenic differentiation and chondrogenic differentiation. Extensive studies have shown that not only miRNAs can directly trigger targeted genes to regulate the tri-lineage differentiation of C3H10T1/2, but it also can indirectly regulate the differentiation by triggering different signaling pathways or various downstream molecules. This paper aims to clarify the regulatory roles of different miRNAs on C3H10T1/2 differentiation, and discussing their balance effect among osteogenic differentiation, adipogenic differentiation and chondrogenic differentiation of C3H10T1/2. We also review the biogenesis of miRNAs, Wnt signaling pathways, MAPK signaling pathways and BMP signaling pathways and provide some specific examples of how these signaling pathways act on C3H10T1/2 tri-lineage differentiation. On this basis, we hope that a deeper understanding of the differentiation and regulation mechanism of miRNAs in C3H10T1/2 can provide a promising therapeutic method for the clinical treatment of bone defects, osteoporosis, osteoarthritis and other diseases.
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NR 161
TC 7
Z9 8
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U2 24
PU BMC
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J9 STEM CELL RES THER
JI Stem Cell Res. Ther.
PD NOV 22
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DI 10.1186/s13287-022-03205-3
PG 24
WC Cell & Tissue Engineering; Cell Biology; Medicine, Research & Experimental
SC Cell Biology; Research & Experimental Medicine
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AU Schwendich, E
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TI Modulation of Dopamine Receptors on Osteoblasts as a Possible Therapeutic Strategy for Inducing Bone Formation in Arthritis
SO CELLS
LA English
DT Article
DE rheumatoid arthritis; dopamine; osteoblast; osteoclasts; mineralization
ID rheumatoid-arthritis; cells; disease; neurobiology; expression
AB Rheumatoid arthritis (RA) is associated with systemic osteoporosis, which leads to severe disability and low quality of life. Current therapies target osteoclasts to reduce bone degradation, but more treatment options would be required to promote bone protection by acting directly on osteoblasts (OB). Recently, the local production of dopamine in inflamed joints of RA has been observed. Thus, in this project, we aimed to determine the implication of the neurotransmitter dopamine in the bone formation process in RA. Dopamine receptors (DR) in the human bone tissue of RA or osteoarthritis (OA) patients were examined by immunohistochemistry. DR in isolated human osteoblasts (OB) was analyzed by flow cytometry, and dopamine content was evaluated by ELISA. Osteoclasts (OC)

were differentiated from the PBMCs of healthy controls (HC) and RA patients. Isolated cells were treated with specific dopamine agonists. The effect of dopamine on mineralization was evaluated by Alizarin red staining. Cytokine release in supernatants was measured by ELISA. Osteoclastogenesis was evaluated with TRAP staining. OC markers were analyzed via real-time PCR and bone resorption via staining of resorption pits with toluidine blue. All DR were observed in bone tissue, especially in the bone remodeling area. Isolated OB maintained DR expression, which allowed their study in vitro. Isolated OB expressed tyrosine hydroxylase, the rate-limiting enzyme for dopamine production, and contained dopamine. The activation of D2-like DR significantly increased bone mineralization in RA osteoblasts and increased osteoclastogenesis but did not alter the expression of OC markers nor bone resorption. DR were found in the bone remodeling area of human bone tissue and dopamine can be produced by osteoblasts themselves, thus suggesting a local autocrine/paracrine pathway of dopamine in the bone. D2-like DRs are responsible for bone mineralization in osteoblasts from RA patients without an increase in bone resorption, thus suggesting the D2-like DR pathway as a possible future therapeutic target to counteract bone resorption in arthritis.
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NR 46
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Z9 13
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J9 CELLS-BASEL
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WC Cell Biology
SC Cell Biology
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AF Zeng, Zhipeng
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Guo, Jianmin
Wang, Ping
Yang, Yajing
TI Mitophagy-A New Target of Bone Disease
SO BIOMOLECULES
LA English
DT Review
DE mitophagy; osteoarthritis; intervertebral disc degeneration; osteoporosis; osteosarcoma
ID nucleus pulposus cells; intervertebral disc degeneration; mitochondrial dysfunction; regulates autophagy; therapeutic target; oxidative stress; in-vitro; apoptosis; osteosarcoma; inhibition
AB Bone diseases are usually caused by abnormal metabolism and death of cells in bones, including osteoblasts, osteoclasts, osteocytes, chondrocytes, and bone marrow mesenchymal stem cells. Mitochondrial dysfunction, as an important cause of abnormal cell metabolism, is widely involved in the occurrence and progression of multiple bone diseases, including osteoarthritis, intervertebral disc degeneration, osteoporosis, and osteosarcoma. As selective mitochondrial autophagy for damaged or dysfunctional mitochondria, mitophagy is closely related to mitochondrial quality control and homeostasis. Accumulating evidence suggests that mitophagy plays an important regulatory role in bone disease, indicating that regulating the level of mitophagy may be a new strategy for bone-related diseases. Therefore, by reviewing the relevant literature in recent years, this paper reviews

the potential mechanism of mitophagy in bone-related diseases, including osteoarthritis, intervertebral disc degeneration, osteoporosis, and osteosarcoma, to provide a theoretical basis for the related research of mitophagy in bone diseases.
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NR 165
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U2 61
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TI Senescence-accelerated mice prone 8 (SAMP8) in male as a spontaneous osteoarthritis model
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Article
DE Osteoarthritis; Aging; Mouse models; Subchondral bone; Meniscus
ID cellular senescence; senile osteoporosis; subchondral bone; marrow injection; knee-joint; mouse; cells; pathogenesis
AB Background Animal models of spontaneous osteoarthritis (OA) are sparse and not well characterized. The purpose of the present study is to examine OA-related changes and mechanisms in senescence-accelerated mouse prone 8 (SAMP8) that displays a phenotype of accelerated aging. Methods Knees of male SAMP8 and SAM-resistant 1 (SAMR1) mice as control from 6 to 33 weeks of age were evaluated by histological grading systems for joint tissues (cartilage, meniscus, synovium, and subchondral bone), and mu CT analysis. Gene expression patterns in articular cartilage were analyzed by real-time PCR. Immunohistochemistry was performed for OA-related factors, senescence markers, and apoptosis. Results Starting at 14 weeks of age, SAMP8 exhibited mild OA-like changes such as proteoglycan loss and cartilage fibrillation. From 18 to 33 weeks of age, SAMP8 progressed to partial or full-thickness defects with exposure of subchondral bone on the medial tibia

and exhibited synovitis. Histological scoring indicated significantly more severe OA in SAMP8 compared with SAMR1 from 14 weeks [median (interquartile range): SAMR1: 0.89 (0.56-1.81) vs SAMP8: 1.78 (1.35-4.62)] to 33 weeks of age [SAMR1: 1.67 (1.61-1.04) vs SAMP8: 13.03 (12.26-13.57)]. Subchondral bone sclerosis in the medial tibia, bone mineral density (BMD) loss of femoral metaphysis, and meniscus degeneration occurred much earlier than the onset of cartilage degeneration in SAMP8 at 14 weeks of age. Conclusions SAMP8 are a spontaneous OA model that is useful for investigating the pathogenesis of primary OA and evaluating therapeutic interventions.
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TI Trends in osteoporosis prevalence over a 10-year period in Japan: the ROAD study 2005-2015
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Osteoporosis; Prevalence; Secular trend; Population-based cohort study; ROAD study
AB Introduction This study aimed to clarify the trends in the prevalence of osteoporosis among general inhabitants using population-based cohort data of the baseline and the survey 10 years later. Materials and Methods The baseline survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study was conducted in 2005-2007; 1690 participants (596 men, 1094 women, mean age 65.2 years) completed all examinations of osteoporosis, including a questionnaire of medical information in the present/past and bone mineral density measurement using dual-energy absorptiometry. The fourth survey was performed in 2015-2016; 1906 individuals (637 men, 1269 women, 65.0 years) completed assessments identical to those at the baseline survey. Osteoporosis was defined using the World Health Organization criteria. Results The prevalence of lumbar spine (L2-L4) osteoporosis at the baseline survey was 13.6% (men, 3.4%; women, 19.2%) and that at the fourth survey was 9.7% (men, 1.4%; women, 13.9%), which decreased significantly ($p < 0.01$), while that of the femoral neck was not significantly different between the baseline and fourth surveys. Regarding the prevalence of osteoporosis of L2-L4 or the femoral neck, the prevalence of osteoporosis in women aged >= 70 was 38.8% at the fourth survey and 48.9% at the baseline study; thus, the prevalence at the fourth survey was significantly lower than that at the baseline survey ($p < 0.01$). Conclusions In the population-based survey with a 10-year interval, the prevalence of osteoporosis at lumbar spine tended to decrease significantly. This preferable change in osteoporosis could contribute to the decrease in the occurrence of osteoporotic fracture in the future.
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U2 4
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TI The effects of fisetin on bone and cartilage: A systematic review

SO PHARMACOLOGICAL RESEARCH
LA English
DT Review
DE Fisetin; Aging; Osteoporosis; Osteoarthritis
ID signaling pathway; osteoarthritis; osteoporosis; differentiation; sirt1; osteogenesis; inhibition; apoptosis; diagnosis
AB As the worldwide population progresses in age, there is an increasing need for effective treatments for age-associated musculoskeletal conditions such as osteoporosis and osteoarthritis (OA). Fisetin, a natural flavonoid, has garnered attention as a promising pharmaceutical option for treating or delaying the progression of osteoporosis and OA. However, there is no systematic review of the effects of fisetin on bone and cartilage. The aim of this review is to report the latest evidence on the effects of fisetin on bone and cartilage, with a focus on clinical significance. The PubMed, Embase, and Cochrane Library databases were searched up to December 9th 2021 to evaluate the effects of fisetin on bone and cartilage in in vitro studies and in vivo preclinical animal studies. The risk of bias, quality, study design, sample characteristics, dose and duration of fisetin treatment, and outcomes of the 13 eligible studies were analyzed in this systematic review. Qualitative evaluation was conducted for each study due to differences in animal species, cell type, created disease model, dose and duration of fisetin treatment, and time between intervention and assessment among the eligible studies. The beneficial effects of fisetin on osteoporosis have been demonstrated in in vitro and in vivo preclinical studies across animal species. Similarly, the beneficial effects of fisetin on OA have been demonstrated in in vivo preclinical animal studies, but the reports on OA are still limited. Fisetin, a natural supplement can be use in orthobiologics treatment, as adjuvant to orthopaedic surgery, to improve clinical outcome.
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TI Thermogravimetric analysis of cancellous bone of humerus head in patients

undergoing total shoulder arthroplasty
SO JOURNAL OF THERMAL ANALYSIS AND CALORIMETRY
LA English
DT Article
DE Thermogravimetry; Humerus head; Cancellous bone; Rotator cuff tear; Arthropathy; Trauma; Reversed shoulder replacement
ID subchondral bone; avascular necrosis; osteoarthritis; classification
AB Prior to shoulder replacement, the quality of cancellous bone stock of humerus head should be evaluated. Thermogravimetric analysis (TGA) has already been utilized to assess thermal stability of cancellous bone mineral, collected from the femoral head of patients with osteoarthritis and osteoporosis. Our workgroup has recently examined the thermal parameters of rotator cuff of patients undergoing reversed shoulder replacement. We hypothesized that TGA of humerus head would indicate difference in the bone quality of orthopedic and trauma patients. We also hypothesized that the calorimetric data could correlate with the grade of degenerative changes. Cylindrical subchondral humeral head samples were collected from patients subjected to reversed shoulder replacement due to orthopedic or trauma indications. Then, calorimetric parameters were measured using DTA/TG analysis. Radiological evaluation was also performed to classify the grade of osteoarthritis. In case of orthopedic samples, the calorimetric parameters indicated a moderate to severe degree of bone damage and loss of mineralization, because of the progressed osteoarthritis. Meanwhile, the trauma samples exhibited only moderate or minimal subchondral bone degeneration. DTA curves showed different patterns and indicated shifts in transition temperatures, comparing control and pathologic samples. In addition, correlation was found between the degree of osteoarthritis and calorimetric enthalpy. DTA/TG analysis of humerus head samples indicated marked differences in bone quality of orthopedic and trauma patients. Further investigation is needed to differentiate the calorimetric parameters of different layers of subchondral bone.
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TI Interdisciplinary management of FGF23-related phosphate wasting syndromes: a Consensus Statement on the evaluation, diagnosis and care of patients with X-linked hypophosphataemia
SO NATURE REVIEWS ENDOCRINOLOGY
LA English
DT Article
ID fibroblast-growth factor-23; d-resistant rickets; mineral ion homeostasis; iron-deficiency anemia; vitamin-d metabolites; conventional therapy; genetic-disorders; automated-assay; guided growth; clinical-use
AB This Consensus Statement provides robust clinical evidence on the multidisciplinary management of children and adults with X-linked hypophosphataemia, with an emphasis on patients' experiences and needs. It is the

outcome of a working group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases. X-linked hypophosphataemia (XLH) is the most frequent cause of hypophosphataemia-associated rickets of genetic origin and is associated with high levels of the phosphaturic hormone fibroblast growth factor 23 (FGF23). In addition to rickets and osteomalacia, patients with XLH have a heavy disease burden with enthesopathies, osteoarthritis, pseudofractures and dental complications, all of which contribute to reduced quality of life. This Consensus Statement presents the outcomes of a working group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases, and provides robust clinical evidence on management in XLH, with an emphasis on patients' experiences and needs. During growth, conventional treatment with phosphate supplements and active vitamin D metabolites (such as calcitriol) improves growth, ameliorates leg deformities and dental manifestations, and reduces pain. The continuation of conventional treatment in symptom-free adults is still debated. A novel therapeutic approach is the monoclonal anti-FGF23 antibody burosumab. Although promising, further studies are required to clarify its long-term efficacy, particularly in adults. Given the diversity of symptoms and complications, an interdisciplinary approach to management is of paramount importance. The focus of treatment should be not only on the physical manifestations and challenges associated with XLH and other FGF23-mediated hypophosphataemia syndromes, but also on the major psychological and social impact of the disease.
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DE Selenium deficiency; Arthropathies; Kashin-Beck disease; Osteoarthritis; Rheumatoid arthritis; Osteoporosis
ID kashin-beck-disease; bone-mineral density; t-2 toxin; rheumatoid-arthritis; oxidative stress; signaling pathway; plasma selenium; endemic osteochondropathy; gene-expression; cartilage
AB Selenium, an essential trace element for human health, exerts an indispensable effect in maintaining physiological homeostasis and functions in the body. Selenium deficiency is associated with arthropathies, such as Kashin-Beck disease, rheumatoid arthritis, osteoarthritis, and osteoporosis. Selenium deficiency mainly affects the normal physiological state of bone and cartilage through oxidative stress reaction and immune reaction. This review aims to explore the role of selenium deficiency and its mechanisms existed in the pathogenesis of arthropathies. Meanwhile, this review also summarized various experiments to highlight the crucial functions of selenium in maintaining the homeostasis of bone and cartilage.
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TI Accelerated menopausal changes as human disease model 'FOCUM' for the development of osteoarthritis and other degenerative disorders: protocol for a prospective cohort study
SO BMJ OPEN
LA English
DT Article
DE Musculoskeletal disorders; INTERNAL MEDICINE; Magnetic resonance imaging
ID tendon structure; knee; classification; criteria; hand
AB IntroductionThe incidence of degenerative disorders, including osteoarthritis (OA), increases rapidly in women after menopause. However, the influence of the menopause is still insufficiently investigated due to the slowness of menopausal transition. In this study, a novel human model is used in which it is expected that menopausal-related changes will occur faster. This is the Females discontinuing

Oral Contraceptives Use at Menopausal age model. The ultimate aim is to link these changes to OA and other degenerative disorders, including cardiovascular diseases, diabetes, osteoporosis and tendinopathies.Methods and analysisThis is a pilot observational prospective cohort study with 2 years of follow-up. Fifty women aged 50-60 who use oral contraceptive (OC) and have the intention to stop are included. Measurements are performed once before stopping OC, and four times thereafter at 6 weeks, 6 months, 1 year and 2 years. At every time point, a questionnaire is filled in and a sample of blood is drawn. At the first and final time points, a physical examination, hand radiographs and a MRI scan of one knee are performed. The primary OA outcome is progression of the MRI Osteoarthritis Knee Score. Secondary OA outcomes are the development of clinical knee and hand OA, development of knee OA according to the MRI definition, and progression of radiographic features for hand OA. Principal component analysis will be used to assess which changes occur after stopping OC. Univariate and multivariate generalised estimating equation models will be used to test for associations between these components and OA.Ethics and disseminationThe study has been approved by the Medical Ethics Committee of the Erasmus MC University Medical Center Rotterdam (MEC-2019-0592). All participants must give informed consent before data collection. Results will be disseminated in national and international journals.
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TI Application of extracellular vesicles derived from mesenchymal stem cells as potential therapeutic tools in autoimmune and rheumatic diseases
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Article
DE Mesenchymal stromal cells; Exosomes; Microvesicles; Autoimmune diseases; Rheumatic diseases
ID exosm; osteoarthritis; regeneration; colitis
AB Mesenchymal stem cells (MSCs) have been proven to have superior potential to be used as therapeutic candidates in various disorders. Nevertheless, the clinical application of these cells have been restricted because of their tumorigenic properties. Increasing evidence has established that the valuable impacts of MSCs

are mainly attributable to the paracrine factors including extracellular vesicles (EVs). EVs are nanosized double-layer phospholipid membrane vesicles contain various proteins, lipids and miRNAs which mediate cell-to-cell com-munications. Due to their inferior immunogenicity and tumorigenicity, as well as easier management, EVs have drawn attention as potential cell-free replacement therapy to MSCs. For that reason, herein, we reviewed the recent findings of researches on different MSC-EVs and their effectiveness in the treatment of several autoim-mune and rheumatic diseases including multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis, osteoarthritis, osteoporosis, and systemic lupus erythematosus as well as Sjogren's syndrome, systemic sclerosis and other autoimmune diseases.
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TI Icariin promotes the repair of bone marrow mesenchymal stem cells in rabbit knee cartilage defects via the BMP/Smad pathway
SO ANNALS OF TRANSLATIONAL MEDICINE
LA English
DT Article
DE Icariin (ICA); bone marrow mesenchymal stem cell (BMSC); knee cartilage damage; BMP/Smads
ID osteogenic differentiation; morphogenetic protein-2; osteoblasts; osteoarthritis; expression; bmscs; bmp2
AB Background: Icariin (ICA) has been widely used in the treatment of osteoporosis. However, the potential mechanism of its critical role in repairing knee cartilage damage still needs to be further clarified. Methods: First, rabbit bone marrow mesenchymal stem cells (BMSCs) were isolated, cultured, and identified. Subsequently, BMSCs were treated with different concentrations of ICA. Cell Counting Kit 8 (CCK-8) and 5-ethynyl-2'-deoxyuridine (EdU) were used to evaluate the cell proliferation in each group. Alcian Blue staining, immunofluorescence, and western blotting were used to evaluate the ability of BMSCs to differentiate cartilage. In addition, a rabbit knee cartilage injury model was established. Evaluation of cartilage defects in each group was performed according to the classification system outlined by the International Cartilage Repair Society (ICRS). Hematoxylin and eosin (HE), Alcian Blue, and immunohistochemistry were used to analyze the pathological status of knee cartilage. Results: In vitro, the results showed that ICA promoted the cartilage differentiation of BMSCs as well as cell proliferation. In addition, ICA promoted the expression of type II collagen (COL2A1), aggrecan, and bone morphogenetic protein 2 (BMP2) in BMSCs, while BMP-Smad inhibitor (Noggin) reversed the repair effect of ICA on BMSCs. In vivo, our results showed that the ICRS score of the BMSC and ICA treatment group was higher. Moreover, BMSC and ICA treatment promoted the proliferation of chondrocytes and repaired the cartilage-like tissue on the surface of cartilage defect. Conclusions: The combined application of ICA and BMSCs can repair rabbit knee cartilage injury by regulating the BMP/Smads pathway, indicating that ICA and BMSCs may be a viable clinical treatment strategy for knee cartilage damage.
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TI Clinical Efficacy of Melon GliSODin® for the Treatment of Aging-Related Dysfunction in Motor Organs-A Double Blind, Randomized Placebo-Controlled Study
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE body fat percentage; locomotive syndrome; melon glisodin; osteoarthritis; osteoporosis; oxidative stress; sarcopenia; superoxide dismutase
ID superoxide-dismutase; oral supplementation; japanese people; mobility; pain
AB Background: Locomotive syndrome is a concept proposed in Japan involving decreased mobility due to osteoarthritis, osteoporosis, and sarcopenia. This double-blind, randomized study aimed to investigate the effects of superoxide dismutase (SOD)-rich melon extract (Melon GliSODin (R)) on locomotive syndrome. Methods: For 6 months, we administered oral Melon GliSODin (R) (500.4 mg/day) or a placebo to 24 and 22 women, respectively (aged 50-80 years), with knee or lower back discomfort or pain. Using baseline and 6-month data, changes in the Verbal Rating Scale and in subjective symptoms (determined using the Japanese Knee Osteoarthritis Measure, Locomo 25, the Roland-Morris Disability questionnaire, and the Chalder Fatigue Scale) were assessed, along with various oxidative markers, antioxidants, inflammatory markers, renal and liver function biochemical markers, bone metabolism markers, body composition, and motor function. Results: Oral Melon GliSODin (R) administration tended to be associated with a larger improvement in subjective symptom scores, a reduction in oxidative markers (malondialdehyde and diacron reactive oxygen metabolites) and tumor necrosis factor-alpha, and a significant increase in non-fat mass between baseline and 6 months. However, no statistically significant differences were observed between the groups for outcomes at 6 months. Conclusions: Melon GliSODin (R) tended to improve the subjective symptoms of participants who had knee or lower back pain or discomfort. Melon GliSODin (R) administration may help to prevent

the progression of locomotive syndrome. Future studies involving larger sample sizes and more stringent randomization protocols are needed to determine differences between the placebo and Melon GliSODin (R) groups.
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NR 34
TC 2
Z9 2
U1 0
U2 1
PU MDPI
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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PT J
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AF Morrison, R. J. M.
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TI The effect of vitamin D supplementation on outcomes following total hip or knee arthroplasty surgery: a rapid systematic review of current evidence
SO EFORT OPEN REVIEWS
LA English
DT Review
DE vitamin D; PROMs; THR; TKR; arthroplasty
ID d deficiency; replacement; osteoarthritis; association; prevalence; infection; recovery; tha
AB center dot Purpose: Vitamin D deficiency has been linked to poorer outcomes following hip (THR) and knee (TKR) replacement. We review the effect of peri-operative supplementation on clinical and patient-reported outcomes following THR/TKR. center dot Methods: This study was registered with PROSPERO (CRD42021238086). Searches of electronic databases were performed from inception to March 2021. All randomised, cohort, or case-controlled studies reported in English of adults undergoing THR/TKR where vitamin D supplementation was given peri-operatively and at least one outcome was reported were included. Studies reporting on vitamin D in relation to osteoporosis and hip fracture were excluded, as were conference abstracts and those involving preclinical models. Risks of bias were performed using the RoB-2 and ROBINS-I tools. center dot Results: Three studies comprising 413 TKR patients were identified; two were randomised controlled trials and one was a prospective cohort study. No studies meeting the inclusion criteria reported on the outcomes following THR. Supplementation was associated with a statistically significant reduction in the IL6:IL10 ratio at 24- and 48h following surgery, but no effect was noted on Western Ontario and McMaster Universities Osteoarthritis Index scores or the rates of falls. All studies were judged to be limited by bias, with heterogeneity in the supplementation dose and timing of administration, as well as the reported outcome measures used. center dot Discussion: Further adequately powered randomised-controlled trials using vitamin D supplementation and a specific

clinically relevant or patient-reported outcome measure are required to assess if pre-operative vitamin D insufficiency is a modifiable risk factor to improve outcomes following THR/TKR.
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Z9 11
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PT J
AU Sköld, C
Kultima, K
Freyhult, E
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AF Skold, C.
Kultima, K.
Freyhult, E.
Larsson, A.
Gordh, T.
Hailer, N. P.
Mallmin, H.
TI Effects of denosumab treatment on the expression of receptor activator of nuclear kappa-B ligand (RANKL) and TNF-receptor TNFRSF9 after total hip arthroplasty-results from a randomized placebo-controlled clinical trial
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE RANKL; Denosumab; TNFRFS9; Rebound effect; CTX; P1NP
ID bone loss; vertebral fractures; position statement; discontinuation; osteoclastogenesis; osteoporosis; management; therapy; cd137; 4-1bb
AB We investigated whether the drug denosumab modulates the inflammatory

response after total hip arthroplasty in a randomized controlled trial. Significantly increased expression of RANKL was found in patients treated with denosumab. This could provide an explanation for the rebound effect with rapid loss of BMD seen after discontinuation of denosumab treatment. Purpose To evaluate whether denosumab, a human monoclonal antibody directed against receptor activator of nuclear factor kappa-B ligand (RANKL), modulates the inflammatory response after cementless total hip arthroplasty (THA) in patients with osteoarthritis of the hip. Methods Sixty-four patients operated with cementless THA were randomized to two doses of 60-mg denosumab or placebo 1-3 days and 6 months postoperatively. Serum samples were analyzed by a multiplex extension assay detecting 92 inflammation-related proteins. Bone turnover markers were assessed. Proteins were analyzed using linear mixed effect models. Validation of conspicuous findings was performed with ELISA. Results Two proteins were significantly affected by denosumab treatment: RANKL and tumor necrosis factor receptor super family member 9 (TNFRSF9). Serum levels of RANKL were more than twice as high in the denosumab than in the placebo group 3 months after surgery (ratio 2.10, $p<0.001$). Six and 12 months after surgery, the expression of RANKL was still elevated in the denosumab-treated group (ratios 1.50, $p < 0.001$; 1.47, $p =0.002$). The expression of TNFRSF9 was lower in the denosumab group at 3 months (ratio 0.68, $p<0.001$). In the denosumab group, concentrations of bone turnover markers were substantially reduced after 3 months, remained suppressed after 6 and 12 months, but increased above baseline at 24 months after surgery. Conclusion Two subcutaneous denosumab injections 6 months apart increase RANKL and depress TNFRSF9 after THA. This provides a possible explanation for the rebound effect on bone turnover markers as well as bone mineral density (BMD) upon withdrawal of denosumab. None of the other measured markers of inflammation was influenced by denosumab treatment.
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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J9 OSTEOPOROSIS INT
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AU Lian, WS
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Re-Wen Wu
Jih-Yang Ko
TI Gut Microbiota Ecosystem Governance of Host Inflammation, Mitochondrial Respiration and Skeletal Homeostasis
SO BIOMEDICINES
LA English
DT Review
DE oxidative stress; aging; microbiota; gut dysbiosis; mitochondrial; bone and joint disease
ID disease; metabolism; dysbiosis; osteoarthritis; association; mechanisms; severity; receptor; target; cells
AB Osteoporosis and osteoarthritis account for the leading causes of musculoskeletal dysfunction in older adults. Senescent chondrocyte overburden, inflammation, oxidative stress, subcellular organelle dysfunction, and genomic instability are prominent features of these age-mediated skeletal diseases. Age-related intestinal disorders and gut dysbiosis contribute to host tissue inflammation and oxidative stress by affecting host immune responses and cell metabolism. Dysregulation of gut microflora correlates with development of osteoarthritis and osteoporosis in humans and rodents. Intestinal microorganisms produce metabolites, including short-chain fatty acids, bile acids, trimethylamine N-oxide, and liposaccharides, affecting mitochondrial function, metabolism, biogenesis, autophagy, and redox reactions in chondrocytes and bone cells to regulate joint and bone tissue homeostasis. Modulating the abundance of Lactobacillus and Bifidobacterium, or the ratio of Firmicutes and Bacteroidetes, in the gut microenvironment by probiotics or fecal microbiota transplantation is advantageous to suppress age-induced chronic inflammation and oxidative damage in musculoskeletal tissue. Supplementation with gut microbiota-derived metabolites potentially slows down development of osteoarthritis and osteoporosis. This review provides latest molecular and cellular insights into the biological significance of gut microorganisms and primary and secondary metabolites important to cartilage and bone integrity. It further highlights treatment options with probiotics or metabolites for modulating the progression of these two common skeletal disorders.
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NR 150
TC 25
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U2 38
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WC Biochemistry & Molecular Biology; Medicine, Research & Experimental; Pharmacology & Pharmacy
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TI Estrogen-Related Receptor α: A Significant Regulator and Promising Target in Bone Homeostasis and Bone Metastasis
SO MOLECULES
LA English
DT Review
DE ERR alpha; bone; osteoclast; osteoblast; bone metastasis
ID err-alpha; breast-cancer; osteoblast differentiation; osteogenic differentiation; gene-expression; orphan; activation; gamma; cells; osteoclastogenesis
AB Bone homeostasis is maintained with the balance between bone formation and bone resorption, which is involved in the functional performance of osteoblast and osteoclast. Disruption of this equilibrium usually causes bone disorders including osteoporosis, osteoarthritis, and osteosclerosis. In addition, aberrant activity of

bone also contributes to the bone metastasis that frequently occurs in the late stage of aggressive cancers. Orphan nuclear receptor estrogen-related receptor (ERR alpha) has been demonstrated to control the bone cell fate and the progression of tumor cells in bone through crosstalk with various molecules and signaling pathways. However, the defined function of this receptor in bone is inconsistent and controversial. Therefore, we summarized the latest research and conducted an overview to reveal the regulatory effect of ERR alpha on bone homeostasis and bone metastasis, this review may broaden the present understanding of the cellular and molecular model of ERR alpha and highlight its potential implication in clinical therapy.
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NR 70
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J9 MOLECULES
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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AU Suzuki, A
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TI Advanced glycation end products in musculoskeletal system and disorders
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LA English
DT Article
DE Advanced glycation end products (AGEs); RAGE; Cross-link; Diabetes mellitus; Musculoskeletal system; Musculoskeletal diseases
ID collagen cross-links; bone-mineral density; tgf-beta expression; stromal st2 cells; maillard reaction; extracellular-matrix; skeletal-muscle; nonenzymatic glycation; protein modification; neurite outgrowth
AB The human population is ageing globally, and the number of old people is increasing yearly. Diabetes is common in the elderly, and the number of diabetic patients is also increasing. Elderly and diabetic patients often have musculoskeletal disorder, which are associated with advanced glycation end products (AGEs). AGEs are heterogeneous molecules derived from non-enzymatic products of the reaction of glucose or other sugar derivatives with proteins or lipids, and many different types of AGEs have been identified. AGEs are a biomarker for ageing and for evaluating disease conditions. Fluorescence, spectroscopy, mass spectrometry, chromatography, and immunological methods are commonly used to measure AGEs, but there is no standardized evaluation method because of the heterogeneity of AGEs. The formation of AGEs is irreversible, and they accumulate in tissue, eventually causing damage. AGE accumulation has been confirmed in neuromusculoskeletal tissues, including bones, cartilage, muscles, tendons, ligaments, and nerves, where they adversely affect biomechanical properties by causing charge changes and forming cross-linkages. AGEs also bind to receptors, such as the receptor for AGEs (RAGE), and induce inflammation by intracellular signal transduction. These mechanisms cause many varied aging and diabetesrelated pathological conditions, such as osteoporosis, osteoarthritis, sarcopenia, tendinopathy, and neuropathy. Understanding of AGEs related pathomechanism may lead to develop novel methods for the prevention and therapy of such disorders which affect patients' quality of life. Herein, we critically review the current methodology used for detecting AGEs, and present potential mechanisms by which AGEs cause or exacerbate musculoskeletal disorders.

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TI Causal effects of B vitamins and homocysteine on obesity and musculoskeletal diseases: A Mendelian randomization study
SO FRONTIERS IN NUTRITION

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DT Article
DE homocysteine; musculoskeletal diseases; obesity; B vitamins; Mendelian randomization
ID body-mass index; genetic-variants; dna methylation; mthfr gene; determinants; folate; metabolism; acid; risk; hyperhomocysteinemia
AB ObjectivesAlthough homocysteine (Hcy) increases the risk of cardiovascular diseases, its effects on obesity and musculoskeletal diseases remain unclear. We performed a Mendelian randomization study to estimate the associations between Hcy and B vitamin concentrations and their effects on obesity and musculoskeletal-relevant diseases in the general population. MethodsWe selected independent single nucleotide polymorphisms of Hcy (n = 44,147), vitamin B12 (n = 45,576), vitamin B6 (n = 1864), and folate (n = 37,465) at the genome-wide significance level as instruments and applied them to the studies of summary-level data for fat and musculoskeletal phenotypes from the UK Biobank study (n = 331,117), the FinnGen consortium (n = 218,792), and other consortia. Two-sample Mendelian randomization (MR) approaches were utilized in this study. The inverse variance weighting (IVW) was adopted as the main analysis. MR-PRESSO, MR-Egger, the weighted median estimate, bidirectional MR, and multivariable MR were performed as sensitivity methods. ResultsHigher Hcy concentrations were robustly associated with an increased risk of knee osteoarthritis [odds ratio (OR) 1.119; 95% confidence interval (CI) 1.032-1.214; P = 0.007], hospital-diagnosed osteoarthritis (OR 1.178; 95% CI 1.012-1.37; P = 0.034), osteoporosis with pathological fracture (OR 1.597; 95% CI 1.036-2.46; P = 0.034), and soft tissue disorder (OR 1.069; 95% CI 1.001-1.141; P = 0.045) via an inverse variance weighting method and other MR approaches. Higher vitamin B12 levels were robustly associated with decreased body fat percentage and its subtypes (all P < 0.05). Bidirectional analyses showed no reverse causation. Multivariable MR analyses and other sensitivity analyses showed directionally similar results. ConclusionsThere exist significant causal effects of vitamin B12 in the serum and Hcy in the blood on fat and musculoskeletal diseases, respectively. These findings may have an important insight into the pathogenesis of obesity and musculoskeletal diseases and other possible future therapies.
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DE agrochemicals; crop production; personal protection; pesticide handling issues; risk
ID integrated pest-management; safety behavior; determinants; exposure; risks
AB Agriculture in the Yucatan Peninsula, Mexico, grew last year, and pesticide use problems have been reported; however, there is no information about the use and management of pesticides in farms. In this study, the main pesticides used by farmers were identified in two types of agriculture: open-air (milpa) (OA) and enclosed area (shade house and greenhouse) (EA), in order to evaluate their use and management and the related environmental and health perceptions of users. Surveys (38 questions) were applied to 39 farmers in the study area, which consisted of 14 localities in Yucatan State. The most cultivated products were habanero pepper (Capsicum chinense) for enclosed-areas and maize (Zea mays) for open-air agriculture. The use of 33 active ingredients was reported. Some of them have restrictions in Mexico (i.e., dicofol and methamidophos). Paraquat was the most used of all pesticides reported. Organophosphorus pesticides (OP) were the most used. Farmers know about the environmental and health risks related to pesticide use; however, a lack of knowledge about the misuse of these products was evident. The surveys showed deficiencies in personal protection during application and incorrect disposal of empty containers and wastes. The analysis showed that the behavior of farmers about pesticide management and their perception of damage to health and the environment were multifactorial. The results conclude that farmers' personal aspects (i.e., language, education) are the leading cause of problems associated with pesticide misuse and the lack of information and training, representing a risk for human health and the environment.

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NR 52
TC 10

Z9 11
U1 3
U2 13
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JI Rev. Int. Contam. Ambient.
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SC Environmental Sciences & Ecology
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PT J
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AF Ding, Ming
Overgaard, Soren
TI Degenerations in Global Morphometry of Cancellous Bone in Rheumatoid Arthritis, Osteoarthritis and Osteoporosis of Femoral Heads are Similar but More Severe than in Ageing Controls
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE 3-D microarchitecture; Rod- and plate-like trabeculae; Rheumatoid arthritis; Osteoarthritis; Osteoporosis; BV/TV matched
ID plate-like trabeculae; subchondral bone; mechanical-property; rod-like; microarchitecture; decomposition; women
AB We have recently revealed significant differences in microarchitectural properties (i.e. global and local morphometries) and mechanical properties between rheumatoid arthritis (RA), osteoarthritis (OA) and osteoporosis (OP) in cancellous bones. This study compared these properties with those of ageing

controls by matching bone volume fraction (BV/TV), the most important determinant for bones' mechanical properties, to investigate whether these bones have similar properties and degenerative potentials. RA, OA and OP femoral heads were harvested from patients undergoing total hip replacement surgery. The selected patients were matched by similar cancellous bone BV/TV, with seven patients in each group. Four samples were prepared from each femoral head and scanned with micro-CT to quantify microarchitectural properties and compression tested to determine mechanical properties. In terms of global morphometry, no significant differences were observed between these diseased bones. In terms of local morphometry, the number of plates in the RA group was significantly greater than that of the OP and control groups. Plate volume density in the RA group was significantly greater than in the control group. Interestingly, the ultimate stresses in the three diseased groups were 77% to 195% lower than in the control group ($p < 0.001$). Degenerations of global morphometry of cancellous bones in these diseased femoral heads are similar but more severe than in ageing controls matched by BV/TV, as evidenced by pronounced reduction in bone strength. This phenomenon suggests that some local morphometric parameters, along with other factors, such as abnormal collagen, mineralisation, erosion and microdamage, may contribute to further compromising mechanical properties.
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NR 32
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Z9 6
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TI GCTOF-MS Combined LC-QTRAP-MS/MS Reveals Metabolic Difference Between Osteoarthritis and Osteoporotic Osteoarthritis and the Intervention Effect of Erxian Decoction

SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Article
DE knee osteoarthritis; osteoporosis; metabolomics; erxian decoction; osteoporotic osteoarthritis
ID chinese herbal formula; er-xian decoction; cartilage; differentiation; osteoblast
AB PurposeOP and OA are chronic bone diseases with high incidence in the middle-aged and elderly populations. The latest research shows that the pathological environment of OP may be involved in the aggravation of the pathological process of OA, and the pathological state of OP plays an important role in the aggravation of OA pathology. EXD is a traditional Chinese medicine decoction that has been used to treat osteoporosis. Therefore, we further study whether OA will be aggravated in the OP environment and whether EXD can alleviate OA by intervening in the OP environment. The purpose of this study was to analyze the effect of OP on OA metabolites by using metabolomic methods and to explore the intervention mechanism of EXD on osteoporotic OA. MethodThirty-two SD rats were randomly divided into normal group, OA group, OP-OA group, and EXD group. EXD was administered by gavage. Histopathological evaluation of cartilage tissue was performed using Saffron fast green and HE staining. Western blot and qRT-PCR were used to detect the expression levels of chondrogenesis genes SOX9, COL2A1, and COMP in cartilage tissue. GC-TOFMS and LC-QTRAP-MS/MS metabolomics methods were used to analyze the changes of metabolites in serum samples of rats in each group. ResultThe slice results showed that the cartilage damage in the OP-OA group was more serious than that in the OA group, which was significantly relieved after EXD intervention, indicating that the cartilage damage in the OP-OA group was more severe than that in the OA group and further reduced the protein and gene expressions of cartilage markers SOX9, COL2A1, and COMP. Thirty-seven substances were identified, and gentiopicroside, emodin, quercetin, and diosmetin were analyzed as possible active components of EXD. EXD treatment significantly reduced cartilage damage and reversed the expression of these markers. Metabolomics showed that EXD attenuated cartilage destruction by modulating the expression of cystine, chenodeoxycholate, and D-Turanose, involving glycolysis/gluconeogenesis, pantothenate, and CoA biosynthesis metabolic pathways. ConclusionThe OP environment may promote the progression of OA through metabolic factors. The benign intervention of EXD in osteoporotic OA involves cystine, chenodeoxycholate, and D-Turanose, and their associated glycolysis/gluconeogenesis, pantothenate, and CoA biosynthesis metabolic pathways. Therefore, we have a deep understanding of the metabolic-related intervention of EXD in osteoporotic OA and are eager to better understand the mechanism of multi-targeted intervention of EXD in bone metabolic lesions.
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NR 41
TC 15
Z9 18
U1 1
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PU FRONTIERS MEDIA SA
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PT J
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TI Chitosan-based biomaterials for the treatment of bone disorders
SO INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES
LA English
DT Review
DE Natural polymers; Polysaccharides; Bone-related disease; Chitosan; Biomedical applications
ID drug-delivery systems; beta-tricalcium phosphate; in-vitro; hyaluronic-acid; mechanical-property; rheumatoid-arthritis; targeted delivery; tnf-alpha; biomedical applications; articular-cartilage
AB Bone is an alive and dynamic organ that is well-differentiated and originated from mesenchymal tissues. Bone undergoes continuous remodeling during the lifetime of an individual. Although knowledge regarding bones and their disorders has been constantly growing, much attention has been devoted to effective treatments that can be used, both from materials and medical performance points of view. Polymers derived from natural sources, for example polysaccharides, are generally biocompatible and are therefore considered excellent candidates for various biomedical applications. This review outlines the development of chitosan-based biomaterials for the treatment of bone disorders including bone fracture, osteoporosis, osteoarthritis, arthritis rheumatoid, and osteosarcoma. Different examples of chitosan-based formulations in the form of gels,

micro/nanoparticles, and films are discussed herein. The work also reviews recent patents and important developments related to the use of chitosan in the treatment of bone disorders. Although most of the cited research was accomplished before reaching the clinical application level, this manuscript summarizes the latest achievements within chitosan-based biomaterials used for the treatment of bone disorders and provides perspectives for future scientific activities.
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ID mesenchymal stem-cells; glucocorticoid-induced osteonecrosis; femoral-head; osteogenic differentiation; extracellular vesicles; chondrocyte apoptosis; osteoarthritis; osteoporosis; osteocyte; rna
AB Bone and joint diseases are prevalent and often fatal conditions in elderly individuals. Additionally, bone-derived cells may release exosomes that package and distribute a range of active substances, such as proteins, miRNAs, and numerous active factors, thereby facilitating material and information interchange between cells. Exososmes generated from bone may be utilized to manage bone production and resorption balance or even as biological or gene therapy carriers, depending on their properties and composition. In this review, we will discuss the composition, secretion, and uptake theory of exososmes, the role of exososmes in bone metabolism regulation, the pathogenesis and diagnosis of bone and joint diseases, and the application of exososmes in regenerative medicine. The findings will expand our understanding of the potential research and application space regarding exososmes.
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TI Advancement in the Treatment of Osteoporosis and the Effects on Bone Healing
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DT Review
DE osteoporosis; bone-related surgeries
ID atypical femoral fractures; x-ray absorptiometry; vitamin-d supplementation; lumbar interbody fusion; marrow adipose-tissue; mineral density; postmenopausal women; parathyroid-hormone; turnover markers; biochemical markers
AB Osteoporosis (OP) is a major global health concern, with aging being one of the most important risk factors. Osteoarthritis (OA) is also an age-related disorder. Patients with OP and/or OA may be treated surgically for fractures or when their quality of life is impaired. Poor bone quality due to OP can seriously complicate the stability of a bone fixation construct and/or surgical fracture treatment. This review summarizes the current knowledge on the pathophysiology of normal and osteoporotic bone healing, the effect of a bone fracture on bone turnover markers, the diagnosis of a low bone mineral density (BMD) before surgical intervention, and the effect of available anti-osteoporosis treatment. Interventions that improve bone health may enhance the probability of favorable surgical outcomes. Fracture healing and the treatment of atypical femoral fractures are also discussed.
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NR 230
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TI Comparison of the Coincidence of Osteoporosis, Fracture, Arthritis Histories, and DEXA T-Score between Monozygotic and Dizygotic Twins: A Cross-Sectional Study Using KoGES HTS Data
SO NUTRIENTS
LA English
DT Article
DE dizygotic twins; monozygotic twins; aging; bone mineral density; osteoporosis; fracture; osteoarthritis; rheumatoid arthritis; genetic factors; environmental factors
ID bone-mineral density; rheumatoid-arthritis; genetic-factors; elderly-people; healthy twin; risk; osteoarthritis; susceptibility; questionnaire; determinants
AB We explored the genetic and environmental inter-relationships among osteoporosis, fracture, arthritis, and bone mineral density concordance in monozygotic twins compared to those in dizygotic twins. This cross-sectional research assessed data of 1032 monozygotic and 242 dizygotic twin pairs aged >20 years included in the Healthy Twin Study data of the Korean Genome and Epidemiology Study between 2005 and 2014. Outcomes of interest included illness concordance and absolute differences in dual-energy X-ray absorptiometry (DEXA) T-scores. We found comparable concordances of osteoporosis, fractures, osteoarthritis, and rheumatoid arthritis between monozygotic and dizygotic twins. Medical histories of osteoporosis, fractures caused by accident or falling, osteoarthritis, and rheumatoid arthritis were not distinct between monozygotic and dizygotic twins. Accidental fracture occurrence in both monozygotic twins showed

significantly lower odds than that in dizygotic twins. Genetic influence on liability to fracture risk might thus be maintained. DEXA T-scores for bone mineral density indicated more comparable tendencies within monozygotic twin pairs than within dizygotic ones, suggesting the relative importance of genetic contribution to bone mineral density. The relative importance of genetic factors in bone mineral density is sustained between monozygotic twins; overt disease expression of osteoporosis, fractures, or arthritis may be affected by environmental factors.
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NR 43
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Z9 5
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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Huang, Xinqi
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TI CircRNA-miRNA networks in regulating bone disease
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Review
DE circRNA; miRNA; osteoarthritis; osteoporosis; osteosarcoma
ID nf-kappa-b; circular rna; oxidative stress; inflammasome activation; cartilage degradation; chondrocyte apoptosis; feedback circuitry; cell-proliferation; emerging roles; ovarian-cancer
AB Circular RNA (circRNA) is a class of endogenous noncoding RNA (ncRNA), presenting as a special covalent closed loop without a 5 ' cap or 3 ' tail, maintaining resistance to RNA exonuclease and keeping high stability. Although lowly expressed in most situations, circRNA makes an active difference in regulating physiological or pathological processes by modulating gene expression by regulation of transcription, protein, and miRNA functions through various mechanisms in particular tissues. Recent studies have demonstrated the roles of the miRNA-circRNA network in the development of several bone diseases such as osteoporosis, a multiple-mechanism disease resulting from defective bone quality and low bone mass, osteoarthritis, whose main pathomechanism is inflammation and articular cartilage degradation, as well as osteosarcoma, known as one of the most common bone cancers. However, the specific mechanism of how circRNA along with miRNA influences those diseases is not well documented, showing potential for the development of new therapies for those bone diseases.
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TI Medial tibial plateau sustaining higher physiological stress than the lateral plateau: based on 3D printing and finite element method
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DT Article
DE Knee; Femoral condyle trabeculae; 3D printing; Finite element method; Mechanical properties
ID vertebral trabecular bone; mechanical-property; articular-cartilage; cancellous bone; cortical bone; compressive property; volume fraction; knee; model; density
AB Background Medial compartment knee osteoarthritis (KOA) accounts for most KOA cases, and increased trabecular bone volume fraction (BV/TV) is one of the pathological changes in the tibial plateau of KOA. How BV/TV changes before and after the menopause and its effects on medial compartment KOA are yet to be clarified. Methods Twenty femurs from twenty 12-week-old rats were included. The operated group underwent ovariectomy (to represent the osteoporosis condition), called the O group, and the non-operated group was the normal control, called the

N group. Micro-CT scans of the femoral condyles were acquired 12 weeks after the surgery, and the volume of interest (VOI) of medial-, inter-, and lateral-condyle trabeculae were three-dimensional (3D) printed for uniaxial compression mechanical test and simulated by the finite element (FE) method. Results The results demonstrated that the O group indicated poorer trabecular architecture than the N group in three parts of the femoral condyle, especially in the intercondyle. Within the group, the BV/TV, trabecular thickness (Tb.Th), and trabecular number (Tb.N) ratios between the medial and lateral condyles were greater than 1 in both N and O groups. The medial condyle trabeculae's mechanical properties were higher than those of the lateral condyle, and this superiority appears to be broadened under osteoporotic conditions. FE modelling well reproduced these mechanical differentiations. Conclusions According to Wolff's law, the higher BV/TV and mechanical properties of the medial femoral condyle may be due to inherent imbalanced loading on the knee component. Alterations in BV/TV and their corresponding mechanical properties may accompany KOA.
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TI Mapping knowledge landscapes and emerging trends of the links between osteoarthritis and osteoporosis: A bibliometric analysis
SO FRONTIERS IN PUBLIC HEALTH
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DT Article
DE osteoarthritis; osteoporosis; bibliometric analysis; visualization; CiteSpace; VOSviewer
ID bone-mineral density; musculoskeletal diseases; european-society; subchondral bone; economic-aspects; fracture risk; management; prevention; knee; hip
AB BackgroundOsteoarthritis has the characteristics of degenerative changes in articular cartilage and secondary osteoporosis, and it is a common chronic irreversible joint disease. In addition to affecting articular cartilage, subchondral bone, joint capsule and synovial membrane also undergo pathological changes during the development of the disease. Multiple studies have revealed that patients with osteoarthritis were found to have a significantly increased risk of osteoporosis,

which also contributes to the progression of osteoarthritis. However, in the current existing studies, we found that no scholars have used bibliometric analysis in the study of the relationship between osteoarthritis and osteoporosis. From the perspective of bibliometrics, this study summarizes in detail the degree of cooperation between countries, research institutions, authors, and related journals in the field of osteoarthritis and osteoporosis research and their respective influence. In this way, the evolution of knowledge structure, the change of research focus and the hot topics with research potential in the future can be further visualized and analyzed. MethodsSearch the Web of Science core collection in Science Citation Index Expanded for articles and reviews of research on osteoarthritis and osteoporosis from 1998 to 2021. Bibliometric tools such as VOSviewer, CiteSpace, were be frequently used in our study. They are mainly used to analyze collaborations between countries, research institutions, and publication authors. Meantime, co-citation analysis of journals, co-occurrence analysis of keywords and subject categories will also be reflected in the study. ResultsAccording to the search strategy, 1,078 publications were included during the period 1998-2021. And the number of annual publications on the relationship between osteoarthritis and osteoporosis is on the rise. The United States has achieved the most and contributed the most in this field and the Boston University was the most prolific institution. For the statistical analysis of published publications, Reginster JY had the highest number of publications, while Felson DT had the highest co-citation frequency. Respectively, Osteoarthritis And Cartilage was the most productive journal in this area of research. The keywords "inflammation," "expression," and "mesenchymal stem cells" may also be the development trend and research hotspot of the future research direction in this field. ConclusionsIn our study, the relationship between osteoarthritis and osteoporosis was analyzed by using literature measurement. These analysis results can lead researchers to learn more directly about the trend in this area and provide guidance for determining popular research directions.
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TI The anti-inflammation effect of strontium ranelate on rat chondrocytes with or without IL-1β in vitro
SO EXPERIMENTAL AND THERAPEUTIC MEDICINE
LA English
DT Article
DE strontium ranelate; chondrocytes; anti-inflammation; IL-1 beta; beta-catenin
ID osteoarthritis; cartilage; expression; chondrogenesis; pathogenesis; proteases; cells; sox9
AB Temporomandibular joint osteoarthritis (TMJ-OA) is a common disease with a high level of inflammation in the joint micro-environment and cartilage degradation. Anti-inflammation and cartilage regeneration are the key therapies for TMJ-OA, but currently, there are no novel medicines or treatments that can control its pathogenic progression. Strontium ranelate (SrR) is an anti-osteoporosis drug and is now considered a promising anti-OA drug, but the anti-inflammatory effect of SrR remains to be elucidated. In the present study, the anti-inflammatory

effect of SrR in a normal or high IL-1 beta environment was observed. Cell viability under the treatment of SrR was tested using Cell Counting Kit-8. Toluidine blue staining, immunofluorescence staining, hydroxyproline assay, PCR assay and western blotting were used to detect the expression of collagen (Col)II, proteoglycans (PG) and aggrecan as a reflection of extracellular matrix synthesis and MMP-9,13 hydroxyproline was used as an inflammation indicator. IL-1 beta of 10 ng/ml was added to the culture medium as inflammation environment and the tests of those biomarkers were done again. Then, the changes in beta-catenin were also studied by immunofluorescence staining, PCR assay and western blotting to explore the possible involvement of the Wnt/beta-catenin pathway. The results showed a significant inhibition of MMP-9, MMP-13, beta-catenin and promotion of Col-II, PG and aggrecan in normal chondrocytes. The presence of IL-1 beta markedly upregulated the expression of MMP-9, MMP-13 and beta-catenin while suppressing Col-II and PG and SrR partially reversed this trend. In conclusion, SrR decreased MMPs but promoted Col-II, aggrecan and PG synthesis in rat chondrocytes with or without the presence of IL-1 beta and SrR attenuated the IL-1 beta-induced increase in beta-catenin, thus reducing the inflammatory reaction.
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TI Automated Text-Messaging After Hip Arthroscopy: A Randomized-Controlled Trial of "Post-Op Buddy"
SO ARTHROSCOPY-THE JOURNAL OF ARTHROSCOPIC AND RELATED SURGERY

LA English
DT Article
ID patient education; surgery; communication
AB Purpose: To assess an automated text-messaging system for patients after hip arthroscopy and its impact at 90 days on the Hip Disability Osteoarthritis Outcome Score Physical Function Short form (HOOS-PS, HOOS-Pain), compliance with rehabilitation guidelines, and patient satisfaction. Methods: One hundred twenty-one participants (average age 29 +/- 8.7 years, 52% female) undergoing hip arthroscopy at 2 academic institutions were prospectively enrolled and randomized to receive (1) standard perioperative communication or (2) additional automated mobile phone text messages. Inclusion criteria included ability to communicate in written English and access to a mobile phone with text-messaging capability. Patients undergoing revision surgery or simultaneous femoral or acetabular osteotomy were excluded. HOOS-PS and HOOS-Pain were collected preoperatively, and after surgery an automated mobile phone robot sent participants in the therapeutic arm intermittent text messages for 90 days. At 90 days all participants again completed HOOS-PS, HOOS-Pain, and additional survey questions on satisfaction with their experience (10-point scale), communication from the surgical team (10-point scale) and adherence to physical therapy exercises, weight-bearing guidelines, and brace use, The primary outcome assessed was a statistically significant change in HOOS-PS and HOOS-Pain; secondary outcomes included change in satisfaction, communication, and adherence to physical therapy exercises, weightbearing guidelines, or brace use. Wilcoxon rank sum was used to compare HOOS-PS and HOOS-Pain scores at 0 and 90 days. Demographic characteristics and survey variables were compared using Students t test for continuous variables and chi(2) or Fisher exact test for categorical variables as appropriate. Results: There were statistically significant and clinically relevant improvements in HOOS-PS and HOOS-Pain in both groups ($P < .05$). Subjective feedback was strongly positive, with 96% of text message participants reporting they would choose automated messages if it was offered to them again in the future. Conclusions: Ninety days of automated text messaging after hip arthroscopy failed to show a significant difference in HOOS-PS ($P = .09$), HOOS-Pain ($P = .13$), patient-reported compliance with postoperative guidelines, or satisfaction with support and communication from the surgical team.
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NR 33
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Z9 6
U1 0
U2 3
PU W B SAUNDERS CO-ELSEVIER INC
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J9 ARTHROSCOPY
JI Arthroscopy
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WC Orthopedics; Sport Sciences; Surgery
SC Orthopedics; Sport Sciences; Surgery
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PT J
AU Wan, Y
Zeng, F
Tan, H
Lu, Y
Zhang, Y
Zhao, L
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AF Wan, Y.
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TI Cost-effectiveness analyses of denosumab for osteoporosis: a systematic review
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Review
DE Cost-effectiveness; Denosumab; Osteoporosis; Systematic review
ID discrete-event simulation; postmenopausal osteoporosis; oral bisphosphonates; economic-evaluation; utility analysis; zoledronic acid; women; fractures; prevention; older
AB This paper systematically reviewed and assessed all retrievable pharmacoeconomic studies on denosumab for the treatment of osteoporosis. Denosumab was more cost-effective in patients with older age, prior fracture experience, lower BMD T-scores, and more risk factors. ESCEO-IOF guidelines were more applicable to improve the quality of pharmacoeconomic studies in osteoporosis. Introduction There are many pharmacoeconomic studies on denosumab for osteoporosis. However, the corresponding reviews are outdated or incomplete and need to be updated and refined. This article aims to systematically review and evaluate all retrievable pharmacoeconomic studies of denosumab for osteoporosis. Methods A systematic literature search was performed utilizing PubMed, EMBASE(Ovid), Proquest(EconLit), Chongqing VIP, WanFang Database, and Chinese National Knowledge Infrastructure to identify full-text articles published before September 2021. The quality of full-text articles was evaluated by the Consolidated Health Economic Evaluation Reporting Standards(CHEERS) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases International Osteoporosis Foundation guideline(ESCEO-IOF). Results In total, 21 full-text articles were eligible for inclusion. Denosumab for postmenopausal osteoporosis was not dominant compared to zoledronate and teriparatide. However, denosumab was dominant compared with strontium ranelate, raloxifene, and ibandronate in patients over 65 years. The probabilities of denosumab being cost-effective or dominant were more than 85% compared with no treatment and risedronate in patients aged over 70 years. Compared to alendronate, the highest rate of denosumab dominance occurred in patients aged 65 to 75 years, at about 65%. Most of the articles had higher CHEERS scores than ESCEO-IOF scores (converted into percentages). Conclusions The cost-effectiveness of denosumab for the treatment of osteoporosis was influenced by multiple factors. Generally, denosumab was more cost-effective in patients with older age, prior fracture experience, lower BMD T-scores, and more risk factors. ESCEO-IOF guidelines were more applicable to

improve the transparency, generalization, and quality of pharmacoeconomic studies in osteoporosis.
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NR 55

TC 17
Z9 22
U1 1
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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JI Osteoporosis Int.
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EA JAN 2022
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA 0M8WV
UT WOS:000744765000001
PM 35059777
DA 2026-02-10
ER

PT J
AU Menz, HB
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AF Menz, Hylton B.
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TI Identification of Radiographic Foot Osteoarthritis: Sensitivity of Views and

Features Using the La Trobe Radiographic Atlas
SO ARTHRITIS CARE & RESEARCH
LA English
DT Article
AB Objective To compare the sensitivity of alternative case finding approaches for the identification of foot osteoarthritis (OA) based on the La Trobe radiographic atlas. Methods This was a cross-sectional study of 533 adults age >= 50 years with foot pain in the past year. Weightbearing dorsoplantar (DP) and lateral radiographs were taken of both feet. The La Trobe radiographic atlas was used to document the presence of osteophytes (OPs) and joint space narrowing (JSN). The prevalence of OA in each joint was documented using both views and features in combination (as recommended in the original atlas), and by using a single view (DP or lateral only) and a single feature (OP or JSN only). Results Compared to the recommended case definition based on OPs and JSN using both views, a DP-only view identified between 15% and 77% of OA cases, while a lateral-only view identified between 28% and 97% of OA cases. Compared to the recommended case definition of using both features, using only OPs identified between 46% and 94% of OA cases, while using only JSN identified between 19% and 76% of OA cases. Conclusion Applying the La Trobe radiographic atlas but using only 1 radiograph view (DP or lateral) or 1 feature (OP or JSN) in isolation misses a substantial number of OA cases, and the sensitivity of these approaches varies considerably between different foot joints. These findings indicate that, where possible, the atlas should be administered according to the original description to avoid under-ascertainment of radiographic foot OA.
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NR 14
TC 4
Z9 4
U1 0
U2 1
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 2151-464X
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J9 ARTHRIT CARE RES
JI Arthritis Care Res.
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BP 1369
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WC Rheumatology
SC Rheumatology
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Liu, Liu
Wang, Shiyong
Chen, Jiaqian
Liao, Ying
TI The Efficacy of Pulsed Electromagnetic Fields on Pain, Stiffness, and Physical Function in Osteoarthritis: A Systematic Review and Meta-Analysis
SO PAIN RESEARCH & MANAGEMENT
LA English
DT Review
ID knee osteoarthritis; double-blind; therapy; placebo; differentiation; stimulation; strength; cells; pemf
AB Background. Although there are many pharmacological interventions for adults with osteoarthritis (OA) who do not meet the indications for surgery, side effects and adverse effects cannot be ignored. Physical interventions are known for their effectiveness and safety, and pulsed electromagnetic fields (PEMFs) have already been applied to skeletal diseases such as osteoporosis. Objective. In this systematic review and meta-analysis, we aimed to assess the efficacy of PEMF on the major symptoms of patients with OA compared with efficacy of other interventions.

Methods. Randomized controlled trials (RCTs) investigating OA patients treated with PEMF and with pain, stiffness, and physical function impairment since 2009 were included. The Visual Analog Scale (VAS) and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scores were used for assessment. All extracted data were analyzed using RevMan V.5.3. Results. Eleven RCTs consisting of 614 patients were enrolled in this meta-analysis, of which 10 trials comprised knee OA and one comprised hand OA. Compared with the control groups, the PEMF treatment yielded a more favorable output. PEMF alleviated pain (standardized mean differences [SMD] = 0.71, 95% confidence interval [CI]: 0.08-1.34, p = 0.03), improved stiffness (SMD = 1.34, 95% CI: 0.45-2.23,p=0.003), and restored physical function (SMD = 1.52, 95% CI: 0.49-2.55,p=0.004). Conclusions. PEMF therapy ameliorates OA symptoms such as pain, stiffness, and physical function in patients compared to other conservative treatments. There is an urgent need to search for different types of OA in multiple locations.
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FU National Natural Science Foundation of China [81804155]; National Natural Science Foundation of Hunan Province [2021JJ30615, 2021JJ40507]; Hunan

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PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1203-6765
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J9 PAIN RES MANAG
JI Pain Res. Manag.
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WC Clinical Neurology
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PT J
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TI P62/SQSTM1 beyond Autophagy: Physiological Role and Therapeutic Applications in Laboratory and Domestic Animals
SO LIFE-BASEL
LA English
DT Review
DE p62; SQSTM1; inflammation; aging; inflammatory diseases; degenerative diseases
ID canine mammary-tumors; poor-prognosis; dna vaccine; protein p62; disease; dogs; osteoarthritis; degeneration; inflammation; mutation
AB Inflammation is the preceding condition for the development of mild and severe pathological conditions, including various forms of osteopenia, cancer, metabolic syndromes, neurological disorders, atherosclerosis, cardiovascular, lung diseases, etc., in human and animals. The inflammatory status is induced by multifarious intracellular signaling cascades, where cytokines, chemokines, arachidonic acid metabolites, adhesion molecules, immune cells and other components foster a "slow burn" at a local or systemic level. Assuming that countering inflammation limits the development of inflammation-based diseases, a series of new side-effects-free therapies was assessed in experimental and domestic animals. Within the targets of the drug candidates for quenching inflammation, an archetypal autophagic gear, the p62/sqstm1 protein, has currently earned attention from researchers. Intracellular p62 has been recently coined as a multi-task tool associated with autophagy, bone remodeling, bone marrow integrity, cancer progression, and the maintenance of systemic homeostasis. Accordingly, p62 can act as an effective suppressor of inflamm-aging, reducing oxidative stress and proinflammatory signals. Such an operational schedule renders this protein an effective watchdog for degenerative diseases and cancer development in laboratory and pet animals. This review summarizes the current findings concerning p62 activities as a molecular hub for cell and tissues metabolism and in a variety of inflammatory diseases and other pathological conditions. It also specifically addresses the applications of exogenous p62 (DNA plasmid) as an anti-inflammatory and homeostatic regulator in the treatment of osteoporosis, metabolic syndrome, age-related macular degeneration and cancer in animals, and the possible application of p62 plasmid in other inflammation-associated diseases.
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J9 LIFE-BASEL
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WC Biology; Microbiology
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PT J
AU Jadzic, J
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AF Jadzic, Jelena
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TI Hip structure analysis and femoral osteodensitometry in aged postmenopausal women with hip osteoarthritis and femoral neck fracture
SO INTERNATIONAL ORTHOPAEDICS
LA English
DT Article
DE Coxarthrosis; Osteoarthritis; Femoral neck fracture; Postmenopausal women; Bone mineral density; Hip structure analysis
ID bone-mineral density; osteoporosis; tomography; fragility; risk; head
AB Purpose Osteoarthritis (OA), osteoporosis, and bone fractures are frequent aging-related conditions. Regardless of the growing research interest in the effects of hip OA on femoral fracture risk, data about the region specificity of osteodensitometric and hip structure analysis (HSA) parameters of the proximal femora are lacking in aged postmenopausal women with hip OA compared to individuals with femoral neck fragility fracture. Methods This study included 76 postmenopausal women admitted for total hip arthroplasty due to non-traumatic femoral neck fracture (FN_Fx group, n = 39) and hip osteoarthritis (OA group, n =

37). Results Osteodensitometric parameters differed significantly between the OA and FN_Fx groups, depicting lower bone mineral density in the FN_Fx group ($p < 0.05$). The most significant increase in these parameters was registered in the intertrochanteric region of the OA group. Moreover, the OA-induced changes in HSA-derived parameters displayed significant regional heterogeneity, with the intertrochanteric region showing the most notable difference between OA and FN_Fx group. Conclusion Our data may indicate that OA displayed the most prominent positive effect on the intertrochanteric femoral region, revealing the regional heterogeneity in structural geometry and biomechanical indices of proximal femora in OA individuals. Since we did not observe significant differences in the femoral neck region, we may speculate that OA does not have a substantial protective effect on the femoral neck fracture risk in aged postmenopausal women.
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TI Is Osteoarthritis Always Associated with Low Bone Mineral Density in Elderly Patients?
SO MEDICINA-LITHUANIA
LA English
DT Article
DE osteoarthritis; bone mineral density; osteoporosis
ID postmenopausal women; knee osteoarthritis; radiographic osteoarthritis; inverse relationship; hand osteoarthritis; older-adults; osteoporosis; fracture; hip; risk
AB Background and Objectives: The relationship between osteoarthritis (OA) and osteoporosis (OP) has been analysed for over four decades. However, this relationship has remained controversial. Numerous observational and longitudinal studies have shown an inverse association between the two diseases and a protective effect of one against the other. On the other hand, some studies show that patients with OA have impaired bone strength and are more prone to fractures. The study's main objective was to determine the bone mineral density (BMD) of the spine and hip (femoral neck) of postmenopausal women of different ages, with radiologically determined OA of the hip and knee, as well as to determine the correlation between BMD values and age in the experimental group.

Materials and Methods: The retrospective cohort study included 7018 patients with osteoarthritis of peripheral joints and the spine, examined by a rheumatologist in an outpatient rheumatology clinic at the Institute for Treatment and Rehabilitation, Niska Banja from July 2019 to March 2021. A nested anamnestic study was conducted within the cohort study of patients, and it included two groups: an experimental group composed of 60 postmenopausal women, and a control group composed of the same number of women. Out of 120 patients, 24 did not meet the criteria for the continuation of the study (due to technical errors-radiographic and/or densitometry artefacts). Fifty-six postmenopausal women (aged 45-77 years) with hip and knee radiological OA were examined as an experimental group. The participants were divided into two subgroups according to age (45-60 years and over 61 years). The control group included 40 healthy postmenopausal women of the same age range, without radiological OA, with normal BMD of the hip and spine. All patients with OA met the American College of Radiology (ACR) criteria. OA of the hip and knee was determined radiologically according to Kellgren and Lawrence (K&L) classification, and patients were included in the study if a K&L grade of at least >= 2 was present. Hip and spine BMD was measured by dual-energy X-ray absorptiometry (DXA). Results: Compared to the control group, we found statistically significantly lower BMD and T-scores of the spine in older postmenopausal women: BMD (g/cm(2)), p = 0.014; T-score, p = 0.007, as well as of the hip: BMD (g/cm(2)), p = 0.024; T-score p < 0.001. The values of BMD and T-score of the spine and hip are lower in more severe forms of OA (X-ray stage 3 and 4, according to K&L), p < 0.001. We found negative correlation between BMD and T-score and age only for the hip: BMD (g/cm(2)), rho = 0.378, p = 0.005; T-score rho = -0.349, p = 0.010. Conclusions: Older postmenopausal women with radiographic hip and knee OA had significantly lower BMD of the hip and spine as compared to the control group without OA, pointing to the need for the prevention and treatment of OA, as well as early diagnosis, monitoring, and treatment of low bone mineral density.

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TI A Key Metabolic Regulator of Bone and Cartilage Health
SO ENDOCRINOLOGY AND METABOLISM
LA English
DT Review
DE Taurine; Osteoblasts; Osteoclasts; Osteoporosis; Cartilage; Osteoarthritis
ID mesenchymal stem-cells; taurine chloramine; oxidative stress; osteoblast differentiation; antioxidant activity; induced apoptosis; mouse model; expression; osteoporosis; mechanism
AB Taurine, a cysteine-derived zwitterionic sulfonic acid, is a common ingredient in energy drinks and is naturally found in fish and oth-er seafood. In humans, taurine is produced mainly in the liver, and it can also be obtained from food. In target tissues, such as the ret-ina, heart, and skeletal muscle, it functions as an essential antioxidant, osmolyte, and antiapoptotic agent. Taurine is also involved in energy metabolism and calcium homeostasis. Taurine plays a considerable role in bone growth and development, and high-profile reports have demonstrated the importance of its metabolism for bone health. However, these reports have not been collated for more than 10 years. Therefore, this review focuses on taurine-bone interactions and covers recently discovered aspects of taurine's effects on osteoblastogenesis, osteoclastogenesis, bone structure, and bone pathologies (e.g., osteoporosis and fracture healing), with due at-tention to the taurine-cartilage relationship.

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TI Early impairment of cartilage poroelastic properties in an animal model of ACL tear
SO ORTHOPAEDICS & TRAUMATOLOGY-SURGERY & RESEARCH
LA English
DT Article
DE Cartilage poroelasticity; Tear; ACL; Early deterioration; Post-traumatic osteoarthritis
ID anterior cruciate ligament; articular-cartilage; osteoarthritis; injury; bone
AB Background: In more than 50% of cases, anterior cruciate ligament (ACL) lesions lead to post-traumatic osteoarthritis. Ligament reconstruction stabilizes the joint, but the tear seems to impair the poroelasticity of the cartilage: synovial membrane fluid inflammation is observed 3 weeks after tearing. There have been some descriptions of visible cartilage changes, but poroelasticity has never been analyzed at this early stage. The present animal study aimed to determine (1) whether cartilage showed early poroelastic deterioration after ACL tear; (2) whether an impairment correlated with macroscopic changes; and (3) whether cartilage poroelasticity deteriorated over time. Hypothesis: In the days following trauma, cartilage poroelasticity is greatly impaired, without macro-scopically visible change. Material and methods: ACL tear was surgically induced in 18 New-Zealand rabbits. Cartilage poroelasticity was assessed on indentation-relaxation test in 3 groups: "early ", at 2 weeks postoperatively (n = 6), "mid-early " at 6 weeks (n = 6) and in a non-operated control group ("non-op "). Macroscopic changes were scored in the same groups. Results: Poroelastic impairment was greatest at the early time-point (2 weeks). Permeability ranged from a mean 0.08 +/- 0.05 x 10-15 m4/Ns (range, 0.028-0.17) in the "non-op " group to 1.03 +/- 0.60 x 10(-15) m(4)/Ns (range, 0.24-2.15) in the "early " group (p = 0.007). Shear modulus ranged from 0.53 +/- 0.11 MPa (range, 0.36-0.66) to 0.23 +/- 0.10 MPa (range, 0.12-0.43), respectively (p = 0.013). Macroscopic deterioration, on the other hand, differed significantly only between the "mid-early " and the "non-op " groups: p = 0.011 for cartilage deterioration and p = 0.008 for osteophyte formation. At the "mid-early " time point, poroelastic deterioration was less marked, with 0.33 +/- 0.33 x 10(-15) m4/Ns permeability (range, 0.06-1.06) and shear modulus 0.30 +/- 0.10 MPa (range, 0.13-0.41: respectively p = 0.039 and p = 0.023 compared to the "non -op " group. Discussion: The severe rapid deterioration in poroelasticity following ACL tear in an animal model, as notably seen in increased permeability, corresponds to changes in cartilage microstructure, with easier outflows of interstitial fluid. This

mechanical degradation may underlie onset of microcracks within the cartilage, leading to physiological loading that the cartilage by its nature is unable to repair. Further investigations are needed to correlate these experimental data with clinical findings. Level of evidence: III; comparative study with control group. (c) 2021 Published by Elsevier Masson SAS.
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TI Potential and Most Relevant Applications of Total Body PET/CT Imaging
SO CLINICAL NUCLEAR MEDICINE
LA English
DT Article
DE FDG; global disease assessment; musculoskeletal disease; NaF; total body PET; vascular disease
ID positron-emission-tomography; early-stage osteoarthritis; deep venous thrombosis; fdg pet/ct; pet/computed tomography; quantitative assessment; f-18-fluoride pet; bone; disease; cancer

AB The introduction of total body (TB) PET/CT instruments over the past 2 years has initiated a new and exciting era in medical imaging. These instruments have substantially higher sensitivity (up to 68 times) than conventional modalities and therefore allow imaging the entire body over a short period. However, we need to further refine the imaging protocols of this instrument for different indications. Total body PET will allow accurate assessment of the extent of disease, particularly, including the entire axial and appendicular skeleton. Furthermore, delayed imaging with this instrument may enhance the sensitivity of PET for some types of cancer. Also, this modality may improve the detection of venous thrombosis, a common complication of cancer and chemotherapy, in the extremities and help prevent pulmonary embolism. Total body PET allows assessment of atherosclerotic plaques throughout the body as a systematic disease. Similarly, patients with widespread musculoskeletal disorders including both oncologic and nononcologic entities, such as degenerative joint disease, rheumatoid arthritis, and osteoporosis, may benefit from the use of TB-PET. Finally, quantitative global disease assessment provided by this approach will be superior to conventional measurements, which do not reflect overall disease activity. In conclusion, TB-PET imaging may have a revolutionary impact on day-to-day practice of medicine and may become the leading imaging modality in the future.
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TI Multimodal Multidisciplinary Management of Patients with Moderate to Severe Pain in Knee Osteoarthritis: A Need to Meet Patient Expectations
SO DRUGS
LA English

DT Article
ID nonsteroidal antiinflammatory drugs; crystalline glucosamine sulfate; articular-cartilage; double-blind; celecoxib; efficacy; safety; trials; acetaminophen; metaanalysis
AB Knee osteoarthritis (OA) is one of the most common and disabling medical conditions. In the case of moderate to severe pain, a single intervention may not be sufficient to allay symptoms and improve quality of life. Examples include first-line, background therapy with symptomatic slow-acting drugs for OA (SYSADOAs) or non-steroidal anti-inflammatory drugs (NSAIDs). Therefore, the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) performed a review of a multimodal/multicomponent approach for knee OA therapy. This strategy is a particularly appropriate solution for the management of patients affected by knee OA, including those with pain and dysfunction reaching various thresholds at the different joints. The multimodal/multicomponent approach should be based, firstly, on different combinations of non-pharmacological and pharmacological interventions. Potential pharmacological combinations include SYSADOAs and NSAIDs, NSAIDs and weak opioids, and intra-articular treatments with SYSADOAs/NSAIDs. Based on the available evidence, most combined treatments provide benefit beyond single agents for the improvement of pain and other symptoms typical of knee OA, although further high-quality studies are required. In this work, we have therefore provided new, patient-centered perspectives for the management of knee OA, based on the concept that a multimodal, multicomponent, multidisciplinary approach, applied not only to non-pharmacological treatments but also to a combination of the currently available pharmacological options, will better meet the needs and expectations of patients with knee OA, who may present with various phenotypes and trajectories.
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NR 55
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U1 0
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TI Pentosan polysulfate regulates hepcidin 1-facilitated formation and function of osteoclast derived from canine bone marrow
SO PLOS ONE
LA English
DT Article
ID intracellular iron; differentiation; anemia; arthritis; activation; osteoarthritis; family; cells
AB Hepcidin which is the crucial regulator of iron homeostasis, produced in the liver in response to anemia, hypoxia, or inflammation. Recent studies have suggested that hepcidin and iron metabolism are involved in osteoporosis by inhibiting osteoblast function and promoting osteoclastogenesis. Pentosan polysulfate (PPS) is a heparin analogue and promising novel therapeutic for osteoarthritis (OA). This study was undertaken to determine whether PPS inhibits hepcidin-facilitated osteoclast (OC) differentiation and iron overload. Canine (n = 3) bone marrow mononuclear cells were differentiated to OC by macrophage colony-stimulating factor and receptor-activator of nuclear factor kappaB ligand with the treatment of hepcidin1 (200, 400, 800, 1200 nmol/L) and PPS (1, 5, 10, 20, 40 mu g/mL). Differentiation and function of OC were accessed using tartrate-resistant acid phosphate staining and bone resorption assay while monitoring ferroportin1 (FPN1) and iron concentration by immunocytochemistry. Gene expression of OC for cathepsin K (CTK), matrix metallopeptidase-9, nuclear factor of activated-T-cells cytoplasmic 1 and FPN1 was examined. Hepcidin1 showed significant enhancement of OC number at 800 nmol/L ($p<0.01$). PPS impeded hepcidin-facilitated OC at 1, 5 and 10 <mu>g/mL and reduction of resorption pits at 5 and 10 mu g/mL ($p< 0.01$). All OC specific genes were downregulated with PPS, specifically in significant manner with CTK at higher concentrations. However, heparin induced FPN1 internalization and degradation was inhibited at higher concentrations of PPS while restoring iron-releasing capability of OC. We demonstrate for the first time that PPS is a novel-inhibitor of hepcidin-facilitated OC formation/function which might be beneficial for treatment of OA and osteoporosis.
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TI Prevalence of osteoporosis and osteopenia in elderly patients scheduled for total knee arthroplasty
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article
DE Osteoporosis; Total knee arthroplasty; Osteoarthritis; Bone mineral density; DXA
ID bone-mineral density; periprosthetic bone; postmenopausal women; osteoarthritis; migration
AB Introduction Osteoporosis is a common comorbidity in elderly patients with osteoarthritis (OA) and may increase perioperative complications in orthopedic surgery (e.g., component migration, periprosthetic fractures). As there is no investigation of bone mineral density (BMD) in elderly patients prior to total knee arthroplasty (TKA) in Europe, we investigated this issue with a particular focus on a potential treatment gap. Materials and methods We assessed the BMD by dual-energy X-ray absorptiometry (DXA) in 109 consecutive elderly patients (age >= 70 years) scheduled for TKA. In addition to a detailed assessment of osteoporosis and osteopenia, the influence of clinical risk factors and radiological OA severity on BMD was evaluated using group comparisons and linear regression models. In addition, we analyzed differences in BMD between patients scheduled for TKA vs. total hip arthroplasty (THA). Results Of the included 109 patients, 19 patients (17.4%) were diagnosed with osteoporosis and 50 (45.9%) with osteopenia. In the osteoporotic patients, a clinically relevant underdiagnosis concomitant with a serious treatment gap was observed in 95.0% of the patients. Body mass index, OA grade, and glucocorticoid use were identified as independent factors associated with BMD. No differences in BMD were found between the patients scheduled for TKA vs. THA. Conclusions Considering the high prevalence of osteoporosis and osteopenia in elderly patients, DXA screening should be recommended for patients >= 70 years indicated for TKA.

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Yoshimura, Noriko
TI The discrepancy between radiographically-assessed and self-recognized hallux

valgus in a large population-based cohort
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Hallux valgus; Hallux valgus interphalangeus; Prevalence; Radiograph; Self-recognition
ID older-people; risk-factors; foot pain; interphalangeus; prevalence; falls; validation; etiology
AB Background There has been a paucity of literature revealing the discrepancy between self-recognition about hallux valgus (HV) and radiographically-evaluated foot configuration. Knowing this discrepancy will help to make a comparative review of the findings of previous literatures about epidemiological studies about the prevalence of HV. Questions/purposes (1) Is there a discrepancy between radiographically-assessed and self-recognized HV in the general population? (2) What factors affect the self-recognition of HV in the general population? Methods The fifth survey of the Research on Osteoarthritis/Osteoporosis against Disability study involved 1996 participants who had undergone anterior-posterior radiography of bilateral feet and answered a simple dichotomous questionnaire on self-recognition of HV. Measurements of the HV angle (HVA), interphalangeal angle of the hallux (IPA), and intermetatarsal angle between 1st and 2nd metatarsals (IMA) were performed using radiographs. Radiographic diagnosis of HV was done using the definition of hallux valgus angle of 20 degrees or more. After univariate comparison of the participant backgrounds and radiographic measurements between participants with or without self-recognition of HV, multivariable logistic regression analysis was conducted in order to reveal independent factors affecting self-recognition. Results Significant difference was found between the prevalence of radiographically-assessed and self-recognized HV (29.8% vs. 16.5%, $p < 0.0001$). The prevalence of self-recognized HV increased with the progression of HV severity from a single-digit percentage (normal grade, HVA < 20 degrees) up to 100% (severe grade, HVA >= 40 degrees). A multivariable logistic regression analysis demonstrated that HVA, IMA, and female sex were independent positive factors for self-recognition of HV (HVA [per 1 degrees increase]: OR, 1.18; 95% CI, 1.15-1.20; $p < 0.0001$; IMA [per 1 degrees increase]: OR, 1.15; 95% CI, 1.09-1.20; $p < 0.0001$; and female sex [vs. male sex]: OR, 3.47; 95% CI, 2.35-5.18; $p < 0.0001$). Conclusions There was a significant discrepancy between radiographically-assessed and self-recognized HV which narrowed with the progressing severity of HV. HVA, IMA, and female sex were independent positive factors for self-recognition of HV. Attention needs to be paid to potentially lowered prevalence of HV in epidemiological studies using self-reporting based on self-recognition.
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TI Engineered extracellular vesicles for bone therapy
SO NANO TODAY
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DE Extracellular vesicles; Bone therapy; Modification; Biomaterials; Nanotechnology
ID mesenchymal stem-cells; drug-delivery; global burden; stromal cells; in-vitro; osteogenic differentiation; musculoskeletal disorders; surface functionalization; click chemistry; exosm
AB Extracellular vesicles, which are secreted by living cells and play a critical role in cellular communication, have emerged as a promising cell-free strategy in the treatment of many diseases. Recently, EVs are con-sidered excellent delivery systems for various therapeutic agents, including nucleic acids, proteins, drugs, and nanomaterials, owing to their superior physiochemical stability and biocompatibility. Yet, drawbacks such as the the uncertain distribution, unfavorable therapeutic efficiency and low yields are still the pri-mary obstacles that hinder the application of EVs in the clinical. An increasing number of studies show that EVs can be "internally" engineered via cargo loading and "externally" engineered via surface modification to track their distributions, obtain scalable production and improve bone-targeting capacity for bone therapy. Herein, we provide a brief overview of the present applications and therapeutic mechanism of EVs for bone-related diseases. Thereafter, a comprehensive overview of methodological advances made recently in in-ternally and externally engineering EVs is presented. Moreover, the potential applications of modified EVs are discussed by presenting prominent examples for the treatment of osteoarthritis, osteoporosis, and bone fracture and defects, as well as the prospective engineering approaches to address these issues.(c) 2022 Elsevier Ltd. All rights reserved.
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TI Telemedicine in rheumatology care: A systematic review
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English
DT Review
DE Telemedicine; Rheumatology; Patient-reported outcomes; Quality of life; Access to care
ID face-to-face; digital divide; health-care; arthritis; telerheumatology; technology; covid-19; program
AB Objective: The COVID-19 pandemic led to a sudden uptake of telemedicine in rheumatology. We analyzed the recent published literature on telemedicine for the diagnosis and management of inflammatory, noninflammatory and/or autoimmune rheumatic diseases. Methods: We performed a registered systematic search

(CRD42020202063) for interventional or observational studies published between August 2015 and January 2022. We included studies of telemedicine that reported outcomes (e.g., satisfaction, disease activity, quality of life) in ten or more people with rheumatic disease. Reviewers screened manuscripts, extracted data, and assessed bias. Results: Of the 2,988 potentially eligible studies, 36 reports were included: 27 observational studies, 7 randomized clinical trials, and 2 controlled clinical trials. Studies focused on general rheumatology (n = 18), rheumatoid arthritis (n = 9), gout (n = 3), osteoarthritis (n = 2), unspecified inflammatory arthritis (n = 1), osteoporosis (n = 2), and systemic lupus erythematosus (n = 1). Patient satisfaction with telemedicine was the most common reported outcome (n = 23) with majority of studies demonstrating high levels of satisfaction. Among interventional studies, the effect of telemedicine on the primary outcomes varied, with most finding that telemedicine was as good as usual / in-person care for disease activity control, patient satisfaction, total societal costs, and other patient reported outcomes. Effectiveness and feasibility were high across studies, though most demonstrated a high risk of bias. Meta-analysis was not feasible given the heterogeneity of interventions and outcome instruments utilized. Conclusion: Although the number of studies to date is low, telemedicine may be an effective mode to deliver care for people with rheumatic diseases. Most studies demonstrated limitations due to study design and risk of bias. Randomized clinical studies are needed to determine best uses of telemedicine for the diagnosis and management of rheumatic conditions.
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TI Relationship between postural changes, osteoarthritis and bone mineral density in postmenopausal women
SO GYNECOLOGICAL ENDOCRINOLOGY
LA English
DT Article
DE Postural changes; osteoarthritis; osteoporosis; bone mass content; bone mineral density
ID balance; strength; quality
AB Objectives To assess the relationship between postural changes, osteoarthritis (OA) and bone mineral density (BMD) in postmenopausal women. Methods A total of 127 Brazilian women, aged 45 years or older, were included in this retrospective study. Subjects were divided in two groups: study group with postural changes (SG) and control group without postural changes (CG). Possible postural changes considered were scoliosis, kyphosis and lordosis. All women underwent BMD assessment and OA was identified at the region of the hip and lumbar spine by dual energy X-ray absorptiometry (DXA) analysis. Results SG was older (66.0 +/- 7.3 years) than the CG (61.0 +/- 8.6 years). In the entire sample we found thirteen women with OA and low BMD. Overall, the lumbar spine area was more affected by OA than the hip. The value of BMD T-score accounted for up to 77% of the changes observed in the SG group. Conclusion Postural changes identified in women are directly related to aging and associated with bone loss and joint degeneration. Postural changes may be the primary sign of frailty as a result of body adaptation to pain related to musculoskeletal diseases.
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NR 18
TC 4
Z9 4
U1 1
U2 4
PU TAYLOR & FRANCIS LTD
PI ABINGDON
PA 2-4 PARK SQUARE, MILTON PARK, ABINGDON OR14 4RN, OXON, ENGLAND
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J9 GYNECOL ENDOCRINOL
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WC Endocrinology & Metabolism; Obstetrics & Gynecology
SC Endocrinology & Metabolism; Obstetrics & Gynecology
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ER

PT J
AU Janssens, K
Verstreken, F
AF Janssens, Kathleen
Verstreken, Frederik
TI Outcome of the MatOrtho arthroplasty for PIP osteoarthritis with a minimum follow-up of two years
SO ACTA ORTHOPAEDICA BELGICA
LA English
DT Article
DE Proximal interphalangeal joint; PIP; osteoarthritis; arthroplasty; prosthesis; MatOrtho
ID proximal interphalangeal joint; surface replacement arthroplasty; implant arthroplasty; term outcm; pyrocarbon; hand; complications; reliability; prevalence; validity
AB The aim of this study is to report the early results of the MatOrtho arthroplasty, a newer generation resurfacing implant of the proximal interphalangeal joint. We performed a prospective cohort review of all MatOrtho arthroplasties implanted between 12/2013 and 05/2018 by a single surgeon at a single institution because of primary osteoarthritis, with a minimum follow-up of two years. Patient demographics, diagnosis, implant revision and other surgical interventions were recorded. Subjective and objective outcomes were evaluated, including range of motion, Patient Reported Outcome Measures and radiographic assessment. A total of 34 implants were inserted in 25 patients. Two implants were lost to follow-up. Pain scores improved significantly (mean VAS preop 7, mean VAS post-op 1, $p < 0.05$). Active range of motion improved in 83% (25/30) of joints, with a mean improvement of the total arc of motion of 25 degrees. On radiographic assessment, no signs of circumferential lucency or subsidence were observed. Additional surgery was necessary for three out of 32 implants, including implant removal in two cases. 93.75% (30/32) implants survived after a mean follow-up of 33 months. Our results confirm that at least at short term follow up, the MatOrtho PIP arthroplasty can be a successful procedure with high patient satisfaction and functional improvement.
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NR 40
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Z9 1
U1 0
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AU Xia, K
Yu, LY
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Liu, J
AF Xia, Kai
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Liu, Jun
TI Epigenetic regulation by long noncoding RNAs in osteo-/adipogenic differentiation of mesenchymal stromal cells and degenerative bone diseases
SO WORLD JOURNAL OF STEM CELLS
LA English
DT Review
DE Long noncoding RNA; Epigenetics; DNA methylation; Histones; Cell differentiation; Bone diseases
ID stem-cells; dna methylation; adipogenesis; binding; lncrna; h19; osteoarthritis; targets; tissue; genes
AB Bone is a complex tissue that undergoes constant remodeling to maintain homeostasis, which requires coordinated multilineage differentiation and proper proliferation of mesenchymal stromal cells (MSCs). Mounting evidence indicates that a disturbance of bone homeostasis can trigger degenerative bone diseases, including osteoporosis and osteoarthritis. In addition to conventional genetic modifications, epigenetic modifications (i.e., DNA methylation, histone modifications, and the expression of noncoding RNAs) are considered to be contributing factors that affect bone homeostasis. Long noncoding RNAs (lncRNAs) were previously regarded as 'transcriptional noise' with no biological functions. However, substantial evidence suggests that lncRNAs have roles in the epigenetic regulation of biological processes in MSCs and related diseases. In this review, we summarized the interactions between lncRNAs and epigenetic modifiers associated with osteo-/adipogenic differentiation of MSCs and the pathogenesis of degenerative bone diseases and highlighted promising lncRNA-based diagnostic and therapeutic targets for bone diseases.
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PT J
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TI Identification of PDXDC1 as a novel pleiotropic susceptibility locus shared between lumbar spine bone mineral density and birth weight
SO JOURNAL OF MOLECULAR MEDICINE-JMM
LA English
DT Article
DE Osteoporosis; Bone mineral density; Birth weight; Pleiotropy; Conditional false discovery rate
ID growth-factor-i; fatty-acids; binding protein; osteoporosis; association; risk; osteoarthritis; n-3; metabolism; pufas
AB An increasing number of epidemiological studies have suggested that birth weight (BW) may be a determinant of bone health later in life, although the underlying genetic mechanism remains unclear. Here, we applied a pleiotropic conditional false discovery rate (cFDR) approach to the genome-wide association study (GWAS) summary statistics for lumbar spine bone mineral density (LS BMD) and BW, aiming to identify novel susceptibility variants shared between these two traits. We detected 5 novel potential pleiotropic loci which are located at or near 7 different genes (NTAN1, PDXDC1, CACNA1G, JAG1, FAT1P1, CCDC170, ESR1), among which PDXDC1 and FAT1P1 have not previously been linked to these phenotypes. To partially validate the findings, we demonstrated that the expression of PDXDC1 was dramatically reduced in ovariectomized (OVX) mice in comparison with sham-operated (SHAM) mice in both the growth plate and trabecula bone. Furthermore, immunohistochemistry assay with serial sections showed that both osteoclasts and osteoblasts express PDXDC1, supporting its potential role in bone metabolism. In conclusion, our study provides insights into some shared genetic mechanisms for BMD and BW as well as a novel potential therapeutic target for the prevention of OP in the early stages of the disease development. Key messages We investigated pleiotropy-informed enrichment between LS BMD and BW. We identified genetic variants related to both LS BMD and BW by utilizing a cFDR approach. PDXDC1 is a novel pleiotropic gene which may be related to both LS BMD and BW. Elevated expression of PDXDC1 is related to higher BMD and lower ratio n-6/n-3 PUFA indicating a bone protective effect of PDXDC1.
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NR 49
TC 2
Z9 2
U1 0
U2 10
PU SPRINGER HEIDELBERG
PI HEIDELBERG
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WC Genetics & Heredity; Medicine, Research & Experimental
SC Genetics & Heredity; Research & Experimental Medicine
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AU Zhang, WK
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TI α-Mangostin inhibits LPS-induced bone resorption by restricting osteoclastogenesis via NE-κB and MAPK signaling
SO CHINESE MEDICINE
LA English
DT Article
DE Osteoclast; alpha-mangostin; NF-kappa B; MAPK; Osteolysis
ID pathway; activation; apoptosis; differentiation; osteoarthritis; chondrocytes; inflammation; progression; arthritis; cells
AB Background: Excessive osteoclast activation is an important cause of imbalanced bone remodeling that leads to pathological bone destruction. This is a clear feature of many osteolytic diseases such as rheumatoid arthritis, osteoporosis, and osteolysis around prostheses. Because many natural compounds have therapeutic potential for treating these diseases by suppressing osteoclast formation and function, we hypothesized that alpha-mangostin, a natural compound isolated from mangosteen, might be a promising treatment as it exhibits anti-inflammatory, anticancer, and cardioprotective effects. Methods: We evaluated the therapeutic effect of alpha-mangostin on the processes of osteoclast formation and bone resorption. The receptor activator of nuclear factor-kappa B (NF-kappa B) ligand (RANKL) induces osteoclast formation in vitro, and potential pathways of alpha-mangostin to inhibit osteoclast differentiation and function were explored. A mouse model of lipopolysaccharide-induced calvarial osteolysis was established. Subsequently, micro-computed tomography and histological assays were used to evaluate the effect of alpha-mangostin in preventing inflammatory osteolysis. Results: We found that alpha-mangostin could inhibit RANKL-induced osteoclastogenesis and reduced osteoclast-related gene expression in vitro. F-actin ring immunofluorescence and resorption pit assays indicated that alpha-mangostin also inhibited osteoclast functions. It achieved these effects by disrupting the activation of NF-kappa B/mitogen-activated protein kinase signaling pathways. Our in vivo data revealed that alpha-mangostin could protect mouse calvarial bone from osteolysis. Conclusions: Our findings demonstrate that alpha-mangostin can inhibit osteoclastogenesis both in vitro and in vivo and may be a potential option for treating osteoclast-related diseases.
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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WC Integrative & Complementary Medicine; Pharmacology & Pharmacy
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TI Patients' Perspectives on Transforming Clinical Trial Participation: Large Online Vignette-based Survey
SO JOURNAL OF MEDICAL INTERNET RESEARCH
LA English
DT Article
DE randomized controlled trial; remote trial; telemedicine; patient experience; trial participation; RCTs; participation; recruitment; patient preferences; remote medicine; pharmacological treatments
ID improve; care
AB Background: Patients' participation is crucial to the success of randomized controlled trials (RCTs). However, recruiting and retaining patients in trials remain a challenge. Objective: This study aims to describe patients' preferences for the organization of RCTs (visits on- site or remotely) and evaluate the potential impact of fulfilling preferences on their willingness to participate in a clinical trial. Methods: This was a vignette-based survey. Vignettes were case scenarios of real clinical trials assessing pharmacological treatments. These RCTs evaluated 6 prevalent chronic diseases (ie, osteoporosis, osteoarthritis, asthma, cardiovascular diseases, diabetes, and endometriosis). Each vignette described (1) the RCT and characteristics of the treatment tested (ie, doses, administration routes) and (2) the trial procedures and different options (on-site or remotely) for how the trial was organized for informed consent, follow-up visits, and communication of results when the trial was completed. We recruited 628 participants from ComPaRe (www.compare.aphp.fr), a French e-cohort of patients with chronic diseases. The outcomes were the participants' preferences for the way the trial was organized (on-site or remotely) and their willingness to participate in the trial. Results: Of the 628 participants who answered the vignettes, 491 (78.2%) were female (median age 55 years), with different chronic diseases ranging from endometriosis in 59 of 491 (12%) patients to asthma in 133 of 628 (21.2%) patients. In addition, 38 (6.1%) participants wanted to provide informed consent and all trial visits on-site, 176 (28%) wished to participate in the trial entirely remotely, and 414 (65.9%) wanted to combine remote-based and hospital-based visits. Considering the trial as a whole, when the trial was organized in a way that the patients preferred, the median (Q1-Q3) likelihood of participation in the trial was 90% (80-100) versus 60% (30-80) if the trial followed the patients' nonpreferred model. Furthermore, 256

(40.8%) patients responded to open-ended questions expressing their experience with trial participation and visits to the hospital and providing suggestions for improvement. The patients emphasized the need to personalize the way a trial is organized according to each patient's needs and conditions. Conclusions: There was a significant diversity in the participants' preferences. Most participants preferred hybrid organization involving both on-site and remote visits. Participants were more likely to participate in a trial organized according to their preferences.
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NR 34
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U1 0
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ER

PT J
AU Wu, ZY
Liu, LY
AF Wu, Zhenyu
Liu, Luying
TI The protective activity of genistein against bone and cartilage diseases
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE genistein; osteoporosis; osteoarthritis; rheumatoid arthritis; intervertebral disc degeneration
ID intervertebral disc degeneration; rheumatoid-arthritis; postmenopausal women; mineral density; soy protein; osteoclastic differentiation; phytoestrogen genistein; soybean isoflavone; ros production; estrogen
AB Genistein, a natural isoflavone rich in soybean and leguminous plants, has been shown various biological effects, such as anti-inflammation, anti-oxidation, anti-cancer, and bone/cartilage protection. Due to the structural similarity to estrogen, genistein exhibits estrogen-like activity in protecting against osteoporosis and osteoarthritis. Furthermore, genistein has been considered as an inhibitor of tyrosine kinase, which has been found to be dysregulated in the pathological development of osteoporosis, osteoarthritis, and intervertebral disc degeneration (IDD). Many signaling pathways, such as MAPK, NF-kappa B, and NRF2/HO-1, are involved in the regulatory activity of genistein in protecting against bone and cartilage diseases. The potential molecular mechanisms of genistein in therapeutic management of bone and cartilage diseases have been investigated, but remain to be fully understood. In this article, we mainly discuss the current knowledge of genistein in protecting against bone and cartilage diseases, such as osteoporosis, osteoarthritis, rheumatoid arthritis (RA), and IDD.
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TI Positron emission tomography: a horse in the musculoskeletal imaging race
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DT Article
ID f-18-sodium fluoride pet; joint inflammation; back-pain; bone; f-18-fluoride; f-18-fdg; hip; osteoarthritis; scintigraphy; diagnosis
AB Positron emission tomography (PET) has established itself as a pertinent tool in equine musculoskeletal imaging in the last few years. With the ability to provide functional information regarding both bone and soft tissues, PET has found several clinical applications in horses. PET is currently used in horses as an enhanced bone scan, providing high-resolution 3-dimensional information, in particular for imaging of the racehorse fetlock. Combined with CT and MRI, PET is particularly pertinent in horses for the assessment of subchondral bone and enthesis. The development of a dedicated PET scanner to image the distal limb of horses with standing sedation led to new applications, where PET is used as a first-line advanced imaging tool, in particular for foot, fetlock, and tarsal imaging. A complimentary clinical review of when to seek advanced imaging in equine athletes can be found in the companion Currents in One Health by Garrett in the July 2022 issue of the Journal of American Veterinary Medical Association. The clinical use of PET in human medicine remains mainly focused on oncological imaging; however, numerous small-scale clinical studies have demonstrated valuable applications for musculoskeletal imaging. These include assessment of foot and ankle pain, osteoarthritis of the knee and hip, osteoporosis, response to bisphosphonates, and chronic osteomyelitis. The use of musculoskeletal PET in dogs remains quite limited, but a few studies have recently been published and clinical interest is growing. The available research data and clinical applications between horses, humans, and dogs are currently quite disparate, but all suggest great promises for earlier and more accurate clinical diagnosis, as well as better understanding of pathophysiology and response to treatment. Translating knowledge from a species to another will undoubtedly help further growth of musculoskeletal PET.
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TI Different n-6/n-3 PUFA diets with fish oil attenuated osteoarthritis in ovariectomized mice via targeting the NLRP3 inflammasome
SO FOOD BIOSCIENCE
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DT Article
DE n-3 PUFAs; n-6 PUFAs; Osteoarthritis; Osteoporosis; Fish oil; NLRP3
ID polyunsaturated fatty-acids; n-3; omega-3-fatty-acids; osteoporosis; pathogenesis; association; metabolism; plays; model
AB Osteoporosis(OP) and osteoarthritis(OA) co-exist with increased inflammatory cytokines as a common feature. Modern diet containing high n-6/n-3 PUFA was suggested contributing to these chronic inflammatory diseases. Although fish oil (FO) rich in n-3 PUFAs has been confirmed beneficial for OA and bone loss in previous studies, whether small amounts of FO could alleviate osteoporotic OA under a high n-6/n-3 PUFA condition has not been reported. In this study, the osteoporotic OA mice were fed with 20:1 or 6:1 n-6/n-3 PUFA diets with or without FO for 12 weeks. The results showed that 20:1 diet with FO ameliorated systemic inflammation and cartilage degradation in model mice, compared to the non-FO 20:1 diet. Specifically, diets with FO altered the fatty acids composition with elevating n-3/n-6 PUFA in articular cartilage, thus restoring the cartilage homeostasis by inhibiting the catabolic process. Mechanistically, 20:1 non-FO diet promoted the expression of NLRP3 via PGE2/EP4/NF kappa B. However, 20:1 FO-H diet significantly inhibited the expression of NLRP3 and further exhibited a greater affinity for GPR120 than 20:1 non-FO diet to inactivate caspase-1-dependent NLRP3 inflammasome. As a consequence, 20:1 FO-H diet inhibited chondrocyte pyroptosis and followed by the reduction of the two catabolic cytokines: IL-1 beta

and IL-18. Notably, the 20:1 FO-H diet performed as well as the 6:1 non-FO diet, and 6:1 diet with FO could further improve osteoporotic OA in a dose-dependent manner. This study demonstrated that FO could attenuate the adverse effect of 20:1 n-6/n-3 PUFA diet on osteoporotic OA, providing skeletal evidence for healthy diet.
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U1 1
U2 28
PU ELSEVIER
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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JI Food Biosci.
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PT J
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TI Could radiofrequency echographic multispectrometry (REMS) overcome the overestimation in BMD by dual-energy X-ray absorptiometry (DXA) at the lumbar spine?
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Osteoporosis; Osteoarthritis; Vertebral fractures; Radiofrequency echographic multi-spectrometry (REMS); Dual-energy X-ray absorptiometry (DXA)
ID bone; osteoporosis; diagnosis; calcification; densitometry; fractures; artifacts; density
AB Background Osteoarthritis (OA) and vertebral fractures at the lumbar spine lead to an overestimation of bone mineral density (BMD). Recently, a new approach for osteoporosis diagnosis, defined as radiofrequency echographic multi-spectrometry (REMS), represents an innovative diagnostic tool that seems to be able to investigate bone quality and provide an estimation of fracture risk independent of BMD. The aim of this paper was to evaluate whether the use of REMS technology can favor the diagnosis of osteoporosis in subjects with an apparent increase in BMD. Methods In a cohort of 159 postmenopausal (66.2 +/- 11.6 yrs) women with overestimated BMD by DXA at the lumbar spine, we performed an echographic scan with the REMS technique. Results The mean values of BMD at different skeletal sites obtained by the DXA and REMS techniques showed that the BMD T-scores by REMS were significantly lower than those obtained by the DXA technique both at the lumbar spine ($p < 0.01$) and at all femoral subregions ($p < 0.05$). In OA subjects, the percentage of women classified as "osteoporotic" on the basis of BMD by REMS was markedly higher with respect to those classified by DXA (35.1% vs 9.3%, respectively). Similarly, the REMS allows a greater number of fractured patients to be classified as osteoporotic than DXA (58.7% vs 23.3%, respectively). Conclusions REMS technology by the analysis of native raw unfiltered ultrasound signals appears to be able to overcome the most common artifacts, such as OA and vertebral fracture of the lumbar spine, which affect the value of BMD by DXA.

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NR 28
TC 33

Z9 37
U1 0
U2 0
PU BMC
PI LONDON
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SN
EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD MAY 19
PY 2022
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IS 1
BP
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DI 10.1186/s12891-022-05430-6
PG 8
WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
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UT WOS:000798016900005
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TI Relationship between fish size and otolith size of four deep-sea fishes from the Western Bay of Bengal, India
SO INDIAN JOURNAL OF GEO-MARINE SCIENCES
LA English
DT Article

DE Deep-sea fishes; Indian water; Morphometry; Otolith; Western Bay of Bengal
ID length-weight relationships; arabian sea; lophiiformes; waters; north
AB The present study provides the otolith morphology and morphometric relationships with fish size of four deep-sea fishes (Parascombrops pellucidus Alcock, 1889, Alepocephalus blanfordii Alcock, 1892, Lamprogrammus niger Alcock, 1891, Pterygotrigla hemisticta (Temminck & Schlegel, 1843)) collected from western Bay of Bengal during March 2020. Among these, the equations were derived for the first time for three species (P. pellucidus, A. blanfordii, L. niger). Sampling was done as a part of deep-sea exploratory survey of FORV Sagar Sampada along the deeper shelf regions of the Bay of Bengal at a depth range of 200 - 1000 m using high-speed demersal trawl (HSDT-CV). The numerical relations established using regression between fish size (TL) and various otolith morphometric measurements (otolith length (OL), otolith height (OH), otolith weight (OWe), otolith area (OA) and otolith perimeter (OP)) can be used to predict the prey size in food and feeding studies for studying the food web dynamics of less-studied deep-sea fishes. LWR of the otolith of selected species showed a negative allometric growth (t-test, $p < 0.5$). The higher r(2) value (> 0.70) obtained for the relationship between fish size (TL) and various otolith morphometric measurements indicates the robustness of the model. The representative images of otoliths of these fishes will be helpful to the taxonomists for the species confirmation and reconstruction of past species assemblages in the palaeontological studies.
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AU Karim, A
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AF Karim, Asima
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TI The role of disrupted iron homeostasis in the development and progression of arthropathy
SO JOURNAL OF ORTHOPAEDIC RESEARCH

LA English
DT Review
DE cartilage degeneration; hereditary hemochromatosis; iron; osteoarthritis; oxidative stress
ID hereditary hemochromatosis; serum ferritin; genetic hemochromatosis; rheumatoid-arthritis; postmenopausal women; synovial-fluid; overload; osteoarthritis; osteoporosis; deficiency
AB Arthropathy or joint disease leads to significant pain and disability irrespective of etiology. Clinical and experimental evidence point to the presence of considerable links between arthropathy and iron overload. Previous work has suggested that iron accumulation in the joints is often associated with increased oxidative stress, disrupted matrix metabolism, and cartilage degeneration. However, key issues regarding the role of iron overload in the pathogenesis of arthropathy remain ambiguous. For example, significant gaps in our knowledge of the primary cellular targets of iron overload-induced damage and the exact molecular mechanism through which disrupted iron homeostasis leads to joint damage still exist. The exact signaling pathway that links iron metabolism and cellular damage in arthropathy also remains largely unmapped. In this review, we focus on the relationship between iron overload and arthropathy with special emphasis on the adversarial relationship between iron that accumulates in the joints over time and cartilage homeostasis. A better understanding of the mechanisms and pathways underlying iron-induced cartilage degeneration may help in defining new prognostic markers and therapeutic targets in arthropathy.
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TI Metallothionein-1 is Positively Correlated with Inflammation and Ankylosing Spondylitis Activity
SO JOURNAL OF INFLAMMATION RESEARCH
LA English
DT Article
DE metallothionein-1; ankylosing spondylitis; noninfectious inflammatory diseases; inflammation cytokines; regulatory; cytokines
ID necrosis-factor-alpha; disease-activity; tnf-alpha; gene-expression; interleukin-6; zinc; induction; il-6; prevalence; il-1-beta
AB Introduction: Ankylosing spondylitis (AS) is a common form of chronic

inflammatory rheumatic disease. Metallothionein-1 (MT-1) has been known to play an immunosuppressive role in various noninfectious inflammatory diseases, especially osteoarthritis and rheumatoid arthritis, thus inhibiting inflammation and pathogenesis in various diseases. However, whether MT-1 is related to AS is unclear. Here, we examined the levels of MT-1 in patients with AS and its correlation with the disease activity, complication, clinical indexes, and inflammatory cytokines and attempted to explain the effect of MT-1 on inflammation in AS. Methods: The messenger RNA (mRNA) and protein expression of MT-1 in patients with AS were detected through real-time polymerase chain reaction and enzyme-linked immunosorbent assay. The associations between serum MT-1 protein level and clinical indexes or proinflammatory cytokines in AS were analyzed using the Spearman correlation test. Results: The mRNAs and serum protein levels of MT-1 were significantly higher in patients with AS, especially in patients with active AS and patients with osteoporosis (OP) than in healthy controls (HCs), and no difference was observed between patients with inactive AS and HCs. Serum MT-1 levels positively correlated with disease activity, proinflammatory cytokines, and clinical indexes Ankylosing Spondylitis Disease Activity Score with C-Reactive Protein, C-reactive protein level, and erythrocyte sedimentation rate in patients with AS. Conclusion: MT-1 expression was upregulated in patients with active AS but not in those with inactive AS and positively correlated with clinical indexes, especially in OP, as well as with proinflammatory cytokines tumor necrosis factor-alpha, interleukin (IL)-1 beta, and IL-6 in patients with AS.
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NR 48
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TI Connexin43 in Musculoskeletal System: New Targets for Development and Disease Progression
SO AGING AND DISEASE
LA English
DT Article
DE liver; Connexin43; gap junction; hemichannel; musculoskeletal system; rheumatoid arthritis; osteoporosis; osteoarthritis
ID junction protein connexin-43; functional gap-junctions; kinase-c-delta; intercellular communication; articular-cartilage; skeletal development; prostaglandin e-2; fluid-flow; bone mass; osteocytic connexin-43
AB Connexin43, which is the most highly expressed connexin subtype in the musculoskeletal system, exists in a variety of bone cells, synovial tissue, and cartilage tissue. Connexin43 has been suggested to be a key regulator of bone homeostasis. Studies have shown aberrant Connexin43 expression in musculoskeletal disorders, such as osteoporosis, osteoarthritis, and rheumatoid arthritis. During cellular activities, Connexin43 can participate in the formation of functionally specific gap junctions and hemichannels and can exert independent cellular regulatory and signaling functions through special C-termini. The critical role of Connexin43 in physiological development and disease progression has been gradually revealed. In this article, the function of Connexin43 in musculoskeletal tissues is summarized, revealing the potential role of Connexin43 as a key target in

the treatment of related bone and muscle disorders and the need for further discovery.
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FU National Natural Science Foundation of China [81874030, 820 72506, 82102600]; National Key R&D Program of China [2019 YFA0111900]; Shandong Provincial Natural Science Foundation [ZR202102210485]; National Clinical Research Center for Geriatric Disorders (Xiangya Hospital) [2021 KFJJ02]; National Clinical Research Center for Orthopedics, Sports Medicine and Rehabilitation [2021-NCRC-CXJJ-PY-40]; Science and Technology Innovation Program of Hunan Province [2021 RC3025]; Provincial Natural Science Foundation of Hunan [2020JJ3060]; Provincial Clinical Medical Technology Innovation Project of Hunan [2020 SK53709]; Administration of Traditional Chinese Medicine of Hunan Province [2021075]; Guangdong Basic and Applied Basic Research Foundation [2020A151501048]; Independent Exploration and Innovation Project for Postgraduate Students of Central South University; Shenzhen Science and Technology Program [RCBS20200714114856299, JCYJ2019080616 4216661]; Innovation-Driven Project of Central South university [2020CX045]; Wu Jieping Medical Foundation [320.6750.2020-03-14]; CMA Young and Middle-aged Doctors Outstanding Development Program-Osteoporosis Specialized Scientific Research Fund Project [G-X-2019-1107-12]; [81902303]; [2021zzts1030]
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TI Scoping Review of Randomized Trials With Discontinuation of Medicines in Older Adults
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DT Review
DE Scoping review; medicine discontinuation; deprescribing; geriatric medicine
ID benign prostatic hyperplasia; double-blind; alzheimers-disease; controlled withdrawal; combination therapy; elderly-patients; 5-alpha-reductase inhibitor; furosemide withdrawal; zoledronic acid; heart-failure
AB Objectives: To map the randomized trial evidence describing the feasibility of discontinuing active medications with potential adverse effects in older patients. Design: Scoping review with systematic search of PubMed, Embase, and Cochrane Library. Setting and Participants: Randomized trials investigating discontinuation of a single medicine or medicine class in patients with mean age >= 65 years. Methods: We extracted trial characteristics including study design and assessed bias. As proxies for the "feasibility of discontinuation," we extracted the "dropout rate" and "disease recurrence rate." Results: We identified 40 trials investigating discontinuation of symptomatic (n = 26), preventive (n = 6), or both preventive and

symptomatic medicines (n = 8) against psychiatric (n = 10), neurologic (n = 9), musculoskeletal (n = 8), cardiovascular (n = 5), respiratory (n = 4), and urologic diseases (n = 4). Five discontinuation designs were used, 75% (30/40) of trials were placebo-controlled, and 48% (19/40) of trials had bias disfavoring discontinuation. The dropout rate was similar between the discontinuation group and the continuation group in 79% of the trials (30/38), whereas disease recurrence was similar in 72% (23/32) of the trials. In 42% (13/31) of trials reporting both dropout rate and disease recurrence rate, the differences between groups were statistically insignificant and less than 10%; these trials investigated discontinuation of cholinesterase inhibitors for Alzheimer's disease in various settings (n = 3), alendronate for osteoporosis (n = 3), glucosamine for osteoarthritis, lithium as adjunct for unipolar depression, statins for cardiovascular disease in patients with limited life expectancy, droxidopa for neurogenic orthostatic hypotension, tamsulosin for lower urinary tract symptoms, sertraline for major depressive episode, and fentanyl patch for low back or osteoarthritis pain. Conclusions and Implications: We identified 40 randomized trials using a variety of designs investigating discontinuation of both symptomatic and preventive medicines in older patients. Discontinuation of medicines seems feasible for most of the investigated medicines. This scoping review can guide clinical practice and future trials on deprescribing. (c) 2022 The Authors. Published by Elsevier Inc. on behalf of AMDA e The Society for Post-Acute and Long-Term Care Medicine. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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DT Review
DE mTOR; Osteosarcopenia; Rapamycin; Rapalogues; Rheumatoid arthritis; Osteoarthritis
ID renal-transplant patients; rheumatoid-arthritis; protein-synthesis; reduces severity; bone; mtor; metabolism; activation; sirolimus; osteoporosis
AB Background Preclinical studies have shown a therapeutic role of the mechanistic/mammalian target of rapamycin complex 1 (mTORC1) inhibition with rapamycin and its analogues (rapalogues) on several age-related musculoskeletal disorders (MSKD). However, the applicability to humans of these findings is unknown. Objective To assess the efficacy of rapalogues on age-related MSKD in humans. Methods We conducted a systematic review according to the PRISMA guidelines. MEDLINE, EMBase, EMCare, and Cochrane Central Registry of Controlled Trials were searched for original studies examining the effects of rapalogues on outcomes linked to the age-related MSKD in humans. This review is registered in the PROSPERO database (University of New York; registration number CRD42020208167). Results Fourteen studies met the inclusion criteria and were analyzed. The effect of rapamycin and other rapalogues, including everolimus and temsirolimus, on bone, muscle and joints have been evaluated in humans; however, considerable variability concerning the subjects' age, inclusion criteria, and drug administration protocols was identified. In bone, the use of rapamycin is associated with a decrease in bone resorption markers dependent on osteoclastic activity. In muscle, rapamycin and rapalogues are associated with a reduction in muscle protein synthesis in response to exercise. In the context of rheumatoid arthritis, rapamycin and rapalogues have been associated with clinical improvement and a decrease in inflammatory activity. Conclusion Although there are studies that have evaluated the effect of rapamycin and rapalogues on MSKD in humans, the evidence supporting its use is still incipient, and the clinical implication of these results on the development of osteoporosis, sarcopenia, or osteosarcopenia has not been studied, opening an interesting field for future research.
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NR 49
TC 9
Z9 14
U1 0
U2 6
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 1594-0667
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J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA 5Y5LT
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PT J
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AF Nicholls, Mathew
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TI Changes in prescription pain medication and intra-articular corticosteroid utilization after intra-articular bio-fermentation derived hyaluronic acid use in patients undergoing multimodal pain management
SO JOURNAL OF MEDICAL ECONOMICS
LA English
DT Article
DE Bio-fermentation derived hyaluronic acid; opioids; pain management; intra-articular hyaluronic acid; intra-articular corticosteroids
ID knee osteoarthritis; european-society; economic-aspects; adverse events; injections; osteoporosis; algorithm; efficacy; impact; time
AB Background Multiple interventions may be used to treat symptomatic knee osteoarthritis (OA), but concerns have been raised about the safety and efficacy of some therapies. Clinical trials have shown that hyaluronic acid (HA) can provide pain relief up to 6 months and possibly to 12 months, while real-world data has shown that pain medication and intra-articular corticosteroid (CS) injection utilization are reduced within 6 months after HA. Objective To examine changes in prescription pain medication and CS utilization during 1 year after multimodal therapy that included high molecular weight, bio-fermentation derived HA (Bio-HA) use for knee OA. Methods Commercial and Medicare Supplemental claims

data (IBM MarketScan Research Databases) (1 January 2012, through 31 December 2018) was used to identify unilateral Bio-HA patients using multimodal therapy (any combination of CS injection, opioids, and non-opioid pain medication). Monthly therapy utilization was compared in the 12 months after Bio-HA therapy initiation to the 4-month intra-multimodal period. Results A total of 13,999 patients underwent Bio-HA therapy with concurrent multimodal therapy. The number of filled opioid prescriptions decreased from 2,913.0/month to 2,861.5/month after Bio-HA, with a reduction in mean monthly prescriptions from 0.60 to 0.43 per user ($p < 0.001$). A number of opioid days supplied also decreased from 48,914/month to 39,730/month, with a decrease from 10.1/month to 6.0/month per user ($p < 0.001$). Bio-HA patients had prescription pain medication-free days for 71% of the time post-multimodal period compared to 53% during the intra-multimodal period ($p < 0.001$). The proportion of patients with CS injections after Bio-HA decreased from 53.8% to 29.6% ($p < 0.001$). Total monthly CS injections decreased from 2,292 to 663. Conclusions Our data suggest that high molecular weight Bio-HA, as part of multimodal therapy, may be effective in providing longer-term pain relief with the reduction in pain therapy (CS injections and opioids) and increase in prescription pain medication-free days.
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NR 34
TC 1
Z9 1
U1 0
U2 2
PU TAYLOR & FRANCIS LTD
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J9 J MED ECON
JI J. Med. Econ.
PD JAN 1
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IS 1
BP 7
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DI 10.1080/13696998.2021.2009710
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WC Economics; Health Care Sciences & Services; Health Policy & Services; Medicine, General & Internal
SC Business & Economics; Health Care Sciences & Services; General & Internal Medicine
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UT WOS:000728039700001
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TI Speculation on the pathophysiology of musculoskeletal injury with COVID-19 infection
SO FRONTIERS IN MEDICINE
LA English
DT Article
DE COVID-19; ACE2; inflammation; bone; muscle; joint
ID hip fracture; mortality; matriptase; outcm; ace2; care
AB Coronavirus disease 2019 (COVID-19) primarily affects the respiratory tract, but also many other organs and tissues, leading to different pathological pictures, such as those of the musculoskeletal tissues. The present study should be considered as a speculation on the relationship between COVID-19 infection and some frequent musculoskeletal pathologies, in particular sarcopenia, bone loss/osteoporosis (OP) and fracture risk and osteoarthritis (OA), to hypothesize how the virus acts on these

pathologies and consequently on the tissue regeneration/healing potential. The study focuses in particular on the modalities of interaction of COVID-19 with Angiotensin-Converting Enzyme 2 (ACE2) and on the "cytokine storm." Knowing the effects of COVID-19 on musculoskeletal tissues could be important also to understand if tissue regenerative/reparative capacity is compromised, especially in elderly and frail patients. We speculate that ACE2 and serine proteases together with an intense inflammation, immobilization and malnutrition could be the responsible for muscle weakness, altered bone remodeling, increase in bone fracture risk and inflammatory joint pathologies. Future preclinical and clinical studies may focus on the regenerative/reparative properties of the musculoskeletal tissues after COVID-19 infection, toward a personalized treatment usually based on scaffolds, cells, and growth factors.
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10.1016/j.csbj.2020.08.024
NR 50
TC 7
Z9 10
U1 0
U2 9
PU FRONTIERS MEDIA SA
PI LAUSANNE
PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
SN
EI 2296-858X
J9 FRONT MED-LAUSANNE
JI Front. Med.
PD JUL 14
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WC Medicine, General & Internal
SC General & Internal Medicine
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ER

PT J
AU Kapoor, V
Ghosh, MM
Chatterjee, A
Debnath, K
Hasan, GM
AF Kapoor, Vikash
Ghosh, Mriganka M.
Chatterjee, Anirban
Debnath, Kaustav
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TI Ankle and Hindfoot Alignment Changes in Advanced OA Varus Knees After Cruciate Retaining Total Knee Arthroplasty: A Prospective Cohort Study
SO INDIAN JOURNAL OF ORTHOPAEDICS
LA English

DT Article
DE Hindfoot alignment; Mechanical axis; Knee arthroplasty; Varus knee
AB Background Correct alignment of the knee is considered to be one of the most influential factors in determining the long-term outcomes after Total Knee Arthroplasty (TKA), and is believed to decrease both the mechanical and shear stresses placed on the bearing surfaces, as well as the bone/prosthesis interfaces. Compensatory malalignment of ankle and hindfoot is a recognized cause for ankle disability and deformity in long-standing osteoarthritic patients with varus deformity. This study aims to assess changes in ipsilateral ankle and hindfoot if any, pre- and post-operative TKA. Methods 65 knees of 54 patients of osteoarthritis knee were evaluated for alignment in knee, ankle and hindfoot pre- and post-TKA. Pre- and post-operative scanogram were evaluated for knee and ankle alignment. Hindfoot alignment view was used to calculate hindfoot alignment angle. All parameters were compared before TKA and after 10 weeks TKA and Wilcoxon signed rank test was used to test the significance of the values. Results Mean age of the patients was 62.9 years (49-80 years). Mean varus before surgery was 14.49 which changed to 4.01 and mean hindfoot angle valgus reduced from 9.23 to 6.62, both of which was found significant. Significant changes were also observed between pre- and post-op measurements of knee society scores, AOFAS, with improved functional outcomes both in knee and ankle. Conclusion This study reveals the radiological and functional changes occurring in the ankle and hindfoot after acute correction of long-standing varus deformity of the knee using total knee arthroplasty. Hindfoot valgus alignment in varus knees decreased significantly post-TKA without any intervention at ankle level. In cases undergoing knee arthroplasty, effect of the acute change in the alignment of the knee on the ankle and hindfoot should be taken into consideration and the amount of correction of knee alignment can be a predictor of correction of ankle and hindfoot malalignment too. The lateral benefit of improvement in ankle pain after TKA is a significant gain in this study.
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AU Geahchan, S
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TI Marine Collagen: A Promising Biomaterial for Wound Healing, Skin Anti-Aging, and Bone Regeneration
SO MARINE DRUGS
LA English
DT Article

DE marine collagen; wound healing; bone regeneration; collagen peptides; antiaging; osteoporosis; osteoarthritis; fish collagen; marine sponge
ID ultimate tensile-strength; fish collagen; extracellular-matrix; mechanical-property; scale collagen; cell-adhesion; stem-cells; peptides; differentiation; gelatin
AB Marine organisms harbor numerous bioactive substances that can be utilized in the pharmaceutical and cosmetic industries. Scientific research on various applications of collagen extracted from these organisms has become increasingly prevalent. Marine collagen can be used as a biomaterial because it is water soluble, metabolically compatible, and highly accessible. Upon review of the literature, it is evident that marine collagen is a versatile compound capable of healing skin injuries of varying severity, as well as delaying the natural human aging process. From in vitro to in vivo experiments, collagen has demonstrated its ability to invoke keratinocyte and fibroblast migration as well as vascularization of the skin. Additionally, marine collagen and derivatives have proven beneficial and useful for both osteoporosis and osteoarthritis prevention and treatment. Other bone-related diseases may also be targeted by collagen, as it is capable of increasing bone mineral density, mineral deposition, and importantly, osteoblast maturation and proliferation. In this review, we demonstrate the advantages of marine collagen over land animal sources and the biomedical applications of marine collagen related to bone and skin damage. Finally, some limitations of marine collagen are briefly discussed.
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PT J
AU Klein, GL
AF Klein, Gordon L.
TI Is calcium a link between inflammatory bone resorption and heart disease?
SO ELIFE
LA English

DT Review
DE cardiovascular disease; chronic inflammation; calcium-sensing receptor; burns; calcium
ID spinal-cord-injury; coronary-artery-disease; sensing receptor; cardiovascular-disease; burn injury; myocardial-infarction; pth secretion; up-regulation; risk; osteoarthritis
AB Several epidemiologic studies associate bone-resorbing chronic inflammatory conditions with increased risk of atherosclerotic heart disease. These include post-menopausal osteoporosis, spinal cord injury, rheumatoid arthritis, and osteoarthritis. Additional studies have noted that the use of anti-resorptive agents following hip fracture, during rheumatoid arthritis, and prior to intensive care management have resulted in reduced overall mortality and mortality from cardiovascular disorders. The careful study of burn patients has allowed us to detect that children and adolescents have a mechanism that protects them from the entry of calcium into the circulation following inflammatory bone resorption. That is, they respond to pro-inflammatory cytokines by up-regulating the parathyroid calcium-sensing receptor (CaSR) with consequent development of hypocalcemic hypoparathyroidism and hypercalciuria. As extracellular calcium appears to exacerbate and/or prolong the inflammatory response, this responsiveness of the CaSR to inflammatory cytokines may be the factor that reduces cardiovascular morbidity and mortality. In adults with chronic inflammatory conditions, the ability of the CaSR to respond to pro-inflammatory cytokines is lost, suggesting that the calcium that enters the circulation following inflammatory bone resorption may persist in the circulation, entering the small coronary blood vessels and favoring the formation of coronary artery calcification, inflammation, and consequent cardiovascular disease.
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NR 51
TC 10
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Kim, Ji-hyun
TI Predicting the incidence of age-related diseases based on biological age: The 11-year national health examination data follow-up
SO ARCHIVES OF GERONTOLOGY AND GERIATRICS
LA English
DT Article
DE Biomarkers; Biological age; Chronological age; Age-related disease; Incidence of age-related disease
ID models; mortality; index
AB Purpose: As the population ages rapidly, the incidence of age-related diseases (ARDs) is also increasing fast. Predicting the incidence of ARDs is a challenge since the rates of individual aging vary, and objective assessments of the stages of aging based on chronological age (CA) may be inaccurate. Thus, in this study, we developed a biological age (BA) model based on the National Health Examination (NHE) data and analyzed the model prediction results for the incidence of 16 ARDs. Methods: This study was based on the 2002-2019 National Health Information Databases of the National Health Insurance Service (NHIS-NHID). The data from a total of 10,002,494 subjects were selected between 2009 and 2010, and the principal component analysis (PCA) was performed to develop the BA model. The Cox -proportional hazard model was used to perform predictive analysis of the ARD incidence. Results: For the unit increase in the difference between corrected biological age (cBA) and chronological age (CA), the hazard ratios (HRs) of ARDs increased significantly for both sexes ($p < 0.001$). In descending order, the corresponding ARDs' HRs were obesity (1.655), chronic renal failure (1.362), hypertension (1.301), hyperlipidemia (1.264), diabetes mellitus (1.261), fracture (1.119), dementia (1.163), cataract (1.116), myocardial infarction (1.097), stroke (1.169), macular degeneration (1.075), osteoarthritis (1.059), osteoporosis (1.124), Parkinson's disease (1.048), and chronic obstructive pulmonary disease (1.026). Conclusions: In this study, the incidence of 16 ARDs were analyzed based on BA. Therefore, conducting the NHIS health examination can facilitate the prevention of ARDs by estimating HRs for at least 16 diseases.
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TI Interleukin-10 family members: Biology and role in the bone and joint diseases
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Article
DE Interleukin-10 family; Osteoporosis; Bone fracture; Osteoarthritis; Bone tumors
ID anti-interleukin-20 monoclonal-antibody; fibroblast-like synoviocytes; rheumatoid-arthritis; receptor activator; tnf-alpha; il-10 overexpression; interferon-lambda; iii interferons; gene-expression; tgf-beta
AB Interleukin (IL)-10 family cytokines include IL-10, IL-19, IL-20, IL-22, IL-24, IL-26, IL-28A, IL-28B, and IL-29. These cytokines play crucial regulatory roles in various biological reactions and diseases. In recent years, several studies have shown that the IL-10 family plays a vital role in bone and joint diseases, including bone metabolic diseases, fractures, osteoarthritis, rheumatoid arthritis, and bone tumors. Herein, the recent progress on the regulatory role of IL-10 family of cytokines in the occurrence and development of bone and joint diseases has been summarized. This review will provide novel directions for immunotherapy of bone and joint diseases.
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TI ActiveHip plus : A feasible mHealth system for the recovery of older adults after hip surgery during the COVID-19 pandemic
SO DIGITAL HEALTH
LA English
DT Article

DE eHealth; digital health; tele-rehabilitation; hip fracture; osteoarthritis; osteoporosis; functional status; older people; family caregivers; health providers
ID physical performance battery; quality-of-life; fracture; rehabilitation; osteoarthritis; replacement; reliability; disability; mortality; experience
AB ObjectiveHalf of older adults undergoing hip surgery do not recover their previous functional status. mHealth is a promising tool for rehabilitating older adults after hip surgery. This study aimed to test the feasibility of the ActiveHip+ mHealth system in older adults after hip surgery. MethodsSixty-nine older adults who had undergone hip surgery and their family caregivers were recruited from hospitals in Spain and Belgium and used the ActiveHip+ mHealth system for 12 weeks. Assessments were made during hospital stay and 3 months after surgery. Feasibility assessment included: adoption (participation proportion), usage (access to the app), satisfaction with the app (Net Promoter Score) and user perception of the quality of the app (Mobile App Rating Scale). Clinical assessment included: patient-reported outcomes, such as functional status (Functional Independence Measure) and performance-based outcomes, such as physical fitness (Short Physical Performance Battery). ResultsThe ActiveHip+ mHealth system obtained satisfactory feasibility results in both countries. In Spain, we observed 85% adoption, 64% usage, 8.86/10 in satisfaction with the app and 4.42/5 in perceived quality of the app. In Belgium, we observed 82% adoption, 84% usage, 5.16/10 in satisfaction with the app and 3.52/5 in app's perceived quality. The intervention had positive effects on levels of functional status, pain and physical fitness. ConclusionsThe ActiveHip+ mHealth system is a feasible tool to conduct the rehabilitation in older adults after hip surgery. Although the intervention seemed beneficial clinically, we do not recommend its implementation in clinical settings until appropriately designed randomised clinical trials confirm these results.
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NR 66
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Z9 10
U1 2
U2 24
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SN 2055-2076
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J9 DIGIT HEALTH
JI Digit. Health
PD JUN 15
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DI 10.1177/20552076221139694
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WC Health Care Sciences & Services; Health Policy & Services; Public, Environmental & Occupational Health; Medical Informatics
SC Health Care Sciences & Services; Public, Environmental & Occupational Health; Medical Informatics
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UT WOS:000927948400001
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TI Which stem in total hip arthroplasty for developmental hip dysplasia? A comparative study using a 3D CT-based software for pre-operative surgical planning
SO JOURNAL OF ORTHOPAEDICS AND TRAUMATOLOGY
LA English
DT Article
DE Single wedge; Conical tapered; Combined anteversion; Offset; Antetorsion
ID anatomy; osteoarthritis
AB Background Stem choice in total hip arthroplasty (THA) for hip dysplasia is still controversial. The aims of the study were to evaluate (1) which stem design provided the highest percentage of adequate reconstructions in THA for dysplasia and (2) any correlation between the reconstructions provided by the stems and the native femoral morphology. Materials and methods 150 CT scans including 200 adult dysplastic hips were randomly selected. Using the 3D CT-based software Hip-Op for surgical planning, the native hip anatomy was studied. Then, a single wedge tapered stem, an anatomical stem and a conical tapered stem were simulated in every hip. An adequate reconstruction of hip biomechanics was obtained when combined anteversion, offset restoration, coronal and sagittal tilt, canal filling and leg lengthening were inside the normal ranges. Results Conical stems achieved the highest percentage of adequate reconstructions (87%, $p < 0.0001$). The anatomical stem was the worst performer. Single wedge and anatomical stem acceptability was mainly influenced by the combined anteversion. Stem anteversion was correlated with the femoral anteversion (fair correlation), the calcar femorale (fair) and the mediolateral femoral diameter at isthmus (poor). When the femoral anteversion was >= 25 degrees, combined anteversion was very acceptable for the conical stem (99.2%), whereas the rate of acceptable combined anteversion for the single wedge tapered stem was 71.4%, and that for the anatomical stem was 51.6% ($p < 0.0001$). Conclusions Stem choice in developmental hip dysplasia is mainly driven by appropriate combined anteversion, which is dependent on the coronal and axial femoral morphologies. As a rule of thumb, tapered stems are adequate when femoral anteversion is < 25 degrees; conical stems should be adopted for higher anteversions.
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Zimmer Biomet, 2020, CLS STEM, V0, P0
NR 22
TC 8
Z9 11
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JI J. Orthop. Traumatol.
PD DEC 15
PY 2022
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IS 1
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DI 10.1186/s10195-022-00650-x
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WC Orthopedics
SC Orthopedics
GA 2Y6ZV
UT WOS:000826043300001
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TI Clinical code usage in UK general practice: a cohort study exploring 18 conditions over 14 years
SO BMJ OPEN
LA English
DT Article

DE primary care; public health; change management
ID robust maximum association; primary-care; computers
AB Objective To assess the diagnostic Read code usage for 18 conditions by examining their frequency and diversity in UK primary care between 2000 and 2013. Design Population-based cohort study Setting 684 UK general practices contributing data to the Clinical Practice Research Datalink (CPRD) GOLD. Participants Patients with clinical codes for at least one of asthma, chronic obstructive pulmonary disease, diabetes, hypertension (HT), coronary heart disease, atrial fibrillation (AF), heart failure, stroke, hypothyroidism, chronic kidney disease, learning disability (LD), depression, dementia, epilepsy, severe mental illness (SMI), osteoarthritis, osteoporosis and cancer. Primary and secondary outcome measures For the frequency ranking of clinical codes, canonical correlation analysis was applied to correlations of clinical code usage of 1, 3 and 5 years. Three measures of diversity (Shannon entropy index of diversity, richness and evenness) were used to quantify changes in incident and total clinical codes. Results Overall, all examined conditions, except LD, showed positive monotonic correlation. HT, hypothyroidism, osteoarthritis and SMI codes' usage had high 5-year correlation. The codes' usage diversity remained stable overall throughout the study period. Cancer, diabetes and SMI had the highest richness (code lists need time to define) unlike AF, hypothyroidism and LD. SMI (high richness) and hypothyroidism (low richness) can last for 5 years, whereas cancer and diabetes (high richness) and LD (low richness) only last for 2 years. Conclusions This is an under-reported research area and the findings suggest the codes' usage diversity for most conditions remained overall stable throughout the study period. Generated mental health code lists can last for a long time unlike cardiometabolic conditions and cancer. Adopting more consistent and less diverse coding would help improve data quality in primary care. Future research is needed following the transfer to the Systematised Nomenclature of Medicine Clinical Terms (SNOMED CT) coding.
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NR 43
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U2 1
PU BMJ PUBLISHING GROUP
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PA BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND
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WC Medicine, General & Internal
SC General & Internal Medicine
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TI Characterization of titanium ceramic composite for bone implants applications
SO CERAMICS INTERNATIONAL
LA English
DT Article
DE Titanium; Wollastonite; Bioceramic; Mesenchymal stem cells; Bone implants
ID in-vitro bioactivity; mechanical-property; hydroxyapatite coatings; palm stearin; wollastonite; powder; microstructure; tissue; metal; fabrication
AB Bone implants are widely used to restore bone loss due to several factors including but not limited to osteoporosis, osteoarthritis and road injuries. Current bone implant materials restore mechanical stability but suffer from a lack of osteointegration and will need to be replaced after long term use. To circumvent this, tissue engineering which capitalizes on the use of cells, biochemical factors and biodegradable materials aim to develop a biological substitute that restores, maintain or improve tissue functions. Central to the improvement of the tissue function and its stability through the implant relies on its interaction with the host tissue. Hence, a bioactive implant that promotes osteointegration is more desirable than an inert implant. In this study, metal-ceramic composites are explored for their suitability to be used as bone implants in the future. Fabrication of the composite was optimized using hot press compression and vacuum sintering method. Data presented include physicochemical characteristics of titanium-hydroxyapatite and titanium-wollastonite analyzed via SEM, FTIR, XRD, 3D laser microscopy and mechanical test. Evidence of material biocompatibility with primary human osteoprogenitor cells is also provided. Both titanium hydroxyapatite and titanium wollastonite possess the potential as the future of metal-ceramic composites as they possess the bioactivity of ceramic while still maintaining its core titanium body as a source of strength.
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AU Liu, FX
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AF Liu, Fanxiao
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TI Transcriptome Sequencing Reveals Key Genes in Three Early Phases of Osteogenic, Adipogenic, and Chondrogenic Differentiation of Bone Marrow Mesenchymal Stem Cells in Rats
SO FRONTIERS IN MOLECULAR BIOSCIENCES
LA English
DT Article
DE bone marrow mesenchymal stem cells; high-throughput sequencing; osteogenic differentiation; chondrogenic differentiation; adipogenic differentiation; differentially expressed genes
ID identification; candidate
AB Bone mesenchymal stem cells (BMSCs) of multi-directional differentiation and reproductive activity are attractive candidates for bone and cartilage repair. However, the molecular mechanisms underlying the early phase of osteogenesis, adipogenesis, and chondrogenesis of BMSCs are still far from understood. In the current study, BMSCs are isolated from rats, and the gene expressions during the initiation of differentiation (phase I), lineage acquisition (phase II), and early lineage

progression (phase III) of three-directional differentiation of BMSCs were detected by using high-throughput sequencing. Then, 356, 540, and 299 differentially expressed genes (DEGs) were identified in phases I, II, and III of osteogenesis, respectively. The numbers are 507, 287, and 428 for adipogenesis, respectively, and 412, 336, and 513 for chondrogenesis, respectively. Time-dependent expression patterns of genes were also validated during three-directional differentiation in BMSCs. Hub genes including Ccna2, Cdc20, and Il6 may act as common participants in initiating osteogenesis, adipogenesis, and chondrogenesis. Mex3b, Sertad1, and Hopx showed an enhanced expression throughout three early phases during the osteogenic differentiation but no significant change in other two-directional differentiation. A similar pattern of Dtx4 and Ibsp expression occurred in adipogenesis and chondrogenesis, respectively. Our findings will help understand the underlying mechanism determining the differentiation fate of BMSCs and provide theoretical support for the clinical treatment of osteoporosis, osteoarthritis, and other age-related bone diseases.
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NR 33
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TI Nuclear morphology is a deep learning biomarker of cellular senescence
SO NATURE AGING
LA English
DT Article
ID dna-damage; cells; cancer; diseases; pathway; target

AB Senescent cells are typically identified by a combination of senescence-associated markers, and the phenotype is heterogeneous. Here, using deep neural networks, Heckenbach et al. show that nuclear morphology can be used to predict cellular senescence in images of tissues and cell cultures. Cellular senescence is an important factor in aging and many age-related diseases, but understanding its role in health is challenging due to the lack of exclusive or universal markers. Using neural networks, we predict senescence from the nuclear morphology of human fibroblasts with up to 95% accuracy, and investigate murine astrocytes, murine neurons, and fibroblasts with premature aging in culture. After generalizing our approach, the predictor recognizes higher rates of senescence in p21-positive and ethynyl-2'-deoxyuridine (EdU)-negative nuclei in tissues and shows an increasing rate of senescent cells with age in H&E-stained murine liver tissue and human dermal biopsies. Evaluating medical records reveals that higher rates of senescent cells correspond to decreased rates of malignant neoplasms and increased rates of osteoporosis, osteoarthritis, hypertension and cerebral infarction. In sum, we show that morphological alterations of the nucleus can serve as a deep learning predictor of senescence that is applicable across tissues and species and is associated with health outcomes in humans.
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Lehman-Lane, J
Uzlik, RM
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AF Nouraee, Cyrus M.
McGaver, Rebecca Stone
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TI Opioid-Prescribing Practices Between Total Knee and Hip Arthroplasty in an Outpatient Versus Inpatient Setting
SO JOURNAL FOR HEALTHCARE QUALITY
LA English
DT Article
DE opioids; TKA; THA; outpatient ambulatory surgery center; inpatient hospital
ID african-americans; osteoarthritis; prevalence; replacement; pain; caucasians; symptoms

AB Despite trends showing increases in the utilization of outpatient (OP) ambulatory surgery centers (ASCs) and decreases in the utilization of inpatient (IP) facilities for total knee arthroplasty (TKA) and total hip arthroplasty (THA), little is known about opioid prescribing for these procedures between each setting. This study evaluated differences in opioid prescribing and consumption between OP ASC and IP settings for elective TKA and THA surgeries over a 1-year period. Data collection also included pain and satisfaction of pain control postsurgery. In an OP ASC, analysis revealed a significant decrease in pills prescribed ($p < .001$, $p < .001$) and consumed ($p < .001$, $p < .001$) for TKA and THA, respectively. There was a significant decrease in the morphine equivalence units prescribed ($p < .001$, $p < .001$) and consumed ($p < .001$, $p < .001$) for TKA and THA, respectively. For TKA, pain was significantly lower ($p = .018$) and satisfaction of pain control was significantly higher ($p = .007$). For THA, pain ($p = .374$) and satisfaction of pain control ($p = .173$) were similar between the settings. Benefits of performing these surgeries in an OP ASC setting are patients having similar or lower levels of pain and having similar or higher satisfaction of pain control. Patients are also prescribed and consume less opioids. This has important implications for healthcare systems.
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NR 40
TC 4

Z9 4
U1 0
U2 0
PU LIPPINCOTT WILLIAMS & WILKINS
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JI J. Healthc. Qual.
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WC Health Care Sciences & Services; Health Policy & Services
SC Health Care Sciences & Services
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ER

PT J
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TI Prospective evaluation of in situ screw fixation for stable slipped capital femoral epiphysis
SO JOURNAL OF CHILDRENS ORTHOPAEDICS
LA English
DT Article
DE Slipped capital femoral epiphysis; in situ fixation; secondary surgery; patient reported outcomes

ID modified dunn procedure; femoroacetabular impingement; osteoarthritis; osteotomy; outcm
AB Purpose: We aimed to determine which variables were associated with persistent symptoms or need for further surgery in patients treated with in situ fixation for stable slipped capital femoral epiphysis. We hypothesized that patients with greater proximal femoral deformity would require revision surgical intervention. Methods: We prospectively collected data on stable slipped capital femoral epiphysis patients who underwent in situ screw fixation at a single institution. Demographic and radiographic information, as well as patient-reported outcomes, were collected. Results: Forty-six patients (54 hips) with an average follow-up of 3.5 years (range: 2.0-8.5) and mean pre-op Southwick slip angle of 40.5 degrees +/- 19.4 degrees were studied. We observed one complication following the index procedure (2%). Twelve hips (22%) went on to have a secondary procedure 2.7 +/- 2.2 years after the index surgery. Severe slips were 14.8x more likely to undergo a secondary procedure than mild and moderate slips ($p < 0.001$). We found no correlation between slip severity and patient-reported outcomes ($p > 0.6$). Hips requiring a secondary procedure had significantly lower Hip disability and Osteoarthritis Outcome scores (76.8 +/- 18.4) at final follow-up compared to hips that did not require additional surgery (86.8 +/- 15.7) ($p = 0.042$). Conclusion: With minimum 2-year follow-up, 22% of patients required a secondary surgery. Patient-reported outcomes did not correlate with slip severity, but were found to be significantly higher in slipped capital femoral epiphysis patients that did not require a secondary procedure. Prophylactic treatment of all slip-related cam deformity was not found to be necessary in this prospective cohort. Patients with moderate-to-severe slips may require secondary surgery.
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NR 19
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U1 0
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PT J
AU Feng, YA
Ding, L
Li, LG
AF Feng, Yinan
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Li, Longguang
TI LPS-inducible circAtp9b is highly expressed in osteoporosis and promotes the apoptosis of osteoblasts by reducing the formation of mature miR-17-92a
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Osteoporosis; circAtp9b; miR-17-92a; Maturation; Apoptosis
ID osteoarthritis
AB Background Circular RNA circAtp9b is an enhancer of LPS-induced inflammation, which promotes osteoporosis (OS). This study explored the role of circAtp9b in OS. Methods RT-qPCR was performed to detect the expression of circAtp9b and microRNA (miR)-17-92a (both mature and premature) in OS and healthy controls. The subcellular location of circAtp9b was assessed by nuclear fractionation assay. The direct interaction between circAtp9b and premature miR-17-92a was detected by RNA pull-down assay. The role of circAtp9b in regulating the maturation of miR-17-92a in osteoblasts was explored by overexpression assay and RT-qPCR. Cell apoptosis was analyzed by cell apoptosis assay. Results OS patients exhibited upregulation of circAtp9b and premature miR-17-92a, but downregulation of mature miR-17-92a. In osteoblasts, circAtp9b suppressed the maturation of miR-17-92a. LPS upregulated circAtp9b and premature miR-17-92a, and downregulated mature miR-17-92a in osteoblasts. CircAtp9b was detected in both nucleus and cytoplasm, and it directly interacted with premature miR-17-92a. Overexpression of circAtp9b reduced the effects of miR-17-92a on the apoptosis of osteoblasts induced by LPS. Conclusion CircAtp9b is LPS-inducible and upregulation of circAtp9b in OS promotes the apoptosis of

osteoblasts by reducing the formation of mature miR-17-92a.
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NR 22
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U1 0
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PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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PT J
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TI The multifaced role of HtrA1 in the development of joint and skeletal disorders
SO BONE
LA English
DT Review
DE HtrA1; Osteoporosis; Rheumatoid arthritis; Osteoarthritis; Intervertebral disc degeneration; Musculoskeletal disorders
ID serine-protease htra1; articular-cartilage vesicles; a1 htra1; temporomandibular-joint; ifn-gamma; disc degeneration; induced arthritis;

up-regulation; osteoarthritis; requirement
AB HtrA1 (High temperature requirement A1) family proteins include four members, widely conserved from prokaryotes to eukaryotes, named HtrA1, HtrA2, HtrA3 and HtrA4. HtrA1 is a serine protease involved in a variety of biological functions regulating many signaling pathways degrading specific components and playing key roles in many human diseases such as neurodegenerative disorders, pregnancy complications and cancer. Due to its role in the breakdown of many ExtraCellular Matrix (ECM) components of articular cartilage such as fibronectin, decorin and aggrecan, HtrAl encouraged many researches on studying its role in several skeletal diseases (SDs). These studies were further inspired by the fact that HtrA1 is able to regulate the signaling of one of the most important cytokines involved in SDs, the TGF beta-1. This review aims to summarize the data currently available on the role of HtrA1 in skeletal diseases such as Osteoporosis, Rheumatoid Arthritis, Osteoarthritis and Intervertebral Disc Degeneration (IDD). The use of HtrA1 as a marker of frailty in geriatric medicine would represent a powerful tool for identifying older individuals at risk of developing skeletal disorders, evaluating an appropriate intervention to improve quality care in these people avoiding or improving age-related SDs in the elderly population.
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NR 100
TC 49
Z9 49
U1 1
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TI Analysis of hydration and subchondral bone density on the viscoelastic properties of bovine articular cartilage
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Articular cartilage; Bone density; Hydration; Loss; Storage; Viscoelasticity
ID human femoral-head; synovial-fluid; mechanical-property; boundary lubrication; chemical-composition; surface failure; stress transfer; osteoarthritis; collagen; osteoporosis
AB Background Articular cartilage is known to be a viscoelastic material, however little research has explored the impact of cartilage water content and bone density on its viscoelasticity. This study aimed to isolate subchondral bone density and hydration of articular cartilage and analyse their effects on the viscoelastic properties of articular cartilage. Methods Dynamic mechanical analysis was used to test samples at frequencies of 1, 8, 12, 29, 49, 71, and 88 Hz. Synthetic bone material with densities of 663.7 kg/m(3) and 156.8 kg/m(3) were used to mimic the bone mineral density (BMD). Dehydration occurred in a stepwise manner at relative humidity (RH) levels of 100%, 30%, and 1%. These relative humidity levels led to

water contents of approximately 76%, 8.5%, and approximate to 0% by mass, respectively. Results Samples from eight bovine femoral heads were tested under a sinusoidal load. Storage stiffness was lower on the lower substrate density. Storage stiffness, though, increased as cartilage samples were dehydrated from a water content of 76% to 8.5%; decreasing again as the water content was further reduced. Loss stiffness was lower on a lower density substrate and decreased as the water content decreased. Conclusions In conclusions, a decrease in hydration decreases the loss stiffness, but a non-linear relationship between hydration and storage stiffness may exist. Additionally, higher BMD values led to greater storage and loss stiffnesses.
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NR 53
TC 7
Z9 7
U1 0
U2 14
PU BMC
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PT J
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He, Y
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AF Xiong, Yi
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TI Association of IL-6 and TGF-β Gene Polymorphisms with the Risk of Thoracolumbar Osteoporotic Vertebral Compression Fractures
SO PHARMACOGENOMICS & PERSONALIZED MEDICINE
LA English
DT Article
DE OVCF; IL-6; TGF-beta; gene polymorphisms
ID transforming growth-factor-beta-1; osteoarthritis; bone; kyphoplasty; refracture; tgf-beta-1; rs1800796; variant; level
AB Purpose: Osteoporotic vertebral compression fracture (OVCF) is a common disease in the elderly, and genetic factors play a key role in its occurrence. The present study was conducted to investigate the association between interleukin-6 (IL-6) and the transforming growth factor (TGF-beta) gene polymorphisms and the occurrence of thoracolumbar OVCF. Patients and Methods: This case-control study recruited 146 patients with OVCF and 144 osteoporosis patients as the control group. Genotypes of the IL-6 rs1800796 and TGF-beta rs1982073 were analyzed by sequencing. Genotype distribution and allelic frequencies were investigated by the chi(2) test. Odds ratios (OR) and 95% confidence intervals (CI) evaluated the relationship of IL-6 or TGF-beta polymorphism and OVCF susceptibility. Results: Allele G and genotype GG of IL-6 rs1800796 was more frequent in patients with OVCF (40.07% vs.28.47%; 19.18% vs.7.64%) compared with controls. GG genotype (OR=3.394, 95% CI=1.560-7.385, P < 0.001) and G allele (OR=1.680, 95% CI=1.187-2.376, P < 0.001) of IL-6 rs1800796 was significantly associated with increased risk of OVCF. What is more, CT and TT genotypes (41.78 vs.51.39; 19.86 vs.26.39) and allele T (40.75 vs 52.08) of TGF-beta rs1982073 were less frequent in OVCFs, more common in controls and protective against OVCF risk (OR=0.436, 95% CI=0.228-0.835, P = 0.012; OR=0.615, 95% CI=0.443-0.855, P = 0.004). Conclusion: Our results suggest that the G allele and GG genotype of IL-6 rs1800796 may contribute to increased susceptibility to OVCF in elderly Chinese. In contrast, CT and TT genotypes and the T allele of TGF-beta rs1982073 may contribute to lower susceptibility of OVCF.
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PT J
AU Bai, RJ
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AF Bai, Rui-Jun

Li, Yu-Sheng
Zhang, Fang-Jie
TI Osteopontin, a bridge links osteoarthritis and osteoporosis
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE bone metabolism; inflammation; osteoarthritis; osteoporosis; osteopontin
ID bone-mineral density; nf-kappa-b; synovial-fluid; disease severity; messenger-rna; expression; migration; cd44; ovariectomy; osteoblast
AB Osteoarthritis (OA) is the most prevalent joint disease characterized by degradation of articular cartilage, inflammation, and changes in periarticular and subchondral bone of joints. Osteoporosis (OP) is another systemic skeletal disease characterized by low bone mass and bone mineral density (BMD) accompanied by microarchitectural deterioration in bone tissue and increased bone fragility and fracture risk. Both OA and OP are mainly affected on the elderly people. Recent studies have shown that osteopontin (OPN) plays a vital role in bone metabolism and homeostasis. OPN involves these biological activities through participating in the proliferation, migration, differentiation, and adhesion of several bone-related cells, including chondrocytes, synoviocytes, osteoclasts, osteoblasts, and marrow mesenchymal stem cells (MSCs). OPN has been demonstrated to be closely related to the occurrence and development of many bone-related diseases, such as OA and OP. This review summarizes the role of OPN in regulating inflammation activity and bone metabolism in OA and OP. Furthermore, some drugs that targeted OPN to treat OA and OP are also summarized in the review. However, the complex mechanism of OPN in regulating OA and OP is not fully elucidated, which drives us to explore the depth effect of OPN on these two bone diseases.
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Z9 74
U1 4
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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UT WOS:000883827000001
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ER

PT J
AU Yang, JJ
Zhang, XM
AF Yang, Jing-Jin
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TI Clinical Efficacy of Glucosamine plus Sodium Hyaluronate for Osteoporosis Complicated by Knee Osteoarthritis and Its Influence on Joint Function and Bone Metabolic Markers
SO COMPUTATIONAL AND MATHEMATICAL METHODS IN MEDICINE
LA English
DT Article
ID injection; arthritis; health
AB Background. Osteoporosis (OP) associated with knee osteoarthritis (KOA) is common in older men and postmenopausal women, and it is important to find reliable and effective treatments for this disease to improve joint function and bone metabolism in this population. Objective. To clarify the clinical efficacy of glucosamine (GlcN) plus sodium hyaluronate (SH) for OP complicated by KOA (OP + KOA) and its influence on joint function and bone metabolic markers (BMMs). Methods. Admitted from July 2019 to July 2021, 126 patients with OP + KOA were selected, including 76 cases (observation group) treated with GlcN plus SH and 50 cases (control group) given GlcN alone. The pain, joint function, BMMs, and clinical

efficacy were evaluated and compared. Pain and joint function assessments employed the Visual Analogue Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) plus Lysholm Knee Scoring Scale, respectively. BMMs mainly measured bone gla protein (BGP), serum tartrate-resistant acid phosphatase variant (TRACP)-5b, type I collagen cross-linked C-telopeptide (CTX-1), and bonespecific alkaline phosphatase (BALP). Results. Higher posttreatment VAS scores were determined in observation group as compared to control group; observation group showed lower WOMAC scores of joint function and higher Lysholm scores than control group; in terms of BMMs, TRACP-5b and CTX-1 were lower while BGP and BALP were higher in observation group; the curative effect was also higher in observation group. All the above differences were statistically significant. Conclusions. GlcN plus SH has definite clinical efficacy in the treatment of OP + KOA, which can not only significantly improve patients' joint function and bone metabolism but also relieve pain, with high clinical popularization value.
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NR 30
TC 3
Z9 5
U1 0
U2 3
PU HINDAWI LTD
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PA ADAM HOUSE, 3RD FLR, 1 FITZROY SQ, LONDON, W1T 5HF, ENGLAND
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J9 COMPUT MATH METHOD M
JI Comput. Math. Method Med.
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PT J
AU Apitz, S
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AF Apitz, Salome
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TI The Primary Care Research Landscape and its Relationship with Clinical Practice: A Scientometric Analysis
SO ACTA MEDICA PORTUGUESA
LA English
DT Article
DE Bibliometrics; Database Management Systems; Primary Health Care; Publishing
AB Introduction: It is unclear if research published in primary care journals aligns with the broad spectrum of problems managed in primary care practice. The aim of this study was to analyse publication trends concerning the burden of medical conditions reported in primary care journals, and to compare these findings with the burden of problems seen in clinical practice, in order to identify research gaps. Material and Methods: Scientometric tools were used to analyse 9956 articles of primary care journals indexed in MEDLINE. Through keyword analysis, a relations map was built. Literature review and a primary care database were used to identify active problems and reasons for visiting a family physician. Rankings and frequencies of research output and conditions were compared. Results: Keyword analysis identified five clusters of publication trends: cardiovascular conditions and conditions related with unhealthy lifestyles; mental disorders; infections; oncology and health management. By comparing publications with clinical problems, the fields of orthopaedics, endocrinology/metabolism, gastroenterology/hepatology, dermatology, ophthalmology, and the respiratory system show the biggest gaps. Through the relations map, more concrete potential research topics were identified such as palliative care, chronic pain, insomnia, antibiotic prescribing, burnout, osteoporosis, osteoarthritis, and COVID-19. Conclusion: The distribution of publications in primary care journals is distinct from the burden of problems faced in clinical practice and reasons for visiting a family physician. The use of scientometric tools to identify publication trends and their comparison with common problems could be a strategy to identify areas with research gaps in primary care.
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NR 18
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Z9 3
U1 0
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PU ORDEM MEDICOS
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JI Acta Medica Port.
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PT J
AU Barrowclough, J
Kool, B
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TI Fetal malposition in labour and health outcomes for women and their newborn infants: A retrospective cohort study
SO PLOS ONE
LA English
DT Article
ID occiput posterior position; head position; intrapartum sonography; 1st stage; association; delivery; 2nd-stage; risk
AB Introduction Occiput-posterior (OP) or occiput-transverse (OT) fetal malposition has a prevalence of 33-58% in the first-stage of labour with 12-22% persisting until delivery. Malposition is associated with significant maternal and neonatal morbidity. Most previous studies report the incidence and adverse maternal and fetal outcomes of persistent fetal malposition in the second stage of labour and do not include outcomes that may be present in the first stage of labour. Aims To assess the incidence and health outcomes for women and their newborn infants of a fetal malposition in the first or second stage of labour. Materials and methods A retrospective cohort study of 738 maternity records (randomly selected) from a tertiary hospital in New Zealand. Maternal and neonatal characteristics are described. Outcomes for women with a fetus in an OP or OT position in labour are compared to those for women with a fetus in an occiput-anterior position (OA). Results 499 (68%) women had an OP/OT positioned fetus and 239 (32%) had an OA positioned fetus on vaginal examination in labour. Women had similar characteristics except a body mass index >= 30 kg/m(2) was more common in the OP/OT group. Fetal malposition appears to be more likely in women with a right-sided fetal occiput. Three quarters of OP/OT fetuses rotated anteriorly by birth. Fetal malposition compared to no malposition was associated with oxytocin augmentation, epidural use, a longer first stage of labour, fewer normal vaginal births, and more caesarean sections. Fetal malposition during labour was not associated with adverse neonatal outcomes. Conclusion Interventions such as maternal posture in the first and second stage of labour could potentially reduce the incidence of malposition and improve health outcomes for mothers.
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TI Effects of Systemic or Local Administration of Mesenchymal Stem Cells from Patients with Osteoporosis or Osteoarthritis on Femoral Fracture Healing in a Mouse Model
SO BIOMOLECULES
LA English
DT Article
DE mesenchymal stem cells; bone regeneration; animal model; micro-CT; histological study
ID bone; promotes; repair
AB The purpose of this study was to analyze the regenerative capacity of mesenchymal stem cells (MSCs) in the treatment of fractures. MSCs extracted from patients with osteoporotic hip fractures or hip osteoarthritis undergoing hip

replacement surgeries were cultured and injected into mice with femoral fracture. Two experimental models were established, one for the systemic administration of MSCs (n = 29) and another one for local administration (n = 30). Fracture consolidation was assessed by micro-CT and histology. The degree of radiological consolidation and corticalization was better with MSCs from osteoporosis than from osteoarthritis, being significant after systemic administration (p = 0.0302 consolidation; p = 0.0243 corticalization). The histological degree of consolidation was also better with MSCs from osteoporosis than from osteoarthritis. Differences in histological scores after systemic infusion were as follows: Allen, p = 0.0278; Huo, p = 0.3471; and Bone Bridge, p = 0.0935. After local administration at the fracture site, differences in histological scores were as follows: Allen, p = 0.0764; Huo, p = 0.0256; and Bone Bridge, p = 0.0012. As osteoporosis and control groups were similar, those differences depended on an inhibitory influence by MSCs from patients with osteoarthritis. In conclusion, we found an unexpected impairment of consolidation induced by MSCs from patients with osteoarthritis. However, MSCs from patients with osteoporosis compared favorably with cells from patients with osteoarthritis. In other words, based on this study and previous studies, MSCs from patients with osteoporosis do not appear to have worse bone-regenerating capabilities than MSCs from non-osteoporotic individuals of similar age.
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JI Biomolecules
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TI Bone-Targeted Nanoparticle Drug Delivery System: An Emerging Strategy for Bone-Related Disease

SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE bone targeted; drug delivery; bone diseases; nanoparticles; stimulus-responsive
ID stimuli-responsive nanocarriers; poly(d,l-lactide-co-glycolide) nanoparticles; lipid nanoparticles; anabolic therapy; co-delivery; cell-selex; osteoporosis; osteoarthritis; tetracycline; bisphosphonates
AB Targeted delivery by either systemic or local targeting of therapeutics to the bone is an attractive treatment for various bone metabolism diseases such as osteoporosis, osteoarthritis, osteosarcoma, osteomyelitis, etc. To overcome the limitations of direct drug delivery, the combination of bone-targeted agents with nanotechnology has the opportunity to provide a more effective therapeutic approach, where engineered nanoparticles cause the drug to accumulate in the bone, thereby improving efficacy and minimizing side effects. Here, we summarize the current advances in systemic or local bone-targeting approaches and nanosystem applications in bone diseases, which may provide new insights into nanocarrier-delivered drugs for the targeted treatment of bone diseases. We envision that novel drug delivery carriers developed based on nanotechnology will be a potential vehicle for the treatment of currently incurable bone diseases and are expected to be translated into clinical applications.
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U2 114
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WC Pharmacology & Pharmacy
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AU Bao, ZM
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Yang, WS
AF Bao, Zheming
Chen, Mengli
Li, Chen
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TI Monosodium iodoacetate-induced subchondral bone microstructure and inflammatory changes in an animal model of osteoarthritis
SO OPEN LIFE SCIENCES
LA English
DT Article
DE animal model; osteoarthritis; bone microarchitecture; iodoacetic acid
AB The monosodium iodoacetate (MIA)-induced osteoarthritis (OA) may lead to cartilage degeneration and histopathological lesions. However, the correlation between inflammatory reaction and subchondral bone remodeling in a rodent osteoarthritic model is ambiguous. In this study, intra-articular injection of MIA was performed in 36 four-week-old specific pathogen-free male Wistar rats to induce OA. After 4 weeks of intervention, changes in intrinsic structural properties of the subchondral bones were measured, and the histological evaluation, as well as biochemical analysis, was conducted. We found that intra-articular injection of MIA increased chondrocyte apoptosis and promoted cartilage matrix degradation, such as cartilage surface defects and shallow or disappearing staining. MIA also induced inflammation, improved the expression of IL-1 beta, TNF-alpha, and matrix metalloproteinase, and decreased the expression of cartilage-specific proteins with the extension of modeling time. Meanwhile, the MIA also significantly accelerated the subchondral bone remodeling, as shown by the decreased subchondral bone

density, thinning of trabeculae, disordered cartilage structure, and morphology. In conclusion, we have shown that MIA-induced rodent osteoarthritic model would cause decreased subchondral bone density, sparse trabecular bone, and other manifestations of osteoporosis accompanied by an inflammatory response, which would worsen with the progression of modeling time. Our results suggest that different phases of MIA-induced OA are associated with the changes in subchondral bone microstructure and the progression of local inflammation.
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TI Glucosamine delays the progression of osteoporosis in senile mice by promoting osteoblast autophagy
SO NUTRITION & METABOLISM
LA English
DT Article
DE Glucosamine; d-Galactose; Senile osteoporosis; Osteogenesis; Autophagy
ID oxidative-stress; osteoarthritis; sulfate; cell
AB Background Senile osteoporosis (SOP) is one of the most prevalent diseases that afflict the elderly population, which characterized by decreased osteogenic ability. Glucosamine (GlcN) is an over-the-counter dietary supplement. Our previous study reported that GlcN promotes osteoblast proliferation by activating autophagy in vitro. The purpose of this study is to determine the effects and mechanisms of GlcN on senile osteoporosis and osteogenic differentiation in vivo.

Methods Aging was induced by subcutaneous injection of d-Galactose (d-Gal), and treated with GlcN or vehicle. The anti-senile-osteoporosis effect of GlcN was explored by examining changes in micro-CT, serum indicators, body weight, protein and gene expression of aging and apoptosis. Additionally, the effects of GlcN on protein and gene expression of osteogenesis and autophagy were observed by inhibiting autophagy with 3-methyladenine (3-MA). Results GlcN significantly improved bone mineral density (BMD) and bone micro-architecture, decreased skeletal senescence and apoptosis and increased osteogenesis in d-Gal induced osteoporotic mice. While all effect was reversed with 3-MA. Conclusion GlcN effectively delayed the progression of osteoporosis in senile osteoporotic mice by promoting osteoblast autophagy. This study suggested that GlcN may be a prospective candidate drug for the treatment of SOP.
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NR 60
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JI Nutr. Metab.
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WC Nutrition & Dietetics
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TI Trabecular bone porosity and pore size distribution in osteoporotic patients - A low field nuclear magnetic resonance and microcomputed tomography investigation
SO JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS
LA English
DT Article
DE Osteoporosis; Trabecular bone morphology; Microcomputed tomography; Low field nuclear magnetic resonance; Bone porosity
ID micro-computed tomography; human cortical bone; age-related-changes; single-sided nmr; mechanical-property; cancellous bone; rat model; diffusion; mri; water
AB The study of bone morphology is of great importance as bone morphology is influenced by factors such as age and underlying comorbidities and is associated with bone mechanical properties and fracture risk. Standard diagnostic techniques used in bone disease, such as Dual-Energy X-ray absorptiometry and ultrasonography do not provide qualitative and quantitative morphological information. In recent years, techniques such as High Resolution Computed Tomography (HR-CT), micro- CT, Magnetic Resonance Imaging (MRI), and Low Field Nuclear Magnetic Resonance (LF-NMR) have been developed for the study of bone structure and porosity. Data obtained from these techniques have been used to construct models to predict bone mechanical properties thanks to finite element analysis. Cortical porosity has been extensively studied and successfully correlated with disease progression and mechanical properties. Trabecular porosity and pore

size distribution, however, have increasingly been taken into consideration to obtain a comprehensive analysis of bone pathology and mechanic. Therefore, we have decided to evaluate the ability of micro- CT (chosen for its high spatial resolving power) and LF-NMR (chosen to analyze the behavior of water molecules within trabecular bone pores) to characterize the morphology of trabecular bone in osteoporosis. Trabecular bone samples from human femoral heads collected during hip replacement surgery were from osteoporosis (test group) and osteoarthritis (control group) patients. Our data show that both micro- CT and LF-NMR can detect qualitative changes in trabecular bone (i.e., transition from plate-like to rod-like morphology). Micro- CT failed to detect significant differences in trabecular bone morphology parameters between osteoporotic and osteoarthritic specimens, with the exception of Trabecular Number and Connectivity Density, which are markers of osteoporosis progression. In contrast, LF-NMR was able to detect significant differences in porosity and pore size of trabecular bone from osteoporotic versus osteoarthritic (control) samples. However, only the combination of these two techniques allowed the detection of structural morphometric changes (increase in the larger pore fraction and enlargement of the larger pores) in the trabecular bone of osteoporotic specimens compared to osteoarthritic ones. In conclusion, the combined use of LF-NMR and micro- CT provides a valuable tool for characterizing the morphology of trabecular bone and may offer the possibility for a new approach to the study and modeling of bone mechanics in the context of aging and disease.
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TI The Abundance of Trace Elements in Human Bone Relative to Bone Type and Bone Pathology
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ID lead-exposure; long-term; blood lead; osteoporotic fracture; strontium ranelate; mineral density; risk-factors; zinc; cadmium; calcium
AB As the global population ages and the proportion of individuals afflicted with musculoskeletal disease spirals upward, there is an increasing interest in understanding and preventing bone-related diseases. Bone diseases, such as osteoporosis and osteoarthritis, are known to be influenced by a variety of factors

including age, gender, nutrition, and genetics, but are also inherently linked to the human body's ability to produce biominerals of suitable quality. Because the crystal lattice structure and mineralogy of bone hydroxyapatite is surprisingly analogous to geological hydroxyapatite, trace element levels and exposure have long been proposed to influence the structure of biominerals as they do geological minerals (e.g., strontium substitution changes the crystal lattice of bone minerals, while toxic lead disrupt bone cellular processes leading to bone disease). Here, we explore the distribution of trace elements in human bones to evaluate the distribution of these elements with respect to bone type (cortical vs. trabecular) and bone disease (osteoarthritis vs. osteoporosis). We find higher concentrations of many metabolically active transition metals, as well as lead, in cortical bone compared to trabecular bone. When compared to patients who have osteoarthritis, and thus presumably normal bone minerals, osteoporosis patients have higher concentrations of scandium and chromium (Cr) in trabecular bone, and Cr and lead in cortical bone. Lower concentrations of bariumand titanium are associated with osteoporotic trabecular bone. This survey is an exploratory cross-sectional geochemical examination of several trace element concentrations previously understudied in human bone minerals. Plain Language Summary Bone-related diseases, like osteoporosis, are a growing concern as the global population ages. There are many factors which can influence bone health, including age, sex, and genetics, but ultimately osteoporosis is a disease of bone mass and bone strength. Bone minerals are like minerals found in nature, which contain trace element impurities. When these impurities occur in bones, they affect bone strength, with some trace elements increasing bone strength, and others decreasing it. The amount and kind of trace elements found in bone can be affected by environmental exposures or from the body's own processes which may be different between healthy and diseased individuals. This study compares the concentrations of 16 trace elements in bones from people with osteoporosis, a disease where bones themselves are diseased, and osteoarthritis, as disease of joint cartilage that is not expected to impact the trace element chemistry of bone minerals. We find that bones from osteoporosis patients have higher concentrations of some elements, including toxic lead, but lower concentrations of other elements. The location of these element deficiencies or excesses in the bones may suggest if their concentrations are more likely to be a cause of osteoporosis or a symptom of it.
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Z9 14
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WC Environmental Sciences; Public, Environmental & Occupational Health
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PT J
AU Harlaar, J
   Macri, EM
   Wesseling, M
AF Harlaar, J.
   Macri, E. M.
   Wesseling, M.
TI Osteoarthritis year in review 2021: mechanics
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Review
DE Osteoarthritis; Biomechanics; Cartilage; Multiscale modelling; Wearables; Machine learning
ID severe knee osteoarthritis; high tibial osteotomy; joint; individuals; people; forces; pain
AB Osteoarthritis (OA) has a complex, heterogeneous and only partly understood

etiology. There is a definite role of joint cartilage pathomechanics in originating and progressing of the disease. Although it is still not identified precisely enough to design or select targeted treatments, the progress of this year's research demonstrates that this goal became much closer. On multiple scales - tissue, joint and whole body - an increasing number of studies were done, with impressive results. (1) Technology based instrument innovations, especially when combined with machine learning models, have broadened the applicability of biomechanics. (2) Combinations with imaging make biomechanics much more precise & personalized. (3) The combination of Musculoskeletal & Finite Element Models yield valid personalized cartilage loads. (4) Mechanical outcomes are becoming increasingly meaningful to inform and evaluate treatments, including predictive power from biomechanical models. Since most recent advancements in the field of biomechanics in OA are at the level of a proof op principle, future research should not only continue on this successful path of innovation, but also aim to develop clinical workflows that would facilitate including precision biomechanics in large scale studies. Eventually this will yield clinical tools for decision making and a rationale for new therapies in OA. (C) 2022 The Authors. Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.
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TC 23
Z9 27
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PU ELSEVIER SCI LTD
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JI Osteoarthritis Cartilage
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WC Orthopedics; Rheumatology
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PT J
AU Abraham, L
Halsby, K
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Wrona, B
Emir, B
Stevenson, H
AF Abraham, Lucy
Halsby, Kate
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TI An Observational Retrospective Matched Cohort Study of Healthcare Resource Utilisation and Costs in UK Patients with Moderate to Severe Osteoarthritis Pain
SO RHEUMATOLOGY AND THERAPY
LA English
DT Article
DE Analgesia; Arthroplasty; Chronic pain; England; Healthcare cost; Hospitalisation; Length of stay; Osteoarthritis; Primary health care; Regional health planning
ID knee osteoarthritis; work productivity; management; epidemiology; impact; pharmacotherapy; recommendations; burden; hip
AB Introduction Using data from patients residing in Salford, UK, we aimed to compare healthcare resource utilisation (HCRU) and direct healthcare costs between patients with moderate to severe (M-S) or severe osteoarthritis (OA) pain

and those without OA. Methods Patients with a M-S OA pain event within a period of chronic pain were indexed from the Salford Integrated Record (SIR) between 2010 and 2017. Patients with a severe pain event formed an OA subcohort. Patients in each OA pain cohort were independently matched to patients without OA, forming two control cohorts. HCRU, prescribed analgesic drugs, and total direct costs per UK standardised tariffs were calculated for the year post-index. Multivariable models were used to identify drivers of healthcare cost. Results The M-S OA pain and control cohorts each comprised 3123 patients; the severe OA pain and control cohorts each comprised 1922 patients. Patients in both OA pain cohorts had a significantly higher mean number of general practitioner encounters, inpatient, outpatient, and accident and emergency visits, and were prescribed a broader range of analgesic drugs in the year post-index than respective controls. Mean healthcare costs of all types were significantly higher in the M-S and severe OA pain cohorts vs controls (total: M-S 2519 pound vs 1379; pound severe 3389 pound vs 1397) pound. Paracetamol (M-S: 40% of patients had at least one prescription; severe: 50%) and strong opioids (34% and 59%) were the analgesics most prescribed to patients with OA pain. In all cohorts, multivariable models showed that a higher age at index, the presence of gout, osteoporosis, type 2 diabetes, or coronary artery disease, significantly contributed towards higher healthcare costs. Conclusion In the population of Salford, UK, patients with M-S OA pain had significantly higher annual HCRU and costs compared with matched controls without OA; generally, these were even higher in patients with severe OA pain.

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NR 48
TC 3
Z9 3
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PU SPRINGER
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PT J
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TI Changes in Bone Mineral Density of the Femur and Tibia Before Injury to 2 Years After Anterior Cruciate Ligament Reconstruction in Division I Collegiate Athletes
SO AMERICAN JOURNAL OF SPORTS MEDICINE
LA English
DT Article
DE ACL reconstruction; imaging; bone; knee; bone mineral density
ID posttraumatic osteoarthritis; knee; fracture; osteoporosis; kinematics; extremity; calcaneus; kinetics; recovery; risk
AB Background: Osteoarthritis (OA) is a significant long term concern after anterior cruciate ligament (ACL) reconstruction (ACLR). A low bone mineral density (BMD), particularly in the subchondral region, has been associated with the development of OA and is evident at the knee in patients long after ACLR. It is unknown if persistent BMD deficits are present in high level collegiate athletes. Purpose/Hypothesis: The purpose of this study was to evaluate bilateral changes in the BMD of the femur and tibia from before the injury to 24 months after ACLR in collegiate athletes. We hypothesized that the BMD of both the distal femur and the proximal tibia would be significantly reduced within the surgical limb initially postoperatively but return to preinjury levels by 24 months after ACLR. Study Design: Cohort study; Level of evidence, 2. Methods: A total of 33 Division I collegiate athletes were identified between 2010 and 2021 (13 female) who underwent total body dual-energy X-ray absorptiometry (DXA) before sustaining an ACL injury. DXA was repeated at 6, 12, and 24 months after ACLR. Linear mixed effects models assessed differences in the BMD at 5%, 15%, and 50% of the femur's length (F-5, F-15, F-50) and at 5%, 15%, and 50% of the tibia's length (T-5, T-15, T-50) within each limb from before the injury to 24 months after ACLR, reported as Tukey-adjusted P values. Results: Compared with before the injury, the BMD at F-5 of the surgical limb was reduced by 0.15 g/cm(2) (SE, 0.02 g/cm(2)) at 6 months ($P < .001$). The BMD at F-15 of the surgical limb was reduced by 0.06 g/cm(2) (SE, 0.01

g/cm(2)), 0.09 g/cm(2) (SE, 0.01 g/cm(2)), and 0.09 g/cm(2) (SE, 0.01 g/cm(2)) at 6, 12, and 24 months, respectively (all P < .001). The BMD at T-5 of the nonsurgical limb was reduced by 0.07 g/cm(2) (SE, 0.02 g/cm(2)) at 12 months (P = .02) and 0.10 g/cm(2) (SE, 0.02 g/cm(2)) at 24 months (P = .001). The BMD at T-15 of the surgical limb was reduced by 0.07 g/cm(2) (SE, 0.01 g/cm(2)) at 6 months and 0.08 g/cm(2) (SE, 0.02 g/cm(2)) at 12 months (P < .001). Conclusion: BMD deficits at F-15 of the surgical limb persisted out to 24 months (-7.1%) after ACLR compared with before the injury in collegiate athletes. The BMD at F-5 and T-15 of the surgical limb was reduced at 6 and 12 months but not at 24 months compared with preinjury levels. For the nonsurgical limb, no significant differences were detected, except for the T-5 region at 12 months (-5.1%) and 24 months (-7.2%). The BMD at F-50 and T-50 of both limbs was not significantly different than preinjury levels at any time after ACLR.

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TI Association between serum insulin-like growth factor 1 and locomotive syndrome in community-dwelling older people
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE IGF-1; Locomotive syndrome; Community-dwelling; Older people
ID factor-i; igf-i; exercise; sarcopenia; frailty; disability
AB Background Locomotive syndrome (LS) is a condition in which mobility decreases, and it is known as a risk factor for elderly persons needing care in connection with sarcopenia and frailty. Prevention or delay of the onset of these diseases is important for preventing the need for care, and identification of biomarkers as indicators for appropriate intervention is useful. The present study aimed to clarify whether the serum insulin-like growth factor 1 (IGF-1) level, which has been reported to be related to sarcopenia and frailty, is related to LS. Methods The study participants were 133 elderly people living in a rural area in Japan. LS was assessed using Locomo-25, which is a self-administered questionnaire, and LS was defined as a Locomo-25 score >= 7 points. Serum IGF-1 and albumin levels were measured. A self-completed medical history questionnaire was used. Results On multiple linear regression analysis, age, IGF-1, osteoporosis, and osteoarthritis were significantly associated with the Locomo-25 score. The receiver-operating characteristic curve analysis of the IGF-1 level showed a threshold value of 82.0 ng/mL for discriminating non-LS and LS. The logistic regression analysis adjusted for osteoporosis, osteoarthritis, and the propensity score estimated from sex, age, and BMI showed that the odds ratio (OR) of the IGF-1 level for LS was 1.019 (95% confidence interval [CI], 1.002-1.039; p = 0.027), and the OR of IGF-1 <= 82 ng/mL for LS was 2.275 (95% CI 0.993-5.324; p = 0.052). Conclusions The present findings suggest that osteoporosis and osteoarthritis were associated with early LS, and a decrease of the serum IGF-1 level was a significant independent factor for early LS.

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TI Role of Lysine-Specific Demethylase 1 in Metabolically Integrating Osteoclast Differentiation and Inflammatory Bone Resorption Through Hypoxia-Inducible Factor 1α and E2F1
SO ARTHRITIS & RHEUMATOLOGY
LA English
DT Article
ID rheumatoid-arthritis; denosumab; innate; cells; risk
AB Objective Hypoxia occurs in tumors, infections, and sites of inflammation, such as in the affected joints of patients with rheumatoid arthritis (RA). It alleviates inflammatory responses and increases bone resorption in inflammatory arthritis by enhancing osteoclastogenesis. The mechanism by which the hypoxia response is linked to osteoclastogenesis and inflammatory bone resorption is unclear. This study was undertaken to evaluate whether the protein lysine-specific demethylase 1 (LSD1) metabolically integrates inflammatory osteoclastogenesis and bone resorption in a state of inflammatory arthritis. Methods LSD1-specific inhibitors and gene silencing with small interfering RNAs were used to inhibit the expression of LSD1 in human osteoclast precursor cells derived from CD14-positive monocytes, with subsequent assessment by RNA-sequencing analysis. In experimental mouse models of arthritis, inflammatory osteolysis, or osteoporosis, features of accelerated bone loss and inflammatory osteolysis were analyzed. Furthermore, in blood samples from patients with RA, cis-acting expression quantitative trait loci (cis-eQTL) were analyzed for association with the expression of hypoxia-inducible

factor 1 alpha (HIF-1 alpha), and associations between HIF-1 alpha allelic variants and extent of bone erosion were evaluated. Results In human osteoclast precursor cells, RANKL induced the expression of LSD1 in a mechanistic target of rapamycin-dependent manner. Expression of LSD1 was higher in synovium from RA patients than in synovium from osteoarthritis patients. Inhibition of LSD1 in human osteoclast precursors suppressed osteoclast differentiation. Results of transcriptome analysis identified several LSD1-mediated hypoxia and cell-cycle pathways as key genetic pathways involved in human osteoclastogenesis. Furthermore, HIF-1 alpha protein, which is rapidly degraded by the proteasome in a normoxic environment, was found to be expressed in RANKL-stimulated osteoclast precursor cells. Induction of LSD1 by RANKL stabilized the expression of HIF-1 alpha protein, thereby promoting glycolysis, in conjunction with up-regulation of the transcription factor E2F1. Analyses of cis-eQTL revealed that higher HIF-1 alpha expression was associated with increased bone erosion in patients with RA. Inhibition of LSD1 decreased pathologic bone resorption in mice, both in models of accelerated osteoporosis and models of arthritis and inflammatory osteolysis. Conclusion LSD1 metabolically regulates osteoclastogenesis in an energy-demanding inflammatory environment. These findings provide potential new therapeutic strategies targeting osteoclasts in the management of inflammatory arthritis, including in patients with RA.
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TI The Effects of Crocin on Bone and Cartilage Diseases
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DT Review
DE crocin; bone; cartilage; inflammation; cell differentiation
ID nf-kappa-b; mesenchymal stem-cells; collagen-induced arthritis; necrosis-factor-alpha; osteogenic differentiation; rheumatoid-arthritis; osteoclast differentiation; follow-up; matrix metalloproteinases; articular-cartilage
AB Crocin, the main biologically active carotenoid of saffron, generally is derived from the dried trifid stigma of Crocus sativus L. Many studies have demonstrated that crocin has several therapeutic effects on biological systems through its anti-oxidant and anti-inflammatory properties. The wide range of crocin activities is believed to be because of its ability to anchor to many proteins, triggering some cellular pathways responsible for cell proliferation and differentiation. It also has therapeutic potentials in arthritis, osteoarthritis, rheumatoid arthritis, and articular pain probably due to its anti-inflammatory properties. Anti-apoptotic effects, as well as osteoclast inhibition effects of crocin, have suggested it as a natural substance to treat osteoporosis and degenerative disease of bone and cartilage. Different mechanisms underlying crocin effects on bone and cartilage repair have been investigated, but remain to be fully elucidated. The present review aims to undertake current knowledge on the effects of crocin on bone and cartilage degenerative diseases with an emphasis on its proliferative and differentiative properties in mesenchymal stem cells.
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DE mesenchymal stromal cell; cell sheet; osteogenesis; beta-TCP; tricalcium phosphate; tissue engineering; in vitro 3D model
ID mesenchymal stem-cells; osteogenic differentiation; in-vitro; nanofibrous scaffolds; stromal cells; 3d culture; pore-size; tissue; marrow; defect
AB Bone diseases such as osteoporosis, delayed or impaired bone healing, and osteoarthritis still represent a social, financial, and personal burden for affected patients and society. Fully humanized in vitro 3D models of cancellous bone tissue are needed to develop new treatment strategies and meet patient-specific needs. Here, we demonstrate a successful cell-sheet-based process for optimized mesenchymal stromal cell (MSC) seeding on a beta-tricalcium phosphate (TCP) scaffold to generate 3D models of cancellous bone tissue. Therefore, we seeded MSCs onto the beta-TCP scaffold, induced osteogenic differentiation, and wrapped a single osteogenically induced MSC sheet around the pre-seeded scaffold. Comparing the wrapped with an unwrapped scaffold, we did not detect any differences in cell viability and structural integrity but a higher cell seeding rate with osteoid-like granular structures, an indicator of enhanced calcification. Finally, gene expression analysis showed a reduction in chondrogenic and adipogenic markers, but an increase in osteogenic markers in MSCs seeded on wrapped scaffolds. We conclude from these data that additional wrapping of pre-seeded scaffolds will provide a local niche that enhances osteogenic differentiation while repressing chondrogenic and adipogenic differentiation. This approach will eventually lead to optimized preclinical in vitro 3D models of cancellous bone tissue to develop new treatment strategies.
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TI Research progress on the hedgehog signalling pathway in regulating bone formation and homeostasis
SO CELL PROLIFERATION
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DT Review
DE bone homeostasis; bone regeneration; hedgehog; mesenchymal stem cells; osteogenesis
ID mesenchymal stem-cells; osteogenic differentiation; sonic hedgehog; osteoblast differentiation; oxysterol; activation; proliferation; regeneration; promotes; purmorphamine
AB Bone formation is a complex regeneration process that was regulated by many signalling pathways, such as Wnt, Notch, BMP and Hedgehog (Hh). All of these signalling have been demonstrated to participate in the bone repair process. In particular, one promising signalling pathway involved in bone formation and homeostasis is the Hh pathway. According to present knowledge, Hh signalling plays a vital role in the development of various tissues and organs in the embryo. In adults, the dysregulation of Hh signalling has been verified to be involved in bone-related diseases in terms of osteoarthritis, osteoporosis and bone fracture; and during the repair processes, Hh signalling could be reactivated and further modulate bone formation. In this chapter, we summarize our current understanding on the function of Hh signalling in bone formation and homeostasis. Additionally, the current therapeutic strategies targeting this cascade to coordinate and mediate the osteogenesis process have been reviewed.
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TI The cumulative incidence of and risk factors for morphometric severe vertebral fractures in Japanese men and women: the ROAD study third and fourth surveys
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LA English
DT Article
DE Incidence; Risk factor; Vertebral fracture
ID quality-of-life; prevalent; osteoporosis; deformity; prediction; mortality; cohort; hip; bmd
AB This population-based cohort study with a 3-year follow-up revealed that the

annual incidence rates of vertebral fracture (VF) and severe VF (sVF) were 5.9%/year and 1.7%/year, respectively. The presence of mild VF at the baseline was a significant risk factor for incident sVF in participants without prevalent sVF. Introduction This study aimed to estimate the incidence of morphometric vertebral fracture (VF) and severe VF (sVF) in men and women and clarify whether the presence of a mild VF (mVF) increases the risk of incident sVF. Methods Data from the population-based cohort study, entitled the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study, were analyzed. In total, 1190 participants aged >= 40 years (mean age, 65.0 +/- 11.2) years completed whole-spine lateral radiography both at the third (2012-2013, baseline) and fourth surveys performed 3 years later (2015-2016, follow-up). VF was defined using Genant's semi-quantitative (SQ) method: VF as SQ >= 1, mVF as SQ = 1, and sVF as SQ >= 2. Cumulative incidence of VF and sVF was estimated. Multivariate logistic regression analyses were performed to evaluate risk factors for incident sVF. Results The baseline prevalence of mVF and sVF were 16.8% and 6.0%, respectively. The annual incidence rates of VF and sVF were 5.9%/year and 1.7%/year, respectively. The annual incidence rates of sVF in participants without prevalent VF, with prevalent mVF, and with prevalent sVF were 0.6%/year, 3.8%/year, and 11.7%/year ($p < 0.001$), respectively. Multivariate logistic regression analyses in participants without prevalent sVF showed that the adjusted odds ratios for incident sVF were 4.12 [95% confident interval 1.85-9.16] and 4.53 [1.49-13.77] if the number of prevalent mVF at the baseline was 1 and >= 2, respectively. Conclusions The annual incidence rates of VF and sVF were 5.9%/year and 1.7%/year, respectively. The presence of prevalent mVF was an independent risk factor for incident sVF.
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TI Management of patients at very high risk of osteoporotic fractures through sequential treatments
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
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DT Review
DE Osteoporosis; Epidemiology; Imminent; Fracture; Anabolic; Antiresorptive
ID bone-mineral density; term denosumab treatment; parathyroid-hormone 1-34; postmenopausal women; zoledronic acid; patients preferences; vertebral fractures; fragility fracture; cost-effectiveness; hip fracture
AB Osteoporosis care has evolved markedly over the last 50 years, such that there are now an established clinical definition, validated methods of fracture risk assessment and a range of effective pharmacological agents. Currently, bone-forming (anabolic) agents, in many countries, are used in those patients who have continued to lose bone mineral density (BMD), patients with multiple subsequent fractures or those who have fractured despite treatment with antiresorptive agents. However, head-to-head data suggest that anabolic agents have greater rapidity and efficacy for fracture risk reduction than do antiresorptive therapies. The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) convened an expert working group to discuss the tools available to identify patients at high risk of fracture, review the evidence for the use of anabolic agents as the initial intervention in patients at highest risk of fracture and consider the sequence of therapy following their use. This position paper sets out the findings of the group and the consequent recommendations. The key conclusion is that the current evidence base supports an "anabolic first" approach in patients found to be at very high risk of fracture, followed by maintenance therapy using an antiresorptive agent, and with the subsequent need for antiosteoporosis therapy addressed over a lifetime horizon.
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NR 136
TC 88
Z9 100
U1 0
U2 12
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 1594-0667
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J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
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EA MAR 2022
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA 1A5IM
UT WOS:000780286200001
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PT J
AU Otieno, J
Ng, R
Graffen, S
Diebold, R
AF Otieno, James
Ng, Rachel
Graffen, Simon
Diebold, Robin
TI Effect of introduction of routine single shot adductor canal block in primary total knee arthroplasty in a rural Australian setting
SO ANZ JOURNAL OF SURGERY
LA English
DT Article
DE anaesthetics; arthroplasty; orthopaedic surgery
ID efficacy
AB Background There is a growing demand for quality osteoarthritis management available in Australia. There has been increasing emphasis on post-total knee replacement pain relief as a significant issue, especially in the context of postoperative recovery protocols which focus on early mobility. Methods The aim of this study was to assess if the addition of adductor canal blocks (ACB) reduced postoperative pain and affected mobility post primary total knee arthroplasty (TKR) at Armidale Rural Referral Hospital (ARRH). A retrospective cohort study was performed of unilateral TKR patients before and after the addition of adductor canal blocks to the TKR protocol at ARRH. Forty-seven patients were included in the study who are matched for age and radiographic disease severity. All patients were prescribed post-operative analgesia per the protocol. Results Patients who received an ACB had a significant difference in opioid consumption in the first 24 h post-operative compared with those who did not, 115.90 mg oral morphine compared to 66.07 mg (P = 0.0001). This was also supported by a significant difference in patient self-rated numerical pain score between groups, no ACB group 3.09/10 and ACB group 1.05/10 (P = 0.0001). The ACB group were able to

mobilize further on post-op days 1 and 2 than those who did not receive an ACB with the ACB group (P = 0.0001 and 0.0008). Conclusion This adds to the evidence supporting the use of Adductor Canal Blocks in patients undergoing total knee arthroplasty, of especial significance in a rural population.
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NR 9
TC 1
Z9 1
U1 0
U2 0
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1445-1433
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J9 ANZ J SURG
JI ANZ J. Surg.
PD NOV 15
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WC Surgery
SC Surgery
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PT J
AU Moura, R
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Kimmich, N
Mascarenhas, T
Natal, R
AF Moura, Rita
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Oliveira, Dulce
Parente, Marco
Kimmich, Nina
Mascarenhas, Teresa
Natal, Renato
TI A biomechanical study of the birth position: a natural struggle between mother and fetus
SO BIOMECHANICS AND MODELING IN MECHANOBIOLOGY
LA English
DT Article
DE Finite element model; Computational simulations; Childbirth biomechanics; Fetal malposition; Sacrum-flexible position; Fetal head molding
ID pelvic floor muscles; fetal head; behavior; malposition; episiotomy; delivery; stress; suture; strain; skull
AB Birth trauma affects millions of women and infants worldwide. Levator ani muscle avulsions can be responsible for long-term morbidity, associated with 13-36% of women who deliver vaginally. Pelvic floor injuries are enhanced by fetal malposition, namely persistent occipito-posterior (OP) position, estimated to affect 1.8-12.9% of pregnancies. Neonates delivered in persistent OP position are associated with an increased risk for adverse outcomes. The main goal of this work was to evaluate the impact of distinct fetal positions on both mother and fetus. Therefore, a finite element model of the fetal head and maternal structures was used to perform childbirth simulations with the fetus in the occipito-anterior (OA) and OP position of the vertex presentation, considering a flexible-sacrum maternal position. Results demonstrated that the pelvic floor muscles' stretch was similar in

both cases. The maximum principal stresses were higher for the OP position, and the coccyx rotation reached maximums of 2.17 degrees and 0.98 degrees for the OP and OA positions, respectively. Concerning the fetal head, results showed noteworthy differences in the variation of diameters between the two positions. The molding index is higher for the OA position, with a maximum of 1.87. The main conclusions indicate that an OP position can be more harmful to the pelvic floor and pelvic bones from a biomechanical point of view. On the other side, an OP position can be favorable to the fetus since fewer deformations were verified. This study demonstrates the importance of biomechanical analyses to further understand the mechanics of labor.
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FU Portuguese Foundation of Science [SFRH/BD/05876/2021]; NORTE2020, through FEDER; [CEECIND/01522/2020]; [UIDB/50022/2020]; [NORTE-01-0145-FEDER-030062]
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NR 48
TC 7
Z9 7
U1 2
U2 8
PU SPRINGER HEIDELBERG
PI HEIDELBERG
PA TIERGARTENSTRASSE 17, D-69121 HEIDELBERG, GERMANY
SN 1617-7959
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J9 BIOMECH MODEL MECHAN
JI Biomech. Model. Mechanobiol.
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WC Biophysics; Engineering, Biomedical
SC Biophysics; Engineering
GA 1P4RI
UT WOS:000778918400001
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PT J
AU Wang, YJ
Liu, L

Qu, ZC
Wang, D
Huang, WL
Kong, LB
Yan, L
AF Wang, Yanjun
Liu, Lin
Qu, Zechao
Wang, Dong
Huang, Wangli
Kong, Lingbo
Yan, Liang
TI Tanshinone Ameliorates Glucocorticoid-Induced Bone Loss via Activation of AKT1 Signaling Pathway
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Article
DE tanshinone; osteoporosis; AKT1; signaling; bone
ID osteoporosis; osteoarthritis; inhibition; iia; biology
AB Purpose: Osteoporosis, a common disorder especially prevalent in the postmenopausal women and the elderly, is becoming a worldwide public health problem. Osteoporosis can cause severe joint pain, fragility fractures, and other symptoms, which can seriously impair the daily lives of affected patients. Currently, no gold-standard drug is available that can completely cure osteoporosis. Tanshinone is a traditional Chinese medicine, which can exhibit multiple biological activities. It might also display a protective effect on osteoporosis. However, the molecular mechanism through which tanshinone can improve osteoporosis remain unclear. The objective of our study is to explore the underlying mechanism behind the protective actions of tanshinone.Methods: The common KEGG pathways of tanshinone-targeted genes and osteoporosis were analyzed by using bioinformatics analysis. The bioinformatics analysis results were further validated both by in vitro and in vivo experiments.Results: 21 common KEGG pathways were identified between osteoporosis and tanshinone-targeted genes. It was further found that tanshinone could induce expression of AKT1, promote the proliferation of MSCs, and ultimately suppress their apoptosis.Conclusion: Taken together, our findings indicate that tanshinone can alleviate osteoporosis, its effect was potentially mediated through modulating AKT1 expression. Thus, tanshinone could serve as a promising treatment option for osteoporosis.
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NR 38
TC 21
Z9 27
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U2 32
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J9 FRONT CELL DEV BIOL
JI Front. Cell. Dev. Biol.
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WC Cell Biology; Developmental Biology
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AU Zhao, JL
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TI Combination of mesenchymal stem cells (MSCs) and platelet-rich plasma (PRP) in the treatment of knee osteoarthritis: a meta-analysis of randomised controlled trials
SO BMJ OPEN
LA English
DT Article
DE Knee; Adult surgery; Health informatics
ID intraarticular injection; hyaluronic-acid; osteoporosis; management; pain
AB Objectives The purpose of this meta-analysis was to investigate the efficacy and safety of mesenchymal stem cells (MSCs) combined with platelet-rich plasma (PRP) in the treatment of knee osteoarthritis (KOA). Design Systematic review and meta-analysis. Participants Patients with KOA. Interventions Use of MSCs+PRP. Primary and secondary outcomes Visual Analogue Scale (VAS) score, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, Knee Injury and Osteoarthritis Outcome Score (KOOS) and adverse reactions. Data sources PubMed, Cochrane Library, Embase and China National Knowledge Infrastructure were searched from inception to 15 July 2021. Measures The OR or weighted mean difference (WMD) of relevant outcome indicators was calculated. Study quality was evaluated using the risk-of-bias assessment tool version 2.0. Heterogeneity among studies was evaluated by calculating I-2. If I-2<50%, a fixed-effect model was applied; conversely, if I-2 <= 50%, a random-effect model was applied. Results Six controlled clinical trials with 493 cases were included. The meta-analysis results showed that in terms of the VAS score 3 months after treatment, MSCs+PRP had no significant effect on the reduction of the VAS score in patients with KOA compared with the control (p=0.09), hyaluronic acid (HA) (p=0.15) or PRP alone (p=0.07). MSCs+PRP was more effective in reducing the VAS score at 6 and 12 months after treatment than the control (WMD=-0.55, 95% CI -0.87 to -0.22, p<0.001), HA (WMD=-1.20, 95% CI -2.28 to -0.13, p=0.03) or PRP alone (WMD=-0.54, 95% CI -0.89 to -0.18, p=0.003). Regarding the decrease in the total WOMAC score at 3 and 6 months after treatment, MSCs+PRP showed better clinical efficacy than the control or HA alone (p<0.01). Compared with the control, MSCs+PRP exhibited no significant difference in reducing the total WOMAC score 12 months after treatment (p=0.39). There was no significant difference between MSCs+PRP and the control in terms of improvement of the KOOS 12 months after

treatment (p=0.16). Compared with MSCs alone, MSCs+PRP exhibited no significant difference in the incidence of adverse reactions (p=0.22) 12 months after treatment. Conclusions Treatment with MSCs+PRP showed good clinical efficacy in improving pain and joint function in patients with KOA. Compared with MSCs alone, there was no significant difference in the incidence of adverse reactions with MSCs+PRP.
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AF Buckberry, Jo
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TI The dark satanic mills: Evaluating patterns of health in England during the industrial revolution
SO INTERNATIONAL JOURNAL OF PALEOPATHOLOGY
LA English
DT Article
DE Industrialisation; Fractures; Infection; Metabolic disease; Osteoarthritis; Dental disease
ID vitamin-d deficiency; cribra-orbitalia; medieval; london; tuberculosis; population; evolution; pathology; century; anatomy
AB Objective: this research seeks to investigate the impact the industrial revolution had on the population of England. Materials: Pre-existing skeletal data from 1154 pre-Industrial (1066-1700 CE) and 4157 industrial (1700-1905) skeletons from 21 cemeteries (N = 5411). Methods: Context number, sex, age-at-death, stature and presence/absence of selected pathological conditions were collated. The data were compared using chi square, Kolmogorov-Smirnov, t-tests and logistic regression

(alpha = 0.01). Results: There was a statistically significant increase in cribra orbitalia, periosteal reactions, rib lesions, fractures, rickets, osteoporosis, osteoarthritis, enamel hypoplasia, dental caries and periapical lesions in the industrial period. Osteomyelitis decreased from the pre-industrial to industrial period. Conclusion: Our results confirm the industrial revolution had a significant negative impact on human health, however the prevalence of TB, treponemal disease, maxillary sinusitis, osteomalacia, scurvy, gout and DISH did not change, suggesting these diseases were not impacted by the change in environmental conditions. Significance: This is the largest study of health in the industrial revolution that includes non-adults and adults and considers age-at-death alongside disease status to date. This data supports the hypothesis that the rise of industry was associated with a significant decline in general health, but not an increase in all pathological conditions.
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TI Causal Association Between Tea Consumption and Bone Health: A Mendelian

Randomization Study
SO FRONTIERS IN NUTRITION
LA English
DT Article
DE tea consumption; osteoarthritis; rheumatoid arthritis; osteoporosis; SNP; mendelian randomization
ID rheumatoid-arthritis; knee osteoarthritis; instruments; inference; caffeine; risk
AB BackgroundMuch observational research reported that tea consumption decreases the risk of osteoarthritis (OA), rheumatoid arthritis (RA), and osteoporosis (OP) which are the three major bone disorders. However, the observed correlation is inconclusive. To determine the causal relationship between genetically predicted tea intake and OA, RA, and OP, we performed a two-sample Mendelian randomization (MR) study based on large samples. MethodsThe European population's genome-wide association meta-analysis (GWAS) dataset identified SNPs associated with tea consumption was obtained from Neale Lab's analysis of UK Biobank data that comprised 349,376 participants of European ancestry. We extracted genetic data for knee OA (17,885 controls and 4,462 cases), hip OA (50,898 controls and 12,625 cases), and RA (43,923 controls and 14,361 cases) from the UK Biobank and OP cases (93083 controls and 1,175 cases) from FinnGen Data Freeze 2. A MR study was conducted to examine the effect of selected single nucleotide polymorphisms (SNPs) and OA, RA, and OP risk. Several sensitivity analyses were performed with weighted median and inverse-variance weighted methods for estimating the causal effects. ResultsIn this MR study, the genetically predicted per one cup increase of tea consumption was not associated with knee OA (OR 1.11,95% CI: 0.79-1.55) using IVW with random effect. Genetic predisposition to tea consumption was not associated with hip OA (OR: 1.20, 95% CI: 0.84-1.71), RA (OR: 1.24 95% CI: 0.81-1.91), and OP (OR: 1.11, 95% CI: 0.89, 1.39). Following the sensitivity analysis, there was no potential pleiotropy. ConclusionAccording to our study, According to our study, there was no statistical power to confirm a causal relationship between tea consumption and the risk of knee OA, hip OA, RA, and OP.
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NR 41
TC 20
Z9 21
U1 1
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PT J
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TI Phantom limb syndrome: Assessment of psychiatric and medical comorbidities associated with Phantom pain in 44,028 below knee amputees
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE Phantom limb syndrome; Amputation; Comorbidities; Psychiatric; Medical
ID quality-of-life; long-term; amputation; depression; osteoarthritis; prevalence; distress; anxiety
AB Introduction: Phantom limb syndrome is a debilitating complication after extremity amputation that poses significant challenges to recovery. This study aims to examine the relationship between phantom limb syndrome and mental and physical comorbidities, including a comparison between phantom limb pain and phantom limb syndrome without pain in below knee amputees.Methods: This is a retrospective cohort study of patients who underwent below knee amputation of the lower extremity in the PearlDiver database, as identified using CPT codes. Analysis was carried out to evaluate the absence or presence of phantom limb syndrome. Matched bivariate analysis accounting for age, sex, Charlson Comorbidity Index score, and region was used to assess whether the presence of pain in phantom limb syndrome patients was associated with increased comorbidity.Results: In total, 44,028 patients with below knee amputation were examined: 95% (42,493 patients) did not develop phantom limb syndrome while 4.8% (1,535 patients) of patients did develop phantom limb syndrome. Phantom limb syndrome was significantly associated with increased odds of coexistent major depressive disorder (OR = 1.86, p < 0.0 0 01), generalized anxiety disorder (OR = 2.14, p = 0.04), posttraumatic stress disorder (OR = 1.7, p < 0.0 0 01), suicidal ideation (OR = 1.62, p < 0.0 0 01), obesity (OR = 1.28, p = 0.0 0 07), osteoarthritis (OR = 1.53, p < 0.0 0 01), osteoporosis (OR = 1.64, p < 0.0 0 01), and low back pain (OR = 2.31, p < 0.0 0 01). Analysis of patient cohorts of phantom limb syndrome with pain and those without pain did not reveal a statistically significant relationship between the presence of pain and any dependent variable.Conclusions: This investigation of over 44,0 0 0 patients with below knee amputation revealed that pa-tients with phantom limb syndrome exhibit significantly higher rate of psychiatric comorbidities com-pared to those without

documented phantom limb pain. Suicidal ideation, major depressive disorder, gen-eralized anxiety disorder, and post-traumatic stress disorder were especially common, and consequently a multi-disciplinary approach to management is essential.(c) 2022 Elsevier Ltd. All rights reserved.
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10.1080/03093640802016316
NR 24
TC 11
Z9 13
U1 0
U2 9
PU ELSEVIER SCI LTD
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TI 3D Bioprinted Hydroxyapatite or Graphene Oxide Containing Nanocellulose-Based Scaffolds for Bone Regeneration
SO MACROMOLECULAR BIOSCIENCE
LA English
DT Article
DE 3D bioprinting; bioinks; bone; graphene oxide; hydroxyapatite; tissue engineering
ID hydrogels; cells; differentiation
AB Bone tissue is usually damaged after big traumas, tumors, and increasing aging-related diseases such as osteoporosis and osteoarthritis. Current treatments are based on implanting grafts, which are shown to have several inconveniences. In this regard, tissue engineering through the 3D bioprinting technique has arisen to manufacture structures that would be a feasible therapeutic option for bone regenerative medicine. In this study, nanocellulose-alginate (NC-Alg)-based bioink is improved by adding two different inorganic components such as hydroxyapatite (HAP) and graphene oxide (GO). First, ink rheological properties and biocompatibility are evaluated as well as the influence of the sterilization process on them. Then, scaffolds are characterized. Finally, biological studies of embedded murine D1 mesenchymal stem cells engineered to secrete erythropoietin are performed. Results show that the addition of both HAP and GO prevents NC-Alg ink from viscosity lost in the sterilization process. However, GO is reduced due to short cycle autoclave sterilization, making it incompatible with this ink. In addition, HAP and GO have different influences on scaffold architecture and surface as well as in swelling capacity. Scaffolds mechanics, as well as cell viability and functionality, are promoted by both elements addition. Additionally, GO demonstrates an enhanced bone differentiation capacity.
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NR 72
TC 23
Z9 24
U1 7
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PU WILEY-V C H VERLAG GMBH
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AU Franz, A
Ji, SHY
Bittersohl, B
Zilkens, C
Behringer, M
AF Franz, Alexander
Ji, Sanghyeon
Bittersohl, Bernd
Zilkens, Christoph
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TI Impact of a Six-Week Prehabilitation With Blood-Flow Restriction Training on Pre- and Postoperative Skeletal Muscle Mass and Strength in Patients Receiving Primary Total Knee Arthroplasty
SO FRONTIERS IN PHYSIOLOGY
LA English
DT Article
DE venous occlusion; kaatsu training; muscle atrophy; rehabilitation; exercise therapy
ID quality-of-life; exercise; atrophy; performance; disability; outcm; women; thigh; hip
AB Introduction: Total Knee Arthroplasty (TKA) is one of the most successful interventions in gonarthrosis, however the operation is leading to muscle atrophy and long-term muscular deficits. To enhance rehabilitation after TKA, exercise programs try to improve muscle function preoperatively, called prehabilitation. Blood-Flow-Restriction Exercises (BFRE) is a training method which is characterized by using tourniquets to reduce arterial and occlude venous blood flow simultaneously during the exercise to increase metabolic stress. The present study

aimed to evaluate the effects of a 6-week prehabilitation with BFR on pre- and postoperative muscle mass, strength, and quality of life (QoL).Methods: 30 patients with end-stage gonarthrosis participated in this study. Patients were randomized into one of three groups: 1) Control-Group (CON): Standard clinical approach without prehabilitation. 2) Active-Control-Group (AC): Participation in a prehabilitation with sham-BFR. 3) BFR-Group (BFR): Participation in a prehabilitation with BFR. The prehabilitation protocol consist of a cycling-ergometer-based training performed twice per week over 6 weeks. During exercise, BFR was applied periodically three times per leg with a pressure of 40% of the individual-limb-occlusion-pressure. Measurement time points were six- (baseline), 3-weeks and 5-days before the surgery (Pre-OP), as well as three- and 6-months postoperatively. Outcome measures were muscular strength of the thigh muscles, thigh circumference as well as QoL and functional activity, examined by 6-min walking- and chair rising test.Results: Both training groups indicated significantly improved leg muscle strength following the prehabilitation period with a superior effect for the BFR-group (BFR: similar to 170% vs. AC: similar to 91%, $p < 0.05$). No significant changes in leg strength occurred in the CON (similar to 3%, $p = 0.100$). Further, patients in BFR-group indicated significantly improved skeletal muscle mass assessed by femoral circumference following prehabilitation period (similar to 7%, $p < 0.05$), while no significant changes occurred in the CON (-1.14%, $p = 0.131$) and AC-group (similar to 3%, $p = 0.078$). At 3-months Post-OP, the CON and BFR-group revealed a significant decrease in femoral circumference compared to the Pre-OP (CON: similar to 3%, BFR: similar to 4%; $p < 0.05$), but BFR-group remained above the baseline level (similar to 3%, $p < 0.05$). No significant change in femoral circumference was found for AC-group (similar to 2%, $p = 0.078$). In addition, the prehabilitation with BFR provided notably improved Knee Injury and Osteoarthritis Outcome Scores (KOOS) especially in pain perception with significant higher effect compared to other groups (CON: -2%, AC: 13%, BFR: 41%; $p < 0.05$). In long-term rehabilitation after 6-months, all groups showed significantly improved KOOS scores in all dimensions (CON: similar to 110%, AC: similar to 132%, BFR: similar to 225%; $p < 0.01$), and functional examinations (CON: similar to 26%, AC: similar to 16%, BFR: similar to 53%; $p < 0.01$).Conclusion: The present findings show that BFR-prehabilitation induce significant improvements in muscle function and QoL before TKA surgery. In addition, the supporting effect of prehabilitation on postoperative regeneration and QoL should be highlighted, illustrating prolonged beneficial effects of BFR on muscular and functional performance in a "better in, better out"-manner.
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TC 27
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AU Cheng, KM
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TI Mapping Knowledge Landscapes and Emerging Trends of the Links Between Bone Metabolism and Diabetes Mellitus: A Bibliometric Analysis From 2000 to 2021
SO FRONTIERS IN PUBLIC HEALTH
LA English
DT Article
DE diabetes mellitus; bone metabolism; bibliometrics; CiteSpace; VOSviewer; Bibliometrix
ID fracture risk; vertebral fractures; sglt2 inhibitors; type-1; women; men; metaanalysis; mechanisms; expression; density
AB BackgroundDiabetes mellitus (DM) have become seriously threatens to human health and life quality worldwide. As a systemic metabolic disease, multiple studies have revealed that DM is related to metabolic bone diseases and always induces higher risk of fracture. In view of this, the links between bone metabolism (BM) and DM (BMDM) have gained much attention and numerous related papers have been published. Nevertheless, no prior studies have yet been performed to analyze the field of BMDM research through bibliometric approach. To fill this knowledge gap, we performed a comprehensive bibliometric analysis of the global scientific publications in this field. MethodsArticles and reviews regarding BMDM published between 2000 and 2021 were obtained from the Web of Science after manually screening. VOSviewer 1.6.16, CiteSpace V 5.8.R3, Bibliometrix, and two online analysis platforms were used to conduct the bibliometric and visualization analyses. ResultsA total of 2,525 documents including 2,255 articles and 270 reviews were retrieved. Our analysis demonstrated a steady increasing trend in the number of publications over the past 22 years (R-2 = 0.989). The United States has occupied

the leading position with the largest outputs and highest H-index. University of California San Francisco contributed the most publications, and Schwartz AV was the most influential author. Collaboration among institutions from different countries was relatively few. The journals that published the most BMDM-related papers were Bone and Osteoporosis International. Osteoporosis and related fractures are the main bone metabolic diseases of greatest concern in this field. According to co-cited references result, "high glucose environment," "glycation end-product" and "sodium-glucose co-transporter" have been recognized as the current research focus in this domain. The keywords co-occurrence analysis indicated that "diabetic osteoporosis," "osteoarthritis," "fracture risk," "meta-analysis," "osteogenic differentiation," "bone regeneration," "osteogenesis," and "trabecular bone score" might remain the research hotspots and frontiers in the near future. ConclusionAs a cross-discipline research field, the links between bone metabolism and diabetes mellitus are attracting increased attention. Osteoporosis and related fractures are the main bone metabolic diseases of greatest concern in this field. These insights may be helpful for clinicians to recognize diabetic osteopenia and provide more attention and support to such patients.
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U1 28
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TI Is bone marrow oedema in patients with labral tear an indicator of hip pain?
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Bone marrow oedema; Labral tear; Modified Harris hip score; Hip pain
ID transient osteoporosis; cartilage loss; lesions; association; osteoarthritis; osteonecrosis; prevalence; risk
AB Background Hip labral tear (LT) causes various degrees of hip pain, for which there are few objective measures. Bone marrow oedema (BME), characterized by a diffuse, widely spreading change in the bone marrow, is observed in some patients with LT. However, its pathological role has not been fully understood. The purpose of this study was to investigate the prevalence of BME on hip magnetic resonance imaging (MRI) in patients with LT and to determine whether BME was an objective indicator of hip pain. Methods In total, 84 patients with LT who underwent MRI scanning under the same conditions were included. We determined the presence or absence of BME and its size on MRI and evaluated the relationships between BME and sex, age, and pain and total scores on the modified Harris hip score (MHHS). In addition, we collected data on surgical treatments such as hip arthroscopy within a one-year follow-up period and examined whether the presence of BME affected the course of therapy. Results BME was found in 34.5% of patients. MHHS pain and total scores were significantly lower in patients with BME (MHHS pain score: non-BME vs. BME <= 1 cm: $p = 0.022$, non-BME vs. BME > 1 cm: $p < 0.001$; MHHS total score: non-BME vs. BME <= 1 cm: $p = 0.131$, non-BME vs. BME > 1 cm: $p = 0.027$). The presence of BME did not differ between patients who did and did not undergo surgery during follow-up ($p = 0.563$). Conclusion BME on MRI in patients with LT might be an indicator of hip pain and hip joint dysfunction.

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NR 35
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PG 7
WC Orthopedics
SC Orthopedics
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PT J
AU Thoreau, L
Marfil, DM
Thienpont, E
AF Thoreau, L.
Marfil, D. Morcillo
Thienpont, E.
TI Periprosthetic fractures after medial unicompartmental knee arthroplasty: a narrative review
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Review
DE Uni-compartmental knee arthroplasty; Peri-prosthetic fracture; Aseptic loosening; Fracture load; Tibial plateau
ID bone-mineral density; tibial plateau fractures; stress-fracture; vitamin-d; total hip; osteoarthritis; osteoporosis; replacement; mass; penetration
AB Introduction On rare occasions, fractures of the tibial plateau may occur after uni-compartmental knee arthroplasty (UKA) and account for 2% of total UKA failures. The purpose of this narrative review is to identify and discuss potential risk factors that might lead to prevention of this invalidating complication. Materials and methods Electronic database of Pubmed, Scopus, Cochrane and Google Scholar were searched. A total of 457 articles related to the topic were found. Of those, 86 references were included in this narrative review. Results UKA implantation acts as a stress riser in the medial compartment. To avoid fractures, surgeons need to balance load and bone stock. Post-operative lower limb alignment, implant positioning, level of resection and sizing of the tibial tray have a strong influence on load distribution of the tibial bone. Pain on weight-bearing signals bone-load imbalance and acts as an indicator of bone remodeling and should be a trigger for unloading. The first three months after surgery are critical because of transient post-operative osteoporosis and local biomechanical changes. Acquired osteoporosis is a growing concern in the arthroplasty population. Split fractures require internal fixation, while subsidence fractures differ in their management depending of the amount of bone impaction. Loose implants require revision knee arthroplasty. Conclusion Peri-prosthetic fracture is a rare, but troublesome event, which can lead to implant failure and revision surgery. Better knowledge of the multifactorial risk factors in association with a thorough surgical technique is key for prevention.
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NR 82
TC 23
Z9 27
U1 0
U2 7
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J9 ARCH ORTHOP TRAUM SU
JI Arch. Orthop. Trauma Surg.

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TI Comprehensive assessment of multimorbidity burden in a population-based cohort of patients with rheumatoid arthritis
SO RMD OPEN
LA English
DT Article
DE rheumatoid arthritis; epidemiology; cardiovascular diseases
ID records-linkage system; cardiovascular risk; epidemiology; association; impact
AB Objective To comprehensively assess multimorbidity burden in patients with rheumatoid arthritis (RA) in order to unify the multimorbidity definition for RA research and clinical practice. Methods In this population-based study, residents of

eight Minnesota counties with prevalent RA on 1 January 2015 were identified. Age, sex and county-matched non-RA comparators were selected from the same population. Diagnostic codes were retrieved for 5 years before 1 January 2015. Using two codes >= 30 days apart, 44 previously defined morbidities and 78 non-overlapping chronic disease categories based on Clinical Classification Software were defined. Prevalence of each morbidity in the RA versus non-RA cohorts was compared using false discovery rate to adjust for multiple comparisons. Morbidities more common in RA than non-RA and those with prevalence >= 5% were retained. Results 1643 patients with RA and 1643 non-RA subjects (72% women; mean age 63.1 years) were studied. Using the 44 morbidities, multimorbidity (defined as 2+ morbidities) was present in 1411 (86%) of RA and 1164 (71%) of non-RA subjects ($p<0.001$) with 5+ morbidities present in 907 (55%) of RA and 619 (38%) of non-RA ($p<0.001$). Patients with RA had significantly higher prevalence of 24 of the 44 morbidities compared with non-RA, especially interstitial lung disease, fibromyalgia, osteoarthritis and osteoporosis. Among the additional 78 categories, 7 were significantly higher in RA than non-RA, including organic sleep disorders, vitamin D deficiency and foot ulcers. Conclusion Patients with RA have a higher prevalence of multimorbidity compared with non-RA subjects. These results confirm the list of 44 morbidities and add several other morbidities of interest in RA.
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NR 19
TC 23
Z9 25
U1 1
U2 8
PU BMJ PUBLISHING GROUP
PI LONDON
PA BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND
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PD JAN 15
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WC Rheumatology
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TI Sex- and Age-Related Dynamic Changes of the Macroelements Content in the Femoral Bone with Hip Osteoarthritis
SO BIOLOGY-BASEL
LA English
DT Article
DE structural elements; macroelements; femoral bone; Ca; P radio; ICP-OES; arthroplasty; osteoarthrosis; osteoporosis; bone mineral density (BMD)
ID trabecular bone; mineral density; knee; fracture; women; neck; microarchitecture; replacement; head
AB Simple Summary The study assessed the content of macroelements Ca, Mg, P, and Na in the proximal femoral bone tissue in patients with hip osteoarthritis, and it correlated with age, sex, and BMI. The high reduction of macroelements in the femoral bone of patients with hip osteoarthritis is more pronounced in the cortical bone and occurs in women under 60 years of age. In men, it begins in the seventh and increases in the eighth decade of life. Background: The content of macroelements in bones varies with age and depends on sex. The aim of the study was to evaluate the content of macroelements and its correlation with age and sex in the femoral bone obtained during total hip arthroplasty. Methods: In the 86 patients, the content of macroelements (Ca, P, Mg, and Na) in the femoral head and neck (cancellous and cortical bone) was assessed by means of the inductively coupled plasma optical emission spectrometry analytical technique (ICP-OES). Results: There was a decrease in the content of macroelements in the cortical bone with age in the women in the 51-60 years (statistically significant: -0.59 for Ca, -0.65 for P) and over 70 years age groups (correlation not statistically significant: -0.29 for Ca, -0.38 for P). A significant decrease in the content of macroelements in the cortical bone was found in men over 70 years of age. Conclusions: Patterns of increased loss of macronutrients (Ca, P, and Mg) in the femoral neck (cortical bone) were demonstrated in the following patients with osteoarthritis: women aged

51-60 years and patients of both sexes over 70 years of age.
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NR 30
TC 2
Z9 2
U1 0
U2 2
PU MDPI
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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TI Disease consequences of higher adiposity uncoupled from its adverse metabolic effects using Mendelian randomisation
SO ELIFE
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DT Article
DE Mendelian randomisation; obesity; favourable adiposity; cardiovascular disease; cancer; Human
ID body-mass index; genome-wide association; alzheimers-disease; genetic-loci; risk loci; metaanalysis; obesity; causal; identification; psoriasis
AB Background: Some individuals living with obesity may be relatively metabolically healthy, whilst others suffer from multiple conditions that may be linked to adverse metabolic effects or other factors. The extent to which the adverse metabolic component of obesity contributes to disease compared to the non-metabolic components is often uncertain. We aimed to use Mendelian randomisation (MR) and specific genetic variants to separately test the causal roles of higher adiposity with and without its adverse metabolic effects on diseases. Methods: We selected 37 chronic diseases associated with obesity and genetic variants associated with different aspects of excess weight. These genetic variants included those associated with metabolically 'favourable adiposity' (FA) and 'unfavourable adiposity' (UFA) that are both associated with higher adiposity but with opposite effects on metabolic risk. We used these variants and two sample MR to test the effects on the chronic diseases. Results: MR identified two sets of diseases. First, 11 conditions where the metabolic effect of higher adiposity is the likely primary cause of the disease. Here, MR with the FA and UFA genetics showed opposing effects on risk of disease: coronary artery disease, peripheral artery disease, hypertension, stroke, type 2 diabetes, polycystic ovary syndrome, heart failure, atrial fibrillation, chronic kidney disease, renal cancer, and gout. Second, 9 conditions where the non-metabolic effects of excess weight (e.g. mechanical effect) are likely a cause. Here, MR with the FA genetics, despite leading to lower metabolic risk, and MR with the UFA genetics, both indicated higher disease risk: osteoarthritis, rheumatoid arthritis, osteoporosis, gastro-oesophageal reflux disease, gallstones, adult-onset asthma, psoriasis, deep vein thrombosis, and venous thromboembolism. Conclusions: Our results assist in understanding the consequences of higher adiposity uncoupled from its adverse metabolic effects, including the risks to individuals with high body mass index who may be relatively metabolically healthy. Funding: Diabetes UK, UK Medical Research Council, World Cancer Research Fund, National Cancer Institute.
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AF Zhao, Jinlong
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TI The efficacy and safety of Jinwu Gutong capsule in the treatment of knee osteoarthritis: A meta-analysis of randomized controlled trials
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE Efficacy; Safety; Knee osteoarthritis; Jinwu Gutong capsule; Meta-analysis
AB Ethnopharmacological relevance: The Jinwu Gutong (JWGT) capsule is a Chinese patent medicine that is widely used in the treatment of knee osteoarthritis (KOA) and osteoporosis in China and is considered to have the potential for good clinical efficacy.& nbsp;Aim of the study: The purpose of this study was to systematically evaluate the clinical efficacy and safety of JWGT in the treatment of KOA.& nbsp;Materials and methods: We searched the China National Knowledge Infrastructure (CNKI), Wanfang, SinoMed, PubMed, Embase and Cochrane Library databases to identify clinical trials that explore the use of JWGT only or JWGT combined with Western drugs (JWGT group) compared with the use of conventional Western drugs (Western drugs group) for the treatment of KOA. The clinical trials, that were retrieved from each database from the inception of the database to December 2021, were screened. We used the risk of bias assessment tool recommended by Cochrane to evaluate the quality of the included literature and RevMan 5.3 software for data analysis.& nbsp;Results: A total of 17 clinical

randomized controlled trials (RCTs) were included in this study, with a total of 1930 participants, including 1015 people in the experimental group and 915 people in the control group. The results of the meta-analysis showed that the JWGT group exhibited better efficacy than the Western drug group with respect to WOMAC score (WMD =-6.25, 95% CI =-8.09 to-4.41, P < 0.001), VAS score (WMD =-1.36, 95% CI =-2.17 to-0.55, P = 0.001), KSS score (WMD = 23.01, 95% CI = 21.42 to 24.59, P < 0.001), IL-6 (SMD = -3.30, 95% CI =-4.84 to-1.76, P < 0.001), TNF-alpha (SMD =-1.70, 95% CI =-2.02 to-1.38, P < 0.001). The effective rate (OR = 2.56, 95% CI = 1.83 to 3.57, P < 0.001) and incidence of adverse reactions was significantly lower in the JWGT group than in the control group (OR = 0.13, 95% CI = 0.07 to 0.21, P < 0.001). Subgroup analysis showed that JWGT + NSAIDs had more advantages in regard to efficacy (OR = 2.05, 95% CI = 1.35 to 3.12, P < 0.001), and reducing adverse reactions (OR = 0.10, 95% CI = 0.06 to 0.18, P < 0.001), VAS score (WMD =-1.00, 95% CI =-1.93 to-0.07, P = 0.04), KSS score (WMD = 17.39, 95% CI = 15.39 to 19.39, P < 0.001), WOMAC score (WMD =-2.84, 95% CI =-10.75 to 5.08, P < 0.001), IL-6 (SMD =-1.42, 95% CI = -2.08 to-0.75, P < 0.001) and TNF-alpha (SMD =-1.68, 95% CI =-1.93 to-1.43, P < 0.001) than NSAIDs alone. Compared with hyaluronic acid (HA) alone, JWGT + HA had better clinical efficacy (OR = 3.08, 95% CI = 1.48 to 6.40, P < 0.001). Compared with glucosamine (GS) alone, JWGT + GS significantly reduced the Lequesne index score (WMD =-0.53, 95% CI =-0.85 to-0.21, P = 0.001) and the serum TNF-alpha level (SMD =-1.68, 95% CI =-1.93 to-1.43, P < 0.001), but it had no significant advantage in reducing the serum IL-6 level (SMD =-4.53, 95% CI =-10.13 to 1.07, P = 0.11).& nbsp;Conclusion: JWGT is considered effective and safe in the treatment of KOA and is worthy of clinical application. In addition, the application of JWGT combined with NSAIDs, HA or GS can significantly improve the clinical efficacy of the latter agents in KOA treatment.
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Z9 7
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PU ELSEVIER IRELAND LTD
PI CLARE
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AU Xiao, JC
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Chen, Bohao
Wang, Haibin
TI Bioinformatics analysis combined with experimental validation to explore the mechanism of XianLing GuBao capsule against osteoarthritis
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE XianLing GuBao capsule; PI3K/AKT/NF-?B pathway; MAPK pathway; Osteoarthritis; Bioinformatics analysis
ID inflammation; pathway; cartilage; chondrocytes; degradation; expression; inhibitor; health; knee; il-6
AB Ethnopharmacological relevance: XianLing GuBao Capsule (XLGB) is often used to treat osteoarthritis (OA), osteoporosis, fractures, and other musculoskeleton disorders. However, the molecular mechanism of XLGB for treating OA is still unclear. Aim of the study: This study set out to uncover the molecular mechanism underlying the treatment of osteoarthritis with XLGB. Materials and methods: Disease genes were obtained from CTD, DisGeNET, and GeneCards databases, and

XLGB drug targets were obtained from ETCM and target genes predicted by XLGB metabolic components reported in the literature. Then we used the Venn diagram viewer to extract disease and drug intersection genes as potential therapeutic genes for Protein-protein interaction (PPI), GO terminology, and KEGG pathway analysis. Subsequently, we performed qRT-PCR, Western blot and histological analysis to validate the therapeutic effect of XLGB against OA and its molecular mechanism. Results: A total of 1039 OA genes and 949 XLGB target genes were collected, and finally 188 potential therapeutic target genes were obtained. PPI network analysis indicated that the main target genes for XLGB to treat OA include Akt1, Mapk3, Il-6, Il-1 beta, Ptgs2, Mmp9, etc. The results of KEGG and GO enrichment analysis suggested that XLGB may treat OA by anti-inflammatory and reducing extracellular matrix degradation. In vitro, XLGB down regulated the expressions of Mmp3, Mmp9, Mmp12, Mmp13, Cox-2, Il-6, increased the expression of Collagen II and Sox9. Mechanistically, XLGB inhibits the activation of PI3K/AKT/NF-kappa B and MAPK pathways. Moreover, the results of animal experiments indicated that XLGB reduced cartilage destruction, bone resorption, and synovitis in osteoarthritic rats. Conclusions: XLGB has a protective effect against OA by suppressing PI3K/AKT/NF-kappa B and MAPK signaling. Our study provides a theoretical basis for XLGB in the treatment of osteoarthritis.
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U2 24
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AU Wang, B
Wang, H
Li, YC
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TI Lipid metabolism within the bone micro-environment is closely associated with bone metabolism in physiological and pathophysiological stages
SO LIPIDS IN HEALTH AND DISEASE
LA English
DT Review
DE Lipid metabolism; Bone metabolism; Bone destruction diseases
ID mineral density; osteoclast differentiation; serum-cholesterol; ewing sarcoma; stem-cells; in-vitro; osteoporosis; statins; rankl; osteogenesis
AB Recent advances in society have resulted in the emergence of both hyperlipidemia and obesity as life-threatening conditions in people with implications for various types of diseases, such as cardiovascular diseases and cancer. This is further complicated by a global rise in the aging population, especially menopausal women, who mostly suffer from overweight and bone loss simultaneously. Interestingly, clinical observations in these women suggest that osteoarthritis may be linked to a higher body mass index (BMI), which has led many to believe that there may be some degree of bone dysfunction associated with conditions such as obesity. It is also common practice in many outpatient settings to encourage patients to control their BMI and lose weight in an attempt to mitigate mechanical stress and thus reduce bone pain and joint dysfunction. Together, studies show that bone is not only a mechanical organ but also a critical component of metabolism, and various endocrine functions, such as calcium metabolism. Numerous studies have demonstrated a relationship between metabolic dysfunction in bone and abnormal lipid metabolism. Previous studies have also regarded obesity as a metabolic disorder. However, the relationship between lipid metabolism and bone metabolism has not been fully elucidated. In this narrative review, the data describing the close relationship between bone and lipid metabolism was summarized and the impact on both the normal physiology and pathophysiology of these tissues was discussed at both the molecular and cellular levels.

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NR 107
TC 68
Z9 82
U1 5
U2 52
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
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J9 LIPIDS HEALTH DIS
JI Lipids Health Dis.
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SC Biochemistry & Molecular Biology; Nutrition & Dietetics
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AU Nemeria, NS
Nagy, B
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AF Nemeria, Natalia S.
Nagy, Balint
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TI Functional Versatility of the Human 2-Oxoadipate Dehydrogenase in the L-Lysine Degradation Pathway toward Its Non-Cognate Substrate 2-Oxopimelic Acid
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE 2-oxoadipate dehydrogenase; L-lysine degradation pathway; 2-oxopimelate substrate; 2-oxoadipate dehydrogenase complex; E1a promiscuity; H2O2 production; rare E1a variants
ID lipoyl domain; dhtkd1 mutations; e3 components; e1 component; complex; mechanism; identification; visualization; catalysis; enzymes
AB The human 2-oxoadipate dehydrogenase complex (OADHc) in L-lysine catabolism is involved in the oxidative decarboxylation of 2-oxoadipate (OA) to glutaryl-CoA and NADH (+H+). Genetic findings have linked the DHTKD1 encoding 2-oxoadipate dehydrogenase (E1a), the first component of the OADHc, to pathogenesis of AMOXAD, eosinophilic esophagitis (EoE), and several neurodegenerative diseases. A multipronged approach, including circular dichroism spectroscopy, Fourier Transform Mass Spectrometry, and computational approaches, was applied to provide novel insight into the mechanism and functional versatility of the OADHc. The results demonstrate that E1a oxidizes a non-cognate substrate 2-oxopimelate (OP) as well as OA through the decarboxylation step, but the OADHc was 100-times less effective in reactions producing adipoyl-CoA and NADH from the dihydrolipoamide succinyltransferase (E2o) and dihydrolipoamide dehydrogenase (E3). The results revealed that the E2o is capable of producing succinyl-CoA, glutaryl-CoA, and adipoyl-CoA. The important conclusions are the identification of: (i) the functional promiscuity of E1a and (ii) the ability of the E2o to form acyl-CoA products derived from homologous 2-oxo acids with five, six, and even seven carbon atoms. The findings add to our understanding of both the OADHc function in the L-lysine degradative pathway and of the molecular mechanisms leading to the pathogenesis associated with DHTKD1 variants.
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NR 62
TC 8
Z9 8
U1 1
U2 8
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
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PT J
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TI Association Between Race and Radiographic, Symptomatic, and Clinical Hand Osteoarthritis: A Propensity Score-Matched Study Using Osteoarthritis Initiative Data
SO ARTHRITIS & RHEUMATOLOGY
LA English
DT Article
ID knee osteoarthritis; united-states; prevalence; health; hip
AB Objective To determine the associations between Black race and the presence of radiographic, symptomatic, and clinical hand osteoarthritis (OA). Methods Using available hand radiographs from the Osteoarthritis Initiative cohort (total 4,699; n = 849 Black subjects [18.1%], n = 3,850 non-Black subjects [81.9%]), a propensity score-matching method was used to match Black subjects with non-Black subjects for known potential risk factors of hand OA (age, sex, body mass index, smoking status, cardiovascular disease, osteoporosis, excessive occupation- or recreation-related hand use, and knee OA). Posteroanterior radiographs of subjects' dominant hands were reviewed by a musculoskeletal radiologist in a blinded manner. To assess the severity of hand OA, the modified Kellgren/Lawrence (K/L) radiographic OA scoring scale (grades 0-4) was used, and the presence of erosive OA in the hand joints was recorded. Associations between race and the severity of hand OA (measured as the summed modified K/L grade), presence of radiographic hand OA (modified K/L grade >= 2), presence of erosive hand OA, presence of symptomatic hand OA (radiographic OA with hand pain), and presence of clinical hand OA (indicated by clinical findings of Heberden's nodes in the hands) were studied using regression models. In these models, beta coefficients or odds ratios (ORs) with 95% confidence intervals (95% CIs) were calculated for the associations between Black race and any of these radiographic and symptomatic hand OA phenotypes. Results Black subjects had less severe hand OA (beta = -1.93 [95% CI -2.53, -1.34]), as well as a lower risk of developing radiographic hand OA (OR 0.79 [95% CI 0.66, 0.94]), erosive hand OA (OR 0.23 [95% CI 0.11, 0.47]), symptomatic hand OA (OR 0.63 [95% CI 0.49, 0.82]), and clinical hand OA (OR 0.49 [95% CI 0.41, 0.60]), as compared to non-Black subjects. Conclusion In contrast to the well-established association between Black race and knee or hip OA, the findings of this study suggest that the risk of hand OA is lower in Black subjects compared to non-Black subjects, which is not mediated by known hand OA risk factors. Future studies are warranted to determine the mediating protective factors for hand OA among Black subjects.
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NR 26
TC 14
Z9 14
U1 0
U2 0
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 2326-5191
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J9 ARTHRITIS RHEUMATOL
JI Arthritis Rheumatol.
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AF Ding, Dong
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TI Dihydroartemisinin attenuates osteoclast formation and bone resorption via inhibiting the NF-κB, MAPK and NFATc1 signaling pathways and alleviates osteoarthritis
SO INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE
LA English
DT Article
DE osteoarthritis; subchondral bone; osteoclast; dihydroartemisinin; signaling pathway
ID deficiency-induced osteoporosis; subchondral bone; rheumatoid-arthritis; tnf-alpha; c-fos; cartilage; differentiation; ligand; degradation; expression
AB Osteoarthritis (OA) is a chronic, progressive and degenerative disease, and its incidence is increasing on a yearly basis. However, the pathological mechanism of OA at each stage is still unclear. The present study aimed to explore the underlying mechanism of dihydroartemisinin (DHA) in terms of its ability to inhibit osteoclast activation, and to determine its effects on OA in rats. Bone marrow-derived macrophages were isolated as osteoclast precursors. In the presence or absence of DHA, osteoclast formation was assessed by tartrate-resistant acid phosphatase (TRAP) staining, cell viability was assessed by Cell Counting Kit-8 assay, the presence of F-actin rings was assessed by immunofluorescence, bone resorption was determined by bone slices, luciferase activities of NF-kappa B and nuclear factor of activated T cell cytoplasmic 1 (NFATc1) were determined using luciferase assay kits, the protein levels of biomolecules associated with the NF-kappa B, MAPK and NFATc1 signaling pathways were determined using western blotting, and the expression of genes involved in osteoclastogenesis were measured using reverse transcription-quantitative PCR. A knee OA rat model was designed by destabilizing the medial meniscus (DMM). A total of 36 rats were assigned to three groups, namely the sham-operated, DMM + vehicle and DMM + DHA groups, and the rats were administered DHA or DMSO. At 4 and 8 weeks postoperatively, the micro-architecture of the subchondral bone was analyzed using micro-CT, the thickness of the cartilage layers was calculated using H&E staining, the extent of cartilage degeneration was scored using Safranin O-Fast Green staining, TRAP-stained osteoclasts were counted, and the levels of receptor activator of NF-kappa B ligand (RANKL), C-X-C-motif chemokine ligand 12 (CXCL12) and NFATc1 were measured using immunohistochemistry. DHA was found to inhibit osteoclast formation without cytotoxicity, and furthermore, it did not affect bone formation. In addition, DHA suppressed the expression levels of NF-kappa B, MAPK, NFATc1 and genes involved in osteoclastogenesis. Progressive cartilage loss was observed at 8 weeks postoperatively. Subchondral bone remodeling was found to be dominated by bone resorption accompanied by increases in the levels of RANKL, CXCL12 and NFATc1 during the first 4 weeks. DHA was found to delay OA progression by inhibiting osteoclast formation and bone resorption during the

early phase of OA. Taken together, the results of the present study demonstrated that the mechanism through which DHA could inhibit osteoclast activation may be associated with the NF-kappa B, MAPK and NFATc1 signaling pathways, thereby indicating a potential novel strategy for OA treatment.
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NR 59
TC 36
Z9 41
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AU Xiao, PL
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TI Prevalence and treatment rate of osteoporosis in patients undergoing total knee and hip arthroplasty: a systematic review and meta-analysis
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Review
DE Total joint arthroplasty; Osteoporosis; Prevalence; Treatment; Meta-analysis
ID bone-mineral density; postmenopausal women; joint arthroplasty; urban-population; osteoarthritis; revision; bisphosphonates; association; adults; korea
AB Purpose Due to age and gender, patients awaiting total knee or hip arthroplasty (TKA/THA) are at a higher risk of osteoporosis. In joint arthroplasty, low bone mineral density (BMD) is a risk factor for implant osseointegration, durability, and prosthesis complications. This study aims to investigate the prevalence and treatment rate of osteoporosis in patients undergoing total joint arthroplasty (TJA). Methods We applied a comprehensive literature search through PubMed, Cochrane Library, and EMBASE from inception to July 10, 2021, for studies investigating the prevalence and treatment rate of osteoporosis in TJA patients. The aggregated prevalence was calculated with the random-effects model, and the heterogeneity between studies was checked by Cochran's Q test and quantified by the I-2 statistic. We performed subgroup analyses and meta-regression analyses to determine the source of heterogeneity. Publication bias was assessed by a funnel plot and verified by Egger's test. Anti-osteoporosis treatment for TJA patients was described qualitatively and quantitatively. Results Of 4561 citations identified by the search strategy, 11 studies including 3462 patients were eligible for inclusion. The pooled prevalence of osteoporosis and osteopenia in TJA patients was 24.8% (95%CI: 14.1-37.2%) and 38.5% (95%CI: 29.3-48.0%), respectively. The prevalence of osteoporosis/osteopenia in TJA patients was 64.0% (95%CI: 45.8-80.3%). In terms of gender, the pooled prevalence of osteoporosis in males, females, and postmenopausal females were 5.5% (95%CI: 1.5-11.4%), 29.0% (95%CI: 18.3-41.1%), and 38.3% (95%CI: 13.2-67.1%), respectively. The treatment rate of osteoporosis in TJA patients was 32.9% (95%CI: 15.2-53.1%) by a random-effects model. Conclusions Osteoporosis is highly prevalent in patients undergoing TJA, especially in postmenopausal females. However, the treatment rate of osteoporosis is low. Considering the possibility of surgical complications, clinicians should strengthen their awareness of pre-operative BMD assessment and manage osteoporosis in high-risk patients.
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J9 ARCH OSTEOPOROS
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PT J
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AF Wang, Weizhou
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Wang, Zhihua
Yin, Liang
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TI Untargeted Metabolomics Reveal the Protective Effect of Bone Marrow Mesenchymal Stem Cell Transplantation Against Ovariectomy-Induced Osteoporosis in Mice
SO CELL TRANSPLANTATION
LA English
DT Article
DE bone marrow mesenchymal stem cells; ovariectomy-induced osteoporosis; cell therapy; metabolomics; biomarkers

ID stromal cells; osteoarthritis; brain; risk
AB Bone marrow mesenchymal stem cell transplantation (BMSCT) is a potential treatment for osteoporosis, capable of contributing to bone tissue repair. BMSCT has demonstrated osteoinductive effects and the ability to regulate microenvironmental metabolism; however, its role and mechanisms in bone loss due to reduced estrogen levels remain unclear. In this study, the effect of BMSCT on ovariectomy (OVX)-induced osteoporosis in mice was assessed, and liquid chromatography-mass spectrometry (LC-MS) metabolomic studies of bone tissue were conducted to identify potential metabolic molecular markers. The results revealed that BMSCT reduces OVX-induced bone loss in mice while improving the mechanical properties of mouse femurs and increasing the expression of osteogenic markers in peripheral blood. In a metabolomic study, 18 metabolites were screened as potential biomarkers of the anti-osteoporotic effect of BMSCT. These metabolites are mainly involved in arachidonic acid metabolism, taurine and hypotaurine metabolism, and pentose and glucuronate interconversions. Collectively, these results illustrate the correlation between metabolites and the underlying mechanisms of osteoporosis development and are important for understanding the role and mechanisms of exogenous bone marrow mesenchymal stem cells (BMSCs) in osteoporosis management. This study lays the foundation for research on BMSCs as a treatment strategy for osteoporosis.
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TI Mechanical forces couple bone matrix mineralization with inhibition of angiogenesis to limit adolescent bone growth
SO NATURE COMMUNICATIONS
LA English
DT Article
ID protein-1 dmp1; dentin; osteogenesis; fragments; strength; receptor; failure; signals; fusion; sites
AB The study shows that mechanical forces trigger secretion of the extracellular matrix protein dentin matrix protein 1 from osteoblasts. This transforms bone growth-promoting blood vessels into a quiescent subtype to limit bone growth at the end of adolescence. Bone growth requires a specialised, highly angiogenic blood vessel subtype, so-called type H vessels, which pave the way for osteoblasts surrounding these vessels. At the end of adolescence, type H vessels differentiate into quiescent type L endothelium lacking the capacity to promote bone growth. Until now, the signals that switch off type H vessel identity and thus limit adolescent bone growth have remained ill defined. Here we show that mechanical forces, associated with increased body weight at the end of adolescence, trigger the mechanoreceptor PIEZO1 and thereby mediate enhanced production of the kinase FAM20C in osteoblasts. FAM20C, the major kinase of the secreted phosphoproteome, phosphorylates dentin matrix protein 1, previously identified as a key factor in bone mineralization. Thereupon, dentin matrix protein 1 is secreted from osteoblasts in a burst-like manner. Extracellular dentin matrix protein 1 inhibits vascular endothelial growth factor signalling by preventing phosphorylation of vascular endothelial growth factor receptor 2. Hence, secreted dentin matrix protein 1 transforms type H vessels into type L to limit bone growth activity and enhance bone mineralization. The discovered mechanism may suggest new options for the treatment of diseases characterised by aberrant activity of bone and vessels such as osteoarthritis, osteoporosis and osteosarcoma.
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Keen, H. I.
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TI Zoledronic acid does not slow spinal radiographic progression of osteoarthritis in postmenopausal women with osteoporosis and radiographic osteoarthritis
SO THERAPEUTIC ADVANCES IN MUSCULOSKELETAL DISEASE

LA English
DT Article
DE bisphosphonates; spinal osteoarthritis; treatment; zoledronic acid
ID knee osteoarthritis; strontium ranelate; subchondral bone; risedronate; bisphosphonates; fractures; symptoms; risk
AB Introduction: Post hoc analyses of osteoporosis trials have suggested that alendronate and strontium ranelate may be associated with a reduction in the progression of spinal radiographic osteoarthritis (OA). We performed an analysis on a subgroup of participants in the horizon PFT trial (a 3-year randomized controlled trial (RCT) of yearly zoledronic acid (ZA) in postmenopausal women with osteoporosis), to evaluate the effect of ZA on the structural progression of spinal osteophytes (OPh) and disk space narrowing (DN). Methods: Paired lateral spinal X-rays (baseline and 36 months) were selected from the horizon PFT trial records restricted to those with radiographic OA at baseline. The X-rays were analyzed by two readers blinded to the treatment allocation. OPh and DN were scored separately using the Lane atlas (0-3 for increasing severity at each vertebral level) at all evaluable levels from T4-12 and L1-5. Results: A total of 504 sets of paired radiographs were included in the analysis, 245 in the ZA group and 259 in the placebo group. Overall, the rates of change of OPh and DN scores were low, and they were not statistically different between the groups (change in the whole spine OPh ZA 1.0 +/- 1.6, placebo 0.8 +/- 1.3, p = 0.1; DN ZA 0.3 +/- 1.0, placebo 0.3 +/- 0.8, p = 0.7). Conclusion: Yearly ZA for 3 years was not associated with a slowing of progression of OPh or DN in the thoracolumbar spine in patients with pre-existing radiographic OA.
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TI Geroprotectors and Skeletal Health: Beyond the Headlines
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English

DT Review
DE aging; senescence; osteoarthritis; osteoporosis; geroprotectors; mouse models
ID rapamycin reduces severity; life-span extension; senescent cells; bone loss; experimental osteoarthritis; cartilage degeneration; cellular senescence; secretory phenotype; oxidative stress; metformin
AB Osteoporosis and osteoarthritis are the most common age-related diseases of the musculoskeletal system. They are responsible for high level of healthcare use and are often associated with comorbidities. Mechanisms of ageing such as senescence, inflammation and autophagy are common drivers for both diseases and molecules targeting those mechanisms (geroprotectors) have potential to prevent both diseases and their co-morbidities. However, studies to test the efficacy of geroprotectors on bone and joints are scant. The limited studies available show promising results to prevent and reverse Osteoporosis-like disease. In contrast, the effects on the development of Osteoarthritis-like disease in ageing mice has been disappointing thus far. Here we review the literature and report novel data on the effect of geroprotectors for Osteoporosis and Osteoarthritis, we challenge the notion that extension of lifespan correlates with extension of healthspan in all tissues and we highlight the need for more thorough studies to test the effects of geroprotectors on skeletal health in ageing organisms.
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NR 128
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Liu, JJ
Guan, CH
Ma, CX
An, JY
Tang, XL
AF Jiang, Na
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TI Thioredoxin-interacting protein: A new therapeutic target in bone metabolism disorders?
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE Thioredoxin-interacting protein; osteoporosis; osteoarthritis; rheumatoid arthritis; osteoblasts; osteoclasts; chondrocytes
ID carbohydrate response element; nlrp3 inflammasome; oxidative stress; osteoclast differentiation; critical regulator; txnip; activation; expression; glucose; mondoa
AB Target identification is essential for developing novel therapeutic strategies in diseases. Thioredoxin-interacting protein (TXNIP), also known as thioredoxin-binding protein-2, is a member of the alpha-arrestin protein family and is regulated by several cellular stress factors. TXNIP overexpression coupled with thioredoxin inhibits its antioxidant functions, thereby increasing oxidative stress. TXNIP is directly involved in inflammatory activation by interacting with Nod-like receptor protein 3 inflammasome. Bone metabolic disorders are associated with aging, oxidative stress, and inflammation. They are characterized by an imbalance between bone formation involving osteoblasts and bone resorption by osteoclasts, and by chondrocyte destruction. The role of TXNIP in bone metabolic diseases has been extensively investigated. Here, we discuss the roles of TXNIP in the regulatory mechanisms of transcription and protein levels and summarize its involvement in bone metabolic disorders such as osteoporosis, osteoarthritis, and rheumatoid arthritis. TXNIP is expressed in osteoblasts, osteoclasts, and chondrocytes and affects the differentiation and functioning of skeletal cells through both

redox-dependent and -independent regulatory mechanisms. Therefore, TXNIP is a potential regulatory and functional factor in bone metabolism and a possible new target for the treatment of bone metabolism-related diseases.
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AF Han, Juanjuan
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TI Novel insights into the interaction between N6-methyladenosine methylation and noncoding RNAs in musculoskeletal disorders
SO CELL PROLIFERATION
LA English
DT Review
ID mesenchymal stem-cells; intervertebral disc degeneration; messenger-rna; m6a modification; ribosomal-rna; m(6)a methyltransferase; xenopus-laevis; n-6-methyladenosine; osteoporosis; translation
AB Background Musculoskeletal disorder (MSD) are a class of inflammatory and degener-ative diseases, but the precise molecular mechanisms are still poorly understood. Noncoding RNA (ncRNA) N6-methyladenosine (m6A) modification plays an essential role in the pathophysiological process of MSD. This review summarized the interaction be-tween m6A RNA methylation and ncRNAs in the molecular regulatory mechanism of MSD. It provides a new perspective for the pathophysiological mechanism and ncRNA m6A targeted therapy of MSD. Methods A comprehensive search of databases was conducted with musculoskeletal disorders, noncoding RNA, N6-methyladenosine, intervertebral disc degeneration, oste-oporosis, osteosarcoma, osteoarthritis, skeletal muscle, bone, and cartilage as the key-words. Then, summarized all the relevant articles. Results Intervertebral disc degeneration (IDD), osteoporosis (OP), osteosarcoma (OS), and osteoarthritis (OA) are common MSDs that affect muscle, bone, cartilage, and joint, leading to limited movement, pain, and disability. However, the precise pathogenesis remains unclear, and no effective treatment and drug is available at present. Numerous studies confirmed that the mutual regulation between m6A and ncRNAs (i.e., microRNAs, long ncRNAs, and circular RNAs) was found in MSD, m6A modification can regulate ncRNAs, and ncRNAs can also target m6A regulators. ncRNA m6A modification plays an essential role in the pathophysiological process of MSDs by regulating the homeostasis of skeletal muscle, bone, and cartilage. Conclusion m6A interacts with ncRNAs to regulate multiple biological processes and plays important roles in IDD, OP, OS, and OA. These studies provide new insights into the pathophysiological mechanism of MSD and targeting m6A-modified ncRNAs may be a promising therapy approach.
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TI Role of vitamin D supplementation in the management of musculoskeletal diseases: update from an European Society of Clinical and Economical Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) working group
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Vitamin D; Fragility fracture; Falls; Osteoarthritis
ID serum 25-hydroxyvitamin d; postmenopausal women; double-blind; d deficiency; calcium supplementation; knee osteoarthritis; oral vitamin-d-3; fracture risk; older-people; preventing fractures
AB Vitamin D is a key component for optimal growth and for calcium-phosphate homeostasis. Skin photosynthesis is the main source of vitamin D. Limited sun exposure and insufficient dietary vitamin D supply justify vitamin D supplementation in certain age groups. In older adults, recommended doses for vitamin D supplementation vary between 200 and 2000 IU/day, to achieve a goal of circulating 25-hydroxyvitamin D (calcifediol) of at least 50 nmol/L. The target level depends on the population being supplemented, the assessed system, and the outcome. Several recent large randomized trials with oral vitamin D regimens varying between 2000 and 100,000 IU/month and mostly conducted in vitamin D-replete and healthy individuals have failed to detect any efficacy of these approaches for the prevention of fracture and falls. Considering the well-recognized major musculoskeletal disorders associated with severe vitamin D deficiency and taking into account a possible biphasic effects of vitamin D on fracture and fall risks, an European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) working group convened, carefully reviewed, and analyzed the meta-analyses of randomized controlled trials on the effects of vitamin D on fracture risk, falls or osteoarthritis, and came to the conclusion that 1000 IU daily should be recommended in patients at increased risk of vitamin D deficiency. The group also addressed the identification of patients possibly benefitting from a vitamin D loading dose to achieve early 25-hydroxyvitamin D therapeutic level or from calcifediol administration.
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TI Substance P, A Promising Therapeutic Target in Musculoskeletal Disorders
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DE substance P; NK-1 receptor; musculoskeletal disorders; tendinopathy; rheumatoid arthritis; osteoarthritis; osteoporosis
ID gene-related peptide; neurokinin-1 receptor; rheumatoid-arthritis; nk-1 receptor; bone-marrow; induced internalization; tachykinin receptors; systematic analysis; global burden; tendinopathy
AB A large number of studies have focused on the role of substance P (SP) and the neurokinin-1 receptor (NK1R) in the pathogenesis of a variety of medical conditions. This review provides an overview of the role of the SP-NK1R pathway in the pathogenesis of musculoskeletal disorders and the evidence for its role as a therapeutic target for these disorders, which are major public health problems in most countries. To summarize, the brief involvement of SP may affect tendon healing in an acute injury setting. SP combined with an adequate conjugate can be a regenerative therapeutic option in osteoarthritis. The NK1R antagonist is a promising agent for tendinopathy, rheumatoid arthritis, and osteoarthritis. Research on the SP-NK1R pathway will be helpful for developing novel drugs for osteoporosis.
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TI The regulatory role and therapeutic application of pyroptosis in musculoskeletal diseases

SO CELL DEATH DISCOVERY
LA English
DT Review
ID nlrp3 inflammasome activation; cell-death; t-cells; rheumatoid-arthritis; molecular switch; gasdermin d; osteoarthritis; apoptosis; necroptosis; autophagy
AB Pyroptosis is a controlled form of inflammatory cell death characterized by inflammasome activation, pore formation, and cell lysis. According to different caspases, pyroptosis can be divided into canonical, non-canonical, and other pathways. The role of pyroptosis in disease development has been paid more attention in recent years. The trigger factors of pyroptosis are often related to oxidative stress and proinflammatory substances, which coincide with the pathological mechanism of some diseases. Pyroptosis directly leads to cell lysis and death, and the release of cytosolic components and proinflammatory cytokines affects cell activity and amplifies the inflammatory response. All the above are involved in a series of basic pathological processes, such as matrix degradation, fibrosis, and angiogenesis. Since these pathological changes are also common in musculoskeletal diseases (MSDs), emerging studies have focused on the correlations between pyroptosis and MSDs in recent years. In this review, we first summarized the molecular mechanism of pyroptosis and extensively discussed the differences and crosstalk between pyroptosis, apoptosis, and necrosis. Next, we elaborated on the role of pyroptosis in some MSDs, including osteoarthritis, rheumatoid arthritis, osteoporosis, gout arthritis, ankylosing spondylitis, intervertebral disc degeneration, and several muscle disorders. The regulation of pyroptosis could offer potential therapeutic targets in MSDs treatment. Herein, the existing drugs and therapeutic strategies that directly or indirectly target pyroptosis pathway components have been discussed in order to shed light on the novel treatment for MSDs.
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NR 185
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J9 CELL DEATH DISCOV
JI Cell Death Discov.
PD DEC 15
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VL 8
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AU Lee, YS
Park, SJ
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Choi, E
Kim, BJ
AF Lee, Yun Sun
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Choi, Eunah
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TI Benefits of lumican on human bone health: clinical evidence using bone marrow aspirates
SO KOREAN JOURNAL OF INTERNAL MEDICINE
LA English
DT Article
DE Lumican; Hip fractures; Osteogenesis; Bone resorption; Bone density
ID differentiation; expression; women
AB Background/Aims: Lumican, a small leucine-rich proteoglycan, has shown osteoprotective effects by synchronously stimulating bone formation and suppressing bone resorption. To clarify the role of lumican in human bone metabolism, the association between lumican concentrations and osteoporosis-related phenotypes was evaluated using bone marrow (BM) samples directly reflecting local microenvironments. Methods: BM aspirates were obtained from 77 patients during hip surgery for either fragility hip fractures (HF) (n = 29) or osteoarthritis (n = 48) and centrifuged. Concentrations of lumican and biochemical bone markers in BM supernatants were measured using enzyme linked immunosorbent assays. Results: After considering confounders, lumican concentrations in BM supernatants were 16.9% lower in patients with HF than in controls, with each increase in the standard deviation of lumican concentration being associated with a 61% lower likelihood of HF. The odds ratios for HF decreased linearly with increasing lumican tertiles in BM, with the odds of having fragility HF markedly lower in participants in the highest than in the lowest lumican tertile. Higher lumican level correlated significantly with higher femur neck bone mineral density and higher bone-specific alkaline phosphatase levels, but not with tartrate-resistant acid phosphatase 5b concentrations, in BM supernatants. Conclusions: These data clinically validate previous in vitro and animal experiments showing the beneficial roles of lumican for bone homeostasis and suggest that lumican may contribute to a reduction in fracture risk in humans mainly through its stimulation of bone formation.
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PA 101-2501 LOTTE CASTLE PRESIDENT, 109 MAPO-DAERO, MAPO-GU, SEOUL, SOUTH KOREA
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AU Arnold, EL
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AF Arnold, Emily L.
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TI Thermally dynamic examination of local order in nanocrystalline hydroxyapatite
SO JOURNAL OF SOLID STATE CHEMISTRY
LA English
DT Article
DE Hydroxyapatite; Powder X-ray diffraction (PXRD); Total scattering; Pair distribution function (PDF)
ID x-ray-diffraction; crystal-structure; carbonate substitution; apatite; transformation; decomposition; refinement; stability; disorder; ion
AB The main mineral component of bone is hydroxyapatite, a commonly nanocrystalline material which presents many challenges for those trying to characterize it. Here, local structure is analyzed using X-ray total scattering for synthetic samples, to enable a better understanding of the nanocrystalline nature of hydroxyapatite. Two samples were measured dynamically during heat treatment from 25 degrees C to 800 degrees C, and were analyzed using small box modelling.

Analysis of sequential measurements when dwelling at key temperatures showed a significant rela-tionship between time and temperature, indicating a process occurring more slowly than thermal expansion. This indicates a decrease in B-type CO(3)(2-)substitution between 550 degrees C and 575 degrees C and an increase in A-type CO32- substitution above 750 degrees C. A greater understanding of local, intermediate, and long-range order of this complex biomineral during heat treatment can be of interest in several sectors, such as in forensic, biomedical and clinical settings for the study of implant coatings and bone diseases including osteoporosis and osteoarthritis.
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WC Chemistry, Inorganic & Nuclear; Chemistry, Physical
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AF Pei, Wenhui
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Huang, Caoxing
TI Sustainable lignin and lignin-derived compounds as potential therapeutic agents for degenerative orthopaedic diseases: A systemic review
SO INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES
LA English
DT Review
DE Lignin; Biological activity; Degenerative orthopaedic diseases
ID inhibits osteoclast differentiation; antioxidant activity; moderate depolymerization; mechanical-property; carbohydrate complex; bone-resorption; wheat-straw; extraction; osteoarthritis; inflammation
AB Lignin, the most abundant natural and sustainable phenolic compound in biomass, has exhibited medicinal values due to its biological activities decided by physicochemical properties. Recently, the lignin and its derivatives (such as lignosulfonates and lignosulfonate) have been proven efficient in regulating cellular process and the extracellular microenvironment, which has been regarded as the key factor in disease progression. In orthopaedic diseases, especially the degenerative diseases represented by osteoarthritis and osteoporosis, excessive activated inflammation has been proven as a key stage in the pathological process. Due to the excellent biocompatibility, antibacterial and antioxidative activities of lignin and its derivatives, they have been applied to stimulate cells and restore the

uncoupling bone remodeling in the degenerative orthopaedic diseases. However, there is a lack of a systemic review to state the current research actuality of lignin and lignin-derived compounds in treating degenerative orthopaedic diseases. Herein, we summarized the current application of lignin and lignin-derived compounds in orthopaedic diseases and proposed their possible therapeutic mechanism in treating degenerative orthopaedic diseases. It is hoped this work could guide the future preparation of lignin/ligninderived drugs and implants as available therapeutic strategies for clinically degenerative orthopaedic diseases.
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FU Jiangsu Qing Lan Project [82101010]; Young Elite Scientists Sponsorship Program by CAST [BK20190133]; National Natural Science Foun-dation of China; Natural Science Foundation of Jiangsu Province
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TI Dorso-ventral osteophytes of interphalangeal joints correlate with cartilage damage and synovial inflammation in hand osteoarthritis: a histological/radiographical study
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Article
ID numerical scoring systems; bone-marrow lesions; finger joints; progression; prevalence; recommendations; reliability; arthritis; etiology; features
AB Objective To detect dorsally located osteophytes (OP) on lateral x-ray views and to correlate their presence with the extent of structural joint damage, determined by histologic grading (cartilage damage and synovial inflammation) and radiographic scoring in hand osteoarthritis (HOA). Methods Distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints were obtained from post mortem specimens (n = 40). Multiplanar plain x-rays were taken (dorso/palmar (dp) and lateral views). Radiographic OA was determined by the Kellgren and Lawrence classification. Joint samples were prepared for histological analysis and cartilage damage was graded according to the Mankin scoring system. Inflammatory changes of the synovial membrane were scored using the general synovitis score (GSS). Spearman's correlation was applied to examine the relationship between histological and radiographical changes. Differences between groups were determined by Mann-Whitney test. Results Bony proliferations that were only detectable on lateral views but reminiscent of OPs on dp images were termed dorso-ventral osteophytes (dvOPs). All joints displaying dvOPs were classified as OA and the presence of dvOPs in DIP and PIP joints correlated with the extent of histological and radiographic joint damage, as well as with patient age. Joint

damage in osteoarthritic DIP and PIP joints without any dvOPs was less severe compared to joints with dvOPs. Synovial inflammation was mainly present in joints displaying dvOPs and correlated with joint damage. Conclusion dvOPs are associated with increasing structural alterations in DIP and PIP joints and can be seen as markers of advanced joint damage. Detecting dvOPs can facilitate the diagnosis process and improve damage estimation in HOA.
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TI Icariin: A Potential Alternative Against Osteoporosis
SO NATURAL PRODUCT COMMUNICATIONS
LA English
DT Review
DE icariin; flavonoids; osteoporosis; osteogenesis; bone loss; MSCs
ID mesenchymal stem-cells; glucocorticoid-induced osteoporosis; promotes bone-formation; osteogenic differentiation; herba-epimedii; postmenopausal osteoporosis; osteoclast development; ovariectomized rats; estrogen deficiency; signaling pathway
AB Osteoporosis is a metabolic skeletal disorder characterized by increased fragility and fracture risk as s result of reduced bone mineral density and microstructural destruction and caused a heavy burden on families and society. Current medicines, on the other hand, have some limitations, with side effects and doubts regarding long-term efficacy being highlighted. Studies seeking for natural constituents as potential treatment options therefore come into focus. Icariin is a phytochemical derived from a traditional Chinese medicine, Herba epimedium, that has been used to treat orthopedic disorders in ancient China for thousands of years, including osteoporosis, osteoarthritis, and fracture. Icariin belongs to a category of prenylated flavonoids and has been shown to help reduce osteoporosis bone loss while having relatively low side effects. Icariin's anti-osteoporosis properties manifest in a variety of ways, like promoting osteogenesis, suppressing osteoclastogenesis and bone resorption, regulating migration, proliferation, and differentiation of mesenchymal stem cells, enhancing angiogenesis, anti-inflammation, and antioxidation. These procedures entail a slew of critical signaling pathways, such as PPAR., ERa/AKT/ss-catenin, and MAPK. Therefore, icariin can be an applicable alternative to improve osteoporosis although the underlying mechanisms have yet to be fully understood. In this study, we searched using the terms "icariin" and "osteoporosis," and included 64 articles meeting the inclusion criteria and reviewed the research of icariin in anti-osteoporosis over the last 10 years, and discussed new prospects for future study. Therefore, this review may provide some references for further studies.
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TI UK clinical guideline for the prevention and treatment of osteoporosis
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Osteoporosis; Fracture; NOGG; Guideline
ID bone-mineral density; glucocorticoid-induced osteoporosis; hip fracture patients; corticosteroid-induced osteoporosis; vertebral compression fractures; yearly zoledronic acid; quality-of-life; aged 50 years; postmenopausal women; double-blind
AB The National Osteoporosis Guideline Group (NOGG) has revised the UK guideline for the assessment and management of osteoporosis and the prevention of fragility fractures in postmenopausal women, and men age 50 years and older. Accredited by NICE, this guideline is relevant for all healthcare professionals involved in osteoporosis management. Introduction The UK National Osteoporosis Guideline Group (NOGG) first produced a guideline on the prevention and treatment of osteoporosis in 2008, with updates in 2013 and 2017. This paper presents a major update of the guideline, the scope of which is to review the assessment and management of osteoporosis and the prevention of fragility fractures in postmenopausal women, and men age 50 years and older. Methods Where available, systematic reviews, meta-analyses and randomised controlled

trials were used to provide the evidence base. Conclusions and recommendations were systematically graded according to the strength of the available evidence. Results Review of the evidence and recommendations are provided for the diagnosis of osteoporosis, fracture-risk assessment and intervention thresholds, management of vertebral fractures, non-pharmacological and pharmacological treatments, including duration and monitoring of anti-resorptive therapy, glucocorticoid-induced osteoporosis, and models of care for fracture prevention. Recommendations are made for training; service leads and commissioners of healthcare; and for review criteria for audit and quality improvement. Conclusion The guideline, which has received accreditation from the National Institute of Health and Care Excellence (NICE), provides a comprehensive overview of the assessment and management of osteoporosis for all healthcare professionals involved in its management. This position paper has been endorsed by the International Osteoporosis Foundation and by the European Society for the Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases.

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TI Gut Microbiota and Bone Diseases: A Growing Partnership
SO FRONTIERS IN MICROBIOLOGY
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DT Review
DE gut microbiota; bone diseases; osteoporosis; osteoarthritis; rheumatoid arthritis; bone tumor
ID calcium-absorption; double-blind; t-cells; intestinal microbiota; knee osteoarthritis; sodium-butyrate; mineral density; supplementation; metabolism; health
AB Gut microbiota is key to human health and disease. Convincing studies have demonstrated that dysbiosis in the commensal gut microbiota is associated with intestinal and extra-intestinal diseases. Recent explorations have significantly contributed to the understanding of the relationship between gut microbiota and bone diseases (osteoporosis, osteoarthritis, rheumatoid arthritis, and bone cancer). Gut microbiota and its metabolites may become associated with the development and progression of bone disorders owing to their critical role in nutrient absorption, immunomodulation, and the gut-brain-bone axis (regulation hormones). In this work, we review the recent developments addressing the effect

of gut microbiota modulation on skeletal diseases and explore a feasible preventive approach and therapy for bone diseases.
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TI Evaluation of mandibular condyle trabecular structure in patients with rheumatoid arthritis using fractal analysis
SO ORAL SURGERY ORAL MEDICINE ORAL PATHOLOGY ORAL RADIOLOGY
LA English
DT Article
ID bone-mineral density; detecting osteoporosis; dental radiographs; cancellous bone; alveolar bone; iliac crest; dimension; texture; osteoarthritis; pattern
AB Objectives. The aim of this study was to compare the fractal dimension (FD) of trabecular structure of the mandibular condyles in patients with rheumatoid arthritis (RA) to patients without RA. Correlations between condylar FD and bone mineral density T-scores in the femoral neck and lumbar spine were also examined. Study Design. The RA study group patients were divided into 3 categories (33 normal, 33 osteopenic, and 34 osteoporotic) according to T-scores. The control group without RA was sex- and age-matched with the study group. FD was calculated from panoramic radiographs and compared between the study and control groups. The relationships between FD values and femoral neck and L1-L4 lumbar spine T-scores were investigated for study and control groups. Significance was established at P < .05. Results. The mean FD values of the entire study group and of each category in the study group were significantly lower than those of the control group (P < .001). There were no significant differences in FD values among the 3 RA categories (P > .05). No significant correlations appeared between FD and femoral neck or lumbar spine T-scores (P >= .063). Conclusions. Fractal analysis of the condyles on panoramic radiographs can distinguish RA from healthy condyles, even if the patients with RA have normal bone mineral density T-scores.
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TI LncRNA KCNQ1OT1: Molecular mechanisms and pathogenic roles in human diseases
SO GENES & DISEASES
LA English
DT Review
DE Cell functions; Human diseases; KCNQ1OT1; Long non-coding RNA; Regulatory ncRNA
ID long noncoding rnas; cancer incidence; methylation; prevention; pyroptosis; trends; world

AB Long non-coding RNAs (lncRNAs) exhibit a length more than 200 nucleotides and they are characterized by non-coding RNAs (ncRNA) not encoded into proteins. Over the past few years, the role and development of lncRNAs have aroused the rising attention of re-searchers. To be specific, KCNQ1OT1, the KCNQ1 opposite strand/antisense transcript 1, is clearly classified as a regulatory ncRNA. KCNQ1OT1 is capable of interacting with miRNAs, RNAs and proteins, thereby affecting gene expression and various cell functions (e.g., cell prolifer-ation, migration, epithelial-mesenchymal transition (EMT), apoptosis, viability, autophagy and inflammation). KCNQ1OT1 is dysregulated in a wide range of human diseases (e.g., cardio-vascular disease, cancer, diabetes, osteoarthritis, osteoporosis and cataract), and it is specu-lated to act as a therapeutic target for treating various human diseases. On the whole, this review aims to explore the biological functions, underlying mechanisms and pathogenic roles of KCNQ1OT1 in human diseases.Copyright (c) 2021, Chongqing Medical University. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/ by-nc-nd/4.0/).
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TI Biochemical characterization of a disease-causing human osteoprotegerin variant
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ID juvenile pagets-disease; mutation; ligand; osteoporosis; chondrocytes; prevention; apoptosis; cartilage
AB Recently, a human mutation of OPG was identified to be associated with familial forms of osteoarthritis. This missense mutation (c.1205A = > T; p.Stop402Leu) occurs on the stop codon of OPG, which results in a 19-residue appendage to the C-terminus (OPG(+19)). The biochemical consequence of this unusual sequence alteration remains unknown. Here we expressed OPG(+19) in 293 cells and the mutant OPG was purified to homogeneity by heparin affinity chromatography and size exclusion chromatography. We found that in sharp contrast to wildtype OPG,

which mainly exists in dimeric form, OPG(+19) had a strong tendency to form higher-order oligomers. To our surprise, the hyper-oligomerization of OPG(+19) had no impact on how it binds cell surface heparan sulfate, how it inhibits RANKL-induced osteoclastogenesis and TRAIL-induced chondrocytes apoptosis. Our data suggest that in biological contexts where OPG is known to play a role, OPG(+19) functions equivalently as wildtype OPG. The disease-causing mechanism of OPG(+19) likely involves an unknown function of OPG in cartilage homeostasis and mineralization. By demonstrating the biochemical nature of this disease-causing OPG mutant, our study will likely help elucidating the biological roles of OPG in cartilage biology.

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AU Graham, J
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TI Associations of Healthcare Utilization and Costs with Increasing Pain and Treatment Intensity Levels in Osteoarthritis Patients: An 18-Year Retrospective Study
SO RHEUMATOLOGY AND THERAPY
LA English
DT Article
DE Clinical phenotyping; Health economics; Osteoarthritis; Pain
ID knee osteoarthritis; hip; hand; prevalence; phenotypes; arthritis; obesity
AB Introduction Osteoarthritis (OA) is a complex disease, and prior studies have documented the health and economic burdens of patients with OA compared to those without OA. Our goal was to use two strategies to further stratify OA patients based on both pain and treatment intensity to examine healthcare utilization and costs using electronic records from 2001 to 2018 at a large integrated health system. Methods Adult patients with >= 1 pain numerical rating scale (NRS) and diagnosis of OA were included. Pain episodes of >= 90 days were defined as mild (0-3), moderate (4-6), or severe (7-10) based on initial NRS. Patients were initially classified as mild and moved to moderate-severe OA if any of eight

treatment-based criteria were met. Outpatient visits (OP), emergency department visits (ED), inpatient days, and healthcare costs (both all-cause and OA-specific) were compared among pain levels and OA severity levels as frequencies and per-member-per-year rates, using generalized linear regression models adjusting for age, sex, and body mass index, with contrasts of $p < 0.05$ considered significant. Results We identified 127,656 patients, 92,576 with pain scores. Moderate and severe pain were associated with significantly higher rates of OA-related utilization and costs, and all-cause ED visits and pharmacy costs. Moderate-severe OA patients had significantly higher OA-related utilization and costs, and all-cause OP, ED and pharmacy costs. Conclusions Pain and treatment intensity were both strongly associated with OA-related utilization but not consistently with all-cause utilization. Our results provide promising evidence of better criteria and approaches for predicting disease burden and costs in the future.
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TI The Role of Depletion of Gut Microbiota in Osteoporosis and Osteoarthritis: A Narrative Review
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE osteoporosis; osteoarthritis; gut microbiome depletion; bone; immune
ID bone; obesity; health; mice; antibiotics; bacteria; disease; barrier; burden; impact
AB Osteoporosis and osteoarthritis are common diseases in an aging society, are considered metabolic diseases, and affect the quality of life of older adults. In addition, the gut microbiome is considered an additional organ to regulate bone metabolism. In the past decade, people have been studying the relationship between gut microbiota and bone metabolism. The role and mechanism of the gut microbiota in regulating bone metabolism is very important to improve the development of osteoporosis and osteoarthritis. Depletion of the gut microbiota as a method of studying the role of the gut microbiota was provided strategies to enhance the role of the gut microbiota in regulating osteoporosis and osteoarthritis. In this review, we discuss how depletion of the gut microbiota affects osteoporosis and osteoarthritis.
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TI Orang Asli Health and Lifeways Project (OA HeLP): a cross-sectional cohort study protocol
SO BMJ OPEN
LA English
DT Article
DE EPIDEMIOLOGY; PUBLIC HEALTH; Anthropology
ID mechanisms linking obesity; blood-pressure; heart-disease; double burden; risk-factors; inflammation; association; ultrasound; management; aborigines
AB Introduction Non-communicable disease (NCD) risk is influenced by environmental factors that are highly variable worldwide, yet prior research has focused mainly on high-income countries where most people are exposed to relatively homogeneous and static environments. Understanding the scope and complexity of environmental influences on NCD risk around the globe requires more data from people living in diverse and changing environments. Our project will investigate the prevalence and environmental causes of NCDs among the

indigenous peoples of Peninsular Malaysia, known collectively as the Orang Asli, who are currently undergoing varying degrees of lifestyle and sociocultural changes that are predicted to increase vulnerability to NCDs, particularly metabolic disorders and musculoskeletal degenerative diseases. Methods and analysis Biospecimen sampling and screening for a suite of NCDs (eg, cardiovascular disease, type II diabetes, osteoarthritis and osteoporosis), combined with detailed ethnographic work to assess key lifestyle and sociocultural variables (eg, diet, physical activity and wealth), will take place in Orang Asli communities spanning a gradient from remote, traditional villages to acculturated, market-integrated urban areas. Analyses will first test for relationships between environmental variables, NCD risk factors and NCD occurrence to investigate how environmental changes are affecting NCD susceptibility among the Orang Asli. Second, we will examine potential molecular and physiological mechanisms (eg, epigenetics and systemic inflammation) that mediate environmental effects on health. Third, we will identify intrinsic (eg, age and sex) and extrinsic (eg, early-life experiences) factors that predispose certain people to NCDs in the face of environmental change to better understand which Orang Asli are at greatest risk of NCDs. Ethics and dissemination Approval was obtained from multiple ethical review boards including the Malaysian Ministry of Health. This study follows established principles for ethical biomedical research among vulnerable indigenous communities, including fostering collaboration, building cultural competency, enhancing transparency, supporting capacity building and disseminating research findings.
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TI Assessment of Hypothetical Out-of-Pocket Costs of Guideline-Recommended Medications for the Treatment of Older Adults With Multiple Chronic Conditions, 2009 and 2019
SO JAMA INTERNAL MEDICINE
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DT Article
ID clinical-practice guidelines; polypharmacy; association; care
AB IMPORTANCE Most adults 65 years or older have multiple chronic conditions. Managing these conditions with prescription drugs can be costly, particularly for older adults with limited incomes. OBJECTIVE To estimate hypothetical out-of-pocket costs associated with guideline-recommended outpatient medications for the initial treatment of 8 common chronic diseases among older adults with Medicare prescription drug plans (PDPs). DESIGN, SETTING, AND PARTICIPANTS This retrospective cross-sectional study used 2009 and 2019 Medicare prescription drug plan formulary files to estimate annual out-of-pocket costs among hypothetical patients enrolled in Medicare Advantage or stand-alone Medicare Part D plans. A total of 3599 PDPs in 2009 and 3618 PDPs in 2019 were included after inclusion and exclusion criteria were applied. Costs associated with guideline-recommended medications for 8 of the most common chronic diseases

(atrial fibrillation, chronic obstructive pulmonary disease [COPD], heart failure with reduced ejection fraction, hypercholesterolemia, hypertension, osteoarthritis, osteoporosis, and type 2 diabetes), alone and in 2 clusters of commonly comorbid conditions, were examined. MAIN OUTCOMES AND MEASURES Annual out-of-pocket costs for each chronic condition, inflation adjusted to 2019 dollars. RESULTS Among 3599 Medicare PDPs in 2009, 1998 were Medicare Advantage plans and 1601 were stand-alone plans; among 3618 Medicare PDPs in 2019, 2719 were Medicare Advantage plans and 899 were stand-alone plans. For an older adult enrolled in any Medicare PDP in 2019, the median annual out-of-pocket costs for individual conditions varied, from a minimum of $32 (IQR, $6-$ 48) for guideline-recommended management of osteoporosis (a decrease from $128 [IQR, $102-$183] in 2009) to a maximum of $1579 (IQR, $1524-$2229) for guideline-recommended management of atrial fibrillation (an increase from $91 [IQR, $73-$124] in 2009). For an older adult with a cluster of 5 commonly comorbid conditions (COPD, hypertension, osteoarthritis, osteoporosis, and type 2 diabetes) enrolled in any PDP, the median out-of-pocket cost in 2019 was $1999 (IQR, $1630-$2564), a 12% decrease from $2284 (IQR, $1920-$3107) in 2009. For an older adult with all 8 chronic conditions (atrial fibrillation, COPD, diabetes, hypercholesterolemia, heart failure, hypertension, osteoarthritis, and osteoporosis) enrolled in any PDP, the median out-of-pocket cost in 2019 was $3630 (IQR, $3234-$5197), a 41% increase from $2571 (IQR, $2185-$3719) in 2009. CONCLUSIONS AND RELEVANCE In this cross-sectional study, out-of-pocket costs for guideline-recommended outpatient medications for the initial treatment of 8 common chronic diseases varied by condition. Although costs generally decreased between 2009 and 2019, particularly with regard to conditions for which generic drugs were available, out-of-pocket costs remained high and may have presented a substantial financial burden for Medicare beneficiaries, especially older adults with conditions for which brand-name drugs were guideline recommended.

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AU Hu, LH
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TI Circular RNAs: typical biomarkers for bone-related diseases
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LA English
DT Review

DE Circular RNA; Bone-related disease; Competing endogenous RNA (ceRNA); MicroRNA
ID extracellular-matrix degradation; intervertebral disc degeneration; nucleus pulposus cells; multiple-myeloma; osteogenic differentiation; expression profiles; emerging roles; noncoding rna; up-regulation; promotes
AB Bone is a connective tissue that has important functions in the human body. Cells and the extracellular matrix (ECM) are key components of bone and are closely related to bone-related diseases. However, the outcomes of conventional treatments for bone-related diseases are not promising, and hence it is necessary to elucidate the exact regulatory mechanisms of bone-related diseases and identify novel biomarkers for diagnosis and therapy. Circular RNAs (circRNAs) are single-stranded RNAs that form closed circular structures without a 5 & PRIME; cap or 3 & PRIME; tail and polycyclic adenylate tails. Due to their high stability, circRNAs have the potential to be typical biomarkers. Accumulating evidence suggests that circRNAs are involved in bone-related diseases, including osteoarthritis, osteoporosis, osteosarcoma, multiple myeloma, intervertebral disc degeneration, and rheumatoid arthritis. Herein, we summarize the recent research progress on the characteristics and functions of circRNAs, and highlight the regulatory mechanism of circRNAs in bone-related diseases.
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TI Diterbutyl phthalate attenuates osteoarthritis in ACLT mice via suppressing ERK/c-fos/NFATc1 pathway, and subsequently inhibiting subchondral osteoclast fusion
SO ACTA PHARMACOLOGICA SINICA
LA English
DT Article
DE osteoarthritis; Panax notoginseng; diterbutyl phthalate; osteoclastogenesis; subchondral bone; ERK; c-fos; NFATc1 pathway; two-dimensional cell membrane chromatography (2D; CMC); ACLT mice
ID mesenchymal stem-cells; articular-cartilage; knee osteoarthritis; cross-talk; bone; angiogenesis; alendronate; pain; components; exhibit
AB Osteoarthritis (OA) is the most common arthritis with a rapidly increasing prevalence. Disease progression is irreversible, and there is no curative therapy available. During OA onset, abnormal mechanical loading leads to excessive osteoclastogenesis and bone resorption in subchondral bone, causing a rapid

subchondral bone turnover, cyst formation, sclerosis, and finally, articular cartilage degeneration. Moreover, osteoclast-mediated angiogenesis and sensory innervation in subchondral bone result in abnormal vascularization and OA pain. The traditional Chinese medicine Panax notoginseng (PN; Sanqi) has long been used in treatment of bone diseases including osteoporosis, bone fracture, and OA. In this study we established two-dimensional/bone marrow mononuclear cell/cell membrane chromatography/time of flight mass spectrometry (2D/BMMC/CMC/TOFMS) technique and discovered that diterbutyl phthalate (DP) was the active constituent in PN inhibiting osteoclastogenesis. Then we explored the therapeutic effect of DP in an OA mouse model with anterior cruciate ligament transaction (ACLT). After ACLT was conducted, the mice received DP (5 mg center dot kg(-1)center dot d(-1), ip) for 8 weeks. Whole knee joint tissues of the right limb were harvested at weeks 2, 4, and 8 for analysis. We showed that DP administration impeded overactivated osteoclastogenesis in subchondral bone and ameliorated articular cartilage deterioration. DP administration blunted aberrant H-type vessel formation in subchondral bone marrow and alleviated OA pain assessed in Von Frey test and thermal plantar test. In RANKL-induced RAW264.7 cells in vitro, DP (20 mu M) retarded osteoclastogenesis by suppressing osteoclast fusion through inhibition of the ERK/c-fos/NFATc1 pathway. DP treatment also downregulated the expression of dendritic cell-specific transmembrane protein (DC-STAMP) and d2 isoform of the vacuolar (H+) ATPase V0 domain (Atp6v0d2) in the cells. In conclusion, we demonstrate that DP prevents OA progression by inhibiting abnormal osteoclastogenesis and associated angiogenesis and neurogenesis in subchondral bone.
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TI The combination of osteoporosis and low lean mass correlates with physical function in end-stage knee osteoarthritis: A retrospective observational study
SO MEDICINE
LA English
DT Article
DE knee; osteoarthritis; osteoporosis; physical function; prevalence; sarcopenia
ID sarcopenia; osteosarcopenia; validation; bone; muscle; hip; individuals; performance; fracture; outcm
AB We aimed to investigate the prevalence of osteoporosis and low lean mass, either together or in isolation, and their association with physical function, pain, and quality of life (QOL) in patients with end-stage knee osteoarthritis (OA). This retrospective cross-sectional observational study included 578 patients (77 males and 501 females) diagnosed with end-stage knee OA. Patients were divided into 4 groups based on body composition parameters: control, osteoporosis, low lean mass, and osteoporosis + low lean mass. All participants underwent performance-based physical function tests, including a stair climbing test (SCT), a 6-minute walk test, a timed up and go test, and instrumental gait analysis, to examine spatiotemporal parameters. Self-reported physical function and pain levels were measured using the Western Ontario McMaster Universities Osteoarthritis Index and visual analog scale, respectively. Self-reported QOL was measured using the EuroQOL 5 dimensions (EQ-5D) questionnaire. Of 578 patients, 268 (46.4%) were included in the control group, 148 (25.6%) in the osteoporosis group, 106 (18.3%) in the low lean mass group, and 56 (9.7%) in the osteoporosis + low lean mass group. Analysis of variance revealed that the scores for the osteoporosis + low lean mass group in the SCT-ascent, SCT-descent, and timed up and go test were significantly higher, whereas those for the 6-minute walk test, gait speed, and cadence were significantly lower than those for the other groups ($P < .05$). After adjusting for age, sex, and body mass index, multiple linear regression analysis identified SCT-ascent (beta = 0.140, P = .001, R-2 = 0.126), SCT-descent (beta = 0.182, P < .001, R-2 = 0.124), gait speed (beta = -0.116, P = .005, R-2 = 0.079), and cadence (beta = -0.093, P = .026, R-2 = 0.031) as being significantly associated with osteoporosis + low lean mass. Thus, osteoporosis + low lean mass correlates with poor physical function, but not pain and QOL, in patients with end-stage knee OA.
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Parodi, Alessandro
Zamyatnin, Andrey A., Jr.
TI Cathepsin K in Pathological Conditions and New Therapeutic and Diagnostic Perspectives
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE Cathepsin K; protease; diagnostics; therapy; inhibitors
ID bone-mineral density; microphthalmia transcription factor; kappa-b ligand; gene-expression; osteoclast differentiation; osteoprotegerin ligand; postmenopausal women; cysteine cathepsins; receptor activator; messenger-rna
AB Cathepsin K (CatK) is a part of the family of cysteine proteases involved in many important processes, including the degradation activity of collagen 1 and elastin in bone resorption. Changes in levels of CatK are associated with various pathological conditions, primarily related to bone and cartilage degradation, such as pycnodysostosis (associated with CatK deficiency), osteoporosis, and osteoarthritis (associated with CatK overexpression). Recently, the increased secretion of CatK is being highly correlated to vascular inflammation, hypersensitivity pneumonitis, Wegener granulomatosis, berylliosis, tuberculosis, as well as with tumor progression. Due to the wide spectrum of diseases in which CatK is involved, the design and validation of active site-specific inhibitors has been a subject of keen interest in pharmaceutical companies in recent decades. In this review, we

summarized the molecular background of CatK and its involvement in various diseases, as well as its clinical significance for diagnosis and therapy.
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NR 134
TC 29
Z9 32
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U2 7
PU MDPI
PI BASEL
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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TI Metabolomic Analysis of Severe Osteoarthritis in a Spanish Population of Women Compared to Healthy and Osteoporotic Subjects
SO METABOLITES
LA English
DT Article

DE osteoarthritis; osteoporotic fracture; metabolomic analysis; postmenopausal women
ID management; diagnosis; mortality
AB Bone pathologies such as osteoporosis (OTP) and osteoarthritis (OA) are rising in incidence with the worldwide rise in life expectancy. The diagnosis is usually obtained using imaging techniques such as densitometry, but with both being multifactorial diseases, several molecular mechanisms remain to be understood. Metabolomics offers the potential to detect global changes which can lead to the identification of biomarkers and a better insight in the progress of the diseases. Our aim was to compare the metabolic profiles of a cohort of 100 postmenopausal women, including subcapital hip fragility fracture patients, women with severe OA of the hip that required the implantation of a hip prosthesis and controls, to find altered metabolites and networks. Nuclear magnetic resonance (NMR) spectroscopy was used to obtain the metabolomic profiles of peripheral blood derived serum, and statistical analysis was performed using MATLAB V.6.5. 30 of the 73 metabolites analysed showed statistically significant differences in a 3-way ANOVA, and 11 of them were present in the comparison between OA and controls after adjustment by covariates, including amino acids, energy metabolism metabolites and phospholipid precursors. PLS-DA analysis shows a good discrimination between controls and fracture subjects with OA patients, and ROC curve analysis demonstrates that control and fracture subjects were accurately discriminated using the metabolome, but not OA. These results point to OA as an intermediate metabolic state between controls and fracture, and suggest that some metabolic shifts that happen after a fracture are also present at weaker intensity in the OA process.
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NR 27
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U1 0
U2 9
PU MDPI
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EI 2218-1989
J9 METABOLITES
JI Metabolites
PD AUG 15
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WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
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TI Impact of bone health on the mechanics of plate fixation for Vancouver B1 periprosthetic femoral fractures
SO CLINICAL BIOMECHANICS
LA English
DT Article
DE Periprosthetic femoral fracture; Total hip arthroplasty; Finite element analysis; Bone property; Bone strain; Load transfer
ID total hip; risk-factors; osteoporosis; femur; density; muscle; women; osteoarthritis; accuracy; strength
AB Background: Condyle-spanning plate-screw constructs have shown potential to lower the risks of femoral refractures after the healing of a primary Vancouver type B1 periprosthetic femoral fracture. Limited information exists to show how osteoporosis (a risk factor for periprosthetic femoral fractures) may affect the plate fixation during activities of daily living.Methods: Using total hip arthroplasty and plate-implanted finite element models of three osteoporotic femurs, this study simulated physiological loads of three activities of daily living, as well as osteoporosis associated muscle weakening, and compared the calculated stress/strain, load transfer and local stiffness with experimentally validated models of three healthy femurs. Two plating systems and two construct lengths (a diaphyseal construct and a condyle-spanning construct) were modeled.Findings: Osteoporotic femurs showed higher bone strain (21.9%) and higher peak plate stress (144.3%) as compared with healthy femurs. Compared with shorter diaphyseal constructs, condyle-spanning constructs of two plating systems reduced bone strains in both healthy and osteoporotic femurs (both applying 'the normal' and 'the weakened muscle forces') around the most distal diaphyseal screw and in the distal metaphysis, both locations where secondary fractures are typically reported. The lowered resultant compressive force and the increased local compressive stiffness in the distal diaphysis and metaphysis may be associated with strain reductions via condyle-spanning constructs. Interpretation: Strain reductions in condyle-spanning constructs agreed with the clinically reported lowered risks of femoral refractures in the distal diaphysis and metaphysis. Multiple condylar screws may mitigate the concentrated strains in the lateral condyle, especially in osteoporotic femurs.
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NR 44
TC 1
Z9 1
U1 0
U2 3
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 0268-0033
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J9 CLIN BIOMECH
JI Clin. Biomech.
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WC Engineering, Biomedical; Orthopedics; Sport Sciences
SC Engineering; Orthopedics; Sport Sciences
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TI Emerging biomimetic nanotechnology in orthopedic diseases: progress, challenges, and opportunities
SO TRENDS IN CHEMISTRY
LA English
DT Review
ID targeting drug-delivery; bone regeneration; nanoparticles; osteosarcoma; cartilage; collagen; scaffold; nanocarriers; doxorubicin; fabrication
AB Orthopedic diseases (e.g., fracture, bone tumor, osteoarthritis, osteoporosis, chronic inflammation, and infection) can result in locomotion disability, loss of protection for other soft tissues/organs, or dysfunction of hematopoiesis, mineral homeostasis, and other functions. The development of biomimetic nano-technology has advanced the innovation of orthopedic therapies for

restoring the structure, composition, and biophysiological functions of the natural bone tissue. Identification of the pathogenesis and understanding the disease progression can greatly benefit the design and optimization of disease-specific therapy. Herein, we summarize guidelines on how biomimetic nanotechnology can be utilized in more efficiently treating various orthopedic diseases. We also discuss unmet needs and current challenges that might hinder the clinical implementation of biomimetic nanotechnology-based orthopedic therapies.
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TI Molecular Mechanism of Ferroptosis in Orthopedic Diseases
SO CELLS
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DE ferroptosis; regulation of ferroptosis; bone marrow injury; osteoporosis; osteoarthritis; osteosarcoma; orthopedic disease
ID cell-death; marrow suppression; osteosarcoma cells; iron; bone; apoptosis; epidemiology; autophagy; protects; mice
AB Ferroptosis is a new iron-dependent programmed cell death process that is directly mediated by the accumulation of lipid peroxides and reactive oxygen species. Numerous studies have shown that ferroptosis is important in regulating the occurrence and development of bone-related diseases, but the underlying mechanisms are not completely clear. Herein, we review the progress of the mechanism of ferroptosis in bone marrow injury, osteoporosis, osteoarthritis, and osteosarcoma and attempt to deeply understand the regulatory targets of ferroptosis, which will open up a new way for the prevention and treatment of orthopedic diseases.
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DE Cartilage; Equol; Osteoarthritis; Ovariectomised rats; Subchondral bone
ID protein-synthesis initiation; hormone-replacement therapy; estrogen-receptor-beta; isoflavone metabolite; soybean isoflavone; up-regulation; s-equol; soy; cancer; transection
AB Objective(s): This study aimed to determine the therapeutic effect of equol (EQ) on osteoporotic osteoarthritis (OP OA).Materials and Methods: Thirty-six 12-week-old female Sprague-Dawley rats were randomly divided into sham group, OP OA group, and EQ group (n=12). OP OA was induced by anterior cruciate ligament transection (ACLT) combined with ovariectomy (OVX). EQ was orally administrated (10 mu g/g/day) after the operation for 12 weeks. The efficacy was evaluated by gross pathology and histopathologic evaluation. The underlying mechanism was investigated by immunohistochemical analysis, micro-computed tomography (micro-CT) scanning, and tartrate-resistant acid phosphatase (TRAP) staining.Results: EQ effectively retarded cartilage degeneration, decreased the levels of matrix metalloproteinases-13 (MMP-13), a disintegrin and metalloproteinase with thrombospondin motifs 5 (ADAMTS-5), nuclear factor-kappa B P65 (NF-cB P65) and caspase-3, and increased the levels of collagen type II (Col-II), Col-I, aggrecan (AGG), and inhibitor of NF-cB alpha (ficB alpha) in the cartilage. In addition, EQ increased bone mineral density, improved the microstructural parameters of the subchondral bone (SB), and decreased the number of osteoclasts.Conclusion: EQ exerted a chondroprotective effect on OP OA in rats, associated with inhibition of the NF-cB signaling pathway and chondrocyte apoptosis. Furthermore, EQ showed an osteoprotective effect on SB via inhibiting osteoclastic activities.
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NR 41
TC 4
Z9 6
U1 0
U2 4
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PG 6
WC Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Research & Experimental Medicine; Pharmacology & Pharmacy
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ER

PT J
AU Hamdi, T
Gouissem, I
AF Hamdi, T.
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TI Potential effect of Enterolactone and Raloxifene in reversing osteoarthritis markers in cultured Human articular chondrocytes
SO ARP RHEUMATOLOGY
LA English

DT Article
DE Raloxifene; Enterolactone; Osteoarthritis; Collagens; Cartilage; Chondrocytes
ID estrogen-receptor modulators; vertebral fracture risk; postmenopausal women; breast-cancer; reduction; expression; phytoestrogens; osteoporosis; alpha; cells
AB Background: Osteoarthritis (OA) is associated with cartilage destruction. Maintenance of differentiated chondrocyte biomarkers is important in prevention of degeneration. Selective estrogen receptor modulators (SERMs) such as raloxifene (Ral) and phytoestrogens like enterolactone (Ent) which have structural and functional homologies with estrogen can mime their action. This study was undertaken to evaluate in vitro the possible effects of Ral and Ent on the expression of differentiated, dedifferentiated and hypertrophic biomarkers in human articular chondrocytes (HAC). Methods: Chondrocytes of osteoarthritic patients, harvested from one passage cell culture, were treated with Ral (0.1 and 1 mu M) and Ent (1 and 5 mu M) for 10 and 12 days in two- (2D) and three-dimensional (3D) models. Genes expression of type I collagen (COL1A1), type II collagen (COL2A1), type X collagen (COL10A1), aggrecan (ACAN) and small novel rich in cartilage (SNORC), were detected by real-time PCR and by Western-Blotting. Results: Our study revealed that Ral increased COL2A1, ACAN and SNORC and decreased concomitantly COL1A1 and COL10A1 genes expression when compared to untreated OA chondrocytes. Ent increased COL2A1 and decreased genes expression of the other biomarkers cited above like COL1A1. Our results demonstrated that low doses of 17 beta-oestradiol (E2), Ral and Ent had positive effects on the expression of differentiated chondrocyte markers such as COL2A1, ACAN and SNORC whereas high dose of these compounds inhibited their effects. Our results showed that 1 mu M of Ral induced an up-regulation of COL2A1, ACAN and SNORC expression and a downregulation of COL1A1 and COL10A1 expression in HAC incubated in 3D for 12 days. Conclusions: This study showed that SERMs like Ral and a phyto-estrogen like Ent induced the expression of differentiated chondrocyte markers of hyaline cartilage: COL2A1, ACAN and SNORC and decreased COL1A1 and COL10A1 genes expression on HAC of osteoarthritis patients.
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U1 0
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PU PUBLISAUDE-EDICOES MEDICAS LDA
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J9 ARP RHEUMATOL
JI ARP Rheumatol.
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WC Rheumatology
SC Rheumatology

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PT J
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AF Ege, Ferhat
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TI FokI polymorphism in the vitamin D receptor gene in patients with hip osteoarthritis: A case-control study
SO TURKISH JOURNAL OF PHYSICAL MEDICINE AND REHABILITATION
LA English
DT Article
DE FokI; osteoarthritis; polymorphisms; vitamin D receptor gene
ID bone-mineral density; start codon polymorphism; association; knee; osteoporosis; women; risk
AB Objectives: This study aimed to examine whether there is an association between hip osteoarthritis and vitamin D receptor gene FokI polymorphisms. Patients and methods: In this case-control study, a total of 162 volunteers (43 males, 119 females; mean age: 62.4 +/- 9.3; range, 50 to 80 years) were included between March 2011 and March 2012. The patient group included 80 individuals with a diagnosis of coxarthrosis. Eighty-two individuals with normal hip, low back, and sacroiliac joint examination were included in the control group. The American College of Rheumatology hip osteoarthritis classification criteria were used in the diagnosis of coxarthrosis. Analysis of FokI polymorphisms was performed with restriction fragment length polymorphisms. Results: When the genotype and allele distributions of vitamin D receptor FokI polymorphisms were examined, no statistical difference was found in both groups. Conclusion: No significant association between the hip osteoarthritis and FokI polymorphisms could be obtained.
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NR 31
TC 4
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PU BAYCINAR MEDICAL PUBL-BAYCINAR TIBBI YAYINCILIK
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JI Turk. J. Phys. Med. Rehabil.
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WC Rehabilitation
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PT J
AU Little-Letsinger, SE
Rubin, J
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AF Little-Letsinger, Sarah E.
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TI Exercise to Mend Aged-tissue Crosstalk in Bone Targeting Osteoporosis & Osteoarthritis
SO SEMINARS IN CELL & DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE Exercise; Mechanical; Aging; Marrow adipose tissue (MAT); Niche; Senescence;

Osteoarthritis; Osteoporosis; Chondrocyte; Mesenchymal stem cell (MSC); Osteoblast; Adipocyte; Hematopoietic stem cell (HSC); Osteoclast; Loading
ID mesenchymal stem-cells; marrow adipose-tissue; tumor-necrosis-factor; oxidative stress; osteoclast differentiation; articular-cartilage; mechanical signals; physical-activity; mineral density; dna-damage
AB Aging induces alterations in bone structure and strength through a multitude of processes, exacerbating common aging-related diseases like osteoporosis and osteoarthritis. Cellular hallmarks of aging are examined, as related to bone and the marrow microenvironment, and ways in which these might contribute to a variety of age-related perturbations in osteoblasts, osteocytes, marrow adipocytes, chondrocytes, osteoclasts, and their respective progenitors. Cellular senescence, stem cell exhaustion, mitochondrial dysfunction, epigenetic and intracellular communication changes are central pathways and recognized as associated and potentially causal in aging. We focus on these in musculoskeletal system and highlight knowledge gaps in the literature regarding cellular and tissue crosstalk in bone, cartilage, and the bone marrow niche. While senolytics have been utilized to target aging pathways, here we propose non-pharmacologic, exercise-based interventions as prospective "senolytics" against aging effects on the skeleton. Increased bone mass and delayed onset or progression of osteoporosis and osteoarthritis are some of the recognized benefits of regular exercise across the lifespan. Further investigation is needed to delineate how cellular indicators of aging manifest in bone and the marrow niche and how altered cellular and tissue crosstalk impact disease progression, as well as consideration of exercise as a therapeutic modality, as a means to enhance discovery of bone-targeted therapies.
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NR 262
TC 23
Z9 26
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U2 22
PU ACADEMIC PRESS LTD- ELSEVIER SCIENCE LTD
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JI Semin. Cell Dev. Biol.
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WC Cell Biology; Developmental Biology
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PT J
AU Ghasemian, M
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TI Long non-coding RNA MIR4435-2HG: a key molecule in progression of cancer and non-cancerous disorders
SO CANCER CELL INTERNATIONAL
LA English
DT Review
DE MIR4435-2HG; lncRNA; Cancer; Biomarker
ID carcinoma metastasis; poor-prognosis; lncrna-awpph; promotes; cells; growth; contributes; yap/taz; flot2; runx2
AB MIR4435-2HG (LINC00978) is a long non-coding RNA (lncRNA) that acts as an oncogene in almost all cancers. This lncRNA participates in the molecular cascades involved in other disorders such as coronary artery diseases, osteonecrosis, osteoarthritis, osteoporosis, and periodontitis. MIR4435-2HG exerts its functions via the spectrum of different mechanisms, including inhibition of apoptosis, sponging microRNAs (miRNAs), promoting cell proliferation, increasing cell invasion and migration, and enhancing epithelial to mesenchymal transition (EMT). MIR4435-2HG can regulate several signaling pathways, including Wnt, TGF-beta/SMAD, Nrf2/HO-1, PI3K/AKT, MAPK/ERK, and FAK/AKT/beta-catenin signaling pathways; therefore, it can lead to tumor progression. In the present review, we aimed to discuss the potential roles of lncRNA MIR4435-2HG in developing cancerous and non-cancerous conditions. Due to its pivotal role in different disorders, this lncRNA can serve as a potential biomarker in future investigations. Moreover, it may serve as a potential therapeutic target for the treatment of various diseases.
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NR 81
TC 25
Z9 27
U1 3
U2 12
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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WC Oncology
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PT J
AU Weidauer, LA
Harbaugh, ZM
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AF Weidauer, Lee A.
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TI Greater subchondral vBMD at the tibia is observed between 1 and 5 years of anterior cruciate ligament injury
SO JOURNAL OF MUSCULOSKELETAL & NEURONAL INTERACTIONS
LA English
DT Article
DE ACL; Knee; Osteoarthritis; pQCT; Subchondral
ID bone-mineral density; knee; reconstruction; osteoarthritis; risk; strength; prevalence
AB Objectives: This study aimed to determine if differences exist in tibial subchondral bone and muscle imbalances between individuals with and without an Anterior Cruciate Ligament (ACL) repair within the past 1 to 5 years (median 3 years). Methods: Fifteen individuals (ages 18-23 years) that had a unilateral ACL repair with no contralateral knee injuries and 15 age- and sex-matched controls (no prior knee injuries) were recruited to participate. Subchondral bone was measured using peripheral quantitative computed tomography (pQCT) distal to the tibial plateau. Muscle force, power, and force efficiency were measured using single leg jumps performed on a force platform. Results: Within subject analysis showed a greater subchondral vBMD in the injured versus uninjured legs of cases (278 +/- 11 mg/cm(3) and 258 +/- 6 mg/cm(3), respectively, mean +/- SD, p=0.01). Subchondral vBMD was greater on the injured leg of cases than controls (267 +/- 8 mg/cm3 and 237 +/- 8 mg/cm3, respectively, marginal mean +/- SE, p=0.01). No differences were observed between cases and controls for muscle force, power, or force efficiency. Conclusions: Greater subchondral bone mineral density was observed in participants between 1- and 5-years post-op. Given the results of this study and the known long-term effects of ACL injuries, future research must continue to focus on the prevention of these injuries
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NR 25
TC 0
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PA 7 SPILIADOU SQ, NAFPLION, 21 100, GREECE
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J9 J MUSCULOSKEL NEURON
JI J. Musculoskelet. Neuronal Interact.
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TI Novel formulations of oral bisphosphonates in the treatment of osteoporosis
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Osteoporosis; Bisphosphonates; Fragility fracture; Therapy; Risedronate; Alendronate
ID risedronate 35 mg; postmenopausal osteoporosis; randomized-trial; vertebral fractures; bone-density; alendronate; women; adherence; risk; prevention
AB Oral bisphosphonates are a key intervention in the treatment of osteoporosis and in reducing the risk of fragility fractures. Their use is supported by over 3 decades of evidence; however, patient adherence to oral bisphosphonates remains poor in part due to complex dosing instructions and adverse events, including

upper gastrointestinal symptoms. This problem has led to the development of novel oral bisphosphonate formulations. Buffered, effervescent alendronate is dissolved in water and so seeks to reduce upper gastro-intestinal adverse events, and gastro-resistant risedronate aims to reduce the complexity of dosing procedure (e.g. fasting prior to consumption) whilst still maintaining the efficacy of fracture risk reduction. Clinical trials and real-world data have been employed to demonstrate some benefits in terms of reduced upper gastro-intestinal adverse events, adherence, persistence and health economic outcomes. This report describes the result of an ESCEO (European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis) expert working group, which explores where oral bisphosphonates sit in current clinical practice guidelines, review their risk-benefit profile and the consequences of poor adherence before exploring novel oral bisphosphonate formulations and their potential clinical and health economic impact. Further research is required but there are signs that these novel, oral bisphosphonate formulations may lead to improved tolerance of oral bisphosphonates and thus, improved adherence and fracture outcomes.
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TI Effects of the Pulsed Electromagnetic Fields on Experimental Periodontitis and Estrogen Deficiency
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DT Article
DE periodontal diseases; osteoporosis; eletromagnetic fields; experimental periodontitis; animal study
ID ovariectomy-induced osteoporosis; knee osteoarthritis; bone-formation; rats; therapy; osteoprotegerin; consensus; strength; workshop; pattern
AB Periodontitis is an inflammatory disease resulting from a complex polymicrobial infection that causes tissue destruction in susceptible individuals. Osteoporosis has been associated with greater clinical attachment loss in patients with periodontitis. Experimental studies have shown positive results in the treatment of osteoporosis through pulsed electromagnetic field (PEMF) stimulation. The aim of this study was to evaluate the effects of PEMF in the presence of estrogen deficiency associated with periodontitis, verifying its role in bone metabolism and in the inflammatory response. Sixty rats were divided into four groups: Sham surgery + ligature-induced periodontitis (P); Sham surgery + ligature-induced periodontitis + PEMF therapy (P + PEMF); Ovariectomy surgery + ligature-induced periodontitis (P + OVX); Ovariectomy surgery + ligature-induced periodontitis + PEMF therapy (P + OVX + PEMF). The area of bone loss in the furcation region (BL), connective tissue attachment loss (CTAL) and alveolar bone loss (ABL), BV/TV and BMD were evaluated. In addition to immunohistochemical labelling of RANKL, OPG, and TRAP and the inflammatory response of interleukin (IL)-1b, IL-6, TNF-alpha, IL-10, and vascular endothelial growth factor. P + OVX showed significant BL in relation to P + PEMF and the greatest CTAL and ABL. P + OVX and P + OVX + PEMF showed a

significant reduction in BV/TV (%). P and P + PEMF showed a significantly lesser amount of Tb.Sp (mm) while P + OVX and P + OVX + PEMF showed a lesser of Tb.N. P + PEMF had the greatest BMD. P + OVX presented higher RANKL and lower OPG immunolabeling than other groups. P + PEMF and P + OVX + PEMF showed a reduction on all biomarkers evaluated. The application of PEMF seems to attenuate the effects of bone loss in the presence of periodontitis and ovariectomy. (c) 2022 Bioelectromagnetics Society.
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TI Bone-targeted biomaterials: Strategies and applications
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ID iron-oxide nanoparticles; in-vitro evaluation; mesoporous silica; extracellular vesicles; poly(ethylene glycol); gold nanoparticles; polymeric micelles; delivery-system; cellular uptake; alendronate
AB Bone diseases including osteoarthritis, osteoporosis, and bone tumors are

becoming severe threats to public health. Bone-targeted biomaterials-based strategies could improve therapeutic effects while avoiding systemic complications, demonstrating promising translational potential in bone-related diseases treatment. In the present review, we introduced the bone biology, bone-targeting strategies, bone-targeted moieties, and bone-targeted biomaterials for the treatment of bone diseases. The discussions herein presented will provide useful information of bone-targeted biomaterials for the chemists and materials scientists, give clue for the selection of suitable bone-targeted drug for the pharmacists, and offer new insights into the therapy of bone-related diseases for the clinicians.
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U1 19
U2 241
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SC Engineering
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PT J
AU Kalra, S
Kumar, V
Kapoor, N
AF Kalra, Sanjay
Kumar, Vijay
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TI The MOAN (Musculo-Osteo-Arthro-Neuropathic) syndrome
SO JOURNAL OF THE PAKISTAN MEDICAL ASSOCIATION
LA English
DT Article
DE Arthritis; Diabetes; Type 2 diabetes; Endocrinology; Geriatrics; Neuropathy; Osteoarthritis; Osteoporosis; Peripheral neuropathy; Sacropenia
AB We share the concept of a multisystemic syndrome which affects the muscle, bone, joints and nerves, in varying manners. The MOAN (musculo-osteo-arthro-neuropathic) syndrome highlights the close relationship between these four organ-systems, and their contribution to each other's health and disease. The mnemonic MOAN also underscores the discomfort and pain associated with the condition and encourages health professionals to address these patients in a holistic manner, rather than just addressing one of the components.
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NR 11
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WC Medicine, General & Internal; Medicine, Research & Experimental
SC General & Internal Medicine; Research & Experimental Medicine
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ER

PT J
AU Kulyar, MFEA
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Bhutta, Zeeshan Ahmad
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Li, Jiakui
Qi, Desheng
TI Regulatory Role of Apoptotic and Inflammasome Related Proteins and Their Possible Functional Aspect in Thiram Associated Tibial Dyschondroplasia of Poultry
SO ANIMALS
LA English
DT Review
DE poultry; tibial dyschondroplasia; thiram; apoptosis; inflammasome; chondrocytes
ID endothelial-cell survival; nitric-oxide synthase; growth-plate; down-regulation;

hypertrophic chondrocytes; extracellular-matrix; molecular-mechanisms; signal-transduction; dietary calcium; resting zone
AB Simple Summary Tibial dyschondroplasia (TD) is a metabolic disorder that impairs bony and cartilage processes. It is common in broilers due to the consumption of thiram, especially in the industrial and agriculture zones. During the condition, cartilage does not only seem to develop ossification during its occurrence but also causes lameness, mortality, and moral convictions in commercial poultry. Moreover, it has been characterized as an economically significant condition since it causes carcass damage due to the involvement of different biological pathways that lead to a particular change in the chondrocytes. These entire cellular pathways are interconnected through various cellular inputs, including anti-apoptotic, pro-apoptotic, and executioner caspases that modulate the other essential chondrogenic proteins (collagen and aggrecan), extracellular metalloproteinases, and NLRP3 base inflammasome. Tibial dyschondroplasia debilities apoptotic and inflammasomal conditions that can further destroy chondrocytes. Inflammasomes are specialized protein complexes that process pro-inflammatory cytokines, e.g., interleukin-1 beta (IL-1 beta) and IL-18. Moreover, there is mounting evidence that many of the signaling molecules that govern programmed cell death also affect inflammasome activation in a cell-intrinsic way. During the last decade, apoptotic functions have been described for signaling molecules involving inflammatory responses and cell death pathways. Considering these exceptional developments in the knowledge of processes, this review gives a glimpse of the significance of these two pathways and their connected proteins in tibial dyschondroplasia. The current review deeply elaborates on the elevated level of signaling mediators of mitochondrial-mediated apoptosis and the inflammasome. Although investigating these pathways' mechanisms has made significant progress, this review identifies areas where more study is especially required. It might lead to developing innovative therapeutics for tibial dyschondroplasia and other associated bone disorders, e.g., osteoporosis and osteoarthritis, where apoptosis and inflammasome are the significant pathways.
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NR 150
TC 6
Z9 6
U1 1
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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TI Intra-articular Soft Tissue Pathology of the Postpartum Hip: A Systematic Review
SO CURRENT REVIEWS IN MUSCULOSKELETAL MEDICINE
LA English
DT Review
DE Hip; Labrum; Arthroscopy; Pregnancy; Postpartum
ID trochanteric pain syndrome; acetabular labrum; pregnancy; osteoarthritis; osteoporosis; arthroscopy; anatomy; repair
AB Purpose of Review Pregnancy-related lumbopelvic and hip pain affects over half of postpartum females and has multiple aetiologies. The relative contribution of intra-articular soft tissue pathology to pregnancy-related hip pain is unknown. The current review investigates the available evidence regarding underlying intra-articular soft tissue aetiologies of hip pain in females during pregnancy and in the acute postpartum period. Recent Findings Three online databases (Embase, PubMed and Ovid [MEDLINE]) were searched from database inception until 11 April 2021. All titles, relevant abstracts and full-text articles were screened by two reviewers independently. The methodological quality of the included studies was assessed using the Methodological Index for Non-Randomized Studies (MINORS) instrument. Descriptive study characteristics are presented in a narrative summary. Five level IV evidence articles were eligible for inclusion. Twenty-two females were included. Twenty patients presented with labral pathology, 15 of which necessitated hip arthroscopy with labral debridement or repair with or without acetabuloplasty and/or femoroplasty. One patient presented with an incidental labral tear in the context of osteitis condensans illi. One patient presented with posttraumatic osteoarthritis necessitating a hip arthroplasty. The contribution of intra-articular soft tissue injury is a documented, albeit sparse, aetiology

contributing to pregnancy-related hip pain. Further research to better delineate the prevalence, natural history and optimal management options for females who sustained these injuries at a life-altering juncture is necessary to advance the care of these patients.
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TI Icariin alleviates osteoarthritis through PI3K/Akt/mTOR/ULK1 signaling pathway
SO EUROPEAN JOURNAL OF MEDICAL RESEARCH
LA English
DT Article
DE Icariin; Interleukin-1 beta; Autophagy; Chondrocytes; PI3K/Akt/mTOR/ULK1
ID cartilage degeneration; autophagy; apoptosis; osteoporosis; epidemiology; chondrocytes; inflammation; protection; model
AB Objectives: This study aims to investigate the effects of Icariin (ICA) on interleukin-1 beta (IL-I beta)-induced osteoarthritis (OA) and its potential mechanism of action. Methods: SW1353 chondrocytes were pretreated with ICA for 2 h, followed by stimulation with IL-1 beta to mimic OA. Expression levels of matrix metalloproteinases (MMP-3) and collagen II were determined using real-time PCR and Western blot assays. Autophagy activation (by ICA) or inhibition (by shRNA) was determined based on the expression levels of ULK1, Beclin-1, LC3-II/I, and p62, using Western blot analysis. The phosphorylation levels of PI3K, Akt, mTOR, and ULK1 were also detected using Western blot analysis. Results: IL-1 beta increased MMP-3 overproduction, induced collagen 11 degradation, and reduced the level of autophagy-associated proteins, including ULK1, Beclin-1, and LC3-II/I. In contrast, ICA pretreatment attenuated IL-1 beta-induced MMP-3 overproduction, increased collagen II expression, and induced expression of autophagy-related proteins. ICA also decreased PI3K, Akt, and mTOR phosphorylation, increased the production of ULK1, and induced autophagy. Short hairpin RNA-mediated knockdown of ULK1 led to activation of the PI3K/Akt/mTOR pathway, which reversed the protective effects of ICA. Conclusions: Our findings indicate that ICA can induce autophagy by regulating the PI3K/AKT/mTOR/ULK1 signaling pathway. This study suggests that ICA may be effective for treating OA.
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NR 44
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Z9 39
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U2 22
PU BMC
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 EUR J MED RES
JI Eur. J. Med. Res.
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IS 1
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DI 10.1186/s40001-022-00820-x
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WC Medicine, Research & Experimental
SC Research & Experimental Medicine
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AU Zhou, DY
Zhang, H
Xue, X
Tao, YL
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Ren, XX
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AF Zhou, Dongyang
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Xue, Xu
Tao, Yali
Wang, Sicheng
Ren, Xiaoxiang
Su, Jiacan
TI Safety Evaluation of Natural Drugs in Chronic Skeletal Disorders: A Literature Review of Clinical Trials in the Past 20 years
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE natural drugs; chronic skeletal disorders; ageing; clinical trial; safety evaluation
ID wilfordii hook f; double-blind; rheumatoid-arthritis; efficacy; osteoarthritis; osteoporosis; knee; metaanalysis; resveratrol; activation
AB Chronic skeletal disorders (CSDs), including degenerative diseases such as osteoporosis (OP) and autoimmune disorders, have become a leading cause of disability in an ageing society, with natural drugs being indispensable therapeutic options. The clinical safety evaluation (CSE) of natural drugs in CSDs has been given priority and has been intensively studied. To provide fundamental evidence for the clinical application of natural drugs in the elderly population, clinical studies of natural drugs in CSDs included in this review were selected from CNKI, Web of Science, PubMed, Science Direct and Google Scholar since 2001. Seventeen randomized controlled trials (RCTs) met our inclusion criteria: four articles were on OP, seven on osteoarthritis (OA), four on rheumatoid arthritis (RA) and two on gout. Common natural drugs used for the treatment of OP include Epimedium brevicornu Maxim [Berberidaceae], Dipsacus asper Wall ex DC [Caprifoliaceae] root, and Phalaenopsis cornu-cervi (Breda) Blume & Rchb. f[Orchidaceae], which have been linked to several mild adverse reactions, such as skin rash, gastric dysfunction, abnormal urine, constipation and irritability. The safety of Hedera helix L [Araliaceae] extract, Boswellia serrata Roxb [Burseraceae] extract and extract from perna canaliculus was evaluated in OA and upper abdominal pain, and unstable movements were obsrerved as major side effects. Adverse events, including pneumonia, vomiting, diarrhoea and upper respiratory tract infection, were reported when RA was treated with Tripterygium wilfordii, Hook. F [Celastraceae][TwHF] polyglycosides and quercetin (Capsella bursa-pastoris (L.) Medik [Brassicaceae]). The present review aimed to summarize the CSE results of

natural drugs in CSDs and could provide evidence-based information for clinicians.
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NR 68
TC 23
Z9 24
U1 3
U2 37
PU FRONTIERS MEDIA SA
PI LAUSANNE
PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
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EI 1663-9812
J9 FRONT PHARMACOL
JI Front. Pharmacol.
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WC Pharmacology & Pharmacy
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ER

PT J
AU Markowska, A
Antoszczak, M
Markowska, J
Huczynski, A
AF Markowska, Anna
Antoszczak, Michal
Markowska, Janina
Huczynski, Adam
TI Role of Vitamin K in Selected Malignant Neoplasms in Women
SO NUTRIENTS
LA English
DT Review
DE vitamin K; breast cancer; cervical cancer; ovarian cancer
ID ovarian-cancer; tyk-nu; apoptosis; cells; inhibition; mortality; increase; growth; risk
AB The main function of vitamin K in the human organism is its activity in the blood clotting cascade. Epidemiological studies suggest that reduced intake of vitamin K may contribute to an increased risk of geriatric diseases such as atherosclerosis, dementia, osteoporosis, and osteoarthritis. A growing number of studies also indicate that vitamin K may be involved not only in preventing the development of certain cancers but it may also support classical cancer chemotherapy. This review article summarizes the results of studies on the anticancer effects of vitamin K on selected female malignancies, i.e., breast, cervical, and ovarian cancer, published over the past 20 years. The promising effects of vitamin K on cancer cells observed so far indicate its great potential, but also the need for expansion of our knowledge in this area by conducting extensive research, including clinical trials.
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NR 55
TC 16
Z9 17
U1 0
U2 17
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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EI 2072-6643
J9 NUTRIENTS
JI Nutrients
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IS 16
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WC Nutrition & Dietetics
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PT J
AU Zhang, YL
Huang, XY
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Sun, CR
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Liu, N
Zhu, LG
Wei, X
AF Zhang, Yili
Huang, Xinyi
Qi, Baoyu
Sun, Chuanrui
Sun, Kai
Liu, Ning
Zhu, Liguo
Wei, Xu
TI Ferroptosis and musculoskeletal diseases: "Iron Maiden" cell death may be a promising therapeutic target
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE regulated cell death; immunology; oxidative stress; inflammation; mechanism
ID oxidative stress; skeletal-muscle; glutathione-peroxidase; promotes ferroptosis; lipid-peroxidation; global burden; in-vitro; mechanisms; damage; identification
AB Ferroptosis is a novel form of cell death precisely regulated by iron metabolism, antioxidant processes, and lipid metabolism that plays an irreplaceable role in the development of many diseases. Musculoskeletal disorders (MSKs), including osteoporosis, osteoarthritis, rheumatoid arthritis, intervertebral disc degeneration, sarcopenia, and rhabdomyolysis, have become one of the most common causes of disability and a major burden on public health and social care systems. The

mechanism of ferroptosis in MSKs has recently been elucidated. In this review, we briefly introduce the ferroptosis mechanism and illustrate the pathological roles of ferroptosis in MSKs with a focus on how ferroptosis can be exploited as a promising treatment strategy. Notably, because the toxicity of compounds that inhibit or induce ferroptosis in other organs is largely unknown, ferroptosis appears to be a double-edged sword. We point out that more research is needed in the future to verify the therapeutic effects based on ferroptosis in MSKs.
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TI Age-associated callus senescent cells produce TGF-β1 that inhibits fracture healing in aged mice
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ID mesenchymal stem-cells; nf-kappa-b; cellular senescence; transforming growth-factor-beta-1; tgf-beta; lymphatic vessels; bone; differentiation; clearance; gene
AB Cellular senescence plays an important role in human diseases, including osteoporosis and osteoarthritis. Senescent cells (SCs) produce the senescence-associated secretory phenotype to affect the function of neighboring cells and SCs themselves. Delayed fracture healing is common in the elderly and is accompanied by reduced mesenchymal progenitor cells (MPCs). However, the contribution of cellular senescence to fracture healing in the aged has not to our knowledge been studied. Here, we used C57BL/6J 4-month-old young and 20-month-old aged mice and demonstrated a rapid increase in SCs in the fracture callus of aged mice. The senolytic drugs dasatinib plus quercetin enhanced fracture healing in aged mice. Aged callus SCs inhibited the growth and proliferation of callus-derived MPCs (CaMPCs) and expressed high levels of TGF-beta 1. TGF-beta-neutralizing Ab prevented the inhibitory effects of aged callus SCs on CaMPCs and promoted fracture healing in aged mice, which was associated with increased CaMPCs and proliferating cells. Thus, fracture triggered a significant cellular senescence in the callus cells of aged mice, which inhibited MPCs by expressing TGF-beta 1. Short-term administration of dasatinib plus quercetin depleted callus SCs and accelerated fracture healing in aged mice. Senolytic drugs represent a promising therapy, while TGF-beta 1 signaling is a molecular mechanism for fractures in the elderly via SCs.
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TI Impact of Total Hip Replacements on the Incidence of Hip Fractures in Norway During 1999-2019. A Norwegian Epidemiologic Osteoporosis Studies (NOREPOS) Study
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE OSTEOPOROSIS; EPIDEMIOLOGY; GENERAL POPULATION STUDIES; ORTHOPEDICS; IMPLANTS
ID body-mass index; osteoarthritis; arthroplasty; cohort; trends; risk
AB The knowledge about why hip fracture rates in Norway have declined is sparse. Concurrent with decreasing hip fracture rates, the rates of total hip replacements (THRs) have increased. We wanted to investigate if hip fracture rates continued to decline, and whether the increase in THRs had any influence on this decline, assuming that living with a hip prosthesis precludes fracture of the operated hip. Information on hip fractures in Norway 1999-2019 was available from the Norwegian Epidemiologic Osteoporosis Studies (NOREPOS) hip fracture database and population size were available in official population tables from Statistics Norway. Primary THRs (for any cause except hip fracture) 1989-2019 were obtained

from the Norwegian Arthroplasty Register. We calculated the annual age-standardized incidence rates of hip fracture by sex for the period 1999-2019. The hip fracture rates in a scenario with no hip prostheses were calculated by subtracting 0.5 persons from the population at risk for each prevalent hip prosthesis, considering that each person has two hips at risk of fracture. We estimated how much of the decline could be attributed to the increased prevalence of hip prostheses. From 1999 to 2019, age-standardized incidence rates of hip fracture decreased by 27% in women and 20% in men. The rates remained stable in those under 70 years and decreased in those 70 years and above. Excluding replaced hips from the population at risk led to higher incidence rates, and this impact was considerably larger at higher ages. The increased prevalence of hip prostheses over the period accounted for approximately 18% (20% in women and 11% in men) of the observed decline in hip fracture rates. In conclusion, the incidence of hip fractures continued to decline, and the increasing number of people living with hip prostheses contributed significantly to the observed declining time trends. (c) 2022 The Authors. Journal of Bone and Mineral Research published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research (ASBMR).
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TI Superimposition of ground reaction force on tibial-plateau supporting diagnostics and post-operative evaluations in high-tibial osteotomy. A novel methodology
SO GAIT & POSTURE
LA English
DT Article
DE Gait analysis; Ground reaction force; Weight-bearing CT; Data registration; High tibial osteotomy
ID joint coordinate system; knee osteoarthritis; valgus alignment; gait analysis; varus
AB Background: A fully personalised combination of Gait Analysis (GA), including Ground Reaction Force (GRF), and patient-specific knee joint morphology has not yet been reported. This can provide valuable biomechanical insight in normal and pathological conditions. Abnormal knee varus results in medial knee condylar hyper compression and osteoarthritis, which can be prevented by restoring proper condylar load distribution via High Tibial Osteotomy (HTO).Research question: This study was aimed at reporting on an original methodology, merging GA, GRF and Computer-Tomography (CT) to depict a patient-specific representation of the knee mechanical condition during locomotion. It was hypothesised that HTO results in a lateralized pattern of GRF with respect to the tibial plateau. Methods: Four patients selected for HTO received clinical, radiological and instrumental examinations, pre-and post-operatively at 6-month follow-up. GA was performed during level walking and more demanding motor tasks using a 9-camera motion-capture system, combined with two force platforms, and an established protocol. Additional skin markers were positioned around the tibial-plateau rim. Weight-bearing CT scans of the knee were collected while still wearing these markers. Proximal tibial and marker morphological models were reconstructed. The markers from CT reconstruction were then registered to the corresponding trajectories as tracked by GA data. Resulting registration matrices were used to report GRF vectors on the plane best matching the tibial plateau model and the

intersection paths were calculated.Results and significance: The registration procedure was successfully executed, with a max registration error of about 3 mm. GRF intersection paths were found medially to the tibial plateau pre-op, and lateralized post-op, thus much closer to the knee centre, as expected after HTO. The exploitation of the present methodology offers personalised quantification of the original mechanical misalignment and of the effect of surgical correction which could enhance diagnostics and planning of HTO as well as other knee treatments.
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TI Roles of Gut Microbiome in Bone Homeostasis and Its Relationship with Bone-Related Diseases
SO BIOLOGY-BASEL
LA English
DT Review
DE gut microbiome; bone homeostasis; osteoporosis; osteoarthritis; rheumatoid arthritis; diabetes mellitus; obesity; bone cancer; probiotic therapy; pharmacological drugs
ID chain fatty-acids; vitamin-d; probiotic supplementation; rheumatoid-arthritis; calcium-absorption; mineral density; double-blind; t-cells; mice; osteoarthritis
AB Simple Summary In recent years, there has been increasing evidence that communication between the skeletal system and the gut microbiome (GM) can influence bone health and that the GM is a key regulator of bone homeostasis. Here, we review the roles of GM in bone homeostasis. In addition, the relationship between GM composition and selected bone-related diseases (osteoporosis, osteoarthritis, rheumatoid arthritis, diabetes mellitus, obesity and bone cancer) is presented. It is also emphasized that a probiotic supplementation can play an important role in suppressing the symptoms of each of these diseases. The extended microbial genome-the gut microbiome (GM)-plays a significant role in host health and disease. It is able to influence a number of physiological functions. During dysbiosis, GM is associated with the development of various chronic diseases with impaired bone quality. In general, GM is important for bone homeostasis and can affect it via several mechanisms. This review describes the roles of GM in bone homeostasis through influencing the immune and endocrine functions, short-chain fatty acids production, calcium absorption and the gut-brain axis. The relationship between GM composition and several bone-related diseases, specifically osteoporosis, osteoarthritis, rheumatoid arthritis, diabetes mellitus, obesity and bone cancer, is also highlighted and summarized. GM manipulation may become a future adjuvant therapy in the prevention of many chronic diseases. Therefore, the beneficial effects of probiotic therapy to improve the health status of individuals with aforementioned diseases are provided, but further studies are needed to clearly confirm its effectiveness. Recent evidence suggests that GM is responsible for direct and indirect effects on drug efficacy. Accordingly, various GM alterations and interactions related to the treatment of bone-related diseases are

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NR 182
TC 21
Z9 25
U1 2
U2 40
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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EI 2079-7737
J9 BIOLOGY-BASEL
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AU Kim, D
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AF Kim, Dongkeun
Pirshahid, Ali Ahmadi
Li, Yueyang
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TI Prevalence of osteoporosis in osteoarthritis: a systematic review and meta-analysis
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Review
DE Bone mineral density; Meta-analysis; Osteoarthritis; Osteoporosis; Systematic literature review
ID bone-mineral density; elderly-men; radiographic osteoarthritis; postmenopausal women; hand osteoarthritis; knee osteoarthritis; lumbar spine; fracture; hip; association
AB Data are contradictory regarding the relationship between osteoarthritis (OA) and osteoporosis (OP) with some studies showing the increased risk of OP in OA. The study was conducted to determine whether OP prevalence is increased in patients with OA, compared to age and sex-matched population. MEDLINE, EMBASE, Scopus, Web of Science, and Cochrane Library (inception-2019) were searched for studies reporting the frequency, rate, prevalence, incidence, risk, or excess risk of OP in patients with OA compared to age and sex-matched population. Estimates were combined using a random effects model. Consistency was evaluated using the I-2 statistic. Articles with fewer than 200 participants were excluded. Of 2772 articles, 49 had full article screening, and 8 articles met the inclusion criteria. Other articles reporting mean BMD and not OP were excluded. In women, 998 participants with OA were compared with 1903 controls. The pooled estimate of the odds ratio for prevalence of OP vs general matched population was not statistically different. In men, 136 participants with OA were compared with 682 controls. The results did not show a statistically significant difference in the frequency of OP in OA in men. According to the site of bone mineral density measurement, a higher prevalence of OP at lumbar spine was found in both men and women. The frequency of OP overall in participants with OA was not different, except for a higher prevalence of OP in lumbar spine in both men and women compared to the matched controls.
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NR 33
TC 34
Z9 38
U1 2
U2 14
PU SPRINGER LONDON LTD
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PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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J9 OSTEOPOROSIS INT
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PT J
AU Veronese, N
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TI Dietary acrylamide and incident osteoporotic fractures: an 8-year prospective cohort study
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Acrylamide; Fracture; Osteoporosis; Osteoarthritis initiative
ID bone-mineral density; risk; stress; scale
AB Background Acrylamide, a component of fried foods, has been associated with several negative health outcomes. However, the relationship between dietary acrylamide and osteoporotic fractures has been explored by a few cross-sectional studies. Aims To investigate if dietary acrylamide is associated with the onset of fractures in North American participants at high risk/having knee osteoarthritis (OA), over 8 years of follow-up. Methods A Cox's regression analysis, adjusted for baseline confounders was run and the data were reported as hazard ratios (HRs) and 95% confidence intervals (CIs). Dietary acrylamide intake was assessed at the baseline using a food frequency questionnaire and categorized in tertiles (T), whilst fractures' history was recorded using self-reported information. Results Altogether, 4,436 participants were included. Compared to participants with lower acrylamide intake (T1; < 3,313 mu g), those with a higher acrylamide intake (T3; > 10,180 mu g) reported a significantly higher risk of any fracture (HR = 1.37; 95% CI 1.12-1.68; p for trend = 0.009), forearm (HR = 1.73; 95% CI 1.09-2.77; p for trend = 0.04),

spine (HR = 2.21; 95% CI 1.14-4.31; p for trend = 0.04), and hip fracture (HR = 4.09; 95% CI 1.29-12.96; p for trend = 0.046). Conclusions Our study is the first to report that high dietary acrylamide may be associated with an increased risk of osteoporotic fractures.
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NR 45
TC 5
Z9 6
U1 0
U2 4
PU SPRINGER
PI NEW YORK
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J9 AGING CLIN EXP RES
JI Aging Clin. Exp. Res.
PD OCT 15
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PT J
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TI Association of physical activity levels and prevalence of major degenerative diseases: Evidence from the national health and nutrition examination survey (NHANES) 1999-2018
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Article
DE Sarcopenia; Osteoporosis; Osteoarthritis; Exercise; Aging
ID sarcopenic obesity; older-adults; osteoporosis; men; osteoarthritis; mortality; exercise; mass
AB Objectives: Degenerative diseases are associated with lower healthy life expectancy and higher mortality. Physical activity (PA) has demonstrated a fundamental role in the prevention and control of several pathologies associated to the aging process. The aim of this study was to analyze the association of PA with the prevalence of sarcopenia, osteoporosis and osteoarthritis in non-institutionalized American population. Methods: Cross-sectional study carried out in participants aged >50 years from the 1999-2018 National Health and Nutrition Examination Survey (NHANES). Sarcopenia was defined using appendicular lean mass adjusted for body mass index (ALM:BMI; men <0.789 kg/m2, women <0.512 kg/m2). Osteoporosis was defined as bone mineral density T-score <=- 2.5 of femur neck. Osteoarthritis and PA were self-reported, and total PA was used to classify participants in groups. The Odds Ratios among the different PA levels for each disease were examined. Results: Performing at least 150 MET-min/week of PA was associated with reduced odds for sarcopenia; performing >1800 MET-min/week was associated with reduced odds for osteoporosis; and performing 150-1800 MET-min/week of PA was associated with reduced odds for osteoarthritis after adjust the results by several confounders. Conclusions: The benefits of PA in sarcopenia, osteoporosis, and osteoarthritis prevention are evident among Americans aged >50 years.
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NR 46
TC 17
Z9 18
U1 1
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PU PERGAMON-ELSEVIER SCIENCE LTD
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TI Preferred Strategies for Delivering Health Information to Patients With Musculoskeletal Disorders A Qualitative Study
SO JCR-JOURNAL OF CLINICAL RHEUMATOLOGY
LA English
DT Article
DE knee osteoarthritis; osteoporosis; patient education; qualitative methods; rheumatoid arthritis
ID rheumatoid-arthritis; global burden; disease; needs; education; care; osteoporosis; interviews; adherence; literacy
AB Background Patients' information needs may differ from what their care providers may perceive to be the patients' needs. This discordance needs to be recognized and addressed. Objective We conducted a qualitative study to explore the perceptions of patients with selected musculoskeletal disorders and those of rheumatologists, on their preferred strategies for delivery of disease management information. Methods Fifty-two patients diagnosed with either rheumatoid arthritis, knee osteoarthritis, or osteoporosis took part in 6 focus groups and 18 individual

semistructured interviews. In addition, 11 rheumatologists participated in 2 focus groups and 4 semistructured individual interviews. Data were explored by thematic content analysis. Perceived preferences were identified and compared between patients and rheumatologists regarding (a) media, (b) setting, (c) messengers, and (d) key message content. Results Patients' preferred media for disease management information were electronic (television and videos delivered as digital optical discs or the Internet), group instruction, and printed material. Patients preferred the information to be delivered in the setting of their homes, doctor's offices, or clinic waiting areas by the rheumatologists and patients with disease experience, addressing healthy lifestyle changes, medication adherence, and consequences of noncompliance. For rheumatologists, the perceived preference for information delivery was through printed material (brochures, booklets, and pamphlets) delivered in waiting areas by nurses and physicians, addressing nature of the disease, complications, and treatment adverse effects. Conclusions Provider perspectives on strategies for education may differ from those of patients. Our findings highlight the need for considering different stakeholder perspectives in designing educational tools and decision support materials for patients with chronic diseases. Take-Home Message Rheumatologists' preferences on strategies for education (mode of delivery, delivery setting, messengers, and topics) differ from those of patients. For example, patients want to learn about lifestyle changes and consequences of compliance versus noncompliance, whereas rheumatologists considered more important for patients to understand their disease, treatment adverse effects, and consequences of noncompliance.
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NR 34

TC 2
Z9 3
U1 0
U2 0
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 1076-1608
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J9 JCR-J CLIN RHEUMATOL
JI JCR-J. Clin. Rheumatol.
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TI Connections between Orthopedic Conditions and Oxidative Stress: Current Perspective and the Possible Relevance of Other Factors, Such as Metabolic Implications, Antibiotic Resistance, and COVID-19
SO MEDICINA-LITHUANIA
LA English
DT Article
DE oxidative stress; orthopedic; COVID-19; antibacterial resistance; osteoarthritis; osteoporosis; orthopedic surgery
ID loaded bone-cement; antimicrobial resistance; hip; mortality; infection; knee; staphylococcus; osteoarthritis; risk; prophylaxis
AB The general opinion in the literature is that these topics remain clearly understudied and underrated, with many unknown aspects and with controversial results in the respective areas of research. Based on the previous experience of our groups regarding such matters investigated separately, here we attempt a short overview upon their links. Thus, we summarize here the current state of knowledge regarding the connections between oxidative stress and: (a) orthopedic conditions; (b) COVID-19. We also present the reciprocal interferences among them. Oxidative stress is, of course, an interesting and continuously growing area, but what exactly is the impact of COVID-19 in orthopedic patients? In the current paper we also approached some theories on how oxidative stress, metabolism involvement, and even antibiotic resistance might be influenced by either orthopedic conditions or COVID-19. These manifestations could be relevant and of great interest in the context of this current global health threat; therefore, we summarize the current knowledge and/or the lack of sufficient evidence to support the interactions between these conditions.
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TI Therapeutic Effects of Citrus Flavonoids Neohesperidin, Hesperidin and Its Aglycone, Hesperetin on Bone Health
SO BIOMOLECULES
LA English
DT Review
DE flavonoids; bone; bone repair; bone health; neohesperidin; hesperidin; hesperetin
ID in-vitro; matrix metalloproteinases; dentin collagen; dihydrochalcone; suppresses; resorption; inhibition; expression; arthritis; pharmacokinetics
AB Flavonoids are natural phytochemicals that have therapeutic effects and act in the prevention of several pathologies. These phytochemicals can be found in seeds, grains, tea, coffee, wine, chocolate, cocoa, vegetables and, mainly, in citrus fruits. Neohesperidin, hesperidin and hesperetin are citrus flavonoids from the flavanones subclass that have anti-inflammatory and antioxidant potential. Neohesperidin, in the form of neohesperidin dihydrochalcone (NHDC), also has dietary properties as a sweetener. In general, these flavanones have been investigated as a strategy to control bone diseases, such as osteoporosis and osteoarthritis. In this literature review, we compiled studies that investigated the effects of neohesperidin, hesperidin and its aglycone, hesperetin, on bone health. In vitro studies showed that these flavanones exerted an antiosteoclastic and anti-inflammatory effects, inhibiting the expression of osteoclastic markers and reducing the levels of reactive oxygen species, proinflammatory cytokines and matrix metalloproteinase levels. Similarly, such studies favored the osteogenic potential of preosteoblastic cells and induced the overexpression of osteogenic markers. In vivo, these flavanones favored the regeneration of bone defects and minimized inflammation in arthritis- and periodontitis-induced models. Additionally, they exerted a significant anticatabolic effect in ovariectomy models, reducing trabecular bone loss and increasing bone mineral density. Although research should advance to the clinical field, these flavanones may have therapeutic potential for controlling the progression of metabolic, autoimmune or inflammatory bone diseases.
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AU Curtis, EM
Codd, V
Nelson, C
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TI Telomere Length and Risk of Incident Fracture and Arthroplasty: Findings From UK Biobank
SO JOURNAL OF BONE AND MINERAL RESEARCH
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DT Article
DE OSTEOPOROSIS; OSTEOARTHRITIS; EPIDEMIOLOGY; LEUCOCYTE TELOMERE LENGTH; AGING
ID mesenchymal stem-cells; x-ray absorptiometry; bone-mineral density;

osteoporosis; osteoarthritis; senescence; women; inflammation; leukocytes; cartilage
AB We investigated independent associations between telomere length and risk of fracture and arthroplasty in UK Biobank participants. Leukocyte telomere length (LTL) was measured in baseline samples using a validated polymerase chain reaction (PCR) method. We used, in men and women separately, Cox proportional hazards models to calculate the hazard ratio (HR) for incident fracture (any, osteoporotic) or arthroplasty (hip or knee) over 1,186,410 person-years of follow-up. Covariates included age, white cell count, ethnicity, smoking, alcohol, physical activity, and menopause (women). In further analyses we adjusted for either estimated bone mineral density (eBMD) from heel quantitative ultrasound, handgrip strength, gait speed, total fat mass (bioimpedance), or blood biomarkers, all measured at baseline (2006-2010). We studied 59,500 women and 51,895 men, mean +/- standard deviation (SD) age 56.4 +/- 8.0 and 57.0 +/- 8.3 years, respectively. During follow-up there were 5619 fractures; 5285 hip and 4261 knee arthroplasties. In confounder-adjusted models, longer LTL was associated with reduced risk of incident knee arthroplasty in both men (HR/SD 0.93; 95% confidence interval [CI], 0.88-0.97) and women (0.92; 95% CI, 0.88-0.96), and hip arthroplasty in men (0.91; 95% CI, 0.87-0.95), but not women (0.98; 95% CI, 0.94-1.01). Longer LTL was weakly associated with reduced risk of any incident fracture in women (HR/SD 0.96; 95% CI, 0.93-1.00) with less evidence in men (0.98; 95% CI, 0.93-1.02). Associations with incident outcomes were not materially altered by adjustment for heel eBMD, grip strength, gait speed, fat mass, or blood biomarker measures. In this, the largest study to date, longer LTL was associated with lower risk of incident knee or hip arthroplasty, but only weakly associated with lower risk of fracture. The relative risks were low at a population level, but our findings suggest that common factors acting on the myeloid and musculoskeletal systems might influence later life musculoskeletal outcomes. (c) 2022 The Authors. Journal of Bone and Mineral Research published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research (ASBMR).
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TI Tracking Strain-Specific Morphogenesis and Angiogenesis of Murine Calvaria with Large-Scale Optoacoustic and Ultrasound Microscopy
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE ANALYSIS; QUANTIFICATION OF BONE; PRECLINICAL STUDIES; OSTEOGENESIS; INTRAVITAL MICROSCOPY; LONGITUDINAL IMAGING
ID bone-marrow; hematopoietic stem; mouse-brain; osteogenesis; cells
AB Skull bone development is a dynamic and well-coordinated process playing a key role in maturation and maintenance of the bone marrow (BM), fracture healing, and progression of diseases such as osteoarthritis or osteoporosis. At present, dynamic transformation of the growing bone (osteogenesis) as well as its vascularization (angiogenesis) remain largely unexplored due to the lack of suitable in vivo imaging techniques capable of noninvasive visualization of the whole developing calvaria at capillary-level resolution. We present a longitudinal study on skull bone development using ultrasound-aided large-scale optoacoustic microscopy (U-LSOM). Skull bone morphogenesis and microvascular growth patterns were monitored in three common mouse strains (C57BL/6J, CD-1, and Athymic Nude-Foxn1nu) at the whole-calvaria scale over a 3-month period. Strain-specific differences in skull development were revealed by quantitative analysis of bone and vessel parameters, indicating the coupling between angiogenesis and osteogenesis during skull bone growth in a minimally invasive and label-free manner. The method further enabled identifying BM-specific sinusoidal vessels, and superficial skull vessels penetrating into BM compartments. Our approach furnishes a new high-throughput longitudinal in vivo imaging

platform to study morphological and vascular skull alterations in health and disease, shedding light on the critical links between blood vessel formation, skull growth, and regeneration. (c) 2022 The Authors. Journal of Bone and Mineral Research published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research (ASBMR).
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TI Current Research on Subchondral Insufficiency Fracture of the Femoral Head
SO CLINICS IN ORTHOPEDIC SURGERY
LA English
DT Review
DE Subchondral insufficiency fracture; Femoral head; Rapidly progressive osteoarthritis of the hip
ID rapidly destructive osteoarthritis; osteonecrosis; patient; mri; hip; prevalence; appearance; inversion
AB Subchondral insufficiency fracture (SIF) of the femoral head is one of the

predominant etiologies of rapidly progressive osteoarthri-tis of the hip (RPOH). SIF is a rare disease that causes acute pain in the hip joint. It is most frequently found in elderly women with osteoporosis. It is often underdiagnosed or misdiagnosed as osteonecrosis of the femoral head. SIF is currently a well-established cause of RPOH; however, the deeper etiology of SIF is not clear. Good clinical outcomes have been reported for hip preservation therapy and hip replacement. SIF is not obvious radiologically in the early stage, and a T1-weighted magnetic resonance imaging shows a discontinuous low-intensity band under the articular cartilage convex to the articular surface as its characteristic manifes-tation. Some patients will lose the opportunity to preserve the hip joint due to symptoms such as progressive joint space narrowing and subchondral collapse within a very short period. Patients with progressive hip space narrowing and subchondral collapse on X-ray should be converted to total hip arthroplasty. Based on the characteristics of the disease, surgeons need to master the clinical and radiological characteristics of SIF and strive for early diagnosis and treatment.

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TI Role of Primary Cilia in Skeletal Disorders
SO STEM CELLS INTERNATIONAL
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DT Review

ID adolescent idiopathic scoliosis; endoscopic lumbar diskectomy; intraflagellar transport; growth-plate; protein; chondrocytes; cells; bone; expression; cartilage
AB Primary cilia are highly conserved microtubule-based organelles that project from the cell surface into the extracellular environment and play important roles in mechanosensation, mechanotransduction, polarity maintenance, and cell behaviors during organ development and pathological changes. Intraflagellar transport (IFT) proteins are essential for cilium formation and function. The skeletal system consists of bones and connective tissue, including cartilage, tendons, and ligaments, providing support, stability, and movement to the body. Great progress has been achieved in primary cilia and skeletal disorders in recent decades. Increasing evidence suggests that cells with cilium defects in the skeletal system can cause numerous human diseases. Moreover, specific deletion of ciliary proteins in skeletal tissues with different Cre mice resulted in diverse malformations, suggesting that primary cilia are involved in the development of skeletal diseases. In addition, the intact of primary cilium is essential to osteogenic/chondrogenic induction of mesenchymal stem cells, regarded as a promising target for clinical intervention for skeletal disorders. In this review, we summarized the role of primary cilia and ciliary proteins in the pathogenesis of skeletal diseases, including osteoporosis, bone/cartilage tumor, osteoarthritis, intervertebral disc degeneration, spine scoliosis, and other cilium-related skeletal diseases, and highlighted their promising treatment methods, including using mesenchymal stem cells. Our review tries to present evidence for primary cilium as a promising target for clinical intervention for skeletal diseases.
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TI Therapeutic Potential of Human Fetal Mesenchymal Stem Cells in Musculoskeletal Disorders: A Narrative Review
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
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DT Review
DE mesenchymal stem cells; fetal; musculoskeletal disorders; regeneration
ID amniotic-fluid; stromal cells; in-vitro; progenitor cells; bone-marrow; differentiation; tissue; liver; transplantation; identification
AB Mesenchymal stem cells (MSCs) have emerged as a promising therapeutic approach for diverse diseases and injuries. The biological and clinical advantages of human fetal MSCs (hfMSCs) have recently been reported. In terms of promising therapeutic approaches for diverse diseases and injuries, hfMSCs have gained prominence as healing tools for clinical therapies. Therefore, this review assesses not the only biological advantages of hfMSCs for healing human diseases and regeneration, but also the research evidence for the engraftment and immunomodulation of hfMSCs based on their sources and biological components. Of particular clinical relevance, the present review also suggests the potential therapeutic feasibilities of hfMSCs for musculoskeletal disorders, including osteoporosis, osteoarthritis, and osteogenesis imperfecta.
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TC 9
Z9 11

U1 0
U2 4
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
SN 1661-6596
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J9 INT J MOL SCI
JI Int. J. Mol. Sci.
PD FEB 15
PY 2022
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IS 3
BP
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DI 10.3390/ijms23031439
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
GA ZF2PD
UT WOS:000759412800001
PM 35163361
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PT J
AU Min, HK
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Lee, JY
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AF Min, Hong Ki
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TI DJ-1 controls T cell differentiation and osteoclastogenesis in rheumatoid arthritis
SO SCIENTIFIC REPORTS
LA English
DT Article
ID reactive oxygen; potential biomarkers; nadph oxidase; protein; rankl; autoantibody; osteoporosis; tissue; park7
AB Herein, we investigated the effect of DJ-1 on helper T cell differentiation, fibroblast-like synoviocyte (FLS) activation, and osteoclastogenesis in rheumatoid

arthritis (RA). Serum and synovial fluid (SF) of RA and osteoarthritis (OA) patients were collected, and DJ-1 and H2O2 levels were investigated. CD4(+) cells from peripheral blood mononuclear cells (PBMCs) were cultured under type 17 helper T cell (Th17) polarization conditions, and CD4(+) T cell differentiation, pro-inflammatory cytokine levels, and soluble receptor activator of nuclear factor kappa-Beta ligand (RANKL) were assessed. RA-FLSs were stimulated with 50 mu M H2O2, and DJ-1 (10, 50, 100 ng/mL) to evaluate MMP-9, VEGF, TNF-alpha, and sRANKL production, while RANKL(+) FLSs were assessed using flow cytometry. Monocytes were cultured with RANKL or IL-17A with or without DJ-1 and H2O2-pretreated RA-FLS, and tartrate-resistant acid phosphatase (TRAP) staining and RT-qPCR of osteoclast-related genes were performed. The levels of DJ-1 and H2O2 in serum and SF of RA patients were higher than those of OA patients. Under Th17-polarizing conditions, CD4(+)RANKL(+) and CD4(+)CCR4(+)CCR6(+)CXCR3(-) T cells decreased, whereas CD4(+)CD25(high)Foxp3(+) T cell increased after DJ-1 administration. Additionally, IL-17A, TNF-alpha, and sRANKL levels decreased in DJ-1-treated groups. DJ-1 lowered MMP-9, VEGF, TNF-alpha, and sRANKL levels, and RANKL(+) FLS in ROS-stimulated RA-FLS. Both RANKL and IL-17A stimulated osteoclast differentiation, DJ-1 decreased TRAP(+) cell count, and the expression levels of TRAP, ATP6v0d2, NFATc1, and CTSK. These findings were also observed in in vitro osteoclastogenesis with DJ-1 pretreated RA-FLS. As DJ-1 regulates Th17/Treg imbalance, pro-inflammatory cytokine production, RA-FLS activation, and osteoclastogenesis, it holds potential for RA therapy.
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NR 49
TC 8
Z9 11
U1 0
U2 5
PU NATURE PORTFOLIO
PI BERLIN
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SN 2045-2322
EI
J9 SCI REP-UK
JI Sci Rep
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PY 2022
VL 12
IS 1
BP
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DI 10.1038/s41598-022-16285-1
PG 10
WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
GA 3H2RJ
UT WOS:000831887000101
PM 35896699
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PT J
AU Pröbsting, E
Altenburg, B
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AF Proebsting, Eva
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Bellmann, Malte
Krug, Kerstin
Schmalz, Thomas
TI How does ankle power on the prosthetic side influence loading parameters on the sound side during level walking of persons with transfemoral amputation?
SO PROSTHETICS AND ORTHOTICS INTERNATIONAL
LA English
DT Article
DE ankle power; knee loading; powered foot; ankle push off
ID knee osteoarthritis; push-off; foot; gait; adduction
AB Background: Increased ankle power on the prosthetic side seems to decrease biomechanical loading parameters on the sound side. This assumption is based on biomechanical comparisons of different foot constructions. However, such study designs could not show whether the amount of ankle power solely influences the sound side. Objective: To analyze the influence of divergent ankle power, resulting from different foot constructions and from different ankle power settings, on the sound side loading parameters. Study design: Interventional cross sectional study. Methods: Level walking of transfemoral amputees with a microprocessor knee joint and Solid Ankle Cushioned Heel (SACH), energy storing and returning (ESR) and powered foot (PF) was analyzed. The PF was adapted in three configurations: without power (np), low power (lp), and optimal power (op). An optoelectronic camera system with 12 cameras and two force plates were used. Results: The ankle power on the prosthetic side shows significant differences about foot types and different settings of the PF. The knee adduction moment, the knee flexion moment, and the vertical ground reaction forces on the sound side were significantly reduced with PF_op and ESR in comparison to SACH. When analyzing these parameters for the different PF configurations, only some show significant results at normal velocity. Conclusions: The additional positive mechanical work for an active push off in the PF tends to have a relieving effect. The biomechanical sound side loading parameters are reduced with PF_op in comparison to SACH and ESR, resulting in a relief of the sound side of lower limb amputees.
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NR 24
TC 4
Z9 5
U1 0
U2 0
PU WOLTERS KLUWER HEALTH
PI Philadelphia
PA 2001 Market St., Philadelphia, PA, UNITED STATES
SN 0309-3646
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J9 PROSTHET ORTHOT INT
JI Prosthet. Orthot. Int.
PD AUG 15
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VL 46
IS 4
BP 306
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DI 10.1097/PXR.0000000000000099
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WC Orthopedics; Rehabilitation
SC Orthopedics; Rehabilitation
GA 8G6CE
UT WOS:000920430300002
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PT J
AU Peng, X
Zhou, X
Yin, Y
Luo, BB
Liu, Y
Yang, C
AF Peng, Xin
Zhou, Xin
Yin, Ying
Luo, Beibei
Liu, Yang
Yang, Cheng
TI Inflammatory Microenvironment Accelerates Bone Marrow Mesenchymal Stem Cell Aging
SO FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY
LA English
DT Article
DE aging-related skeletal diseases; stem cell therapy; inflammatory microenvironment; bone marrow mesenchymal stem cell; aging
ID senescent cells; differentiation; osteoarthritis; osteoporosis; therapy
AB MSC senescence is considered a contributing factor in aging-related diseases. We investigated the influence of the inflammatory microenvironment on bone marrow mesenchymal stem cells (BMSCs) under aging conditions and the underlying mechanism to provide new ideas for stem cell therapy for age-related osteoporosis. The BMSCs were cultured until passage 3 (P3) (young group) and passage 10 (P10) (aging group) in vitro. The supernatant was collected as the conditioned medium (CM). The young BMSCs were cultured in the CM of P3 or P10 cells. The effects of CM from different groups on the aging and stemness of the young BMSCs were examined. A Quantibody (R) mouse inflammation array on

serum extracts from young (aged 8 weeks) and old (aged 78 weeks) mice was performed, and differentially expressed factors were screened out. We discovered that the CM from senescent MSCs changed the physiology of young BMSCs. Systemic inflammatory microenvironments changed with age in the mice. In particular, the pro-inflammatory cytokine IL-6 increased, and the anti-inflammatory cytokine IL-10 decreased. The underlying mechanism was investigated by GO and KEGG analyses, and there was a change in the JAK-STAT signaling pathway, which is closely related to IL-6 and IL-10. Collectively, our results demonstrated that the age-related inflammatory microenvironment has a significant effect on the biological functions of BMSCs. Targeted reversal of this inflammatory environment may provide a new strategy for stem cell therapy to treat aging-related skeletal diseases.
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TI The Association Between Acupuncture Therapies and Reduced Fracture Risk in Patients with Osteoarthritis: A Nationwide Retrospective Matched Cohort Study
SO JOURNAL OF INTEGRATIVE AND COMPLEMENTARY MEDICINE
LA English
DT Article
DE acupuncture; fracture; National Health Insurance Research Database; osteoarthritis; Traditional Chinese Medicine
ID bone-mineral density; cytokine production; tnf-alpha; knee; population; inflammation; arthritis; viscosupplementation; osteoporosis; trial

AB Objective: The aim of this study is to investigate the association between acupuncture therapy and the risk of fracture in patient with osteoarthritis (OA).Design: The authors performed a 1:1 propensity score-matched cohort study to analyze patient with OA between January 1, 1997 and December 31, 2010 through the Taiwanese National Health Insurance Research Database. Patients who received acupuncture therapy from the initial date of diagnosis of OA to December 31, 2010 were included in the acupuncture cohort. Patients who did not receive acupuncture during the same follow-up period were defined as the no-acupuncture cohort. A Cox regression model was used to adjust for sex, age, comorbidities, prescription, and surgical experiences. Hazard ratios (HRs) were compared between the two cohorts.Results: A total of 3416 patients were identified after 1:1 propensity score matching. The patients had similar basic characteristics. In the final analysis, 292 patients in the acupuncture cohort (30.06 per 1000 person-years) and 431 patients in the no-acupuncture cohort (56.08 per 1000 person-years) developed fractures (adjusted HRs 0.57, 95% confidence interval 0.49-0.67). A reduced cumulative incidence of fracture was found in the acupuncture cohort (log-rank test, $p < 0.001$). The association between acupuncture and reducing the fracture incidence was independent of sex, comorbidities, drugs use, and surgical experiences.Conclusion: Their results revealed the association between acupuncture therapies and a reduced incidence of fracture development in patients with OA. This finding provides noteworthy ideas for further research.
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TI Kruppel-like Factors in Skeletal Physiology and Pathologies
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DT Review

DE Kruppel-like factor; osteoblast; osteoclast; osteoarthritis; osteoporosis; osteosarcoma
ID congenital dyserythropoietic anemia; mesenchymal stem-cells; inducible early gene-1; finger transcription factor; marrow stromal cells; bone-mineral density; factor klf1 causes; tgf-beta; tumor-suppressor; co-repressor
AB Kruppel-like factors (KLFs) belong to a large group of zinc finger-containing transcription factors with amino acid sequences resembling the Drosophila gap gene Kruppel. Since the first report of molecular cloning of the KLF family gene, the number of KLFs has increased rapidly. Currently, 17 murine and human KLFs are known to play crucial roles in the regulation of transcription, cell proliferation, cellular differentiation, stem cell maintenance, and tissue and organ pathogenesis. Recent evidence has shown that many KLF family molecules affect skeletal cells and regulate their differentiation and function. This review summarizes the current understanding of the unique roles of each KLF in skeletal cells during normal development and skeletal pathologies.
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NR 194
TC 14
Z9 14
U1 1
U2 19
PU MDPI
PI BASEL

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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
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AU Wu, YQ
Chao, JQ
Bao, M
Zhang, N
Wang, LX
AF Wu, Yanqian
Chao, Jianqian
Bao, Min
Zhang, Na
Wang, Leixia
TI Construction of predictive model for osteoporosis related factors among postmenopausal women on the basis of logistic regression and Bayesian network
SO PREVENTIVE MEDICINE REPORTS
LA English
DT Article
DE Osteoporosis; Postmenopausal women; Influencing factors; Bayesian network; Multiple logistic regression
ID bone-mineral density; knee osteoarthritis; health
AB Osteoporosis is a prevalent chronic disease that often goes unnoticed in postmenopausal women. Early identification of risk factors for osteoporosis in postmenopausal women is essential. This study aimed to develop predictive models for osteoporosis-related factors among postmenopausal women in the U.S.

and explore the influencing factors. In this cross-sectional study, we included 4417 postmenopausal women from the NHANES (2009-2010, 2013-2014, and 2017-2020). Through multiple regression analysis, we found that age, minutes of sedentary activity, prednisone or cortisone usage, arthritis, bone loss around teeth, and trouble sleeping were risk factors for osteoporosis after menopause. Conversely, height, BMI, and age at the last menstrual period were identified as protective factors. The findings from the Bayesian network analysis indicated that several factors influenced osteoporosis, including age, BMI, bone loss around teeth, prednisone or cortisone usage, arthritis, and age at the last menstrual period. On the other hand, minutes of sedentary activity and height might have indirect effects, while trouble sleeping may not have a significant impact. Both logistic regression and Bayesian network models demonstrated good predictive capabilities in predicting osteoporosis among postmenopausal women. In addition, Bayesian networks offer a more intuitive depiction of the intricate network risk mechanism between diseases and factors.
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NR 39
TC 11
Z9 13
U1 2
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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PT J
AU Kim, H
Lee, HYJ
AF Kim, Hyunsu
Lee, Hyunjung
TI Risk of Stroke and Cardiovascular Disease According to Diabetes Mellitus Status
SO WESTERN JOURNAL OF NURSING RESEARCH
LA English
DT Article
DE cardiovascular disease; diabetes mellitus; national surveys; risk factors; stroke
ID quality-of-care; ischemic-stroke; microvascular complications; physical-activity; age; epidemiology; association; guidelines; management; diagnosis
AB The purpose of this study was to investigate the importance of prevention and management of diabetes by analyzing stroke and cardiovascular disease (CVD) incidence among people with diabetes. This secondary analysis of the Korea National Health and Nutrition Examination Survey VII (2016-2018) data included 15,039 adults. Diabetes status was significantly associated with sex, age, marital status, household size, education level, employment status, household income, hypertension, dyslipidemia, stroke, CVD, osteoarthritis, osteoporosis, kidney failure, depression, level of stress, smoking, drinking, body mass index, weight control, and the number of days of walking per week; however, it was not associated with rheumatoid arthritis. Stroke and CVD risk significantly increased in the presence of diabetes (by 4.123 times and 3.223 times, respectively). The incidences of stroke and CVD were significantly higher among participants with diabetes than among those without diabetes. Thus, preventing and systematically managing diabetes is crucial to reducing related complications and mortality.
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PT J
AU Cui, YJ
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Ma, SS
Ye, ZL
AF Cui, Yaojia
Zhu, Longwei
Wang, Hui

Zhao, Zhuzi
Ma, Shuaishuai
Ye, Zhaolian
TI Characteristics and Oxidative Potential of Ambient PM2.5 in the Yangtze River Delta Region: Pollution Level and Source Apportionment
SO ATMOSPHERE
LA English
DT Article
DE particulate matter; oxidative potential; high-resolution aerosol mass spectrometer; multiple linear regression; positive matrix factorization
ID fine particulate matter; humic-like substances; aerosol mass-spectrometry; water-soluble pm2.5; dithiothreitol dtt; organic aerosols; chemical-composition; trace-elements; redox activity; air-pollution
AB Fine particulate matter (PM2.5) is a major contributor to the degree of air pollution, and it is associated with a range of adverse health impacts. Moreover, the oxidative potential (OP, as a tracer of oxidative stress) of PM2.5 has been thought to be a possible determinant of its health impact. In this study, the OP of 136 fine aerosol filter samples collected in Changzhou in two seasons (spring and summer) were determined using a dithiothreitol (DTT) assay. Source apportionments of the PM2.5 and DTT activity were further performed. Our results showed that the daily average +/- standard deviation of the DTTv (volume-normalized DTT activity) in the PM2.5 was 1.16 +/- 0.58 nmol/min/m(3) and 0.85 +/- 0.16 nmol/min/m(3) in the spring and summer, respectively, and the DTTm (mass-normalized DTT activity) was 13.56 +/- 5.45 pmol/min/mu g and 19.97 +/- 6.54 pmol/min/mu g in the spring and summer, respectively. The DTTv was higher in the spring compared to the summer while the opposite was true for the DTTm. Most of the detected components (including the organic component, element component, NH4+, Mn, Cu, Zn, etc.) exhibited a moderately positive correlation with the DTTv, but the opposite was found with the DTTm. An aerodyne high-resolution aerosol mass spectrometer (HP-AMS) was deployed to probe the chemical properties of the water-soluble organic matter (WSOA). Positive matrix factorization (PMF) coupled with multiple linear regression was used to obtain the relative source contributions to the DTT activity for the WSOA in the PM2.5. The results showed that the sensitivity sequences of the DTTv to the WSOA sources were oxygenated organic aerosol (OOA) > biomass burning OA (BBOA) > hydrocarbon-like OA (HOA) in the spring and HOA > nitrogen-enriched OA (NOA) > OOA in the summer. The PMF suggested the highest contribution from traffic emissions to the DTTv of the PM2.5 in both seasons. Our findings point to the importance of both organic components from secondary formation and transition metals to adverse health effects in this region. This study can provide an important reference for adopting appropriate public health policies regarding the detrimental outcomes of exposure to PM2.5.
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TI Melatonin and bone-related diseases: an updated mechanistic overview of current evidence and future prospects
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ID mesenchymal stem-cells; systemic-lupus-erythematosus; nitric-oxide synthase; quality-of-life; osteoblast differentiation; rheumatoid-arthritis; signaling pathway; oxidative stress; mineral density; osteogenic differentiation
AB PurposeBone diseases account for an enormous cost burden on health systems. Bone disorders are considered as age-dependent diseases. The aging of world population has encouraged scientists to further explore the most effective preventive modalities and therapeutic strategies to overcome and reduce the high cost of bone disorders. Herein, we review the current evidence of melatonin's therapeutic effects on bone-related diseases.MethodsThis review summarized evidences from in vitro, in vivo, and clinical studies regarding the effects of melatonin on bone-related diseases, with a focus on the molecular mechanisms. Electronically, Scopus and MEDLINE & REG;/PubMed databases were searched for articles published on melatonin and bone-related diseases from inception to June 2023.ResultsThe findings demonstrated that melatonin has beneficial effect in bone- and cartilage-related disorders such as osteoporosis, bone fracture healing, osteoarthritis, and rheumatoid arthritis, in addition to the control of sleep and circadian rhythms.ConclusionA number of animal and clinical studies have indicated that various biological effects of melatonin may suggest this molecule as an effective therapeutic agent for controlling, diminishing, or suppressing bone-related disorders. Therefore, further clinical studies are required to clarify whether melatonin can be effective in patients with bone-related diseases.
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TI p62/SQSTM1 indirectly mediates remote multipotent mesenchymal cells and rescues bone loss and bone marrow integrity in ovariectomized rats
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DE bone physiology; DNA plasmid; multipotent mesenchymal cells; osteoporosis; p62
ID plasmid dna; p62; osteoarthritis; autophagy; delivery; vaccine; protein
AB Intramuscular administration of p62/SQSTM1 (sequestosome1)-encoding plasmid demonstrated an anticancer effect in rodent models and dogs as well as a high safety profile and the first evidence of clinical benefits in humans. Also, an anti-inflammatory effect of the plasmid was reported in several rodent disease models. Yet, the mechanisms of action for the p62 plasmid remain unknown. Here, we tested a hypothesis that the p62-plasmid can act through the modulation of bone marrow multipotent mesenchymal cells (MSCs). We demonstrated that a p62 plasmid can affect MSCs indirectly by stimulating p62-transfected cells to secrete an active ingredient(s) sensed by untransfected MSCs. When we transfected MSCs with the p62-plasmid, collected their supernatant, and added it to an untransfected MSCs culture, it switched the differentiation state and prompt osteogenic responses of the untransfected MSCs. According to an accepted viewpoint, ovariectomy leads to bone pathology via dysregulation of MSCs, and restoring the MSC homeostasis would restore ovariectomy-induced bone damage. To validate our in vitro observations in a clinically relevant in vivo model, we administered the p62 plasmid to ovariectomized rats. It partially reversed bone loss and notably reduced adipogenesis with concurrent reestablishing of the MSC subpopulation pool within the bone marrow. Overall, our study suggests that remote modulation of progenitor MSCs via administering a p62-encoding plasmid may constitute a mechanism for its previously reported effects and presents a feasible disease-preventing and/or therapeutic strategy.
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AU Zheng, ML
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DE CD14; CSF1R; gastritis; molecular targets; osteoarthritis
ID expression; diagnosis
AB Osteoarthritis (OA) is a non-inflammatory degenerative joint disease that mainly involves articular cartilage damage and involves the whole joint tissue. Gastritis is a common stomach disorder, typically referring to inflammation or lesions of the gastric mucosa. However, the relationship between CD14 and colony stimulating factor-1 receptor (CSF1R) and these 2 diseases is not yet clear. OA datasets GSE46750, GSE82107 and gastritis datasets GSE54043 profiles were downloaded from gene expression omnibus databases generated by GPL10558 and GPL570.The R package limma was used to screen differentially expressed genes (DEGs). Weighted gene co-expression network analysis was performed. The construction and analysis of protein-protein interaction network, functional enrichment analysis, gene set enrichment analysis and comparative toxicogenomics database analysis were performed. TargetScan was used to screen miRNAs regulating central DEGs. A

total of 568 DEGs were identified. According to the gene ontology (GO) and biological processes analysis, they were mainly enriched in ATP metabolism negative regulation, toll-like receptor TLR1:TLR2 signaling pathway, and intracellular transport. The enrichment terms for OA and gastritis were similar to the GO and Kyoto encyclopedia of gene and genome enrichment terms of DEGs, mainly enriched in ATP metabolism negative regulation, secretion granules, transmembrane receptor protein kinase activity, cytokine-cytokine receptor interaction, Toll-like receptor signaling pathway, MAPK signaling pathway, and TGF-beta signaling pathway. In the Metascape enrichment projects, GO enrichment projects showed functions related to cell-cell receptor interaction, cell secretion, and growth. Two core genes were identified through the construction and analysis of the protein-protein interaction network. The core genes (CD14 and CSF1R) exhibited high expression in OA and gastritis samples and low expression in normal samples. Comparative toxicogenomics database analysis revealed associations between core genes (CD14 and CSF1R) and diseases such as OA, osteoporosis, gastritis, juvenile arthritis, diarrhea, and inflammation. CD14 and CSF1R are highly expressed in OA and gastritis, making them potential therapeutic targets for both diseases.

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TI Sow-Offspring Diets Supplemented with Probiotics and Synbiotics Are Associated with Offspring's Growth Performance and Meat Quality
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE growth performance; carcass traits; meat quality; probiotics; synbiotics; Bama mini-pigs
ID blood characteristics; muscle; breed; expression; health; time; l.
AB Probiotics and synbiotics supplementation have been shown to play potential roles in animal production. The present study aimed to evaluate the effects of dietary probiotics and synbiotics supplementation to sows during gestation and lactation and to offspring pigs (sow-offspring) on offspring pigs' growth performance and meat quality. Sixty-four healthy Bama mini-pigs were selected and randomly allocated into four groups after mating: the control, antibiotics, probiotics, and synbiotics groups. After weaning, two offspring pigs per litter were selected, and four offspring pigs from two litters were merged into one pen. The offspring pigs were fed a basal diet and the same feed additive according to their corresponding sows, representing the control group (Con group), sow-offspring antibiotics group (S-OA group), sow-offspring probiotics group (S-OP group), and sow-offspring synbiotics group (S-OS group). Eight pigs per group were euthanized and sampled at 65, 95, and 125 d old for further analyses. Our findings showed that probiotics supplementation in sow-offspring diets promoted growth and feed intake of offspring pigs during 95-125 d old. Moreover, sow-offspring diets supplemented with probiotics and synbiotics altered meat quality (meat color, pH(45min), pH(24h), drip loss, cooking yield, and shear force), plasma UN and AMM levels, and gene expressions associated with muscle-fiber types (MyHCI, MyHCIIa, MyHCIIx, and MyHCIIb) and muscle growth and development (Myf5, Myf6, MyoD, and MyoG). This study provides a theoretical basis for the maternal-offspring integration regulation of meat quality by dietary probiotics and synbiotics supplementation.
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
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TI Targeting Ferroptosis in Bone-Related Diseases: Facts and Perspectives
SO JOURNAL OF INFLAMMATION RESEARCH
LA English
DT Review
DE ferroptosis; cell death; iron accumulation; lipid peroxidation; bone-related diseases
ID rheumatoid-arthritis; oxidative stress; iron-metabolism; activation; pathway; cancer; ferritinophagy; osteoporosis; osteoclasts; expression
AB Ferroptosis is a new cell fate decision discovered in recent years. Unlike apoptosis, autophagy or pyroptosis, ferroptosis is characterized by iron-dependent lipid peroxidation and mitochondrial morphological changes. Ferroptosis is involved in a variety of physiological and pathological processes. Since its discovery, ferroptosis has been increasingly studied concerning bone-related diseases. In this review, we focus on the latest research progress and prospects, summarize the regulatory mechanisms of ferroptosis, and discuss the role of ferroptosis in the pathogenesis of bone-related diseases, such as osteoporosis (OP), osteoarthritis (OA), rheumatoid arthritis (RA), and osteosarcoma (OS), as well as its therapeutic potential.
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TI Exploring the role and mechanism of Fuzi decoction in the treatment of osteoporosis by integrating network pharmacology and experimental verification
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DT Article
DE Fuzi decoction; Osteoporosis; Network pharmacology; Osteoclast; NF-& kappa;B pathway
ID aconitum-carmichaeli; kappa-b; differentiation; osteoclastogenesis; inhibition; activation; kaempferol
AB Background Fuzi decoction (FZD), a traditional Chinese medicine formula, was used to treat musculoskeletal diseases by warming channels, strengthening yang and dispelling pathogenic cold and dampness. In clinical practice, FZD has been used to treat rheumatoid arthritis and osteoarthritis. It alleviated osteoarticular disorders through ameliorating the degradation of cartilage and improving meniscal damage in osteoarthritis, while its roles and mechanisms in the treatment

of bone loss diseases remain unclear. This study aims to investigate the underlying mechanisms of FZD in treating osteoporosis using an integrative method of network pharmacology and experimental study.Methods In this study, network pharmacology was used to predict the core targets and potential pathways of the bioactive ingredients of FZD to attenuate osteoporosis. Molecular docking was performed to evaluate the interactions between core compounds and key targets. In addition, both cell and animal experiments were carried out to validate the role and potential mechanism in treating osteoporosis.Results In the present study, data revealed that kaempferol, beta-sitosterol, stigmasterol, fumarine, and (+)-catechin may be the primary bioactive ingredients of FZD in the treatment of osteoporosis, which were closely associated with the osteoporosis-related targets. And the KEGG results indicated that the NF-?B pathway was closely associated with the function of FZD in treating osteoporosis. In addition, in vivo demonstrated that FZD ameliorated osteoporosis. In vitro experiments showed that the pro-apoptotic factors indicators including CASP3 and BAX were decreased by FZD and the anti-apoptotic factor BCL2 was increased by FZD. In addition, FZD significantly suppressed the osteoclast differentiation in culture and the expression levels of osteoclast-related genes including TRAF6, CTSK, and MMP9. And the NF-?B pathway was confirmed, via in vitro experiment, to be involved in osteoclast differentiation.Conclusions This study demonstrated that FZD played a pivotal role in suppressing the osteoclast differentiation via regulating the NF-?B pathway, indicating that FZD could be a promising antiosteoporosis drug and deserve further investigation.
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TI Polypharmacy, Potentially Inappropriate Medications, and Drug-to-Drug Interactions in Patients with Chronic Myeloproliferative Neoplasms

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DE myeloproliferative neoplasms; polypharmacy; drug interactions; survival; thrombosis; potentially inappropriate medications; drug-to-drug interactions
ID polycythemia-vera; essential thrombocythemia; survival; mutations; lesions; adults; risk; jak2
AB Polypharmacy, potentially inappropriate medications (PIMs), and drug-to-drug interactions (DDIs) are highly prevalent in the elderly and may have adverse effects on health-related outcomes. Their occurrence and clinical and prognostic associations in patients with chronic myeloproliferative neoplasms (MPN) are unknown. We retrospectively evaluated polypharmacy, PIMs, and DDIs in a cohort of 124 MPN patients (essential thrombocythemia, ET = 63, polycythemia vera, PV = 44, myelofibrosis = 9, MPN unclassifiable = 8) from a single community hematology practice. There were 761 drug prescriptions with a median of five prescribed medications per patient. Polypharmacy, at least one PIM (calculated for persons >60 years of age, n = 101), and at least one DDI were recorded in 76 (61.3%), 46 (45.5%), and 77 (62.1%) of patients, respectively. Seventy-four (59.6%) and twenty-one (16.9%) patients had at least one C or at least one D interaction, respectively. Among other associations, polypharmacy and DDIs were associated with older age, management of disease-related symptoms, osteoarthritis/osteoporosis, and different CV disorders. In multivariate analyses adjusted for clinically meaningful parameters, both polypharmacy and DDIs were significantly associated with inferior overall survival (OS) and time to thrombosis (TTT), whereas PIMs had no significant associations with neither OS nor TTT. There were no associations with bleeding or transformation risks. Polypharmacy, DDIs, and PIMs are very frequent among MPN patients and may have important clinical associations.
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WC Biochemistry & Molecular Biology; Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Biochemistry & Molecular Biology; Research & Experimental Medicine; Pharmacology & Pharmacy
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TI Corrosion Prevention of Biomedical Implants: Surface Coating Techniques Perspective
SO CHEMISTRYSELECT
LA English
DT Review
DE Biodegradable; Biomedical; Coating; Corrosion; Implants
ID sprayed hydroxyapatite coatings; mechanical-property; thin-films; electrophoretic deposition; abrasion-corrosion; chitosan coatings; resistance; electrodeposition; magnesium; behavior
AB No doubt, the use of biomedical implants in the world has been of tremendous benefit to humans (animals as well), still gaining much relevance today, and commands greater prospects in the future. Developments in this field have been from the progression of the use of materials like wood, iron and gold as external limb support and indental applications, to more sophisticated materials today like biodegradable metal alloys, polymers, ceramics and composites materials capable of replacing damaged or worn-out organs (eye, heart, lungs, liver, kidney, etc.), mimicking the bone, or for boosting other physiological features as in cosmetology.Appropriate applications of these implants in the human body still remain a challenge today due to several post-surgical issues like cytotoxicity, thrombogenicity, allergenicity, carcinogenicity and inflammations all of which could be attributed to factors like biocompatibility, osseointegration, mechanical properties and corrosion resistance of these biomedical implants during service. The aspect of implants' corrosion is of much concern in the biomedical industry of which there have been several methods used to tackle it viz -use of corrosion resistant materials and inhibitors, metal plating, environmental and design considerations and protective coating techniques. This paper reviews five different surface coating techniques for preventing corrosion in biomedical implants, their descriptions and working principles. The need for the use of biomedical implants may arise due to several scenarios like osteoporosis, osteoarthritis, heart problems, broken limbs, hips, spinal cords, and teeth problems. Corrosion of these implants in vivo can cause serious adverse effects on the individual's health. This paper reviews five different surface coating techniques for preventing corrosion in biomedical implants, their descriptions, and working principles.image
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TI Oxidative stress as a key modulator of cell fate decision in osteoarthritis and osteoporosis: a narrative review
SO CELLULAR & MOLECULAR BIOLOGY LETTERS
LA English
DT Review
DE Osteoarthritis; Osteoporosis; Senescence; Oxidative stress; ROS; Cell death; Cell fate decision; Mitochondrial dysfunction; Cartilage; Bone
ID mitochondrial superoxide-dismutase; antioxidant response element; foxo transcription factors; activated protein-kinase; lipid-peroxidation; senescent cells; dna-damage; posttraumatic osteoarthritis; chondrocyte hypertrophy; replicative senescence
AB During aging and after traumatic injuries, cartilage and bone cells are exposed to various pathophysiologic mediators, including reactive oxygen species (ROS),

damage-associated molecular patterns, and proinflammatory cytokines. This detrimental environment triggers cellular stress and subsequent dysfunction, which not only contributes to the development of associated diseases, that is, osteoporosis and osteoarthritis, but also impairs regenerative processes. To counter ROS-mediated stress and reduce the overall tissue damage, cells possess diverse defense mechanisms. However, cellular antioxidative capacities are limited and thus ROS accumulation can lead to aberrant cell fate decisions, which have adverse effects on cartilage and bone homeostasis. In this narrative review, we address oxidative stress as a major driver of pathophysiologic processes in cartilage and bone, including senescence, misdirected differentiation, cell death, mitochondrial dysfunction, and impaired mitophagy by illustrating the consequences on tissue homeostasis and regeneration. Moreover, we elaborate cellular defense mechanisms, with a particular focus on oxidative stress response and mitophagy, and briefly discuss respective therapeutic strategies to improve cell and tissue protection.
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FU The authors would like to thank Patrizia Horny for her excellent support in creating the illustrations and Robert Blakytny for the final proofreading of the manuscript.
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TI The need to distinguish intervention thresholds and diagnostic thresholds in the management of osteoporosis
SO OSTEOPOROSIS INTERNATIONAL
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DT Article
DE Definition; Diagnosis; Fracture risk; FRAX; Intervention thresholds; Osteoporosis
ID clinical-practice guidelines; bone-mineral density; hip fracture; postmenopausal women; practice framework; treatment gap; risk-factors; prevention; men; prediction

AB This position paper of the International Osteoporosis Foundation (IOF) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) addresses the rationale for separate diagnostic and intervention thresholds in osteoporosis. We conclude that the current BMD-based diagnostic criteria for osteoporosis be retained whilst clarity is brought to bear on the distinction between diagnostic and intervention thresholds.
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TI Musculoskeletal exercise: Its role in promoting health and longevity
SO PROGRESS IN CARDIOVASCULAR DISEASES
LA English
DT Review
DE Exercise; Resistance exercise; Strength training; Cardiovascular disease

ID muscle strength; resistance exercise; physical-activity; skeletal-muscle; cardiovascular-disease; cancer-mortality; walking pace; all-cause; risk; association
AB Resistance training (RT) is an often ignored but essential component of physical health. The functioning of the musculoskeletal system declines with age, resulting in sarcopenia, loss of muscle strength and power, decrease in muscle flexibility and balance. Other pertinent age-related changes include decline in basal metabolic rate, in-crease in fat mass, and decrease in bone mineral density. Such primary aging can be accentuated by the concom-itant presence of comorbid conditions, such as insulin resistance and diabetes, obesity, inflammatory conditions, and physical inactivity (PI). The latter is often promoted by the presence of musculoskeletal conditions, such as osteoarthritis, back pain, and osteoporosis, which are quite common in society. RT can diminish long-term joint stress, "resist" age-related physiological deterioration and improve health outcomes through its ability to increase muscle strength and mass, balance the distribution of forces within a joint, increase basal metabolic rate and bone density, reduce body fat and cardiac risk factors, enhance endothelial function, and promote cog-nitive function and psychological well-being. Accordingly, health providers should screen for PI, lack of RT, and mobility risks using short screening questions, and employ simple functional tests, when indicated, to evaluate patients for impairment in gait, muscle strength, flexibility, and balance. This review also provides general prin-ciples for initiating and conducting RT and provides general and specific examples of resistance training pro-grams, which should be individualized for patients through the evaluation and guidance by appropriate health providers, physical therapists, and certified trainers.& COPY; 2023 Published by Elsevier Inc.
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NR 95
TC 69
Z9 81
U1 4
U2 86
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J9 PROG CARDIOVASC DIS
JI Prog. Cardiovasc. Dis.
PD MAR-APR 15
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IS
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DI 10.1016/j.pcad.2023.02.006
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WC Cardiac & Cardiovascular Systems
SC Cardiovascular System & Cardiology
GA J8OV3
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PT J
AU Anastasilakis, AD
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Mantzoros, Christos S.
TI Association of activins, follistatins and inhibins with incident hip fracture in women with postmenopausal osteoporosis: a proof of concept, case-control study

SO ENDOCRINE
LA English
DT Article
DE Activin; Follistatin; Inhibin; Hip fracture; Myokine; Postmenopausal osteoporosis
ID bone; differentiation; bimagrumab; receptors; d-3
AB PurposeThe activins-follistatins-inhibins (AFI) hormonal system is considered to regulate muscle and bone mass. We aimed to evaluate AFI in postmenopausal women with an incident hip fracture.MethodsIn this post-hoc analysis of a hospital based case-control study, we evaluated circulating levels of the AFI system in postmenopausal women with a low-energy hip fracture admitted for fixation compared with postmenopausal women with osteoarthritis scheduled for arthroplasty.ResultsCirculating levels of follistatin ($p = 0.008$), FSTL3 ($p = 0.013$), activin B and AB (both $p < 0.001$), as well as activin AB/follistatin and activin AB/FSTL3 ratios ($p = 0.008$ and $p = 0.029$, respectively) were higher in patients than controls in unadjusted models. Differences for activins B and AB remained after adjustment for age and BMI ($p = 0.006$ and $p = 0.009$, respectively) and for FRAX-based risk for hip fracture ($p = 0.008$ and $p = 0.012$, respectively) but were lost when 25OHD was added to the regression models.ConclusionsOur data indicate no major changes in the AFI system in postmenopausal women at the time of hip fracture compared to postmenopausal women with osteoarthritis except for higher activin B and AB levels, whose significance, however, was lost when 25OHD was added to the adjustment models.
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NR 18
TC 3
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U1 0
U2 0
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 1355-008X
EI 1559-0100
J9 ENDOCRINE
JI Endocrine
PD SEP 15
PY 2023
VL 81
IS 3
BP 573
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EA MAY 2023
PG 6

WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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UT WOS:000993336800003
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AU Poullain, F
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Pithioux, Martine
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TI Vertebral trabecular bone texture analysis in opportunistic MRI and CT scan can distinguish patients with and without osteoporotic vertebral fracture: A preliminary study
SO EUROPEAN JOURNAL OF RADIOLOGY
LA English
DT Article
DE Spine; Osteoporosis; Opportunistic; CT; MRI; Texture
ID mineral density; elderly-men; microarchitecture; classification; osteoarthritis; association; diagnosis; standard; women; risk
AB Purpose: To investigate the potential of texture parameters from opportunistic MRI and CT for the detection of patients with vertebral fragility fracture, to design a decision tree and to compute a Random Forest analysis for the prediction of fracture risk. Methods: One hundred and eighty vertebrae of sixty patients with at least one (30) or without (30) a fragility fracture were retrospectively assessed. Patients had a DXA, an MRI and a CT scan from the three first lumbar vertebrae. Vertebrae texture analysis was performed in routine abdominal or lumbar CT and lumbar MRI using 1st and 2nd order texture parameters. Hounsfield Unit Bone

density (HU BD) was also measured on CT-scan images.Results: Twelve texture parameters, Z-score and HU BD were significantly different between the two groups whereas T score and BMD were not. The inter observer reproducibility was good to excellent. Decision tree showed that age and HU BD were the most relevant factors to predict the fracture risk with a 93 % sensitivity and 56 % specificity. AUC was 0.91 in MRI and 0.92 in CT-scan using the Random Forest analysis. The corresponding sensitivity and specificity were 72 % and 93 % in MRI and 83 and 89 % in CT. Conclusions: This study is the first to compare texture indices computed from opportunistic CT and MR images. Age and HU-BD together with selected texture parameters could be used to assess risk fracture. Machine learning algorithm can detect fracture risk in opportunistic CT and MR imaging and might be of high interest for the diagnosis of osteoporosis.
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NR 29
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U2 17
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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WC Radiology, Nuclear Medicine & Medical Imaging
SC Radiology, Nuclear Medicine & Medical Imaging
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PT J
AU Peng, S
Sun, C
Lai, CT
Zhang, L
AF Peng, Song
Sun, Chang
Lai, Chengteng
Zhang, Lei
TI Exosomes derived from mesenchymal stem cells rescue cartilage injury in osteoarthritis through Ferroptosis by GOT1/CCR2 expression
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Article
DE Mesenchymal stem cells; Exosomes; Osteoarthritis; GOT1; CCR2
AB Osteoarthritis is a prevalent joint disease that significantly affects the daily life of the elderly and is one of the primary causes of disability in this population. This study aims to evaluate the potential pro-inflammatory effects and molecular mechanism of Mesenchymal stem cells-derived exosomes (MSC-Exos) in Osteoarthritis. Bilateral ovariectomy was carried out to induce osteoporosis under anesthesia for the mice. MC3T3-E1 cells were induced for 14 days. HE staining, Safranin O staining and Biomechanical parameter analysis were used in this experiment. MSC-Exos improved osteoarthritis in a mouse model by reducing inflammation levels, preventing ferroptosis, and inducing expression of GOT1/CCR2 to regulate ferroptosis. MSC-Exos also promoted cell growth and osteogenic differentiation of bone cells in an in vitro model. Inhibition of GOT1 reduced the effects of MSC-Exos on cell growth and osteogenic differentiation in an osteoarthritis model. MSC-Exos induce Nrf2/HO-1 expression through the GOT1/CCR2 signaling pathway, resulting in the reduction of Ferroptosis. However,

inhibition of Nrf2 reduces the effectiveness of MSC-Exos in treating Osteoarthritis.The results of this study suggest that the GOT1/CCR2/Nrf2/HO-1 signaling pathway plays a crucial role in MSC-Exos-mediated reduction of Ferroptosis in macrophages during Osteoarthritis. These findings may provide a potential therapeutic approach for Osteoarthritis and other orthopedic conditions.
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Wang, Xin
TI The role of autophagy in bone metabolism and clinical significance
SO AUTOPHAGY
LA English
DT Review
DE Autophagy; bone metabolism; mesenchymal stem cell; osteoblast; osteoclast; osteogenesis
ID mesenchymal stem-cells; ameliorates disc degeneration; nucleus pulposus cells; osteogenic differentiation; suppresses apoptosis; modulating autophagy; gold nanoparticles; promotes autophagy; activation; senescence
AB The skeletal system is the basis of the vertebral body composition, which affords stabilization sites for muscle attachment, protects vital organs, stores mineral ions, supplies places to the hematopoietic system, and participates in complex endocrine and immune system. Not surprisingly, bones are constantly reabsorbed, formed, and remodeled under physiological conditions. Once bone metabolic homeostasis is interrupted (including inflammation, tumors, fractures, and bone metabolic diseases), the body rapidly initiates bone regeneration to maintain bone tissue structure and quality. Macroautophagy/autophagy is an essential metabolic process in eukaryotic cells, which maintains metabolic energy homeostasis and plays a vital role in bone regeneration by controlling molecular degradation and organelle renewal. One relatively new observation is that mesenchymal cells, osteoblasts, osteoclasts, osteocytes, chondrocytes, and vascularization process exhibit autophagy, and the molecular mechanisms and targets involved are being explored and updated. The role of autophagy is also emerging in degenerative diseases (intervertebral disc degeneration [IVDD], osteoarthritis [OA], etc.) and bone metabolic diseases (osteoporosis [OP], osteitis

deformans, osteosclerosis). The use of autophagy regulators to modulate autophagy has benefited bone regeneration, including MTOR (mechanistic target of rapamycin kinase) inhibitors, AMPK activators, and emerging phytochemicals. The application of biomaterials (especially nanomaterials) to trigger autophagy is also an attractive research direction, which can exert superior therapeutic properties from the material-loaded molecules/drugs or the material's properties such as shape, roughness, surface chemistry, etc. All of these have essential clinical significance with the discovery of autophagy associated signals, pathways, mechanisms, and treatments in bone diseases in the future.
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TI Bone/cartilage targeted hydrogel: Strategies and applications
SO BIOACTIVE MATERIALS
LA English
DT Review
DE Bone; Cartilage; Hydrogel; Target therapy; Bone disease
ID chondroitin sulfate; drug-delivery; extracellular vesicles; cartilage degeneration; osteochondral unit; bone; acid; osteoarthritis; nanoparticles; osteoporosis
AB The skeletal system is responsible for weight-bearing, organ protection, and movement. Bone diseases caused by trauma, infection, and aging can seriously affect a patient's quality of life. Bone targeted biomaterials are suitable for the treatment of bone diseases. Biomaterials with bone-targeted properties can

improve drug utilization and reduce side effects. A large number of bone-targeted micro-nano materials have been developed. However, only a few studies addressed bone-targeted hydrogel. The large size of hydrogel makes it difficult to achieve systematic targeting. However, local targeted hydrogel still has significant prospects. Molecules in bone/cartilage extra -cellular matrix and bone cells provide binding sites for bone-targeted hydrogel. Drug delivery systems featuring microgels with targeting properties is a key construction strategy for bone-targeted hydrogel. Besides, injectable hydrogel drug depot carrying bone-targeted drugs is another strategy. In this review, we summarize the bone -targeted hydrogel through application environment, construction strategies and disease applications. We hope this article will provide a reference for the development of bone-targeted hydrogels. We also hope this article could increase awareness of bone-targeted materials.
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TI Oviposition behaviour in Drosophila melanogaster: Genetic and behavioural decoupling between oviposition acceptance and preference for natural fruits
SO JOURNAL OF EVOLUTIONARY BIOLOGY
LA English
DT Article
DE natural genetic variation; natural resources; oviposition acceptance; oviposition candidate genes; oviposition preference
ID olfactory behavior; site preferences; host shifts; performance; evolution; selection; architecture; neurons; yeast; heritability
AB In phytophagous insects, oviposition behaviour is an important component of habitat selection and, given the multiplicity of genetic and environmental factors affecting its expression, is defined as a complex character resulting from the sum of interdependent traits. Here, we study two components of egg-laying behaviour: oviposition acceptance (OA) and oviposition preference (OP) in Drosophila melanogaster using three natural fruits as resources (grape, tomato and orange) by means of no-choice and two-choice experiments, respectively. This experimental design allowed us to show that the results obtained in two-choice assays (OP) cannot be accounted for by those resulting from no-choice assays (OA). Since the genomes of all lines used are completely sequenced, we perform a genome-wide association study to identify and characterize the genetic underpinnings of these oviposition behaviour traits. The analyses revealed different candidate genes affecting natural genetic variation of both OA and OP traits. Moreover, our results suggest behavioural and genetic decoupling between OA and OP and that egg-laying behaviour is plastic and context-dependent. Such independence in the genetic architectures of OA and OP variation may influence different aspects of oviposition behaviour, including plasticity, canalization, host shift and maintenance of genetic variability, which contributes to the adoption of adaptive strategies during habitat selection.
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NR 83
TC 6
Z9 6
U1 5
U2 49
PU OXFORD UNIV PRESS
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WC Ecology; Evolutionary Biology; Genetics & Heredity
SC Environmental Sciences & Ecology; Evolutionary Biology; Genetics & Heredity
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PT J
AU Schinzel, E
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TI The effect of aquatic exercise on bone mineral density in older adults. A systematic review and meta-analysis
SO FRONTIERS IN PHYSIOLOGY
LA English
DT Review
DE aquatic exercise; water-based exercise; bone mineral density; systematic review; meta-analysis
ID postmenopausal women; water exercise; program; health; intensity; osteoarthritis; osteoporosis; therapy; quality; fitness
AB Introduction: Aquatic or water-based exercise is a very popular type of exercise in particular for people with physical limitations, joint problems and fear of falling. The present systematic review and meta-analysis aimed to provide evidence for the effect of aquatic exercise on Bone Mineral Density (BMD) in adults.Methods: A systematic literature search of five electronic databases (PubMed/MEDLINE, Cochrane Library, Scopus, Web of Science and CINAHL) according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) was conducted until 2022/01/30, with an update to 2022/10/07. We included controlled trials with a duration of more than 6 months and at least two study groups, aquatic exercise (EG) versus non-training controls (CG) with no language restrictions. Outcome measures were standardized mean differences (SMD) with

95%-confidence intervals (95%-CI) for BMD changes at the lumbar spine (LS) and femoral neck (FN). We applied a random-effects meta-analysis and used the inverse heterogeneity (IVhet) model to analyze the data.Results: Excluding an outlier study with an exceptionally high effect size for LS-BMD, we observed a statistically significant (p = .002) effect (EG vs. CG) of aquatic exercise for the LS-BMD (n = 10; SMD: 0.30; 95%-CI: 0.11-0.49). In parallel, the effect of aquatic exercise on FN-BMD was statistically significant (p = .034) compared to the CG (n = 10; SMD: 0.76, 95%-CI: 0.06-1.46). Of importance, heterogeneity between the trial results was negligible for LS (I-2: 7%) but substantial for FN-BMD (I-2: 87%). Evidence for risks of small study/publication bias was low for LS-BMD and considerable for FN-BMD.Discussion: In summary, the present systematic review and meta-analysis provides further evidence for the favorable effect of exercise on bone health in adults. Due to its safety and attractiveness, we particularly recommend water-based exercise for people unable, afraid or unmotivated to conduct intense land-based exercise programs.
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NR 52
TC 10
Z9 15
U1 2
U2 20
PU FRONTIERS MEDIA SA
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WC Physiology
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TI A review on the role of long non-coding RNA prostate androgen-regulated transcript 1 (PART1) in the etiology of different disorders
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE lncRNA; PART1; cancer; biomarker; diagnsotic marker
ID cell-proliferation; lncrna; apoptosis; carcinoma; cancer; progression; expression; injury; gene
AB LncRNA prostate androgen-regulated transcript 1 (PART1) is an important lncRNA in the carcinogenesis whose role has been firstly unraveled in prostate cancer. Expression of this lncRNA is activated by androgen in prostate cancer cells. In addition, this lncRNA has a role in the pathogenesis intervertebral disc degeneration, myocardial ischemia-reperfusion injury, osteoarthritis, osteoporosis and Parkinson's disease. Diagnostic role of PART1 has been assessed in some types of cancers. Moreover, dysregulation of PART1 expression is regarded as a prognostic factor in a variety of cancers. The current review provides a concise but comprehensive summary of the role of PART1 in different cancers and non-malignant disorders.
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WC Cell Biology; Developmental Biology
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TI Cellular senescence in skeletal disease: mechanisms and treatment
SO CELLULAR & MOLECULAR BIOLOGY LETTERS
LA English
DT Review

DE Cellular senescence; Chronic inflammation; Age-related orthopaedic diseases; Signalling pathways; Bone marrow
ID mesenchymal stem-cells; intervertebral disc degeneration; osteogenic differentiation; aging mouse; bone mass; life-span; age; osteoarthritis; hedgehog; proliferation
AB The musculoskeletal system supports the movement of the entire body and provides blood production while acting as an endocrine organ. With aging, the balance of bone homeostasis is disrupted, leading to bone loss and degenerative diseases, such as osteoporosis, osteoarthritis, and intervertebral disc degeneration. Skeletal diseases have a profound impact on the motor and cognitive abilities of the elderly, thus creating a major challenge for both global health and the economy. Cellular senescence is caused by various genotoxic stressors and results in permanent cell cycle arrest, which is considered to be the underlying mechanism of aging. During aging, senescent cells (SnCs) tend to aggregate in the bone and trigger chronic inflammation by releasing senescence-associated secretory phenotypic factors. Multiple signalling pathways are involved in regulating cellular senescence in bone and bone marrow microenvironments. Targeted SnCs alleviate age-related degenerative diseases. However, the association between senescence and age-related diseases remains unclear. This review summarises the fundamental role of senescence in age-related skeletal diseases, highlights the signalling pathways that mediate senescence, and discusses potential therapeutic strategies for targeting SnCs.
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TI Occurrence of chlorpyrifos and organochlorine pesticides in a native bumblebee (Bombus pauloensis) living under different land uses in the southeastern Pampas, Argentina
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DE Bumblebees; Pollution; Chlorpyrifos
ID apis-mellifera; hymenoptera apidae; honey-bees; exposure; residues; pollinators; endosulfan; soils; term; insecticides
AB Pollinators such as Apidae bees are vital for ecosystems and food security. Unfortunately, their populations have declined due to several factors including pesticide use. Among them, the organophosphate insecticide chlorpyrifos, poses a global threat, while legacy compounds like organochlorine pesticides (OCPs) easily bio-accumulate, increasing the concern. Bombus pauloensis, a widely distributed native bee in Argentina, is used for commercial pollination; however, information regarding their health status is scarce. This study assessed chlorpyrifos and OCP levels in B. pauloensis (workers and males) and related environmental matrices living from three different land uses schemes, by means of GC-ECD and GC-MS. The ornamental horticulture field (OP) showed the highest total pesticide concentrations in workers (13.1 ng/g), flowers and soils, whereas the organic agriculture field (OA) exhibited the lowest. Chlorpyrifos was the most abundant compound, accounting for at least 20 % of pesticide load across all matrices. The food production horticulture field (FH) had the highest chlorpyrifos concentration in workers, males and soils (5.0, 4.4 and 3.3 ng/g, respectively), suggesting a local greater usage, whereas OA showed the lowest. Regarding OCPs groups, Drins and DDTs were predominant in most matrices, with FH males registering the highest levels (4.0 and 2.5 ng/g, respectively), closely followed by OP. However, metabolites' contribution indicated historical use and atmospheric inputs in all sites. Multivariate analyses confirmed the significance of site and bumblebee sex to explain pesticide composition. Males from all sites exhibited higher chlorpyrifos levels than workers and this trend was similar for some OCP groups. Overall, OA differed from FH and OP, indicating a correlation between production modes and pesticide profiles. This study demonstrates the value of B. pauloensis as a pesticide biomonitor but also offers insights into its populations' health in the area. In this sense, this information could be useful towards the preservation of this crucial pollinator.
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TI Age- and sex-specific normative values of bone mineral density in the adult glenoid
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE age; bone mineral density; glenoid; normative values; shoulder
ID anterior shoulder instability; computed-tomography; femoral-neck; erosion; spine; osteoarthritis; arthroplasty; osteoporosis; thickness; quality
AB The objective of this study was to determine the normative bone mineral density (BMD) of cortical and trabecular bone regions in the adult glenoid and its dependence on the subject's age and sex. We analyzed computed tomography (CT) scans of 441 shoulders (310 males, 18-69 years) without any signs of glenohumeral joint pathology. Glenoid BMD was automatically quantified in six volumes of interest (VOIs): cortical bone (CO), subchondral cortical plate (SC), subchondral trabecular bone (ST), and three adjacent layers of trabecular bone (T1, T2, and T3). BMD was measured in Hounsfield unit (HU). We evaluated the association between glenoid BMD and sex and age with the Student's t test and Pearson's correlation coefficient (r), respectively. The lambda-mu-sigma method was used to determine age- and sex-specific normative values of glenoid BMD in cortical (CO and SC) and trabecular (ST, T1, T2, and T3) bone. Glenoid BMD was higher in males than females, in most age groups and most VOIs. Before 40 years old, the effect of age on BMD was very weak in both males and females. After 40 years old, BMD

declined over time in all VOIs. This BMD decline with age was greater in females (cortical: r = -0.45, trabecular: r = -0.41) than in males (cortical: r = -0.30; trabecular: r = -0.32). These normative glenoid BMD values could prove clinically relevant in the diagnosis and management of patients with various shoulder disorders, in particular glenohumeral osteoarthritis and shoulder arthroplasty or shoulder instability, as well as in related research.
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TI Roles of Stem Cell Exosomes and their MicroRNA Carrier in Bone and Cartilage Regeneration
SO CURRENT STEM CELL RESEARCH & THERAPY
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DT Review
DE Stem cells; bone regeneration; exosomes; osteoblasts; osteoclasts; cartilage
ID proliferation; osteogenesis; immunogenicity; tumorigenicity; osteoblasts; release; repair
AB Bone and cartilage regeneration is a dynamic and complex process involving multiple cell types, such as osteoblasts, osteoclasts, endothelial cells, etc. Stem cells have been proved to have an efficient capability to promote bone and cartilage regeneration and repair, but the usage of cells harbors some important safety issues, such as immune rejection and carcinogenicity. Exosomes are non-cell structures secreted from various cells. The content of exosomes is enriched with proteins, such as cytoskeleton proteins, adhesion factors, transcription factors, etc., and a variety of nucleic acids, such as mRNA (Messenger RNA), long-chain non-coding RNA, microRNA (miRNA), etc. Exosomes can deliver a variety of contents from the parent cells to the recipient cells in different tissue backgrounds, influencing the phenotype and function of the recipient cells. Recent studies have demonstrated that miRNAs play significant roles in bone formation, suggesting that miRNAs may be novel therapeutic targets for bone and cartilage diseases. Exosomes have been shown with low/no immune rejection in vivo, no carcinogenic risk of infection, nor other side effects. In recent years, stem cell exosomes have been utilized to promote bone and cartilage regeneration processes during bone defect, bone fracture, cartilage repair, osteoporosis, and osteoarthritis. In this review, we discuss different exosomes derived from stem cells and their interactions with target cells, including osteoblasts, chondrocytes and osteoclasts. We also highlight the various signaling pathways involved in stem cell exosome-related bone and cartilage regeneration.
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PT J
AU Ackert-Bicknell, C
Karasik, D
AF Ackert-Bicknell, Cheryl
Karasik, David
TI Proceedings of the Post-Genome Analysis for Musculoskeletal Biology Workshop
SO CURRENT OSTEOPOROSIS REPORTS
LA English
DT Review
DE Osteoporosis; Osteoarthritis; Sarcopenia; Functional follow-up to GWAS; Animal models
ID bone-density; genetics; osteoarthritis; evolution
AB Purpose of the ReviewHerein, we report on the proceedings of the workshop entitled "Post-Genome analysis for musculoskeletal biology" that was held in July of 2022 in Safed, Galilee, Israel. Supported by the Israel Science Foundation, the goal of this workshop was to bring together established investigators and their trainees who were interested in understanding the etiology of musculoskeletal disease, from Israel and from around the world.Recent FindingsPresentations at this workshop spanned the spectrum from basic science to clinical studies. A major emphasis of the discussion centered on genetic studies in humans, and the limitations and advantages of such studies. The power of coupling studies using human data with functional follow-up studies in pre-clinical models such as mice, rats, and zebrafish was discussed in depth. The advantages and limitations of mice and zebrafish for faithfully modelling aspects of human disease were debated, specifically in the context of age-related diseases such as osteoporosis, osteoarthritis, adult-onset auto-immune disease, and osteosarcopenia.There remain significant gaps in our understanding of the nature and etiology of human musculoskeletal disease. While therapies and medications exist, much work is still needed to find safe and effective interventions for all patients suffering from diseases associated with age-related deterioration of musculoskeletal tissues. The potential of forward and reverse genetic studies has not been exhausted for diseases of muscles, joints, and bones.
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AU Wada, H
Aso, K
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Ikeuchi, M
AF Wada, Hiroyuki
Aso, Koji
Izumi, Masashi
Ikeuchi, Masahiko
TI The effect of postmenopausal osteoporosis on subchondral bone pathology in a rat model of knee osteoarthritis
SO SCIENTIFIC REPORTS
LA English
DT Article
ID mineral density; articular-cartilage; estrogen; association; pain; ovariectomy; turnover; cohort; health; women
AB This study aimed to investigate the additional effect of ovariectomy-induced osteoporosis (OP) on the pathology of knee osteoarthritis (OA) in a rat meniscectomized model, particularly focusing on subchondral bone changes and pain behaviour. Rats were divided into four groups, sham, OP, OA, OP plus OA, and assessed for histology, osteoclast activity, subchondral bone microstructure, and pain-related behaviour. Rats with OP plus OA had significantly increased calcified cartilage and subchondral bone damage scores, increased densities of subchondral osteoclasts in the weight-bearing area, and more porous subchondral trabecular bone compared with rats with OA. Loss of tidemark integrity was observed most frequently in rats with OP plus OA. The density of subchondral osteoclasts correlated with the calcified cartilage and subchondral bone damage score in rats with OA (OA and OP plus OA). No significant differences in the receptor activator of nuclear factor-kappa B ligand (RANKL)/osteoprotegerin (OPG) expression ratio in subchondral bone and pain-related behavioural tests were observed between rats with OA and rats with OP plus OA. In rats with OA, coexisting OP potentially aggravated OA pathology mainly in calcified cartilage and subchondral trabecular bone by increasing subchondral osteoclast activity.
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U1 2
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PU NATURE PORTFOLIO
PI BERLIN
PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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WC Multidisciplinary Sciences
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TI Astaxanthin as a Potent Antioxidant for Promoting Bone Health: An Up-to-Date Review
SO ANTIOXIDANTS
LA English
DT Review
DE astaxanthin; antioxidant; bone; osteoporosis; osteoarthritis; osteosarcoma
ID steroid-induced osteonecrosis; oxidative stress; femoral-head; rat model; osteoblastic differentiation; postmenopausal women; osteosarcoma; cells; bisphosphonates; osteoporosis
AB In recent years, bone loss and its associated diseases have become a significant public health concern due to increased disability, morbidity, and mortality. Oxidative stress and bone loss are correlated, where oxidative stress suppresses osteoblast activity, resulting in compromised homeostasis between bone formation and resorption. This event causes upregulation of bone remodeling turnover rate with an increased risk of fractures and bone loss. Therefore, supplementation of antioxidants can be proposed to reduce oxidative stress, facilitate the bone remodeling process, suppress the initiation of bone diseases, and improve bone health. Astaxanthin (3,3 & PRIME;-dihydroxy-4-4 & PRIME;-diketo-& beta;-& beta; carotene), a potent antioxidant belonging to the xanthophylls family, is a potential ROS scavenger and could be a promising therapeutic nutraceutical possessing various pharmacological properties. In bone, astaxanthin enhances osteoblast differentiation, osteocytes numbers, and/or differentiation, inhibits osteoclast differentiation, cartilage degradation markers, and increases bone mineral density, expression of osteogenic markers, while reducing bone loss. In this review, we presented the up-to-date findings of the potential anabolic effects of astaxanthin on bone health in vitro, animal, and human studies by providing comprehensive evidence for its future clinical application, especially in treating bone diseases.
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TI Longbie capsules reduce bone loss in the subchondral bone of rats with comorbid osteoporosis and osteoarthritis by regulating metabolite alterations
SO FRONTIERS IN MEDICINE
LA English
DT Article
DE geriatric medicine; bone aging; osteoarthritis; osteoporosis; Longbie capsule; plant-based natural products; metabonomics; bone metabolism
ID postmenopausal osteoporosis; 5-hydroxytryptamine; density; alpha
AB Background and objective With the development of global population aging, comorbidity (>= 2 diseases) is a common health problem among elderly people. Osteoarthritis (OA) and osteoporosis (OP) are common in elderly individuals. There is a lack of drug therapy for OA and OP comorbidities. The purpose of this study was to explore the efficacy and mechanism of Longbie capsule (LBJN), which contains various plant herbs, in treating OA and OP comorbidities (OA + OP) in rats using metabolomics techniques.Methods We created an OA + OP rat model through bilateral oophorectomy combined with meniscus instability surgery. Thirty SD rats were randomly divided into five groups (six in each group), namely, the sham group, OA group, OA + OP group, LBJN low-dose group (0.625 g/kg, OA + OP+LB-L group) and LBJN high-dose group (1.25 g/kg, OA + OP+LB-H group). After 8 weeks of intervention, we used micro-CT to detect bone microstructure status, ELISA to measure bone metabolism indicators, and UPLC-MS technology for

metabolomics analysis. Finally, the screened differentially expressed metabolites were subjected to Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway and functional enrichment analysis.Results The micro-CT results showed that LBJN significantly improved the bone mineral density (BMD) and bone quality of subchondral bone in OA + OP rats, and LBJN regulated the expression of bone alkaline phosphatase (BALP), osteoprotegerin (OPG), and tartrate-resistant acid phosphatase (TRACP) in serum to maintain bone metabolism balance. Metabolomics analysis showed that the metabolic trajectory of OA + OP rats after intervention in the OA + OP+LB-H group showed significant changes, and 107 potential biomarkers could be identified. Among them, 50 metabolites were upregulated (such as zeranol) and 57 were downregulated (such as vanillactic acid). The KEGG functional enrichment results indicated that the differentially expressed metabolites are mainly involved in amino acid metabolism, lipid metabolism, and carbohydrate metabolism. The KEGG pathway enrichment results indicated that LBJN may exert therapeutic effects on OA + OP rats by regulating the cAMP signaling pathway, and the FoxO signaling pathway.Conclusion LBJN can maintain bone metabolism balance by regulating serum lipid metabolism, amino acid metabolism, carbohydrate metabolism, and estrogen, thereby reducing bone loss in subchondral bone, which may be a potential mechanism through which LBJN treats OA + OP.

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TI Lower bone mineral density can be a risk for an enlarging bone marrow lesion: A longitudinal cohort study of Japanese women without radiographic knee osteoarthritis
SO MODERN RHEUMATOLOGY
LA English
DT Article
DE Knee osteoarthritis; bone marrow lesion; bone mineral density
ID bisphosphonates; osteoporosis; incident; associations; criteria; fracture; radius; volume; pain
AB Objectives The aim is to elucidate the relationship between bone mineral density (BMD) at baseline and the change of bone marrow lesion (BML) during a

2-year follow-up (2YFU) period. Methods Seventy-eight female participants (mean age: 54.9 +/- 9.6 years) without radiographic knee osteoarthritis were eligible. Based on right-knee magnetic resonance imaging, maximum BML area (BMLa) was calculated by tracing the BML border. The change in BMLa was defined using the following formula: [2YFU] - [Baseline] = Delta BMLa. Positive Delta BMLa was defined as enlarged; negative Delta BMLa was defined as regressed. Dual-energy X-ray absorptiometry was performed to measure the BMD of distal radius. Young adult mean [YAM (%)] of the BMD was used for statistical analysis. Linear regression analysis was conducted with Delta BMLa as the dependent variable and YAM as the independent variable. Receiver operating characteristic curve and logistic regression analyses were conducted for YAM to predict the prevalence of BML enlargement or regression. Results Twenty-six (33.3%) patients had enlarged BMLa, 12 (15.4%) participants showed regressing BMLa, and 40 (51.3%) patients remained stable. YAM was negatively associated with Delta BMLa (beta: - 0.375, P = 0.046). The best predictor of BML enlargement risk was 85% (odds ratio: 8.383, P = 0.025). Conclusions Lower BMD could predict BML enlargement during a 2YFU period.
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TI Osteogenic Differentiation Potential of Mesenchymal Stem Cells Using Single Cell Multiomic Analysis
SO GENES
LA English
DT Article
DE mesenchymal stem cells; single-cell multiome; osteogenic differentiation
ID chromatin; accessibility; rna
AB Mesenchymal stem cells (MSC) are multipotent stem cells that can differentiate into multiple cell types, including osteoblasts, chondrocytes, and adipocytes. Osteoblast differentiation is reduced during osteoporosis development, resulting in reduced bone formation. Further, MSC isolated from different donors possess distinct osteogenic capacity. In this study, we used single-cell multiomic analysis to

profile the transcriptome and epigenome of MSC from four healthy donors. Data were obtained from similar to 1300 to 1600 cells for each donor. These cells were clustered into four groups, indicating that MSC from different donors have distinct chromatin accessible regulatory elements for regulating gene expression. To investigate the mechanism by which MSC undergo osteogenic differentiation, we used the chromatin accessibility data from the single-cell multiome data to identify individual-specific enhancer-promoter pairs and evaluated the expression levels and activities of the transcriptional regulators. The MSC from four donors showed distinct differentiation potential into osteoblasts. MSC of donor 1 showed the largest average motif activities, indicating that MSC from donor 1 was most likely to differentiate into osteoblasts. The results of our validation experiments were consistent with the bioinformatics prediction. We also tested the enrichment of genome-wide association study (GWAS) signals of several musculoskeletal disease traits in the patient-specific chromatin accessible regions identified in the single-cell multiome data, including osteoporosis, osteopenia, and osteoarthritis. We found that osteoarthritis-associated variants were only enriched in the regions identified from donor 4. In contrast, osteoporosis and osteopenia variants were enriched in regions from donor 1 and least enriched in donor 4. Since osteoporosis and osteopenia are related to the density of bone cells, the enrichment of variants from these traits should be correlated with the osteogenic potential of MSC. In summary, this study provides large-scale data to link regulatory elements with their target genes to study the regulatory relationships during the differentiation of mesenchymal stem cells and provide a deeper insight into the gene regulatory mechanism.

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NR 36
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TI Interplay between fat, muscle, bone mass, and oteophytes and risk for tophaceous gout
SO JOURNAL OF INVESTIGATIVE MEDICINE
LA English
DT Article
DE Body Composition; Osteoarthritis; Osteoporosis
ID serum uric-acid; x-ray absorptiometry; morphogenetic protein; postmenopausal women; mineral density; association; accumulation; tophus
AB Tophaceous gout is a common arthritis caused by the deposition of urate crystals and is related to limited joint function. Although there are reports that uric acid (UA) is associated with bone mineral density (BMD), little is known about the relationship between UA, osteophytes, and muscle. This cross-sectional case-control study was performed in patients with tophaceous gout. The control group included patients without gout. All subjects underwent BMD and body composition analyses. Age, sex, alcohol consumption, smoking, and radiography of both knees were recorded. Adjusted ORs for tophaceous gout were calculated using the logistical regression models. A total of 150 male patients were enrolled, including 65 individuals with tophaceous gout and 85 without gout. The mean age of the patients with tophaceous gout was 59.94 +/- 12.40 years, while that of

individuals without gout was 61.29 +/- 11.57 years (p=0.492). Patients with tophaceous gout have a higher mean body mass index, fat mass, appendicular lean mass, BMD, and osteophytes. Multiple logistic regression analysis revealed that fat mass (OR 2.01, 95% CI 1.27 to 3.18), appendicular lean mass (OR 4.27, 95% CI 1.86 to 9.83), and osteophytes (OR 5.88, 95% CI 1.72 to 20.13) were significantly associated with tophaceous gout. In the current study, higher fat mass, high muscle mass, and osteophyte formation were found to increase the risk of tophaceous gout, as the association is the most than can be inferred from a cross-sectional study. Therefore, reducing body fat and weight management may prevent tophaceous gout.
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TI Gender Differences in Potentially Inappropriate Medication Use among Older Adults
SO PHARMACEUTICALS
LA English
DT Article
DE elderly; ageing; Beers criteria; inappropriate prescribing
ID sex-differences; cardiovascular-diseases; elderly-patients; polypharmacy; risk; outcm; prescriptions; events; impact; costs
AB Background: Use of potentially inappropriate medication (PIMs) is a prominent concern that leads to significant medication-related issues among older adults. Notably, older women tend to utilize more medicines than men; older women frequently take more drugs. In addition, some evidence suggests that prescription PIMs vary by gender. This study examines the gender-based variation in prescribing PIM among older adults in Saudi Arabia. Methods: A cross-sectional retrospective analysis of electronic medical records from a large hospital in Saudi Arabia was carried out. Patients over the age of 65 who received ambulatory treatment were included in the study. The utilization of PIM was assessed based on Beers criteria. Descriptive statistics and logistic regression were employed to describe patterns of PIM utilization and identify factors associated with their use. All statistical analyses were performed using Version 9.4 of the Statistical Analysis Software (SAS((R)) 9.4). Results: The study comprised 4062 older people (age 65) who visited ambulatory care clinics; the average age was (72.6 +/- 6.2) years. The majority of the study sample was women (56.8%). Among older adults, 44.7% of older men and 58.3% of older women reported having PIMs that should be avoided, indicating a higher prevalence of PIMs among women compared to men. In terms of the PIM categories used, women had a much higher utilization rate of cardiovascular and gastrointestinal drugs than men. In men, the use of PIMs was frequently associated with hypertension, ischemic heart disease, asthma,

osteoarthritis, and cancer, while in women PIM use was associated with age, dyslipidemia, chronic kidney disease, and osteoporosis. Conclusions: This study revealed sex differences in PIM prescribing among older adults; PIM use is more common among women. Sex differences exist in clinical and socioeconomic characteristics and factors related to using potentially inappropriate medications. This study revealed essential areas that could be targeted by further interventions to improve drug-prescribing practices among older adults at risk of PIM.
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TC 21
Z9 21
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PU MDPI
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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TI Can Organic Pork Help Achieve Sustainable Development Goals in Thailand?
SO AGRICULTURE-BASEL
LA English
DT Article
DE organic pork; food security; willingness to pay; Sustainable Development Goals; sustainable livestock systems; sustainable production and consumption; Life Cycle Assessment; Thailand
ID willingness-to-pay; environmental impacts; animal-welfare; food; systems; safety; products
AB This paper examines how organic pork (OP) production, marketing and

consumption in Thailand contributes to global Sustainable Development Goals (SDGs) that affect food agri-food system sustainability. The paper discusses technical debates and academic literature sources about OP, socioeconomic and environmental impacts of organic agriculture (OA), food security and SDGs. It reflects on theoretical, practical, policy and empirical issues utilizing Thai case study data on willingness to pay (WTP) for OP to illustrate SDG linkages. The study raises broader questions, complications and contradictions about universal access to safe, healthy and affordable organic food. It suggests that WTP as a niche strategy supporting OP producers has responded to consumer demand and has potential for increased farmer incomes. But WTP for OP is an inadequate, problematic priority if it does not better address ecological, social and economic sustainability concerns, cross-cutting SDGs and national policies including inequities among richer and poorer consumers and farmers. It shows how OP may modestly contribute to SDG2 achievement or help realize other interlinked SDGs in Thailand but can also hinder some SDGs. We conclude that the OA movement and governments must better address difficult challenges affecting livestock systems sustainability, meat production, consumption, value chains and socioeconomic equity.
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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J9 AGRICULTURE-BASEL
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PT J
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TI Reducing diagnostic delay in hypophosphatasia: a case series of 14 patients presenting to general rheumatology
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Alkaline phosphatase; Hypophosphatasia; Musculoskeletal pain
AB ObjectivesHypophosphatasia (HPP) is a rare genetic metabolic bone disease that can cause chronic pain and fractures. Its hallmark is a persistently low serum ALP. HPP is now recognised by many osteoporosis specialists, but other specialists, such as rheumatologists and primary care physicians, may be less aware of this condition, causing diagnostic delay and possible harm to these patients. Our objective was to highlight features that can reduce this delay.MethodsWe retrospectively analysed 14 patients that presented with musculoskeletal pain to general rheumatology clinic at St. George's Hospital and were subsequently diagnosed with HPP.ResultsMedian diagnostic delay was 13 years. All patients had an ALP below reference range for age and gender, with lowest mean ALP of 16 IU/L. All but one patient were women with median age of 51 years. Most common presentation was peripheral joint pain in 85.7% of patients. This was due to early-onset CPPD (calcium pyrophosphate deposition disease) in 71.4% of patients, osteoarthritis in 50%, or bursitis in 50%. Axial pain was reported in 64% of patients due to osteoarthritis or spinal stenosis. Fifty percent of patients had a history of long bone pain. Fifty percent had previous fracture(s). A total of 28.6% of patients had psoriatic arthritis, of which 1 patient had spondyloarthropathy, and 4 patients also had enthesitis.ConclusionPatients with HPP can present to rheumatology with musculoskeletal pain, and if a persistently low ALP is confirmed, this may reduce the diagnostic delay of this rare disease. Similar to other rheumatologic patients, musculoskeletal pain in HPP was noted in peripheral joints and in the spine with almost a third of patients having psoriatic arthritis. Pain was also noted in the long bones, a feature consistent with metabolic bone disease. The diagnosis of HPP was also more likely in those patients with a personal or family history of dental disease or arthritis.
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SC Endocrinology & Metabolism
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AU Ryan, JM
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TI Prevalence and incidence of chronic conditions among adults with cerebral palsy: A systematic review and meta-analysis
SO DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY
LA English

DT Review
ID privately insured adults; chronic kidney-disease; young-adults; physical-activity; risk-factors; health; care; multimorbidity; osteoporosis; polypharmacy
AB AimTo assess the prevalence and incidence of chronic conditions among adults with cerebral palsy (CP) and compare them to the prevalence and incidence among adults without CP. MethodWe searched MEDLINE and Embase for studies reporting the prevalence or incidence of one or more chronic conditions among adults with CP. Two independent reviewers screened titles, abstracts, and full-text articles. Two independent reviewers extracted data relating to prevalence and incidence and appraised study quality. We performed random-effects meta-analyses to pool prevalence and incidence. ResultsWe identified 69 studies; 65 reported the prevalence of 53 conditions and 13 reported the incidence of 21 conditions. At least 20% of adults had the following conditions: depression (21%); anxiety (21%); mood affective disorders (23%); asthma (24%); hypertension (26%); epilepsy (28%); urinary incontinence (32%); malnutrition (38%); and scoliosis (46%). Adults with CP were more likely to have type 2 diabetes, anxiety, bipolar disorder, depression, schizophrenia, hypertension, ischaemic heart disease, stroke, cerebrovascular disease, asthma, liver disease, osteoarthritis, osteoporosis, underweight, and chronic kidney disease than adults without CP. InterpretationThese data from 18 countries, which provide an international perspective, may be used to promote awareness, identify targets for intervention, and inform the development of appropriate supports for adults with CP.
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0012-1622
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JI Dev. Med. Child Neurol.
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AU Xi, YJ
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TI Regulatory Effects of Quercetin on Bone Homeostasis: Research Updates and Future Perspectives
SO AMERICAN JOURNAL OF CHINESE MEDICINE
LA English
DT Article
DE Bone Homeostasis; Quercetin; Therapeutic Mechanisms; Bioavailability; Review

ID nf-kappa-b; pi3k/akt signaling pathway; cell-cycle arrest; oxidative stress; osteoblastic differentiation; hydrogen-peroxide; induced apoptosis; delivery-system; activation; mapk
AB The imbalance of bone homeostasis has become a major public medical problem amid the background of an aging population, which is closely related to the occurrence of osteoporosis, osteoarthritis, and fractures. Presently, most drugs used in the clinical treatment of bone homeostasis imbalance are bisphosphonates, calcitonin, estrogen receptor modulators, and biological agents that inhibit bone resorption or parathyroid hormone analogs that promote bone formation. However, there are many adverse reactions. Therefore, it is necessary to explore potential drugs. Quercetin, as a flavonol compound with various biological activities, is widely distributed in plants. Studies have found that quercetin can regulate bone homeostasis through multiple pathways and targets. An in-depth exploration of the pharmacological mechanism of quercetin is of great significance for the development of new drugs. This review discusses the therapeutic mechanisms of quercetin on bone homeostasis, such as regulating the expression of long non-coding RNA, signaling pathways of bone metabolism, various types of programmed cell death, bone nutrients supply pathways, anti-oxidative stress, anti-inflammation, and activation of Sirtuins. We also summarize recent progress in improving quercetin bioavailability and propose some issues worth paying attention to, which may help guide future research efforts.
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TI Estradiol as the Trigger of Sirtuin-1-Dependent Cell Signaling with a Potential Utility in Anti-Aging Therapies
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE estradiol; sirtuin 1; aging
ID acanthopanax-senticosus harms; sirt1; estrogen; muscle; osteoarthritis; 17-beta-estradiol; testosterone; apoptosis; inflammation; chondrocytes
AB Aging entails the inevitable loss of the structural and functional integrity of cells and tissues during the lifetime. It is a highly hormone-dependent process; although, the exact mechanism of hormone involvement, including sex hormones, is unclear. The marked suppression of estradiol synthesis during menopause suggests that the hormone may be crucial in maintaining cell lifespan and viability in women. Recent studies also indicate that the same may be true for men. Similar anti-aging features are attributed to sirtuin 1 (SIRT1), which may possibly be linked at the molecular level with estradiol. This finding may be valuable for understanding the aging process, its regulation, and possible prevention against unhealthy aging. The following article summarizes the initial studies published in this field with a focus on age-associated diseases, like cancer, cardiovascular disease and atherogenic metabolic shift, osteoarthritis, osteoporosis, and muscle damage, as well as neurodegenerative and neuropsychiatric diseases.
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TC 12
Z9 14
U1 0
U2 8
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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PT J
AU Zhang, W
Han, JK
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TI Enzymatic preparation of chondroitin sulfate oligosaccharides and its alleviating effect on ovariectomy-induced osteoporosis in rats
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Chondroitin sulfate oligosaccharides; Chondroitinase; Postmenopausal osteoporosis
ID glucosamine sulfate; adipose-tissue; bone turnover; estrogen; prevention; glycosaminoglycans; nutraceuticals; pathogenesis; metabolism; diagnosis
AB Postmenopausal osteoporosis is the most common type of osteoporosis. Chondroitin sulfate (CS) has been suc-cessfully employed as food supplement against osteoarthritis, while the therapeutic potential on postmenopausal osteoporosis is little explored. In this study, CS oligosaccharides (CSOs) were enzymatically prepared through the lysis of CS by a chondroitinase from Microbacterium sp. Strain. The alleviating effects of CS, CSOs and Caltrate D (a clinically used supplement) on ovariectomy (OVX) -induced rat's osteoporosis were comparatively investi-gated. Our data showed that the prepared CSOs was basically unsaturated CS disaccharide mixture of Delta Di4S (53.1%), Delta Di6S (27.7%) and Delta Di0S (17.7%). 12 weeks' intragastric administration of Caltrate D (250 mg/kg/d), CS or CSOs (500 mg/kg/d, 250 mg/kg/d, 125 mg/kg/d) could obviously regulate the disorder of serum indices, recover the mechanical strength and mineral content of bone, improve the cortical bones' density and the number and length of trabecular bones in OVX rats. Both CS and CSOs in 500 mg/kg/d and 250 mg/kg/d could restore more efficiently the serum indices, bone fracture deflection and femur Ca than Caltrate D. As compared with CS at the same dosage, CSOs exhibited a more significant alleviating effect. These findings suggested that there was great potential of CSOs as daily interventions for delaying the progression of postmenopausal osteoporosis.
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NR 77
TC 6
Z9 7
U1 5
U2 46
PU ELSEVIER FRANCE-EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER
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J9 BIOMED PHARMACOTHER
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WC Medicine, Research & Experimental; Pharmacology & Pharmacy
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PT J
AU Garcia, SA
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AF Garcia, Steven A.
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TI Walking speed differentially affects lower extremity biomechanics in individuals with anterior cruciate ligament reconstruction compared to uninjured controls
SO CLINICAL BIOMECHANICS
LA English
DT Article
DE Ground reaction force; Asymmetry; Gait biomechanics
ID cartilage morphology; gait mechanics; knee; kinetics; osteoarthritis; kinematics; return; progression; asymmetry; deficits
AB Background: Walking biomechanics are commonly affected after anterior cruciate ligament reconstruction and differ compared to uninjured controls. Manipulating task difficulty has been shown to affect the magnitude of walking impairments in those early after knee surgery but it is unclear if patients in later phases post-op are similarly affected by differing task demands. Here, we evaluated the effects of manipulating walking speed on between-limb differences in ground reaction force and knee biomechanics in those with and without anterior cruciate ligament reconstruction.Methods: We recruited 28 individuals with anterior cruciate ligament reconstruction and 20 uninjured control participants to undergo walking assessments at three speeds (self-selected, 120%, and 80% self-selected speed). Main outcomes included sagittal plane knee moments, angles, excursions, and ground reaction forces (vertical and anterior-posterior).Findings: We observed walking speed differentially impacted force and knee-outcomes in those with

anterior cruciate ligament reconstruction. Between-limb differences increased at fast and decreased at slow speeds in those with anterior cruciate ligament reconstruction while uninjured participants maintained between-limb differences regardless of speed (partial eta(2) = 0.13-0.33, $p < 0.05$). Anterior cruciate ligament reconstruction patients underloaded the surgical limb relative to both the contralateral, and uninjured controls in GRFs and sagittal plane knee moments (partial eta(2) range = 0.13-0.25, $p < 0.05$).Interpretation: Overall, our findings highlight the persistence of walking impairments in those with anterior cruciate ligament reconstruction despite completing formal rehabilitation. Further research should consider determining if those displaying larger changes in gait asymmetries in response to fast walking also exhibit poorer strength and/or joint health outcomes.
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NR 52
TC 6
Z9 6
U1 0
U2 10
PU ELSEVIER SCI LTD
PI London
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TI Cannabidiol for musculoskeletal regenerative medicine
SO EXPERIMENTAL BIOLOGY AND MEDICINE

LA English
DT Review
DE Cannabidiol; orthopedics; regenerative medicine; inflammation; exosome
ID cannabinoid receptor; tendon disease; cb2 receptor; pain; pathophysiology; tendinopathy; inflammation; osteoarthritis; epidemiology; osteoporosis
AB Chronic musculoskeletal (MSK) pain is one of the most prevalent causes, which lead patients to a physician's office. The most common disorders affecting MSK structures are osteoarthritis, rheumatoid arthritis, back pain, and myofascial pain syndrome, which are all responsible for major pain and physical disability. Although there are many known management strategies currently in practice, phytotherapeutic compounds have recently begun to rise in the medical community, especially cannabidiol (CBD). This natural, non-intoxicating molecule derived from the cannabis plant has shown interesting results in many preclinical studies and some clinical settings. CBD plays vital roles in human health that go well beyond the classic immunomodulatory, anti-inflammatory, and antinociceptive properties. Recent studies demonstrated that CBD also improves cell proliferation and migration, especially in mesenchymal stem cells (MSCs). The foremost objective of this review article is to discuss the therapeutic potential of CBD in the context of MSK regenerative medicine. Numerous studies listed in the literature indicate that CBD possesses a significant capacity to modulate mammalian tissue to attenuate and reverse the notorious hallmarks of chronic musculoskeletal disorders (MSDs). The most of the research included in this review report common findings like immunomodulation and stimulation of cell activity associated with tissue regeneration, especially in human MSCs. CBD is considered safe and well tolerated as no serious adverse effects were reported. CBD promotes many positive effects which can manage detrimental alterations brought on by chronic MSDs. Since the application of CBD for MSK health is still undergoing expansion, additional randomized clinical trials are warranted to further clarify its efficacy and to understand its cellular mechanisms.
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NR 118
TC 8
Z9 10
U1 0
U2 14
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SC Research & Experimental Medicine
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PT J
AU Rivkin, G
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AF Rivkin, Gurion
Kandel, Leonid
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Nasrawy, Tarek
Liebergall, Meir
TI Total knee arthroplasty using a computerized assisted stereotaxic navigation system with bluetooth communication in obese patients-A randomized controlled study
SO COMPUTER ASSISTED SURGERY
LA English
DT Article
DE Total knee arthroplasty; obese; coronal alignment; navigation; prospective randomized trial
ID body-mass index; tibial alignment; osteoarthritis; metaanalysis
AB Correct mechanical alignment (180 degrees hip-knee-angle (HKA)) may be difficult to obtain on a consistent basis in obese patients. This is a randomized controlled study comparing the post-operative coronal alignment in obese patients between two surgical total knee arthroplasty (TKA) techniques - conventional and computer assisted navigation. The primary outcome was the post-operative HKA. A total of 60 patients were assigned to undergo conventional total knee arthroplasty (30 patients) or computerized assisted stereotaxic navigation system with Bluetooth communication surgery (30 patients). One patient from the study group was excluded due to malfunction of the navigation system. Good quality x-rays were available in 57 patients. There was no difference between the groups. Post-operative HKA was 2.8 degrees and 2.9 degrees in the study and control groups, respectively (p = 0.87). In obese patients undergoing TKA, computerized navigation had no impact on post-op HKA.
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NR 25
TC 3
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U2 12
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J9 COMPUT ASSIST SURG
JI COMPUT. ASSIST. SURG.
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WC Surgery
SC Surgery
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UT WOS:000913383000001
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PT J
AU Xu, K
Li, J
Wen, RM
Chang, B
Cheng, Y
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AF Xu, Ke
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Wen, Ruiming
Chang, Bo
Cheng, Yang
Yi, Xuejie
TI Role of SIRT3 in bone homeostasis and its application in preventing and treating bone diseases

SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE SIRT3; bone homeostasis; osteoblasts; osteoclasts; motility
ID osteoblast differentiation; osteogenic differentiation; oxidative stress; cells; osteoarthritis; marrow; transcription; activation; inhibition; apoptosis
AB Bone homeostasis refers to the balance between osteoblast-mediated bone formation and osteoclast-mediated bone resorption and the maintenance of stable bone mass. SIRT3 is a class of mitochondrial protein deacetylase that influences various mitochondrial functions and is involved in the mechanisms underlying resistance to aging; regulation of bone marrow mesenchymal stem cells, osteoblasts, and osteoclasts; and development of osteoporosis, osteoarthritis, and other bone diseases. Moreover, exercise affects bones through SIRT3. Thus, studies on SIRT3 may provide insights for the treatment of bone diseases. Although SIRT3 can exert multiple effects on bone, the specific mechanism by which it regulates bone homeostasis remains unclear. By evaluating the relevant literature, this review discusses the structure and function of SIRT3, reveals the role and associated mechanisms of SIRT3 in regulating bone homeostasis and mediating bone health during exercise, and highlights the potential pharmacological value of SIRT3 in treating bone diseases.
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TI Weight Loss and Vitamin D Improve Hyporesponsiveness to Corticosteroids in Obese Asthma
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DE Asthma; Bariatric surgery; Corticosteroid. Obesity; Obesity; Vitamin D
ID bariatric surgery; lung-function; systemic inflammation
AB Background: Obesity negatively impacts on the response of asthma patients to inhaled corticosteroids. The mechanisms underlying this impact are unknown. Objective: To demonstrate that the poor response to inhaled corticosteroids in obese asthma patients is associated with impaired antiinflammatory activity of corticosteroids and vitamin D deficiency, both of which are improved by weight loss. Methods: The study population comprised 23 obese asthma patients (OA) (18 females; median (IQR) age 56 [51-59] years), 14 nonobese asthma patients (NOA) (11 females; 53 [43-60] years), 15 obese patients (OP) (13 females; 47 [45-60] years), and 19 healthy controls (HC) (14 females; 43 [34-56] years). Ten OA and 11

OP were evaluated at baseline (V1) and 6 months after bariatric surgery (V2). Corticosteroid response was measured using dexamethasone-induced inhibition of peripheral blood mononuclear cell (PBMC) proliferation. Lung function and serum levels of leptin, adiponectin, and vitamin D were measured at V1 and V2. Results: We found a reduced response to dexamethasone in PBMCs of OP and OA with respect to NOA and HC; this inversely correlated with the adiponectin/leptin ratio and vitamin D levels. Bariatric surgery improved corticosteroid responses in OP and OA and normalized the adiponectin/leptin ratio and vitamin D levels. Exposure of PBMCs to vitamin D potentiated the antiproliferative effects of corticosteroids. Dexamethasone and vitamin D induced similar MKP1 expression in OP and OA. Conclusions: The efficacy of weight loss to improve symptoms and lung function in OA may be due, at least in part, to the recovered antiinflammatory effects of corticosteroids. Vitamin D deficiency may contribute to corticosteroid hyporesponsiveness in OA.
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Yang, Xingfen
TI An aqueous extract of Prunella vulgaris L. ameliorates cadmium-induced bone loss by promoting osteogenic differentiation in female rats
SO FOOD AND CHEMICAL TOXICOLOGY
LA English
DT Article
DE Prunella vulgaris L; Cadmium; Bone loss; Osteogenic differentiation; BMP/Smad signal pathway
ID herbal antiarthritic agent; mineral density; stem-cells; exposure; osteoporosis; metabolism; osteoarthritis; population; fractures; model
AB Cadmium (Cd) causes bone loss, concerning inhibiting osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs). Prunella vulgaris L. (PV) has the potential for promoting osteogenic differentiation, but its influence on Cd-induced bone loss is unclear. This study investigated the effect of PV aqueous extract (PVE) on Cd-induced bone loss and its underlying mechanisms. Eight-week-old female SD rats were randomly assigned into four groups and treated for 16 weeks: Control, Cd (50 mg/L of Cd chloride), Cd + PV Low (125 mg/kg bw of PVE), and Cd + PV High (250 mg/kg bw of PVE). PV ameliorated femoral bone loss in Cd-treated rats manifested as increases in bone mineral density, bone volume, trabecular thickness, number, and area, and decreases in trabecular separation. Compared with Cd group, PV-treatment groups had higher serum levels of bone formation markers (ALP, BGP). Additionally, in PV-treatment groups, expressions of bone formation markers (Osterix, Runx2) and molecules involved in osteogenic differentiation signal pathway BMP/Smad (BMP4, Smad1/5/9) in the tibia of rats and isolated rat primary BMSCs were upregulated. These results suggest that PV alleviates Cd-induced bone loss by promoting

osteogenic differentiation, which is likely associated with BMP/Smad pathway.
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PT J
AU Lee, JH
Yun, IL
Nam, CM
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AF Lee, Jung Hyun
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Nam, Chung-Mo
Jang, Suk-Yong

Park, Eun-Cheol
TI Association between physical activity and health-related quality of life in middle-aged and elderly individuals with musculoskeletal disorders: Findings from a national cross-sectional study in Korea
SO PLOS ONE
LA English
DT Article
ID older-adults; exercise; osteoarthritis; reliability; speed
AB PurposeThis study aimed to identify the association between physical activity and health-related quality of life (HRQoL) in middle-aged and elderly individuals with musculoskeletal disorders.MethodsThis study used data from the 2016-2020 Korea National Health and Nutrition Examination Survey (KNHANES). We included only those over 40 years of age diagnosed with one or more of the following: osteoarthritis, rheumatism, and osteoporosis. In total, 4,731 participants (783 men and 3,948 women) were included as the study population. Multiple logistic regression analysis was performed to examine the association between physical activity and HRQoL.ResultsIn the case of middle-aged and elderly individuals with musculoskeletal disorders, the likelihood of HRQoL worsening was significantly lower for those who regularly engaged in physical activity compared with that of those who did not engage in physical activity at all (men: OR 0.58, 95% CI 0.37-0.90; women: OR 0.64, 95% CI 0.53-0.79). Stratified analysis by the type and intensity of physical activity revealed that the possibility of poor HRQoL was lowest when leisure-related moderate-intensity physical activities were performed (men: OR 0.44, 95% CI 0.22-0.89; Women: OR 0.50, 95% CI 0.36-0.69).ConclusionsOur findings suggest that engaging in regular physical activity contributes to preventing exacerbation of HRQoL, even if the individual suffers from musculoskeletal disorders. It is necessary to provide an appropriate type and intensity of physical activity in consideration of the patients' pain and severity.
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PT J
AU Littman, J
Gil, H
Aaron, R
AF Littman, Jake
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Aaron, Roy
TI Spontaneous Bone Marrow Edema: Perfusion Abnormalities and Treatment with Surgical Decompression
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE MRI; pathophysiology; venous stasis; bone pain; surgical decompression; intraosseous hypertension
ID intraosseous pressure; transient osteoporosis; core decompression; avascular necrosis; venous congestion; blood-flow; osteoarthritis; hip; oxygen; pain
AB Bone marrow edema (BME), also termed bone marrow lesions, is a syndrome characterized by bone pain and the appearance of high signal intensity on T2

fat-suppressed and short tau inversion recovery (STIR) MRI sequences. BME can be related to trauma or a variety of non-traumatic diseases, and current treatment modalities include non-steroidal anti-inflammatory drugs (NSAIDS), bisphosphonates, denosumab, extracorporeal shockwave therapy (ESWT), the vasoactive prostacyclin analogue iloprost, and surgical decompression. Spontaneous BME is a subset that has been observed with no apparent causative conditions. It is most likely caused by venous outflow obstruction and intraosseous hypertension. These are mechanistically related to impaired perfusion and ischemia in several models of BME and are related to bone remodeling. The association of perfusion abnormalities and bone pain provides the pathophysiological rationale for surgical decompression. We present a case of spontaneous BME and a second case of spontaneous migratory BME treated with surgical decompression and demonstrate resolution of pain and the high signal intensity on MRI. This report provides an integration of the clinical syndrome, MR imaging characteristics, circulatory pathophysiology, and treatment. It draws upon several studies to suggest that both the bone pain and the MRI characteristics are related to venous stasis, and when circulatory pathologies are relieved by decompression or fenestration, both the bone pain and the MRI signal abnormalities resolve.
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PT J
AU Dong, ZC
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TI Modulation of SIRT6 activity acts as an emerging therapeutic implication for pathological disorders in the skeletal system
SO GENES & DISEASES
LA English
DT Review
DE Intervertebral disc degeneration (IDD); Osteoarthritis (OA); Osteoporosis (OP); Rheumatoid arthritis (RA); SIRT6 (SIR2-Like protein 6); SIRT6 activator
ID nf-kappa-b; mesenchymal stem-cell; gene-related peptide; osteogenic differentiation; deacetylase sirt6; oxidative stress; posttraumatic osteoarthritis; osteoblast differentiation; osteoclast differentiation; rheumatoid-arthritis
AB The skeletal system is a dynamically balanced system, which undergoes continuous bone resorption and formation to maintain bone matrix homeostasis. As an important ADP-ribosylase and NAD thorn -dependent deacylase, SIRT6 (SIR2-like protein 6) is widely expressed on various kinds of bone cells, such as

chondrocytes, osteoblasts, osteoclasts. The aberration of SIRT6 impairs gene expression (e.g., NF-KB and Wnt target genes) and cellular functions (e.g., DNA repair, glucose and lipid metabolism, telomeric maintenance), which disturbs the dynamic balance and ultimately leads to several bone-related diseases. In this review, we sum-marize the critical roles of SIRT6 in the onset and progression of bone-related diseases including osteoporosis, osteoarthritis, rheumatoid arthritis, and intervertebral disc degenera-tion, as well as the relevant signaling pathways. In addition, we discuss the advances in the development of SIRT6 activators and elucidate their pharmacological profiles, which may pro-vide novel treatment strategies for these skeletal diseases. & COPY; 2022 The Authors. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co., Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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TI Regulatory mechanisms of autophagy-related ncRNAs in bone metabolic diseases
SO FRONTIERS IN PHARMACOLOGY
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DT Review
DE autophagy; ncRNAs; bone metabolism; osteoporosis; osteoarthritis; rheumatoid arthritis
ID long noncoding rna; mesenchymal stem-cells; osteogenic differentiation; cartilage degradation; targeted deletion; oxidative stress; apoptosis; promotes; chondrocytes; activation
AB Bone metabolic diseases have been tormented and are plaguing people worldwide due to the lack of effective and thorough medical interventions and the poor understanding of their pathogenesis. Non-coding RNAs (ncRNAs) are heterogeneous transcripts that cannot encode the proteins but can affect the expressions of other genes. Autophagy is a fundamental mechanism for keeping cell viability, recycling cellular contents through the lysosomal pathway, and maintaining the homeostasis of the intracellular environment. There is growing evidence that ncRNAs, autophagy, and crosstalk between ncRNAs and autophagy play complex roles in progression of metabolic bone disease. This review investigated the complex mechanisms by which ncRNAs, mainly micro RNAs (miRNAs), long noncoding RNAs (lncRNAs), and circular RNAs (circRNAs), regulate autophagic pathway to assist in treating bone metabolism disorders. It aimed at identifying the autophagy role in bone metabolism disorders and understanding the role, potential, and challenges of crosstalk between ncRNAs and autophagy for bone metabolism disorders treatment.
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TI Mendelian randomization to evaluate the causal relationship between liver enzymes and the risk of six specific bone and joint-related diseases
SO FRONTIERS IN IMMUNOLOGY
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DT Article
DE Mendelian randomization; liver enzyme; bone and joint-related diseases; causality; genome-wide association studies
ID primary sclerosing cholangitis; mesenchymal stem-cells; alkaline-phosphatase; osteogenic differentiation; hepatic osteodystrophy; rheumatoid-arthritis; wide association; dna methylation; acid; determinant
AB Background: Studies of liver dysfunction in relation to bone and joint-related diseases are scarce, and its causality remains unclear. Our objective was to investigate whether serum liver enzymes are causally associated with bone and joint-related diseases using Mendelian randomization (MR) designs. Methods: Genetic data on serum liver enzymes (alkaline phosphatase (ALP); alanine transaminase (ALT); gamma-glutamyl transferase (GGT)) and six common bone and joint-related diseases (rheumatoid arthritis (RA), osteoporosis, osteoarthritis (OA), ankylosing spondylitis, psoriatic arthritis, and gout) were derived from independent genome-wide association studies of European ancestry. The inverse variance-weighted (IVW) method was applied for the main causal estimate. Complementary sensitivity analyses and reverse causal analyses were utilized to confirm the robustness of the results. Results: Using the IVW method, the positive causality between ALP and the risk of osteoporosis diagnosed by bone mineral density (BMD) at different sites was indicated (femoral neck, lumbar spine, and total body BMD, odds ratio (OR) [95% CI], 0.40 [0.23-0.69], 0.35 [0.19-0.67], and

0.33 [0.22-0.51], respectively). ALP was also linked to a higher risk of RA (OR [95% CI], 6.26 [1.69-23.51]). Evidence of potential harmful effects of higher levels of ALT on the risk of hip and knee OA was acquired (OR [95% CI], 2.48 [1.39-4.41] and 3.07 [1.49-6.30], respectively). No causal relationship was observed between GGT and these bone and joint-related diseases. The study also found that BMD were all negatively linked to ALP levels (OR [95% CI] for TBMD, FN-BMD, and LS-BMD: 0.993 [0.991-0.995], 0.993 [0.988-0.998], and 0.993 [0.989, 0.998], respectively) in the reverse causal analysis. The results were replicated via sensitivity analysis in the validation process. Conclusions: Our study revealed a significant association between liver function and bone and joint-related diseases.
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DE Shoulder arthroplasty; Cementless glenoid; Metal back; Keeled glenoid; Pegged glenoid; Midterm results; Primary osteoarthritis
ID arthroplasty; replacement; survival; prosthesis; young
AB Introduction Cemented all-polyethylene glenoid components are considered the gold standard in anatomic shoulder arthroplasty. New designs of cementless metal backed glenoid components showed promising early and midterm results. The aim of this matched-pair analysis was to compare the radiologic results of two cemented glenoid components and a cementless glenoid component in patients

with primary osteoarthritis (OA). Methods Sixty shoulders were clinically and radiologically evaluated after a mean follow-up of 59 months. Mean patient age was 70.4 years at surgery. Based on the design of the glenoid component (keel, peg, MB), 3 groups with, respectively, 20 shoulders were formed according to the matching criteria time of follow-up, patient age and gender. RLL and osteolysis in anteroposterior and axillary X-ray images were quantified and combined in a radiologic score (R-Score). Higher scores expressed worse radiologic outcomes. Further radiological parameters such as lateral glenohumeral offset (LGHO) and subluxation index were measured according to Walch. The functional results were documented using the age and gender normalized Constant-Murley score. Results Postoperative R-Score was highest in pegged components (peg: 5.7, keel: 2.4, MB: 1.6; $p < 0.001$) when combining both radiographs and after separate analysis of anteroposterior radiographs. MB glenoids had the lowest R-score in axillary radiographs (peg: 2.2, keel: 1.4, MB: 0.6; MB vs. keel: $p = 0.004$, MB vs peg: $p < 0.001$). RLL were more common ($p = 0.004$) and severe ($p = 0.005$) in pegged glenoids (RLL incidence: 77.8%, RLL-score: 2.5) than in MB glenoids (RLL incidence: 30%, RLL-score 0.7) and tended ($p = 0.084$) to have a higher RLL-score than keeled glenoids (RLL incidence: 63.2%, RLL-score:1.4). Both the osteolysis score (keel vs. peg: $p < 0.001$, MB vs. peg $p < 0.001$) and the incidence of osteolysis (keel vs. peg: $p = 0.008$, MB vs peg: $p = 0.003$) were significant higher in pegged glenoids (peg: osteolysis score: 3.2, osteolysis incidence: 100%; keel: osteolysis score: 1.0, osteolysis incidence: 63.2%, MB: osteolysis score: 0.9, osteolysis incidence: 60%), while the osteolysis score in axillary images was lowest for MB glenoids (peg: 1.2, keel: 0.9, MB: 0.4; peg vs. MB: $p = 0.009$, keel vs. MB: $p = 0.047$). Osteolysis in the central axillary zone was least common in MB glenoids (peg: 50%, keel: 47.4%, MB: 15%; peg vs. MB $p = 0.035$, keel vs. MB $p = 0.041$). LGHO was highest in MB glenoids (peg: 54.1, keel: 54.5, MB: 57.8; $p < 0.001$) but did not increase radiographic loosening ($r = 0.007$; $p = 0.958$). Preoperative posterior humeral head subluxation seemed to affect incidence of RLL negatively (pre-op posterior decentered 64.3%, pre-op centered 31.9%; $p = 0.201$) but did not reach statistical significance. Conclusion Pegged glenoid components had a concerning rate of RLL and osteolysis. MB glenoid components had a better outcome in axillary radiographs concerning RLL and osteolysis. Increased LGHO did not increase radiographic loosening.

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TI Association of a femoral neck T score with knee joint osteophyte formation but not with skeletal muscle mass
SO CLINICAL RHEUMATOLOGY
LA English
DT Article
DE Femoral neck; Knee; Musclemass; Osteophyte; T score
ID bone-mineral density; postmenopausal women; hand osteoarthritis; metabolic syndrome; elderly-men; osteoporosis; prevalence; cartilage; hip; relevance
AB Background Osteophyte formation is an important radiographic sign of osteoarthritis (OA) and limited joint motion in knee osteoarthritis patients. Some studies revealed relationships of osteophyte formation with a high bone mineral density and a high muscle mass, while others showed no correlations. The aim of this study was to identify relationships of osteophyte formation with bone mineral density and muscle mass. Methods A cross sectional study of knee osteoarthritis was conducted. Cases were classified as patients with osteophyte formation, while controls were those without osteophytes. All subjects underwent a knee x-ray and bone mineral density and body composition evaluation. General patient characteristics, covariates, and the results of biochemical analyses were also recorded. Statistical analysis was conducted using SPSS Version 22.0. Logistic regression and the chi-square test were utilized to analyze the relationships between the presence of knee osteophytes and the study variables. Results A total of 228 patients were enrolled, including 78 with osteophytes in the knee joint and 150 without. A total of 162/228 are females; knee OA is commonly explained among females. (p = 0.001). The mean age was 73.23 +/- 11.10 years in the osteophyte group and 71.86 +/- 12.23 in the no osteophyte group (p = 0.409). The mean body mass index was 24.15 +/- 3.27 kg/m(2) in the osteophyte group and 23.37 +/- 3.48 kg/m(2) in the no osteophyte group (p = 0.433). More patients in the osteophyte group had hypertension (p = 0.002), so the age group 73 years expected to have OA and hypertension along other metabolic diseases, and the femoral neck T score was higher in the osteophyte group (p = 0 .044) . Logistic regression analysis showed that the male gender was associated with less osteophyte formation (p = 0.001, odds ratio (OR) 0.11 (0.03-0.37)), and hypertension was associated with increased muscle loss (p = 0.005). Femoral neck T

score was associated with the presence of osteophyte formation (p = 0.011, OR 1.98 (1.17-3.36)). Conclusions The results demonstrated an association of knee osteophyte formation with the femoral neck T score and hypertension, but no association with muscle mass. We speculated that in patients with osteophytosis and increased bone mass, metabolic factors such as hypertension should be considered. Further study of the molecular mechanisms regulating these processes is needed in the future.
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TI Association of the visceral adiposity index with femur bone mineral density and osteoporosis among the US older adults from NHANES 2005-2020: a cross-sectional study
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Article
DE visceral adiposity index; femur bone mineral density; osteoporosis; U-shaped; cross-sectional study; National Health and Nutrition Examination Survey
ID type-2 diabetes-mellitus; obesity; fat; women; body; mass; osteoarthritis; men; bmi
AB BackgroundThe visceral adiposity index (VAI) is a marker of abdominal fat distribution and adipose tissue function. However, the association between VAI and femur bone mineral density (BMD) and osteoporosis is unclear among the U.S. older adults.MethodsCross-sectional data for adults aged 60 years and older from the 2007-2020 National Health and Nutrition Examination Survey (NHANES) were included. Multivariable linear and logistic regression were used to evaluate the association between VAI and femur BMD and osteoporosis. We used the smooth curve fitting to address nonlinearity. Moreover, a two-piecewise linear regression model was used to explain the nonlinearity further.ResultsThe findings of the multivariable logistic regression models showed that as the VAI value increased by one unit, the prevalence of osteoporosis decreased by 1.2% after adjusting for covariates associated with osteoporosis. The multivariable linear regression models

demonstrated that VAI was positively correlated with femur BMD. Further analysis revealed an inverted L-shaped and inverted U-shaped relationship between VAI and femur BMD at different sites.ConclusionsOur findings indicated that an increased VAI is independently linked to a higher prevalence of osteoporosis among the U.S. older adults. Further analysis reveals that once VAI reaches a certain threshold, femur BMD no longer increases and may even decrease. This suggests that a moderate accumulation of visceral fat may be beneficial for bone health, while excessive visceral fat could potentially have detrimental effects.
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TI Current comprehensive understanding of denosumab (the RANKL neutralizing antibody) in the treatment of bone metastasis of malignant tumors, including pharmacological mechanism and clinical trials
SO FRONTIERS IN ONCOLOGY
LA English
DT Review
DE denosumab; RANK; RANKL; OPG system; bone metastasis; skeletal-related events; osteoclast
ID resistant prostate-cancer; squamous-cell carcinoma; phase-iii trial; zoledronic acid; breast-cancer; skeletal metastases; adjuvant denosumab; multiple-myeloma; double-blind; open-label
AB Denosumab, a fully humanized monoclonal neutralizing antibody, inhibits activation of the RANK/RANKL/OPG signaling pathway through competitive binding with RANKL, thereby inhibiting osteoclast-mediated bone resorption. Denosumab inhibits bone loss; therefore, it is used to treat metabolic bone diseases (including postmenopausal osteoporosis, male osteoporosis, and glucocorticoid-induced osteoporosis), in clinical practice. Since then, multiple effects of denosumab have been discovered. A growing body of evidence suggests that denosumab has a variety of pharmacological activities and broad potential in clinical diseases such as osteoarthritis, bone tumors, and other autoimmune diseases. Currently, Denosumab is emerging as a treatment for patients with malignancy bone metastases, and it also shows direct or indirect anti-tumor effects in preclinical models and clinical applications. However, as an innovative drug, its clinical use for bone metastasis of malignant tumors is still insufficient, and its mechanism of action needs to be further investigated. This review systematically summarizes the pharmacological mechanism of action of denosumab and the current understanding and clinical practice of the use of denosumab for bone metastasis of malignant tumors to help clinicians and researchers deepen their understanding of denosumab.
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TI Extracellular vesicles derived from host and gut microbiota as promising nanocarriers for targeted therapy in osteoporosis and osteoarthritis
SO FRONTIERS IN PHARMACOLOGY
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DT Review
DE osteoporosis; gut microbiota; microbiota extracellular vesicles; microbiota-host communications; osteoarthritis; exosome
ID outer-membrane vesicles; bone loss; vessel formation; exosm; osteogenesis; cells; angiogenesis; immune; differentiation; microvesicles
AB Osteoporosis (OP), a systemic bone disease that causes structural bone loss and bone mass loss, is often associated with fragility fractures. Extracellular vesicles (EVs) generated by mammalian and gut bacteria have recently been identified as

important mediators in the intercellular signaling pathway that may play a crucial role in microbiota-host communication. EVs are tiny membrane-bound vesicles, which range in size from 20 to 400 nm. They carry a variety of biologically active substances across intra- and intercellular space. These EVs have developed as a promising research area for the treatment of OP because of their nanosized architecture, enhanced biocompatibility, reduced toxicity, drug loading capacity, ease of customization, and industrialization. This review describes the latest development of EVs derived from mammals and bacteria, including their internalization, isolation, biogenesis, classifications, topologies, and compositions. Additionally, breakthroughs in chemical sciences and the distinctive biological features of bacterial extracellular vesicles (BEVs) allow for the customization of modified BEVs for the therapy of OP. In conclusion, we give a thorough and in-depth summary of the main difficulties and potential future of EVs in the treatment of OP, as well as highlight innovative uses and choices for the treatment of osteoarthritis (OA).
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AU Chen, X
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AF Chen, Xun
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TI Accumulation of advanced glycation end products promotes atrophic nonunion incidence in mice through a CtBP1/2-dependent mechanism
SO EXPERIMENTAL CELL RESEARCH
LA English
DT Article
DE Atrophic nonunion; C-terminal binding protein; Histone deacetylase 1; Runt-related transcription factor 2; Advanced glycation end products
ID fracture; pathogenesis; ages

AB Atrophic nonunion (AN) is a complex and poorly understood pathological condition resulting from impaired fracture healing. Advanced glycation end products (AGEs) have been implicated in the pathogenesis of several bone disorders, including osteoporosis and osteoarthritis. However, the role of AGEs in the development of AN remains unclear. This study found that mice fed a high-AGE diet had a higher incidence of atrophic nonunion (AN) compared to mice fed a normal diet following tibial fractures. AGEs induced two C-terminal binding proteins (CtBPs), CtBP1 and CtBP2, which were necessary for the development of AN in response to AGE accumulation. Feeding a high-AGE diet after fracture surgery in CtBP1/2-/- and RAGE-/- (receptor of AGE) mice did not result in a significant occurrence of AN. Molecular investigation revealed that CtBP1 and CtBP2 formed a heterodimer that was recruited by histone deacetylase 1 (HDAC1) and runt-related transcription factor 2 (Runx2) to assemble a complex. The CtBP1/2-HDAC1-Runx2 complex was responsible for the downregulation of two classes of bone development and differentiation genes, including bone morphogenic proteins (BMPs) and matrix metalloproteinases (MMPs). These findings demonstrate that AGE accumulation promotes the incidence of AN in a CtBP1/2-dependent manner, possibly by modulating genes related to bone development and fracture healing. These results provide new insights into the pathogenesis of AN and suggest new therapeutic targets for its prevention and treatment.
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AU Daher, M
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Boufadel, P
Khanna, A
Zalaquett, Z
Abboud, JA
AF Daher, Mohammad
Fares, Mohamad Y.
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TI Osteoporosis in the Setting of Shoulder Arthroplasty: A Narrative Review
SO GERIATRIC ORTHOPAEDIC SURGERY & REHABILITATION
LA English
DT Review
DE osteoporosis; osteoarthritis; shoulder arthroplasty; management; bone mineral density
ID fractures
AB Patients who undergo shoulder surgery are frequently affected by osteoporosis and osteopenia, and the prevalence of this association is expected to increase due to the growing number of elderly individuals undergoing these procedures. It may be advisable to conduct a preoperative DXA scan for orthopedic surgical candidates at high risk, to detect those who could benefit from early intervention and avoid any related adverse events. Some of these complications include periprosthetic fractures, infection, subsequent fragility fractures, and have an all-cause revision arthroplasty at 2 years post-op. Some studies analyzed the beneficence of antiresorptive medications pre-operatively but the latter did not show favorable outcomes. Surgical management may include cementing components of the prosthesis as well as modifying the diameter of the shoulder stem. Nevertheless, more studies are needed to evaluate the efficacy of any intervention, whether medical or surgical, to avoid any shoulder arthroplasty related-complication that may be precipitated by the reduced bone mineral

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AU Yu, YJ
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TI Mussel-Based Biomimetic Strategies in Musculoskeletal Disorder Treatment: From Synthesis Principles to Diverse Applications

SO INTERNATIONAL JOURNAL OF NANOMEDICINE
LA English
DT Review
DE mussel; biomimetic; musculoskeletal disorder; tissue engineering; biomaterials
ID cruciate ligament reconstruction; inspired adhesive; enhanced cytocompatibility; artificial ligament; cross-linking; wet adhesion; hydrogel; catechol; protein; polydopamine
AB Musculoskeletal disorders are the second leading cause of disability worldwide, posing a huge global burden to the public sanitation system. Currently, tissue engineering-based approaches act as effective strategies, which are, however, challenging in limited application scenarios. Mussel-based biomimetic materials, exhibit numerous unique properties such as intense adhesion, biocompat-ibility, moisture resistance, and injectability, to name only a few, and have attracted extensive research interest. In particular, featuring state-of-the-art properties, mussel-inspired biomaterials have been widely explored in innumerable musculoskeletal disorder treatments including osteochondral defects, osteosarcoma, osteoarthritis, ligament rupture, and osteoporosis. Nevertheless, a comprehensive and timely discussion of their applications in musculoskeletal disorders is insufficient. In this review, we emphasize on (1) the main categories and characteristics of mussel foot proteins and their fundamental mechanisms for the spectacular adhesion in mussels; (2) the diverse synthetic methods and modification of various polymers; and (3) the emerging applications of mussel-biomimetic materials, the future perspectives, and challenges, especially in the area of musculoskeletal disorder. We envision that this review will provide a unique and insightful perspective to improve the development of a new generation of mussel biomimetic strategies.
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TI UPLC/Q-TOF-MS-based metabolomics evaluate the efficacy of oroxylin A against postmenopausal osteoporosis
SO BIOMEDICAL CHROMATOGRAPHY

LA English
DT Article
DE metabolic pathway; metabolites; metabolomics; oroxylin A; osteoporosis
ID bone-mineral density; expression; turnover
AB Post-menopausal osteoporosis (PMOP) is a common metabolic bone malady characterized by bone mass loss and bone microarchitectural deterioration; however, there is currently no effective drug for its management. According to our previous study, oroxylin A (OA) could effectively protect ovariectomized (OVX)-osteoporotic mice from bone loss; however, its therapeutic targets are still unclear. From a metabolomic perspective, we studied serum metabolic profiles to discover potential biomarkers and OVX-related metabolic networks, which could assist us to comprehend the impact of OA on OVX. Five metabolites were identified as biomarkers associated with 10 related metabolic pathways, including phenylalanine, tyrosine and tryptophan biosynthesis, and phenylalanine, tryptophan and glycerophospholipid metabolism. After OA treatment, the expression of multiple biomarkers changed, with lysophosphatidylcholine (18:2) being a major significantly regulated biomarker. Our study demonstrated that OA's effects on OVX are probably related to the regulation of phenylalanine, tyrosine and tryptophan biosynthesis. Our findings explain the role of OA against PMOP in terms of metabolism and pharmacology and provide a pharmacological foundation for OA treatment of PMOP.
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TI Advances in the study of traditional Chinese medicine affecting bone metabolism through modulation of oxidative stress
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE oxidative stress; osteoblast; osteoclast; bone metabolism; traditional Chinese medicine
ID nf-kappa-b; dexamethasone-induced apoptosis; endothelial progenitor cells; signaling pathway; map kinase; osteoporosis; osteoclastogenesis; activation; inhibition; osteoblast
AB Bone metabolic homeostasis is dependent on coupled bone formation dominated by osteoblasts and bone resorption dominated by osteoclasts, which is a process of dynamic balance between bone formation and bone resorption. Notably, the formation of bone relies on the development of bone vasculature. Previous studies have shown that oxidative stress caused by disturbances in the antioxidant system of the whole organism is an important factor affecting bone metabolism. The increase in intracellular reactive oxygen species can lead to disturbances in bone metabolism, which can initiate multiple bone diseases, such as osteoporosis and osteoarthritis. Traditional Chinese medicine is considered to be an effective antioxidant. Cumulative evidence shows that the traditional Chinese medicine can alleviate oxidative stress-mediated bone metabolic disorders by modulating multiple signaling pathways, such as Nrf2/HO-1 signaling, PI3K/Akt signaling, Wnt/beta-catenin signaling, NF-kappa B signaling, and MAPK signaling. In this paper, the potential mechanisms of traditional Chinese medicine to regulate bone me-tabolism through oxidative stress is summarized to provide direction and theoretical basis for future research related to the treatment of bone diseases with traditional Chinese medicine.
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TI Current insights into the functional roles of ferroptosis in musculoskeletal diseases and therapeutic implications
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE clinical implications; ferroptosis; musculoskeletal diseases; oxidative stress; therapeutic strategies
ID intervertebral disc degeneration; hypoxia-inducible factor-2-alpha; transsulfuration pathway; lipid-peroxidation; oxidative stress; iron-deficiency; cell-death; apoptosis; erastin; ferritinophagy
AB Ferroptosis is a novel type of cell death associated with iron accumulation and excessive lipid peroxidation. Elucidating the underlying molecular mechanisms of ferroptosis is intensively related to the development and treatment of multiple diseases, including musculoskeletal disorders. Moreover, in vitro and in vivo studies have shown the importance of oxidative stress in musculoskeletal conditions such as osteoporosis, osteoarthritis, rheumatoid arthritis, and osteosarcoma. Ferroptosis-derived clinical management of musculoskeletal diseases offers tremendous and attractive opportunities. Notably, ferroptosis agonists have been proven to enhance the sensitivity of osteosarcoma cells to conventional therapeutic strategies. In this review, we have mainly focused on the implications of ferroptosis regulation in the pathophysiology and therapeutic response of musculoskeletal disorders. Understanding roles of ferroptosis for controlling musculoskeletal diseases might provide directions for ferroptosis-driven therapies, which could be promising for the development of novel therapeutic strategies.
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TI Implications and theragnostic potentials of circular RNAs in rheumatic diseases
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DE circRNAs; Rheumatic diseases; Therapeutic potential; Diagnostic potential; Circular RNAs
ID inflammatory-bowel-disease; promotes osteogenic differentiation; systemic-lupus-erythematosus; blood mononuclear-cells; t-cells; cartilage degradation; expression profile; emerging roles; arthritis; apoptosis
AB Circular RNAs (circRNAs), a class of non-coding RNAs (ncRNAs), are highly stable and ubiquitous molecules that exhibit tissue-specific expression. Accumulating evidence has shown that aberrant expression of circRNAs can play a role in the pathogenesis of several diseases. Rheumatic diseases are a varied group of autoimmune and inflammatory disorders affecting mainly the musculoskeletal system. Notably, circRNAs, which are essential immune system gene modulators, are strongly linked to the occurrence and progression of autoimmune disorders. Here, we present and discuss the current findings concerning the roles, implications and theragnostic potentials of circRNAs in common rheumatic diseases, including ankylosing spondylitis (AS), osteoarthritis (OA), osteoporosis (OP), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Crohn's disease (CD), and gout. This review aims to provide new insights to support the development of novel diagnostic and therapeutic strategies for these disabling diseases.
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NR 176
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Z9 13
U1 2
U2 13
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PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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J9 INT J BIOL MACROMOL
JI Int. J. Biol. Macromol.

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WC Biochemistry & Molecular Biology; Chemistry, Applied; Polymer Science
SC Biochemistry & Molecular Biology; Chemistry; Polymer Science
GA 9X2HF
UT WOS:000949593000001
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PT J
AU Cao, SY
Wei, YH
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Liu, P
Zeng, H
AF Cao, Siyang
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TI Global research landscape on the crosstalk between ferroptosis and musculoskeletal diseases: A bibliometric and visualized analysis
SO HELIYON
LA English
DT Article
DE Global research trend; Ferroptosis; Musculoskeletal diseases; Bibliometrics; Visualized analysis
ID cancer-cells; glutathione; metabolism; biology; head
AB Over the past 11 years, mounting evidence has suggested a significant association between ferroptosis and the development and progression of musculoskeletal (MSK) diseases, such as osteoporosis and osteoarthritis. However, a comprehensive bibliometric analysis summarizing the relationship between ferroptosis and MSK diseases is currently lacking. The present study collected articles and reviews on the topic of ferroptosis in MSK diseases. The data were collected from January 1st, 2012 to June 30th, 2023 by screening the Web of Science database. Various tools, including VOSviewer, CiteSpace, Pajek, the R

package, and others, were used to conduct bibliometric and visualization analyses. Notably, China, the USA, and Italy emerged as primary contributors, jointly accounting for over 80 % of published documents, thereby shaping research in this domain. Among the diverse institutions, Shanghai Jiao Tong University, Soochow University, and Huazhong University of Science and Technology displayed the highest productivity levels. The most prolific authors include Sun Kai, Shang Peng, and Jing Xingzhi. Oxidative Medicine and Cellular Longevity stood out with the largest number of publications in this area. The five most significant disorders in this field are bone fractures, osteosarcoma, bone neoplasms, joint diseases, and osteoporotic fractures. This study represents an inaugural comprehensive bibliometric analysis, presenting a holistic view of the knowledge framework and developmental patterns in ferroptosis concerning MSK diseases over the previous eleven years. This information can aid researchers in acquiring a thorough grasp of this domain and offer invaluable insights for forthcoming explorations.
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FU National Natural Science Foundation of China [82172432, 82102568, 82001319]; National & Local Joint Engineering Research Centre of Orthopaedic Biomaterials [XMHT20190204007]; Guangdong Basic and Applied Basic Research Foundation [2021A1515012586, 2021A1515220054, 2022B1515120046, 2022A1515220038, 2022A1515220111, 2021A1515220037, 2022A1515220165]; Shenzhen High-Level Hospital Construction Fund; Shenzhen Key Medical Discipline Construction Fund [SZXK023]; Sanming Project of Medicine in Shenzhen [SZSM202211038]; Research and Development Projects of Shenzhen [JCYJ20210324110214040, JCYJ20220531094214032, JCYJ20190809152409606, JCYJ20210324105806016, JCYJ20220531094406015]; Shenzhen Sustainable Development Project [KCXFZ20201221173411031]; Scientific Research Foundation of Peking University Shenzhen Hospital [KYQD2021099]
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NR 51
TC 13
Z9 13
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U2 32
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PA 50 HAMPSHIRE ST, FLOOR 5, CAMBRIDGE, MA 02139 USA
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TI Assessing oxidative stress induction ability and oxidative potential of PM2.5 in cities in eastern and western Japan
SO CHEMOSPHERE
LA English
DT Article
DE Oxidative stress induction ability; Oxidative potential; Heme oxygenase-1 assay; Dithiothreitol assay; Positive matrix factorization; Biomass burning
ID humic-like substances; particulate-matter; organic aerosols; transition-metals; soluble metals; redox activity; black carbon; particles; toxicity; airway
AB Oxidative stress is an important cause of respiratory diseases associated with exposure to PM2.5. Accordingly, acellular methods for assessing the oxidative potential (OP) of PM2.5 have been evaluated extensively for use as indicators of oxidative stress in living organisms. However, OP-based assessments only reflect the physicochemical properties of particles and do not consider particle-cell interactions. Therefore, to determine the potency of OP under various PM2.5 scenarios, oxidative stress induction ability (OSIA) assessments were performed using a cell-based method, the heme oxygenase-1 (HO-1) assay, and the findings were compared with OP measurements obtained using an acellular method, the dithiothreitol assay. For these assays, PM2.5 filter samples were collected in two cities in Japan. To quantitatively determine the relative contribution of the quantity of metals and subtypes of organic aerosols (OA) in PM2.5 to the OSIA and the OP, online measurements and offline chemical analysis were also performed. The findings showed a positive relationship between the OSIA and OP for water-extracted samples, confirming that the OP is generally well suited for use as an indicator of the OSIA. However, the correspondence between the two assays differed for samples with a high water-soluble (WS)-Pb content, which had a higher OSIA than would be expected from the OP of other samples. The results of reagentsolution experiments showed that the WS-Pb induced the OSIA, but not the OP, in 15-min reactions, suggesting a reason for the inconsistent relationship between the two assays across samples. Multiple linear regression analyses and reagent-solution experiments showed that WS transition metals and biomass burning OA accounted for approximately 30-40% and 50% of the total OSIA or the total OP of water-extracted PM2.5 samples, respectively.
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NR 71
TC 9
Z9 9
U1 2
U2 25
PU PERGAMON-ELSEVIER SCIENCE LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND
SN 0045-6535
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J9 CHEMOSPHERE
JI Chemosphere
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WC Environmental Sciences
SC Environmental Sciences & Ecology
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ER

PT J
AU Alsaikhan, F
Mahmoud, MZ
Suliman, M
AF Alsaikhan, Fahad
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Suliman, Muath
TI Synthesis and characterization of novel denosumab/magnesium-based metal organic frameworks nanocomposite prepared by ultrasonic route as drug delivery system for the treatment of osteoporosis
SO FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY
LA English
DT Article
DE bone; denosumab; drug delivery system; metal organic framework; osteoporotic
ID magnesium; denosumab; mechanism; co2
AB Introduction: The metal-organic frameworks (MOF) have shown fascinating possibilities in biomedical applications, and designing a drug delivery system (DDS) based on the MOF is important. This work aimed at developing a suitable DDS based on Denosumab-loaded Metal Organic Framework/ Magnesium (DSB@MOF (Mg)) for attenuating osteoarthritis. Materials and Methods: The MOF (Mg) ($Mg_3(BPT)_2(H_2O)_4$) was synthesized using a sonochemical protocol. The efficiency of MOF (Mg) as a DDS was evaluated by loading and releasing DSB as a drug. In addition, the performance of MOF (Mg) was evaluated by releasing Mg ions for bone formation. The MOF (Mg) and DSB@MOF (Mg) cytotoxicity towards the MG63 cells were explored by MTT assay. Results: MOF (Mg) characterized by using XRD, SEM, EDX, TGA, and BET. Drug loading, and releasing experiments proved that DSB was loaded on the MOF (Mg) and approximately 72% DSB was released from it after 8 h. The characterization techniques showed that MOF (Mg) was successfully synthesized with good crystal structure and thermal stability. The result of BET showed that MOF (Mg) had high surface areas and pore volume. This is the reason why its 25.73% DSB was loaded in the subsequent drug-loading experiment. Drug release and ion release experiments indicated DSB@MOF (Mg) had a good controlled release of DSB and Mg ions in solution. Cytotoxicity assay confirmed that the optimum dose of it had excellent biocompatibility and could stimulate the proliferation of MG63 cells as time went on. Conclusion: Due to the high loading amount of DSB and releasing time, DSB@ MOF (Mg) can be promising as a suitable candidate for relieving bone pain caused by osteoporosis, with ossification-reinforcing functions.
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TI Osteochondral junction leakage and cartilage joint lubrication
SO COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE
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DT Article
DE Cartilage; Subchondral bone plate region; Osteochondral junction leakage; Coefficient of friction; Mixed-mode lubrication duration; Permeability
ID subchondral bone plate; interstitial fluid pressurization; tension-compression nonlinearity; articular-cartilage; solute transport; tibial plateau; model; osteoarthritis; interface; friction
AB Background and Objectives: Previous studies have shown that there is potentially interstitial fluid ex-change between cartilage tissue and the subarticular spongiosa region in the case of injury or disease (e.g., osteoarthritis and osteoporosis). Interstitial flow is also required for cartilage lubrication under joint load. A key question then is how cartilage lubrication is modified by increased interstitial fluid leakage across the osteochondral junction. Thus, the purpose of this study is to develop a numerical model to investigate changes in cartilage lubrication with changes in osteochondral junction leakage. Methods: The multi-phase coupled model includes domains corresponding to the contact gap, cartilage tissue and subchondral bone plate region (ScBP). Each of these domains are treated as poroelastic sys-tems, with their coupling implemented through mass and pressure continuity. The effects of osteochon-dral junction leakage on

lubrication were investigated with a parametric study on the relative permeabil-ity between the ScBP and cartilage tissue. Results: Significant effects of ScBP permeability were predicted, especially during the early stage of the junction leakage development (early stage of the disease). There is a significant reduction in mixed-mode lubrication duration under the effect of increased junction leakage (the cartilage tissue mixed-mode lubri-cation duration is about 33% decrease for a relative permeability ratio of 0.1 between ScBP and cartilage tissue, and about 52% decrease under the osteoarthritis condition). In addition, the time for cartilage to reach steady-state consolidation is significantly reduced when ScBP permeability increases (the consoli-dation time reduces from roughly 2 h to 1.2 h when the relative permeability ratio increases from 0.001 to 0.1, and it reduces to 0.8 h for an advanced osteoarthritis condition). It is predicted that the initial fric-tion coefficient could increase by over 60% when the ScBP permeability is consistent with an advanced osteoarthritis (OA) condition. Conclusion: Increased osteochondral junction leakage induced by joint injury and disease could result in increased cartilage surface wear rates due to more rapid interstitial fluid depressurization within articular cartilage. (c) 2023 Elsevier B.V. All rights reserved.
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TI Biochanin A protects against iron overload associated knee osteoarthritis via regulating iron levels and NRF2/System xc-/GPX4 axis
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Biochanin A; Iron overload; Knee osteoarthritis; Iron level; Nrf2; system xc-; GPX4; ROS accumulation
ID blood-induced damage; murine model; articular-cartilage; ferroptosis; progression; antagonizes; mechanisms
AB Background: Iron homeostasis plays a positive role in articular cartilage health. Excessive iron or iron overload can induce oxidative stress damage in chondrocytes and ferroptosis cell death, advancing knee osteoarthritis (KOA). However, up to date, few effective agents treat iron overload-induced KOA (IOKOA). Chinese herbal medicine (CHM) provides abundant resources for drug selection to manage bone metabolic conditions, including osteoporosis. Biochanin A (BCA) is a novel bioactive multifunctional natural compound isolated from Huangqi, which has protective effects on bone loss. Nevertheless, the function and mechanism of BCA in treating IOKOA are still elusive.Purpose: This study seeks to uncover the potential therapeutic targets and mechanisms of BCA in the management of KOA with iron accumulation.Methods: Iron dextrin (500 mg/kg) was intraperitoneally injected into mice to establish the iron overloaded mice model. OA was induced through surgery, and the progression was evaluated eight weeks following surgery. OA severity was evaluated with micro-CT and Safranin-O/Fast green staining in vivo. Iron deposition in the knee joint and synovium was assessed using Perl's Prussian blue staining. Ferric ammonium citrate (FAC) was then administered to primary chondrocytes to evaluate iron regulators mediated iron homeostasis. Toluidine blue staining was utilized to identify chondrocytes in vitro. The vitality of the cells was assessed using the CCK-8 test. The apoptosis rate of cells was measured using Annexin V-FITC/PI assay. The intracellular iron level was detected utilizing the calcein-AM test. Reactive oxygen species (ROS), lipid-ROS, and

mitochondrial membrane potentiality were reflected via fluorescence density. Utilizing RT-qPCR and western blotting, the expression level was determined.Results: Micro-CT and histological staining of knee joints showed greater cartilage degradation and higher iron buildup detected in iron-overloaded mice. BCA can reduce iron deposition and the severity of KOA. Toluidine blue staining and the CCK-8 assay indicated that BCA could rescue chondrocytes killed by iron. Cell apoptosis rates were increased due to iron overload but improved by BCA. Further, the intracellular content of iron, ROS, and lipid-ROS was increased with ferric ammonium citrate (FAC) treatment but restored after treatment with different concentrations of BCA. JC-1 staining revealed that BCA could reduce mitochondrial damage induced by iron overload.Conclusion: Iron overload was shown to promote chondrocyte ferroptosis in vivo and in vitro. Moreover, iron overload suppressed the expression of collagen II and induced MMP expression by catalyzing ROS generation with mitochondrial dysfunction. Our results showed that BCA could directly reduce intracellular iron concen-tration by inhibiting TfR1 and promoting FPN but also target the Nrf2/system xc-/GPX4 signaling pathway to scavenge free radicals and prevent lipid peroxidation. The results of this research indicate that BCA regulates iron homeostasis during the progression of osteoarthritis, which can open a new field of treatment for KOA.
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TI Mechanisms of tissue degeneration mediated by periostin in spinal degenerative diseases and their implications for pathology and diagnosis: a review

SO FRONTIERS IN MEDICINE
LA English
DT Review
DE periostin; pathway; biomarker; mechanical stress; inflammation; spinal degenerative diseases; bone metabolic diseases
ID ligamentum-flavum hypertrophy; intervertebral disc degeneration; nf-kappa-b; serum periostin; knee osteoarthritis; tnf-alpha; periodontal-ligament; postmenopausal women; gene-expression; bone loss
AB Periostin (POSTN) serves a dual role as both a matricellular protein and an extracellular matrix (ECM) protein and is widely expressed in various tissues and cells. As an ECM protein, POSTN binds to integrin receptors, transduces signals to cells, enabling cell activation. POSTN has been linked with various diseases, including atopic dermatitis, asthma, and the progression of multiple cancers. Recently, its association with orthopedic diseases, such as osteoporosis, osteoarthritis resulting from cartilage destruction, degenerative diseases of the intervertebral disks, and ligament degenerative diseases, has also become apparent. Furthermore, POSTN has been shown to be a valuable biomarker for understanding the pathophysiology of orthopedic diseases. In addition to serum POSTN, synovial fluid POSTN in joints has been reported to be useful as a biomarker. Risk factors for spinal degenerative diseases include aging, mechanical stress, trauma, genetic predisposition, obesity, and metabolic syndrome, but the cause of spinal degenerative diseases (SDDs) remains unclear. Studies on the pathophysiological effects of POSTN may significantly contribute toward the diagnosis and treatment of spinal degenerative diseases. Therefore, in this review, we aim to examine the mechanisms of tissue degeneration caused by mechanical and inflammatory stresses in the bones, cartilage, intervertebral disks, and ligaments, which are crucial components of the spine, with a focus on POSTN.
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TI Identification of 12 hub genes associated to the pathogenesis of osteoporosis based on microarray and single-cell RNA sequencing data
SO FUNCTIONAL & INTEGRATIVE GENOMICS
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DT Article
DE Osteoporosis; Immune microenvironment; Chemokines; Mesenchymal stromal cells; Osteoblasts; Bone remodeling
ID mesenchymal stem-cells; bone-resorption; expression; fractures; differentiation; osteoprotegerin; osteoarthritis; icam-1; women; ccl3
AB Osteoporosis is a common disease, especially among the elderly. This study aimed to comprehensively examine the roles of immune microenvironment in osteoporosis pathogenesis. Expression profiles of GSE35959, GSE7158, and GSE13850 datasets were used to analyze differential expression and identify hub genes related to immune features. Based on the single-cell RNA sequencing (scRNA-seq) data of an osteoporosis patient, different cell types were classified and

the relation between immune environment and osteoporosis was explored. Twelve hub genes significantly associated with immune features were selected and 11 subgroups were defined using scRNA-seq data. The expression of two hub genes (CDKN1A and TEFM) was greatly altered during the transformation from mesenchymal stem cells (MSCs) to osteoblasts. Chemokines and chemokine receptors were differentially enriched in different cell types. CXCL12 was high-expressed in MSCs. This study emphasized that immune microenvironment played a critical role in the pathogenesis of osteoporosis. Chemokines and chemokine receptors can modify cell development and affect the interactions among different cell types, leading to unbalanced bone remodeling.
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TI Applications of 3D printing in aging
SO INTERNATIONAL JOURNAL OF BIOPRINTING
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DT Article
DE Aging; 3D-printing; Biomaterials; Disease model; Regenerative medicine; Aging care
ID alzheimers-disease; extracellular-matrix; global burden; knee osteoarthritis; european-society; amyloid-beta; osteoporosis; mechanisms; cartilage; stereolithography
AB Aging is inevitable, and how to age healthily is a key concern. Additive manufacturing offers many solutions to this problem. In this paper, we first briefly introduce various 3D printing technologies commonly used in the biomedical field, particularly in aging research and aging care. Next, we closely examine

aging-related health conditions of nervous system, musculoskeletal system, cardiovascular system, and digestive system with a focus on the application of 3D printing in these fields, including the creation of in vitro models and implants, production of drugs and drug delivery systems, and fabrication of rehabilitation and assistive medical devices. Finally, the opportunities, challenges, and prospects of 3D printing in the field of aging are discussed.
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TI Acupoint Thread Embedding Combined With Wenshen Bugu Decoction for the Treatment of Aromatase Inhibitor-Associated Musculoskeletal Symptom Among Postmenopausal Breast Cancer Patients: Study Protocol of a Randomized Controlled Trial
SO INTEGRATIVE CANCER THERAPIES
LA English
DT Article
DE aromatase inhibitor-associated musculoskeletal symptom (AIMSS); acupoint thread embedding (ATE); Wenshen Bugu Decoction; breast cancer; endocrine therapy
ID quality-of-life; acupuncture; therapy; women; validity; osteoporosis; management; tamoxifen; adherence
AB Background:Aromatase inhibitors (AIs) are recommended as the preferred therapy for postmenopausal women with hormone receptor-positive (HR+) breast cancer. As a result, aromatase inhibitor-associated musculoskeletal symptom (AIMSS) have become a major problem leading to therapy discontinuation and decreased quality of life in patients receiving adjuvant AIs treatment. Multiple therapies have been attempted, but have yielded limited clinical results. This study will be performed to determine whether acupoint thread embedding (ATE) combined with Wenshen Bugu Decoction can effectively treat AIMSS, so as to improve the AIs medication compliance of postmenopausal breast cancer patients. Methods:This study will utilize a randomized, 2 parallel groups controlled trial design. A total of 128 eligible postmenopausal breast cancer women with AIMSS will be randomized to receive a 12-week treatment with Wenshen Bugu Decoction alone (control group) or in combination with ATE (treatment group) in a 1:1 ratio. The primary outcome will be the 12 week Brief Pain Inventory Worst Pain (BPI-WP) score. The secondary outcome measures will include response rate, Brief Pain Inventory-Short Form (BFI-SF), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Functional Assessment of Cancer

Therapy-Endocrine Symptom (FACT-ES), Functional Assessment of Cancer Therapy-Breast (FACT-B), bone marrow density (BMD), blood markers of bone metabolite, Morisky medication adherence scale-8 (MMAS-8), credibility and expectancy, and survival outcomes. Discussion:This trial may provide clinical evidence that ATE combined with Wenshen Bugu Decoction can be beneficial for treating AIMSS among postmenopausal breast cancer survivors. Our findings will be helpful to enhance the quality of life and reduce the occurrence of AIs withdrawal.
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TI Low-molecular-weight fucoidan ameliorates calcium-deficient-diet-induced bone loss and osteoarthritis via CaSR level regulation
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DT Article
DE Extracellular calcium ion concentration; Calcium deficiency; Calcium-sensing receptor; Low-molecular-weight fucoidan; Osteoarthritis; Osteoblast
ID human trabecular bone; sensing-receptor; osteogenic differentiation; osteoblastic differentiation; expression; osteoporosis; growth; cells; supplementation; osteoprotegerin
AB Fucoidans-sulfated and fucosylated polysaccharides extracted from brown seaweed-reportedly accelerate bone growth and prevent osteoarthritis (OA) progression. In this study, we examined the effects of lowmolecular-weight

fucoidan (LMF) on the molecular mechanism of extracellular calcium concentration in vitro and in vivo. In MG63 cells, LMF significantly increased the activity of alkaline phosphatase (ALP) and expression of calcium-sensing receptor (CaSR), runt-related transcription factor 2 (Runx2), and osteoprotegerin (OPG) under low- and normal-[Ca+2]0 conditions, but only decreased the expression of receptor activator of the nuclear factor kappa B ligand (RANKL) under normal-[Ca+2]0 conditions. In the calcium-deficient diet model, LMF significantly increased body length, growth rate, bone-specific ALP secretion, trabecular number, and CaSR protein expression, without body weight changes. In the OA model, LMF significantly increased bone volume and CaSR protein expression and reduced joint inflammation. Overall, our results indicate that LMF reduced calcium-deficientdiet-induced bone loss and OA via CaSR level regulation.
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TI Impact of Environmental and Epigenetic Changes on Mesenchymal Stem Cells during Aging
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DT Review
DE bone marrow stromal cells; mesenchymal stem cells; epigenetics; osteogenic; bone; skeleton; DNA methylation; histone methylation; histone acetylation
ID human-bone-marrow; regulates osteogenic differentiation; dna methylation; gene-expression; life-span; in-vitro; progenitor cells; dietary-protein; messenger-rna; self-renewal
AB Many crucial epigenetic changes occur during early skeletal development and throughout life due to aging, disease and are heavily influenced by an individual's lifestyle. Epigenetics is the study of heritable changes in gene expression as the result of changes in the environment without any mutation in the underlying DNA sequence. The epigenetic profiles of cells are dynamic and mediated by different mechanisms, including histone modifications, non-coding RNA-associated gene silencing and DNA methylation. Given the underlining role of dysfunctional mesenchymal tissues in common age-related skeletal diseases such as osteoporosis and osteoarthritis, investigations into skeletal stem cells or mesenchymal stem cells (MSC) and their functional deregulation during aging has been of great interest and how this is mediated by an evolving epigenetic landscape. The present review describes the recent findings in epigenetic changes of MSCs that effect growth and cell fate determination in the context of aging, diet, exercise and bone-related diseases.
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TI Structural characterization and anti-lipotoxicity effects of a pectin from okra (Abelmoschus esculentus (L.) Moench)
SO INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES

LA English
DT Article
DE Okra; Chemical structure; Lipotoxicity
ID activated protein-kinase; oleic-acid; antioxidant activity; lipid-accumulation; in-vitro; polysaccharide; purification; inhibition; metabolism; ampk
AB Okra (Abelmoschus esculentus (L.) Moench) is rich in various bioactive ingredients and used as a medicinal plant in traditional medicine. In the present study, to find the polysaccharide with anti-lipotoxicity effects from okra and clarify its structure, a pectin OP-1 was purified from okra, which had a backbone containing -> 4)-alpha-GalpA-(1 -> residues, and 1,5-Ara linked the main chain through the O-3 of the residue -> 3,4)-alpha-GalpA-(1 ->, and the C-6 of residue 1, 4-alpha-GalpA replaced by methyl ester. In vitro experiments showed that OP-1 pretreatment alleviated oleic acid (OA)-induced lipid accumulation, ROS generation, apoptosis, transaminase leakage, and inflammatory cytokine secretion in HepG2 cells, resulting in reduced lipotoxicity. Further molecular results revealed that OP-1 increased Adenosine 5 '-monophosphate (AMP)-activated protein kinase (AMPK) phosphorylation and affected the expression of AMPK downstream targets, including inhibit SREBP1c and FAS, as well as activate CPT-1A. Impressively, AMPK inhibitor dorsomorphin (Compound C) blocked the effects of OP-1 against lipotoxicity. The effects of OP-1 on lipid metabolism were also diminished by dorsomorphin. Our results demonstrated that OP-1 possesses a potent function in preventing lipotoxicity via regulating AMPK-mediated lipid metabolism and provide a novel insight into the future utilization of okra polysaccharide.
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NR 65
TC 14
Z9 14
U1 2
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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TI The intricate mechanism of PLS3 in bone homeostasis and disease
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE PLS3; bone cells; mechanotransduction; calcium regulation; osteogenesis; bone diseases
ID x-linked osteoporosis; t-plastin; terminal differentiation; beta-catenin; nitric-oxide; cancer-cells; osteocytes; expression; protein; mutations
AB Since our discovery in 2013 that genetic defects in PLS3 lead to bone fragility, the mechanistic details of this process have remained obscure. It has been established that PLS3 variants cause syndromic and nonsyndromic osteoporosis as well as osteoarthritis. PLS3 codes for an actin-bundling protein with a broad pattern of expression. As such, it is puzzling how PLS3 specifically leads to bone-related disease presentation. Our review aims to summarize the current state of knowledge regarding the function of PLS3 in the predominant cell types in the bone tissue, the osteocytes, osteoblasts and osteoclasts. This is related to the role of PLS3 in regulating mechanotransduction, calcium regulation, vesicle trafficking, cell differentiation and mineralization as part of the complex bone pathology presented by PLS3 defects. Considering the consequences of PLS3 defects on multiple aspects of bone tissue metabolism, our review motivates the study of its mechanism in bone diseases which can potentially help in the design of suitable therapy.
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TI Distinct Stocks of the Redtail Scad Decapterus kurroides Bleeker, 1855 (Perciformes: Carangidae) from the Northern Sulu and Southern Sibuyan Seas, Philippines Revealed from Otolith Morphometry and Shape Analysis
SO FISHES
LA English
DT Article
DE morphometry; shape analysis; otolith; Decapterus kurroides; stock delineation
ID rastrelliger-kanagurta; population-structure; discrimination; chemistry; atlantic; morphology; history; growth; cod; microchemistry
AB A recent study was performed to assess the morphometric variation of otoliths of the Decapterus kurroides collected in the northern Sulu and southern Sibuyan seas in delineating fish stocks. Seven of the otolith morphometric descriptors (otolith length, OL; otolith height, OH; otolith weight OW; otolith area, OA; otolith perimeter, OP; ellipticity, EL; and aspect ratio, AR) demonstrated a significant positive correlation with fish length and six (rectangularity, RE; squareness, SQ; roundness, RO; circularity, CI; compactness, CO; and form factor, FF) demonstrated a significant negative correlation. In terms of intraspecific comparisons, almost all the otolith morphometric descriptors were significantly different between the two sites (except RE and OH). Further, principal component (PC) analysis showed that direct otolith morphometric descriptors such as OL, OH, OW, OA, and OP explained 61.71% of the differences (PC1). In contrast, derived otolith descriptors such as EL, AR, and CO explained 22.00% of the variations (PC2) for a total of 83.71% explained variations with the eight otolith morphometric descriptors. Statistics reveal that D. kurroides from the Sibuyan Sea have significantly larger, heavier, and more elliptical otoliths than those from the Sulu Sea. Results suggested that the D. kurroides from Sulu and Sibuyan seas are two different phenotypic stocks. Further studies such as otolith microchemistry, genetics, other life history-based studies, and present exploitation levels should be carried out to supplement the results of this study to fully establish the D. kurroides stock structures within Philippine waters.
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TI Teriparatide ameliorates articular cartilage degradation and aberrant subchondral bone remodeling in DMM mice
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Article
DE Teriparatide (PTH (1-34)); Knee osteoarthritis; Cartilage; Subchondral bone; Osteoprotegerin (OPG)
ID knee osteoarthritis; degeneration; chondrocytes; progression
AB Objective: Knee osteoarthritis (KOA) is a highly prevalent musculoskeletal disorder characterized by degeneration of cartilage and abnormal remodeling of subchondral bone (SCB). Teriparatide (PTH (1-34)) is an effective anabolic drug for osteoporosis (OP) and regulates osteoprotegerin (OPG)/receptor activator of nuclear factor ligand (RANKL)/RANK signaling, which also has a therapeutic effect on KOA by ameliorating cartilage degra-dation and inhibiting aberrant remodeling of SCB. However, the mechanisms of PTH (1-34) in treating KOA are still uncertain and remain to be explored. Therefore, we compared the effect of PTH (1-34) on the post-traumatic KOA mouse model to explore the potential therapeutic effect and mechanisms.Methods: In vivo study, eight-week-old male mice including wild-type (WT) (n = 54) and OPG-/- (n = 54) were investigated and compared. Post-traumatic KOA model was created by destabilization of medial meniscus (DMM). WT mice were randomly assigned into three groups: the sham group (WT-sham; n = 18), the

DMM group (WT-DMM; n = 18), and the PTH (1-34)-treated group (WT-DMM + PTH (1-34); n = 18). Similarly, the OPG-/- mice were randomly allocated into three groups as well. The designed mice were executed at the 4th, 8th, and 12th weeks to evaluate KOA progression. To further explore the chondro-protective of PTH (1-34), the ATDC5 chondrocytes were stimulated with different concentrations of PTH (1-34) in vitro. Results: Compared with the WT-sham mice, significant wear of cartilage in terms of reduced cartilage thickness and glycosaminoglycan (GAG) loss was detected in the WT-DMM mice. PTH (1-34) exhibited cartilage-protective by alleviating wear, retaining the thickness and GAG contents. Moreover, the deterioration of the SCB was alleviated and the expression of PTH1R/OPG/RANKL/RANK were found to increase after PTH (1-34) treatment. Among the OPG-/- mice, the cartilage of the DMM mice displayed typical KOA change with higher OARSI score and thinner cartilage. The damage of the cartilage was alleviated but the abnormal remodeling of SCB didn't show any response to the PTH (1-34) treatment. Compared with the WT-DMM mice, the OPG-/--DMM mice caught more aggressive KOA with thinner cartilage, sever cartilage damage, and more abnormal remodeling of SCB. Moreover, both the damaged cartilage from the WT-DMM mice and the OPG-/--DMM mice were alleviated but only the deterioration of SCB in WT-DMM mice was alleviated after the administration of PTH (1-34). In vitro study, PTH (1-34) could promote the viability of chondrocytes, enhance the synthesis of extracellular matrix (ECM) (AGC, COLII, and SOX9) at the mRNA and protein level, but inhibit the secretion of inflammatory cyto-kines (TNF-alpha and IL-6).Conclusion: Both wear of the cartilage was alleviated and aberrant remodeling of the SCB was inhibited in the WT mice, but only the cartilage-protective effect was observed in the OPG-/- mice. PTH (1-34) exhibited chondro-protective effect by decelerating cartilage degeneration in vivo as well as by promoting the proliferation and enhancing ECM synthesis of chondrocytes in vitro. The current investigation implied that the rescue of the disturbed SCB is dependent on the regulation of OPG while the chondro-protective effect is independent of modulation of OPG, which provides proof for the treatment of KOA. The translational potential of this article: Systemic administration of PTH (1-34) could exert a therapeutic effect on both cartilage and SCB in different mechanisms to alleviate KOA progression, which might be a novel therapy for KOA.
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AU Nie, YP
Liu, HY
Lei, L
Wu, QS
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Liu, Huanyan
Lei, Lei
Wu, Qishan
TI Effect of Berberine on Treatment of Periodontitis: a Meta-Analysis
SO LATIN AMERICAN JOURNAL OF PHARMACY
LA English
DT Article
DE berberine; clinical use; inflammation; in vitro and in vivo experiment periodontitis
ID in-vitro; bone; fibroblast; differentiation; degradation; expression; osteoblast; pathway; vivo
AB Berberine, an isoquinoline alkaloid derived from medicinal plants, can prevent extracellular MMPs from degrading. Berberine's influence on periodontal MMP expression was studied in vitro and in vivo. Berberine contains anti-inflammatory, anti-tumor, lower blood cholesterol, lower blood glucose, anti -osteoporosis, anti-osteoarthritis, and anti-osteoarthritis properties, according to pharmacological investigations. The goal of this review study was to look at berberine's preventive effects on inflammation and alveolar bone loss in ligature-induced periodontitis, as well as its mechanism of action and future usage and development. To determine the effect of berberine on periodontitis, PubMed, EMBASE, the Cochrane Library, Google Scholar were searched. All the above databases were searched from the available date of inception until the latest issue of 2022. With the removal of duplicates, the titles and abstract of 9 studies have remained. Finally, 6articles were included in our meta-analysis. The heterogeneity result showed that the included studies had clinical and statistical homogeneity. As shown in plot analysis, the berberine-containing group had a higher reduction of inflammation than the control group. BBR's anti-inflammatory properties in periodontitis. BBR as a pleiotropic agent is efficacious in exerting anti-inflammatory effects
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AU Mcphee, S
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AF Mcphee, Samuel
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Pena Fernandez, Marta
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TI QCT-based computational bone strength assessment updated with MRI-derived 'hidden' microporosity
SO JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS
LA English
DT Article
DE Subchondral bone; Strength; MRI; QCT; Fracture risk; Microdamage; Finite element model

ID 3rd metacarpal bone; scanning-electron-microscopy; vertebral trabecular bone; finite-element model; subchondral bone; thoroughbred racehorses; metacarpophalangeal joint; cortical bone; mechanical-property; damage accumulation
AB Microdamage accumulated through sustained periods of cyclic loading or single over-loading events contributes to bone fragility through a reduction in stiffness and strength. Monitoring microdamage in vivo remains unattainable by clinical imaging modalities. As such, there are no established computational methods for clinical fracture risk assessment that account for microdamage that exists in vivo at any specific timepoint. We propose a method that combines multiple clinical imaging modalities to identify an indicative surro-gate, which we term 'hidden porosity', that incorporates pre-existing bone microdamage in vivo. To do so, we use the third metacarpal bone of the equine athlete as an exemplary model for fatigue induced microdamage, which coalesces in the subchondral bone. N=10 metacarpals were scanned by clinical quantitative computed tomography (QCT) and mag-netic resonance imaging (MRI). We used a patch-based similarity method to quantify the signal intensity of a fluid sensitive MRI sequence in bone regions where microdamage coa-lesces. The method generated MRI-derived pseudoCT images which were then used to de-termine a pre-existing damage (D-pex) variable to quantify the proposed surrogate and which we incorporate into a nonlinear constitutive model for bone tissue. The minimum, median, and maximum detected D-pex of 0.059, 0.209, and 0.353 reduced material stiffness by 5.9%, 20.9%, and 35.3% as well as yield stress by 5.9%, 20.3%, and 35.3%. Limb-specific voxel-based finite element meshes were equipped with the updated material model. Lateral and medial condyles of each metacarpal were loaded to simulate physiological joint loading dur-ing gallop. The degree of detected D-pex correlated with a relative reduction in both condylar stiffness ($p = 0.001$, $R\text{-}2 > 0.74$) and strength ($p < 0.001$, $R\text{-}2 > 0.80$). Our results illustrate the complementary value of looking beyond clinical CT, which neglects the inclusion of micro-damage due to partial volume effects. As we use clinically available imaging techniques, our results may aid research beyond the equine model on fracture risk assessment in human diseases such as osteoarthritis, bone cancer, or osteoporosis.
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NR 109
TC 1
Z9 2
U1 0
U2 13
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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J9 J MECH BEHAV BIOMED
JI J. Mech. Behav. Biomed. Mater.
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PT J
AU Swan, JT
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TI Specification, validation, and adherence of quality indicators to optimize the safe use of nonsteroidal anti-inflammatory drugs for knee osteoarthritis pain in the primary care setting
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Osteoarthritis; Pain; Quality indicators; Primary care; NSAIDs
ID european-society; economic-aspects; task-force; nsaid use; management; hand; hip; recommendations; osteoporosis; prevention
AB BackgroundNonsteroidal anti-inflammatory drugs (NSAIDs) used for osteoarthritis (OA) in primary care may cause gastrointestinal or renal injury. This study estimated adherence to two quality indicators (QIs) to optimize NSAID safety: add proton pump inhibitors (PPI) to NSAIDs for patients with gastrointestinal (GI) risk (QI #1 NSAID-PPI) and avoid oral NSAIDs in chronic kidney disease (CKD) stage G4 or G5 (QI #2 NSAID-CKD).MethodsThis retrospective study included index primary care clinic visits for knee OA at our health system in 2019. The validation cohort consisted of a random sample of 60 patients. The remainder were included in the expanded cohort. Analysis of structured data extracts was validated against chart review of clinic visit notes (validation cohort) and estimated QI adherence (expanded cohort).ResultsAmong 60 patients in the validation cohort, analysis of data extracts was validated against chart review for QI #1 NSAID-PPI (100%

sensitivity and 91% specificity) and QI #2 NSAID-CKD (100% accuracy). Among 335 patients in the expanded cohort, 44% used NSAIDs, 27% used PPIs, 73% had elevated GI risk, and only 2% had CKD stage 4 or 5. Twenty-one percent used NSAIDs and had elevated GI risk but were not using PPIs. Therefore, adherence to QI #1 NSAID-PPI was 79% (95% CI, 74-83%). No patients with CKD stage 4 or 5 used NSAIDs. Therefore, adherence to QI #2 NSAID-CKD was 100%.ConclusionA substantial proportion of knee OA patients with GI risk factors did not receive PPI with NSAID therapy during primary care visits.
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NR 31
TC 2
Z9 3
U1 0
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 BMC MUSCULOSKEL DIS
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SC Orthopedics; Rheumatology

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AU Gany, SLS
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TI Preventative and therapeutic potential of tocotrienols on musculoskeletal diseases in ageing
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE musculoskeletal; ageing; tocotrienol; muscle ageing; sarcopenia; osteoporosis; arthritis; TRF
ID low-back-pain; breast-cancer cells; vitamin-e; oxidative stress; knee osteoarthritis; older-adults; skeletal-muscle; palm tocotrienols; gamma-tocotrienol; satellite cells
AB Musculoskeletal health is paramount in an ageing population susceptible to conditions such as osteoporosis, arthritis and fractures. Age-related changes in bone, muscle, and joint function result in declining musculoskeletal health, reduced mobility, increased risk of falls, and persistent discomfort. Preserving musculoskeletal wellbeing is essential for maintaining independence and enhancing the overall quality of life for the elderly. The global burden of musculoskeletal disorders is significant, impacting 1.71 billion individuals worldwide, with age-related muscle atrophy being a well-established phenomenon. Tocotrienols, a unique type of vitamin E found in various sources, demonstrate exceptional antioxidant capabilities compared to tocopherols. This characteristic positions them as promising candidates for addressing musculoskeletal challenges, particularly in mitigating inflammation and oxidative stress underlying musculoskeletal disorders. This review paper comprehensively examines existing research into the preventive and therapeutic potential of tocotrienols in addressing age-related musculoskeletal issues. It sheds light on the promising role of tocotrienols in enhancing musculoskeletal health and overall wellbeing, emphasizing their significance within the broader context of age-related health

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AU Sun, JF
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AF Sun, Jianfeng
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Mikhail, Herasimenka
Pavel, Volotovski
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Li, Yusheng
TI Role and molecular mechanism of ghrelin in degenerative musculoskeletal disorders
SO JOURNAL OF CELLULAR AND MOLECULAR MEDICINE
LA English
DT Review
DE ageing; ghrelin; intervertebral disc degeneration; osteoarthritis; osteoporosis; sarcopenia
ID intervertebral disc degeneration; nucleus pulposus cells; necrosis-factor-alpha; bone-mineral density; low-back-pain; growth-hormone; skeletal-muscle; acyl-ghrelin; unacylated ghrelin; serum ghrelin
AB Ghrelin is a brain-gut peptide, and the first 28-peptide that was found in the gastric mucosa. It has a growth hormone (GH)-releasing hormone-like effect and can potently promote the release of GH from pituitary GH cells; however, it is unable to stimulate GH synthesis. Therefore, ghrelin is believed to play a role in promoting bone growth and development. The correlation between ghrelin and some degenerative diseases of the musculoskeletal system has been reported recently, and ghrelin may be one of the factors influencing degenerative

pathologies, such as osteoporosis, osteoarthritis, sarcopenia and intervertebral disc degeneration. With population ageing, the risk of health problems caused by degenerative diseases of the musculoskeletal system gradually increases. In this article, the roles of ghrelin in musculoskeletal disorders are summarized to reveal the potential effects of ghrelin as a key target in the treatment of related bone and muscle diseases and the need for further research.
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TI A systematic review of cost-effectiveness analyses of sequential treatment for osteoporosis
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Review
DE Cost-effectiveness; Osteoporosis; Sequential treatment; Systematic review
ID health economic-evaluation; discrete-event simulation; postmenopausal osteoporosis; oral bisphosphonates; risk; women; abaloparatide; combination; alendronate; management
AB Sequential treatment of osteoporosis has been increasingly mentioned in recent years. However, the corresponding systematic review has not been reported. This study aims to systematically review and assess all full-text pharmacoeconomic studies of sequential treatment for osteoporosis. A comprehensive literature search was performed using PubMed, EMBASE (Ovid), CNKI, and Wanfang Database to identify original articles, published before June 17, 2022. The quality of included articles was evaluated by the updated Consolidated Health Economic Evaluation Reporting Standards (CHEERS 2022) and the Euro-pean Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases International Osteoporosis Foundation (ESCEO-IOF). In general, ten articles were

included in this review. For the comparison between sequential treatment and bisphosphonate monotherapy, more than 75% of studies demonstrated the sequential treatment was cost-effective or dominant, with the exception of sequential treatment involving teriparatide. When the comparisons occurred between the two sequential treatment groups, the sequential treatments associated with either abaloparatide or romosozumab were cost-effective or dominant compared to the sequential treatment involving teriparatide. Several major key drivers of cost-effectiveness included drug cost, medication persistence and adherence, drug effect on fracture risk, offset effect, time horizon, and baseline fracture risk. The most of studies were identified as high quality in CHEERS (2022) and ESCEO-IOF. The cost-effectiveness of sequential treatment for osteoporosis is influenced by multiple factors. Generally, the sequential treatments involving abaloparatide, romosozumab, denosumab, and bisphosphonates may be considered as the preferred option for osteoporosis with high fracture risk, while the sequential treatment with teriparatide was not a cost-effectiveness strategy. The ESCEO-IOF and CHEER (2022) increase the transparency, comparability, extrapolation, and quality of research, engage patients and the general public in research on health services and policies, and help improve the quality of health technology assessment.
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TI Italian Orthopaedic and Traumatology Society (SIOT) position statement on the non-surgical management of knee osteoarthritis
SO JOURNAL OF ORTHOPAEDICS AND TRAUMATOLOGY
LA English
DT Review
DE Osteoarthritis; Knee OA; SIOT position statement; Non-surgical management
ID oarsi recommendations; american-college; european-society; economic-aspects; spa therapy; hip; osteoporosis; stimulation; guidelines; consensus
AB BackgroundKnee osteoarthritis (OA) is a chronic disease associated with a severe impact on quality of life. However, unfortunately, there are no evidence-based guidelines for the non-surgical management of this disease. While recognising the gap between scientific evidence and clinical practice, this position statement aims to present recommendations for the non-surgical management of knee OA, considering the available evidence and the clinical knowledge of experienced surgeons. The overall goal is to offer an evidenced-based expert opinion, aiding clinicians in the management of knee OA while considering the condition, values, needs and preferences of individual patients.MethodsThe study design for this position statement involved a preliminary search of PubMed, Google Scholar, Medline and Cochrane databases for literature spanning the period between January 2021 and April 2023, followed by screening of relevant articles (systematic reviews and meta-analyses). A Societa Italiana Ortopedia e Traumatologia (SIOT) multidisciplinary task force (composed of four orthopaedic surgeons and a rheumatologist) subsequently formulated the recommendations.ResultsEvidence-based recommendations for the non-surgical management of knee OA were developed, covering assessment, general approach, patient information and education, lifestyle changes and physical therapy, walking aids, balneotherapy, transcutaneous electrical nerve stimulation, pulsed electromagnetic field therapy, pharmacological interventions and injections.ConclusionsFor non-surgical management of knee OA, the recommended first step is to bring about lifestyle changes, particularly management of body weight combined with physical exercise and/or hydrotherapy. For acute symptoms, non-steroidal anti-inflammatory drugs

(NSAIDs), topic or oral, can be used. Opioids can only be used as third-line pharmacological treatment. Glucosamine and chondroitin are also suggested as chronic pharmacological treatment. Regarding intra-articular infiltrative therapy, the use of hyaluronic acid is recommended in cases of chronic knee OA [platelet-rich plasma (PRP) as second line), in the absence of active acute disease, while the use of intra-articular injections of cortisone is effective and preferred for severe acute symptoms. NSAIDs (topical or oral formulations) are a better choice for acute symptoms, compared with acetaminophen in knee osteoarthritis non-surgical treatment.SIOT recommend opioid use only while patients are waiting for surgical treatment, if NSAIDs are ineffective against pain.Considering intra-articular infiltrative therapy, the use of hyaluronic acid is recommended in cases of chronic knee OA in the absence of active acute disease, while the use of intra-articular injections of cortisone is effective and preferred for severe acute symptoms.The use of growth factor injections and/or PRP in symptomatic knee OA is only favoured in highly specialised centres
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TI Bone marrow edema of the hip: a narrative review
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Review
DE Bone marrow edema; Hip; Review; Total hip arthroplasty; Core decompression; Avascular necrosis femoral head
ID transient osteoporosis; femoral-head; syndrome/transient osteoporosis; core decompression; avascular necrosis; risk-factors; osteonecrosis; lesions; osteoarthritis; fractures
AB Bone marrow edema (BME) of the hip is a radiological-clinical condition with symptoms ranging from asymptomatic to severe, and it is characterized by

increased interstitial fluid within the bone marrow, usually at the femur. Depending on the etiology it can be classified as primary or secondary. The primary cause of BME is unknown, while the secondary forms include traumatic, degenerative, inflammatory, vascular, infectious, metabolic, iatrogenic, and neoplastic etiologies. BME could be classified as reversible or progressive. Reversible forms include transient BME syndrome and regional migratory BME syndrome. Progressive forms include avascular necrosis of the femoral head (AVNH), subchondral insufficiency fracture, and hip degenerative arthritis. The diagnosis can be difficult, because at the beginning, the outbreak of hip pain, typically acute and disabling without any prior trauma or exceptional physical activity, is poorly supported by radiographic findings. MRI is the gold standard, and it shows an area of intermediate signal on T1-weighted MRI scans and a high signal on T2-weighted scans, usually lacking sharps margins. In the reversible form, BME is typically self-limiting, and it can be managed conservatively by means of pharmacological and physical therapy. Surgery is generally required for progressive forms in patients who failed non-operative treatment, and it ranges from femoral head and neck core decompression to total hip arthroplasty.
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NR 85
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Z9 7
U1 1
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SN 0936-8051
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J9 ARCH ORTHOP TRAUM SU
JI Arch. Orthop. Trauma Surg.
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PT J
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TI MRI-based T1rho and T2 cartilage compositional imaging in osteoarthritis: what

have we learned and what is needed to apply it clinically and in a trial setting?
SO SKELETAL RADIOLOGY
LA English
DT Review
DE Cartilage; MRI; Quantitative imaging; Biomarkers; Osteoarthritis
ID t2 relaxation-time; gadolinium-enhanced mri; focal knee lesions; articular-cartilage; quantitative mri; weight-loss; progression; association; degeneration; t-1-rho
AB Cartilage MRI-based T-1rho and T-2 compositional measurements have been developed to characterize cartilage matrix quality and diagnose cartilage damage before irreversible defects are found, allowing intervention at an early, potentially reversible disease stage. Over the last 2 decades, this technology was investigated in numerous studies and was validated using specimen studies and arthroscopy; and longitudinal studies documented its ability to predict progression of degenerative disease and radiographic osteoarthritis (OA). While T-1rho and T-2 measurements have shown promise in early disease stages, several hurdles have been encountered to apply this technology clinically. These include (i) challenges with cartilage segmentation, (ii) long image acquisition times, (iii) a lack of standardization of imaging, and (iv) an absence of reference databases and definitions of abnormal cut-off values. Progress has been made by developing deep-learning based automatic cartilage segmentation and faster imaging methods, enabling the feasibility of T-1rho and T-2 imaging for clinical and scientific trial applications. Also, the Radiological Society of North America (RSNA) Quantitative Imaging Biomarker Alliance mechanism was used to establish standardized profiles for compositional T-1rho and T-2 imaging, and multi-center feasibility testing is work in progress. The last hurdles are the development of reference databases and establishing a definition of normal versus abnormal cartilage T-1rho and T-2 values. Finally, effective treatments for prevention and slowing progression of OA are required in order to establish T-1rho and T-2 as imaging biomarkers for initiating and monitoring therapies, analogous to the role of dual X-ray absorptiometry (DXA) bone mineral density measurements in the management of osteoporosis.
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NR 66
TC 15
Z9 19
U1 1
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SN 0364-2348
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JI Skeletal Radiol.
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WC Orthopedics; Radiology, Nuclear Medicine & Medical Imaging
SC Orthopedics; Radiology, Nuclear Medicine & Medical Imaging
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AU Li, M
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AF Li, Miao

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TI Integrating network pharmacology and experimental verification strategies to reveal the active ingredients and molecular mechanism of Tenghuang Jiangu Capsule against osteoporosis
SO HELIYON
LA English
DT Article
DE Teng Huang Jian Gu capsule (THJGC); Osteoporosis; Network pharmacology; Bone formation; Experimental validation
ID oxidative stress; in-vitro; differentiation; kaempferol; management; decoction
AB Tenghuang Jiangu Capsule (THJGC) is a Chinese herbal formula used for the treatment of osteoporosis and osteoarthritis in China, but its mechanism for treating osteoporosis is not clear. The aim of this study was to investigate the therapeutic effect of THJGC on osteoporosis and its intrinsic mechanism through network pharmacology and experimental validation. Drugs and potential targets were obtained from several reliable databases through network pharmacology, and these targets were integrated and analyzed using bioinformatics and molecular docking strategies. Quercetin, lignans and kaempferol were identified as key components, and the key targets included Akt1, MAPKs, and CASP3. Subsequently, UPLC-MS/MS analysis confirmed the presence of components in THJGC for the treatment of osteoporosis. In addition, using ex vivo and in vivo models, it was confirmed that THJGC inhibited H2O2-induced ROS generation and apoptosis, and reduced OVX-induced bone loss in a mouse model of osteoporosis. Our data suggest that THJGC has antioxidant, bone formation-promoting, bone resorption-inhibiting, and MC3T3-E1 apoptosis-reducing effects, and thus has anti-osteoporotic properties. In conclusion, it may be a promising pharmacologic adjuvant treatment for osteoporosis.
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NR 41
TC 6
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U1 1
U2 15
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JI Heliyon
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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PT J
AU Ma, MX
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Lu, Xiaoshuai
Yue, Chen
Zhang, Xue
TI Mesenchymal stem cell-derived extracellular vesicles, osteoimmunology and orthopedic diseases
SO PEERJ
LA English
DT Article
DE Mesenchymal stem cell; Extracellular vesicles; Osteoimmunology; Orthopedic diseases
ID in-vitro; bone; exosm; osteonecrosis; inflammation; osteoarthritis; osteoclastogenesis; pathophysiology; differentiation; degeneration
AB Mesenchymal stem cells (MSCs) play an important role in tissue healing and regenera-tive medicine due to their self-renewal and multi-directional differentiation properties. MSCs exert their therapeutic effects mainly via the paracrine pathway, which involves the secretion of extracellular vesicles (EVs). EVs have a high drug loading capacity and can transport various molecules, such as

proteins, nucleic acids, and lipids, that can modify the course of diverse diseases. Due to their ability to maintain the therapeutic effects of their parent cells, MSC-derived EVs have emerged as a promising, safe cell-free treatment approach for tissue regeneration. With advances in inflammation research and emergence of the field of osteoimmunology, evidence has accumulated pointing to the role of inflammatory and osteoimmunological processes in the occurrence and progression of orthopedic diseases. Several studies have shown that MSC-derived EVs participate in bone regeneration and the pathophysiology of orthopedic diseases by regulating the inflammatory environment, enhancing angiogenesis, and promoting the differentiation and proliferation of osteoblasts and osteoclasts. In this review, we summarize recent advances in the application and functions of MSC-derived EVs as potential therapies against orthopedic diseases, including osteoarthritis, intervertebral disc degeneration, osteoporosis and osteonecrosis.
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TI Harnessing Stem Cell-Derived Extracellular Vesicles for the Regeneration of Degenerative Bone Conditions
SO INTERNATIONAL JOURNAL OF NANOMEDICINE
LA English
DT Review
DE nanomedicine; extracellular vesicles; stem cells; regeneration; therapy
ID intervertebral disc degeneration; inflammation; exosm; tissue; osteoarthritis; pathogenesis; osteoporosis; cartilage; protect; biology
AB Degenerative bone disorders such as intervertebral disc degeneration (IVDD), osteoarthritis (OA), and osteoporosis (OP) pose significant health challenges for aging populations and lack effective treatment options. The field of regenerative medicine holds promise in addressing these disorders, with a focus on utilizing extracellular vesicles (EVs) derived from stem cells as an innovative therapeutic approach. EVs have shown great potential in stimulating biological responses, making them an attractive candidate for rejuvenating degenerative bone disorders. However, a comprehensive review summarizing the current state of this field and providing a clear assessment of EV-based therapies in degenerative bone disorders is currently deficient. In this review, we aim to fill the existing gap by outlining the current knowledge on the role of EVs derived from different types of stem cells, such as mesenchymal stem cells, embryonic stem cells, and induced pluripotent stem cells, in bone regeneration. Furthermore, we discuss the therapeutic potential of EV-based treatments for IVDD, OA, and OP. By substantiating the use of stem cell-derived EVs, we highlight their promising potential as a cell-free strategy to improve degenerative bone disorders.
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Wen, Chiung-Jung
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TI Urban-rural differences in outcomes and management of vertebral fractures: A real- world observational study
SO JOURNAL OF THE FORMOSAN MEDICAL ASSOCIATION
LA English
DT Article

DE Fracture liaison service; Osteoporosis; Vertebral fracture; Urban-rural differences
ID bone-mineral density; hip fracture; increased mortality
AB Background: A fracture liaison services (FLSs) and its modified services reduce refractures and mortality and can be cost-effective. Limited studies have addressed whether urban-rural dif-ferences exist in vertebral fracture outcomes and management. Therefore, the aims of the study were to investigate any urban-rural differences in refracture, mortality, prescription pattern, and associated factors of vertebral fractures after receiving assistance from an FLSs. Methods: Baseline characteristics and osteoporosis medication prescription patterns of partic-ipants were collected. After 1-year follow-up, mortality, refracture rate, and osteoporosis medication switching and adherence were evaluated. Multivariate logistic regressions were performed to identify baseline correlates on one-year mortality. Results: There was higher mortality rate in the rural group but no urban-rural difference in the 1-year refracture rate after implementation of FLSs and medication management services (MMSs). The types of osteoporosis medications prescribed for both groups were similar, but participants in the rural group were less likely to change their osteoporosis medications during the 1-year follow-up timeframe and with lower adherence rate. The likelihood of being older and having chronic kidney disease, osteoarthritis, and neurological disease was higher in the rural group. Conclusion: Our multicomponent services have similar effectiveness in osteoporosis treatment between urban and rural areas. The overall adherence rate was lower in the rural group with higher mortality but no difference in the refracture rate in one year. Copyright 2022, Formosan Medical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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TI Unlock the power of bovine milk-derived exosomes for degenerative diseases associated with aging
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LA English
DT Article
DE Bovine milk-derived exosomes; Aging; Identification and labeling; Application
ID parkinsons-disease; extracellular vesicles; oral delivery; dairy foods; microrna; risk; mechanisms; expression; system; growth
AB Bovine milk-derived exosomes (BMDEs) have emerged as a fruitful area of investigation in age-related disease therapeutics. Through the utilization of BMDEs, researchers possess the capacity to unveil novel treatments and therapeutic interventions that have the potential to enhance the quality of life for elderly individuals across the globe. Studies have provided evidence of the efficacy of BMDEs in facilitating the regenerative processes of bone and cartilage, thus establishing their potential as a viable therapeutic avenue for addressing conditions like osteoarthritis. Although BMDEs show promise as a prospective research route for tackling age-related illnesses, including Parkinson's disease, osteoporosis, and skin rejuvenation, other unanswered questions still demand more exploration. Concerns have been raised regarding the safety and efficacy of BMDEs, especially regarding their human administration, and researchers must

carefully examine these concerns to identify alternatives. In conclusion, BMDEs are an area ripe for investigation into the prevention and treatment of age-related diseases.
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TI Management of bone diseases: looking at scaffold-based strategies for drug delivery
SO DRUG DELIVERY AND TRANSLATIONAL RESEARCH
LA English
DT Review
DE Scaffolds; Local drug delivery; Bone diseases; Bone regeneration
ID of-the-art; chronic osteomyelitis; hyaluronic-acid; regeneration; hydrogel;

system; biomaterials; tgf-beta-3; efficacy
AB The bone tissue can regenerate itself completely and continuously; however, large-scale bone defects may overpower this self-regenerative process. Furthermore, the aging population, the increment in obesity incidence, and the sedentary lifestyles are serious risk factors for bone diseases' development which are associated with the self-regenerative process's failure, high morbidity, and mortality rates. Thus, there is an ever-growing need for strategic approaches targeting bone replacement, its remodelling, and its regeneration. Bone scaffolds have successfully been used as synthetic bone grafts for many years, yet recent bone tissue engineering strategies attempt to explore their multifunctionality by investigating them as drug delivery systems. Bone diseases' treatments can be substantially difficult due to the avascular nature of the surrounding cartilage; thus, targeted drug delivery to the bone can be advantageous: it provides local high drug concentrations and minimizes adverse effects while securing a space for new, healthy tissue growth. Despite the promising scientific progress, studies underlining bone scaffolds' use as local drug delivery systems are not abundant. Hence, this work reviews bone scaffolds' therapeutic interest for local drug delivery in five distinct bone disorders-osteomyelitis, osteoporosis, osteoarthritis, osteosarcoma, and cancer bone metastasis. Additionally, it presents the challenges of this possible therapeutic approach and its future perspectives. Albeit bone scaffolds present therapeutic benefits by acting as drug delivery systems, further pre-clinical and clinical assessments are needed to strengthen their understanding and enable research evidence translation into clinical practice. The mismatch between scientific evolution and regulatory frameworks remains one of the major future challenges.
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NR 81
TC 14
Z9 16
U1 2
U2 39
PU SPRINGER HEIDELBERG
PI HEIDELBERG
PA TIERGARTENSTRASSE 17, D-69121 HEIDELBERG, GERMANY
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J9 DRUG DELIV TRANSL RE
JI Drug Deliv. Transl. Res.
PD JAN 15
PY 2023
VL 13
IS 1
BP 79
EP 104
DI 10.1007/s13346-022-01191-w
EA JUL 2022
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WC Instruments & Instrumentation; Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Instruments & Instrumentation; Research & Experimental Medicine; Pharmacology & Pharmacy
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UT WOS:000825082300002

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PT J
AU Yoon, HK
Choi, MH
Lee, H
Park, J
Ahn, J
AF Yoon, Hyung Ku
Choi, Min-Ho
Lee, Ho
Park, Jinyong
Ahn, Joosuk
TI Subchondral stress fracture of the femoral head (SSFFH) in young and healthy military recruits: clinical recommendations and fracture configurations on MRI
SO INTERNATIONAL ORTHOPAEDICS
LA English
DT Article
DE Subchondral stress fracture of the femoral head; Stress fracture; SSFFH; Fatigue type; Military
ID bone-marrow edema; insufficiency fracture; transient osteoporosis; avascular necrosis; osteonecrosis; hip; joint
AB PurposeThis study aimed to evaluate the clinical and radiologic characteristics of the fatigue-type of SSFFH in healthy military recruits.Materials and methodWe retrospectively analyzed 39 hips from 32 patients who were treated for SSFFH between 2014 and 2018. Clinical variables were analyzed. We devised a categorization system that divided SSFFH into five types (A-E) according to the extent of the fracture line MRI axial view. The femoral head was divided into three parts for the categorization: the anterior third, middle third, and posterior third.ResultsThe included patients were 39 hips from 32 patients with the mean age 22.3 years. Almost all patients with SSFFH (96.9%) complained of hip pain with limping at the time of diagnosis. The mean time to the onset of the hip pain from the beginning of military training was 24.8 days. There were seven patients (21.9%) with concomitant stress fractures on whole-body bone scan. Six hips (15.4%) developed osteoarthritis and required surgery. Almost all the cases (94.9%) involved the anterior compartment of the femoral head.ConclusionsMilitary recruits with the hip pain and limping within one month of military training should undergo detailed evaluation. A whole-body bone scan with SPECT is useful for identifying other concomitant stress fractures. Majority of SSFFH involved the anterior compartment of the femoral head.
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10.1007/s11999-011-2209-z
NR 33
TC 4
Z9 5
U1 1
U2 5
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 0341-2695
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J9 INT ORTHOP
JI Int. Orthop.
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DI 10.1007/s00264-023-05739-4
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WC Orthopedics
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PT J
AU Xu, TP
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Li, Bin
Zhao, Xin
TI Injectable, Self-Contained, Subaqueously Cross-Linking Laminous Adhesives for Biophysical-Chemical Modulation of Osteochondral Microenvironment
SO ADVANCED FUNCTIONAL MATERIALS
LA English
DT Article
DE cell microenvironments; injectable adhesives; osteochondral regeneration; subaqueous cross-linking
ID stem-cell differentiation; mechanical-property; articular-cartilage; growth-factors; chondrogenesis; hydrogel; proliferation; regeneration; pathway; bmp-2
AB Current osteochondral (OC) defect repair approaches using premade scaffolds face clinical limitations due to invasiveness, weak integrity, and/or insufficient interfacial bonding. An injectable hydrophobic laminous adhesive is developed that rapidly photocross-link subaqueously and forms robust bi-layered structure that orchestrates biophysical-chemical cues for stimulating OC repair. Liquid hydrophobic photo-cross-linkable poly (lactide-co-propylene glycol-co-lactide) dimethacrylates (P(m)L(n)DMA) are adopted as cartilage phase and P(m)L(n)DMA encapsulating methacrylated hydroxyapatite nanoparticles (P(m)L(n)DMA/MH) as the mineralized subchondral bone phase. Both phases exhibit strong interfacial bonding due to the presence of "C(sic)C". Mechanotransduction and growth factor-mediated signaling pathways are enchanced by matching the mechanical properties of two phases to native cartilage and bone via systematical modulation of the adhesives' composition and encapsulated growth factors' release profile. This enhances mesenchymal stem cells' commitment to corresponding chondrocytes and osteoblasts to augment OC repair in vitro and in vivo, and ultimately benefits patients suffering from OC fracture, osteoarthritis, and osteoporosis.
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NR 55
TC 11
Z9 11

U1 11
U2 141
PU WILEY-V C H VERLAG GMBH
PI WEINHEIM
PA POSTFACH 101161, 69451 WEINHEIM, GERMANY
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EI 1616-3028
J9 ADV FUNCT MATER
JI Adv. Funct. Mater.
PD JUN 15
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DI 10.1002/adfm.202213428
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WC Chemistry, Multidisciplinary; Chemistry, Physical; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary; Physics, Applied; Physics, Condensed Matter
SC Chemistry; Science & Technology - Other Topics; Materials Science; Physics
GA H8TX6
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PT J
AU Sophocleous, A
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Huesa, C
Stylianou, E
Ralston, SH
AF Sophocleous, Antonia
Azfer, Asim
Huesa, Carmen
Stylianou, Eleni
Ralston, Stuart H.
TI Probiotics Inhibit Cartilage Damage and Progression of Osteoarthritis in Mice
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Microbiome; Probiotics; DMM; Osteoarthritis
ID bone-formation

AB Increasing interest has focussed on the possible role of alterations in the microbiome in the pathogenesis of metabolic disease, inflammatory disease, and osteoporosis. Here we examined the role of the microbiome in a preclinical model of osteoarthritis in mice subjected to destabilisation of medical meniscus (DMM). The intestinal microbiome was depleted by broad-spectrum antibiotics from 1 week before birth until the age of 6 weeks when mice were subjected reconstitution of the microbiome with faecal microbial transplant (FMT) followed by the administration of a mixture of probiotic strains Lacticaseibacillus paracasei 8700:2, Lactiplantibacillus plantarum HEAL9 and L. plantarum HEAL19 or vehicle. All mice were subjected to DMM at the age of 8 weeks. The severity of osteoarthritis was evaluated by histological analysis and effects on subchondral bone were investigated by microCT analyses. The combination of FMT and probiotics significantly inhibited cartilage damage at the medial femoral condyle such that the OARSI score was 4.64 +/- 0.32 (mean +/- sem) in the FMT and probiotic group compared with 6.48 +/- 0.53 in the FMT and vehicle group ($p = 0.007$). MicroCT analysis of epiphyseal bone from the femoral condyle showed that the probiotic group had higher BV/TV, increased Tb.Th, and moderately thicker subchondral bone plates than the control group. There was no difference between groups in joint inflammation or in serum concentrations of inflammatory cytokines and chemokines. We conclude that treatment with probiotics following FMT in mice where the microbiome has been depleted inhibits DMM-induced cartilage damage and impacts on the structure of subchondral bone particularly at the femoral condyle. While further studies are required to elucidate the mechanism of action, our research suggests that these probiotics may represent a novel intervention for the treatment of osteoarthritis.
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SC Endocrinology & Metabolism
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PT J
AU Wakelin, EA
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AF Wakelin, Edgar A.
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TI Intra-operative laxity and balance impact 2-year pain outcomes in TKA: a prospective cohort study
SO KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY
LA English
DT Article
DE Total knee arthroplasty; Joint balance; Laxity; Outcome; 2 Years; Robotics; Digital balancer

ID total knee arthroplasty; functional outcm; clinical-outcm; alignment
AB Purpose The objective of this study was to determine if intra-operatively measured joint gaps are associated with 2-year pain outcomes in total knee arthroplasty (TKA) and whether balance and laxity windows could be defined throughout flexion to optimize 2-year pain outcomes. Our hypothesis is that intra-operative joint gaps are associated with 2 year post-operative pain outcome. Methods A prospective study investigating 310 robotically assisted TKAs was performed. Final intra-operative joint gap data were recorded using a digital tensioner and component alignment data were recorded by the robotics system. Patient demographics and Knee Injury and Osteoarthritis Outcome Score (KOOS) were recorded pre-operatively and KOOS and Hospital for Special Surgery (HSS) satisfaction were recorded at 2 years post-op. A random search Simulated Annealing (SANN) optimisation algorithm was used to determine global optimum laxity and balance windows at different flexion angles which maximized the 2-year KOOS pain scores. The windows were combined to determine the impact of achieving optimal laxity and balance throughout flexion. To improve clinical utility, boundaries identified by the SANN algorithm were rounded to the nearest 0.5 mm before statistical analysis. Results Laxity and balance windows were defined in extension (Med lax: -2.0 to 2.5 mm, Lat lax: -0.5 to 2.5 mm, Balance: -3.0 to 0.0 mm), mid-flexion (Med lax: -1.0 to 2.5 mm, Lat lax: -0.5 to 3.0 mm, Balance: -2.0 to 2.0 mm), and flexion (Med lax: -2.0 to 3.5 mm, Lat lax: -2.0 to 1.5 mm, Balance: -3.0 to 3.0 mm). When all windows were satisfied, the greatest difference in KOOS pain score was observed (100.0 vs 94.4, $p<0.0001$). The highest percentage of knees satisfying the Patient Acceptable Symptom State (PASS) for KOOS pain was also observed in knees which satisfied all windows compared to knees which did not (93% vs 71%, $p=0.0009$). The proportion of knees which satisfy the PASS threshold decreased in knees which only satisfied 1-3 (29%) or 4-6 (69%) windows ($p <= 0.0018$). No optimal windows were found between component alignment and KOOS pain outcome ($p >= 0.1180$). High satisfaction was found across all groups (>= 95%). Conclusion Intra-operatively measured joint gaps are associated with all KOOS sub-score outcomes at 2 years after TKA. Optimal windows for a clinically relevant improvement in post-operative KOOS pain were defined for laxity and balance but not for alignment indicating balance may have a greater impact on outcome than alignment.
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TC 23
Z9 23
U1 0
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AU Jung, UJ
AF Jung, Un Ju
TI Sarcopenic Obesity: Involvement of Oxidative Stress and Beneficial Role of

Antioxidant Flavonoids
SO ANTIOXIDANTS
LA English
DT Review
DE sarcopenic obesity; pathophysiology; oxidative stress; flavonoids
ID endoplasmic-reticulum stress; activated protein-kinase; skeletal-muscle atrophy; diet-induced obesity; onion peel extract; nf-kappa-b; mitochondrial dysfunction; molecular-mechanisms; adipose-tissue; er stress
AB Sarcopenic obesity, which refers to concurrent sarcopenia and obesity, is characterized by decreased muscle mass, strength, and performance along with abnormally excessive fat mass. Sarcopenic obesity has received considerable attention as a major health threat in older people. However, it has recently become a health problem in the general population. Sarcopenic obesity is a major risk factor for metabolic syndrome and other complications such as osteoarthritis, osteoporosis, liver disease, lung disease, renal disease, mental disease and functional disability. The pathogenesis of sarcopenic obesity is multifactorial and complicated, and it is caused by insulin resistance, inflammation, hormonal changes, decreased physical activity, poor diet and aging. Oxidative stress is a core mechanism underlying sarcopenic obesity. Some evidence indicates a protective role of antioxidant flavonoids in sarcopenic obesity, although the precise mechanisms remain unclear. This review summarizes the general characteristics and pathophysiology of sarcopenic obesity and focuses on the role of oxidative stress in sarcopenic obesity. The potential benefits of flavonoids in sarcopenic obesity have also been discussed.
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TI Roles of focal adhesion proteins in skeleton and diseases
SO ACTA PHARMACEUTICA SINICA B
LA English
DT Review
DE Focal adhesion; Skeleton; Mechanotransduction; Signal transduction; Integrin; Cartilage; Intervertebral disc; Skeletal diseases
ID nucleus pulposus cells; integrin-linked kinase; annulus fibrosus cells; bone-resorption; osteogenic differentiation; matrix interactions; gene-expression; mice lacking; promotes; alpha-5-beta-1
AB The skeletal system, which contains bones, joints, tendons, ligaments and other elements, plays a wide variety of roles in body shaping, support and movement, protection of internal organs, pro-duction of blood cells and regulation of calcium and phosphate metabolism. The prevalence of skeletal diseases and disorders, such as osteoporosis and bone fracture, osteoarthritis, rheumatoid arthritis, and intervertebral disc degeneration, increases with age, causing pain and loss of mobility and creating a huge social and economic burden globally. Focal adhesions

(FAs) are macromolecular assemblies that are composed of the extracellular matrix (ECM), integrins, intracellular cytoskeleton and other proteins, including kindlin, talin, vinculin, paxillin, pinch, Src, focal adhesion kinase (FAK) and integrin-linked protein kinase (ILK) and other proteins. FA acts as a mechanical linkage connecting the ECM and cyto-skeleton and plays a key role in mediating cell-environment communications and modulates important processes, such as cell attachment, spreading, migration, differentiation and mechanotransduction, in different cells in skeletal system by impacting distinct outside-in and inside-out signaling pathways. This review aims to integrate the up-to-date knowledge of the roles of FA proteins in the health and disease of skeletal system and focuses on the specific molecular mechanisms and underlying therapeutic targets for skeletal diseases.
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TI Real-world evidence: new opportunities for osteoporosis research.

Recommendations from a Working Group from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)
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LA English
DT Article
DE Drug effectiveness; Fracture; Osteoporosis; Real-world evidence; Epidemiology; Registry
ID medication adherence; patient registry; bone-density; fractures; risk; identification; epidemiology; alendronate; validation; therapy
AB This narrative review summarises the recommendations of a Working Group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) for the conduct and reporting of real-world evidence studies with a focus on osteoporosis research. Purpose Vast amounts of data are routinely generated at every healthcare contact and activity, and there is increasing recognition that these real-world data can be analysed to generate scientific evidence. Real-world evidence (RWE) is increasingly used to delineate the natural history of disease, assess real-life drug effectiveness, understand adverse events and in health economic analysis. The aim of this work was to understand the benefits and limitations of this type of data and outline approaches to ensure that transparent and high-quality evidence is generated. Methods A ESCEO Working Group was convened in December 2022 to discuss the applicability of RWE to osteoporosis research and approaches to best practice. Results This narrative review summarises the agreed recommendations for the conduct and reporting of RWE studies with a focus on osteoporosis research. Conclusions It is imperative that research using real-world data is conducted to the highest standards with close attention to limitations and biases of these data, and with transparency at all stages of study design, data acquisition and curation, analysis and reporting to increase the trustworthiness of RWE study findings.
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ID skeletal-muscle atrophy; kappa-b; antisense oligonucleotide; rheumatoid-arthritis; synovial fibroblasts; glucose-uptake; tnf-alpha; bone loss; osteoporosis; osteoarthritis
AB Age-related disorders of the musculoskeletal system including sarcopenia, osteoporosis and arthritis represent some of the most common chronic conditions worldwide, for which there remains a great clinical need to develop safer and more efficacious pharmacological treatments. Collectively, these conditions involve multiple tissues, including skeletal muscle, bone, articular cartilage and the synovium within the joint lining. In this review, we discuss the potential for oligonucleotide therapies to combat the unmet clinical need in musculoskeletal disorders by evaluating the successes of oligonucleotides to modify candidate pathological gene targets and cellular processes in relevant tissues and cells of the musculoskeletal system. Further, we discuss the challenges that remain for the clinical development of oligonucleotides therapies for musculoskeletal disorders and evaluate some of the current approaches to overcome these.
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NR 143
TC 7
Z9 7

U1 2
U2 8
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 1999-4923
J9 PHARMACEUTICS
JI Pharmaceutics
PD JAN 15
PY 2023
VL 15
IS 1
BP
EP
DI 10.3390/pharmaceutics15010237
PG 19
WC Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
GA 8R3EG
UT WOS:000927776900001
PM 36678864
DA 2026-02-10
ER

PT J
AU Ruan, CY
Jiang, WY
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TI Analysis of risk factors for axial symptoms after posterior cervical open-door laminoplasty
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Cervical spondylotic myelopathy; Laminoplasty; Axial symptoms; Risk factors;

Cutoff value
ID longitudinal ligament; compressive myelopathy; spondylotic myelopathy; joint pain; neck pain; ossification; decompression; preservation; alignment; anterior
AB BackgroundLaminoplasty (LP), a procedure commonly used to treat cervical spondylotic myelopathy (CSM), often results in the development of axial symptoms (AS) postoperatively. This study aims to analyze the risk factors associated with the occurrence of AS after LP.MethodsWe collected and evaluated clinical data from 264 patients with CSM who underwent LP treatment at our institution from January 2018 to January 2022 through a single-center retrospective study. Of the patients, 153 were male and 111 were female, with an average age of 58.1 +/- 6.7 years. All patients underwent C3-7 posterior laminoplasty. Based on the occurrence of postoperative axial symptoms, the patients were divided into an AS group and a non-AS group. General information, including age, gender, disease duration, Japanese Orthopaedic Association (JOA) score, postoperation early function training, and collar-wearing time, was recorded and compared between the two groups. Surgical-related data, such as operative segments, surgical time, intraoperative blood loss, intraoperative facet joint destruction, and destruction of the C7 spinous process muscle insertion, were also compared. Imaging data, including preoperative cervical curvature, cervical range of motion, preoperative encroachment rate of the anterior spinal canal, and angle of laminar opening, were collected. Univariate and multivariate logistic regression analyses were used to identify risk factors for the development of AS after LP, and receiver operator characteristic (ROC) curves were utilized to explore the optimal preoperative parameters.ResultsAll 264 patients successfully underwent surgery and were followed up for an average of 19.5 +/- 6.8 months. At the 6-month follow-up, 117 patients were diagnosed with AS, resulting in an incidence rate of 40.2%. The multivariate logistic regression analysis identified that preoperative encroachment rate of anterior spinal canal (Pre-op ERASC), intraoperative facet joints destruction (Intra-op FJD), intraoperative open-door angle (Intra-op OA), destroy the C7 spinous process muscle insertion (Destroy C7 SPMI), postoperative loss of cervical curvature (Post-op LCC), and postoperative loss of cervical range of motion (Post-op LCROM) were independent risk factors for AS. Conversely, preoperative cervical curvature (Pre-op CC) and postoperation early function training (Post-op EFT) were protective factors against AS. According to the ROC curve, the cutoff values for preoperative anterior spinal canal occupation rate and preoperative cervical curvature were 28.5% and 16.5 degrees, respectively. When the preoperative anterior spinal canal occupation rate was greater than 28.5% or the preoperative cervical curvature was less than 16.5 degrees, AS was more likely to occur after surgery.ConclusionHigh preoperative anterior spinal canal occupation rate, facet joint damage during surgery, C7 spinous process muscle stop point damage, larger angle of laminar opening, and greater postoperative cervical curvature loss and cervical range of motion loss are associated with an increased risk of developing AS after cervical laminoplasty. Conversely, a larger preoperative cervical curvature and early postoperative functional exercises can help reduce the

occurrence of AS.
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NR 37
TC 14
Z9 16
U1 0
U2 5
PU BMC
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN 1749-799X
EI
J9 J ORTHOP SURG RES
JI J. Orthop. Surg. Res.
PD DEC 11
PY 2023
VL 18
IS 1
BP
EP
DI 10.1186/s13018-023-04426-9
PG 11
WC Orthopedics
SC Orthopedics
GA CF0Y8
UT WOS:001123730900001
PM 38082364
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AU Ryou, IS
Lee, SW
Mun, H
Lee, JK

Chun, S
Cho, K
AF Ryou, In Sun
Lee, Sang Wha
Mun, Hanbit
Lee, Jae Kwang
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TI Trend of incidence rate of age-related diseases: results from the National Health Insurance Service-National Sample Cohort (NHIS-NSC) database in Korea: a cross-sectional study
SO BMC GERIATRICS
LA English
DT Article
DE Age-related disease; Senescence cell; Burden of disease; Disability-adjusted life-years
ID burden
AB BackgroundThis study aimed to identify and select age-related diseases (ARDs) in Korea, which is about to have a super-aged society, and to elucidate patterns in their incidence rates.MethodsThe National Health Insurance Service-National Sample Cohort, comprising 1 million health insurance and medical benefit beneficiaries in Korea from 2002 to 2019, was utilized. We selected 14 diseases with high disease burden and prevalence among Koreans from the 92 diseases defined in the Global Burden of Diseases, Injuries, and Risk Factors Study as ARDs. The annual incidence rate represented the number of patients newly diagnosed with an ARD each year from 2006 to 2019, excluding those with a history of ARD diagnosis from 2002 to 2005. The incidence rate by age was categorized into 10-year units based on age as of 2019. The number of patients with ARDs in each age group was used as the numerator, and the incidence rate for each age group was calculated with the age group as the denominator.ResultsRegarding the annual incidence rates of ARDs from 2006 to 2019, chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease decreased annually, whereas dyslipidemia, chronic kidney disease, cataracts, hearing loss, and Parkinson's disease showed a significant increase. Hypertension, diabetes, cerebrovascular disease, osteoporosis, osteoarthritis, and age-related macular degeneration initially displayed a gradual decrease in incidence but exhibited a tendency to increase after 2015. Concerning age-specific incidence rates of ARDs, two types of curves emerged. The first type, characterized by an exponential increase with age, was exemplified by congestive heart failure. The second type, marked by an exponential increase peaking between ages 60 and 80, followed by stability or decrease, was observed in 13 ARDs, excluding congestive heart failure. However, hypertension, ischemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, and hearing loss in men belonged to the first type.ConclusionsFrom an epidemiological perspective, there are similar characteristics in age-specific ARDs

that increase with age, reaching a peak followed by a plateau or decrease in Koreans.
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FU National Health Insurance Service Ilsan Hospital Fund
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NR 32
TC 5
Z9 7
U1 2
U2 5
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1471-2318
J9 BMC GERIATR
JI BMC Geriatr.
PD DEC 12
PY 2023
VL 23
IS 1
BP
EP
DI 10.1186/s12877-023-04578-7
PG 11
WC Geriatrics & Gerontology; Gerontology
SC Geriatrics & Gerontology
GA CK1V0
UT WOS:001125063700001
PM 38087197
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ER

PT J
AU Qu, YD
Chen, SB
Han, ML
Gu, ZQ
Zhang, YJ
Fan, TX
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Yang, Q
Ding, CH

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Zhu, ZH
AF Qu, Yudun
Chen, Shibo
Han, Mengling
Gu, Ziqi
Zhang, Yujie
Fan, Tianxiang
Zeng, Muhui
Ruan, Guangfeng
Cao, Peihua
Yang, Qian
Ding, Changhai
Zhang, Yan
Zhu, Zhaohua
TI Osteoporosis and osteoarthritis: a bi-directional Mendelian randomization study
SO ARTHRITIS RESEARCH & THERAPY
LA English
DT Article
DE Osteoporosis; Osteoarthritis; Mendelian randomization; Gene ontology enrichment analyses; Expression quantitative trait locus analyses
ID bone-mineral density; radiographic osteoarthritis; subchondral bone; knee; risk; hip; bmd; metaanalysis; association; incident
AB ObjectiveTo investigate the causal relationship between low bone mineral density (BMD) and osteoarthritis (OA) using Mendelian randomization (MR) design.MethodsTwo-sample bi-directional MR analyses were performed using summary-level information on OA traits from UK Biobank and arcOGEN. Sensitivity analyses including MR-Egger, simple median, weighted median, MR pleiotropy residual sum, and outlier approaches were utilized in conjunction with inverse variance weighting (IVW). Gene ontology (GO) enrichment analyses and expression quantitative trait locus (eQTL) colocalization analyses were used to investigate the potential mechanism and shared genes between osteoporosis (OP) and OA.ResultsThe IVW method revealed that genetically predicted low femoral neck BMD was significantly linked with hip (beta = 0.105, 95% CI: 0.023-0.188) and knee OA (beta = 0.117, 95% CI: 0.049-0.184), but not with other site-specific OA. Genetically predicted low lumber spine BMD was significantly associated with OA at any sites (beta = 0.048, 95% CI: 0.011-0.085), knee OA (beta = 0.101, 95% CI: 0.045-0.156), and hip OA (beta = 0.150, 95% CI: 0.077-0.224). Only hip OA was significantly linked with genetically predicted reduced total bone BMD (beta = 0.092, 95% CI: 0.010-0.174). In the reverse MR analyses, no evidence for a causal effect of OA on BMD was found. GO enrichment analysis and eQTL analysis illustrated that DDN and SMAD-3 were the most prominent co-located genes.ConclusionsThese findings suggested that OP may be causally linked to an increased risk of OA, indicating that measures to raise BMD may be effective in

preventing OA. More research is required to determine the underlying processes via which OP causes OA.
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NR 45
TC 31
Z9 33
U1 3
U2 21
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN 1478-6354
EI 1478-6362
J9 ARTHRITIS RES THER
JI Arthritis Res. Ther.
PD DEC 13
PY 2023
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IS 1
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DI 10.1186/s13075-023-03213-5
PG 11
WC Rheumatology
SC Rheumatology
GA CH8Q4
UT WOS:001124458200001
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ER

PT J
AU Lee, YJ
Kim, YG
AF Lee, Yeo-Jin
Kim, Yong-Gil
TI Subchondral insufficiency fracture of the femoral head in a patient with ankylosing spondylitis: Case report and literature review
SO INTERNATIONAL JOURNAL OF RHEUMATIC DISEASES
LA English
DT Review
DE ankylosing spondylitis; femoral head; subchondral insufficiency fracture
AB Subchondral insufficiency fracture (SIF) of the femoral head occurs in patients with osteoporosis, elderly women, and renal or liver transplant recipients. Although SIF has been reported in several patients with rheumatic disease, SIF of the femoral head has not been reported in patients with ankylosing spondylitis (AS), and the

association between AS and SIF has not been determined. A 48-year-old man with AS presented with pain in his left hip for 2 months. He had been diagnosed with AS and radiographic bilateral grade 3 sacroiliitis 11 years earlier. He had been treated with subcutaneous adalimumab 40 mg biweekly for more than 10 years, during which time his condition remained stable. This patient was obese but had no other known predisposing conditions, such as old age, overexertion, osteoporosis, steroid use, or transplantation. He had never taken steroids. X-rays showed no specific findings, other than mild osteoarthritis in both hips. However, pelvic magnetic resonance imaging demonstrated flattening and subchondral irregularity with a large amount of bone marrow edema, confirming a diagnosis of SIF of the femoral head. Thus, even in patients with AS having no significant risk factors, SIF should be considered as part of the differential diagnosis of hip pain.
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U2 5
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PT J
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Jang, I
AF Kwak, Yeunhee
Jang, Insil
TI Exploring factors influencing health-related quality of life in adult females with injuries: a cross-sectional nationwide study
SO FRONTIERS IN PUBLIC HEALTH
LA English
DT Article
DE women; injury; quality of life; middle age; health promotion
ID road traffic injury; osteoarthritis; knee
AB ObjectivesThis study aimed to identify the types of injury experiences affecting

adult females and the associations between injury experiences and health-related quality of life.MethodsThis study used a secondary analysis of cross-sectional data from the Korea National Health and Nutrition Examination Survey, which employed a stratified multistage probability sampling design to obtain nationally representative data. Health-related quality of life was measured with the EuroQol Five-Dimension and consisted of mobility, self-care, usual activity, pain/discomfort, and anxiety/depression.ResultsAmong women aged 19-64, the prevalence of injury experience was 5.9%. Women's injury experience varied by age, subjective health perception, menstruation details, osteoporosis status, and osteoarthritis status. The following injury experience-related factors were significantly associated with health-related quality of life: self-care (odds ratio [OR] = 0.32, 95% confidence interval [CI]: 0.17-0.60), usual activity (OR = 0.43, 95% CI: 0.27-0.70), and pain/discomfort (OR = 0.56, 95% CI: 0.44-0.72).ConclusionHealth-related quality of life among adult women was significantly associated with injury experience. The results of this study highlight risk factors for injury that are associated with aging, such as menopause, osteoporosis, and osteoarthritis. Accurate assessments of pain and discomfort, as well as daily activities, are essential for designing effective interventions for injured women. Tailored training and education can promote self-management and improve outcomes for recovery.
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FU The authors would like to thank the reviewers for their critical and helpful comments.
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TI Peonidin-3-O-glucoside and Resveratrol Increase the Viability of Cultured Human hFOB Osteoblasts and Alter the Expression of Genes Associated with Apoptosis, Osteoblast Differentiation and Osteoclastogenesis
SO NUTRIENTS
LA English
DT Article
DE apoptosis; Bcl-2; DLX5; HIF1 & alpha;; IL-18; RNA-seq; Rankl; Sp7/osterix; osteoporosis
ID bone-mineral density; growth-factor; cancer cells; osteogenesis; combinations; regulator; synergy; protein; stress; dlx5
AB High-throughput RNA-sequencing can determine the impact of nutrients and their combinations on gene transcription levels in osteocytes, and clarify the biological pathways associated with their impact on bone tissues. Previously, we reported that resveratrol (RES) and peonidin-3-O-glucoside (POG) increased osteoblastogenesis, as well as reduced osteoclastogenesis in transgenic teleost fish models. Here, we perform whole-genome transcriptomic profiling of osteoblasts treated with POG or RES to provide a comprehensive understanding of alterations in gene expression and the molecular mechanisms involved. Cultured human fetal osteoblastic hFOB 1.19 cells were treated with the test compounds, and then RNA was used to prepare RNA-seq libraries, that were sequenced using a NovaSeq 6000. Treatment with POG or RES increased osteoblast proliferation and reduced apoptosis. Transcriptomic profiling showed that of the 29,762 genes investigated, 3177 were differentially expressed (1481 upregulated, 1696 downregulated, FDR = 0.05) in POG-treated osteoblasts. In the RES-treated osteoblasts, 2288 genes were differentially expressed (DGEs, 1068 upregulated, 1220 downregulated, FDR = 0.05). Ingenuity((R)) Pathway Analysis (IPA) of DGEs from RES or POG-treated osteoblasts revealed significant downregulation of the apoptosis, osteoarthritis and HIF1a canonical pathways, and a significant reduction in Rankl mRNA expression. The data suggest that RES and POG have both anabolic and anticlastogenic effects.
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NR 69
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U1 0
U2 3
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AF Heng, Boon Chin
Bai, Yunyang
Li, Xiaochan
Lim, Lee Wei
Li, Wang
Ge, Zigang
Zhang, Xuehui
Deng, Xuliang
TI Electroactive Biomaterials for Facilitating Bone Defect Repair under Pathological Conditions
SO ADVANCED SCIENCE
LA English
DT Review
DE biomaterials; bone; degenerative; disease; electric; scaffold
ID glycation end-products; electrical-stimulation; osteogenic differentiation; composite scaffolds; mineral density; stem-cells; osteoclast differentiation; postmenopausal women; tissue regeneration; angiogenic factors
AB Bone degeneration associated with various diseases is increasing due to rapid aging, sedentary lifestyles, and unhealthy diets. Living bone tissue has bioelectric properties critical to bone remodeling, and bone degeneration under various pathological conditions results in significant changes to these bioelectric properties. There is growing interest in utilizing biomimetic electroactive biomaterials that recapitulate the natural electrophysiological microenvironment of healthy bone tissue to promote bone repair. This review first summarizes the etiology of degenerative bone conditions associated with various diseases such as type II diabetes, osteoporosis, periodontitis, osteoarthritis, rheumatoid arthritis, osteomyelitis, and metastatic osteolysis. Next, the diverse array of natural and synthetic electroactive biomaterials with therapeutic potential are discussed. Putative mechanistic pathways by which electroactive biomaterials can mitigate bone degeneration are critically examined, including the enhancement of osteogenesis and angiogenesis, suppression of inflammation and osteoclastogenesis, as well as their anti-bacterial effects. Finally, the limited research on utilization of electroactive biomaterials in the treatment of bone degeneration associated with the aforementioned diseases are examined. Previous studies have mostly focused on using electroactive biomaterials to treat bone traumatic injuries. It is hoped that this review will encourage more research efforts on the use of electroactive biomaterials for treating degenerative bone conditions.
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NR 229
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PT J
AU Wang, H
AF Wang, Hsiuying
TI The Potential of Collagen Treatment for Comorbid Diseases
SO POLYMERS
LA English
DT Review
DE collagen; disease; inflammation; tissue damage; treatment
ID diabetes-mellitus; osteoporosis; extraction; expression; peptides; gout
AB Collagen, the most abundant protein in our bodies, plays a crucial role in maintaining the structural integrity of various tissues and organs. Beyond its involvement in skin elasticity and joint health, emerging research suggests that collagen may significantly impact the treatment of complex diseases, particularly those associated with tissue damage and inflammation. The versatile functions of collagen, including skin regeneration, improving joint health, and increasing bone strength, make it potentially useful in treating different diseases. To the best of my knowledge, the strategy of using collagen to treat comorbid diseases has not been widely studied. This paper aims to explore the potential of collagen in treating comorbid diseases, including rheumatoid arthritis, osteoarthritis, osteoporosis, psoriatic arthritis, sarcopenia, gastroesophageal reflux, periodontitis, skin aging, and diabetes mellitus. Collagen-based therapies have shown promise in managing comorbidities due to their versatile properties. The multifaceted nature of collagen positions it as a promising candidate for treating complex diseases and addressing comorbid conditions. Its roles in wound healing, musculoskeletal disorders, cardiovascular health, and gastrointestinal conditions highlight the diverse therapeutic applications of collagen in the context of comorbidity management.
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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J9 POLYMERS-BASEL
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AU Sato, M
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TI Contributions of Resin Cast Etching to Visualising the Osteocyte Lacuno-Canalicular Network Architecture in Bone Biology and Tissue Engineering
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Review
DE Bone; Osteocyte; Lacuno-canalicular network; Scanning electron microscopy; Resin cast etching
ID electron-microscopic observations; rabbit cortical bone; transgenic expression; transmission electron; targeted disruption; titanium implants; system; morphology; osseointegration; osteoblasts
AB Recent years have witnessed an evolution of imaging technologies towards sophisticated approaches for visualising cells within their natural environment(s) and for investigating their interactions with other cells, with adjacent anatomical structures, and with implanted biomaterials. Resin cast etching (RCE) is an uncomplicated technique involving sequential acid etching and alkali digestion of resin embedded bone to observe the osteocyte lacuno-canalicular network using scanning electron microscopy. This review summarises the applicability of RCE to bone and the bone-implant interface. Quantitative parameters such as osteocyte size, osteocyte density, and number of canaliculi per osteocyte, and qualitative metrics including osteocyte shape, disturbances in the arrangement of osteocytes and canaliculi, and physical communication between osteocytes and implant surfaces can be investigated. Ageing, osteoporosis, long-term immobilisation, spinal cord injury, osteoarthritis, irradiation, and chronic kidney disease have been shown to impact osteocyte lacuno-canalicular network morphology. In addition to titanium, calcium phosphates, and bioactive glass, observation of direct connectivity between osteocytes and cobalt chromium provides new insights into the osseointegration potential of materials conventionally viewed as non-osseointegrating. Other applications include in vivo and in vitro testing of polymer-based tissue engineering scaffolds and tissue-engineered ossicles, validation of ectopic osteochondral defect models, ex vivo organ culture of whole bones, and observing the effects of gene dysfunction/deletion on the osteocyte

lacuno-canalicular network. Without additional contrast staining, any resin embedded specimen (including clinical biopsies) can be used for RCE. The multitude of applications described here attest to the versatility of RCE for routine use within correlative analytical workflows, particularly in biomaterials science.
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TI Novel insights of EZH2-mediated epigenetic modifications in degenerative musculoskeletal diseases
SO AGEING RESEARCH REVIEWS
LA English
DT Review
DE EZH2; Epigenesis; EZH2 inhibitor; Degenerative musculoskeletal disease
ID intervertebral disc regeneration; mesenchymal stem-cells; zeste homolog 2; skeletal-muscle; osteogenic differentiation; extracellular vesicles; gene-expression; bone-formation; ezh2; osteoarthritis
AB Degenerative musculoskeletal diseases (Osteoporosis, Osteoarthritis, Degenerative Spinal Disease and Sarcopenia) are pathological conditions that affect the function and pain of tissues such as bone, cartilage, and muscles, and are closely associated with ageing and long-term degeneration. Enhancer of zeste homolog 2 (EZH2), an important epigenetic regulator, regulates gene expression mainly through the PRC2-dependent trimethylation of histone H3 at lysine 27 (H3K27me3). Increasing evidence suggests that EZH2 is involved in several biological processes closely related to degenerative musculoskeletal diseases, such as osteogenic-adipogenic differentiation of bone marrow mesenchymal stem cells, osteoclast activation, chondrocyte functional status, and satellite cell proliferation and differentiation, mainly through epigenetic regulation (H3K27me3). Therefore, the synthesis and elucidation of the role of EZH2 in degenerative musculoskeletal diseases have attracted increasing attention. In addition, although EZH2 inhibitors have been approved for clinical use, whether they can be repurposed for the treatment of degenerative musculoskeletal diseases needs to be considered. Here, we reviewed the role of EZH2 in the development of degenerative musculoskeletal diseases and brought forward prospects of its pharmacological inhibitors in the improvement of the treatment of the diseases.

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NR 121
TC 12
Z9 13
U1 3
U2 22
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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J9 AGEING RES REV
JI Ageing Res. Rev.
PD SEP 15
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EA AUG 2023
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WC Cell Biology; Geriatrics & Gerontology
SC Cell Biology; Geriatrics & Gerontology
GA S4EG2
UT WOS:001070709800001
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ER

PT J
AU Han, BX
Yan, SS
Han, Y
Xu, Q
Zhao, QG
Ma, XL
Ni, JJ
Zhang, L
Pei, YF
AF Han, Bai-Xue
Yan, Shan-Shan
Han, Yu
Xu, Qian
Zhao, Qi-Gang
Ma, Xin-Ling
Ni, Jing-Jing
Zhang, Lei
Pei, Yu-Fang
TI Causal Effects of Plasma Proteome on Osteoporosis and Osteoarthritis
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Mendelian randomization; Bone; Plasma proteome; Causal relationship
ID bone-mineral density

AB The two-sample Mendelian randomization (MR) study revealed a causal association of plasma proteins with osteoporosis (OP) and osteoarthritis (OA). Bone mineral density (BMD) is the gold standard for the clinical assessment of OP. Recent studies have shown that plasma proteins play an essential role in the regulation of bone development. However, the causal association of plasma proteins with BMD and OA remains unclear. We estimated the effects of 2889 plasma proteins on 2 BMD phenotypes and 6 OA phenotypes using two-sample MR analysis based on the genome-wide association study summary statistics. Then, we performed sensitivity analysis and reverse-direction MR analysis to evaluate the robustness of the MR analysis results, followed by gene ontology (GO) enrichment analysis and KEGG pathway analysis to explore the functional relevance of the identified plasma proteins. Overall, we observed a total of 257 protein-estimated heel BMD associations, 17 protein-total-body BMD associations, 2 protein-all-OA associations, and 2 protein-knee-OA associations at P-FDR < 0.05. Reverse-direction MR analysis demonstrated that there was little evidence of the causal association of BMD and OA with plasma proteins. GO enrichment analysis and KEGG pathway analysis identified multiple pathways, which may be involved in the development of OP and OA. Our findings recognized plasma proteins that could be used to regulate changes in OP and OA, thus, providing new insights into protein-mediated mechanisms of bone development.
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NR 32
TC 11
Z9 11
U1 0
U2 14
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EI 1432-0827
J9 CALCIFIED TISSUE INT
JI Calcif. Tissue Int.
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VL 112
IS 3
BP 350
EP 358
DI 10.1007/s00223-022-01049-w
EA DEC 2022
PG 9
WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA CN1F0
UT WOS:000905517100002
PM 36576504
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ER

PT J
AU Bhattacharyya, R
Alloush, A
Wilson, C
Doonan, J
Rooney, B
Walker, C
Maclean, A
Blyth, M
AF Bhattacharyya, Rahul
Alloush, Almothenna
Wilson, Christina
Doonan, James
Rooney, Brian
Walker, Colin
Maclean, Angus
Blyth, Mark
TI Survivorship of high tibial osteotomy in the treatment of osteoarthritis of the knee: a retrospective cohort study with fourteen years' follow-up
SO INTERNATIONAL ORTHOPAEDICS
LA English
DT Article
DE High tibial osteotomy; HTO; Survivorship; Medial compartment osteoarthritis

ID arthroplasty; score
AB PurposeThis study was to evaluate the survivorship of HTO for the treatment of medial compartment osteoarthritis (OA) in young and active patients from two teaching hospitals in a single city.MethodsThis is a retrospective cohort multicenter study looking at HTO for treatment of medial compartment OA. We analyzed a case series of HTO's performed by four surgeons in two centres over a 14-year period. Failure was defined as conversion to total knee replacement (TKR). All cases where additional procedures for instability of the knee were performed at the time of the index surgery were excluded. Time to failure was recorded, and a Kaplan-Meir (KM) analysis was performed to evaluate survivorship. Univariate binary regression analysis was undertaken to identify associations between risk factors and failure.ResultsA total of 96 patients were included in the study with a median age was 45 years. The survivorship at five years post-op was 90.3%, and at ten years post-op, it was 82%. Patients that were 14 years after surgery had a survivorship of 65%. Also, 18.8% of patients required the removal of their metalwork. The overall complication rate was 6.3%. The univariate regression analysis showed that higher age (p = 0.02) and larger corrections requiring the use of bone graft increased the risk of failure (p = 0.02). There was no statistically significant correlation between laterality, gender, complication rate, and pre-operative alignment to survivorship.ConclusionThis is one of the largest reported case series of HTO's with comparable survivorship at five and ten year follow-up compared to the reported literature. There was an association found between increasing age and larger corrections requiring bone graft at index procedure to increasing failure rate.
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CR Agneskirchner JD, 2007, ARTHROSCOPY, V23, P852, DOI 10.1016/j.arthro.2007.05.018
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10.2106/00004623-198870040-00011
NR 17
TC 5
Z9 5
U1 0
U2 3
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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JI Int. Orthop.
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WC Orthopedics
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PT J
AU Hu, YX
Wang, YF

Liu, SM
Wang, H
AF Hu, Yunxiang
Wang, Yufei
Liu, Sanmao
Wang, Hong
TI The Potential Roles of Ferroptosis in Pathophysiology and Treatment of Musculoskeletal Diseases-Opportunities, Challenges, and Perspectives
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Review
DE ferroptosis; osteoporosis; osteoarthritis; osteosarcoma; intervertebral disc degeneration; spinal cord injury
ID iron overload; cell-death; bone loss; differentiation; glutathione; protects
AB Ferroptosis is different from other forms of cell death, such as apoptosis, autophagy, pyroptosis, and cuproptosis, mainly involving iron metabolism and lipid peroxidation. Ferroptosis plays an important role in various disease, such as malignant tumors, neuron-degenerative diseases, and cardiovascular diseases, and has become the focus of current research. Both iron overload and lipid peroxide accumulation contribute to the occurrence, development, and treatment of musculoskeletal diseases, such as osteoporosis, osteoarthritis, osteosarcoma, intervertebral disc degeneration, and spinal cord injury. For a better understanding of the potential roles ferroptosis may play in pathophysiology and treatment of common musculoskeletal disorders, this article briefly reviewed the relationship and possible mechanisms. Through an investigation of ferroptosis' role in musculoskeletal diseases' occurrence, development, and treatment, ferroptosis could offer new opportunities for clinical diagnosis and treatment.
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FU National Natural Science Foundation of China [31971275] Funding Source: Medline
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NR 70
TC 12
Z9 13
U1 2
U2 26
PU MDPI

PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 2077-0383
J9 J CLIN MED
JI J. Clin. Med.
PD MAR 15
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IS 6
BP
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DI 10.3390/jcm12062125
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WC Medicine, General & Internal
SC General & Internal Medicine
GA A5IL4
UT WOS:000955455700001
PM 36983130
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PT J
AU Van Wynsberghe, J
   Vanakker, OM
AF Van Wynsberghe, Judith
   Vanakker, Olivier M.
TI Significance of Premature Vertebral Mineralization in Zebrafish Models in Mechanistic and Pharmaceutical Research on Hereditary Multisystem Diseases
SO BIOMOLECULES
LA English
DT Review
DE zebrafish model; multisystemic disorders; premature mineralization; axial skeleton
ID generalized arterial calcification; familial tumoral calcinosis; danio-rerio ostariophysi; matrix gla protein; gene-expression; tgf-beta; pseudoxanthoma elasticum; axial skeleton; hox-genes; vitamin-k
AB Zebrafish are increasingly becoming an important model organism for studying the pathophysiological mechanisms of human diseases and investigating how these mechanisms can be effectively targeted using compounds that may open avenues to novel treatments for patients. The zebrafish skeleton has been particularly instrumental in modeling bone diseases as-contrary to other model organisms-the lower load on the skeleton of an aquatic animal enables mutants to survive to early adulthood. In this respect, the axial skeletons of zebrafish have

been a good read-out for congenital spinal deformities such as scoliosis and degenerative disorders such as osteoporosis and osteoarthritis, in which aberrant mineralization in humans is reflected in the respective zebrafish models. Interestingly, there have been several reports of hereditary multisystemic diseases that do not affect the vertebral column in human patients, while the corresponding zebrafish models systematically show anomalies in mineralization and morphology of the spine as their leading or, in some cases, only phenotype. In this review, we describe such examples, highlighting the underlying mechanisms, the already-used or potential power of these models to help us understand and amend the mineralization process, and the outstanding questions on how and why this specific axial type of aberrant mineralization occurs in these disease models.
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TI Assessing the knowledge, attitude and practice of osteoporosis among Pakistani women: A national social-media based survey
SO PLOS ONE
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ID beliefs; care
AB BackgroundThere are numerous risk factors for osteoporosis and understanding and recognizing these risk factors is critical when deciding whether to take preventive measures. It is critical to reduce the healthcare expenditure burden of the Pakistani population by raising awareness and implementing osteoporosis-preventable measures. This survey aims to assess the knowledge, attitudes, and practices (KAP) of Pakistani women as well as their misconceptions about osteoporosis.MethodsA cross-sectional survey was conducted from August 2021 to January 2022 by the Bone & Mineral Disease research group at Section of Chemical Pathology, Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi, with exemption from the ethical review committee. Using snowball sampling, a validated Osteoporosis Prevention and Awareness Tool (OPAAT) was disseminated online via social media. With informed consent, 400 Pakistani women aged >= 18 years were included in the study. SPSS Statistics version 25.0 was used for data analysis. Chi-square test for association and Fisher-exact test were applied, and significance level was alpha<0.05.ResultsBased on the OPAAT scores of all (n = 400) participants, 22% (n = 88) had low knowledge, 44% (n = 176) had average knowledge, while 34% (n = 136) had good knowledge of osteoporosis. The most common misconceptions were about age-related risk, presentation of symptoms, radiation risk, associated risk factors like tooth loss, osteoarthritis, and knowledge about predictors of bone health.ConclusionAdult Pakistani women have a fair understanding of osteoporosis, but the OPAAT tool

clarifies some common misconceptions. There is a need to develop educational strategies to increase the knowledge of osteoporosis among Pakistani adults and to promote a bone-healthy lifestyle.
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SC Science & Technology - Other Topics
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Chen, Yan
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TI Role of irisin in bone diseases
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE irisin; bone diseases; osteoarthritis; osteoporosis; rheumatoid arthritis
ID lower circulating irisin; nf-kappa-b; mitochondrial biogenesis; activation; muscle; injury; alpha; cells; serum; fat
AB Bone diseases are common among middle-aged and elderly people, and harm to activities of daily living (ADL) and quality of life (QOL) for patients. It is crucial to search for key regulatory factors associated with the development of bone diseases and explore potential therapeutic targets for bone diseases. Irisin is a novel myokine that has been discovered in recent years. Accumulating evidence indicates that irisin has beneficial effects in the treatment of various diseases such as metabolic, cardiovascular and neurological disorders, especially bone-related diseases. Recent studies had shown that irisin plays the role in various bone diseases such as osteoarthritis, osteoporosis and other bone diseases, suggesting that irisin may be a potential molecule for the prevention and treatment of bone diseases. Therefore, in this review, by consulting the related domestic and international literature of irisin and bone diseases, we summarized the specific regulatory mechanisms of irisin in various bone diseases, and provided a systematic theoretical basis for its application in the diagnosis and treatment of the bone diseases.
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AU Hwang, JS
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AF Hwang, Ji Sup
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TI Three-Dimensional Analysis of the Trapezium Subchondral Bone and its Association with Trapeziometacarpal Joint Osteoarthritis
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Trapezium; Trapeziometacarpal joint; Subchondral bone; Osteoporosis
ID mineral density; carpometacarpal joint; postmenopausal women; hand osteoarthritis; articular-cartilage; trabecular bone; prevalence; morphology; thumb
AB Subchondral bone properties are associated with the pathogenesis of osteoarthritis (OA), but this relationship has not been confirmed in the

trapeziometacarpal joint (TMCJ). We aimed to evaluate the thickness (SBT) and density (SBD) of three-dimensional (3D) trapezium subchondral bone models derived from computed tomography (CT) images, and their relationships with early-stage TMCJ OA. We reviewed patients with a distal radius fracture who underwent conventional CT scans and such osteoporosis evaluations as bone mineral density (BMD) and bone turnover markers (BTMs). From 3D trapezium subchondral bone models, we measured SBT and SBD according to the OA stage and performed multivariate analyses to evaluate their associations with age, sex, body mass index, BMD, and BTMs. As results, a total of 156 patients (78 men and 78 age-matched women; mean age, 67 +/- 10 years) were analyzed. There were 30 (19%) with grade 0, 71 (45%) with grade 1, 13 (8%) with grade 2, and 42 (27%) with grade 3 TMCJ OA. SBT was significantly lower in patients with grade 1 OA than those with grade 0 or grade 3 OA, but SBD generally increased according to the OA severity. Low SBT was associated with low BMD, and low SBD with low BMD, high osteocalcin levels, and severe OA grades. In conclusion, patients with early-stage radiographic TMCJ OA have a lower SBT at the trapezium, which may support the potential role of subchondral bone in OA pathogenesis. This study also shows that subchondral bone properties are associated with BMD and osteocalcin levels.
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TI Effect of Conventional Treatment on Dental Complications and Ectopic Ossifications Among 30 Adults With XLH
SO JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM
LA English
DT Article
DE X-linked hypophosphatemia; fibroblast growth factor 23; dental complication; ectopic ossification; enthesopathy; treatment
ID x-linked hypophosphatemia; d-resistant rickets; abnormality; prevalence
AB Context Conventional treatment of X-linked hypophosphatemia (XLH) was reported to prevent dental complications, but whether the preventive effect was different among different types of teeth, including anterior teeth and molar teeth, is uncertain. Evidence of the preventive effect of conventional treatment on ectopic ossifications is also limited. Objective To compare dental complications and ectopic ossifications among adults with XLH with early (<5 years old) or late (>= 5 years old) conventional treatment. Methods This retrospective observational study included a total of 30 adults with XLH; orthopantomograms, spinal computed tomography scans, and X-rays of hip/knee joints were studied. Dental complications, including the decayed, missing, filled (DMF) index and devitalized teeth, apical periodontitis, and periodontitis, were evaluated. The ossification of the anterior/posterior longitudinal ligament and yellow ligament indexes (OA/OP/OY indexes) and the sum of the OA/OP/OY indexes (OS index) were utilized to evaluate the severity of spinal ligament ossification. The severity of the hip/knee osteophytes was evaluated using the Kellgren-Lawrence (KL) classification. Results The number of sound teeth was significantly lower and the DMF index was significantly higher in patients with late treatment. The severity of dental complications in the anterior tooth and molar tooth, OA/OP/OY/OS index, and KL grade were not significantly different among patients with early treatment and those with late treatment. Conclusion Early treatment could prevent dental complications but did not prevent ectopic ossification in adult patients with XLH. The difference in the preventive effect was not observed among different types of teeth.
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TI Primary Total Knee Arthroplasty for Fractures Around the Knee
SO ZEITSCHRIFT FUR ORTHOPADIE UND UNFALLCHIRURGIE
LA English
DT Review
DE primary total knee arthroplasty; knee; distal femoral fracture; proximal tibial fracture
ID distal femoral fractures; tibial plateau; femur fractures; hip fracture; replacement; mortality; fixation; joint; osteosynthesis; management
AB Primary arthroplasty for fractures of the femoral neck is a very common procedure and even the gold standard for the geriatric patient. In contrast, primary arthroplasty for perigenicular fractures is a rare event. On the other hand, it can be a therapeutic option, especially for geriatric patients with prior osteoarthritis or complex fractures and severe osteoporosis. The operative procedure can be complex and requires experience in primary and revision arthroplasty as well as suitable implants and good preoperative planning. There are case series reporting primary arthroplasty in a total of approximately 200 cases of both distal femoral and proximal tibial fractures. Complication rates are between 0 and 90% and mostly concern wound healing problems and infections. From a functional point of view, predominantly good results and a range of motion of 100 degrees can be achieved. Primary arthroplasty can be a therapeutic option for selected cases of perigenicular fractures and gives good functional results. The most frequent complications are wound healing problems and infections.
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TI Simultaneous extracting area and quantity of agricultural greenhouses in large scale with deep learning method and high-resolution remote sensing images
SO SCIENCE OF THE TOTAL ENVIRONMENT
LA English
DT Article
DE Agricultural greenhouses; Google earth remote sensing images; Convolutional neural network; Area and quantity; Automatic extraction
ID object-based classification; sentinel-2 msi; technology; simulation; design
AB Greenhouses are an important part of modern facility-based agriculture. While creating well-being for human society, greenhouses also bring negative impacts such as air pollution, soil pollution, and water pollution. Therefore, it is of great signiflcance to obtain information such as the area and quantity of greenhouses. It is still a challenging task to flnd a low-cost, high-efflciency, and easy-to-use method for the dual extraction of greenhouse area and quantity on a large scale. In

this study, relatively easy-to-obtain high-resolution Google Earth remote sensing images are used as the experimental data source, and an area and quantity simultaneous extraction framework (AQSEF) is constructed to extract both the area and quantity of greenhouses. The AQSEF uses UNet and YOLO v5 series networks as core op-erators to complete model training and prediction, and main components such as SWP, OSW&NMS and GCA complete data postprocessing. To evaluate the feasibility of our method, we take Beijing, China, as the research area and select multiple accuracy evaluation indicators in the two branches for accuracy veriflcation. The results show that the mIoU, OA, Kappa, Recall and Precision with the best performance model in the area extraction branch can reach 0.931, 0.987, 0.867, 0.91 and 0.914, respectively. Additionally, the Recall, Precision, AP@0.5 and mAP@0.5: 0.95 values of the best performance model are 0.781, 0.891, 0.812 and 0.509, respectively, in the extraction of the quantity of greenhouses. Finally, in Beijing, the area covered by greenhouses is approximately 85.443 km2, and the quantity of greenhouses is approximately 155,464. With the proposed method, the time consumed for area extraction and quan-tity extraction is 6.73 h and 12.97 h, respectively. The experimental results show that AQSEF helps to overcome the spatiotemporal diversity of greenhouses and quickly and accurately map a high-spatial-resolution greenhouse distribu-tion product within the research area.
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U1 6
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TI The Molecular Role of Polyamines in Age-Related Diseases: An Update
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE polyamines; spermidine; spermine; putrescine; aging; age-related diseases; aging biomarkers
ID cerebrospinal-fluid; spermidine; autophagy; mechanisms; atp13a2; serum; transport; stress; brain

AB Polyamines (Pas) are short molecules that exhibit two or three amine groups that are positively charged at a physiological pH. These small molecules are present in high concentrations in a wide variety of organisms and tissues, suggesting that they play an important role in cellular physiology. Polyamines include spermine, spermidine, and putrescine, which play important roles in age-related diseases that have not been completely elucidated. Aging is a natural process, defined as the time-related deterioration of the physiological functions; it is considered a risk factor for degenerative diseases such as cardiovascular, neurodegenerative, and musculoskeletal diseases; arthritis; and even cancer. In this review, we provide a new perspective on the participation of Pas in the cellular and molecular processes related to age-related diseases, focusing our attention on important degenerative diseases such as Alzheimer's disease, Parkinson's disease, osteoarthritis, sarcopenia, and osteoporosis. This new perspective leads us to propose that Pas function as novel biomarkers for age-related diseases, with the main purpose of achieving new molecular alternatives for healthier aging.
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TI The effects of monoplanar and biplanar medial open wedge high tibial osteotomy on pain and functional capacity
SO EUROPEAN REVIEW FOR MEDICAL AND PHARMACOLOGICAL SCIENCES
LA English
DT Review
DE Monoplanar; Biplanar; Medial open wedge; Tibial osteotomy
ID stage knee osteoarthritis; patellar height; compartment
AB - OBJECTIVE: This prospective cross-sectional study aimed to compare the ef-fects of operation types on pain and function-al capacity in patients who underwent monopla-nar and biplanar medial open wedge high tibial osteotomy. PATIENTS AND METHODS: The study in-cluded a total of 117 patients who presented at our clinic between January 2012 -January 2016 and underwent monoplanar (n=63) and biplanar (n=54) medial open wedge high tibial osteoto-my. The groups were evaluated in age, gender, Body Mass Index (BMI), operation side, opera-tion time, follow-up period, Modified Insall Sal-vati ratio, Blackburn Peel Index (BPI), Slope, Knee Society Function Score (KSSF), Knee So-ciety Score (KSSK), Visual Analog Scale (VAS), Kellgren Lawrence score, tibiofemoral angle var-us, and Tegner score. RESULTS: Most of the patients in the mono -planar group were operated on the right side, while most patients in the biplanar group on the left side, and the difference between the groups was significant ($p<0.05$). The operation time was significantly longer in the biplanar group, while the duration of follow-up was statistically signifi-cantly longer in the monoplanar group ($p<0.05$). The preoperative BPI and Kellgren Lawrence scores were significantly higher in the monop-lar group, while BMI, KSSK, and tibiofemoral an-gle varus scores were statistically significantly higher in the biplanar group ($p<0.05$). Postoper-ative VAS and Kellgren Lawrence scores were higher in the monoplanar group, and the Modi-fied Insall Salvati ratio, BPI, BMI,

KSS function score, KSSK score, tibiofemoral angle varus, and Tegner scores were statistically significant-ly higher in the biplanar group ($p<0.05$). Postop-eratively, the mean VAS score was lower in the biplanar group, and the range of change was greater. In the monoplanar group, the postoper-ative VAS values were closer to each other and were higher than in the biplanar group. The mean postoperative KSS function score was higher in the biplanar group, and the range of change was higher in the monoplanar group.CONCLUSIONS: The study results showed that biplanar medial open wedge high tibial os-teotomy was more successful in terms of both pain and functional capacity. However, the op-eration time was longer than the monoplanar method.

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TI Effect of immunology biomarkers associated with hip fracture and fracture risk in older adults
SO IMMUNITY & AGEING
LA English
DT Article
DE Cytokines; Hip fractures; Biomarkers; Prognosis; FRAX
ID prognostic-factors; osteoarthritis; osteoporosis; surgery; validation; proteomics; outcm; density; frailty; genes
AB Osteoporosis is a skeletal disease that can increase the risk of fractures, leading to adverse health and socioeconomic consequences. However, current clinical methods have limitations in accurately estimating fracture risk, particularly in older adults. Thus, new technologies are necessary to improve the accuracy of fracture risk estimation. In this observational study, we aimed to explore the association between serum cytokines and hip fracture status in older adults, and their associations with fracture risk using the FRAX reference tool. We investigated the use of a proximity extension assay (PEA) with Olink. We compared the characteristics of the population, functional status and detailed body composition (determined using densitometry) between groups. We enrolled 40 participants, including 20 with hip fracture and 20 without fracture, and studied 46 cytokines in their serum. After conducting a score plot and two unpaired t-tests using the Benjamini-Hochberg method, we found that Interleukin 6 (IL-6), Lymphotoxin-alpha (LT-alpha), Fms-related tyrosine kinase 3 ligand (FLT3LG), Colony stimulating factor 1 (CSF1), and Chemokine (C-C motif) ligand 7 (CCL7) were significantly different between fracture and non-fracture patients ($p < 0.05$). IL-6 had a moderate correlation with FRAX ($R2 = 0.409$, $p < 0.001$), while CSF1 and CCL7 had weak correlations with FRAX. LT-alpha and FLT3LG exhibited a negative correlation with the risk of fracture. Our results suggest that targeted proteomic tools have the capability to identify differentially regulated proteins and may serve as potential markers for estimating fracture risk. However, longitudinal studies will be necessary to validate these results and determine the temporal patterns of changes in cytokine profiles.
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NR 70
TC 7
Z9 7
U1 0
U2 4
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 IMMUN AGEING
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WC Geriatrics & Gerontology; Immunology
SC Geriatrics & Gerontology; Immunology
GA W1HL0
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PT J
AU Yammine, T
Aprahamian, R
Souaid, M
Salem, N
Awwad, J
Farra, C
AF Yammine, Tony
Aprahamian, Raffi
Souaid, Mirna
Salem, Nabiha
Awwad, Johnny
Farra, Chantal
TI Novel SCN9A variant associated with congenital insensitivity to pain
SO MOLECULAR BIOLOGY REPORTS
LA English
DT Article
DE Congenital insensitivity to Pain; SCN9A gene; Lebanese; Whole exome sequencing; Urinary incontinence
ID mutation; deletion; child
AB BackgroundCongenital insensitivity to pain (CIP) is a rare autosomal recessive syndrome characterized by lack of pain perception and a wide spectrum of clinical signs such as anosmia and hyposmia. Variants in SCN9A gene are associated with CIP. We here report on a Lebanese family with three CIP patients referred for genetic investigations.Methods and resultsWhole exome sequencing analysis revealed the presence of a novel nonsense, homozygous SCN9A pathogenic variant: SCN9A (NM_001365536.1): c.4633G > T, p.(Glu1545*) in exon 26.ConclusionOur three Lebanese patients had CIP, urinary incontinence and

normal olfactory function while two of them also presented with osteoporosis and osteoarthritis; this association of features has not been previously reported in the literature. We hope that this report would contribute to a better delineation of the phenotypic spectrum associated with SCN9A pathogenic variants.
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NR 25
TC 1
Z9 3
U1 2
U2 4
PU SPRINGER
PI DORDRECHT
PA VAN GODEWIJCKSTRAAT 30, 3311 GZ DORDRECHT, NETHERLANDS
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PT J
AU Jeong, S
Lee, JW
Boucher, HR
AF Jeong, Suin
Lee, Ji Won
Boucher, Henry R.
TI The Effect of Preoperative Bisphosphonate Use on Total Hip Arthroplasty Outcomes
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE total hip arthroplasty; osteoporosis; bisphosphonates; patient outcomes;

infection; preoperative optimization
ID joint arthroplasty; femoral fixation; fracture; association; revision
AB Background: Patients undergoing total hip arthroplasty (THA) commonly have osteoporosis for which bisphosphonates (BPs) are Food and Drug Administration (FDA)-approved for treatment. Bisphosphonate use post-THA is associated with decreased periprosthetic bone loss or revisions, and increased longevity of implants. However, evidence is lacking for preoperative bisphosphonate use in THA recipients. This study investigated the association between bisphosphonate use pre-THA and outcomes. Methods: A retrospective review of a national administrative claims database was conducted. Among THA recipients who had a prior diagnosis of hip osteoarthritis and osteoporosis/osteopenia, the treatment group (BP-exposed) consisted of patients who had a history of bisphosphonate use at least 1 year before THA; controls (BP-naive) comprised patients who did not have preoperative bisphosph-onate use. The BP-exposed were matched to BP-naive in a 1:4 ratio by age, sex, and comorbidities. Lo-gistic regressions were used to calculate the odds ratio for intraoperative and 1-year postoperative complications.Results: The BP-exposed group had significantly higher rates of intraoperative and 1-year postoperative periprosthetic fractures (odds ratio (OR): 1.39, 95% confidence interval (CI): 1.23, 1.57) and revisions (OR: 1.14, 95% CI: 1.04, 1.25) compared with the BP-naive controls. BP-exposed also experienced higher rates of aseptic loosening, dislocation, periprosthetic osteolysis, and stress fracture of the femur or hip/pelvis compared to the BP-naive controls, but these values were not statistically significant.Conclusion: The use of bisphosphonates in THA patients preoperatively is associated with higher rates of intraoperative and 1-year postoperative complications. These findings may impact the management of patients undergoing THA who have a prior diagnosis of osteoporosis/osteopenia and use of bisphosphonates. Level of evidence: Retrospective Cohort Study (Level 3).(c) 2023 Elsevier Inc. All rights reserved.
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PT J
AU Chen, RQ
Cheng, YA
Zhang, WT
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AF Chen, Ruiqin
Cheng, Yanan
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Zhang, Hongbiao
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TI The biological applications of exosomal-based materials in bone/cartilage tissue engineering
SO FRONTIERS IN MATERIALS
LA English
DT Review
DE exosome; bone tissue engineering; bone defect; regenerative materials; exosomal-based materials
ID extracellular vesicles; bone-formation; delivery; cartilage; osteoarthritis; inflammation; regeneration; osteoporosis; biogenesis; strategy
AB Exosomes are secreted by various cells including stem cells, dendritic cells, and tumor cells, also known as the cell-derived extracellular vesicles. Exosomes, can carry informative cargos from host cells, thus have been employed as potential nanomaterials for their multifarious biological functions in biomedical fields, such as drug and genes delivery, tumor targeting, and disease treatment. Recently, the biological applications of exosomes in bone tissue engineering have gained

increasing attention. Some important progress has been made while the tissue regeneration and functional recovery of boneremain as the key challenges to be addressed. In this article, we first made a summary of exosomes and their applications in the regeneration of bone and cartilage tissue. Then, modification approaches used for exosomes to equip them with excellent capacities are summarized. Finally, current concerns and future outlooks of exosomes in bone/cartilage tissue engineering and regeneration are discussed.
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FU Medical Health Science and Technology Project of Zhejiang Province [2021KY068, 2023KY028]; Hainan Provincial Natural Science Foundation High-level Talents Project of China [821RC725]
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TI Type H vessels: functions in bone development and diseases
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
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DT Review
DE type H blood vessel; bone development; bone formation; osteogenesis; bone disease; osteoblast; VEGF; PDGF-BB
ID endothelial growth-factor; hypoxia-inducible factor-1-alpha; angiogenesis; osteogenesis; resorption; cells; survival; repair; vascularization; activation
AB Type H vessels are specialized blood vessels found in the bone marrow that are closely associated with osteogenic activity. They are characterized by high expression of endomucin and CD31. Type H vessels form in the cancellous bone area during long bone development to provide adequate nutritional support for cells near the growth plate. They also influence the proliferation and differentiation of osteoprogenitors and osteoclasts in a paracrine manner, thereby creating a suitable microenvironment to facilitate new bone formation. Because of the close relationship between type H vessels and osteogenic activity, it has been found that type H vessels play a role in the physiological and pathological processes of bone diseases such as fracture healing, osteoporosis, osteoarthritis, osteonecrosis, and tumor bone metastasis. Moreover, experimental treatments targeting type H vessels can improve the outcomes of these diseases. Here, we reviewed the molecular mechanisms related to type H vessels and their associated osteogenic activities, which are helpful in further understanding the role of type H vessels in bone metabolism and will provide a theoretical basis and ideas for comprehending bone diseases from the vascular perspective.

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TI Solvent exchange-motivated and tunable in situ forming implants sustaining triamcinolone acetonide release for arthritis treatment
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DT Article
DE In situ forming implants; Triamcinolone acetonide; Poly (lactic-co-glycolic acid); Sustaining release; Arthritis; In situ forming implants; Triamcinolone acetonide; Poly (lactic-co-glycolic acid); Sustaining release; Arthritis
ID bone loss; solubility parameters; rheumatoid-arthritis; delivery; osteoarthritis; polymer; gel; inflammation; osteoporosis; miscibility
AB Arthritis is a syndrome characterized by inflammation in the joints. Triamcinolone acetonide (TA) was used as an anti-inflammatory agent in the treatment of this disease. However, there are limitations to its clinical application, including rapid clearance from the joint cavity, potential joint damage from multiple injections, and adverse joint events. To address these drawbacks, we

developed a tunable in situ forming implant loaded with TA. This injectable polymer solution utilized poly (lactic-co-glycolic acid) (PLGA) as an extended-release material. When injected into the joints, the solution solidifies into implants through a solvent exchange in the aqueous environment. The implants demonstrated robust retention at the injection site and released TA over several weeks even months through diffusion and erosion. By adding different proportions of low water-miscible plasticizers, the release period of the drug could be precisely adjusted. The plasticizers-optimized implants exhibited a tough texture, enhancing the therapeutic efficiency and drug safety in vivo. In arthritic model studies, the tunable TAloaded implants significantly reduced swelling, pain, and motor discoordination, and also showed suppression of arthritis progression to some extent. These findings suggested that TA-loaded ISFI holds promise for managing inflammatory disorders in individuals with arthritis.
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J9 INT J PHARMACEUT
JI Int. J. Pharm.
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WC Pharmacology & Pharmacy
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TI CLAHE-CapsNet: Efficient retina optical coherence tomography classification using capsule networks with contrast limited adaptive histogram equalization
SO PLOS ONE
LA English
DT Article
ID convolutional neural-networks; diabetic macular edema; fully automated detection; degeneration; oct; segmentation; ranibizumab; diseases; images; drusen
AB Manual detection of eye diseases using retina Optical Coherence Tomography (OCT) images by Ophthalmologists is time consuming, prone to errors and tedious. Previous researchers have developed a computer aided system using deep learning-based convolutional neural networks (CNNs) to aid in faster detection of the retina diseases. However, these methods find it difficult to achieve better classification performance due to noise in the OCT image. Moreover, the pooling operations in CNN reduce resolution of the image that limits the performance of the model. The contributions of the paper are in two folds. Firstly, this paper makes a comprehensive literature review to establish current-state-of-act methods successfully implemented in retina OCT image classifications. Additionally, this paper proposes a capsule network coupled with contrast limited adaptive histogram equalization (CLAHE-CapsNet) for retina OCT image classification. The CLAHE was implemented as layers to minimize the noise in the retina image for better performance of the model. A three-layer convolutional capsule network was designed with carefully chosen hyperparameters. The dataset used for this study was presented by University of California San Diego (UCSD). The dataset consists of 84,495 X-Ray images (JPEG) and 4 categories (NORMAL, CNV, DME, and DRUSEN). The images went through a grading system consisting of multiple layers of trained graders of expertise for verification and correction of image labels. Evaluation experiments were conducted and comparison of results was done with state-of-the-art models to find out the best performing model. The evaluation metrics; accuracy, sensitivity, precision, specificity, and AUC are used to determine the performance of the models. The evaluation results show that the proposed model achieves the best performing model of accuracies of 97.7%, 99.5%, and 99.3% on overall accuracy (OA), overall sensitivity (OS), and overall precision (OP), respectively. The results obtained indicate that the proposed model can be adopted and implemented to help ophthalmologists in detecting retina OCT diseases.
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VL 18
IS 11
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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TI Emphatic information on bone mineral loss using quantitative ultrasound sonometer for expeditious prediction of osteoporosis
SO SCIENTIFIC REPORTS
LA English
DT Article
AB Osteoporosis (OP) and osteoarthritis (OA) are skeletal disorders characterized by a reduction in bone density and quality, resulting in increased fragility and susceptibility to fractures. These illnesses are exhibiting a higher prevalence among both males and females. Fracture risk is determined by using the BMD score (Bone Mineral Density). Looking at the bone loss that comes with osteoarthritis (OA) and osteoporosis (OP), this study also looks at the technological methods used to test for these conditions in order to improve therapies and treatment plans for older people. As a matter of consideration, the prevalence of osteoporosis is higher among postmenopausal women (20%) compared to premenopausal women (14.28%) and males (6.77%). The utilization of a preliminary calcaneal Quantitative Ultrasound (QUS) examination is warranted in order to effectively handle the matter of osteoporosis. The prompt assessment of a patient can provide valuable insights into potential fractures and aid in the prevention of bone injury. In a nutshell, it is imperative to comprehend the impact of OA (osteoarthritis) and OP (osteoporosis) on bone health in order to effectively manage the escalating apprehensions surrounding these conditions. Sophisticated diagnostic techniques, such as the calcaneal quantitative ultrasound (QUS) test, have the potential to enhance the well-being of older individuals by enabling early detection and treatment of many ailments.
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DI 10.1038/s41598-023-44407-w
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WC Multidisciplinary Sciences
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AU Wei, JY
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Tong, BD
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AF Wei, Junyu
Ou, Zixuan
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Liao, Zhiwei
Yang, Cao
TI Engineered extracellular vesicles as therapeutics of degenerative orthopedic diseases
SO FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY
LA English
DT Review
DE extracellular vesicles (EVs); native EVs; engineered EVs; degenerative orthopedic

diseases (DODs); osteoarthritis (OA); osteoporosis (OP); intervertebral disc degeneration (IDD); osteonecrosis of the femoral head (ONFH)
ID mesenchymal stem-cells; intervertebral disc degeneration; oxidative stress; cellular uptake; femoral-head; in-vitro; exosm; inflammation; delivery; osteoarthritis
AB Degenerative orthopedic diseases, as a global public health problem, have made serious negative impact on patients' quality of life and socio-economic burden. Traditional treatments, including chemical drugs and surgical treatments, have obvious side effects and unsatisfactory efficacy. Therefore, biological therapy has become the focus of researches on degenerative orthopedic diseases. Extracellular vesicles (EVs), with superior properties of immunoregulatory, growth support, and drug delivery capabilities, have emerged as a new cell-free strategy for the treatment of many diseases, including degenerative orthopedic diseases. An increasing number of studies have shown that EVs can be engineered through cargo loading, surface modification, and chemical synthesis to improve efficiency, specificity, and safety. Herein, a comprehensive overview of recent advances in engineering strategies and applications of engineered EVs as well as related researches in degenerative orthopedic diseases, including osteoarthritis (OA), osteoporosis (OP), intervertebral disc degeneration (IDD) and osteonecrosis of the femoral head (ONFH), is provided. In addition, we analyze the potential and challenges of applying engineered EVs to clinical practice.
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ID mesoporous silica nanoparticles; up-conversion nanoparticles; mesenchymal stromal cells; quantum-dot nanoparticles; iron-oxide nanoparticles; long-term tracking; gold nanoparticles; osteogenic differentiation; carbon nanotubes; in-vitro
AB Stem cells (SC) are a kind of cells with self renewing ability and multipotent differentiation, which can differentiate into many types of cells such as osteoblast, chondrocyte, neurocyte to treat disease like osteoporosis, osteoarthritis and Alzheimer's disease. Despite the development of novel methods for inducing cell differentiation, the inefficiency and complexity of controlling differentiation of stem cells remain a serious challenge, which necessary to develop a new and alternative approach for effectively controlling the direction of stem cell differentiation in vitro and in vivo in stem cells therapy. Recent advancement in nanotechnology for developing a new class of inorganic nanoparticles that exhibit unique chemical and physical properties holds promise for the treatment of stem cells. Over the last decade, inorganic nanoparticle-based approaches against stem cells have been directed toward developing nanoparticles with drug delivery, or utilizing nanoparticles for controlled cell behaviors, and applying nanoparticles for inducing cell differentiation directly. In addition, a strategy to functionalize inorganic nanoparticles as a nanoprobe towards enhanced penetration through near-infrared light or nuclear magnetic resonance has been receiving considerable interest by means of long-term tracking stem cell in vivo. This review summarizes and highlights the recent development of these inorganic nanoparticle-based approaches as potential therapeutics for controlling differentiation of stem cells and so on for stem cell therapy, along with current opportunities and challenges that need to be overcome for their successful clinical translation.
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TI Identifying and visualising multimorbidity and comorbidity patterns in patients in the English National Health Service: a population-based study
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DT Article
ID disease; prevalence; cancer; asthma; impact; breast; care; age
AB Background Globally, there is a paucity of multimorbidity and comorbidity data, especially for minority ethnic groups and younger people. We estimated the frequency of common disease combinations and identified non-random disease associations for all ages in a multiethnic population. Methods In this population-based study, we examined multimorbidity and comorbidity patterns stratified by ethnicity or race, sex, and age for 308 health conditions using electronic health records from individuals included on the Clinical Practice Research Datalink linked with the Hospital Episode Statistics admitted patient care dataset in England. We included individuals who were older than 1 year and who had been registered for at least 1 year in a participating general practice during the study period (between April 1, 2010, and March 31, 2015). We identified the most common combinations of conditions and comorbidities for index conditions. We defined comorbidity as the accumulation of additional conditions to an index

condition over an individual's lifetime. We used network analysis to identify conditions that co-occurred more often than expected by chance. We developed online interactive tools to explore multimorbidity and comorbidity patterns overall and by subgroup based on ethnicity, sex, and age. Findings We collected data for 3 872 451 eligible patients, of whom 1 955 700 (50 & BULL;5%) were women and girls, 1 916 751 (49 & BULL;5%) were men and boys, 2 666 234 (68 & BULL;9%) were White, 155 435 (4 & BULL;0%) were south Asian, and 98 815 (2 & BULL;6%) were Black. We found that a higher proportion of boys aged 1-9 years (132 506 [47 & BULL;8%] of 277 158) had two or more diagnosed conditions than did girls in the same age group (106 982 [40 & BULL;3%] of 265 179), but more women and girls were diagnosed with multimorbidity than were boys aged 10 years and older and men (1 361 232 [80 & BULL;5%] of 1 690 521 vs 1 161 308 [70 & BULL;8%] of 1 639 593). White individuals (2 097 536 [78 & BULL;7%] of 2 666 234) were more likely to be diagnosed with two or more conditions than were Black (59 339 [60 & BULL;1%] of 98 815) or south Asian individuals (93 617 [60 & BULL;2%] of 155 435). Depression commonly co-occurred with anxiety, migraine, obesity, atopic conditions, deafness, soft-tissue disorders, and gastrointestinal disorders across all subgroups. Heart failure often co-occurred with hypertension, atrial fibrillation, osteoarthritis, stable angina, myocardial infarction, chronic kidney disease, type 2 diabetes, and chronic obstructive pulmonary disease. Spinal fractures were most strongly non-randomly associated with malignancy in Black individuals, but with osteoporosis in White individuals. Hypertension was most strongly associated with kidney disorders in those aged 20-29 years, but with dyslipidaemia, obesity, and type 2 diabetes in individuals aged 40 years and older. Breast cancer was associated with different comorbidities in individuals from different ethnic groups. Asthma was associated with different comorbidities between males and females. Bipolar disorder was associated with different comorbidities in younger age groups compared with older age groups. Interpretation Our findings and interactive online tools are a resource for: patients and their clinicians, to prevent and detect comorbid conditions; research funders and policy makers, to redesign service provision, training priorities, and guideline development; and biomedical researchers and manufacturers of medicines, to provide leads for research into common or sequential pathways of disease and inform the design of clinical trials.

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TI A Novel, Image-Based Method for Characterization of the Porosity of Additively Manufactured Bone Scaffolds With Complex Microstructures
SO JOURNAL OF MANUFACTURING SCIENCE AND ENGINEERING-TRANSACTIONS OF THE ASME
LA English
DT Article
DE bone tissue engineering; digital image processing; bone pathology; regenerative medicine; biomedical manufacturing

ID pore-size
AB Bone tissue engineering has emerged as a promising strategy for the treatment of osseous fractures, defects, and ultimately diseases caused by, for example, bone tumor resection, accident trauma, and congenital malformation. Additive fabrication of stem cell-seeded, osteoconductive porous scaffolds has been an effective method in clinical practice for the treatment of bone pathologies (such as osteoporosis, osteoarthritis, and rheumatic diseases). Porosity is known to be one of the main morphological characteristics of bone tissues, which affects the functional performance of an implanted bone scaffold. Hence, in situ detection and quantification of scaffold porosity implemented to ensure functional integrity prior to implantation/surgery is an unavoidable need. The objective of this research work is to introduce a robust, image-based method for identification and subsequently characterization of the surface porosity and dimensional accuracy of additively manufactured bone tissue scaffolds, with a focus on pneumatic micro-extrusion (PME) process. It was observed that the presented method would be capable of detecting complex individual pores based on a micrograph. Using the proposed method, not only were scaffold pores detected, but also scaffold porosity was characterized on the basis of various defined quality metrics/traits (such as the relative standard deviation of distance to the nearest pore). The proposed method was validated by contrasting its performance in "surface pore detection " against that of a standard method, tested on a complex benchmark in four different simulated lighting environments. Besides, the performance of the method in terms of "pore filling " was compared to that of a standard method, tested on a real PME-fabricated bone scaffold. It was observed that the proposed method had a better performance in pore filling, detection, and consolidation. Overall, the outcomes of this work pave the way for high-resolution fabrication of patient-specific, structurally complex, and porous bone scaffolds with easily validatable, functional, and medical properties for the treatment of bone pathologies.
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TI Calcium phosphate bone cements as local drug delivery systems for bone cancer treatment
SO BIOMATERIALS ADVANCES
LA English
DT Review
DE Calcium phosphate cements; Drug delivery; Bone cancer; Antineoplastic drugs; Bisphosphonates
ID controlled-release; hydroxyapatite particles; artificial joints; nanoparticles; doxorubicin; wear; cell; methotrexate; composites; resorption
AB Bone cancer is usually a metastatic disease, affecting people of all ages. Its effective therapy requires a targeted drug administration locally at the cancer site so that the surrounding healthy organs and tissues stay unharmed. Upon a thorough literature search, a tremendous number of published articles are reporting on development of calcium phosphate cements (CPCs) for the treatment of a variety of diseases, such as osteoporosis, osteoarthritis, osteomyelitis, and other musculoskeletal disorders. However, just a limited number of research employs CPCs specifically for bone cancer treatment. In this review article, we study the factors influencing the local drug release from CPCs and particularly focus on bone cancer therapy. Finally, we locate the deficiencies in the literature regarding this specific topic and propose which other perspectives should be considered and discussed in future articles.
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TI Novel insights on the effect of sclerostin on bone and other organs
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LA English
DT Review
DE sclerostin; Wnt signalling; therapeutic; bone
ID glucocorticoid-induced osteoporosis; hematopoietic stem-cells; postmenopausal women; multiple-myeloma; antibody treatment; sost gene; circulating sclerostin; missense mutations; mineral density; cross-talk
AB As a key regulator of bone homeostasis, sclerostin has garnered a lot of interest over the last two decades. Although sclerostin is primarily expressed by osteocytes and is well known for its role in bone formation and remodelling, it is also

expressed by a number of other cells and potentially plays a role in other organs. Herein, we aim to bring together recent sclerostin research and discuss the effect of sclerostin on bone, cartilage, muscle, liver, kidney and the cardiovascular and immune systems. Particular focus is placed on its role in diseases, such as osteoporosis and myeloma bone disease, and the novel development of sclerostin as a therapeutic target. Anti-sclerostin antibodies have recently been approved for the treatment of osteoporosis. However, a cardiovascular signal was observed, prompting extensive research into the role of sclerostin in vascular and bone tissue crosstalk. The study of sclerostin expression in chronic kidney disease was followed by the investigation of its role in liver-lipid-bone interactions, and the recent discovery of sclerostin as a myokine prompted new research into sclerostin within the bone-muscle relationship. Potentially, the effects of sclerostin reach beyond that of bone alone. We further summarise recent developments in the use of sclerostin as a potential therapeutic for osteoarthritis, osteosarcoma and sclerosteosis. Overall, these new treatments and discoveries illustrate progress within the field, however, also highlight remaining gaps in our knowledge.
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NR 167
TC 22
Z9 28
U1 0
U2 15
PU BIOSCIENTIFICA LTD
PI BRISTOL
PA STARLING HOUSE, 1600 BRISTOL PARKWAY N, BRISTOL, ENGLAND
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AU Gao, ZQ
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TI Enpp1 deficiency caused chondrocyte apoptosis by inhibiting AMPK signaling

pathway
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Enpp1; Osteoarthritis; Apoptosis; AMPK; AICAR
ID osteoarthritis; pyrophosphate; progression; proliferation; osteoporosis; metabolism; atp
AB Objective and backgroundThe deficiency of ectonucleotide pyrophosphatase/phosphodiesterase 1 (Enpp1) causes the phenotype similar to knee osteoarthritis (OA). However, the molecular mechanism is poorly understood.MethodThe global deletion of Enpp1 (Enpp1(-/-)) mice was created to analyze the role of Enpp1 in the progress of knee OA. The apoptosis, proliferation and chondrogenic differentiation ability of chondrocytes from wild-type (WT) and Enpp1(-/-) joints were compared. According to the results of high-throughput quantitative molecular measurements, the proteins of chondrocytes from WT and Enpp1(-/-) mice were used to explore the mechanism of Enpp1 deficiency-associated knee OA.ResultIn Enpp1(-/-) knee joints, we found significant chondrocyte apoptosis and proteomic results showed that abnormal expression of AMP-activated protein kinase (AMPK) signaling pathway may contribute to this phenotype. In primary chondrocyte cultures in vitro, Enpp1 deletion dramatically enhancing chondrocyte apoptosis. Meanwhile, we found Enpp1 deletion inhibits the phosphorylation of AMPK (P-AMPK). We also found that decreased level of P-AMPK and chondrocyte apoptosis, which are caused by Enpp1 deficiency, can be reversed by Acadesine (AICAR), the activator of AMPK.ConclusionConsequently, Enpp1 deficiency plays an essential role in knee OA by regulating AMPK signaling pathway.
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NR 38
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PI LONDON
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TI Bone Tissue and the Nervous System: What Do They Have in Common?
SO CELLS
LA English
DT Review
DE stem cells; bone; neurogenesis; differentiation
ID mesenchymal stem-cells; marrow-derived microglia; in-vitro model; mouse model; transcription factor; alzheimers-disease; stromal cells; osteoblast differentiation; intellectual disability; extracellular-matrix

AB Degenerative diseases affecting bone tissues and the brain represent important problems with high socio-economic impact. Certain bone diseases, such as osteoporosis, are considered risk factors for the progression of neurological disorders. Often, patients with neurodegenerative diseases have bone fractures or reduced mobility linked to osteoarthritis. The bone is a dynamic tissue involved not only in movement but also in the maintenance of mineral metabolism. Bone is also associated with the generation of both hematopoietic stem cells (HSCs), and thus the generation of the immune system, and mesenchymal stem cells (MSCs). Bone marrow is a lymphoid organ and contains MSCs and HSCs, both of which are involved in brain health via the production of cytokines with endocrine functions. Hence, it seems clear that bone is involved in the regulation of the neuronal system and vice versa. This review summarizes the recent knowledge on the interactions between the nervous system and bone and highlights the importance of the interaction between nerve and bone cells. In addition, experimental models that study the interaction between nerve and skeletal cells are discussed, and innovative models are suggested to better evaluate the molecular interactions between these two cell types.
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NR 214
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TI Osteoporosis does not affect bone mineral density change in the proximal humerus or the functional outcome after open reduction and internal fixation of unilateral displaced 3-or 4-part fractures at 12-month follow-up
SO JOURNAL OF SHOULDER AND ELBOW SURGERY
LA English
DT Article
DE Proximal humerus fracture; bone mineral density; angle stable locking plate; disuse osteoporosis; disuse osteopenia; functional outcomes
ID locking compression plate; quality; osteoarthritis; questionnaire; support; dxa
AB Background: The aim of this prospective study was to investigate bone mineral density (BMD) changes in the proximal humerus of the shoulder during a healing period of 12 months after displaced 3-or 4-part proximal humerus fractures treated with open reduction and internal fixation (ORIF) with an anatomic angular stable locking plate and the influence on fracture healing and functional outcomes. Methods: In a prospective multicenter study, 36 patients (29F and 7M, age range: 38-83) with unilateral displaced 3-or 4-part proximal humerus fractures were included for ORIF. Dual-energy x-ray absorptiometry for osteoporosis status was employed. Postoperative and 6-week, 3-, 6-, and 12-month shoulder radiographs and dual-energy x-ray absorptiometry of the shoulder with BMD measures in 4

tem-plated regions of interest (ROIs) were performed. Functional outcomes, Western Ontario Osteoarthritis of the Shoulder index, Constant score, visual analog scale pain (VAS), and 36-Item Short Form Survey, were collected. Results: A total of 17 of 36 patients had osteoporosis. We found no differences in BMD changes, functional outcomes, radiology, or need for revision surgery between the osteoporosis and nonosteoporosis groups. The BMD values gradually declined from baseline to 3 -month follow-up in all 4 ROIs of the operated shoulders. All 4 ROIs in the operated shoulder presented with a reduction in BMD at 3, 6, and 12 months compared with baseline, whereas no significant BMD changes were seen in the healthy shoulder during the study period. The functional outcomes displayed an increase in Constant score from 3 to 12 months, but a decrease in domains of the 36-Item Short Form Survey from preinjury to 12 months (physical functioning, general health, and bodily pain). Preinjury and 12-month Western Ontario Osteoarthritis of the Shoulder index, VAS pain at rest, and VAS pain at activity were comparable.Conclusion: BMD changes appeared swiftly in the proximal humerus, after the treatment of displaced 3-or 4-part fractures with ORIF, particularly affecting the proximal diaphysis of the humerus. Shoulder function was restored to preinjury levels for most of the patients. Osteoporosis may not be regarded as a contraindication for the treatment of displaced 3-or 4-part fractures with ORIF.Level of Evidence: Level I; Prospective Cohort Design; Prognosis Study (c) 2022 The Author(s). This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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NR 32
TC 5
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U2 4
PU MOSBY-ELSEVIER
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J9 J SHOULDER ELB SURG
JI J. Shoulder Elbow Surg.
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PT J
AU Wang, XW
Tian, HD
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Li, Yi
TI Mesenchymal Stem Cells-Derived Extracellular Vesicles in Orthopedic Diseases: Recent Advances and Therapeutic Potential
SO ADVANCED THERAPEUTICS
LA English
DT Review
DE exosome; extracellular vesicles; mesenchymal stem cells; orthopedic diseases
ID stromal cells; bone-marrow; cartilage repair; exosm; regeneration; mechanisms; immunomodulation; differentiation; transplantation; proliferation
AB Ever since the first application of mesenchymal stem cell (MSC) transplantation treating human hematologic malignancies in 1995, MSC-based treatments have demonstrated great therapeutic potential in clinical settings. However, only a few MSC-based cell therapy products have been clinically approved. Accumulating evidence suggests that the beneficial effects of MSCs are mainly attributed to the release of paracrine factors or extracellular vesicles (EVs) rather than their mesodermal differentiation potential. Therefore, MSC-derived EVs (MSC-EVs), such as exosomes and microvesicles, have merged as promising alternatives to traditional cell-based therapeutics in clinical practice. They offer several advantages such as better safety, lower immunogenicity, protection of cargoes from degradation, and the ability to overcome biological barriers. Moreover, there have been multiple clinical studies exploring the potential of MSC-EVs for treating various diseases, including orthopedic disorders. However, there is no definitive "cure" for conditions such as osteoporosis and other bone disorders, but MSC-EVs have displayed significant therapeutic potential for these orthopedic ailments. Therefore, the objective of this study is to conduct a systematic review of current knowledge related to MSC-EVs and emphasize their potential application in treating orthopedic diseases, such as bone defects, osteoarthritis, osteoporosis, intervertebral disc degeneration, osteosarcoma, and osteoradionecrosis. Mesenchymal stem cell (MSC)-derived extracellular vesicles (EVs) (MSC-EVs), such as exosomes and microvesicles, have been proposed as promising alternatives to traditional cell-based therapeutics in clinical settings. This study aims to systematically review the current knowledge of MSC-EVs and highlight their potential application in treating orthopedic diseases, such as bone defects, osteoarthritis, osteoporosis, intervertebral disc degeneration, osteosarcoma, and osteoradionecrosis.image
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TI Curcumin nanoparticles and the therapeutic potential of curcumin for musculoskeletal disorders
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DE Musculoskeletal; Curcumin; Nanomaterials; Osteo-porosis; Osteoarthritis
ID glucocorticoid-induced osteoporosis; in-vitro; gold nanoparticles; clinical-trial; double-blind; tetrahydrocurcumin; arthritis; bioavailability; inflammation; liposm
AB - Musculoskeletal disorders (MSD) are a collection of degenerative conditions im-pacting the body's bones, joints, muscles, ten-dons, ligaments, and nerves. MSDs affect ap-proximately 1.71 billion individuals worldwide and are a significant cause of disability. Cur -cumin is a polyphenolic compound with anti-in-flammatory, antioxidant, and antitumor proper-ties. In this review, we will discuss the research progress of structural analogs, derivatives, and nanomaterials that can improve the bioavailabil-ity of this natural drug. Curcumin may potential-ly retard the progression of osteoporosis, osteo-arthritis, and rheumatoid arthritis. These effects may be related to curcumin's targeting of multi-ple signalling pathways.
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TI Midterm clinical outcome of uncemented short-stem reversed shoulder arthroplasty
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article
DE Total shoulder arthroplasty; Reverse; Uncemented; Short stem; Risk factors; Clinical outcome
ID primary glenohumeral osteoarthritis; rotator cuff; classification; management; younger; designs
AB Introduction While the incidence of reverse total shoulder arthroplasty (rTSA) is increasing constantly, newer implants with designs other than the classic Grammont geometry are gaining importance. More anatomic inclination angles and lateralization are supposed to have a positive impact on clinical results and complication rates. Presentation of midterm results therefore is important to support these assumptions. The aim of this study was to report the midterm clinical outcome of primary rTSA with an uncemented humeral short-stem prosthesis (USSP) with a humeral inclination angle of 145 degrees and the analysis of different

variables on the outcome. Methods This is a retrospective study of all patients with primary rTSA using an USSP and a combined humeral inclination angle of 145 degrees (Ascend (TM) flex, Stryker) with a minimum clinical follow-up of 2 years. The implant combines a 132.5 degrees inclination for the humeral stem with an additional 12.5 degrees for the polyethylene inlay. Primary outcomes were patient-reported outcome measures: ASES score, simple shoulder test (SST) and subjective shoulder value (SSV). Secondary outcomes were complication and revision rates. We analyzed different variables: preoperatively gender, age, indication for surgery and status of rotator cuff. Also, the glenoid morphology was classified according to Walch and a proximal humerus cortical bone thickness measurement (CBT avg) of 6 mm was used as a threshold for osteoporosis. Postoperatively, we analyzed different radiologic parameters: filling ratio, distalization and lateralization angles according to Boutsiadis. Results A total of 84 out of 99 (85%) patients with a mean FU of 46.7 months (range 24-80 months) could be included: 62 women and 22 men with a mean age of 74.7 years. Mean ASES score significantly increased from 47 preoperatively to 85.8 at the last follow-up ($p = 0.001$). The postoperative SST reached an average of 65.3 and the mean SSV was 83%. None of the variable parameters analyzed could be identified as a risk factor for a lower outcome defined as a SSV < 70. Three patients (3.6%) had a complication: one incomplete lower plexus lesion, one dislocation and one major hematoma. Surgical revision was needed in two cases (2.4%). Conclusion The midterm clinical outcome of primary reverse total shoulder arthroplasty (rTSA) with an uncemented humeral short stem and a humeral inclination angle of 145 degrees showed good-to-excellent results with a low complication and revision rate independent from a wide range of pre- and postoperative variables. PROMs are comparable to those reported for anatomic TSA with a low complication rate, different to historical studies especially with the Grammont design.
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TI Novel insights into the METTL3-METTL14 complex in musculoskeletal diseases
SO CELL DEATH DISCOVERY
LA English
DT Review
ID methyltransferase mettl3 promotes; messenger-rna methylation; structural basis; m(6)a; n-6-methyladenosine; osteosarcoma; osteoporosis; epigenetics; apoptosis; genetics
AB N6-methyladenosine (m(6)A) modification, catalyzed by methyltransferase complexes (MTCs), plays many roles in multifaceted biological activities. As the most important subunit of MTCs, the METTL3-METTL14 complex is reported to be the initial factor that catalyzes the methylation of adenosines. Recently, accumulating evidence has indicated that the METTL3-METTL14 complex plays a key role in musculoskeletal diseases in an m(6)A-dependent or -independent manner. Although the functions of m(6)A modifications in a variety of musculoskeletal diseases have been widely recognized, the critical role of the METTL3-METTL14 complex in certain musculoskeletal disorders, such as osteoporosis, osteoarthritis, rheumatoid arthritis and osteosarcoma, has not been

systematically revealed. In the current review, the structure, mechanisms and functions of the METTL3-METTL14 complex and the mechanisms and functions of its downstream pathways in the aforementioned musculoskeletal diseases are categorized and summarized.
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TI Direct Reprogramming in Bone and Joint Degenerative Diseases: Applications,

Obstacles and Directions
SO CURRENT STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE Direct reprogramming; bone and joint degenerative diseases; pluripotent cell; obstacles; osteoarthritis (OA); microenvironment
ID pluripotent stem-cells; pioneer transcription factors; mouse somatic-cells; direct conversion; intervertebral disc; human fibroblasts; cardiac fibroblasts; chondrogenic cells; functional-neurons; in-vitro
AB With a booming aging population worldwide, bone and joint degenerative diseases have gradually become a major public health focus, attracting extensive scientific attention. However, the effective treatments of these degenerative diseases have been confined to traditional medications and surgical interventions, which easily lead to the possibility of drug abuse or loss of physiological function to varying degrees. Recently, given that the development of reprogramming has overcome shackles in the field of degenerative diseases, direct reprogramming would provide a new concept to accelerate progress in the therapy of bone and joint degenerative diseases. The process of direct reprogramming would directly induce ordinary somatic cells to the desired targeted cells without passing through pluripotent cell states. In this review, we summarize some direct reprogramming of cells that has been attempted for the repair of common bone and joint degenerative diseases, such as osteoarthritis, osteoporosis-related fracture and intervertebral disc degeneration. However, it is inevitable that some obstacles, such as accurate transcription factors, an appropriate extracellular microenvironment and efficient delivery carriers in vivo, need to be resolved. In addition, developmental and promising directions associated with direct reprogramming have attracted public attention. Investigation of the regulation of the transient genome, metabolic conversion and cellular skeleton would provide superior potential candidates for the revolution of direct reprogramming. The aim of direct reprogramming is to directly provide target cells for cell therapy and even tissue reconstruction in bone and joint degenerative diseases. Moreover, the development of direct reprogramming have potential to achieve repair and even reconstruct in situ, which would be breakthrough effect for the repair of bone and joint degenerative diseases. The advance of direct reprogramming has opened numerous opportunities for new therapeutic strategies in regenerative medicine.
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TI α-Linolenic Acid Inhibits RANKL-Induced Osteoclastogenesis In Vitro and Prevents Inflammation In Vivo
SO FOODS
LA English
DT Article
DE alpha-linolenic acid; osteoclastogenesis; anti-inflammation; ovariectomized rat; Zanthoxylum bungeanum seed oil
ID bungeanum maxim seed; bone loss; lipoic acid; lymphocyte ratio; osteoporosis; promotes; extract; gpr120; marker; cells
AB Inflammation is an important risk factor for bone-destroying diseases. Our preliminary research found that Zanthoxylum bungeanum seed oil (ZBSO) is abundant in unsaturated fatty acids and could inhibit osteoclastogenesis in receptor activator of nuclear factor kappa B ligand (RANKL)-induced RAW264.7

cells. However, the key constituents in ZBSO in the prevention of osteoclastogenesis and its possible mechanism related to inflammation are still unclear. Therefore, in this study, oleic acid (OA), linoleic acid (LA), palmitoleic acid (PLA), and alpha-linolenic acid (ALA) in ZBSO, havingthe strongest effect on RANKL-induced osteoclastogenesis, were selected by a tartrate-resistant acid phosphatase (TRAP) staining method. Furthermore, the effects of the selected fatty acids on anti-inflammation and anti-osteoclastogenesis in vitro and in vivo were assessed using RT-qPCR. Among the four major unsaturated fatty acids we tested, ALA displayed the strongest inhibitory effect on osteoclastogenesis. The increased expression of free fatty acid receptor 4 (FFAR4) and beta-arrestin2 (beta arr2), as well as the decreased expression of nuclear factor-kappa B (NF-kappa B), tumor necrosis factor-alpha (TNF-alpha), nuclear factor of activated T-cells c1 (NFATc1), and tartrate-resistant acid phosphatase (TRAP) in RAW264.7 cells after ALA treatment were observed. Moreover, in ovariectomized osteoporotic rats with ALA preventive intervention, we found that the expression of TNF-alpha, interleukin-6 (IL-6), interleukin-1 beta (IL-1 beta), NFATc1, and TRAP were decreased, while with the ALA therapeutic intervention, downregulated expression of NF-kappa B, NFATc1, TRAP, and transforming growth factor beta-activated kinase 1 (TAK1) were noticed. These results indicate that ALA, as the major unsaturated fatty acid in ZBSO, could inhibit RANKL-induced osteoclastogenesis via the FFAR4/beta arr2 signaling pathway and could prevent inflammation, suggesting that ZBSO may be a promising potential natural product of unsaturated fatty acids and a dietary supplement for the prevention of osteoclastogenesis and inflammatory diseases.
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TI Regulating spleen and stomach can improve bone and joint function of knee osteoarthritis patients complicated with osteoporosis
SO AMERICAN JOURNAL OF TRANSLATIONAL RESEARCH
LA English
DT Article
DE Spleen and stomach conditioning treatment; bone and joint function; osteoarthritis; osteoporosis
ID traditional chinese medicine
AB Objective: This study was designed to determine the influences of spleen and stomach conditioning treatment in Traditional Chinese Medicine (TCM) on patients with both knee osteoarthritis (KOA) and osteoporosis (OP). Methods: The medical records of 108 patients with both KOA and OP treated in Wuhan No. 1 Hospital between February 2020 and December 2021 were retrospectively studied. Among them, 58 patients treated with western medicine alone were assigned to a control

group, and 50 patients who received spleen and stomach conditioning treatment in TCM based on western medicine treatment were assigned to an observation group. The efficacy on the two groups was compared. The joint function, pain, inflammatory factors and bone turnover markers in the two groups before and after treatment were analyzed, as well as the incidence of adverse reactions after treatment. The prognosis of the patients at 12 months after treatment was counted, and the influencing factors of poor prognosis were analyzed by multivariate analysis. Results: The observation group showed a notably higher total effective rate than the control group (P<0.05). After treatment, the observation group had notably higher Lysholm score, but notably lower Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and visual analogue scale (VAS) scores than the control group (all P<0.05). After treatment, the bone turnover markers (beta collagen degradation products (beta-CTx) and procollagen type I amino-terminal propeptide (P1NP)) in both groups decreased notably (P<0.05), with notably lower levels of them in the observation group than those in the control group (both P<0.05). Additionally, after the treatment, the inflammatory indexes (interleukin-1 beta (IL-1 beta), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha)) in both groups decreased notably (all P<0.05), with notably lower levels of them in the observation group than those in the control group (all P<0.05). Moreover, the observation group presented a notably lower incidence of adverse reactions than the control group (P<0.05). The rate of poor prognosis in the observation group was notably lower than that in the control group. According to multiple logistic regression analysis, older age, higher BMI, higher Kellgren-Lawrence grading based on X-ray and history of bone fracture were independent risk factors for poor prognosis, and spleen and stomach conditioning treatment was an independent protective factor. Conclusion: Additional TCM spleen and stomach conditioning treatment can substantially improve the efficacy in patients with both KOA and OP by adjusting the inflammatory factors and bone turnover markers of patients, improving their joint function, alleviating their pain, and strongly preventing adverse reactions, so it is of great clinical application value.
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TI Radiological Features in Type II Odontoid Fractures in Older Adults After High- and Low-Energy Trauma
SO GLOBAL SPINE JOURNAL
LA English
DT Article
DE cervical spine; elderly; trauma; type II odontoid fractures; low-energy trauma; high-energy trauma; cervical malalignment; osteoporosis
ID cervical-spine fractures; injury; epidemiology; management; age
AB Study design: Retrospective study. Objectives: Although type II odontoid fractures mainly occur due to high-energy trauma (HET), the number of odontoid type II fractures after low-energy trauma (LET) in the elderly is on the rise. However, there is a paucity of conclusive evidence on the relationship between trauma mechanism and cervical spine alignment in the elderly population. Consequently, we examined cervical alignment and osteoporotic and osteoarthritic patterns in elderly individuals (aged >= 65 years) with type II odontoid fractures. Methods: We retrospectively assessed cervical spine alignment in 76 elderly individuals who experienced type II odontoid fractures after HET (n = 36) and LET (n = 40) between 2005 and 2020. Osteoporotic and osteoarthritic changes on computed tomography and cervical alignment parameters on sagittal plane radiographs were examined. Results: Moderate and severe osteoporosis of the dens-body junction and osteoarthritis of the atlanto-odontoid joint were more prevalent in the LET than the HET group (P<.005). The anterior atlantodental interval (ADI) was significantly smaller in the LET group than in the HET group (.7 [.7] millimeter vs 1.2 [.8] mm; P=.003). An ADI equal 0 mm indicative for anterior fusion of C1 /C2 was present in 37.5% of patients of the LET group. The C0-C2 angle, C1 -C2 lordosis, and C2-C7 sagittal vertical axis were significantly different (HET vs LET: 33.2 [7.2]degrees vs 41.6 [11.4]degrees, P=.005; 28.1 [7.0]degrees vs 34.0 [8.0]degrees, P=.002; and 16.1 [11.1] millimeter vs 27.1 [12.4] mm, P=.008; respectively). Conclusion: Significantly higher rates of osteoporotic and degenerative changes were observed after LET. Furthermore, previous cervical malalignment represents a risk factor for type II odontoid fractures after LET.
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NR 21
TC 2
Z9 2
U1 0
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PU SAGE PUBLICATIONS LTD
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PA 1 OLIVERS YARD, 55 CITY ROAD, LONDON EC1Y 1SP, ENGLAND
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J9 GLOB SPINE J
JI Glob. Spine J.
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WC Clinical Neurology; Orthopedics
SC Neurosciences & Neurology; Orthopedics
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PT J
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TI A comparison of radiographic degeneration features of older Chinese women and older Italian Caucasian women with a focus on thoracic spine
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Spine; Thoracic; Vertebral deformities; Degeneration; Chinese; Caucasians
ID low-back-pain; disc degeneration; risk-factors; lumbar spine; osteoarthritis; osteoporosis; prevalence; age; kyphosis
AB Background Compared with Caucasians, East Asians have a lower incident of back pain, lower prevalence and severity of osteoporotic vertebral fracture and lumbar spine degeneration.Aim This study compares radiographic spine degeneration features of older Chinese women (as an example of East Asians) and older Italian women (as an example of Caucasians) with a focus on the thoracic spine.Methods From two population-based epidemiological studies conducted in Hong Kong, China and Rome, Italy, 297 pairs (mean age: 73.6 years) age-matched older community women's lateral spine radiographs were sampled. Existence (or absence) of seven degeneration features were assessed including: (1) hyper-kyphosis, (2) disc space narrowing (T3/T4 similar to T11/T12), (3)

osteoarthritic (OA) wedging (T4 similar to T12), (4) generalised osteophyte formation (T4 similar to T12); (5) acquired short vertebrae (T4 similar to T12), (6) Schmorl node (T4 - L5), (7) disc calcification (T4-L5).Results Italian women were more likely to have hyper-kyphosis (53.4% vs 25.6%), disc space narrowing (34.4% vs. 17.2%), OA wedging (6.4% vs. 0.67%), Schmorl node (19.5% vs. 4.4%, all P < 0.001). However, there was no statistically significant difference in osteophyte formation (7.7% vs. 9.4%, P > 0.1) and acquired short vertebrae (8.0% vs. 10.4%, P > 0.1). Disc calcification was uncommon among both Chinese and Italians.Discussion and conclusion For the first time, this study documented a lower prevalence of a number of thoracic spine degeneration features among Chinese. This study further affirms the concept of a generally healthier spine in older Chinese relative to older Caucasians. The observed differences may reflect a foundational background influence of genetic predisposition that represents an important line of future research.
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NR 47
TC 12
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PU SPRINGER
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J9 AGING CLIN EXP RES
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
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TI Dynamic knee stiffness during walking is increased in individuals with anterior cruciate ligament reconstruction
SO JOURNAL OF BIOMECHANICS
LA English
DT Article
DE ACLR; Quasi -stiffness; Knee osteoarthritis; Knee loading; Kinematics; Kinetics
ID joint stiffness; quadriceps strength; gait; osteoarthritis; rehabilitation; cocontraction; biomechanics; association; kinematics; kinetics
AB Individuals with anterior cruciate ligament (ACL) reconstruction often display abnormal gait mechanics reflective of a "stiff-knee" gait (i.e., reduced knee flexion angles and moments). However, dynamic knee stiffness, which is the dynamic relationship between the position of the knee and the moment acting on it, has not been directly examined during walking in individuals with ACL reconstruction. Here, we aimed to evaluate dynamic knee stiffness in the involved compared to the uninvolved limb during weight-acceptance and mid-stance phases of walking. Twenty-six individuals who underwent ACL reconstruction (Age: 20.2 +/- 5.1 yrs., Time post-op: 7.2 +/- 0.9 mo.) completed an overground walking assessment using a three-dimensional motion capture system and two force plates. Dynamic knee stiffness (Nm/degrees) was calculated as the slope of the regression line during weightacceptance and midstance, obtained by plotting the sagittal plane knee angle versus knee moment. Paired t-tests with Bonferroni corrections were used to compare differences in dynamic stiffness, knee excursions, and moment ranges between limbs during both stance phases. Greater dynamic knee stiffness was found in the involved compared with the uninvolved limb during weight-acceptance and mid-stance ($p < 0.01$). Knee flexion and extension excursions were reduced in the involved limb during both weight-acceptance and mid-stance, respectively ($p < 0.01$). Sagittal plane knee moment ranges were not different between limbs during weightacceptance ($p = 0.1$); however, the involved limb moment range was reduced relative to the uninvolved limb during mid-stance ($p < 0.01$). These results indicate that individuals with ACL reconstruction walk with a stiffer knee throughout stance, which may influence knee contact forces and could contribute to the high propensity for post-traumatic knee osteoarthritis development in this population.
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NR 41
TC 10
Z9 10
U1 0
U2 17
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
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JI J. Biomech.
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WC Biophysics; Engineering, Biomedical
SC Biophysics; Engineering
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TI The Efficacy and Safety of Bionic Tiger Bone Powder for the Treatment of Knee Osteoarthritis in Early Stage: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial
SO ALTERNATIVE THERAPIES IN HEALTH AND MEDICINE
LA English
DT Article

ID expert consensus
AB Objective center dot This study evaluated the efficacy and safety of bionic tiger bone powder (Jintiange) in comparison to placebo in treating knee osteoarthritis osteoporosis. Methods center dot A total of 248 patients were randomly allocated to a Jintiange group or a placebo group, undergoing 48 weeks of double-blind treatment. The Lequesne index, clinical symptoms, safety index (adverse events), and Patient's Global Impression of Change score were recorded at pre-determined time intervals. All P values <= .05 were deemed statistically significant. Results center dot Both groups showed a decreasing trend in the Lequesne index, with the Jintiange group's reduction significantly larger from the 12th week (P = .01). Similarly, the effective rate of Lequesne score in the Jintiange group was significantly higher (P < .001). After 48 weeks, clinical symptom score differences between the Jintiange group (2.46 +/- 1.74) and the placebo group (1.51 +/- 1.73) were statistically significant (P < .05), as were differences in the Patient's Global Impression of Change score (P < .05). Adverse drug reactions were minimal with no significant difference between the groups (P > .05). Conclusion center dot Jintiange demonstrated superior efficacy over placebo in treating knee osteoporosis, with comparable safety profiles. Findings warrant further comprehensive real-world studies.
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Zhang ZY, 2020, ANN TRANSL MED, V8, P0, DOI 10.21037/atm-20-4665
NR 17
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J9 ALTERN THER HEALTH M
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PD SEP 15
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DI
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WC Integrative & Complementary Medicine
SC Integrative & Complementary Medicine

GA P3XJ9
UT WOS:001050004000057
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ER

PT J
AU Plapler, PG
Cecatto, RB
Socolowski, MD
Martins, F
AF Plapler, Perola Grinberg
Cecatto, Rebeca Boltes
Socolowski, Mariela Diament
Martins, Fernanda
TI Disability prevalent conditions in women
SO REVISTA DA ASSOCIACAO MEDICA BRASILEIRA
LA English
DT Article
DE Disability evaluations; Women's health; Osteoporosis; Osteoarthritis; Lymphedema; Pregnancy
ID osteoarthritis; epidemiology; pain
AB Women and men can have the same illnesses, but with different prevalence and reactions to symptoms. OBJECTIVE: This study aimed to emphasize that distinct traits between men and women require a different approach for each of them.METHODS: PubMed and Google Scholar were searched using the following terms: Disability Evaluations, Women's health, Osteoporosis, Osteoarthritis,RESULTS/CONCLUSION: Disease management can go beyond the symptoms, assessing the long-term consequences and possibly the disabilities they can generate, compromising the quality of life of the person, his/her family members, and eventually caregivers.
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10.1016/S0002-9610(99)00008-2
NR 25
TC 0
Z9 0
U1 0
U2 1
PU ASSOC MEDICA BRASILEIRA
PI SAO PAULO

PA RUA SAO CARLOS DO PINHAL 324, CAIXA POSTAL 8904, SAO PAULO, SP, BRAZIL
SN 0104-4230
EI 1806-9282
J9 REV ASSOC MED BRAS
JI Rev. Assoc. Med. Bras.
PD JUN 15
PY 2023
VL 69
IS
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DI 10.1590/1806-9282.2023S115
PG 5
WC Medicine, General & Internal
SC General & Internal Medicine
GA O9XP4
UT WOS:001047277100007
PM 37556634
DA 2026-02-10
ER

PT J
AU Dong, WL
Beynnon, BD
AF Dong, Willie
Beynnon, Bruce D.
TI A prospective study of joint position sense after anterior cruciate ligament injury, reconstruction with a bone-patella tendon-bone graft, and rehabilitation
SO KNEE
LA English
DT Article
DE Anterior cruciate ligament; Posttraumatic osteoarthritis; Reconstruction; Joint position
ID proprioception; knee; deficient; rupture; tears
AB Background: Disruption of the anterior cruciate ligament (ACL) is associated with signifi-cant biomechanical and neuromuscular changes including deficits in joint proprioception. While previous studies have assessed joint position sense (JPS) in ACL deficient knees, methods have varied and few have done so with prospective study designs. The specific aim of this investigation was to determine the effect(s) of ACL reconstruction and recovery time may have on JPS.Methods: In this prospective study, we assess the effects of ACL reconstruction and rehabil-itation on joint position sense in a temporal study. Twelve patients with unilateral ACL injuries were assessed pre-operatively and at 2, 4, 8 months post-op.

JPS measurements were performed, while the subject was standing, with passive-active (P-A) and active-active (A-A) tests. Comparisons between the injured/reconstructed and contralateral, unin-jured knee were evaluated in terms of real and absolute mean errors. Results: There were no statistically significant differences between the injured/recon-structed and contralateral/normal side with P-A or A-A testing at 2, 4, or 8 months.Conclusion: We conclude that there is no difference in joint position sense between the injured and contralateral leg after ACL disruption and reconstruction beginning as early as 2 months post-op. This study provides further evidence that knee proprioception is not altered by ACL injury and reconstruction. Level of evidence: II.(c) 2023 Elsevier B.V. All rights reserved.
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NR 29
TC 3
Z9 3
U1 1
U2 8
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 0968-0160
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J9 KNEE
JI Knee
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EA MAR 2023
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WC Orthopedics; Sport Sciences; Surgery
SC Orthopedics; Sport Sciences; Surgery
GA 9Z8ZW
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PT J
AU Yuan, WQ
Liu, WJ
Zhang, YH
Wang, XL
Xu, CH
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Wu, Yanfeng
Shen, Huiyong
Wang, Peng
TI Reduced APPL1 impairs osteogenic differentiation of mesenchymal stem cells by facilitating MGP expression to disrupt the BMP2 pathway in osteoporosis
SO JOURNAL OF BIOLOGICAL CHEMISTRY
LA English
DT Article
ID matrix gla-protein; bone morphogenetic protein-2; osteoblast differentiation; tgf-beta; adiponectin; osteoarthritis; activation; mechanisms; imbalance; mice
AB An imbalance of human mesenchymal stem cells (MSCs) adipogenic and

osteogenic differentiation plays an important role in the pathogenesis of osteoporosis. Our previous study verified that Adaptor protein, phosphotyrosine interacting with PH domain and leucine zipper 1 (APPL1)/myoferlin deficiency promotes adipogenic differentiation of MSCs by blocking autophagic flux in osteoporosis. However, the function of APPL1 in the osteogenic differentiation of MSCs remains unclear. This study aimed to investigate the role of APPL1 in the osteogenic differentiation of MSCs in osteoporosis and the underlying regulatory mechanism. In this study, we demonstrated the downregulation of APPL1 expression in patients with osteoporosis and osteoporosis mice. The severity of clinical osteoporosis was negatively correlated with the expression of APPL1 in bone marrow MSCs. We found that APPL1 positively regulates the osteogenic differentiation of MSCs in vitro and in vivo. Moreover, RNA sequencing showed that the expression of MGP, an osteocalcin/matrix Gla family member, was significantly upregulated after APPL1 knock-down. Mechanistically, our study showed that reduced APPL1 impaired the osteogenic differentiation of mesenchymal stem cells by facilitating Matrix Gla protein expression to disrupt the BMP2 pathway in osteoporosis. We also evaluated the significance of APPL1 in promoting osteogenesis in a mouse model of osteoporosis. These results suggest that APPL1 may be an important target for the diagnosis and treatment of osteoporosis.
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FU National Natural Science Foundation of China [82172349]; Shenzhen Key Medical Discipline Construction Fund [ZDSYS20190902092851024]; Shenzhen Science and Technology Program [RCBS20210609104445097]; Natural Science Foundation of Guangdong Province, China [2021A1515111057]; Futian Healthcare Research Project [FTWS2021013]
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NR 51
TC 8
Z9 9
U1 0
U2 15
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN
EI 1083-351X
J9 J BIOL CHEM
JI J. Biol. Chem.
PD JUN 15
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PG 17
WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
GA G7H7A
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ER

PT J
AU Azuma, K
Osuka, Y
Kojima, N

Sasai, H
Inoue, S
AF Azuma, Kotaro
Osuka, Yosuke
Kojima, Narumi
Sasai, Hiroyuki
Inoue, Satoshi
TI Vitamin K insufficiency predicts incidence of frailty in community-dwelling older adults: The Otassha Study
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Vitamin K; Undercarboxylated osteocalcin (ucOC); Osteocalcin (OC); Frailty; Longitudinal study
ID health
AB IntroductionVitamin K is a fat-soluble vitamin discovered as an essential factor for blood coagulation. It is suggested that vitamin K can benefit several aging-related diseases, including osteoporosis, osteoarthritis, and dementia. We previously reported the cross-sectional association of vitamin K insufficiency with frailty in community-dwelling older adults.Materials and methodsIn October 2020, a health examination of community-dwelling older adults (The Otassha Study) was performed, including frailty evaluation and blood tests. We used a ucOC and OC ratio (ucOC/OC) to indicate vitamin K insufficiency. One year later, we conducted a follow-up evaluation of frailty on 518 people who were not frail at baseline. The serum ucOC/OC at the baseline examination was divided into quartiles (Q1, Q2, Q3, and Q4). Odds ratio (OR) and 95% confidence interval (CI) were calculated using multivariate binary logistic regression for each quartile of ucOC/OC to determine the risk of incident frailty in the follow-up study, with the lowest quartile (Q1) as the reference.ResultsAmong the 518 older adults who were not frail at baseline, 66 people (12.7%) became frail in the follow-up study. In the multivariate binary logistic regression analysis, setting the lowest quartile of ucOC/OC (Q1) as a reference, the OR of the incident frailty in the highest quartile (Q4) was 2.53 (95% CI 1.07, 4.92) which was significantly different from Q1.ConclusionThe findings of this longitudinal study suggest that vitamin K insufficiency has nutritional importance in predicting the future incidence of frailty in the Japanese older adult population.
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CR Azuma K, 2022, AM J GERIAT PSYCHIAT, V30, P1051, DOI 10.1016/j.jagp.2022.04.012
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NR 23
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U1 0
U2 1
PU SPRINGER JAPAN KK

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TI Nrf2: A promising therapeutic target in bone-related diseases
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Review
DE Nrf2; Oxidative; Osteoporosis; Facture; Osteoarthritis; Therapeutic target
ID rankl-induced osteoclastogenesis; ech-associated protein-1; heme oxygenase 1; oxidative stress; rheumatoid-arthritis; reactive oxygen; inflammatory response; nlrp3 inflammasome; signaling pathway; nuclear factor
AB Nuclear factor erythroid-2-related factor 2 (Nrf2) plays an important role in maintaining cellular homeostasis, as it suppresses cell damage caused by external stimuli by regulating the transcription of intracellular defense -related genes.

Accumulating evidence has highlighted the crucial role of reduction-oxidation (REDOX) imbal-ance in the development of bone-related diseases. Nrf2, a transcription factor linked to nuclear factor-erythrocyte 2, plays a pivotal role in the regulation of oxidative stress and induction of antioxidant defenses. Therefore, further investigation of the mechanism and function of Nrf2 in bone-related diseases is essential. Considerable evidence suggests that increased nuclear transcription of Nrf2 in response to external stimuli promotes the expression of intracellular antioxidant-related genes, which in turn leads to the inhibition of bone remodeling imbalance, improved fracture recovery, reduced occurrence of osteoarthritis, and greater tumor resistance. Certain natural extracts can selectively target Nrf2, potentially offering therapeutic benefits for osteogenic arthropathy. In this article, the biological characteristics of Nrf2 are reviewed, the intricate interplay between Nrf2-regulated REDOX imbalance and bone-related diseases is explored, and the potential preventive and pro-tective effects of natural products targeting Nrf2 in these diseases are elucidated. A comprehensive under-standing of the role of Nrf2 in the development of bone-related diseases provides valuable insights into clinical interventions and can facilitate the discovery of novel Nrf2-targeting drugs.
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AU Sun, HQ
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TI The sleep and wake electroencephalogram over the lifespan
SO NEUROBIOLOGY OF AGING
LA English
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DE Sleep; Aging; Electroencephalogram; Brain health; Age norm
ID eeg; age; childhood; spindles; performance; maturation; infants; gender; apnea
AB Both sleep and wake encephalograms (EEG) change over the lifespan. While prior studies have charac-terized age-related changes in the EEG, the datasets span a particular age group, or focused on sleep and wake macrostructure rather than the microstructure. Here, we present sex-stratified data from 3372 community-based or clinic-based otherwise neurologically and psychiatrically healthy participants rang -ing from 11 days to 80 years of age. We estimate age

norms for key sleep and wake EEG parameters in-cluding absolute and relative powers in delta, theta, alpha, and sigma bands, as well as sleep spindle den-sity, amplitude, duration, and frequency. To illustrate the potential use of the reference measures devel-oped herein, we compare them to sleep EEG recordings from age-matched participants with Alzheimer's disease, severe sleep apnea, depression, osteoarthritis, and osteoporosis. Although the partially clinical nature of the datasets may bias the findings towards less normal and hence may underestimate pathol-ogy in practice, age-based EEG reference values enable objective screening of deviations from healthy aging among individuals with a variety of disorders that affect brain health. (c) 2023 Elsevier Inc. All rights reserved.
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TI Hybrid Techniques of X-ray Analysis to Predict Knee Osteoarthritis Grades Based on Fusion Features of CNN and Handcrafted
SO DIAGNOSTICS
LA English
DT Article
DE deep learning; knee osteoarthritis; fusion features; handcrafted features; FFNN

AB Knee osteoarthritis (KOA) is a chronic disease that impedes movement, especially in the elderly, affecting more than 5% of people worldwide. KOA goes through many stages, from the mild grade that can be treated to the severe grade in which the knee must be replaced. Therefore, early diagnosis of KOA is essential to avoid its development to the advanced stages. X-rays are one of the vital techniques for the early detection of knee infections, which requires highly experienced doctors and radiologists to distinguish Kellgren-Lawrence (KL) grading. Thus, artificial intelligence techniques solve the shortcomings of manual diagnosis. This study developed three methodologies for the X-ray analysis of both the Osteoporosis Initiative (OAI) and Rani Channamma University (RCU) datasets for diagnosing KOA and discrimination between KL grades. In all methodologies, the Principal Component Analysis (PCA) algorithm was applied after the CNN models to delete the unimportant and redundant features and keep the essential features. The first methodology for analyzing x-rays and diagnosing the degree of knee inflammation uses the VGG-19 -FFNN and ResNet-101 -FFNN systems. The second methodology of X-ray analysis and diagnosis of KOA grade by Feed Forward Neural Network (FFNN) is based on the combined features of VGG-19 and ResNet-101 before and after PCA. The third methodology for X-ray analysis and diagnosis of KOA grade by FFNN is based on the fusion features of VGG-19 and handcrafted features, and fusion features of ResNet-101 and handcrafted features. For an OAI dataset with fusion features of VGG-19 and handcrafted features, FFNN obtained an AUC of 99.25%, an accuracy of 99.1%, a sensitivity of 98.81%, a specificity of 100%, and a precision of 98.24%. For the RCU dataset with the fusion features of VGG-19 and the handcrafted features, FFNN obtained an AUC of 99.07%, an accuracy of 98.20%, a sensitivity of 98.16%, a specificity of 99.73%, and a precision of 98.08%.
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TI Ubiquitin-specific proteases: Vital regulatory molecules in bone and bone-related diseases
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Review
DE Ubiquitin-specific proteases; Deubiquitination; Osteoclastogenesis; Osteogenesis; Bone-related diseases; Molecular mechanisms
ID nf-kappa-b; epithelial-mesenchymal transition; ror-gamma-t; tgf-beta; rheumatoid-arthritis; positive regulator; articular chondrocytes; ligase smurf1; stem-cells; promotes
AB Stabilization of bone structure and function involves multiple cell-to-cell and molecular interactions, in which the regulatory functions of post-translational modifications such as ubiquitination and deubiquitination shouldn't be underestimated. As the largest family of deubiquitinating enzymes, the ubiquitin-specific proteases (USPs) participate in the development of bone homeostasis and bone-related diseases through multiple classical osteogenic and osteolytic signaling pathways, such as BMP/TGF-beta pathway, NF-xB/p65 pathway, EGFR-MAPK pathway and Wnt/beta-catenin pathway. Meanwhile, USPs may also broadly regulate regulate hormone expression level, cell proliferation and differentiation, and may further influence bone homeostasis from gene fusion and nuclear translocation of transcription factors. The number of patients with bone-related diseases is currently enormous, making exploration of their pathogenesis and targeted therapy a hot topic. Pathological increases in the levels of inflammatory mediators such as IL-1 beta and TNF-alpha lead to inflammatory bone diseases such as osteoarthritis, rheumatoid arthritis and periodontitis. While impaired body metabolism greatly increases the probability of osteoporosis. Abnormal physiological activity of bone-associated cells results in a variety of bone tumors. The regulatory role of USPs in bone-related disease has received particular attention from academics in recent studies. In this review, we focuse on the roles and mechanisms of USPs in bone homeostasis and bonerelated diseases, with the expectation of informing targeted therapies in the clinic.
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DT Review
DE musculoskeletal system; drug delivery; tissue barriers; cartilage; muscle; bone
ID targeted delivery; zoledronic acid; bone; osteoporosis; transport; biodistribution; bisphosphonate; nanoparticle; restoration; carnitine
AB The musculoskeletal system (MSKS) is composed of specialized connective tissues including bone, muscle, cartilage, tendon, ligament, and their subtypes. The primary function of the MSKS is to provide protection, structure, mobility, and mechanical properties to the body. In the process of fulfilling these functions, the MSKS is subject to wear and tear during aging and after injury and requires subsequent repair. MSKS diseases are a growing burden due to the increasing population age. The World Health Organization estimates that 1.71 billon people suffer from MSKS diseases worldwide. MSKS diseases usually involve various dysfunctions in bones, muscles, and joints, which often result in pain, disability, and a decrease in quality of life. The most common MSKS diseases are osteoporosis (loss of bone), osteoarthritis (loss of cartilage), and sarcopenia (loss of skeletal

muscle). Because of the disease burden and the need for treatment, regenerative drug therapies for MSKS disorders are increasingly in demand. However, the difficulty of effective drug delivery in the MSKS has become a bottleneck for developing MSKS therapeutics. The abundance of extracellular matrix and its small pore size in the MSKS present a formidable barrier to drug delivery. Differences of vascularity among various MSKS tissues pose complications for drug delivery. Novel strategies are necessary to achieve successful drug delivery in different tissues composing the MSKS. Those considerations include the route of administration, mechanics of surrounding fluids, and biomolecular interactions, such as the size and charge of the particles and targeting motifs. This review focuses on recent advances in challenges to deliver drugs to each tissue of the MSKS, current strategies of drug delivery, and future ideas of how to overcome drug delivery challenges in the MSKS.
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TI Biochemical Markers of Musculoskeletal Health and Aging to be Assessed in Clinical Trials of Drugs Aiming at the Treatment of Sarcopenia: Consensus Paper from an Expert Group Meeting Organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the Centre Academique de Recherche et d'Experimentation en Sante (CARES SPRL), Under the Auspices of the World Health Organization Collaborating Center for the Epidemiology of Musculoskeletal Conditions and Aging
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Review
DE Sarcopenia; Biomarkers; Biochemical markers; Recommendations; Clinical trial; Pharmacological drugs
ID terminal agrin fragment; skeletal-muscle mass; older-adults; neurotrophic factor; serum creatinine; nutritional supplementation; adiponectin levels; growth-hormone; adipose-tissue; plasma leptin
AB In clinical trials, biochemical markers provide useful information on the drug's mode of action, therapeutic response and side effect monitoring and can act as surrogate endpoints. In pharmacological intervention development for sarcopenia management, there is an urgent need to identify biomarkers to measure in clinical trials and that could be used in the future in clinical practice. The objective of the current consensus paper is to provide a clear list of biochemical markers of musculoskeletal health and aging that can be recommended to be measured in Phase II and Phase III clinical trials evaluating new chemical entities for sarcopenia treatment. A working group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) proposed classifying biochemical markers into 2 series: biochemical markers

evaluating musculoskeletal status and biochemical markers evaluating causal factors. For series 1, the group agreed on 4 biochemical markers that should be assessed in Phase II or Phase III trials (i.e., Myostatin-Follistatin, Brain Derived Neurotrophic Factor, N-terminal Type III Procollagen and Serum Creatinine to Serum Cystatin C Ratio - or the Sarcopenia Index). For series 2, the group agreed on 6 biochemical markers that should be assessed in Phase II trials (i.e., the hormones insulin-like growth factor-1 (IGF-I), dehydroepiandrosterone sulphate, and cortisol, and the inflammatory markers C-reactive protein (CRP), interleukin-6 and tumor necrosis factor-alpha), and 2 in Phase III trials (i.e., IGF-I and CRP). The group also proposed optional biochemical markers that may provide insights into the mode of action of pharmacological therapies. Further research and development of new methods for biochemical marker assays may lead to the evolution of these recommendations.

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TI Fighting age-related orthopedic diseases: focusing on ferroptosis
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ID mesenchymal stem-cells; iron overload; intervertebral disc; bone-resorption; osteoclast differentiation; thalassemia major; gasdermin-d; hereditary hemochromatosis; synovial fibroblasts; lipid-peroxidation
AB Ferroptosis, a unique type of cell death, is characterized by iron-dependent accumulation and lipid peroxidation. It is closely related to multiple biological processes, including iron metabolism, polyunsaturated fatty acid metabolism, and the biosynthesis of compounds with antioxidant activities, including glutathione. In the past 10 years, increasing evidence has indicated a potentially strong relationship between ferroptosis and the onset and progression of age-related orthopedic diseases, such as osteoporosis and osteoarthritis. Therefore, in-depth knowledge of the regulatory mechanisms of ferroptosis in age-related orthopedic diseases may help improve disease treatment and prevention. This review provides an overview of recent research on ferroptosis and its influences on bone and cartilage homeostasis. It begins with a brief overview of systemic iron metabolism and ferroptosis, particularly the potential mechanisms of ferroptosis. It presents a discussion on the role of ferroptosis in age-related orthopedic diseases, including promotion of bone loss and cartilage degradation and the inhibition of osteogenesis. Finally, it focuses on the future of targeting ferroptosis to treat age-related orthopedic diseases with the intention of inspiring further clinical research and the development of therapeutic strategies.
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SO AGING AND DISEASE
LA English
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DE bonem metabolism; GPR120; fatty acids
ID fatty-acid; oxidative stress; osteoclast differentiation; gpr120; inhibition; omega-3-fatty-acids; osteoporosis; pathway; inflammation; activation
AB The link between fatty acids and bone metabolism is complex and can be direct and indirect. This link has been reported in different types of bone cells and various stages of bone metabolism. G-protein coupled receptor 120 (GPR120), also called free fatty acid receptor 4 (FFAR4), is a member of the recently discovered G protein-coupled receptor family that can interact with both long-chain saturated fatty acids (C14-C18) and long-chain unsaturated fatty acids (C16-C22). Research shows that GPR120 regulates processes in different types of bone cells, directly or indirectly affecting bone metabolism. Our research reviewed the literature on the effects of GPR120 on bone marrow mesenchymal stem cells (BMMSCs), osteoblasts, osteoclasts, and chondrocytes, focusing on the research findings regarding the mechanism by which GPR120 alters specific bone metabolic diseases-osteoporosis and osteoarthritis. The data reviewed here provide a basis for clinical and basic research into the role of GPR120 on bone metabolic diseases.
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TI Health benefits of astaxanthin against age-related diseases of multiple organs: A comprehensive review
SO CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
LA English
DT Review
DE Aging-associated diseases; anti-aging; apoptosis; astaxanthin; autophagy; inflammation; oxidative stress
ID induced oxidative stress; nf-kappa-b; helicobacter-pylori infection; acid-acylated astaxanthin; exercise-induced skeletal; nitric-oxide synthase; fatty liver-disease; growth-factor vegf; early brain-injury; in-vitro
AB Age-related diseases are associated with increased morbidity in the past few decades and the cost associated with the treatment of these age-related diseases exerts a substantial impact on social and health care expenditure. Anti-aging strategies aim to mitigate, delay and reverse aging-associated diseases, thereby improving quality of life and reducing the burden of age-related pathologies. The natural dietary antioxidant supplementation offers substantial pharmacological and therapeutic effects against various disease conditions. Astaxanthin is one such natural carotenoid with superior antioxidant activity than other carotenoids, as well as well as vitamins C and E, and additionally, it is known to exhibit a plethora of pharmacological effects. The present review summarizes the protective molecular mechanisms of actions of astaxanthin on age-related diseases of multiple organs such as Neurodegenerative diseases [Alzheimer's disease (AD), Parkinson's disease (PD), Stroke, Multiple Sclerosis (MS), Amyotrophic lateral sclerosis (ALS), and Status Epilepticus (SE)], Bone Related Diseases [Osteoarthritis (OA) and Osteoporosis], Cancers [Colon cancer, Prostate cancer, Breast cancer, and Lung Cancer], Cardiovascular disorders [Hypertension, Atherosclerosis and Myocardial infarction (MI)], Diabetes associated complications [Diabetic nephropathy (DN), Diabetic neuropathy, and Diabetic retinopathy (DR)], Eye disorders [Age related macular degeneration (AMD), Dry eye disease (DED), Cataract and Uveitis], Gastric Disorders [Gastritis, Colitis, and Functional dyspepsia], Kidney Disorders [Nephrolithiasis, Renal fibrosis, Renal Ischemia reperfusion (RIR), Acute kidney injury (AKI), and hyperuricemia], Liver Diseases [Nonalcoholic fatty liver disease (NAFLD), Alcoholic Liver Disease (AFLD), Liver fibrosis, and Hepatic Ischemia-Reperfusion (IR) Injury], Pulmonary Disorders [Pulmonary Fibrosis, Acute Lung injury (ALI), and Chronic obstructive pulmonary disease (COPD)], Muscle disorders (skeletal muscle atrophy), Skin diseases [Atopic dermatitis (ATD), Skin Photoaging, and Wound healing]. We have also briefly discussed astaxanthin's protective effects on reproductive health.
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TI Use of Poly Lactic-co-glycolic Acid Nano and Micro Particles in the Delivery of Drugs Modulating Different Phases of Inflammation
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DT Review
DE PLGA nanoparticles; oxidative stress; IBD; cardiovascular diseases; transplant rejection; neurologic diseases; osteoarthritis; bone regeneration; skin wound healing; eye diseases
ID loaded plga nanoparticles; to-brain delivery; in-vitro; rat model; extracellular-matrix; bone regeneration; oxidative stress; reactive oxygen; bowel-disease; cell sheet
AB Chronic inflammation contributes to the pathogenesis of many diseases, including apparently unrelated conditions such as metabolic disorders, cardiovascular diseases, neurodegenerative diseases, osteoporosis, and tumors, but

the use of conventional anti-inflammatory drugs to treat these diseases is generally not very effective given their adverse effects. In addition, some alternative anti-inflammatory medications, such as many natural compounds, have scarce solubility and stability, which are associated with low bioavailability. Therefore, encapsulation within nanoparticles (NPs) may represent an effective strategy to enhance the pharmacological properties of these bioactive molecules, and poly lactic-co-glycolic acid (PLGA) NPs have been widely used because of their high biocompatibility and biodegradability and possibility to finely tune erosion time, hydrophilic/hydrophobic nature, and mechanical properties by acting on the polymer's composition and preparation technique. Many studies have been focused on the use of PLGA-NPs to deliver immunosuppressive treatments for autoimmune and allergic diseases or to elicit protective immune responses, such as in vaccination and cancer immunotherapy. By contrast, this review is focused on the use of PLGA NPs in preclinical in vivo models of other diseases in which a key role is played by chronic inflammation or unbalance between the protective and reparative phases of inflammation, with a particular focus on intestinal bowel disease; cardiovascular, neurodegenerative, osteoarticular, and ocular diseases; and wound healing.
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TI Clinical Potential of Mesenchymal Stem Cell-Derived Exosomes in Bone Regeneration
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DT Review
DE regenerative medicine; bone; mesenchymal stem cells; extracellular vesicles; exosomes; biomaterials; cell-free therapy
ID endothelial growth-factor; extracellular vesicles; stromal cells; macrophage polarization; skeletal development; osteogenesis; enhance; marrow; repair; angiogenesis
AB Bone metabolism is regulated by osteoblasts, osteoclasts, osteocytes, and stem cells. Pathologies such as osteoporosis, osteoarthritis, osteonecrosis, and traumatic fractures require effective treatments that favor bone formation and regeneration. Among these, cell therapy based on mesenchymal stem cells (MSC) has been proposed. MSC are osteoprogenitors, but their regenerative activity depends in part on their paracrine properties. These are mainly mediated by extracellular vesicle (EV) secretion. EV modulates regenerative processes such as inflammation, angiogenesis, cell proliferation, migration, and differentiation. Thus, MSC-EV are currently an important tool for the development of cell-free therapies in regenerative medicine. This review describes the current knowledge of the effects

of MSC-EV in the different phases of bone regeneration. MSC-EV has been used by intravenous injection, directly or in combination with different types of biomaterials, in preclinical models of bone diseases. They have shown great clinical potential in regenerative medicine applied to bone. These findings should be confirmed through standardization of protocols, a better understanding of the mechanisms of action, and appropriate clinical trials. All that will allow the translation of such cell-free therapy to human clinic applications.
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TI Identification of kukoamine a as an anti-osteoporosis drug target using network pharmacology and experiment verification
SO MOLECULAR MEDICINE

LA English
DT Article
DE Osteoporosis; Kukoamine A; Osteoblast cells; Ovariectomized mice; Network pharmacology
ID oxidative stress; in-vitro; insulin-resistance; down-regulation; cortex lycii; bone mass; osteoarthritis; polymorphisms; metabolism; osteoblast
AB BackgroundOsteoporosis (OP) is a major and growing public health problem characterized by decreased bone mineral density and destroyed bone microarchitecture. Previous studies found that Lycium Chinense Mill (LC) has a potent role in inhibiting bone loss. Kukoamine A (KuA), a bioactive compound extract from LC was responsible for the anti-osteoporosis effect. This study aimed to investigate the anti-osteoporosis effect of KuA isolated from LC in treating OP and its potential molecular mechanism.MethodIn this study, network pharmacology and molecular docking were investigated firstly to find the active ingredients of LC such as KuA, and the target genes of OP by the TCMSP platform. The LC-OP-potential Target gene network was constructed by the STRING database and network maps were built by Cytoscape software. And then, the anti-osteoporotic effect of KuA in OVX-induced osteoporosis mice and MC3T3-E1 cell lines were investigated and the potential molecular mechanism including inflammation level, cell apoptosis, and oxidative stress was analyzed by dual-energy X-ray absorptiometry (DXA), micro-CT, ELISA, RT-PCR, and Western Blotting.ResultA total of 22 active compounds were screened, and we found KuA was identified as the highest active ingredient. Glycogen Phosphorylase (PYGM) was the target gene associated with a maximum number of active ingredients of LC and regulated KuA. In vivo, KuA treatment significantly increased the bone mineral density and improve bone microarchitecture for example increased BV/TV, Tb.N and Tb.Th but reduced Tb.Sp in tibia and lumber 4. Furthermore, KuA increased mRNA expression of osteoblastic differentiation-related genes in OVX mice and protects against OVX-induced cell apoptosis, oxidative stress level and inflammation level. In vitro, KuA significantly improves osteogenic differentiation and mineralization in cells experiment. In addition, KuA also attenuated inflammation levels, cell apoptosis, and oxidative stress level.ConclusionThe results suggest that KuA could protect against the development of OP in osteoblast cells and ovariectomized OP model mice and these found to provide a better understanding of the pharmacological activities of KuA again bone loss.
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TI Cell-Based Therapies for Degenerative Musculoskeletal Diseases
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ID mesenchymal stem-cells; autologous chondrocyte implantation; intervertebral disc repair; bone-marrow; skeletal-muscle; stromal cells; osteogenic differentiation; mitochondrial transfer; tricalcium phosphate; matrix stiffness
AB Degenerative musculoskeletal diseases (DMDs), including osteoporosis, osteoarthritis, degenerative disc disease, and sarcopenia, present major challenges in the aging population. Patients with DMDs present with pain, functional decline, and reduced exercise tolerance, which result in long-term or permanent deficits in their ability to perform daily activities. Current strategies for dealing with this cluster of diseases focus on relieving pain, but they have a limited capacity to repair function or regenerate tissue. Cell-based therapies have attracted considerable attention in recent years owing to their unique mechanisms of action and remarkable effects on regeneration. In this review, current experimental attempts to use cell-based therapies for DMDs are highlighted, and the modes of action of different cell types and their derivatives, such as exosomes, are generalized. In addition, the latest findings from state-of-the-art clinical trials are reviewed, approaches to improve the efficiency of cell-based therapies are summarized, and unresolved questions and potential future research directions for the translation of cell-based therapies are identified.
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NR 197
TC 30
Z9 34
U1 8

U2 70
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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SC Chemistry; Science & Technology - Other Topics; Materials Science
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PT J
AU Sharma, A
Martin, PR
Rodriguez, FR
AF Sharma, Aseem
Martin, Parker R.
Rodriguez, Francisco Rivas
TI Lumbar osteoporotic fractures develop in segments with less degenerated discs which then become more degenerated
SO EUROPEAN SPINE JOURNAL
LA English
DT Article
DE Osteoporosis; Vertebral compression fracture; Disc degeneration; Magnetic resonance imaging
ID bone-mineral density; postmenopausal women; vertebral fractures; osteoarthritis; association; risk; men
AB PurposeOur aim was to study the influence of segmental variations in intervertebral disc degeneration on the location of acute osteoporotic compression

fractures and to investigate chronic effect of such fractures on adjacent discs.MethodsThis retrospective study included 83 patients (69 females; mean +/- SD age: 72.3 +/- 14.0 years) with osteoporotic vertebral fractures. Using lumbar MRI, two neuroradiologists evaluated 498 lumbar vertebral segments for the presence and acuity of fractures and graded adjacent intervertebral disc degeneration on Pfirrmann's scale. Absolute and relative (to average patient-specific degeneration grade) segmental degeneration grades were compared against the presence and chronicity of vertebral fractures for all segments and for upper (T12-L2) and lower (L3-L5) subgroups. Intergroup analysis was conducted using Mann-Whitney U tests, with p value of < .05 considered significant.ResultsFractures involved 149/498 (29.9%; 15.1% acute) vertebral segments, majority (61.1%) involving T12-L2 segments. Segments with acute fractures had significantly lower degeneration grades (mean +/- SD: absolute: 2.72 +/- 0.62; relative: 0.91 +/- 0.17) than those with no (absolute: 3.03 +/- 0.79, p = 0.003; relative: 0.99 +/- 0.16, p < 0.001) or chronic fractures (absolute: 3.03 +/- 0.62, p = 0.003; relative: 1.02 +/- 0.16, p < 0.001). Degeneration grades were higher in the lower lumbar spine (p < 0.001) in the absence of fractures, but comparable to upper spine for segments with acute or chronic fractures (p = 0.28 and 0.56, respectively).ConclusionsOsteoporotic vertebral fractures favour segments with lower burden of disc degeneration, but likely contribute to subsequent worsening of adjacent disc degeneration.
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NR 20
TC 3
Z9 3
U1 0
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PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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PT J
AU Takematsu, E
Murphy, M

Hou, S
Steininger, H
Alam, A
Ambrosi, TH
Chan, CKF
AF Takematsu, Eri
Murphy, Matthew
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Steininger, Holly
Alam, Alina
Ambrosi, Thomas H.
Chan, Charles K. F.
TI Optimizing Delivery of Therapeutic Growth Factors for Bone and Cartilage Regeneration
SO GELS
LA English
DT Review
DE therapeutic growth factor delivery; osteoarthritis; osteoporosis; controlled delivery; osteoimmunology; biomaterials
ID mesenchymal stem-cells; in-vitro; drug-delivery; osteoblast differentiation; morphogenetic protein-2; parathyroid-hormone; articular-cartilage; controlled-release; hybrid scaffold; indian hedgehog
AB Bone- and cartilage-related diseases, such as osteoporosis and osteoarthritis, affect millions of people worldwide, impairing their quality of life and increasing mortality. Osteoporosis significantly increases the bone fracture risk of the spine, hip, and wrist. For successful fracture treatment and to facilitate proper healing in the most complicated cases, one of the most promising methods is to deliver a therapeutic protein to accelerate bone regeneration. Similarly, in the setting of osteoarthritis, where degraded cartilage does not regenerate, therapeutic proteins hold great promise to promote new cartilage formation. For both osteoporosis and osteoarthritis treatments, targeted delivery of therapeutic growth factors, with the aid of hydrogels, to bone and cartilage is a key to advance the field of regenerative medicine. In this review article, we propose five important aspects of therapeutic growth factor delivery for bone and cartilage regeneration: (1) protection of protein growth factors from physical and enzymatic degradation, (2) targeted growth factor delivery, (3) controlling GF release kinetics, (4) long-term stability of regenerated tissues, and (5) osteoimmunomodulatory effects of therapeutic growth factors and carriers/scaffolds.
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U1 0
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PU MDPI
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
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J9 GELS-BASEL
JI Gels
PD MAY 3
PY 2023
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IS 5
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DI 10.3390/gels9050377
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WC Polymer Science
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GA K6VT9
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TI Epidemiological analysis of patients with psoriatic arthritis in follow-up at the brazilian Unified Health System
SO ADVANCES IN RHEUMATOLOGY
LA English
DT Article
DE Psoriatic arthritis; Prevalence; Incidence; Epidemiology; Comorbidities.
ID risk-factors; prevalence; malignancy; management; mortality; disease
AB Introduction/ObjectivesPsoriatic arthritis (PsA) is a chronic multisystem osteoarticular disease that requires specialized care. Most Brazilians depend on the public healthcare provided by the Unified Health System (Sistema unico de Saude, SUS). This study aimed to describe the epidemiological characteristics of patients with PsA in follow-up in SUS, focusing on the incidence and prevalence of the disease, comorbidities, and hospitalizations.MethodsWe collected data from the Outpatient Data System of SUS (Sistema de Informacoes Ambulatoriais do SUS, SIA/SUS) regarding outpatient visits and hospitalizations in the Brazilian public healthcare system from January 2008 to March 2021 using the Techtrials Disease Explorer & REG; platform and the medical code related to PsA were selected.ResultsWe evaluated 40,009 patients and found a prevalence of 24.4 cases of visits due to PsA per 100,000 patients in follow-up in SUS. Female patients were predominant (54.38%). The incidence of visits due to PsA has been increasing in recent years and we observed an incidence of 8,982 new visits in 2020. The main comorbidities of these patients were osteoarthritis, lower back pain, shoulder injuries, oncological diseases, crystal arthropathies, and osteoporosis. Hospitalizations were mainly due to treating clinical or cardiovascular conditions and performing orthopedic procedures.ConclusionThe number of visits due to PsA in SUS has increased in recent years, mainly on account of new diagnoses of the disease, although the prevalence found in this study's population was lower than that observed in the general population.
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NR 45
TC 1
Z9 1
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PU BMC
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J9 ADV RHEUMATOL
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TI Correlation between Bone Mineral Density and Progression of Hip Osteoarthritis in Adult Men and Women in Bulgaria-Results from a 7-Year Study
SO LIFE-BASEL
LA English
DT Article
DE bone mineral density; osteoarthritis progression; subchondral bone remodeling
ID urinary ctx-ii; knee osteoarthritis; health-status; risk-factors; osteoporosis; prevalence; patterns; position; criteria; outcm
AB Changes in clinical presentation, radiographic progression (RP), bone mineral density (BMD), bone turnover (BT), and cartilage turnover (CT) markers were compared in two groups of patients with hip osteoarthritis (HOA) over a period of 7 years. Each group consisted of 150 patients, including a control group on standard-of-care therapy (SC) with simple analgesics and physical exercises, and a study group (SG) on standard-of-care therapy supplemented by vitamin D3 and intravenous administration of zoledronic acid (5 mg) yearly for 3 consecutive years. Patient groups were homogenized regarding the following: (1) radiographic grade (RG), including 75 patients with hip OA RG II according to the Kellgren-Lawrence grading system (K/L), and 75 with RG III on K/L; (2) radiographic model (RM), as each of the K/L grades was subdivided into three subgroups consisting of 25 patients of different RMs: atrophic ('A'), intermediate ('I'), and hypertrophic ('H'); (3) gender-equal ratio of men and women in each subgroup (Female/Male = 15/10). The following parameters were assessed: (1) clinical parameters (CP), pain at walking (WP-VAS 100 mm), functional ability (WOMAC-C), and time to total hip

replacement (tTHR); (2) radiographic indicators(RI)-joint space width (JSW) and speed of joint space narrowing (JSN), changes in BMD (DXA), including proximal femur (PF-BMD), lumbar spine (LS-BMD), and total body (TB-BMD); (3) laboratory parameters (LP)-vitamin D3 levels and levels of BT/CT markers. RV were assessed every 12 months, whereas CV/LV were assessed every 6 months. Results: Cross-sectional analysis (CsA) at baseline showed statistically significant differences (SSD) at $p < 0.05$ in CP (WP, WOMAC-C); BMD of all sites and levels of CT/BT markers between the 'A' and 'H' RM groups in all patients. Longitudinal analysis (LtA) showed SSD ($p < 0.05$) between CG and SG in all CP (WP, WOMAC-C, tTHR) parameters of RP (mJSW, JSN), BMD of all sites, and levels of CT/BT markers for all 'A' models and in 30% of 'I'-RMs (those with elevated markers for BT/CT at baseline and during the observation period). Conclusion: The presence of SSD at baseline ('A' vs. 'H') supported the thesis that at least two different subgroups of HOA exist: one associated with 'A' and the other with 'H' models. D3 supplementation and the intravenous administration of bisphosphonate were the treatment strategies that slowed down RP and postponed tTHR by over 12 months in the 'A' and 'I' RM with elevated BT/CT markers.
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NR 54
TC 2
Z9 2
U1 0
U2 4
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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JI Life-Basel
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WC Biology; Microbiology
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AF Zhao, Amy Y.
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TI The Association of Prior Fragility Fractures on 8-Year Periprosthetic Fracture Risk Following Total Hip Arthroplasty
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE total hip arthroplasty; fragility fracture; periprosthetic fracture; osteoporosis; bone health
ID osteoporosis; barriers; care
AB Background: Fragility fractures are often the initial clinical presentation of osteoporosis. Patients who have a history of fragility fractures undergoing total hip arthroplasty (THA) have an increased risk of 2-year postoperative complications. However, the association of recent fragility fractures with complications beyond 2 years following THA remains unknown. The purpose of this study was to characterize the association of prior fragility fractures with 8-year risks of revision THA, periprosthetic fracture (PPF), and secondary fragility fracture. Methods: Patients aged 50 years and more who underwent THA for osteoarthritis were identified in a large national database. Patients were stratified based on whether they sustained a fragility fracture within 3 years prior to THA. There were 18,529 patients who had a prior fragility fracture and 408,753 who did not have a prior fragility fracture. Demographics and comorbidities were collected. Kaplan-Meier and Cox Proportional Hazards analyses were used to observe the cumulative incidences of all-cause revision, PPF, and secondary fragility fracture within 8 years of index surgery. Results: Patients who had recent fragility fracture had significantly higher risks of revision THA (Hazard Ratio [HR] 1.7; P <.001), PPF (HR 2.2; P <.001), and secondary fragility fracture (HR 4.9; P <.001). Conclusion: Prior fragility fracture was shown to be a significant risk factor for revision THA, PPF, and secondary fragility fracture within 8 years of THA. Identification of these high-risk patients with an emphasis on preoperative and postoperative bone health optimization may

help minimize these complications. (c) 2023 Elsevier Inc. All rights reserved.
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TI High-resolution peripheral quantitative computed tomography: research or clinical practice?
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DT Review
ID estimated bone strength; systemic-lupus-erythematosus; 2nd-generation hr-pqct; in-vivo assessment; cortical bone; postmenopausal women; microarchitectural deterioration; skeletal microstructure; rheumatoid-arthritis; mineral density
AB High-resolution peripheral quantitative CT (HR-pQCT) is a low-dose three-dimensional imaging technique, originally developed for in vivo assessment of bone microarchitecture at the distal radius and tibia in osteoporosis. HR-pQCT has the ability to discriminate trabecular and cortical bone compartments, providing densitometric and structural parameters. At present, HR-pQCT is mostly used in research settings, despite evidence showing that it may be a valuable tool in osteoporosis and other diseases. This review summarizes the main applications of HR-pQCT and addresses the limitations that currently prevent its integration into routine clinical practice. In particular, the focus is on the use of HR-pQCT in primary and secondary osteoporosis, chronic kidney disease (CKD), endocrine disorders affecting bone, and rare diseases. A section on novel potential applications of HR-pQCT is also present, including assessment of rheumatic diseases, knee osteoarthritis, distal radius/scaphoid fractures, vascular calcifications, effect of medications, and skeletal muscle. The reviewed literature seems to suggest that a more widespread implementation of HR-pQCT in clinical practice would offer notable opportunities. For instance, HR-pQCT can improve the prediction of incident fractures beyond areal bone mineral density provided by dual-energy X-ray absorptiometry. In addition, HR-pQCT may be used for the monitoring of anti-osteoporotic therapy or for the assessment of mineral and bone disorder associated with CKD. Nevertheless, several obstacles currently prevent a broader use of HR-pQCT and would need to be targeted, such as the small number of installed machines worldwide, the uncertain cost-effectiveness, the need for improved reproducibility, and the limited availability of reference normative data sets.
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TI The role of retinoic acid receptor-related orphan receptors in skeletal diseases
SO FRONTIERS IN ENDOCRINOLOGY
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DE RORs; bone homeostasis; osteoporosis; rheumatoid arthritis; osteoarthritis
ID ror-gamma-t; collagen-induced arthritis; th17 cells; inverse agonists; bone loss; rheumatoid-arthritis; alpha; differentiation; expression; beta
AB Bone homeostasis, depending on the balance between bone formation and bone resorption, is responsible for maintaining the proper structure and function of the skeletal system. As an important group of transcription factors, retinoic acid receptor-related orphan receptors (RORs) have been reported to play important roles in bone homeostasis by regulating the transcription of target genes in skeletal cells. On the other hand, the dysregulation of RORs often leads to various skeletal diseases such as osteoporosis, rheumatoid arthritis (RA), and osteoarthritis (OA). Herein, we summarized the roles and mechanisms of RORs in skeletal diseases, aiming to provide evidence for potential therapeutic strategies.
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TI Differential Expression of Non-Coding RNAs in Stem Cell Development and Therapeutics of Bone Disorders
SO CELLS
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DT Review
DE stem cells; lncRNA; miRNA; osteoblastogenesis; osteoclastogenesis; osteoporosis; osteoarthritis; and bone cancer
ID promotes osteogenic differentiation; inhibits osteoblastic differentiation; double-stranded-rna; signaling pathway; poor-prognosis; extracellular vesicles; decreased expression; osteosarcoma cells; mineral density; up-regulation
AB Stem cells' self-renewal and multi-lineage differentiation are regulated by a complex network consisting of signaling factors, chromatin regulators, transcription factors, and non-coding RNAs (ncRNAs). Diverse role of ncRNAs in stem cell development and maintenance of bone homeostasis have been discovered recently. The ncRNAs, such as long non-coding RNAs, micro RNAs, circular RNAs, small interfering RNA, Piwi-interacting RNAs, etc., are not translated into proteins but act as essential epigenetic regulators in stem cells' self-renewal and differentiation. Different signaling pathways are monitored efficiently by the differential expression of ncRNAs, which function as regulatory elements in determining the fate of stem cells. In addition, several species of ncRNAs could serve as potential molecular biomarkers in early diagnosis of bone diseases, including osteoporosis, osteoarthritis, and bone cancers, ultimately leading to the development of new therapeutic strategies. This review aims to explore the specific roles of ncRNAs and their effective molecular mechanisms in the growth and development of stem cells, and in the regulation of osteoblast and osteoclast activities. Furthermore, we focus on and explore the association of altered ncRNA

expression with stem cells and bone turnover.
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TI Focal adhesion kinase (FAK): its structure, characteristics, and signaling in skeletal system
SO CELLULAR SIGNALLING
LA English
DT Article
DE FAK; Mesenchymal stem cell; Osteoblast differentiation; Osteoarthritis; Osteosarcoma
ID intensity pulsed ultrasound; mesenchymal stem-cells; enhance osteogenic differentiation; human chondrosarcoma cells; gtpase-activating protein;

growth-factor; in-vitro; alpha-v-beta-3 integrin; terminal domain; migration
AB Focal adhesion kinase (FAK) is a non-receptor tyrosine kinase and distributes important regulatory functions in skeletal system. Mesenchymal stem cell (MSC) possesses significant migration and differentiation capacity, is an important source of distinctive bone cells production and a prominent bone development pathway. MSC has a wide range of applications in tissue bioengineering and regenerative medicine, and is frequently employed for hematopoietic support, immunological regulation, and defect repair, although current research is insufficient. FAK has been identified to cross-link with many other keys signaling pathways in bone biology and is considered as a fundamental "crossroad" on the signal transduction pathway and a "node" in the signal network to mediate MSC lineage development in skeletal system. In this review, we summarized the structure, characteristics, cellular signaling, and the interactions of FAK with other signaling pathways in the skeletal system. The discovery of FAK and its mediated molecules will lead to a new knowledge of bone development and bone construction as well as considerable potential for therapeutic use in the treatment of bone-related disorders such as osteoporosis, osteoarthritis, and osteosarcoma.
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TI Insights into the Notch signaling pathway in degenerative musculoskeletal disorders: Mechanisms and perspectives
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DT Review
DE Notch signaling pathway; Degenerative musculoskeletal disorders; Osteoarthritis; Osteoporosis; Sarcopenia; Intervertebral disc degeneration; Stem/progenitor cells
ID nucleus pulposus cells; intervertebral disc degeneration; hypoxia-inducible factor-1-alpha; matrix-metalloproteinase 13; mesenchymal stem-cells; osteoblast differentiation; knee osteoarthritis; articular-cartilage; chondrogenic differentiation; postmenopausal osteoporosis
AB Degenerative musculoskeletal disorders are a group of age-related diseases of the locomotive system that severely affects the patient's ability to work and cause adverse sequalae such as fractures and even death. The incidence and prevalence of degenerative musculoskeletal disorders is rising owing to the aging of the world's population. The Notch signaling pathway, which is expressed in almost all organ systems, extensively regulates cell proliferation and differentiation as well as cellular fate. Notch signaling shows increased activity in degenerative musculoskeletal disorders and retards the progression of degeneration to some extent. The review focuses on four major degenerative musculoskeletal disorders (osteoarthritis, intervertebral disc degeneration, osteoporosis, and sarcopenia) and summarizes the pathophysiological functions of Notch signaling in these disorders, especially its role in stem/progenitor cells in each disorder. Finally, a conclusion will be presented to explore the research and application of the perspectives on Notch signaling in degenerative musculoskeletal disorders.
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TI Association of temporomandibular joint osteoarthrosis with dentoskeletal morphology in males: A cone-beam computed tomography and cephalometric analysis
SO ORTHODONTICS & CRANIOFACIAL RESEARCH
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DT Article
DE CBCT; Cephalometrics; cone-beam computed tomography; temporomandibular joint; temporomandibular joint osteoarthrosis
ID craniofacial morphology; adolescents; disorders; bone; features; rdc/tmd; growth; age
AB ObjectiveThe objective of the study was to assess the differences in dentoskeletal morphology in males with and without temporomandibular joint osteoarthrosis (TMJOA). MethodsThree hundred seventy-one male participants seeking orthodontic treatment were enrolled in this cross-sectional study. Each participant's osseous status was evaluated using cone-beam computed tomography (CBCT) and classified into normal (N = 104), indeterminate for TMJOA (N = 110) and TMJOA (N = 157) groups. The dentoskeletal characteristics were evaluated using cephalograms. Stratified analysis was performed based on age and skeletal pattern. Descriptive statistics and one-way analysis of variance were performed to investigate dentoskeletal differences among groups. P < .05 was considered statistically significant. ResultsThe differences in posterior cranial base length, FMA, MP-OP, anterior facial height, articular angle, ramus height and L1-MP were statistically significant. After stratification by age, the differences in FMA, maxillomandibular angle, posterior facial height, facial height ratio, gonial angle and mandibular body length were statistically significant in adults. No statistical difference except for articular angle was observed in adolescents. After stratification by skeletal pattern, statistical differences were mainly apparent in skeletal Class II adults. ConclusionMales with TMJOA showed a posteriorly positioned and backward-rotated mandible, especially in skeletal Class II adults. Compared with women, the craniofacial morphology of men is less affected by TMJOA. The association between TMJOA and craniofacial morphology also varied across different age groups and skeletal patterns. Prospective studies are required to clarify the cause-effect relationship between TMJOA and craniofacial morphology in males.
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U1 1
U2 11
PU WILEY
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 ORTHOD CRANIOFAC RES
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PT J
AU Kim, H
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TI Therapeutic Effect of Enzymatically Hydrolyzed Cervi Cornu Collagen NP-2007 and Potential for Application in Osteoarthritis Treatment
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE enzyme hydrolyzation; cervi cornu collagen; NP-2007; osteoarthritis; monosodium iodoacetate
AB Cervi cornu extracts have been used in traditional medicine for the treatment of various disorders, including osteoporosis. However, since it is not easy to separate the active ingredients, limited research has been conducted on their functional properties. In this study, we extracted the low-molecular-weight (843 Da) collagen NP-2007 from cervi cornu by enzyme hydrolyzation to enhance absorption and evaluated the therapeutic effect in monosodium iodoacetate-induced rat osteoarthritis (OA) model. NP-2007 was orally administered at 50, 100, and 200 mg/kg for 21 days. We showed that the production of matrix metalloproteinase-2,

-3, and -9, decreased after NP-2007 treatment. The levels of tumor necrosis factor (TNF)-& alpha;, interleukin (IL)-1 & beta;, IL-6, and prostaglandin E2 were also reduced after treatment of NP-2007. Furthermore, the administration of NP-2007 resulted in effective preservation of both the synovial membrane and knee cartilage and significantly decreased the transformation of fibrous tissue. We verified that the treatment of NP-2007 significantly reduced the production of nitric oxide and pro-inflammatory cytokines including TNF-& alpha;, IL-1 & beta;, and IL-6 in lipopolysaccharides-stimulated RAW 264.7 cells by regulation of the NF-kB and MAPK signaling pathways. This study indicates that NP-2007 can alleviate symptoms of osteoarthritis and can be applied as a novel treatment for OA treatment.
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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Ma, N
Zhao, Z
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TI Mid- to Long-Term Clinical Outcomes of Cartilage Restoration of Knee Joint with Allogenic Next-Generation Matrix-Induced Autologous Chondrocyte Implantation (MACI)
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE Cartilage; Chondral Defect; MACI; Matrix-Induced Autologous Chondrocyte Implantation; Tissue Engineer
ID chondral defects; collagen membrane; follow-up; osteoarthritis; repair; transplantation; microfracture; hypertrophy; scaffold
AB ObjectiveCartilage defect is a common pathology still lacking a unified treating option. The purpose of this retrospective study is to evaluate the safety, efficacy, and clinical and radiological outcome of cartilage restoration of knee joint with allogenic next-generation Matrix-Induced Autologous Chondrocyte Implantation (MACI) for the first time, as well as the correlation between postoperative clinical and radiological outcomes and preoperative patient history and demographics. MethodsFrom July 2014 to August 2020, 15 patients who went through cartilage restoration with allogenic next-generation MACI were included in this study. Patient demographics and PROM including the International Knee Documentation Committee (IKDC) subjective knee score, Lysholm score, Tegner Activity Scale (TAS), and Knee Injury and Osteoarthritis Outcome Score (KOOS) were obtained preoperatively, at 3, 6, 12 months postoperatively and the last follow-up using an online questionnaire platform. MOCART 2.0 score was calculated at the last

follow-up. Analysis of variance (ANOVA) was used to compare PROM pre- and post-operation, with two-tailed $p < 0.05$ defined as statistical significant. Pearson correlation coefficient was used to evaluate correlation between the PROM and MOCART 2.0 score at the last follow-up with patients demorgraphics. ResultsAll patients were followed for an average of 66.47 +/- 24.15 months (range, 21-93). All patients were satisfied with the outcome of the surgery and no complication was reported at the end of the study. No significant improvement was observed until 1 year after the implantation, except for IKDC score at 6 months. All PROM showed significant improvement 1 year post-op except for Lysholm score and TAS, which also increased significantly at the time of the last follow-up. Pearson correlation coefficient showed that the size of the defect, before or after debridement, was significantly negatively correlated with final KOOS-Pain (before debridement: $r = -0.57$, $p < 0.05$; after debridement: $r = -0.54$, $p < 0.05$) and KOOS-Symptoms score (before debridement: $r = -0.66$, $p < 0.05$; after debridement: $r = -0.67$, $p < 0.05$). The MOCART 2.0 score was found significantly and negatively correlated with BMI ($r = -0.60$, $p < 0.05$), and significantly and positively correlated with Lysholm score ($r = 0.70$, $p < 0.05$). ConclusionThe next generation MACI with autologous chondrocyte and allogenic chondrocyte ECM scaffold could be used to treat focal articular cartilage defect in the knee joint safely and efficiently with lasting promising outcomes for more than 5 years. The size of the defects should be considered the most negatively correlated parameters influencing the postoperative clinical outcomes.
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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JI Orthop. Surg.
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TI Meat Analogues from Pea Protein: Effect of Different Oat Protein Concentrates and Post Treatment on Selected Technological Properties of High-Moisture Extrudates
SO APPLIED SCIENCES-BASEL
LA English
DT Article
DE high-moisture extrusion; oat protein concentrates; pea protein; microstructure; texture; color; dry fractionation
ID soy protein; color
AB The effect of using oat protein concentrates from different sources on the techno/functional properties of pea protein high-moisture extrudates (HME) have been investigated. The oat protein fractions were commercially produced by wet milling (OP) or produced by dry fractionation (OA) in our pilot plant facilities. The texture cutting force of HME was significantly increased by the inclusion of OP and had higher anisotropy, while addition of OA did not influence the texture. Addition of both oat sources to the pea mixture led to higher water and oil binding ability on both initial dry ingredients and extrudates. The color of the meat analogues was significantly affected by the type of oat added. CLSM image analysis of the extrudates showed that the type of oat used influenced fiber alignment and apparent porosity of the protein network. Post-extrusion treatment with water at 80 degrees C/20 min of the extrudates significantly reduced the cutting strength of the meat analogues and significantly caused a shift toward a lighter color. The reduction of texture strength of extrudates with OP rendered it similar to cooked chicken samples, while extrudates with OA showed a more resilient fiber strength to the hot water treatment.
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AU Qin, XR
Xi, Y
Jiang, QF
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Yang, GL
AF Qin, Xiaoru
Xi, Yue
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Chen, Chaozhen
Yang, Guoli
TI Type H vessels in osteogenesis, homeostasis, and related disorders
SO DIFFERENTIATION
LA English
DT Review
DE Type H vessels; Osteogenesis; Angiogenesis; Osteoporosis; Osteoarthritis
ID angiogenesis; osteoporosis; vegf; mechanisms; organoids; cells
AB The vascular system plays a crucial role in bone tissue. Angiogenic and osteogenic processes are coupled through a spatial-temporal connection. Recent studies have identified three types of capillaries in the skeletal system. Compared with type L and E vessels, type H vessels express high levels of CD31 and endomucin, and function to couple angiogenesis and osteogenesis. Endothelial cells in type H vessels interact with osteolineage cells (e.g., osteoblasts, osteoclasts, and osteocytes) through cytokines or signaling pathways to maintain bone growth and homeostasis. In imbalanced bone homeostases, such as osteoporosis and osteoarthritis, it may be a new therapeutic strategy to regulate the endothelial cell activity in type H vessels to repair the imbalance. Here, we reviewed the latest progress in relevant factors or signaling pathways in coupling angiogenesis and osteogenesis. This review would contribute to further understanding the role and mechanisms of type H vessels in coupling angiogenic and osteogenic processes. Furthermore, it will facilitate the development of therapeutic approaches for bone disorders by targeting type H vessels.
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TI Otolith Morphometric and Shape Distinction of Three Redfin Species under the Genus Decapterus (Teleostei: Carangidae) from Sulu Sea, Philippines
SO FISHES
LA English
DT Article
DE Decapterus kurroides; Decapterus smithvanizi; Decapterus tabl; small pelagics; species delineation; taxonomy
ID sagittal otolith; stable-isotope; pristipomoides-multidens; comparative morphology; northern australia; pisces scombridae; western-australia; stock structure; mackerel; snapper
AB Otoliths are paired calcified structures in the inner ear of teleosts that function in hearing and balance. In this study, the use of otolith morphometrics and shape analysis were explored to delineate the redfin species under the genus Decapterus from the Sulu Sea, Philippines, namely, Decapterus kurroides, D. smithvanizi, and D. tabl. Results showed that the mean otolith shapes are unique within species ($p < 0.001$). The otolith size-related (OW-otolith weight, OL-otolith length, OH-otolith height, OA-otolith area, and OP-otolith perimeter) and shape-related (RE-rectangularity, SQ-squareness, EL-ellipticity, RO-roundness, AR-aspect ratio, FF-form factor, CO-compactness, and CI-circularity) morphometric indices also showed significant variations ($p < 0.001$) among the three species. Distinct regions differentiating D. kurroides from the other two species were seen along the dorsal margin of the otoliths, which was supported by its significantly higher values for OH (size-related index) and RO (shape-related index). In addition, the morphometric indices showed significant variations ($p < 0.001$), except for RE. Furthermore, it was revealed that the size-related indices were able to separate D. kurroides from the other two species, which turned out to be indifferent. The results provided relevant data on the use of otoliths as an additional confirmatory tool in species delineation of the identified redfin species, and, therefore, offer opportunities of applying the same method in delineation and, eventually, identification of species from other genera, especially those that closely resemble each other.
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NR 62
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U1 1
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PU MDPI
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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AF Huang, Jinming
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TI MiR-30 Family: A Novel Avenue for Treating Bone and Joint Diseases?
SO INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
LA English
DT Review
DE metabolic bone diseases; miR-30; osteoporosis; osteoarthritis; bone tumor; vascular calcification; extracellular vesicles
ID mesenchymal stem-cells; regulates chondrogenic differentiation; transcription factor; osteosarcoma cells; osteogenic differentiation; lineage progression; articular-cartilage; matrix degradation; down-regulation; proliferation
AB Bone and joint diseases are a group of clinically heterogeneous diseases characterized by various bone strength disorders, bone structural defects and bone mass abnormalities. Common bone diseases include osteoporosis, skeletal dysplasia, and osteosarcoma, and common joint diseases include osteoarthritis, rheumatoid arthritis, and degenerative disc disease. all of them lead to high

medical costs. The miR-30 family consists of a total of 5 members: miR-30a, miR-30b, miR-30c, miR-30d and miR-30e. Accumulating evidence has indicated that the miR-30 family may be involved in the occurrence and development of bone and joint diseases. For example, miR-30a is highly expressed in blood samples of osteoporosis patients, miR-30a/b increases in cartilage tissue of osteoarthritis patients, and lower expression of miR-30c is associated with higher malignance and shorter survival time of osteosarcoma. Mechanistically, by targeting crucial transcription factors (RUNX2, SOX9, beclin-1, etc.), the miR-30 family regulates some critical pathways of bone homeostasis (Wnt/beta-Catenin, mTOR, PI3K/AKT, etc.). In view of the distinct actions of the miR-30 family on bone metabolism, we hypothesize that the miR-30 family may be a new remedy for the clinical treatment and prevention of some bone and joint diseases.
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TI Astragalin: a food-origin flavonoid with therapeutic effect for multiple diseases
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE Astragalin; pharmacological activities; diseases; molecular mechanisms; natural source
ID nf-kappa-b; induced inflammatory response; rat plasma application; allergic inflammation; signaling pathway; breast-cancer; ms/ms method; in-vitro; cells; hyperglycemia
AB Naturally occurring flavonoids have long been utilized as essential templates for the development of novel drugs and as critical ingredients for functional foods. Astragalin (AG) is a natural flavonoid that can be isolated from a variety of familiar edible plants, such as the seeds of green tea, Morus alba L., and Cuscuta chinensis. It is noteworthy that AG has a wide range of pharmacological activities and possesses therapeutic effects against a variety of diseases, covering cancers, osteoarthritis, osteoporosis, ulcerative colitis, mastitis, obesity, diabetes mellitus, diabetic complications, ischemia/reperfusion injury, neuropathy, respiratory diseases, and reproductive system diseases. This article reviewed the natural source and pharmacokinetics of AG and systematically summarized the pharmacological activities and potential mechanisms of AG in treating diverse diseases in order to promote the development of AG as a functional food, in doing so providing references for its clinical application in disease therapy.
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TI Relationship between medial partite hallux sesamoid and hallux valgus in the general population
SO FOOT AND ANKLE SURGERY
LA English
DT Article
DE Medial partite hallux sesamoid; Population-based cohort; Radiography; Hallux valgus
ID accessory ossicles; bones; feet
AB <bold>Background: </bold>An association between the medial partite hallux sesamoid (MPHS) and hallux valgus (HV) has been suggested; however, a causal relationship has not been confirmed. This study aimed to determine their causal relationship using a cross-sectional radiographic survey of a large-scale population cohort covering a wide age group.<bold>Patients and methods: </bold>The fifth survey of the Research on Osteoarthritis/Osteoporosis against Disability study involved 1997 participants aged 21-95 years who had undergone anteroposterior radiography of bilateral feet. The presence of MPHS, its morphology, and radiographic parameters related to the HV were assessed using radiographs. Changes in the prevalence of MPHS with age were assessed using trend tests. The relationship between the MPHS and HV was assessed based on sex and age.<bold>Results: </bold>MPHS was found in 508 out of 3994 feet (12.7 %), with a significant difference in prevalence between men and women (10.0 % vs. 13.7 %, $p < 0.001$). Trend analysis demonstrated a significant decrease in MPHS occurrence with age in both sexes. HV angle was significantly higher in feet with MPHS than in those without (Men: 17.8 +/- 7.0 degrees vs. 14.0 +/- 5.9 degrees, $p < 0.0001$; Women: 19.6 +/- 7.7 degrees vs. 17.7 +/- 7.9 degrees, $p < 0.0001$). The prevalence of HV angle >= 20 degrees was also significantly higher in feet with MPHS than in those without (Men: 33.3 % vs. 14.6 %, $p < 0.0001$; Women: 46.5 % vs. 34.6 %, $p < 0.0001$). This association between MPHS and HV was noticeable in younger adults and became less prominent with age.<bold>Conclusions: </bold>MPHS is associated with HV. The weakening of this relationship and the decreased prevalence of MPHS with age suggest that MPHS is not caused by HV, but is one of the causes of HV, especially in younger adults.
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NR 21
TC 2
Z9 2
U1 0
U2 2
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 1268-7731
EI 1460-9584
J9 FOOT ANKLE SURG
JI Foot Ankle Surg.
PD DEC 15
PY 2023
VL 29
IS 8
BP 621
EP 626
DI 10.1016/j.fas.2023.07.011
EA NOV 2023
PG 6
WC Orthopedics
SC Orthopedics
GA DB7V0
UT WOS:001129646600001
PM 37679197
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PT J
AU Choi, YS
Jeong, JU
Lee, SH
AF Choi, Yun Seong
Jeong, Jin-Uk
Lee, Seung Hoon
TI Comparison of both lower leg bone mineral density in single limb knee osteoarthritis patients
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article

DE Total knee arthroplasty; Osteoarthritis; Osteoporosis; Alignment
ID varus alignment; proximal tibia; progression; women
AB PurposeThe relationship between knee osteoarthritis (OA), bone mineral density (BMD), and alignment has not yet been clarified. This study aimed to investigate the relationship between the two limbs in patients with single-limb knee OA.MethodsPatients who underwent single-limb total knee arthroplasty between March 2019 and February 2021 were retrospectively analyzed. Only patients with Kellgren-Lawrence (KL) grades III and IV on the operated side and KL I and II on the opposite side were included. Patients with traumatic OA, a surgery that could change the alignment of both lower extremities and previous fractures were excluded. The proximal femur BMD on the OA and non-OA sides were compared. In addition, the difference in BMD was compared between a group with a difference in alignment of both lower extremities (> 5 & DEG;) and a group without a difference (< 5 & DEG;).ResultsIn total, 149 patients were included. The BMD T-score of the femoral neck on the OA side was lower than that of the non-OA side ($p < 0.001$). There was no correlation between BMD and alignment, and there was no difference in BMD according to the difference in alignment.ConclusionThe femoral neck BMD of the leg on the side with knee OA was lower than that on the side without OA. However, the alignment difference between the legs did not affect BMD. BMD was lowered because of OA and not because of alignment.
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NR 16
TC 2
Z9 2
U1 0
U2 2
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 0936-8051
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J9 ARCH ORTHOP TRAUM SU
JI Arch. Orthop. Trauma Surg.
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IS 12
BP 7147
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DI 10.1007/s00402-023-04928-5
EA AUG 2023
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WC Orthopedics; Surgery
SC Orthopedics; Surgery
GA Y1GB9
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PT J
AU Su, GY
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Xie, Jing
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TI Annexin A5 derived from matrix vesicles protects against osteoporotic bone loss via mineralization
SO BONE RESEARCH
LA English
DT Article
ID osteoblast differentiation; calcification; chondrocytes; biogenesis; proteome; cells
AB Matrix vesicles (MVs) have shown strong effects in diseases such as vascular ectopic calcification and pathological calcified osteoarthritis and in wound repair of the skeletal system due to their membranous vesicle characteristics and abundant calcium and phosphorus content. However, the role of MVs in the progression of osteoporosis is poorly understood. Here, we report that annexin A5, an important component of the matrix vesicle membrane, plays a vital role in bone matrix homeostasis in the deterioration of osteoporosis. We first identified annexin A5 from adherent MVs but not dissociative MVs of osteoblasts and found that it could be sharply decreased in the bone matrix during the occurrence of osteoporosis based on ovariectomized mice. We then confirmed its potential in mediating the mineralization of the precursor osteoblast lineage via its initial binding with collagen type I to achieve MV adhesion and the subsequent activation of cellular autophagy. Finally, we proved its protective role in resisting bone loss by applying it to osteoporotic mice. Taken together, these data revealed the importance of annexin A5, originating from adherent MVs of osteoblasts, in bone matrix

remodeling of osteoporosis and provided a new strategy for the treatment and intervention of bone loss.
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NR 86
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PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON, N1 9XW, ENGLAND
SN 2095-4700
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J9 BONE RES
JI Bone Res.
PD NOV 9
PY 2023
VL 11
IS 1
BP
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DI 10.1038/s41413-023-00290-9
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WC Cell & Tissue Engineering
SC Cell Biology
GA X3HO9
UT WOS:001097399000001
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AU Feng, ST
Li, JH
Tian, JJ
Lu, S
Zhao, Y
AF Feng, Site
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Tian, Jingjing
Lu, Sheng
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TI Application of Single-Cell and Spatial Omics in Musculoskeletal Disorder Research
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE single cell; spatial omics; musculoskeletal disorders; fracture; dysplasia; heterotopic ossification; osteoporosis; osteoarthritis; intervertebral disc;

tendinopathy
ID estrogen-receptor-alpha; trabecular bone-formation; messenger-rna-seq; stem-cells; endochondral ossification; chromatin accessibility; regeneration reveals; dural ossification; induced osteopenia; skeletal growth
AB Musculoskeletal disorders, including fractures, scoliosis, heterotopic ossification, osteoporosis, osteoarthritis, disc degeneration, and muscular injury, etc., can occur at any stage of human life. Understanding the occurrence and development mechanism of musculoskeletal disorders, as well as the changes in tissues and cells during therapy, might help us find targeted treatment methods. Single-cell techniques provide excellent tools for studying alterations at the cellular level of disorders. However, the application of these techniques in research on musculoskeletal disorders is still limited. This review summarizes the current single-cell and spatial omics used in musculoskeletal disorders. Cell isolation, experimental methods, and feasible experimental designs for single-cell studies of musculoskeletal system diseases have been reviewed based on tissue characteristics. Then, the paper summarizes the latest findings of single-cell studies in musculoskeletal disorders from three aspects: bone and ossification, joint, and muscle and tendon disorders. Recent discoveries about the cell populations involved in these diseases are highlighted. Furthermore, the therapeutic responses of musculoskeletal disorders, especially single-cell changes after the treatments of implants, stem cell therapies, and drugs are described. Finally, the application potential and future development directions of single-cell and spatial omics in research on musculoskeletal diseases are discussed.
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TI Fine-tuning osteoclastogenesis: An insight into the cellular and molecular regulation of osteoclastogenesis
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ID mesenchymal stem-cells; b ligand rankl; bone-resorption; in-vitro; promotes osteoclastogenesis; dendritic cells; osteogenic differentiation; multiple-myeloma; cathepsin k; stimulated osteoclastogenesis
AB Osteoclasts, the bone-resorbing cells, are essential for the bone remodeling process and are involved in the pathophysiology of several bone-related diseases. The extensive corpus of in vitro research and crucial mouse model studies in the 1990s demonstrated the key roles of monocyte/macrophage colony-stimulating factor, receptor activator of nuclear factor kappa B ligand (RANKL) and integrin alpha v beta 3 in osteoclast biology. Our knowledge of the molecular mechanisms by which these variables control osteoclast differentiation and function has significantly advanced in the first decade of this century. Recent developments have revealed a number of novel insights into the fundamental mechanisms governing the differentiation and functional activity of osteoclasts; however, these mechanisms have not yet been adequately documented. Thus, in the present review, we discuss various regulatory factors including local and hormonal factors, innate as well as adaptive immune cells, noncoding RNAs (ncRNAs), etc., in the molecular regulation of the intricate and tightly regulated process of osteoclastogenesis. ncRNAs have a critical role as epigenetic controllers of osteoclast physiologic activities, including differentiation and bone resorption. The primary ncRNAs, which include micro-RNAs, circular RNAs, and long noncoding RNAs, form a complex network that affects gene transcription activities associated with osteoclast biological activity. Greater knowledge of the involvement of ncRNAs in osteoclast biological activities will contribute to the treatment and management of several skeletal diseases such as osteoporosis, osteoarthritis, rheumatoid arthritis, etc. Moreover, we further outline potential therapies targeting these regulatory pathways of osteoclastogenesis in distinct bone pathologies.
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NR 293
TC 21
Z9 21
U1 3
U2 17
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0021-9541
EI 1097-4652
J9 J CELL PHYSIOL
JI J. Cell. Physiol.
PD JUL 15
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IS 7
BP 1431
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DI 10.1002/jcp.31036
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WC Cell Biology; Physiology
SC Cell Biology; Physiology
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UT WOS:000986475700001
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ER

PT J
AU Jie, LS
Ma, ZY
Gao, YF
Shi, XQ
Yu, LK
Mao, J
Wang, PM
AF Jie, Lishi
Ma, Zhenyuan
Gao, Yifan
Shi, Xiaoqing
Yu, Likai
Mao, Jun
Wang, Peimin
TI The mechanism of palmatine-mediated intestinal flora and host metabolism intervention in OA-OP comorbidity rats
SO FRONTIERS IN MEDICINE
LA English
DT Article
DE osteoarthritis; osteoporosis; palmatine; gut microbiota; metabonomics
ID in-vitro; osteoarthritis; 5-methoxytryptophol; osteoporosis; arthritis; vivo
AB BackgroundErXian decoction is a Chinese herbal compound that can prevent and control the course of osteoarthritis (OA) and osteoporosis (OP). OP and OA are two age-related diseases that often coexist in elderly individuals, and both are associated with dysregulation of the gut microbiome. In the initial study, Palmatine (PAL) was obtained by liquid chromatography-tandem mass spectrometry (LC-MS/MS) and network pharmacological screening techniques, followed by 16S rRNA sequencing and serum metabolomics of intestinal contents, to explore the mechanism of PAL in the treatment of OA and OP. MethodsThe rats selected for this study were randomly divided into three groups: a sham group, an OA-OP group and a PAL group. The sham group was intragastrically administered normal saline solution, and the PLA group was treated with PAL for 56 days. Through microcomputed tomography (micro-CT), ELISA, 16S rRNA gene sequencing and non-targeted metabonomics research, we explored the potential mechanism of intestinal microbiota and serum metabolites in PAL treatment of OA-OP rats. ResultsPalmatine significantly repair bone microarchitecture of rat femur in OA-OP rats and improved cartilage damage. The analysis of intestinal microflora showed that PAL could also improve the intestinal microflora disorder of OA-OP rats. For example, the abundance of Firmicutes, Bacteroidota, Actinobacteria, Lactobacillus, unclassified_f_Lachnospiraceae, norank_f_Muribaculaceae, Lactobacillaceae, Lachnospiraceae and Muribaculaceae increased after PAL intervention. In addition, the results of metabolomics data analysis showed that PAL also change the

metabolic status of OA-OP rats. After PAL intervention, metabolites such as 5-methoxytryptophol, 2-methoxy acetaminophen sulfate, beta-tyrosine, indole-3-carboxylic acid-O-sulfate and cyclodopa glucoside increased. Association analysis of metabolomics and gut microbiota (GM) showed that the communication of multiple flora and different metabolites played an important role in OP and OA. ConclusionPalmatine can improve cartilage degeneration and bone loss in OA-OP rats. The evidence we provided supports the idea that PAL improves OA-OP by altering GM and serum metabolites. In addition, the application of GM and serum metabolomics correlation analysis provides a new strategy for uncovering the mechanism of herbal treatment for bone diseases.
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NR 45
TC 12
Z9 13
U1 4

U2 27
PU FRONTIERS MEDIA SA
PI LAUSANNE
PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
SN
EI 2296-858X
J9 FRONT MED-LAUSANNE
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WC Medicine, General & Internal
SC General & Internal Medicine
GA F2SP3
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PT J
AU Yilmaz, E
Ünver, S
AF Yilmaz, Ebru
Unver, Sena
TI Investigation of the relationship between magnesium level and vitamin D, bone mineral density, and chronic diseases in patients with knee osteoarthritis
SO MAGNESIUM RESEARCH
LA English
DT Article
DE magnesium; vitamin D; osteoporosis; chronic diseases; knee osteoarthritis
ID osteoporosis; deficiency; inflammation
AB Objective. The maintenance of various physiological cellular processes requires mineral magnesium (Mg). The purpose of the study was to determine a possible association between Mg level and vitamin D levels, bone mineral density (BMD), chronic diseases, and radiographic stage in individuals with knee osteoarthritis (OA). Methods. The study included 98 individuals (62 female and 36 male) who had been diagnosed with at least grade 1 knee menopausal status, duration of menopause, the presence of chronic diseases hypothyroidism) and radiological stage of knee OA were gathered from all pa(PTH) and 25(OH)-vitamin D levels were

recorded. Additionally, dual-energy X-ray absorptiometry (DEXA) was used to measure the BMD of the lumbar vertebrae (L1-L4) and femoral neck as well as anteroposterior radiography of the knee in all patients. T scores <=-2.5 were accepted as evidence of osteoporosis. Results: The mean age of the study population was 59.15 +/- 10.58 years. The level of Mg significantly correlated with age, smoking, presence of chronic disease, duration of menopause, the level of vitamin D and PTH, and femoral neck T score ($p<0.05$). Conclusion: This study provides data supporting the relationship between magnesium levels and PTH and vitamin D levels, bone mineral density, and chronic disease. Future research is needed to examine the potential link between knee osteoarthritis and magnesium status.
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NR 28
TC 1
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U1 2
U2 9
PU JLE
PI ARCUEIL
PA 30, RUE BERTHOLLET, BATIMENT A, 94110 ARCUEIL, ?, FRANCE
SN 0953-1424
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JI Magnes. Res.
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WC Biochemistry & Molecular Biology; Endocrinology & Metabolism
SC Biochemistry & Molecular Biology; Endocrinology & Metabolism
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ER

PT J
AU Lin, AQ
Liu, SJ
Wei, H
AF Lin, Anqi
Liu, Shujie
Wei, Hui

TI Nanozymes for biomedical applications in orthopaedics
SO PARTICUOLOGY
LA English
DT Article
DE Nanozymes; Arti ficial enzymes; Orthopaedics; Nanomedicine; Nanomaterials
ID cerium oxide nanoparticles; oxidative stress; osteoporosis; peroxidase; therapy; gold; pathophysiology; osteoarthritis; polarization; replacement
AB As the next generation of artificial enzymes, nanozymes have attracted increasing attention in biomedical applications due to their multienzyme-like characteristics, multifunctionalities, low cost, and high stability. By taking advantage of their diverse activities, a growing number of nanozyme-mediated therapeutic strategies have been developed for various diseases. Herein, we provide a brief review of the representative studies of nanozymes, especially in orthopaedic diseases over the past decade, which include arthritis, osteoporosis, bone regeneration, bacteria-associated infections, and osteosarcoma. Moreover, the future potential applications and some major challenges are also discussed. This review would not only provide some instructive views of nanozymes but also promote the development of enzyme-mimetic strategies in orthopaedics.(c) 2022 Chinese Society of Particuology and Institute of Process Engineering, Chinese Academy of Sciences. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http:// creativecommons.org/licenses/by-nc-nd/4.0/).
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TI Anti-Inflammatory and Anti-Osteoclastogenesis Activities of Different Kinds of Zanthoxylum bungeanum Seed Oil in Vitro
SO CHEMISTRY & BIODIVERSITY
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DT Article
DE Zanthoxylum bungeanum seed oil; fatty acids; anti-inflammation; osteoclastogenesis
ID nf-kappa-b; polyunsaturated fatty-acids; inflammation
AB Our previous study has exhibited that one kind of Zanthoxylum bungeanum seed oil (ZSO), extracted from Zanthoxylum bungeanum seed, had inhibitory effects on osteoclastogenesis. However, the anti-osteoclastogenesis activities of different kinds of ZSO are scarcely reported. Since inflammation is related to bone loss and osteoporosis, in this study, three kinds of ZSO, Zanthoxylum schinifolium Siebold et Zucc seed oil (ZSSO), Zanthoxylum armatum DC. seed oil (ZDSO) and Zanthoxylum bungeanum maximum seed oil (ZBSO), were obtained with Soxhlet extraction and their fatty acid constituents were detected by GC-FID. RAW264.7 macrophages induced by lipopolysaccharide (LPS) were used to evaluate the inhibitory effects of three kinds of ZSO on inflammation via detecting the expression levels of inflammatory factors by RT-qPCR. Moreover, RANKL-induced osteoclastogenesis was applied to demonstrate the anti-osteoclastogenesis activities of them through tartrate-resistant acid phosphatase (TRAP) staining and RT-qPCR. The GC-FID results exhibited that the highest constituent in ZSSO and ZDSO was oleic acid (OA) and palmitoleic acid (PLA), respectively. While linoleic acid (LA) and alpha-Linolenic acid (ALA) in ZBSO were dominant. At the concentration of 0.5 mu L/mL, all three kinds of ZSO could decrease the expression levels of inducible NO synthase (iNOS), cyclooxygenase-2 (COX-2), tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6), interleukin-1 beta (IL-1 beta) in

LPS-induced macrophages. At the concentration of 0.25 mu L/mL, only ZSSO could decrease the expression levels of iNOS and COX-2, which implied the inhibitory effects of ZSSO were stronger than other ZSOs. The number of RANKL-induced osteoclasts and the expressions of nuclear factor kappa-B (NF-kappa B), TNF-alpha and IL-6 in the cells were decreased after being treated with ZSOs at the concentration of 0.5 mu L/mL, while the number of RANKL-induced osteoclasts after treated with ZBSO were less than those treated with other ZSOs, this indicated that the anti-osteoclastogenesis effect of ZBSO were stronger than other ZSOs. In conclusion, the fatty acid compositions of three major kinds of ZSO were compared and the content of unsaturated fatty acids especially omega-3 polyunsaturated fatty acids in ZBSO were the highest among them. All ZSOs tested had anti-inflammatory and anti-osteoclastogenesis activities. And their anti-osteoclastogenesis effects might be related to the suppression of the NF-kappa B pathway.

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TI Advanced Hydrogel-Based Strategies for Enhanced Bone and Cartilage Regeneration: A Comprehensive Review
SO GELS
LA English
DT Review
DE tissue engineering and regenerative medicine (TERM); advanced hydrogels; bone regeneration; extracellular matrix (ECM); scaffolds; stem cells (SCs)
ID matrix proteins; repair; osteocyte; fracture; delivery; chitosan; system; composite; release; burden
AB Bone and cartilage tissue play multiple roles in the organism, including kinematic support, protection of organs, and hematopoiesis. Bone and, above all, cartilaginous tissues present an inherently limited capacity for self-regeneration.

The increasing prevalence of disorders affecting these crucial tissues, such as bone fractures, bone metastases, osteoporosis, or osteoarthritis, underscores the urgent imperative to investigate therapeutic strategies capable of effectively addressing the challenges associated with their degeneration and damage. In this context, the emerging field of tissue engineering and regenerative medicine (TERM) has made important contributions through the development of advanced hydrogels. These crosslinked three-dimensional networks can retain substantial amounts of water, thus mimicking the natural extracellular matrix (ECM). Hydrogels exhibit exceptional biocompatibility, customizable mechanical properties, and the ability to encapsulate bioactive molecules and cells. In addition, they can be meticulously tailored to the specific needs of each patient, providing a promising alternative to conventional surgical procedures and reducing the risk of subsequent adverse reactions. However, some issues need to be addressed, such as lack of mechanical strength, inconsistent properties, and low-cell viability. This review describes the structure and regeneration of bone and cartilage tissue. Then, we present an overview of hydrogels, including their classification, synthesis, and biomedical applications. Following this, we review the most relevant and recent advanced hydrogels in TERM for bone and cartilage tissue regeneration.
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TI Post-traumatic osteoarthritis: the worst associated injuries and differences in patients' profile when compared with primary osteoarthritis
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Comorbidity; Hip; Injury; Knee; Post-traumatic osteoarthritis
ID total knee arthroplasty; high prevalence; soccer players; risk-factor; anterior; metaanalysis; outcm; burden; tear
AB BackgroundThe estimated prevalence of post-traumatic osteoarthritis (PTOA) is 10-12% and in this study 12.4%. Different knee and hip injuries have been identified as risk factors for PTOA, but there is no consensus regarding the most painful and disabling injuries. Identifying these injuries might help in the prevention of PTOA. Additionally, patients with PTOA have a higher risk for complications after arthroplasty than patients with primary OA, perhaps due to differences in the profile and comorbidity that might help to explain the difference. This work aims 1) to identify the most common past injuries associated with the most painful and disabling PTOA cases in non-athlete patients and 2) to compare the comorbidities and characteristics between PTOA and primary OA.MethodsRetrospective hospital-based cohort study with 1290 participants with joint complaints or who received arthroplasty. Medical records included demographic information, diagnosis, medication, smoking, alcohol history and comorbidities. Data from January 2012 orthopaedic consults till December 2019 was reviewed and had the type and date of injury, pain score by the numerical rating scale and walking disability. Odds Ratio (OR) and 95% confidence intervals are presented.ResultsThere were 641 cases with primary OA (65% females) and 104 with PTOA (61% males). Patients with PTOA were 7.5 years younger (P < 0.001), reported more alcohol consumption (P = 0.01) and had higher odds of osteoporotic fractures (OP) and psychosis than patients with primary OA (OR = 2.0, CI = 1.06-3.78 and OR = 2.90, CI = -0.91-9.18, respectively). Knee fractures were most common in males and hip fractures in females (31% and 37.5%, respectively, P < 0.005). The PTOA-associated injuries with the highest pain and disability scores were meniscal injuries and hip fractures. Besides, in the group with primary OA, there were more diabetes, hypertension and hypothyroidism cases than in PTOA. However, after adjustment, differences were only significant for diabetes (OR(ad)j = 1.78, CI = 1.0-3.2).ConclusionsPast meniscal injuries and hip fractures were the most relevant PTOA-associated injuries regarding pain and walking disability. This, together with differences in their profile when compared with primary OA, might help to decide the orthopaedic management of these injuries to prevent complications such as PTOA and recurrence, with appropriate preoperative

planning, surgery choice and comorbidity treatment.
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NR 40
TC 24
Z9 29
U1 0
U2 4
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD JUL 12
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PG 9
WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA L6LE6
UT WOS:001024350100002
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PT J
AU Mazzotti, A
Langone, L
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AF Mazzotti, Antonio
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TI Probiotics in Orthopedics: From Preclinical Studies to Current Applications and Future Perspective
SO MICROORGANISMS
LA English
DT Review
DE probiotics; orthopedic; bone; osteoporosis; cartilage; muscles; skin; wounds; SAP
ID clostridium-difficile infection; lactobacillus-plantarum; double-blind; beneficial bacteria; skeletal-muscle; gut microbiota; bone health; supplementation; immune; metabolism
AB In recent years, probiotics have been emerging as an attractive therapeutic strategy for several diseases. In orthopedics, probiotics seem to be a promising supplementation for treatment of osteoporosis, osteoarthritis, muscle loss-related disease, wound and ulcer issues, and prevention of surgical antibiotic prophylaxis side effects. Although probiotics are still not included in guidelines for these conditions, several studies have reported theoretical benefits of their administration. Further high-level clinical trials are necessary to convert research into solid clinical practice. However, probiotics represent a cost-effective future perspective and may play a role in association with traditional orthopedic therapies.

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NR 103
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U1 0
U2 11
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PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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J9 MICROORGANISMS
JI Microorganisms
PD AUG 15
PY 2023
VL 11
IS 8
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DI 10.3390/microorganisms11082021
PG 16
WC Microbiology
SC Microbiology
GA Q4SS7
UT WOS:001057441200001
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AU Zhou, GH
Zhang, XQ
Gu, ZX
Zhao, JL
Luo, MH
Liu, J
AF Zhou, Guanghui
Zhang, Xianquan

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Zhao, Jinlong
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TI Research progress on the treatment of knee osteoarthritis combined with osteoporosis by single-herb Chinese medicine and compound
SO FRONTIERS IN MEDICINE
LA English
DT Review
DE geriatric medicine; knee osteoarthritis; osteoporosis; bone aging; metabolism; plant-based natural products; signaling pathway
ID components
AB Knee osteoarthritis (KOA) is a degenerative disease with synovial inflammation, articular surface cartilage degeneration, meniscus degeneration, ligament and muscle changes, subchondral bone changes, and osteophyte formation around the joint as the main pathological changes. Osteoporosis (OP) is a disease characterized by low bone mass and deterioration of the microstructure of bone tissue. KOA and OP are both geriatric diseases, and the incidence of KOA combined with OP is high, but there is a lack of specific drugs, and the major treatments are limited to drug therapy. Most traditional Chinese medicine (TCM) treatments use plant-based natural products, and they help patients obtain good clinical benefits and at the same time provide researchers with ideas to study the mechanism of disease occurrence and the relationship between the two diseases. This article summarizes the research progress of TCM monomers and TCM compounds that are frequently used to treat KOA combined with OP to provide ideas for future clinical treatments and related basic research.
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[赵金龙 Zhao Jinlong], 2020, 中国骨质疏松杂志 CHINESE JOURNAL OF OSTEOPOROSIS, V26, P755
NR 40
TC 10
Z9 14
U1 4
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PU FRONTIERS MEDIA SA
PI LAUSANNE
PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
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EI 2296-858X

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PT J
AU Aziz, H
Trout, SM
Jethanandani, R
Bub, CD
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Goldman, AT
AF Aziz, Hadi
Trout, Sally M.
Jethanandani, Rishabh
Bub, Christine D.
Collins, Lewis
Goldman, Ariel T.
TI Postoperative Outcomes in Malleolar Fractures Fixed With a 3.5-mm Locking Compression Plate Hook Plate
SO ORTHOPEDICS
LA English
DT Article
ID ankle fractures; complications; epidemiology
AB Ankle fractures are among the most common types of fractures seen in the United States. Few studies have analyzed the use of a locking compression plate (LCP) hook plate in the fixation of malleolar fractures. The goal of this study was to analyze postoperative outcomes in malleolar fractures fixed with a 3.5-mm LCP hook plate. A cohort of 74 patients with ankle fractures treated operatively with hook plates between 2011 and 2021 by a single orthopedic surgeon was retrospectively reviewed. Time to union, duration of non-weight bearing, final

range of motion, postoperative complications, demographics, and comorbidities were recorded. A total of 66 patients fulfilled our inclusion criteria. There were 5 isolated medial malleolar, 34 bimalleolar, and 27 trimalleolar fractures. There were 46 women and 20 men with a mean age of 60.9 +/- 18.9 years. Fourteen patients had diabetes, 27 had osteoporosis, and 4 were current or former tobacco users. All patients achieved union, with a mean time to union of 10.9 +/- 5.3 weeks. The mean time to weight bearing was 50.2 +/- 18.4 days. The mean length of follow-up was 8.1 +/- 5.6 months. At final follow-up, mean dorsiflexion was 9.9 degrees +/- 4.3 degrees and mean plantarflexion was 14.1 degrees +/- 5.1 degrees. Six patients experienced postoperative complications such as surgical site infections and posttraumatic osteoarthritis. This study demonstrates that the use of a 3.5-mm LCP hook plate in the operative fixation of malleolar fractures has a high rate of union while maintaining low rates of postoperative complications.
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TI Update on the clinical use of trabecular bone score (TBS) in the management of osteoporosis: results of an expert group meeting organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO), and the International Osteoporosis Foundation (IOF) under the auspices of WHO Collaborating Center for Epidemiology of Musculoskeletal Health and Aging
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Trabecular bone score; TBS; Fracture; Osteoporosis; Guidelines
ID rheumatoid-arthritis patients; fracture risk-assessment; x-ray absorptiometry; ms. os cohort; postmenopausal women; mineral density; vertebral fractures; aromatase-inhibitors; glucocorticoid therapy; spine bmd
AB PurposeTrabecular bone score (TBS) is a grey-level textural measurement acquired from dual-energy X-ray absorptiometry lumbar spine images and is a validated index of bone microarchitecture. In 2015, a Working Group of the European Society on Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) published a review of the TBS literature, concluding that TBS predicts hip and major osteoporotic fracture, at least partly independent of bone mineral density (BMD) and clinical risk factors. It was also concluded that TBS is potentially amenable to change as a result of pharmacological therapy. Further evidence on the utility of TBS has since accumulated in both primary and secondary osteoporosis, and the introduction of FRAX and BMD T-score adjustment for TBS has accelerated adoption. This position paper therefore presents a review of the updated scientific literature and provides expert consensus statements and corresponding operational guidelines for the use of TBS.MethodsAn Expert Working Group was convened by the ESCEO and a systematic review of the evidence undertaken, with defined search strategies for four key topics with respect to the potential use of TBS: (1) fracture prediction in men and women; (2) initiating and monitoring treatment in postmenopausal osteoporosis; (3) fracture prediction in secondary osteoporosis; and (4) treatment monitoring in secondary osteoporosis. Statements to guide the clinical use of TBS

were derived from the review and graded by consensus using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach.ResultsA total of 96 articles were reviewed and included data on the use of TBS for fracture prediction in men and women, from over 20 countries. The updated evidence shows that TBS enhances fracture risk prediction in both primary and secondary osteoporosis, and can, when taken with BMD and clinical risk factors, inform treatment initiation and the choice of antiosteoporosis treatment. Evidence also indicates that TBS provides useful adjunctive information in monitoring treatment with long-term denosumab and anabolic agents. All expert consensus statements were voted as strongly recommended.ConclusionThe addition of TBS assessment to FRAX and/or BMD enhances fracture risk prediction in primary and secondary osteoporosis, adding useful information for treatment decision-making and monitoring. The expert consensus statements provided in this paper can be used to guide the integration of TBS in clinical practice for the assessment and management of osteoporosis. An example of an operational approach is provided in the appendix.This position paper presents an up-to-date review of the evidence base, synthesised through expert consensus statements, which informs the implementation of Trabecular Bone Score in clinical practice.

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TI Gut-spine axis: a possible correlation between gut microbiota and spinal degenerative diseases
SO FRONTIERS IN MICROBIOLOGY
LA English
DT Review
DE gut microbiota; gut dysbiosis; spinal degenerative disease; inflammation; gut-spine axis; gut-bone axis
ID intestinal microbiome; knee osteoarthritis; metabolic syndrome; immune-system; double-blind; short-chain; bone; senescence; inflammation; transplantation
AB As society ages, the number of patients with spinal degenerative diseases (SDD) is increasing, posing a major socioeconomic problem for patients and their families. SDD refers to a generic term for degenerative diseases of spinal structures, including osteoporosis (bone), facet osteoarthritis (joint), intervertebral disk degeneration (disk), lumbar spinal canal stenosis (yellow ligament), and spinal sarcopenia (muscle). We propose the term "gut-spine axis" for the first time, given the influence of gut microbiota (GM) on the metabolic, immune, and endocrine environment in hosts through various potential mechanisms. A close cross-talk is noted between the aforementioned spinal components and degenerative diseases. This review outlines the nature and role of GM, highlighting GM abnormalities associated with the degeneration of spinal components. It also summarizes the evidence linking GM to various SDD. The gut-spine axis perspective can provide novel insights into the pathogenesis and treatment of SDD.
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TI Clinical and Radiographic Outcomes of Total Elbow Arthroplasty Using a Semi-constrained Prosthesis with a Triceps-preserving Approach over a Minimum

Follow-up Period of 4 Years
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE Distal humerus fracture; Joint prosthesis; Osteoporosis; Total elbow arthroplasty
ID distal humeral fractures; rheumatoid-arthritis; internal-fixation; replacement; experience; failure; trends
AB ObjectiveComplications related to triceps after total elbow arthroplasty (TEA) have become a major surgical concern. The triceps-preserving approach has the advantage of not disturbing the insertion of triceps but is disadvantaged by the reduced exposure of the elbow joint. The aim of this study was to investigate the clinical and radiological outcomes of TEA with a triceps-preserving approach and to compare the outcomes of TEA to treat arthropathy with that of TEA to treat acute distal humerus fracture. MethodsFrom January 2010 to December 2018, 23 patients undergoing primary TEAs were retrospectively reviewed with a mean follow-up time of 92.6 months (range, 52-136 months). Each TEA was performed using the triceps-preserving approach with a semi-constrained Coonrad-Morrey prosthesis. Patient demographics, range of motion (ROM), pain visual analogue scale (VAS), and triceps strength (Medical Research Council [MRC] scale) were compared before and after surgery. The Mayo Elbow Performance Score (MEPS), Disabilities of the Arm, Shoulder, and Hand (DASH) score, radiographic outcome, and complications were evaluated at follow-up. ResultsIn total, seven males and 16 females were included in this study, with a mean age of 66.1 years (range:46-85 years). By the last follow-up, pain had been significantly relieved in all patients. The average MEPS in the arthropathy group and fracture group were 90.8 +/- 10.3 points (range: 68-98 points) and 91.7 +/- 0.4 (range: 76-100 points), respectively. The average DASH of the arthropathy group and fracture group was 37.3 +/- 18.8 points (range: 18-52 points) and 38.4 +/- 20.1 (range: 16-60 points). At the last follow-up after surgery, the mean flexion arcs in the arthropathy group and fracture group were 100.4 degrees +/- 24.1 degrees and 97.8 degrees +/- 28.1 degrees, respectively. The mean pro-supination arcs in the arthropathy group and fracture group were 142.4 degrees +/- 15.2 degrees and 139.2 degrees +/- 17.5 degrees, respectively. There were no significant differences in clinical outcomes between the two groups (P >= 0.05). Triceps strength was normal (MRC grade V) in 15 elbows and good in eight elbows. None of the cases experienced weakness of the triceps strength, infection, periprosthetic fractures, or prosthesis breakage. ConclusionsThe clinical and radiographical outcomes of TEA with the triceps-preserving approach were satisfactory in patients with distal humerus fracture, osteoarthritis and rheumatoid arthritis.
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TI A Bibliometric Analysis of Acupuncture Therapy in the Treatment of Musculoskeletal Pain from 2003 to 2022
SO JOURNAL OF PAIN RESEARCH
LA English
DT Review
DE musculoskeletal pain; acupuncture therapy; bibliometrics; CiteSpace
ID low-back-pain; breast-cancer patients; chronic knee pain; systematic reviews; trials; electroacupuncture; osteoarthritis; metaanalysis; multicenter; blind
AB Background: Acupuncture therapy has been widely used in the treatment of musculoskeletal pain (MP) in many countries around the world. However, there are no bibliometric studies on acupuncture therapy for MP. Therefore, the aim of this study was to analyze the current status, frontiers and hot spots in the use of acupuncture therapy for the treatment of MP.Methods: Literature on acupuncture therapy for MP was extracted from the Web of Science Core Collection database from 2003 to 2022. CiteSpace 6.2.R4 (64-bit) software was used to analyze the number and centrality of journals, countries, institutions, authors, references and keywords, and the functions of co-occurrence and clustering were applied to draw a visual knowledge map.Results: Over the past 20 years, the annual journal publications have been on a steady upward trend, with 438 articles published in 143 journals, including Acupuncture in Medicine Journal published the most (28, 6.39%), JAMA-Journal of the American Medical Association was the journal with the highest impact factor (IF = 120.7003), USA dominated with the most publications (140, 31.96%) among 44 countries, and among 196 research organizations Kyung Hee University was the most prolific (19, 4.34%) and Ha, In-Hyuk was the most published author (9, 2.05%). "Acupuncture" is the most popular and highly sought after keywords. "Low back pain" is the keyword with the highest centrality.Conclusion: This article provides the current situation of the use of acupuncture therapy in the treatment of MP in the past 20 years, and statistical analysis reveals that "low back pain", "knit osteoporosis" and "break cancer" are new research diseases related to acupuncture therapy for MP, and "myobasic trigger point" is a new research direction of acupuncture therapy for MP. Therefore, this study helps researchers grasp the research hotspots and provide certain references for in-depth research and future topic selection.
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AF Alenazi, Aqeel M.
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TI Hypertension Is Associated with Joint Pain Severity Among Individuals with Osteoarthritis
SO PAIN MANAGEMENT NURSING
LA English
DT Article
ID knee osteoarthritis; metabolic syndrome; intensity; risk
AB Previous studies have reported an association between hypertension (HTN) and osteoarthritis (OA). How-ever, limited research has examined the association between HTN and symptoms, such as pain severity, in people with OA. Therefore, the aim was to investigate the prevalence of HTN in individuals with OA and the association between HTN and pain severity in this population. This study was cross-sectional and included participants aged 50 years and older from the community. Demographic data were included and self-reported history of chronic illnesses including diabetes, HTN, cardiovascular disease, dyslipidemia, anemia, osteoporosis, neurological disease, and back pain were obtained. Numerous medications and chronic diseases were included. A subsample of people who self-reported osteoarthritis was included in this study. Pain severity was measured over the past 7 days using a pain numeric rating scale. Multiple linear regression was used after adjusting for covariates. A total of 82 participants with OA were included, and the prevalence of HTN among individuals with OA was 28.91%. Hypertension was significantly associated with increased joint pain severity in this population after adjustments for covariates (B = 1.81; 95% CI, 0.65, 2.97; p = .003). Hypertension is prevalent in individuals with OA and is significantly associated with pain severity in this population. Future research should consider the effect of HTN control and medication on symptoms in people with OA. Clinicians may implement screening for HTN among individuals with OA because of the association between HTN and symptoms, such as pain, in this population.(c) 2023 American Society for

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TI Insights into the underlying pathogenesis and therapeutic potential of endoplasmic reticulum stress in degenerative musculoskeletal diseases
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DE Endoplasmic reticulum stress; Degenerative musculoskeletal diseases; Pathogenesis; Treatment
ID glycation end-products; nucleus pulposus cells; intervertebral disc degeneration; unfolded protein response; mesenchymal stem-cells; bone-mineral density; nf-kappa-b; er stress; induced-apoptosis; skeletal-muscle
AB Degenerative musculoskeletal diseases are structural and functional failures of the musculoskeletal system, including osteoarthritis, osteoporosis, intervertebral disc degeneration (IVDD), and sarcopenia. As the global population ages, degenerative musculoskeletal diseases are becoming more prevalent. However, the pathogenesis of degenerative musculoskeletal diseases is not fully understood. Previous studies have revealed that endoplasmic reticulum (ER) stress is a stress response that occurs when impairment of the protein folding capacity of the ER leads to the accumulation of misfolded or unfolded proteins in the ER, contributing to degenerative musculoskeletal diseases. By affecting cartilage degeneration, synovitis, meniscal lesion, subchondral bone remodeling of osteoarthritis, bone remodeling and angiogenesis of osteoporosis, nucleus pulposus degeneration, annulus fibrosus rupture, cartilaginous endplate degeneration of IVDD, and sarcopenia, ER stress is involved in the pathogenesis of degenerative musculoskeletal diseases. Preclinical studies have found that regulation of ER stress can delay the progression of multiple degenerative musculoskeletal diseases. These pilot studies provide foundations for further evaluation of the feasibility, efficacy, and safety of ER stress modulators in the treatment of musculoskeletal degenerative diseases in clinical trials. In this review, we have integrated up-to-date research findings of ER stress into the pathogenesis of degenerative musculoskeletal diseases. In a future perspective, we have also discussed possible directions of ER stress in the investigation of degenerative musculoskeletal disease, potential therapeutic strategies for degenerative musculoskeletal diseases using ER stress modulators, as well as underlying challenges and obstacles in bench-to-beside research.
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TI The Development of Naringin for Use against Bone and Cartilage Disorders
SO MOLECULES
LA English
DT Review
DE naringin; osteoporosis; intervertebral disc degeneration; osteoarthritis; rheumatoid arthritis; osteogenic differentiation; bone tissue engineering
ID nf-kappa-b; endoplasmic-reticulum stress; mesenchymal stem-cells; nucleus pulposus cells; osteogenic differentiation; signaling pathway; induced osteoporosis; femoral-head; nontraumatic osteonecrosis; morphogenetic protein-2
AB Bone and cartilage disorders are the leading causes of musculoskeletal disability. There is no absolute cure for all bone and cartilage disorders. The exploration of natural compounds for the potential therapeutic use against bone and cartilage disorders is proving promising. Among these natural chemicals, naringin, a flavanone glycoside, is a potential candidate due to its multifaceted pharmacological activities in bone and cartilage tissues. Emerging studies indicate that naringin may promote osteogenic differentiation, inhibit osteoclast formation,

and exhibit protective effects against osteoporosis in vivo and in vitro. Many signaling pathways, such as BMP-2, Wnt/beta-catenin, and VEGF/VEGFR, participate in the biological actions of naringin in mediating the pathological development of osteoporosis. In addition, the anti-inflammatory, anti-oxidative stress, and antiapoptosis abilities of naringin also demonstrate its beneficial effects against bone and cartilage disorders, including intervertebral disc degeneration, osteoarthritis, rheumatoid arthritis, bone and cartilage tumors, and tibial dyschondroplasia. Naringin exhibits protective effects against bone and cartilage disorders. However, more efforts are still needed due to, at least in part, the uncertainty of drug targets. Further biological and pharmacological evaluations of naringin and its applications in bone tissue engineering, particularly its therapeutic effects against osteoporosis, might result in developing potential drug candidates.
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TI AnnexinA6: a potential therapeutic target gene for extracellular matrix mineralization
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE AnnexinA6; Ca2+ regulation; matrix vesicles; extracellular matrix mineralization; osteogenesis; bone regeneration
ID vesicle-mediated mineralization; growth-plate cartilage; arterial calcification; vascular calcification; alkaline-phosphatase; cell-proliferation; nucleational core; crystal-structure; membrane-binding; down-regulation
AB The mineralization of the extracellular matrix (ECM) is an essential and crucial process for physiological bone formation and pathological calcification. The abnormal function of ECM mineralization contributes to the worldwide risk of developing mineralization-related diseases; for instance, vascular calcification is attributed to the hyperfunction of ECM mineralization, while osteoporosis is due to hypofunction. AnnexinA6 (AnxA6), a Ca2+-dependent phospholipid-binding protein, has been extensively reported as an essential target in mineralization-related diseases such as osteoporosis, osteoarthritis, atherosclerosis, osteosarcoma, and calcific aortic valve disease. To date, AnxA6, as the largest

member of the Annexin family, has attracted much attention due to its significant contribution to matrix vesicles (MVs) production and release, MVs-ECM interaction, cytoplasmic Ca2+ influx, and maturation of hydroxyapatite, making it an essential target in ECM mineralization. In this review, we outlined the recent advancements in the role of AnxA6 in mineralization-related diseases and the potential mechanisms of AnxA6 under normal and mineralization-related pathological conditions. AnxA6 could promote ECM mineralization for bone regeneration in the manner described previously. Therefore, AnxA6 may be a potential osteogenic target for ECM mineralization.
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NR 197
TC 7
Z9 8
U1 0
U2 24
PU FRONTIERS MEDIA SA
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J9 FRONT CELL DEV BIOL
JI Front. Cell. Dev. Biol.
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DI 10.3389/fcell.2023.1201200
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WC Cell Biology; Developmental Biology
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PT J
AU Ye, ZQ
Liu, YY
Song, JT
Gao, Y
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Zhang, M
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Cui, L
Liu, YZ
AF Ye, Zhiqiang
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Song, Jintong
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Fang, Haiping
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Zhang, Min
Liao, Wenwei
Cui, Liao
Liu, Yanzhi
TI Expanding the therapeutic potential of Salvia miltiorrhiza: a review of its pharmacological applications in musculoskeletal diseases
SO FRONTIERS IN PHARMACOLOGY
LA English

DT Review
DE bone; joint; osteoarthritis; osteoporosis; Salvia miltiorrhiza; musculoskeletal diseases
ID fibroblast-like synoviocytes; tanshinone iia; osteoclast differentiation; rheumatoid-arthritis; kappa-b; danshen; apoptosis; cell; osteoarthritis; osteoblast
AB Salvia miltiorrhiz, commonly known as "Danshen" in Chinese medicine, has longstanding history of application in cardiovascular and cerebrovascular diseases. Renowned for its diverse therapeutic properties, including promoting blood circulation, removing blood stasis, calming the mind, tonifying the blood, and benefiting the "Qi", recent studies have revealed its significant positive effects on bone metabolism. This potential has garnered attention for its promising role in treating musculoskeletal disorders. Consequently, there is a high anticipation for a comprehensive review of the potential of Salvia miltiorrhiza in the treatment of various musculoskeletal diseases, effectively introducing an established traditional Chinese medicine into a burgeoning field. Aim of the review: Musculoskeletal diseases (MSDs) present significant challenges to healthcare systems worldwide. Previous studies have demonstrated the high efficacy and prospects of Salvia miltiorrhiza and its active ingredients for treatment of MSDs. This review aims to illuminate the newfound applications of Salvia miltiorrhiza and its active ingredients in the treatment of various MSDs, effectively bridging the gap between an established medicine and an emerging field. Methods: In this review, previous studies related to Salvia miltiorrhiza and its active ingredients on the treatment of MSD were collected, the specific active ingredients of Salvia miltiorrhiza were summarized, the effects of Salvia miltiorrhiza and its active ingredients for the treatment of MSDs, as well as their potential molecular mechanisms were reviewed and discussed. Results: Based on previous publications, Salvianolic acid A, salvianolic acid B, tanshinone IIA are the representative active ingredients of Salvia miltiorrhiza. Their application has shown significant beneficial outcomes in osteoporosis, fractures, and arthritis. Salvia miltiorrhiza and its active ingredients protect against MSDs by regulating different signaling pathways, including ROS, Wnt, MAPK, and NF-kappa B signaling. Conclusion: Salvia miltiorrhiza and its active ingredients demonstrate promising potential for bone diseases and have been explored across a wide variety of MSDs. Further exploration of Salvia miltiorrhiza's pharmacological applications in MSDs holds great promise for advancing therapeutic interventions and improving the lives of patients suffering from these diseases.
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NR 100
TC 18
Z9 22
U1 3
U2 29
PU FRONTIERS MEDIA SA
PI LAUSANNE
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J9 FRONT PHARMACOL
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WC Pharmacology & Pharmacy
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PT J
AU Shohet, J
Justeson, D
Wilkins, A
AF Shohet, Jack
Justeson, Drew
Wilkins, Allison
TI Transcanal Excision of Exostoses: Large Series Comparing Bone Removal Methods
SO OTOLARYNGOLOGY-HEAD AND NECK SURGERY
LA English
DT Article
DE cutting drill; exostosis; osteotome; piezoelectric; transcanal approach

ID osteotome
AB ObjectiveExternal auditory exostosis (EAE) is a condition of progressive temporal bone growth into the external auditory canal most commonly from repeat cold water and wind exposure. Several tools have been utilized for EAE excision with varying implications for intra- and postoperative complications. However, comparisons of osteotome and microdrill are made difficult due to the few published cases and intervariability between surgeons. Furthermore, evidence is needed to analyze the safety of novel supplemental tools such as the piezoelectric bone-cutting device. Study DesignRetrospective chart review. SettingMedical clinic and surgery center. MethodsA total of 413 subjects representing 472 ears met the inclusion criteria. Of which 159 ears were operated on using osteotome alone (OA), 271 using osteotome with a drill (OD), and 42 with osteotome with piezoelectric (OP). Charts were analyzed for the most reported intraoperative complications and postoperative symptoms and complications. ResultsThere were no significant differences in the rate of tympanic membrane perforations nor in total intraoperative complications between OA, OD, or OP. The OD group contained the only nonperforation intraoperative event. OA had the lowest or near lowest incidence of all symptoms analyzed. OA showed a significantly lower incidence of tinnitus when compared to OD and OP. ConclusionWe found that OA performed the best, though not statistically significant in most measures, with regard to mitigating rates of complications postsurgery. Our findings suggest OA provides lower risk intraoperatively and postoperatively for patients undergoing transcanal exostosis excision.
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NR 8
TC 2
Z9 2
U1 0
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PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0194-5998
EI 1097-6817
J9 OTOLARYNG HEAD NECK
JI Otolaryngol. Head Neck Surg.
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SC Otorhinolaryngology; Surgery
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PT J
AU Ju, SH
Liu, PW
Tan, LR
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Wang, MJ
AF Ju, Shaohua

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TI Hydroxysafflor Yellow A Regulates Inflammation and Oxidative Stress by Suppressing the HIF-1α/JAK/STAT3 Signaling Pathway to Attenuate Osteoarthritis
SO REVISTA BRASILEIRA DE FARMACOGNOSIA-BRAZILIAN JOURNAL OF PHARMACOGNOSY
LA English
DT Article
DE Inflammation; Collagen; Oxidative stress; quinochalcone C-glycosidic structure; Osteoporosis
ID low-grade inflammation; safflower yellow; transcription; epidemiology; chondrocytes; pathogenesis; association; progression; inhibition; transducer
AB Hydroxysafflor yellow A is extracted from Carthamus tinctorius L., Asteraceae, and has extensive pharmacological properties. In this study, interleukin-1 beta was used to establish the osteoarthritis model in vitro, and the impacts of hydroxysafflor yellow A on the cell model were analyzed. CCK8 was used to measure cell viability, and flow cytometry was used to evaluate apoptosis and reactive oxygen species. An enzyme-linked immunosorbent assay was performed to calculate the release of inflammatory cytokines and oxidative stress index. Western blotting was performed to measure the expression of collagen-related proteins. The protein levels in the HIF-1a/JAK/STAT3 signaling pathway were also measured. The results showed that hydroxysafflor yellow A promoted cell viability and inhibited apoptosis and oxidative stress. In addition, quinochalcone C-glycoside upregulated the expression of collagen II and Sry-related HMG box-9, while downregulating the expression of matrix metalloproteinase-13. Interleukin-1 beta induced high levels of interleukin-6 and tumor necrosis factor-a that were inhibited by hydroxysafflor yellow A. Meanwhile, hydroxysafflor yellow A inhibited the interleukin-1 beta-induced high levels of reactive oxygen species and malondialdehyde and enhanced the interleukin-1 beta-induced low levels of superoxide dismutase and glutathione peroxidase. Furthermore, hydroxysafflor yellow A downregulated the mRNA expression of HIF-1a, JAK, STAT3, and interleukin-6 as well as the protein expression of HIF-1a, p-JAK, and p-STAT3. The results suggest that hydroxysafflor yellow A inhibited the JAK/STAT3 signaling pathways by inhibiting HIF-1a. Therefore, hydroxysafflor yellow A regulates the inflammatory response and oxidative stress in vitro.
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NR 42
TC 3
Z9 4
U1 1
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JI Rev. Bras. Farmacogn.-Braz. J. Pharmacogn.
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PT J
AU Chen, S
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Li, ZW
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Jin, Jie
Zhou, Guowei
Li, Zhiwei
TI Osteoarthritis and sarcopenia-related traits: the cross-sectional study from NHANES 2011-2014 and Mendelian randomization study
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Osteoarthritis; Sarcopenia; Grip strength; Mendelian randomization; NHANES
ID knee osteoarthritis; muscle mass; risk-factor; epidemiology; women; burden; osteoporosis; inflammation; instruments; prevalence
AB BackgroundOsteoarthritis (OA) and sarcopenia are common musculoskeletal disorders in the aged population, and a growing body of evidence indicated that they mutually influence one another. Nevertheless, there was still substantial controversy and uncertainty about the causal relationship between sarcopenia and OA. We explored the complex association between sarcopenia-related traits and OA using cross-sectional analysis and Mendelian randomization (MR).MethodsThe cross-sectional study used the data from the National Health and Nutrition Examination Survey (NHANES) 2011-2014. Weighted multivariable-adjusted logistic regression and subgroup analyses were used to evaluate the correlation between sarcopenia, grip, appendicular lean mass (ALM) and the risk of OA. Then, we further performed MR analysis to examine the causal effect of sarcopenia-related traits (grip strength, ALM) on OA. Instrumental variables for grip strength and ALM were from the UK Biobank, and the summary-level data for OA was derived from the

Genetics of Osteoarthritis (GO) Consortium GWAS (n = 826,690).ResultsIn this cross-sectional analysis, we observed that sarcopenia, grip were significantly linked with the risk of OA (OR 1.607, 95% CI 1.233-2.094, P < 0.001), (OR 0.972, 95% CI 0.964-0.979, P < 0.001). According to subgroup analyses stratified by gender, body mass index (BMI), and age, the significant positive relationship between sarcopenia and OA remained in males, females, the age (46-59 years) group, and the BMI (18.5-24.9 kg/m(2)) group (P < 0.05). Furthermore, MR analysis and sensitivity analyses showed causal associations between right grip, left grip and KOA (OR 0.668; 95% CI 0.509 to 0.877; P = 0.004), (OR 0.786; 95% CI 0.608 to 0.915; P = 0.042). Consistent directional effects for all analyses were observed in both the MR-Egger and weighted median methods. Subsequently, sensitivity analyses revealed no heterogeneity, directional pleiotropy or outliers for the causal effect of grip strength on KOA (P > 0.05).ConclusionsOur research provided evidence that sarcopenia is correlated with an increased risk of OA, and there was a protective impact of genetically predicted grip strength on OA. These findings needed to be verified in further prospective cohort studies with a large sample size.
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U1 4
U2 31
PU BMC

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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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JI J. Orthop. Surg. Res.
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WC Orthopedics
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GA M4OY8
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PT J
AU Schreiber, H
Cohen, G
Maor, GS
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Biron-Shental, T
Markovitch, O
AF Schreiber, Hanoch
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Maor, Gil Shechter
Herzberger, Einat Haikin
Biron-Shental, Tal
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TI Head position and vacuum-assisted delivery using the Kiwi Omnicup
SO INTERNATIONAL JOURNAL OF GYNECOLOGY & OBSTETRICS
LA English
DT Article
DE adverse maternal outcomes; adverse neonatal outcomes; Kiwi Omnicup; occiput posterior; vacuum-assisted delivery
ID occiput posterior position; randomized controlled-trial; operative delivery; fetal position; hand-held; association; labor; extraction; 2nd-stage; risk
AB Objective To evaluate the association between fetal head position during

prevacuum assessment and adverse outcomes. Method This retrospective cohort study included all vacuum-assisted deliveries using the Kiwi Omnicup over 5 years. Primary outcomes were third- or fourth-degree perineal tear, pH < 7.1, and subgaleal hematoma (SGH). AGAR, neonatal intensive care unit admission, cephalohematoma, Erb's palsy, third-stage duration, and postpartum hemorrhage were secondary. Outcomes were compared between the occiput posterior (OP) and occiput anterior (OA) positions. Results The study included 1960 patients. OP position was more likely to involve epidural analgesia (311 [82.5%] vs. 1216 [77%], P = 0.020), higher fetal head station (P = 0.001), higher percentage of cup detachments (121 cases [32.1%] vs. 307 [19.4%], P = 0.001), and longer procedure (5.5 +/- 3.7 min vs. 4.7 +/- 2.8 min, P = 0.001). OP was associated with umbilical cord pH < 7.1 (21 [5.5%] vs. 52 [3.9%], P = 0.032), NICU admissions (16 [4.2%] vs. 38 [2.4%], P = 0.049), SGH (18 [4.8%] vs. 38 [2.4%], P = 0.013), and high-degree perineal tears (12 [3.2%] vs. 26 [1.7%], with borderline significance, P = 0.051). SGH and high-grade tears remained significantly associated with OP position (P = 0.008 and P = 0.016, respectively) after adjusting for maternal age, nulliparity, diabetes, epidural anesthesia, preprocedure head station, and birth weight. Conclusion OP position is an independent risk-factor for anal sphincter injury and SGH during vacuum-assisted delivery.
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NR 25
TC 6
Z9 7
U1 2
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PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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JI Int. J. Gynecol. Obstet.
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WC Obstetrics & Gynecology
SC Obstetrics & Gynecology
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TI The molecular mechanisms underlying anti-inflammatory effects of galangin in different diseases
SO PHYTOTHERAPY RESEARCH
LA English
DT Review
DE galangin; inflammation; MAPK; molecular docking; NF-kappa B; NLRP3
ID nf-kappa-b; activated protein-kinases; cisplatin-induced nephrotoxicity; idiopathic pulmonary-fibrosis; collagen-induced arthritis; oxidative stress; nlrp3 inflammasome; risk-factors; suppress osteoclastogenesis; hepatocellular-carcinoma
AB When used as an alternative source of drugs to treat inflammation-associated diseases, phytochemicals with anti-inflammatory properties provide beneficial impacts. Galangin is one of the most naturally occurring flavonoids. Galangin has many biological activities, such as anti-inflammatory, antioxidant, antiproliferative, antimicrobial, anti-obesity, antidiabetic, and anti-genotoxic activities. We observed that galangin was well tolerated and positively impacted disease underlying

inflammation for the renal, hepatic, central nervous system, cardiovascular, gastrointestinal system, skin, and respiratory disorders, as well as ulcerative colitis, acute pancreatitis, retinopathy, osteoarthritis, osteoporosis, and rheumatoid arthritis. Galangin anti-inflammatory effects are mediated mainly by suppressing p38 mitogen-activated protein kinases, nuclear factor-kappa B, and nod-like receptor protein 3 signals. These effects are confirmed and supported by molecular docking. Clinical translational research is required to accelerate the bench-to-bedside transfer and determine whether galangin can be utilised as a safe, natural source of pharmaceutical anti-inflammatory medication for humans.
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TI Atraumatic Bone Marrow Edema Involving the Epiphyses
SO SEMINARS IN MUSCULOSKELETAL RADIOLOGY
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DT Article
DE transient bone marrow edema syndrome; subchondral insufficiency fracture; avascular necrosis; osteoarthritis; bone neoplasms
ID subchondral insufficiency fractures; femoral-head; transient osteoporosis; hip osteoarthritis; avascular necrosis; imaging findings; mri findings; osteonecrosis; lesions; pattern
AB Bone marrow edema (BME)-like signal intensity involving the epiphyses of tubular bones represents a frequent magnetic resonance imaging finding associated with a wide spectrum of bone and joint disorders. It is important to distinguish this finding from cellular infiltration of bone marrow and to be aware of the differential diagnosis of underlying causes. With a general focus on the adult musculoskeletal system, this article reviews the pathophysiology, clinical presentation, histopathology, and imaging findings of nontraumatic conditions associated with epiphyseal BME-like signal intensity: transient bone marrow edema syndrome, subchondral insufficiency fracture, avascular necrosis, osteoarthritis,

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TI "Bone-SASP" in Skeletal Aging
SO CALCIFIED TISSUE INTERNATIONAL
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DT Review
DE Bone-SASP; Cellular senescence; Osteoarthritis; Osteoporosis; Premature aging syndromes; Progeria syndrome; Senescence-associated secretory phenotype (SASP); Skeletal aging
ID mesenchymal stem-cells; telomeric dna-damage; nf-kappa-b; cellular senescence; secretory phenotype; posttraumatic osteoarthritis; osteogenic differentiation; metabolic syndrome; induced expression; oxidative stress
AB Senescence is a complex cell state characterized by stable cell cycle arrest and a unique secretory pattern known as the senescence-associated secretory phenotype (SASP). The SASP factors, which are heterogeneous and tissue specific, normally include chemokines, cytokines, growth factors, adhesion molecules, and lipid components that can lead to multiple age-associated disorders by eliciting local and systemic consequences. The skeleton is a highly dynamic organ that changes constantly in shape and composition. Senescent cells in bone and bone marrow produce diverse SASP factors that induce alterations of the skeleton through paracrine effects. Herein, we refer to bone cell-associated SASP as "bone-SASP." In this review, we describe current knowledge of cellular senescence and SASP, focusing on the role of senescent cells in mediating bone pathologies during natural aging and premature aging syndromes. We also summarize the role of cellular senescence and the bone-SASP in glucocorticoids-induced bone damage. In addition, we discuss the role of bone-SASP in the development of osteoarthritis, highlighting the mechanisms by which bone-SASP drives subchondral bone changes in metabolic syndrome-associated osteoarthritis.

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NR 220
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Z9 41
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TI Pro-Osteogenic and Anti-Inflammatory Synergistic Effect of Orthosilicic Acid, Vitamin K2, Curcumin, Polydatin and Quercetin Combination in Young and Senescent Bone Marrow-Derived Mesenchymal Stromal Cells
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE mesenchymal stromal cells; senescence; natural compounds; osteogenesis; inflammaging; osteoporosis
ID nf-kappa-b; osteoblast differentiation; stem-cells; osteoporosis; activation; promotes; premenopausal
AB During aging, bone marrow mesenchymal stromal cells (MSCs)-the precursors of osteoblasts-undergo cellular senescence, losing their osteogenic potential and acquiring a pro-inflammatory secretory phenotype. These dysfunctions cause bone loss and lead to osteoporosis. Prevention and intervention at an early stage of bone loss are important, and naturally active compounds could represent a valid help in addition to diet. Here, we tested the hypothesis that the combination of two pro-osteogenic factors, namely orthosilicic acid (OA) and vitamin K2 (VK2), and three other anti-inflammatory compounds, namely curcumin (CUR), polydatin (PD) and quercetin (QCT)-that mirror the nutraceutical BlastiMin Complex((R)) (Mivell, Italy)-would be effective in promoting MSC osteogenesis, even of replicative senescent cells (sMSCs), and inhibiting their pro-inflammatory phenotype in vitro. Results showed that when used at non-cytotoxic doses, (i) the association of OA and VK2 promoted MSC differentiation into osteoblasts, even when cultured

without other pro-differentiating factors; and (ii) CUR, PD and QCT exerted an anti-inflammatory effect on sMSCs, and also synergized with OA and VK2 in promoting the expression of the pivotal osteogenic marker ALP in these cells. Overall, these data suggest a potential role of using a combination of all of these natural compounds as a supplement to prevent or control the progression of age-related osteoporosis.
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TC 18
Z9 21
U1 4
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PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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UT WOS:000997532300001
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TI Amelioration of Osteoarthritis Development by Daily Oral Supplementation of Royal Jelly
SO BIOLOGICAL & PHARMACEUTICAL BULLETIN
LA English
DT Article
DE osteoarthritis; royal jelly; chondrocyte
ID 10-hydroxy-2-decenoic acid
AB Royal jelly (RJ), an essential food for the queen honeybee, has a variety of biological activities. Although RJ exerts preventive effects on various lifestyle-related diseases, such as osteoporosis and obesity, no study evaluated the effect of RJ on the development of osteoarthritis (OA), the most common degenerative joint disease. Here, we showed that daily oral administration of raw RJ significantly prevented OA development in vivo following surgically-induced knee joint instability in mice. Furthermore, in vitro experiments using chondrocytes, revealed that raw RJ significantly reduced the expression of inflammatory cytokines and enzymes critical for the degradation of the extracellular matrix (ECM). Similar results were observed after treatment with 10-hydroxy-2-decenoic acid, the most abundant and unique fatty acid in raw RJ. Our results suggest that oral supplementation with RJ would benefit the maintenance of joint health and prophylaxis against OA, possibly by suppressing the activity of inflammatory cytokines and ECM-degrading enzymes.
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NR 32
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PU PHARMACEUTICAL SOC JAPAN
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PA 2-12-15 SHIBUYA, SHIBUYA-KU, TOKYO, 150-0002, JAPAN
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TI Galangin: A food-derived flavonoid with therapeutic potential against a wide spectrum of diseases
SO PHYTOTHERAPY RESEARCH
LA English
DT Review
DE anti-cancer; bioactivities; flavonoid; food; Galangin
ID cisplatin-induced nephrotoxicity; hepatocellular-carcinoma cells; oxidative stress; inhibits proliferation; mmp-9 expression; down-regulation; in-vivo; growth; apoptosis; metastasis
AB Galangin is an important flavonoid with natural activity, that is abundant in galangal and propolis. Currently, various biological activities of galangin have been disclosed, including anti-inflammation, antibacterial effect, anti-oxidative stress and aging, anti-fibrosis, and antihypertensive effect. Based on the above bioactivities, more and more attention has been paid to the role of galangin in neurodegenerative diseases, rheumatoid arthritis, osteoarthritis, osteoporosis, skin diseases, and cancer. In this paper, the natural sources, pharmacokinetics, bioactivities, and therapeutic potential of galangin against various diseases were systematically reviewed by collecting and summarizing relevant literature. In addition, the molecular mechanism and new preparation of galangin in the treatment of related diseases are also discussed, to broaden the application prospect and provide reference for its clinical application. Furthermore, it should be noted that current toxicity and clinical studies of galangin are insufficient, and more evidence is needed to support its possibility as a functional food. image
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TI Harnessing cerium-based biomaterials for the treatment of bone diseases
SO ACTA BIOMATERIALIA

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DT Review
DE Bone diseases; Cerium-based biomaterials; Controllable synthesis; Nanoenzyme; Tailored strategies
ID enzyme-like activity; oxide nanoparticles; ceo2 nanoparticles; hydrogen-peroxide; osteoblast differentiation; antibacterial activity; dioxide nanoparticles; escherichia-coli; bacterial-growth; hollow spheres
AB Bone, an actively metabolic organ, undergoes constant remodeling throughout life. Disturbances in the bone microenvironment can be responsible for pathologically bone diseases such as periodontitis, osteoarthritis, rheumatoid arthritis and osteoporosis. Conventional bone tissue biomaterials are not adequately adapted to complex bone microenvironment. Therefore, there is an urgent clinical need to find an effective strategy to improve the status quo. In recent years, nanotechnology has caused a revolution in biomedicine. Cerium(III, IV) oxide, as an important member of metal oxide nanomaterials, has dual redox properties through reversible binding with oxygen atoms, which continuously cycle between Ce(III) and Ce(IV). Due to its special physicochemical properties, cerium(III, IV) oxide has received widespread attention as a versatile nanomaterial, especially in bone diseases. This review describes the characteristics of bone microenvironment. The enzyme-like properties and biosafety of cerium(III, IV) oxide are also emphasized. Meanwhile, we summarizes controllable synthesis of cerium(III, IV) oxide with different nanostructural morphologies. Following resolution of synthetic principles of cerium(III, IV) oxide, a variety of tailored cerium-based biomaterials have been widely developed, including bioactive glasses, scaffolds, nanomembranes, coatings, and nanocomposites. Furthermore, we highlight the latest advances in cerium-based biomaterials for inflammatory and metabolic bone diseases and bone-related tumors. Tailored cerium-based biomaterials have already demonstrated their value in disease prevention, diagnosis (imaging and biosensors) and treatment. Therefore, it is important to assist in bone disease management by clarifying tailored properties of cerium(III, IV) oxide in order to promote the use of cerium-based biomaterials in the future clinical setting.
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TI No Significant Differences between Bisphosphonates and Placebo for the Treatment of Bone Marrow Lesions of the Knee: A Systematic Review and Meta-Analysis of Randomized Controlled Trials
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Review
DE bisphosphonates; bone marrow lesions; knee; bone marrow edema
ID transient osteoporosis; cartilage volume; zoledronic acid; edema syndrome; osteoarthritis; osteonecrosis; alendronate; mechanism; women
AB Objectives: The purpose of the present systematic review and meta-analysis is to summarize the current evidence on the role of bisphosphonates in the treatment of knee bone marrow lesions (BMLs), to understand whether they are truly effective in improving symptoms and restoring the subchondral bone status at imaging evaluation. Methods: A literature search was carried out on PubMed, Cochrane, and Google Scholar databases in accordance with the PRISMA guidelines. Potential risk of bias was evaluated using the Cochrane Risk of Bias 2 tool for randomized controlled trials (RCTs) and the ROBINS-I tool for non-randomized studies. Results:

A total of 15 studies were included in the present systematic review and meta-analysis. Seven studies were RCTs, two were prospective cohort studies, three were retrospective, and three were case series. Our meta-analysis revealed that bisphosphonates did not significantly improve clinical scores or reduce BML size compared to placebo. Accordingly, the rate of adverse events was also non-significantly higher among bisphosphonate users versus placebo users. Conclusions: The main finding of the present meta-analysis and systematic review is that bisphosphonates show neither significant benefits nor significant adverse events when compared to placebo in the treatment of BMLs of the knee. Level of Evidence: Level IV systematic review of level II-III-IV studies. Level I meta-analysis of level I studies.
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WC Medicine, General & Internal
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PT J
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Leslie, WD
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TI Association of vertebral fractures with worsening degenerative changes of the spine: a longitudinal study
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE osteoporosis < diseases and disorders of/related to bone; osteoarthritis < diseases and disorders of/related to bone; general population studies < epidemiology; other < analysis/quantitation of bone; radiology
ID physical-activity; postmenopausal women; facet joints; follow-up; osteoarthritis; cohort; heart; risk; orientation; prevalence
AB Vertebral compression fractures (VFs) and spinal degeneration are both common causes of back pain, particularly in older adults. Previous cross-sectional

studies have shown a potential association between these entities, but there is limited evidence on the role of VFs in spinal degeneration. In this longitudinal study, we evaluated the association between prevalent VFs and the subsequent progression of facet joint osteoarthritis (FJOA) and intervertebral disc height narrowing (DHN), using data from the Framingham Heart Study Offspring and Third Generation Multi-Detector Computed Tomography study. Summary indices representing the total burden of each spinal parameter (VFs, DHN, and FJOA) were calculated for each individual. We hypothesized that prevalent VFs are associated with worsening spinal degeneration. Three hundred and seventy (31%) of 1197 participants had a baseline (prevalent) VF. The change in summary index of DHN over the follow-up period was significantly higher in those with vs without prevalent VF (difference in change in DHN 0.38, 95% CI 0.18 to 0.59, p<.001), but the change in summary index of FJOA was similar between those with and without prevalent VF. However, once adjusted for age, sex, cohort, smoking status, BMI, and baseline DHN, the change in summary index of DHN did not differ by prevalent VF status. There was a modestly higher change in the FJOA summary index in those with prevalent VFs compared to those without in the fully adjusted model (difference in change in FJOA 0.62, 95% CI -0.01 to 1.24, p = .054), driven primarily by those with severe (grade 3) VF (difference in change in FJOA 4.48, 95% CI 1.99-6.97). Moreover, there was greater change in the summary index of FJOA with increasing severity of prevalent VF (linear trend p = .005). Beyond the established morbidity and mortality associated with VFs, our study suggests that VFs may also lead to worsening spine osteoarthritis.

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NR 45
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PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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JI J. Bone Miner. Res.
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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PT J
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TI Multimorbidity and risk of falls, fractures, and joint replacements over two decades: Findings from the Hertfordshire Cohort Study
SO GERIATRICS & GERONTOLOGY INTERNATIONAL
LA English
DT Article
DE fracture; joint replacement; multimorbidity; osteoarthritis; osteoporosis

ID care
AB Aim: To examine the relationship between level of morbidity burden and long-term risk of fractures, falls, and joint replacements in the community-dwelling participants of the Hertfordshire Cohort Study. Methods: Data were analyzed from 2997 individuals (age 59-73 at baseline). Outcomes (fractures, falls, and lower limb joint replacements) were identified using ICD-10 and OPCS-4 codes from Hospital Episode Statistics data, available from baseline (1998-2004) until December 2018. Number of systems medicated (marker of morbidity level) in relation to risk of outcomes was examined using sex-stratified Cox regression. Results: Among both men and women, a greater number of systems medicated was related to increased risk of falls ($P < 0.001$) and lower limb joint replacements ($P < 0.003$). More systems medicated was only related to increased risk of fracture among women (P-values for trend of <0.001 among women and 0.186 among men). Conclusions: Higher morbidity was associated with increased risk of adverse health outcomes related to poor musculoskeletal health, but these relationships varied according to the musculoskeletal outcome studied. Intervention strategies to reduce multimorbidity among middle-aged and older people may hence reduce the burden of musculoskeletal aging.
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NR 34
TC 1
Z9 1
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WC Geriatrics & Gerontology; Gerontology
SC Geriatrics & Gerontology
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PT J
AU Cakmak, MF
Cigdem-Karacay, B
AF Cakmak, Mehmet-Fevzi
Cigdem-Karacay, Basak
TI The effect of kinesio taping on edema, pain, and functionality after total knee arthroplasty: A randomised sham-controlled double blinded clinical study
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English
DT Article
DE Total knee arthroplasty; Kinesiotape; Taping; Edema; Pain; Joint range of motion
ID oxford knee; osteoarthritis; metaanalysis
AB Background: There are current studies on kinesio taping (KT) application after total knee arthroplasty (TKA), but there is no definite consensus on its effectiveness and application method yet. This study aims to evaluates the effectiveness of KT applied added to the conservative postoperative physiotherapy program (CPPP) after TKA on postoperative edema, pain, range of motion, and functions on the early period. Materials and methods: This prospective, randomized, controlled, double-blind study was conducted in with 187 patients undergoing TKA. The patients were divided into 3 groups as kinesio taping (KTG), sham taping (STG) and control group (CG). KT lymphedema technique and epidermis, dermis, fascia

technique were applied on the 1st and 3rd days postoperatively. Extremity circumference and joint range of motion (ROM) were measured. Visual Analog Scale, Oxford Knee Scale filled. All patients were evaluated preoperatively, on the 1st day, 3rd day, and 10th day postoperatively. Results: There were 62 patients in CTG, 62 patients in STG, and 63 patients in CG. In all circumference measurements, the difference between post-op10th day (PO10D) diameter and preoperative diameter measurement was less in KTG than in CG and STG ($p < 0.001$). CG was higher than the STG in the ROM values measured at PO10D.There was no significant difference between the groups in terms of OKS values (P:0.648). CG was higher than STG in post-op 1st day VAS values (P:0.042). Conclusion: Adding KT to CPP after TKA reduces edema in the acute phase, but has no additive effect on pain, functionality, and ROM. (c) 2023 The Japanese Orthopaedic Association. Published by Elsevier B.V. All rights reserved.
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NR 21
TC 8
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PT J
AU Tekeoglu, S
AF Tekeoglu, Senem
TI Comprehensive analysis of rheumatic diseases, comorbidities, and mortality in geriatric population: Real-world data of 515 patients in a single rheumatology clinic
SO MEDICINE
LA English

DT Article
DE geriatrics; mortality; multimorbidity; rheumatology
ID 2022 american-college; classification criteria; arthritis; osteoarthritis; multimorbidity; prevalence; league; spondyloarthritis; fibromyalgia; efficacy
AB Rheumatic diseases present unique challenges in the elderly, with changes in the immune system contributing to varied clinical presentations. More individuals are now living with chronic diseases due to greater life expectancy, but there is a lack of real-world data about rheumatic diseases and comorbidities in older people. This study aimed to investigate disease types, comorbidities, treatments, and mortality in geriatric patients in comparison to non-geriatric patients at a rheumatology clinic. This retrospective observational cohort study reviewed the medical records of 2610 patients from January 2021 to January 2024 at 2 branches of a private hospital's rheumatology clinics. Demographic information and data on rheumatic diseases, noninflammatory conditions, treatments, comorbidities, and mortality were collected, and geriatric patients were compared to non-geriatric patients. Geriatric patients (n = 515) had a significantly higher prevalence of rheumatoid arthritis (50.6% vs 28.8%, P < .001), polymyalgia rheumatica (11.1% vs 0.2%, P < .001), and crystal arthritis (19.6% vs 8.8%, P < .001), with more frequent geriatric-onset cases. Osteoarthritis was also more prevalent in geriatric patients (51.2% vs 11.3%, P < .001), while fibromyalgia was more common in the non-geriatric group (15.9% vs 4.1%, P < .001). Geriatric patients experienced higher rates of comorbidities, including hypertension (72.4% vs 17.8%, P < .001), diabetes (33.6% vs 12.1%, P < .001), and osteoporosis (64.9% vs 35.4%, P < .001). These patients used more corticosteroids (74.5% vs 44%, P < .001), and conventional synthetic disease-modifying antirheumatic drugs (62.4% vs 49.4%, P < .001) but fewer biological disease-modifying antirheumatic drugs (9.2% vs 23.1%, P < .001). Mortality rates were significantly higher in geriatric patients (6% vs 0.3%), with cancer (P = .001), ischemic heart disease (P = .04), heart failure (P = .01), chronic kidney disease (P = .02), and interstitial lung disease (P = .01) being associated with increased mortality. Geriatric rheumatology should receive greater focus in future research to help address the anticipated increases in demand and to develop tailored management strategies for elderly patients with rheumatic diseases and comorbidities.
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TI The connection between aging, cellular senescence and gut microbiome alterations: A comprehensive review
SO AGING CELL
LA English
DT Review
DE aging; cellular senescence; gut microbiome; musculoskeletal diseases; senotherapeutics
ID chain fatty-acids; appendicular lean mass; intestinal stem-cells; bone-mineral density; double-blind; premature senescence; secretory phenotype; osteoarthritis; inflammation; clearance
AB The intricate interplay between cellular senescence and alterations in the gut microbiome emerges as a pivotal axis in the aging process, increasingly recognized for its contribution to systemic inflammation, physiological decline, and predisposition to age-associated diseases. Cellular senescence, characterized by a cessation of cell division in response to various stressors, induces morphological and functional changes within tissues. The complexity and heterogeneity of senescent cells, alongside the secretion of senescence-associated secretory phenotype, exacerbate the aging process through pro-inflammatory pathways and influence the microenvironment and immune system. Concurrently, aging-associated changes in gut microbiome diversity and composition contribute to dysbiosis, further exacerbating systemic inflammation and undermining the integrity of various bodily functions. This review encapsulates the burgeoning research on the reciprocal relationship between cellular senescence and gut dysbiosis, highlighting their collective impact on age-related musculoskeletal

diseases, including osteoporosis, sarcopenia, and osteoarthritis. It also explores the potential of modulating the gut microbiome and targeting cellular senescence as innovative strategies for healthy aging and mitigating the progression of aging-related conditions. By exploring targeted interventions, including the development of senotherapeutic drugs and probiotic therapies, this review aims to shed light on novel therapeutic avenues. These strategies leverage the connection between cellular senescence and gut microbiome alterations to advance aging research and development of interventions aimed at extending health span and improving the quality of life in the older population. The review "Cellular senescence and gut microbiome alterations" by J. Dong-Hyun et al. demonstrates that gut microbiome dysbiosis and cellular senescence interact bidirectionally and contribute significantly to aging. It also highlights possible ways to target this axis to restore intestine homeostasis, which promotes healthy aging and mitigates the effects of age-related musculoskeletal diseases.image
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NR 173
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U1 15
U2 42
PU WILEY
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1474-9718
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J9 AGING CELL
JI Aging Cell
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SC Cell Biology; Geriatrics & Gerontology
GA J4R2B
UT WOS:001291076200001
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PT J
AU Cheng, BL
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AF Cheng, Bolun
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TI Long-term ambient air pollution and the risk of musculoskeletal diseases: A prospective cohort study
SO JOURNAL OF HAZARDOUS MATERIALS
LA English
DT Article
DE Air pollution; Musculoskeletal diseases; Socioeconomic status; Prospective cohort

ID use regression-models; systematic analysis; national burden; global burden; nitric-oxide; osteoarthritis; osteoporosis; associations; pollutants; exposure
AB Evidence of the associations of air pollution and musculoskeletal diseases is inconsistent. This study aimed to examine the associations between air pollutants and the risk of incident musculoskeletal diseases, such as degenerative joint diseases (n = 38,850) and inflammatory arthropathies (n = 20,108). An air pollution score was constructed to assess the combined effect of PM2.5, PM2.5-10, NO2, and NOX. Cox proportional hazard model was applied to assess the relationships between air pollutants and the incidence of each musculoskeletal disease. The air pollution scores exhibited the modest association with an increased risk of osteoporosis (HR = 1.006, 95% CI: 1.002-1.011). Among the individual air pollutants, PM2.5 and PM2.5-10 exhibited the most significant effect on elevated risk of musculoskeletal diseases, such as PM2.5 on osteoporosis (HR = 1.064, 95% CI: 1.020-1.110), PM2.5-10 on inflammatory arthropathies (HR = 1.059, 95% CI: 1.037-1.081). Females were found to have a higher risk of incident musculoskeletal diseases when exposed to air pollutants. Individuals with extreme BMI or lower socioeconomic status had a higher risk of developing musculoskeletal diseases. Our findings reveal that long-term exposure to ambient air pollutants may contribute to an increased risk of musculoskeletal diseases.
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NR 71
TC 11
Z9 12
U1 3
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PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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TI Bioceramic materials in bone-implantable drug delivery systems: A review
SO JOURNAL OF DRUG DELIVERY SCIENCE AND TECHNOLOGY
LA English
DT Review
DE Bioceramic; Bone-implants; Bone drug delivery; Bone regeneration; Osteomyelitis
ID mesoporous bioactive glass; calcium-sulfate beads; in-vitro evaluation; antibacterial activity; nano-hydroxyapatite; growth-factor; phosphate; vancomycin; scaffolds; osteomyelitis
AB Since long, the applications of bioceramics in bone-implantable drug delivery has revealed a significant impact due to some favorable merits, such as excellent biocompatibility, good bioactivity, nonimmunogenicity, osteoconductivity, bone resorbability and controllable porous microstructure. To treat different disorders and diseases, such as fracture, osteoporosis, osteoarthritis, osteomyelitis, osseous cancer, etc., various drug releasing bone-implants composed of bioceramics have widely been investigated. During the last few decades, a large number of drugs (like antibiotics, anticancer agents, anti-inflammatory agents, proteins and peptides, growth factors, etc.) have been investigated for the controlled release by bone-implants made up of bioceramics. Amongst various bioceramics, calcium sulfate, calcium phosphates and bioactive glasses are being mostly used in the formula of drug releasing bone-implants. This review article describes about different bioceramic materials, which are being used to formulate drug releasing bone-implants to treat different bone diseases and disorders.
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TI Extracellular derivatives for bone metabolism
SO JOURNAL OF ADVANCED RESEARCH
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DT Review
DE Extracellular matrix; Extracellular vesicles; Bone regeneration; Osteoporosis
ID stem-cells; molecular-mechanisms; tissue regeneration; exosm; vesicles; growth; matrix; differentiation; angiogenesis; expression
AB Background: Bone metabolism can maintain the normal homeostasis and function of bone tissue. Once the bone metabolism balance is broken, it will cause osteoporosis, osteoarthritis, bone defects, bone tumors, or other bone diseases. However, such orthopedic diseases still have many limitations in clinical treatment, such as drug restrictions, drug tolerance, drug side effects, and implant rejection. Aim of review: In complex bone therapy and bone regeneration, extracellular derivatives have become a promising research focus to solve the problems of bone metabolic diseases. These derivatives, which include components such as extracellular matrix, growth factors, and extracellular vesicles, have significant therapeutic potential. It has the advantages of good biocompatibility, low immune response, and dynamic demand for bone tissue. The purpose of this review is to provide a comprehensive perspective on extracellular derivatives for bone metabolism and elucidate the intrinsic properties and versatility ofextracellular derivatives. Further discussion of them as innovative advanced orthopedic materials for improving the effectiveness of bone therapy and regeneration processes. Key scientific concepts of review: In this review, we first listed the types and functions of three extracellular derivatives. Then, we discussed the effects of extracellular derivatives of different cell sources on bone metabolism. Subsequently, we collected applications of extracellular derivatives in the treatment of bone metabolic diseases and summarized the advantages and challenges of extracellular derivatives in clinical applications. Finally, we prospected the extracellular derivatives in novel orthopedic materials and clin- ical applications. We hope that

the comprehensive understanding of extracellular derivatives in bone metabolism will provide new solutions to bone diseases. (c) 2023 Production and hosting by Elsevier B.V. on behalf of Cairo University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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TI Emerging role and function of Hippo-YAP/TAZ signaling pathway in

musculoskeletal disorders
SO STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE Hippo; YAP/TAZ; Musculoskeletal diseases; Osteoblast; Osteoclast; Cartilage; Skeletal muscle
ID myogenic regulatory factors; cell contact inhibition; mesenchymal stem-cells; skeletal-muscle; satellite cells; tgf-beta; chondrocyte differentiation; yap oncoprotein; tissue-growth; taz
AB Hippo pathway is an evolutionarily conservative key pathway that regulates organ size and tissue regeneration by regulating cell proliferation, differentiation and apoptosis. Yes-associated protein 1 (YAP)/ WW domain-containing transcription regulator 1 (TAZ) serves as a pivotal transcription factor within the Hippo signaling pathway, which undergoes negative regulation by the Hippo pathway. The expression of YAP/TAZ affects various biological processes, including differentiation of osteoblasts (OB) and osteoclasts (OC), cartilage homeostasis, skeletal muscle development, regeneration and quality maintenance. At the same time, the dysregulation of the Hippo pathway can concurrently contribute to the development of various musculoskeletal disorders, including bone tumors, osteoporosis (OP), osteoarthritis (OA), intervertebral disc degeneration (IDD), muscular dystrophy, and rhabdomyosarcoma (RMS). Therefore, targeting the Hippo pathway has emerged as a promising therapeutic strategy for the treatment of musculoskeletal disorders. The focus of this review is to elucidate the mechanisms by which the Hippo pathway maintains homeostasis in bone, cartilage, and skeletal muscle, while also providing a comprehensive summary of the pivotal role played by core components of this pathway in musculoskeletal diseases. The efficacy and feasibility of Hippo pathway-related drugs for targeted therapy of musculoskeletal diseases are also discussed in our study. These endeavors offer novel insights into the application of Hippo signaling in musculoskeletal disorders, providing effective therapeutic targets and potential drug candidates for treating such conditions.
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TI Ligusticum chuanxiong Hort.: a review of its phytochemistry, pharmacology, and toxicology
SO JOURNAL OF PHARMACY AND PHARMACOLOGY

LA English
DT Review
DE Ligusticum chuanxiong Hort; chemistry; pharmacology; toxicology; review
ID nf-kappa-b; ferulic acid; essential oil; phthalide derivatives; chemical ingredients; parkinsons-disease; rhizoma chuanxiong; receptor activator; cerebral-ischemia; tetramethylpyrazine
AB Background Conioselinum anthriscoides (H. Boissieu) Pimenov & Kljuykov, also known as Ligusticum chuanxiong Hort. is a perennial Umbelliferae herb, whose dried rhizome commonly called Chuanxiong Rhizoma. Chuanxiong Rhizoma is widely used in TCM, especially for cardiocerebrovascular and gynecological diseases. However, these studies are scattered and there is no review that can centralize the results of these studies. The authors summarized this review by collecting research results on the chemical, pharmacological, and toxicological of Chuanxiong Rhizoma published in various publications over the past 20 years.Aims The purpose of this review is to summarize the current experimental studies on Chuanxiong Rhizoma and explore its mechanism of action.Methods Web of Science, PubMed, CBM, CNKI, Medline, Embase, Elsevier, Springer, Wiley Online Library, Scholar, and other databases were searched, and nearly one hundred experimental studies were collected to summarize this review.Results and Discussion Chuanxiong Rhizoma is composed of essential oil, terpenes, alkaloids, polysaccharide, organic acids, ceramides, and cerebrosides. It has the functions of promoting blood circulation, removing blood stasis, antibacterial, antiviral, and calming the mind to sleep. Now it can be used to treat cardiocerebrovascular and gynecological diseases, neurodegenerative disease, psoriasis, rectal cancer, osteoporosis, and osteoarthritis.Conclusions In the past 20 years, a large number of research data have confirmed that Chuanxiong Rhizoma contains rich effective metabolites, has huge medicinal potential, and has a wide range of effective treatments.
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TI Individuals with Knee Osteoarthritis and Osteoporosis Represent a Distinctive Subgroup Whose Symptoms Originate from Differences in Subchondral Bone

Rather than Cartilage
SO CALCIFIED TISSUE INTERNATIONAL
LA English
DT Article
DE Osteoporosis; Knee osteoarthritis; Bone marrow lesion; Cartilage; Symptoms
ID mineral density; trauma fractures; marrow lesions; women; progression; prevalence; protects; healthy; obesity; damage
AB To explore the hypothesis that knee osteoarthritis patients with osteoporosis represent a sub-cohort with different disease characteristics and origin of symptoms. Men and women in the Osteoarthritis Initiative (OAI) at visit 5 (36 months) were examined for osteoporosis (N = 1483) using DXA (T-score at femoral neck <= -2.5), use of bisphosphonates, or having experienced a fracture. Those with and without osteoporosis were compared by subchondral bone quality, bone marrow lesion (BML) properties, and cartilage thickness from MRI, with general linear modeling. Relationships between symptoms (12 months later) and each of cartilage or subchondral bone features were examined conditional on osteoporosis status. Overall, 15.2% of 1246 participants (825 women, 658 men, mean age: 64.4 +/- 8.9yrs, BMI: 30.1 +/- 4.9 kg/m(2)) with knee OA likely had osteoporosis and showed lower medial and lateral subchondral bone density, smaller trabecular number and larger trabecular separation (all $p < 0.01$) compared to those without. Cartilage thickness appeared lower in this group ($p = 0.04$) but only by a small amount. Knee symptoms correlated with both BML properties and cartilage thickness; the latter but not the former being moderated by osteoporosis status. Those with osteoporosis showed no relationship between cartilage and knee symptoms, but demonstrated bone-related associations with symptoms. Osteoporosis affects the pattern of subchondral bone and cartilage properties in individuals with knee osteoarthritis. Knee symptoms in this subgroup likely originates in bone instead of cartilage. Osteoporosis screening may help identify knee osteoarthritis patients at further risk of subchondral bone damage leading to pain.
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TI Inflammatory diseases causing joint and bone destruction: rheumatoid arthritis and hemophilic arthropathy
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Review
DE Rheumatoid arthritis; Hemophilia; Hemophilic arthropathy; Joint destruction
ID single-nucleotide polymorphism; tnf-alpha; matrix metalloproteinases; inhibitor development; synovial-fluids; damage; cells; il-6; il-1-beta; target
AB Various diseases and conditions cause joint disorders. Osteoarthritis (OA) is characterized by the degeneration of articular cartilage, synovitis, and anabolic changes in surrounding bone tissues. In contrast, rheumatoid arthritis (RA) and hemophilic arthropathy (HA) display marked destruction of bone tissues caused by synovitis. RA is a representative autoimmune disease. The primary tissue of RA pathogenesis is the synovial membrane and involves various immune cells that produce catabolic cytokines and enzymes. Hemophilia is a genetic disorder caused by a deficiency in blood clotting factors. Recurrent intra-articular bleeding leads to chronic synovitis through excessive iron deposition and results in the destruction of affected joints. Although the triggers for these two joint diseases are completely different, many cytokines and enzymes are common in the pathogenesis of both RA and HA. This review focuses on the similarities between joint and bone destruction in RA and HA. The insights may be useful in developing better treatments for hemophilia patients with arthropathy and osteoporosis by leveraging advanced therapeutics for RA.
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PT J
AU Hillman, SJ
Dodds, RM
Granic, A
Witham, MD
Sayer, AA
Cooper, R
AF Hillman, Susan J.
Dodds, Richard M.

Granic, Antoneta
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Sayer, Avan A.
Cooper, Rachel
TI Identifying combinations of long-term conditions associated with sarcopenia: a cross-sectional decision tree analysis in the UK Biobank study
SO BMJ OPEN
LA English
DT Article
DE aging; epidemiology; chronic disease; machine learning
ID grip strength; health; multimorbidity; mobility; life
AB Objectives This study aims to determine whether machine learning can identify specific combinations of long-term conditions (LTC) associated with increased sarcopenia risk and hence address an important evidence gap-people with multiple LTC (MLTC) have increased risk of sarcopenia but it has not yet been established whether this is driven by specific combinations of LTC. Design Decision trees were used to identify combinations of LTC associated with increased sarcopenia risk. Participants were classified as being at risk of sarcopenia based on maximum grip strength of <32 kg for men and <19 kg for women. The combinations identified were triangulated with logistic regression. Setting UK Biobank. Participants UK Biobank participants with MLTC (two or more LTC) at baseline. Results Of 140 001 participants with MLTC (55.3% women, median age 61 years), 21.0% were at risk of sarcopenia. Decision trees identified several LTC combinations associated with an increased risk of sarcopenia. These included drug/alcohol misuse and osteoarthritis, and connective tissue disease and osteoporosis in men, which showed the relative excess risk of interaction of 3.91 (95% CI 1.71 to 7.51) and 2.27 (95% CI 0.02 to 5.91), respectively, in age-adjusted models. Conclusion Knowledge of LTC combinations associated with increased sarcopenia risk could aid the identification of individuals for targeted interventions, recruitment of participants to sarcopenia studies and contribute to the understanding of the aetiology of sarcopenia.
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AU Wu, Q
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AF Wu, Qun
Yao, Xianbao
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TI Platelet-rich plasma ameliorates cartilage degradation in rat models of osteoarthritis via the OPG/RANKL/RANK system
SO FOLIA HISTOCHEMICA ET CYTOBIOLOGICA
LA English
DT Article
DE platelet-rich plasma; osteoarthritis; cartilage degradation; inflammation; extracellular matrix; OPG/RANKL/RANK system
ID extracellular-matrix; articular-cartilage; ii collagen; suppresses degradation; human chondrocytes; tissue; cells; opg; osteoporosis; inflammation
AB Introduction. Osteoarthritis (OA) is one of the most common degenerative joint diseases in the elderly, which is featured by the degradation of articular cartilage. Recently, platelet-rich plasma (PRP) injection into the affected joint has become one biological therapy for OA treatment. The OPG/RANKL/RANK signalling has been reported to mediate OA progression. Our study aimed to confirm whether PRP injection retards OA development through the regulation of the OPG/RANKL/RANK system. Material and methods. The OA rat models were induced by medial menisci resection combined with anterior cruciate ligament transection. Four weeks after surgery, OA-induced rats received intra-articular injection with 50 mu L mu L PRP once a week for 6 weeks. Rats were euthanised one week after the 6 th injection. Rat knee joints were subjected to histopathological examination by haematoxylin-eosin (H&E) and safranin O staining. Osteoprotegerin (OPG), receptor activator of nuclear factor kappa B (RANK), and RANK ligand (RANKL) in the articular cartilage of rats were tested through immunofluorescence staining and western blotting. Serum interleukin-1(3 (IL-1(3) and interleukin-6 (IL-6) levels were measured by enzyme-linked

immunosorbent assay (ELISA). Matrix metalloproteinase-13 (MMP-13), aggrecan, collagen alpha, IL-1(3, IL-6, tumour necrosis factor-alpha (TNF-alpha), and nuclear factor kappa-B (NF-kappa B) mRNA and protein expression in rat articular cartilage were examined by real-time quantitative polymerase chain reaction (RT-qPCR) and western blotting, respectively. Results. Intra-articular injections of PRP significantly improved the structural integrity of the articular cartilage and enhanced the synthesis of glycosaminoglycans. PRP reduced MMP-13 protein level but increased aggrecan and collagen alpha protein levels in articular cartilage of OA rats. OA-induced increase in serum IL-1(3, IL-6, and TNF-alpha concentrations as well as increased MMP-13, and decreased collagen II mRNA levels were reversed by the administration of PRP. OA increased IL-1(3, TNF-alpha, and NF-kappa B mRNA expression in rat articular cartilage whereas PRP administration ameliorated these changes. Moreover, in the articular tissue of OA-induced rats the increased OPG protein level was further elevated by PRP injections whereas the protein level of RANK did not change. The increase in the protein level of RANKL in OA-induced articular tissue was offset by PRP administration. PRP elevated OPG mRNA expression and the OPG/RANKL mRNA ratio, but reduced RANKL mRNA expression and the RANKL/RANK mRNA ratio in the articular tissue of OA-induced rats. Conclusions. PRP mitigates cartilage degradation and inflammation in experimental knee OA by regulating the OPG/RANKL/RANK signalling system.
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TI Ferroptosis and its implications in bone-related diseases
SO PEERJ
LA English
DT Article
DE Osteoporosis; Osteoarthritis; Osteosarcoma; Ferroptosis
ID cell-death; diabetes-mellitus; osteoporotic fractures; osteosarcoma cells;

activation; biology; proliferation; progression; mechanisms; inhibition
AB Ferroptosis, a recently recognized form of regulated cell death (RCD) characterized by iron-dependent lipid peroxide accumulation, has emerged as a noteworthy regulator in various bone-related diseases, including osteoporosis (OP), osteoarthritis (OA), and osteosarcoma (OS). OS primarily afflicts the elderly, rendering them susceptible to fractures due to increased bone fragility. OA represents the most prevalent arthritis in the world, often observed in the aging population. OS predominantly manifests during adolescence, exhibiting an aggressive nature and bearing a significantly unfavorable prognosis. In this review article, we present an overview of the characteristics and mechanism of ferroptosis and its involvement in bone-related diseases, with a particular focus on OP, OA, and OS. Furthermore, we summarize chemical compounds or biological factors that impact bone-related diseases by regulating ferroptosis. Through an in-depth exploration of ferroptosis based on current research fi ndings, this review provides promising insights for potential therapeutic approaches to effectively manage and mitigate the impact of these bone-related pathological conditions.
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TI Protective effects of polydatin against bone and joint disorders: the in vitro and in vivo evidence so far
SO NUTRITION RESEARCH REVIEWS
LA English
DT Review
DE Polydatin; Osteoporosis; Osteosarcoma; Osteoarthritis; Rheumatic arthritis
ID osteosarcoma treatment; rheumatoid-arthritis; trans-piceid; resveratrol; apoptosis; osteoarthritis; pathway; differentiation; metabolism; disease
AB Polydatin is an active polyphenol displaying multifaceted benefits. Recently, growing studies have noticed its potential therapeutic effects on bone and joint disorders (BJDs). Therefore, this article reviews recent in vivo and in vitro progress on the protective role of polydatin against BJDs. An insight into the underlying mechanisms is also presented. It was found that polydatin could promote osteogenesis in vitro, and symptom improvements have been disclosed with animal models of osteoporosis, osteosarcoma, osteoarthritis and rheumatic arthritis. These beneficial effects obtained in laboratory could be mainly attributed

to the bone metabolism-regulating, anti-inflammatory, antioxidative, apoptosis-regulating and autophagy-regulating functions of polydatin. However, studies on human subjects with BJDs that can lead to early identification of the clinical efficacy and adverse effects of polydatin have not been reported yet. Accordingly, this review serves as a starting point for pursuing clinical trials. Additionally, future emphasis should also be devoted to the low bioavailability and prompt metabolism nature of polydatin. In summary, well-designed clinical trials of polydatin in patients with BJD are in demand, and its pharmacokinetic nature must be taken into account.
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TI Prevalence of cardiovascular and other selected diseases among Greenlanders with and without type 2 diabetes
SO INTERNATIONAL JOURNAL OF CIRCUMPOLAR HEALTH
LA English
DT Article
DE Diabetes; complications; Inuit; co-morbidities; Greenland
ID atrial-fibrillation; risk-factors; 1st nations; mellitus; population; care; osteoarthritis; association; psoriasis; stress
AB This study aims to estimate the prevalence of cardiovascular disease, kidney disease, and other selected diseases including hypertension, atrial fibrillation, asthma, chronic obstructive lung disease, osteoarthritis, osteoporosis, psoriasis and depression among Greenlanders living in Nuuk with and without type 2 diabetes (T2D). The study was designed as a cross-sectional case-control study based on data from the electronic medical record (EMR) in Greenland. Persons with a registered T2D diagnosis in EMR and residence in Nuuk (N = 435) were included. The prevalence of cardiovascular disease was 17.9% among persons with T2D and significantly higher compared to the control group (10.1%). In addition, our results showed a significantly higher prevalence of ischaemic heart disease, hypertension, heart failure, atrial fibrillation, osteoarthritis and psoriasis among persons with T2D compared to the control group.Our study found a higher prevalence in five out of 10 selected diseases in regularly followed persons with T2D in Nuuk compared to unselected controls. This enlightens the importance of a broad multifaceted approach in combination of changing primary health care to focus on early detection of controllable risk factors and chronic conditions care in Artic Greenland.
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TI KLF transcription factors in bone diseases
SO JOURNAL OF CELLULAR AND MOLECULAR MEDICINE
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DT Review
DE bone disease; Kruppel-like factors; osteoarthritis; osteoporosis; osteosarcoma; rheumatoid arthritis
ID kruppel-like factor; cancer stem-cells; musculoskeletal disorders; global burden; beta-catenin; inflammatory injury; articular-cartilage; breast-cancer; self-renewal;

cross-talk
AB Kruppel-like factors (KLFs) are crucial in the development of bone disease. They are a family of zinc finger transcription factors that are unusual in containing three highly conserved zinc finger structural domains interacting with DNA. It has been discovered that it engages in various cell functions, including proliferation, apoptosis, autophagy, stemness, invasion and migration, and is crucial for the development of human tissues. In recent years, the role of KLFs in bone physiology and pathology has received adequate attention. In addition to regulating the normal growth and development of the musculoskeletal system, KLFs participate in the pathological process of the bones and joints and are intimately linked to several skeletal illnesses, such as osteoarthritis (OA), rheumatoid arthritis (RA), osteoporosis (OP) and osteosarcoma (OS). Consequently, targeting KLFs has emerged as a promising therapeutic approach for an array of bone disorders. In this review, we summarize the current literature on the importance of KLFs in the emergence and regulation of bone illnesses, with a particular emphasis on the pertinent mechanisms by which KLFs regulate skeletal diseases. We also discuss the need for KLFs-based medication-targeted treatment. These endeavours offer new perspectives on the use of KLFs in bone disorders and provide prognostic biomarkers, therapeutic targets and possible drug candidates for bone diseases.
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TI Total ankle arthroplasty improves discrete and continuous stance phase gait symmetry
SO GAIT & POSTURE
LA English
DT Article
DE Total Ankle Arthroplasty; Ankle Arthritis; Symmetry; Normalized Symmetry Index; Statistical Parameter Mapping
ID replacement; arthrodesis; osteoarthritis; mechanics; biomechanics; arthritis; outcm; knee
AB Background: Total ankle arthroplasty (TAA) is used to treat symptomatic end-stage ankle arthritis (AA). However, little is known about TAA's effects on gait symmetry. Research question: Determine if symmetry changes from before surgery through two years following TAA utilizing the normalized symmetry index (NSI) and statistical parametric mapping (SPM). Methods: 141 patients with end-stage unilateral AA were evaluated from a previously collected prospective database, where each participant was tested within two weeks of surgery (Pre-Op), one year and two years following TAA. Walking speed, hip extension angle and moment, hip flexion angle, ankle plantarflexion angle and moment, ankle dorsiflexion angle, weight acceptance (GRF1), and propulsive (GRF2) vertical ground reaction forces were calculated for each limb. Gait symmetry was assessed using the NSI. A linear

mixed effects model with a single response for each gait symmetry variable was used to examine the fixed effect of follow-up time (Pre-Op, Post-1 yr, Post-2 yr) and the random effect of participant with gait speed as a covariate in the model. A one-dimensional repeated measures analysis of variance (ANOVA) statistical parameter mapping (SPM) was completed to examine differences in the time-series NSI to determine regions of significant differences between follow-up times. Results: Relative to Pre-Op values, GRF1, and GRF2 showed increased symmetry for discrete metrics and the timeseries NSI across sessions. Hip extension moment had the largest symmetry improvement. Ankle plantarflexion angle was different between Pre-Op and Post-2 yr ($p=0.010$); and plantarflexion moment was different between Pre- Op and each post-operative session ($p<0.001$). The time-series Ankle Angle NSI was greater during the early stance phase in the Pre-Op session compared to Post-2 yr. Significance: Symmetry across most of the stance phase improved following TAA indicating that TAA successfully improves gait symmetry and future work should determine if these improvements restore symmetry to levels equivalent with health age-match controls.
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WC Neurosciences; Orthopedics; Sport Sciences
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AU Wang, XL
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TI Association between serum iron status and the risk of five bone and joint-related diseases: a Mendelian randomization analysis
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Article
DE bone and joint-related diseases; Mendelian randomization; iron status; genome wide association studies; genetics
ID rheumatoid-arthritis; metabolism

AB Background According to reports, iron status has been associated with the risk of bone and joint-related diseases. However, the exact role of iron status in the development of these conditions remains uncertain.Method We obtained genetic data on iron status, specifically serum iron, ferritin, transferrin saturation (TSAT), and transferrin, as well as data on five common bone and joint-related diseases (osteoarthritis, osteoporosis, rheumatoid arthritis [RA], ankylosing spondylitis [AS], and gout) from independent genome-wide association studies involving individuals of European ancestry. Our primary approach for causal estimation utilized the inverse variance weighted (IVW) method. To ensure the reliability of our findings, we applied complementary sensitivity analysis and conducted reverse causal analysis.Result Using the IVW method, we revealed a positive causal relationship between ferritin levels and the risk of osteoarthritis (OR [95% CI], 1.0114 [1.0021-1.0207]). Besides, we identified a protective causal relationship between serum iron levels and TSAT levels in the risk of RA (OR [95% CI] values of serum iron and TSAT were 0.9987 [0.9973-0.9999] and 0.9977 [0.9966-0.9987], respectively). Furthermore, we found a positive causal relationship between serum iron levels and the risk of AS (OR [95% CI], 1.0015 [1.0005-1.0026]). Regarding gout, both serum iron and TSAT showed a positive causal relationship (OR [95% CI] values of 1.3357 [1.0915-1.6345] and 1.2316 [1.0666-1.4221] for serum iron and TSAT, respectively), while transferrin exhibited a protective causal relationship (OR [95% CI], 0.8563 [0.7802-0.9399]). Additionally, our reverse causal analysis revealed a negative correlation between RA and ferritin and TSAT levels (OR [95% CI] values of serum iron and TSAT were 0.0407 [0.0034-0.4814] and 0.0049 [0.0002-0.1454], respectively), along with a positive correlation with transferrin (OR [95% CI], 853.7592 [20.7108-35194.4325]). To ensure the validity of our findings, we replicated the results through sensitivity analysis during the validation process.Conclusion Our study demonstrated a significant correlation between iron status and bone and joint-related diseases.
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AF Silva, Julia Tavares e
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TI The Impact of Long Noncoding RNAs in Tissue Regeneration and Senescence
SO CELLS
LA English
DT Review
DE aging; cellular senescence; long noncoding RNAs; upregulation; downregulation; neurodegeneration; cardiovascular disease
ID cellular senescence; cells
AB Overcoming senescence with tissue engineering has a promising impact on multiple diseases. Here, we provide an overview of recent studies in which cellular senescence was inhibited through the up/downregulation of specific lncRNAs. This approach prevented senescence in the bones, joints, nervous system, heart, and

blood vessels, with a potential impact on regeneration and the prevention of osteoarthritis and osteoporosis, as well as neurodegenerative and cardiovascular diseases. Senescence of the skin and liver could also be prevented through the regulation of cellular levels of specific lncRNAs, resulting in the rejuvenation of cells from these organs and their potential protection from disease. From these exciting achievements, which support tissue regeneration and are not restricted to stem cells, we propose lncRNA regulation through RNA or gene therapies as a prospective preventive and therapeutic approach against aging and multiple aging-related diseases.
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WC Cell Biology
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TI IRON OXIDE NANOPARTICLES FOR DIAGNOSING AND TREATING DEGENERATIVE ORTHOPAEDIC DISEASES: A REVIEW
SO EUROPEAN CELLS & MATERIALS
LA English
DT Review
DE Iron oxide nanoparticles; magnetism; molecular diagnosis; orthopaedic diseases
ID mesenchymal stem-cells; magnetic nanoparticles; articular-cartilage; toxicity; tracking; hydroxyapatite; particles; contrast; fracture; delivery
AB The prevalence of degenerative orthopaedic diseases, such as osteoarthritis, osteoporosis, and intervertebral disc disease, has increased due to the increasing prevalence and unsatisfactory therapeutic methods. Recently, different types of bioactive nanomaterials, such as iron oxide nanoparticles (IONPs), have raised much concern due to their ability to positively regulate the bone remodelling balance. Due to their magnetic characteristics, IONPs have been applied in magnetic resonance imaging in the clinic, but their ability to treat degenerative orthopaedic diseases has recently been shown both in vitro and in vivo. However, a comprehensive review of the potential utilization of IONPs in the orthopaedic field is lacking. Here, we summarize previous works in this review and discuss future research directions in this field.
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DE lifestyle-related disease; advanced glycation end-products; urine; biomarker;

membrane chromatography; slot blot; Takata's lysis buffer; electrospray ionization-mass spectrometry; matrix-assisted laser desorption/ionization-mass spectrometry
ID human serum-albumin; cross-links; maillard reaction; extracellular-matrix; protein glycation; pentosidine; methylglyoxal; saliva; osteoarthritis; glucosepane
AB Proteins, saccharides, and low molecular organic compounds in the blood, urine, and saliva could potentially serve as biomarkers for diseases related to diet, lifestyle, and the use of illegal drugs. Lifestyle-related diseases (LSRDs) such as diabetes mellitus (DM), non-alcoholic steatohepatitis, cardiovascular disease, hypertension, kidney disease, and osteoporosis could develop into life-threatening conditions. Therefore, there is an urgent need to develop biomarkers for their early diagnosis. Advanced glycation end-products (AGEs) are associated with LSRDs and may induce/promote LSRDs. The presence of AGEs in body fluids could represent a biomarker of LSRDs. Urine samples could potentially be used for detecting AGEs, as urine collection is convenient and non-invasive. However, the detection and identification of AGE-modified proteins in the urine could be challenging, as their concentrations in the urine might be extremely low. To address this issue, we propose a new analytical approach. This strategy employs a method previously introduced by us, which combines slot blotting, our unique lysis buffer named Takata's lysis buffer, and a polyvinylidene difluoride membrane, in conjunction with electrospray ionization-mass spectrometry (ESI)/matrix-assisted laser desorption/ionization-mass spectrometry (MALDI-MS). This novel strategy could be used to detect AGE-modified proteins, AGE-modified peptides, and free-type AGEs in urine samples.
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TI Effects and Mechanisms of Polyunsaturated Fatty Acids on Age-Related Musculoskeletal Diseases: Sarcopenia, Osteoporosis, and Osteoarthritis-A Narrative Review
SO NUTRIENTS

LA English
DT Review
DE polyunsaturated fatty acids; PUFAs; musculoskeletal disease; sarcopenia; osteoporosis; osteoarthritis
ID knee osteoarthritis; bone-resorption; n-3; omega-3-fatty-acids; supplementation; consensus; health; mass; differentiation; interleukin-6
AB Background: The process of the globally aging population has been accelerating, leading to an increasing social burden. As people age, the musculoskeletal system will gradually go through a series of degenerative and loss of function and eventually develop age-related musculoskeletal diseases, like sarcopenia, osteoporosis, and osteoarthritis. On the other hand, several studies have shown that polyunsaturated fatty acids (PUFAs) possess various important physiological functions on the health of muscles, bones, and joints. Objective: This narrative review paper provides a summary of the literature about the effects and mechanisms of PUFAs on age-related musculoskeletal diseases for the prevention and management of these diseases. Methods: Web of Science, PubMed, Science Direct, and Scopus databases have been searched to select the relevant literature on epidemiological, cellular, and animal experiments and clinical evidence in recent decades with keywords "polyunsaturated fatty acids", "PUFAs", "omega-3", "omega-6", "musculoskeletal diseases", "sarcopenia", "osteoporosis", "osteoarthritis", and so on. Results: PUFAs could prevent and treat age-related musculoskeletal diseases (sarcopenia, osteoporosis, and osteoarthritis) by reducing oxidative stress and inflammation and controlling the growth, differentiation, apoptosis, and autophagy of cells. This review paper provides comprehensive evidence of PUFAs on age-related musculoskeletal diseases, which will be helpful for exploitation into functional foods and drugs for their prevention and treatment. Conclusions: PUFAs could play an important role in the prevention and treatment of sarcopenia, osteoporosis, and osteoarthritis.
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TI The essential roles of m6A modification in osteogenesis and common bone diseases
SO GENES & DISEASES
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DE Bone diseases; Regulatory role; Stem cells; m6A modification; Osteogenesis
ID mesenchymal stem-cells; messenger-rna; nuclear-rna; demethylase alkbh5; m(6)a methylation; gene-regulation; n6-methyladenosine; methyltransferase; recognition; adipocytes
AB N6-methyladenosine (m6A) is the most prevalent modification in the eukaryotic transcriptome and has a wide range of functions in coding and noncoding RNAs. It affects the fate of the modified RNA, including its stability, splicing, and translation, and plays an important role in post-transcriptional regulation. Bones play a key role in supporting and protecting muscles and other organs, facilitating the movement of the organism, ensuring blood production, etc. Bone diseases such as osteoarthritis, osteoporosis, and bone tumors are serious public health problems. The processes of bone development and osteogenic differentiation require the precise regulation of gene expression through epigenetic mechanisms including histone, DNA, and RNA modifications. As a reversible dynamic epigenetic mark, m6A modifications affect nearly every important biological process, cellular component, and molecular function, including skeletal development and homeostasis. In recent years, studies have shown that m6A modification is involved in osteogenesis and bone-related diseases. In this review, we summarized the

proteins involved in RNA m6A modification and the latest progress in elucidating the regulatory role of m6A modification in bone formation and stem cell directional differentiation. We also discussed the pathological roles and potential molecular mechanisms of m6A modification in bone-related diseases like osteoporosis and osteosarcoma and suggested potential areas for new strategies that could be used to prevent or treat bone defects and bone diseases. & COPY; 2023 The Authors. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co., Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons. org/licenses/by-nc-nd/4.0/).
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TI Recent advances of m6A methylation in skeletal system disease
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DT Review
DE m6A modification; Osteosarcoma; Osteoporosis; Rheumatoid arthritis; Osteoarthritis
ID messenger-rna; promotes proliferation; reader ythdf2; self-renewal; nuclear-rna; osteosarcoma; cells; progression; n6-methyladenosine; osteoarthritis
AB Skeletal system disease (SSD) is defined as a class of chronic disorders of skeletal system with poor prognosis and causes heavy economic burden. m6A, methylation at the N6 position of adenosine in RNA, is a reversible and dynamic modification in posttranscriptional mRNA. Evidences suggest that m6A modifications play a crucial role in regulating biological processes of all kinds of diseases, such as malignancy. Recently studies have revealed that as the most abundant epigentic modification, m6A is involved in the progression of SSD. However, the function of m6A modification in SSD is not fully illustrated. Therefore, make clear the relationship between m6A modification and SSD pathogenesis might provide novel sights for prevention and targeted treatment of SSD. This article will summarize the recent advances of m6A regulation in the biological processes of SSD, including osteoporosis, osteosarcoma, rheumatoid arthritis and osteoarthritis, and discuss the potential clinical value, research challenge and future prospect of m6A modification in SSD.
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TI The effect of coffee consumption on three main bone disorders: a Mendelian randomization trial
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LA English
DT Article
DE Osteoarthritis; Osteoportic fracture; Rheumatoid arthritis; Coffee consumption; Mendelian randomization
ID acid phenethyl ester; mineral density; caffeine consumption; risk-factors; body-weight; green tea; growth; osteoporosis; health; osteoarthritis
AB IntroductionDespite a large number of observational studies examining the

effect of coffee consumption(CC) on bone disorders(BDs), particularly, osteoarthritis(OA), osteoportic fracture(OF), and rheumatoid arthritis(RA), the conclusions are highly controversial. Thus, it is essential to examine the causal association between CC and BDs.Materials and methodsMendelian randomization (MR) analysis was performed to assess the causal influence of CC on OF, RA, and OA. The main endpoint was the odds ratio (OR) of the inverse variance weighted (IVW) approach. In addition, the weighted median (WM), MR-Egger regressions, MR-pleiotropy residual sum and outlier (MR-PRESSO) and multivariable MR (MVMR) were included in sensitivity analyses. Furthermore, the function of causal SNPs was evaluated by gene ontology (GO) analysis, Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis, and protein-protein interaction networks.ResultsPrimary MR analysis based on the IVW method suggested that changes in CC alter risk of OF (OR = 1.383, 95%CI 1.079-1.853, P = 0.039), RA(OR: 1.623, 95%CI 1.042-2.527, P = 0.032) and HOA (hip osteoarthritis, OR = 1.536, 95% CI 1.044-2.259, P = 0.021). However, these causal relationships were not robust in sensitivity analyses. In contrast, there is a positive causal relationship between increased CC and the risk of KOA (knee osteoarthritis, OR: 2.094, 95%CI: 1.592-2.754, P = 1.41 x 10-7), as evidenced by the IVW using random effect. A similar effect size was observed across all MR sensitivity analyses, with no evidence of horizontal pleiotropy.ConclusionBased on our MR analysis, increased CC was causally linked to an increase in the risk of KOA. Genetic predictions suggested that CC reduction may have benefits for bone health.
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TI Proteomics in orthopedic research: Recent studies and their translational implications
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Review
DE biomarker; bone; cartilage; orthopedics; proteomics
ID spinal-cord-injury; inhibition; expression; apoptosis; cells; atp
AB Proteomics is a growing field that offers insights into various aspects of disease processes and therapy responses. Within the field of orthopedics, there are a variety of diseases that have a poor prognosis due to a lack of targeted curative therapy or disease modifying therapy. Other diseases have been difficult to manage in part due to lack of clinical biomarkers that offer meaningful insight into disease progression or severity. As an emerging technology, proteomics has been increasingly applied in studying bone biology and an assortment of orthopedics related diseases, such as osteoarthritis, osteosarcoma and bone tumors, osteoporosis, traumatic bone injury, spinal cord injury, hip and knee arthroplasty,

and fragile healing. These efforts range from mechanistic studies for elucidating novel insights in tissue activity and metabolism to identification of candidate biomarkers for diagnosis, prognosis, and targeted treatment. The knowledge gained from these proteomic and functional studies has provided unique perspectives in studying orthopedic diseases. In this review, we seek to report on the current state of the proteomic study in the field of orthopedics, overview the advances in clinically applicable discoveries, and discuss the opportunities that may guide us for future research.
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TI Pyrocarbon radial head arthroplasty offers satisfactory clinical and radiological outcomes with low revision rate: A systematic review
SO ORTHOPAEDICS & TRAUMATOLOGY-SURGERY & RESEARCH
LA English
DT Review
DE Pyrocarbon; Pyrolytic carbon; Radial head arthroplasty; MoPyC; Revisions
ID replacement; prosthesis; fractures; stability
AB Introduction: Pyrocarbon promises to be an optimal material choice for radial head arthroplasty (RHA) due to an elastic modulus comparable to the radial diaphysis and thus providing higher biocompatibility. Primary objective was to determine the complications and revision rates related to the usage of these prostheses. The secondary objective was to assess the clinical and radiological outcomes of Pyrocarbon RHAs. Hypothesis: Pyrocarbon RHAs have good clinical and radiological outcomes with low complications and revisions. Methods: Ovid

MEDLINE and Embase databases were used to search for studies on outcomes and complications of the RHAs using Pyrocarbon radial head prostheses. The systematic review was designed in accordance with the PRISMA guidelines and included studies were appraised using the MINORS tool. Complications and RHA revision rates were assessed. Functional outcomes were reviewed using PROMs (like MEPI, DASH and BMS), post -op range of motion (using goniometer) and grip strength (using the dynamometer). Postoperative radiological outcomes like peri-prosthetic lucency, radial neck osteolysis, radio-capitellar congruence, capitellar erosion, overstuffing/understuffing and osteoarthritis were reported using radiographs. Results: A total of 12 studies cumulatively reporting 353 patients who underwent Pyrocarbon RHAs were included in the review. The mean age of patients across the studies ranged from 47 to 54 years of which 50.5% were males. The majority of radial head replacements were done for acute trauma (87.5%) with the remainder done for arthritis (1.7%) and trauma sequelae (10.8%). Mean follow-up period in the selected studies ranged from 18 to 110 months with minimum follow-up across all studies being 12 months. Modular Pyrocarbon (MoPyC, TornierTM) was the implant of choice in ten studies while two studies used the Ascension Pyrocarbon radial head (Ascension OrthopaedicsTM). Ten studies demonstrated mean MEPI ranging from 75.5 to 96. Mean extension deficit ranged from 6 to 19 degrees, mean flexion from 120 to 140 degrees, mean pronation from 71 to 87 degrees and mean supination from 63 to 85 degrees. Relative grip strength ranged from 69 to 96% of the contralateral limb. Revisions due to implant -related reasons (intra-prosthetic dissociation, prosthetic fracture, peri-prosthetic loosening, radio-capitellar subluxation and understuffed/overstuffed elbow) was 6.8% (24/353). Radial stress shielding and peri-prosthetic lucency was reported in 10 to 100% of patients across different studies but symptomatic implant loosening leading to revision remained rare (2%, 7/353). Radio-capitellar congruence was reported in 81% to 100% cases while capitellar erosion ranged from 0% to 89%. Pyrocarbon implants specific complications included head -neck intra-prosthetic decoupling (1.1%) and pyrocarbon head fractures (0.9%). In total, 5.7% cases underwent re -surgery due to non-RHA related reasons. Discussion: The pyrocarbon RHA shows good functional outcome, range of motion and low revision rates. This aligns with the working hypothesis of this review. However, pyrocarbon radial head implants have implant -specific complications like pyrocarbon radial head fractures and intra-prosthetic decoupling between stem and head. Despite promising in vitro biomechanical properties, capitellar wear is still a common finding with pyrocarbon RHAs. Despite these factors, pyrocarbon radial head implants are a viable option for radial head arthroplasty. Level of evidence: II; Systematic review. (c) 2023 Published by Elsevier Masson SAS.

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TI Preoperative Education Prior to Hip or Knee Arthroplasty Is Associated With Home Discharge but Not Reduced Length of Stay
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DT Article
DE hip; knee; preoperative education; physical therapy; osteoarthritis; arthroplasty; length of stay; discharge disposition
ID outcm; care
AB Background:Increasing numbers of patients are undergoing total joint arthroplasty as a treatment for osteoarthritis, which can be an anxiety-provoking experience. Setting expectations through a preoperative physical therapy (pre-op PT) session can alleviate some of these stressors, potentially decrease hospital length of stay (LOS), and promote home discharge.Purpose:We sought to determine whether attending a pre-op PT session is associated with decreased hospital LOS and home discharge in total hip arthroplasty (THA) and total knee arthroplasty (TKA) patients.Methods:A retrospective cohort study was performed of 20,822 patients who underwent THA or TKA between January 2020 and December 2023. Pre-op PT attendance and covariates, including patient demographics and clinical data, were collected and analyzed for association with LOS and discharge disposition.Results:Unadjusted univariate analysis revealed that THA and TKA patients who received pre-op PT had a significantly lower average LOS and were more likely to be discharged home. Our multivariate regression model showed that pre-op PT was not significantly associated with LOS in both groups but was significantly associated with home discharge among THA patients.Conclusions:Our retrospective study of the effect of pre-op PT education on LOS and discharge disposition for elective THA and TKA patients found different results in univariate and multivariate analysis. Further study is needed to confirm the association found on multivariate analysis between pre-op PT and home discharge in THA patients.
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TI Bone development in fetuses with intrauterine growth restriction caused by maternal endocrine-metabolic dysfunctions
SO BONE
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DT Review
DE Thyroid dysfunctions; Obesity; Hypertension; Diabetes mellitus; Intramembranous ossification; Endochondral ossification
ID gestational-age infants; vitamin-d deficiency; congenital hyperparathyroidism secondary; mesenchymal stem-cells; diet-induced obesity; serum-free culture; thyroid-hormones; birth-weight; fetal-growth; parathyroid-hormone
AB Intrauterine growth restriction (IUGR) affects a large proportion of infants, particularly in underdeveloped countries. Among the main causes of IUGR, maternal endocrine-metabolic dysfunction is highlighted, either due to its high incidence or due to the severity of the immediate and mediated changes that these dysfunctions cause in the fetus and the mother. Although the effects of endocrine and metabolic disorders have been widely researched, there are still no reviews that bring together and summarize the effects of these conditions on bone development in cases of IUGR. Therefore, the present literature review was conducted with the aim of discussing bone changes observed in fetuses with IUGR caused by maternal endocrine-metabolic dysfunction. The main endocrine dysfunctions that occur with IUGR include maternal hyperthyroidism, hypothyroidism, and hypoparathyroidism. Diabetes mellitus, hypertensive disorders, and obesity are the most important maternal metabolic dysfunctions that compromise fetal growth. The bone changes reported in the fetus are, for the

most part, due to damage to cell proliferation and differentiation, as well as failures in the synthesis and mineralization of the extracellular matrix, which results in shortening and fragility of the bones. Some maternal dysfunctions, such as hyperthyroidism, have been widely studied, whereas conditions such as hypoparathyroidism and gestational hypertensive disorders require further study regarding the mechanisms underlying the development of bone changes. Similarly, there is a gap in the literature regarding changes related to intramembranous ossification, as most published articles only describe changes in endochondral bone formation associated with IUGR. Furthermore, there is a need for more research aimed at elucidating the late postnatal changes that occur in the skeletons of individuals affected by IUGR and their possible relationships with adult diseases, such as osteoarthritis and osteoporosis.

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TI Identification of potential pathogenic genes related to osteoporosis and osteoarthritis

SO TECHNOLOGY AND HEALTH CARE
LA English
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DE Osteoarthritis; osteoporosis; hub DEGs
ID reveals
AB BACKGROUND: Osteoarthritis (OA) and osteoporosis (OS) are the most common orthopedic diseases. OBJECTIVE: To identify important genes as biomarkers for the pathogenesis of OA and OS. METHODS: Microarray data for OA and OS were downloaded from the Gene Expression Omnibus database. Differentially expressed genes (DEGs) between the OA and healthy control groups and between the OS and healthy control groups were identified using the Limma software package. Overlapping hub DEGs were selected using MCC, MNC, DEGREE, and EPC. Weighted gene co-expression network analysis (WGCNA) was used to mine OA- and OS-related modules. Shared hub DEGs were identified, human microRNA disease database was used to screen microRNAs associated with OA and OS, and an miRNA-target gene network was constructed. Finally, the expression of shared hub DEGs was evaluated. RESULTS: A total of 104 overlapping DEGs were identified in both the OA and OS groups, which were mainly related to inflammatory biological processes, such as the Akt and TNF signaling pathways Forty-six hub DEGs were identified using MCC, MNC, DEGREE, and EPC modules using different algorithms. Seven modules with 392 genes that highly correlated with disease were identified in the WGCNA. Furthermore, 10 shared hub DEGs were identified between the OA and OS groups, including OGN, FAP, COL6A3, THBS4, IGFBP2, LRRC15, DDR2, RND3, EFNB2, and CD48. A network consisting of 8 shared hub DEGs and 55 miRNAs was constructed. Furthermore, CD48 was significantly upregulated in the OA and OS groups, whereas EFNB2, DR2, COL6A3, and RND3 were significantly downregulated in OA and OS. Other hub DEGs were significantly upregulated in OA and downregulated in OS. CONCLUSIONS: The ten genes may be promising biomarkers for modulating the development of both OA and OS.
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TI Clinical presentation and burden of ENPP1 deficiency in adults
SO ARCHIVES DE PEDIATRIE
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DE ENPP1; Early-Onset Osteoporosis; Spinal Hyperostosis; DISH; OPLL/OALL
ID cole disease; mineralization; osteoarthritis; association; mutations; cartilage; gene
AB While the clinical consequences of severe ENPP1 deficiency leading to the rare disorders generalized arterial calcification of infancy (GACI) and autosomal recessive hypophosphatemic rickets type 2 (ARHR2) are well defined and understood, much less is known about how this evolves into adulthood and how moderate ENPP1 deficiency can first manifest in adulthood. Moreover, growing evidence substantiates an association of genetic variants in the ENPP1 gene with a wide range of further clinical manifestations including early-onset osteoporosis, osteoarthritis, and different forms of spinal ligament calcifications, i.e., diffuse idiopathic skeletal hyperostosis (DISH) and ossification of the posterior/anterior longitudinal ligament (OPLL/OALL). Furthermore, conditions with primarily extraskeletal signs and symptoms such as Cole disease, coagulopathies, and metabolic syndrome can seemingly result from ENPP1 variants. The causality and the pathophysiology behind these different clinical presentations appear complex and require further research, especially since the coincidence of these different phenotypes is rarely described and available evidence suggests that part of the aforementioned manifestations may result from ENPP1 effects beyond the catalytic activity of processing ATP to AMP and inorganic pyrophosphate (PPi). Growing awareness of the additional ENPP1-related manifestations across the lifespan will advance our understanding of this complex condition and help to standardize diagnostic approaches and develop individually tailored treatment concepts. (c) 2024 Published by Elsevier Masson SAS on behalf of French Society of Pediatrics.
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TI Decoding ferroptosis: transforming orthopedic disease management
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE lipid peroxidation; antioxidant system; iron metabolism; orthopedic disorders;

mechanisms; therapy
ID hydroperoxide glutathione-peroxidase; programmed cell-death; embryonic cortical-neurons; unfolded protein response; transferrin-bound iron; oxidative stress; rheumatoid-arthritis; gene-expression; vitamin-e; intervertebral disc
AB As a mechanism of cell death, ferroptosis has gained popularity since 2012. The process is distinguished by iron toxicity and phospholipid accumulation, in contrast to autophagy, apoptosis, and other cell death mechanisms. It is implicated in the advancement of multiple diseases across the body. Researchers currently know that osteosarcoma, osteoporosis, and other orthopedic disorders are caused by NRF2, GPX4, and other ferroptosis star proteins. The effective relief of osteoarthritis symptoms from deterioration has been confirmed by clinical treatment with multiple ferroptosis inhibitors. At the same time, it should be reminded that the mechanisms involved in ferroptosis that regulate orthopedic diseases are not currently understood. In this manuscript, we present the discovery process of ferroptosis, the mechanisms involved in ferroptosis, and the role of ferroptosis in a variety of orthopedic diseases. We expect that this manuscript can provide a new perspective on clinical diagnosis and treatment of related diseases.
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U2 14
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AU Zhu, PF
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AF Zhu, Pengfei
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TI TRPA1 aggravates osteoclastogenesis and osteoporosis through activating endoplasmic reticulum stress mediated by SRXN1
SO CELL DEATH & DISEASE
LA English
DT Article
ID oxidative stress; in-vitro; differentiation; inflammation; induction; apoptosis; pathway; cells; smoke
AB Osteoporosis (OP) is a disorder of bone remodeling caused by an imbalance between bone resorption by osteoclasts and bone formation by osteoblasts. Therefore, inhibiting excessive osteoclast activity is one of the promising strategies for treating OP. A major transient receptor potential cation channel, known as transient receptor potential ankyrin 1 (TRPA1), was found to alleviate joint pain and cartilage degeneration in osteoarthritis. However, little research has focused on TRPA1 function in OP. As a result, this study aimed to explore the TRPA1 characteristics and its potential therapeutic function during osteoclastogenesis. The TRPA1 expression gradually increased in the osteoclast differentiation process; however, its suppression with small interfering RNA and an inhibitor (HC030031) significantly controlled the osteoclast count and the expression of osteoclast characteristic genes. Its suppression also inhibited endoplasmic reticulum (ER) stress-related pancreatic ER kinase (PERK) pathways. An ER stress inhibitor (thapsigargin) reversed the down-regulated levels of ER stress and osteoclast differentiation by suppressing TRPA1. Transcriptome sequencing results

demonstrated that TRPA1 negatively regulated reactive oxygen species (ROS) and significantly increased the expression of an antioxidant gene, SRXN1. The osteoclast differentiation and the levels of ER stress were enhanced with SRXN1 inhibition. Finally, TRPA1 knockdown targeting macrophages by adeno-associated virus-9 could relieve osteoclast differentiation and osteopenia in ovariectomized mice. In summary, silencing TRPA1 restrained osteoclast differentiation through ROS-mediated down-regulation of ER stress via inhibiting PERK pathways. The study also indicated that TRPA1 might become a prospective treatment target for OP.

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WC Cell Biology
SC Cell Biology
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PT J
AU Chin, KY
AF Chin, Kok-Yong
TI Updates in the skeletal and joint protective effects of tocotrienol: a mini review
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE bone; cartilage; osteoarthritis; osteoporosis; vitamin E
ID bone histomorphometric parameters; bixa-orellana annatto; vitamin-e; oxidative stress; alpha-tocopherol; palm tocotrienol; calcium content; mc3t3-e1 cells; male rats; supplementation
AB Osteoporosis and osteoarthritis continue to pose significant challenges to the aging population, with limited preventive options and pharmacological treatments often accompanied by side effects. Amidst ongoing efforts to discover new therapeutic agents, tocotrienols (TTs) have emerged as potential candidates. Derived from annatto bean and palm oil, TTs have demonstrated efficacy in improving skeletal and joint health in numerous animal models of bone loss and osteoarthritis. Mechanistic studies suggest that TTs exert their effects through antioxidant, anti-inflammatory, Wnt-suppressive, and mevalonate-modulating

mechanisms in bone, as well as through self-repair mechanisms in chondrocytes. However, human clinical trials in this field remain scarce. In conclusion, TTs hold promise as agents for preventing osteoporosis and osteoarthritis, pending further evidence from human clinical trials.
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TI Changes in Muscle Mass and Bone Density and Their Relationship After Total Knee Arthroplasty
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE knee; osteoarthritis; arthroplasty; sarcopenia; osteoporosis; bone mineral density
ID mineral density; postmenopausal women; renal-function; sarcopenia; prevalence; age; osteoarthritis; mortality; dhea; hip
AB Purpose: To investigate the effects of total knee arthroplasty (TKA) on muscle mass and bone density in end-stage knee osteoarthritis (OA). Methods: This prospective study was conducted on 111 patients with Kellgren-Lawrence grade 4 knee OA who underwent TKA after failing to respond to conservative treatment for more than 3 months at a single institution from June 2022 to May 2023. Appendicular lean mass index (ALMI) and bone mineral density (BMD) were measured using dual-energy X-ray absorptiometry before and every 6 months after surgery. The average follow-up period was 15.5 +/- 2.31 months (range, 11.6-24 months). Results: During the follow-up period after TKA, the ALMI increased relatively continuously and consistently. The BMD of the L-spine and proximal femur did not change significantly until 12 months after TKA surgery but began to increase steeply after 12 months and slowed down after 18 months. The increase in muscle mass showed a significant positive correlation with the increase in BMD. Conclusions: Muscle mass gradually increased after TKA for end-stage knee OA, whereas bone density also increased but not until 12 months after surgery. The significant positive correlation between the increase in muscle mass and bone density suggests that the increase in muscle mass after TKA may be one of the causes of the increase in bone density.
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NR 47
TC 4
Z9 4
U1 0
U2 1
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 2077-0383
J9 J CLIN MED
JI J. Clin. Med.
PD NOV 15
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WC Medicine, General & Internal
SC General & Internal Medicine
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ER

PT J
AU Luo, HH
Zheng, ZT
Xiong, YJ
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Xue, QY
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AF Luo, Huanhuan
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TI Association between folate intake and radiographic progression, pain function scores in subjects with radiographic knee osteoarthritis: Data from the osteoarthritis initiative
SO INTERNATIONAL JOURNAL OF RHEUMATIC DISEASES
LA English
DT Article
DE dietary risk factors; epidemiology; folate; knee osteoarthritis; pain
ID dietary-intake; homocysteine; stress; risk
AB Background Folate has an important role in the functioning of the musculoskeletal system, including modulation of inflammation, immunity, cartilage regeneration, prevention of osteoporosis, and maintenance of muscle strength, but evidence on the association between folate intake and knee pain, functional scores, and radiographic progression in patients with knee osteoarthritis (OA) is still limited. Methodology Our population-based cohort was extracted from the osteoarthritis initiative (OAI), focusing on individuals with prevalent radiographic knee OA (with a Kellgren-Lawrence score >= 2). Folate consumption was determined using the food frequency questionnaire. Data regarding the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores and radiographic readings were collected over 48 months. We analyzed the compiled data using generalized additive mixed models. Results Our cohort consisted of 1472 OA patients (626 men and 846 women, mean [SD] age 62.35 [8.92]). At the 48-month follow-up, we observed a significant correlation between higher folate intake and a slower progression of knee pain and functional scores, as evidenced by a statistically significant decrease in the WOMAC total score, WOMAC pain subscale score, and WOMAC function/disability subscale score ($p < .05$). The fully adjusted models estimated a reduction of -0.028 points per 50 mu g/1000 kcal of daily folate intake on the WOMAC pain subscale, -0.117 points on the WOMAC function subscale, and -0.160 points on the total WOMAC scale. Furthermore, our nonparametric fit analysis suggested that a higher intake of folate might decelerate

the radiographic progression of OA. Stratified analyses indicated that an increase in folate consumption might particularly benefit men, older adults, overweight and obese individuals, and those with a higher dietary fiber intake. Conclusion Higher folate intake is correlated with improved knee function and reduced pain in patients with knee OA and might deter the radiographic progression of OA. The benefits appear to be more pronounced in men, older adults, overweight and obese individuals, and those with a higher dietary fiber intake.
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Z9 2
U1 0
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PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1756-1841
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J9 INT J RHEUM DIS
JI Int. J. Rheum. Dis.
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IS 9
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WC Rheumatology
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PT J
AU Zhang, QY
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Gao, FQ
Sun, W
AF Zhang, Qingyu
Li, Junyou

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TI N6-Methyladenosine in Cell-Fate Determination of BMSCs: From Mechanism to Applications
SO RESEARCH
LA English
DT Review
ID mesenchymal stem-cells; nf-kappa-b; osteogenic differentiation; osteoblast differentiation; methyltransferase mettl3; promotes osteogenesis; m(6)a modification; runx2; proliferation; adipogenesis
AB The methylation of adenosine base at the nitrogen-6 position is referred to as "N6-methyladenosine (m6A)" and is one of the most prevalent epigenetic modifications in eukaryotic mRNA and noncoding RNA (ncRNA). Various m6A complex components known as "writers," "erasers," and "readers" are involved in the function of m6A. Numerous studies have demonstrated that m6A plays a crucial role in facilitating communication between different cell types, hence influencing the progression of diverse physiological and pathological phenomena. In recent years, a multitude of functions and molecular pathways linked to m6A have been identified in the osteogenic, adipogenic, and chondrogenic differentiation of bone mesenchymal stem cells (BMSCs). Nevertheless, a comprehensive summary of these findings has yet to be provided. In this review, we primarily examined the m6A alteration of transcripts associated with transcription factors (TFs), as well as other crucial genes and pathways that are involved in the differentiation of BMSCs. Meanwhile, the mutual interactive network between m6A modification, miRNAs, and lncRNAs was intensively elucidated. In the last section, given the beneficial effect of m6A modification in osteogenesis and chondrogenesis of BMSCs, we expounded upon the potential utility of m6A-related therapeutic interventions in the identification and management of human musculoskeletal disorders manifesting bone and cartilage destruction, such as osteoporosis, osteomyelitis, osteoarthritis, and bone defect.
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TI Salidroside: A Promising Agent in Bone Metabolism Modulation
SO NUTRIENTS
LA English
DT Review
DE salidroside; osteoporosis; Rhodiola rosea; fracture healing; osteoarthritis; adaptogens
ID rhodiola-rosea; extract shr-5

AB Rhodiola rosea, a long-lived herbaceous plant from the Crassulaceae group, contains the active compound salidroside, recognized as an adaptogen with significant therapeutic potential for bone metabolism. Salidroside promotes osteoblast proliferation and differentiation by activating critical signaling pathways, including bone morphogenetic protein-2 and adenosine monophosphate-activated protein kinase, essential for bone formation and growth. It enhances osteogenic activity by increasing alkaline phosphatase activity and mineralization markers, while upregulating key regulatory proteins including runt-related transcription factor 2 and osterix. Additionally, salidroside facilitates angiogenesis via the hypoxia-inducible factor 1-alpha and vascular endothelial growth factor pathway, crucial for coupling bone development with vascular support. Its antioxidant properties offer protection against bone loss by reducing oxidative stress and promoting osteogenic differentiation through the nuclear factor erythroid 2-related factor 2 pathway. Salidroside has the capability to counteract the negative effects of glucocorticoids on bone cells and prevents steroid-induced osteonecrosis. Additionally, it exhibits multifaceted anti-inflammatory actions, notably through the inhibition of tumor necrosis factor-alpha and interleukin-6 expression, while enhancing the expression of interleukin-10. This publication presents a comprehensive review of the literature on the impact of salidroside on various aspects of bone tissue metabolism, emphasizing its potential role in the prevention and treatment of osteoporosis and other diseases affecting bone physiology.
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TI A deep learning approach to identify the fetal head position using transperineal ultrasound during labor
SO EUROPEAN JOURNAL OF OBSTETRICS & GYNECOLOGY AND REPRODUCTIVE BIOLOGY
LA English
DT Article
DE Artificial intelligence; Pattern recognition; Intrapartum ultrasound; Fetal head

malposition; Translabial ultrasound
ID transvaginal digital examination; placement; 2nd-stage; delivery; diagnosis; station; improve
AB Objectives: To develop a deep learning (DL)-model using convolutional neural networks (CNN) to automatically identify the fetal head position at transperineal ultrasound in the second stage of labor. Material and methods: Prospective, multicenter study including singleton, term, cephalic pregnancies in the second stage of labor. We assessed the fetal head position using transabdominal ultrasound and subsequently, obtained an image of the fetal head on the axial plane using transperineal ultrasound and labeled it according to the transabdominal ultrasound findings. The ultrasound images were randomly allocated into the three datasets containing a similar proportion of images of each subtype of fetal head position (occiput anterior, posterior, right and left transverse): the training dataset included 70%, the validation dataset 15%, and the testing dataset 15% of the acquired images. The pre-trained ResNet18 model was employed as a foundational framework for feature extraction and classification. CNN1 1 was trained to differentiate between occiput anterior (OA) and non-OA positions, CNN2 2 classified fetal head malpositions into occiput posterior (OP) or occiput transverse (OT) position, and CNN3 3 classified the remaining images as right or left OT. The DL-model was constructed using three convolutional neural networks (CNN) working simultaneously for the classification of fetal head positions. The performance of the algorithm was evaluated in terms of accuracy, sensitivity, specificity, F1-score and Cohen's kappa. Results: Between February 2018 and May 2023, 2154 transperineal images were included from eligible participants across 16 collaborating centers. The overall performance of the model for the classification of the fetal head position in the axial plane at transperineal ultrasound was excellent, with an of 94.5 % (95 % CI 92.0--97.0), a sensitivity of 95.6 % (95% CI 96.8-100.0), a specificity of 91.2 % (95% CI 87.3-95.1), a F1-score of 0.92 and a Cohen's kappa of 0.90. The best performance was achieved by the CNN1 1 - OA position vs fetal head malpositions - with an accuracy of 98.3 % (95 % CI 96.9-99.7), followed by CNN2 2 - OP vs OT positions - with an accuracy of 93.9 % (95 % CI 89.6-98.2), and finally, CNN3 3 - right vs left OT position - with an accuracy of 91.3 % (95 % CI 83.5-99.1). Conclusions: We have developed a DL-model capable of assessing fetal head position using transperineal ultrasound during the second stage of labor with an excellent overall accuracy. Future studies should validate our DL model using larger datasets and real-time patients before introducing it into routine clinical practice.
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TI Plasma pentosidine concentration is associated with ligament ossification and high-grade osteoarthritis: The ROAD study
SO GERIATRICS & GERONTOLOGY INTERNATIONAL
LA English
DT Article
DE advanced glycation end-products; diffuse idiopathic skeletal hyperostosis; knee osteoarthritis; ossification of the posterior longitudinal ligament of the cervical spine; plasma pentosidine
ID posterior longitudinal ligament; glycation end-products; skeletal hyperostosis dish; body-mass index; diabetes-mellitus; cervical-spine; whole spine; prevalence; age
AB Aim: No studies have examined the association between plasma pentosidine levels and ossification diseases in large cohorts of Japanese residents. This study aimed to investigate the association between cervical ossification of the posterior longitudinal ligament (OPLL) and other ossification diseases, including diffuse idiopathic skeletal hyperostosis, lumbar spondylosis and knee osteoarthritis (OA), by examining plain radiographs of the knee, and cervical, thoracic and lumbar spine from 1690 participants, and the association between these diseases and plasma pentosidine. Design: We enrolled 1690 participants (596 men and 1094 women) from mountainous and coastal areas from the study population of the previous Research on Osteoarthritis/ Osteoporosis Against Disability study. X-ray examination of the cervical/thoracic/lumbar spine and knee was carried out only in these individuals, and not those from urban areas. Plasma pentosidine concentrations were determined using enzyme-linked immunoassays. Results: Radiographic OPLL was detected in 30 (17 men, 13 women) of 1562 individuals who underwent X-ray examination of the cervical spine. OPLL, diffuse idiopathic skeletal hyperostosis, lumbar spondylosis Kellgren-Lawrence (KL) grade, and knee OA KL grade were associated with high plasma pentosidine concentrations (all $P < 0.05$). Furthermore, significant intragroup differences (KL grade 4 vs 3) of plasma pentosidine concentration were observed between the lumbar spondylosis and knee OA groups. The plasma pentosidine concentration was significantly associated with age, OPLL, lumbar spondylosis (KL grade 4) and knee OA (KL grade 4). Conclusions: OPLL is significantly associated with other ossification diseases. The development of more severe OA might lead to the accumulation of plasma pentosidine. Plasma pentosidine levels were associated with OPLL and severe OA. Geriatr Gerontol Int 2023; center dot center dot: center dot center dot-center dot center dot.
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TI The impact of ageing mechanisms on musculoskeletal system diseases in the elderly
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE ageing; cell senescence; SASP; osteoarthritis; osteoporosis; sarcopenia
ID deficiency-induced osteoporosis; inhibiting oxidative stress; cell-cycle arrest; senescent cells; skeletal-muscle; mitochondrial-dna; tumor-suppressor; secretory phenotype; adipose-tissue; stem-cells
AB Ageing is an inevitable process that affects various tissues and organs of the human body, leading to a series of physiological and pathological changes. Mechanisms such as telomere depletion, stem cell depletion, macrophage dysfunction, and cellular senescence gradually manifest in the body, significantly increasing the incidence of diseases in elderly individuals. These mechanisms interact with each other, profoundly impacting the quality of life of older adults. As the ageing population continues to grow, the burden on the public health system is expected to intensify. Globally, the prevalence of musculoskeletal system diseases in elderly individuals is increasing, resulting in reduced limb mobility and prolonged suffering. This review aims to elucidate the mechanisms of ageing and their interplay while exploring their impact on diseases such as osteoarthritis, osteoporosis, and sarcopenia. By delving into the mechanisms of ageing, further research can be conducted to prevent and mitigate its effects, with the ultimate

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TI The Emerging Roles of Hydrogen Sulfide in Ferroptosis
SO ANTIOXIDANTS & REDOX SIGNALING
LA English
DT Review
DE ferroptosis; hydrogen sulfide; mechanism; signaling molecule; disease
ID transcription factor nrf2; cell-death; oxidative stress; nitric-oxide; mediated generation; glutamate toxicity; s-sulfhydration; protein-kinase; small-molecule; cancer-cells
AB Significance: Ferroptosis, a form of regulated cell death characterized by a large amount of lipid peroxidation-mediated membrane damage, joins the evolution of multisystem diseases, for instance, neurodegenerative diseases, chronic obstructive pulmonary disease, acute respiratory distress syndrome, osteoporosis, osteoarthritis, and so forth. Since being identified as the third gasotransmitter in living organisms, the intricate role of hydrogen sulfide (H2S) in ferroptosis has emerged at the forefront of research.Recent Advances: Novel targets in the relevant metabolic pathways have been found, including transferrin receptor 1, cystine/glutamate antiporter, and others, coupled with the exploration of new signaling pathways, particularly the p53 signaling pathway, the nitric oxide/nuclear factor erythroid 2-related factor 2 signaling pathway, and so on. Many diseases such as emphysema and airway inflammation, myocardial diseases, endothelial dysfunction in aging arteries, and traumatic brain injury have recently been found to be alleviated directly by H2S inhibition of ferroptosis. Safe, effective, and tolerable novel H2S donors have been developed and have shown promising results in phase I clinical trials.Critical Issues: Complicated cross talk between the ferroptosis signaling pathway and oncogenic factors results in the risk of cancer when inhibiting ferroptosis. Notably, targeted delivery of H2S is still a challenging task.Future Directions: Discovering more reliable and stable novel H2S donors and achieving their targeted delivery will enable further clinical trials for diseases associated with ferroptosis inhibition by H2S, determining their safety, efficacy, and tolerance.
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TI Sex-Specific Association of Clinical Parameters and Components of Femoral Bone Quality in Patients Undergoing Total Hip Arthroplasty
SO CALCIFIED TISSUE INTERNATIONAL
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DE Osteoporosis; DXA; THA; Osteoarthritis; Osteocytes
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AB Poor bone quality is a critical factor associated with an increased risk of complications after total hip arthroplasty (THA). However, no consistent recommendations have yet been established for assessing indicators of bone quality preoperatively. Thus, it remains unclear which preoperatively available and readily accessible parameters are most closely associated with femoral bone quality. Here, we obtained femoral neck specimens from 50 patients undergoing THA. Preoperative Dual-energy X-ray absorptiometry (DXA) scans, pelvic radiographs, and laboratory parameters were analyzed. In the obtained specimens, bone microstructure was assessed using micro-CT and histomorphometry. Additionally, matrix mineralization and osteocyte lacunar morphology were evaluated using quantitative backscattered electron imaging. Our analysis revealed that DXA-derived T-scores correlated with trabecular microstructure. Furthermore, radiographic indices and body mass index correlated differentially with aspects of bone quality in women and men. Contrary to previous observations, no correlation was found between serum vitamin D levels and osteoid indices, nor between clinical parameters and matrix mineralization. Age was strongly associated with the number of mineralized osteocyte lacunae, a factor that appeared to be independent of sex. Taken together, our study demonstrates that no single preoperatively available parameter exhibits a strong and consistent association with femoral bone quality. However, DXA remains a reliable preoperative measure for determining the trabecular microstructure of the femoral neck. In clinical practice, surgeons should adopt an individualized approach to preoperative assessments by considering age, sex, BMI, and radiographic indices to enhance their insight into femoral bone quality, particularly when DXA is unavailable.
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TI Targeting Mitophagy as a Potential Therapeutic Approach for Age-Related Bone Diseases
SO ADVANCED THERAPEUTICS
LA English
DT Review
DE age-related bone diseases; bone metabolism; mitochondrial dysfunction; mitophagy; osteogenesis
ID mitochondria-associated membranes; parkin-mediated mitophagy; mesenchymal stem-cells; endoplasmic-reticulum; osteogenic differentiation; extracellular vesicles; disc degeneration; pink1 import; autophagy; receptor
AB Accumulating evidence has suggested a strong correlation between age-related bone diseases and abnormal metabolism of bone microenvironment-related cells, including mesenchymal stem cells (MSCs), osteoblasts, osteoclasts, osteocytes, and chondrocytes. Mitochondrial dysfunction significantly impacts cell metabolism and initiates the development and progress of numerous age-related bone diseases. Mitochondrial autophagy or mitophagy, a process that selectively removes damaged or dysfunctional mitochondria, is closely associated with maintaining mitochondrial quality control and homeostasis. Recent studies indicate a decisive regulatory role of mitophagy in age-related bone diseases, thereby pointing toward the potential for manipulating mitophagy levels as a new treatment paradigm. Based on the importance and novelty of mitophagy, the present review offers an overview of the pathways involved in mitophagy and meticulously examines its function in age-related bone diseases. Various treatment methods targeting mitophagy are also discussed, mainly including biomaterials with mitophagy-modulatory capabilities, "old drugs in a new bottle" (e.g., Metformin, Rapamycin), natural compounds, endogenous factors, and stem cell-based therapies. In conclusion, these innovative approaches uncover mitophagy-related signals, pathways, and mechanisms, and may shed light on mitophagy-targeting treatments for age-related bone diseases in the future. Mitophagy deficiency is a key mechanism in aging and age-related bone diseases (such as osteoporosis, osteoarthritis, intervertebral disc degeneration, and periodontitis), which hinders the removal of dysfunctional mitochondria and hence aggravates ROS and inflammation. Therapeutic approaches targeting mitophagy have significant potential for restoring normal bone metabolism or enhancing endogenous bone regeneration. image
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PT J
AU Katz, J
Bartels, CM
AF Katz, Jonathan
Bartels, Christie M.
TI Multimorbidity in Rheumatoid Arthritis: Literature Review and Future Directions
SO CURRENT RHEUMATOLOGY REPORTS
LA English

DT Review
DE Multimorbidity; Rheumatoid Arthritis; Comorbidity; COPD; Depression; Pain
AB Purpose of ReviewTo offer a narrative review of literature and an update on rheumatoid arthritis (RA) multimorbidity research over the past five years as well as future directions.Recent FindingsPatients with RA experience higher prevalence of multimorbidity (31-86% vs 18-71% in non-RA) and faster accumulation of comorbidities. Patients with multimorbidity have worse outcomes compared to non-RA multimorbid patients and RA without multimorbidity including mortality, cardiac events, and hospitalizations. Comorbid disease clusters often included: cardiopulmonary, cardiometabolic, and depression and pain-related conditions. High-frequency comorbidities included interstitial lung disease, asthma, chronic obstructive pulmonary disease, cardiovascular disease, fibromyalgia, osteoarthritis, and osteoporosis, thyroid disorders, hypertension, and cancer. Furthermore, patients with RA and multimorbidity are paradoxically at increased risk of high RA disease activity but experience a lower likelihood of biologic use and more biologic failures.SummaryRA patients experience higher prevalence of multimorbidity and worse outcomes versus non-RA and RA without multimorbidity. Findings call for further studies.
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PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES

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AU Hirashima, S
Kiyooka, Y
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AF Hirashima, Shunsuke
Kiyooka, Yukino
Kaetsu, Shinichiro
Nakagawa, Kimie
TI Vitamin K converting enzyme UBIAD1 plays an important role in osteogenesis and chondrogenesis in mice
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS
LA English
DT Article
DE Vitamin K; Menaquinone-4; UBIAD1; Osteogenesis; Chondrogenesis
ID menaquinone-4 vitamin-k-2; phylloquinone vitamin-k-1; osteoarthritis; fractures; genes
AB Dietary vitamin K1 (phylloquinone: PK) and menaquinone (MK-n) are converted to menadione (MD) in the small intestine and then translocated to various tissues where they are converted to vitamin K2 (menaquinone-4: MK-4) by UbiA prenyltransferase domain containing protein 1 (UBIAD1). MK-4 is effective in bone formation and is used to treat osteoporosis in Japan. UBIAD1 is expressed in bone and osteoblasts and shows conversion to MK-4, but the role of UBIAD1 in

osteogenesis is unknown. In this study, we investigated the function of UBIAD1 in osteogenesis using a tamoxifen-dependent UBIAD1-deficient mouse model. When UBIAD1 deficiency was induced from the first week of life, the femur was significantly shortened, and bone mineral density (BMD) was reduced. In addition, the expression of bone and chondrocyte matrix proteins and chondrocyte differentiation factors was significantly decreased. In primary cultured chondrocytes, chondrocyte differentiation was significantly reduced by UBIAD1 deficiency. These results suggest that UBIAD1 is an important factor for the regulation of chondrocyte proliferation and differentiation during osteogenesis.
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AF Verma, P. K.
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TI Summertime oxidative potential of atmospheric PM2.5 over New Delhi: Effect of aerosol ageing
SO SCIENCE OF THE TOTAL ENVIRONMENT
LA English
DT Article

DE Aerosol composition; Dithiothreitol (DTT) assay; HR-Tof-AMS; Megacity; Indo-Gangetic Plain
ID polycyclic aromatic-hydrocarbons; ambient particulate matter; oxygen species generation; chemical-composition; redox activity; air-pollution; seasonal variability; ultrafine particles; dithiothreitol dtt; diesel exhaust
AB Exposure to elevated particulate matter (PM) concentrations in ambient air has become a major health concern over urban areas worldwide. Reactive oxygen species (ROS) generation due to ambient PM (termed as their oxidative potential, OP) is shown to play a major role in PM-induced health effects. In the present study, the OP of the ambient PM2.5 samples, collected during summer 2019 from New Delhi, were measured using the dithiothreitol (DTT) assay. Average volume-normalized OP (OPV) was 2.9 +/- 1.1 nmol DTT min(-1) m(-3), and mass-normalized OP (OPm) was 61 +/- 29 pmol DTT min(-1) mu g(-1). The regression statistics of OPv vs chemical species show the maximum slope of OPV with the elemental carbon (EC, r(2) = 0.72) followed by water-soluble organic carbon (WSOC, r(2) = 0.72), and organic carbon (OC, r(2) = 0.64). A strong positive correlation between OPm and secondary inorganic aerosols (SIA, such as NH4+ and NO3- mass fractions) was also observed, indicating that the sources emitting NO2 and NH3, precursors of NO3- and NH4+, also emit DTT-active species. Interestingly, the slope value of OPv vs OC for aged aerosols (OM/OC > 1.7, f44 > 0.12 and f43 < 0.04) was 1.7 times higher than relatively fresh organic aerosols (OA, OM/OC < 1.7, f44 < 0.12, f43 > 0.04). An increase in OPv and OPoc with f44 indicates the formation of more DTT active species with the ageing of OA. A linear increase in OPoc with increasing Nitrogen/Carbon (N/C) ratio suggests that nitrogenous OA have higher OP.
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AU Nakahara, E
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TI Identifying factors associated with locomotive syndrome using machine learning methods: The third survey of the research on osteoarthritis/osteoporosis against disability study
SO GERIATRICS & GERONTOLOGY INTERNATIONAL
LA English
DT Article
DE associated factor; cohort study; locomotive syndrome; machine learning; prevalence
ID validation; arthritis; scale
AB AimTo identify factors associated with locomotive syndrome (LS) using medical questionnaire data and machine learning.MethodsA total of 1575 participants underwent the LS risk tests from the third survey of the research on osteoarthritis/osteoporosis against disability study (ROAD) study. LS was defined as stage 1 or higher based on clinical decision limits of the Japanese Orthopaedic Association. A total of 1335 items of medical questionnaire data came from this study. The number of medical questionnaire items was reduced from 1335 to 331 in data cleaning. From the 331 items, identify factors associated with LS use by light gradient boosting machine-based recursive feature elimination with cross-validation. The performance of each set was evaluated using an average of seven performance metrics, including 95% confidence intervals, using a bootstrapping method. The smallest set of items is determined with the highest average of receiver operating characteristic area under the curve (ROC-AUC) under 20 items as association factors of LS. Additionally, the performance of the selected items was compared with the LS risk tests and Loco-check.ResultsThe nine items have the best average ROC-AUC under 20 items. The nine items show an average ROC-AUC of 0.858 (95% confidence interval 0.816-0.898). Age and back pain during walking were strongly associated with the prevalence of LS. The ROC-AUC of nine items is higher than that of existing questionnaire-based LS assessments, including the 25-question Geriatric Locomotor Scale and Loco-check.ConclusionsThe identified nine items could aid early LS detection, enhancing understanding and prevention. Geriatr Gerontol Int 2024; center dot center dot: center dot center dot-center dot center dot. We aimed to identify factors associated with locomotive syndrome using machine learning. The 9 items were identified, and an average ROC-AUC value of the 9 items was 0.858. Age and low back pain during walking were strongly associated with locomotive syndrome. image
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AF Inigo, S. Arun
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TI A Review on Imaging Techniques and Artificial Intelligence Models for Osteoporosis Prediction
SO CURRENT MEDICAL IMAGING
LA English
DT Review
DE Medical image; Bone mineral density (BMD); Image processing; Artificial intelligence; Dataset quality; Deep learning (DL)
ID noise-reduction; deep
AB Osteoporosis causes harmful influences on both men and women of all races. Bone mass, also referred to as "bone density," is frequently used to assess the health of bone. Humans frequently experience bone fractures as a result of trauma, accidents, metabolic bone diseases, and disorders of bone strength, which are

typically led by changes in mineral composition and result in conditions like osteoporosis, osteoarthritis, osteopenia, etc. Artificial intelligence holds a lot of promise for the healthcare system. Data collection and preprocessing seem to be more essential for analysis, so bone images from different modalities, such as X-ray, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), are taken into consideration that help to recognize, classify, and evaluate the patterns in clinical images. This research presents a comprehensive overview of the performance of various image processing techniques and deep learning approaches used to predict osteoporosis through image segmentation, classification, and fault detection. This survey outlined the proposed domain-based deep learning model for image classification in addition to the initial findings. The outcome identifies the flaws in the existing literature's methodology and lays the way for future work in the deep learning-based image analysis model.
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TI Predicting the Fracture Toughness of Human Cancellous Bone in Fractured Neck of Femur Patients Using Bone Volume and Micro-Architecture
SO LIFE-BASEL
LA English
DT Article
DE cancellous bone; fracture toughness; BV/TV; micro-architecture; crack growth; microCT; multi-regression predictions
ID age-related-changes; trabecular bone; mechanical-behavior; density; surface; architecture; strength; strain
AB The current protocol used to determine if an individual is osteoporotic relies on assessment of the individual's bone mineral density (BMD), which allows clinicians to judge the condition of a patient with respect to their peers. This, in essence, evaluates a person's fracture risk, because BMD is a good surrogate measure for strength and stiffness. In recent studies, the authors were the first to produce fracture toughness (FT) data from osteoporotic (OP) and osteoarthritic (OA) patients, by using a testing technique which basically analyzes the prerequisite stress conditions for the onset of growth of a major crack through cancellous bone tissue. FT depends mainly on bone quantity (BV/TV, bone volume/tissue volume), but also on bone micro-architecture (mArch), the inner trabecular design of the bone. The working research hypothesis of the present study is that mArch offers

added prediction power to BV/TV in determining FT parameters. Consequently, our aim was to investigate the use of predictive models for fracture toughness and also to investigate if there are any significant differences between the models produced from samples loaded across (AC, transverse to) the main trabecular orientation and along (AL, in parallel) the trabeculae. In multilinear regression analysis, we found that the strength of the relationships varied for a crack growing in these two orthogonal directions. Adding mArch variables in the Ac direction helped to increase the R2 to 0.798. However, in the AL direction, adding the mArch parameters did not add any predictive power to using BV/TV alone; BV/TV on its own could produce R2 = 0.730. The present results also imply that the anisotropic layout of the trabeculae makes it more difficult for a major crack to grow transversely across them. Cancellous bone models and remodels itself in a certain way to resist fracture in a specific direction, and thus, we should be mindful that architectural quality as well as bone quantity are needed to understand the resistance to fracture.
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TI Sensing the future: A review on emerging technologies for assessing and monitoring bone health
SO BIOMATERIALS ADVANCES
LA English
DT Review
DE Bone health; Bone degenerative disorders; Early diagnosis; Bone turnover markers; Biosensors
ID quantitative ultrasound; rheumatoid-arthritis; raman-spectroscopy; turnover markers; osteoporosis; diagnosis; differentiation; resorption; management; rankl
AB Bone health is crucial at all stages of life. Several medical conditions and changes in lifestyle affect the growth, structure, and functions of bones. This may lead to the development of bone degenerative disorders, such as osteoporosis, osteoarthritis, rheumatoid arthritis, etc., which are major public health concerns worldwide. Accurate and reliable measurement and monitoring of bone health are

important aspects for early diagnosis and interventions to prevent such disorders. Significant progress has recently been made in developing new sensing technologies that offer non-invasive, low-cost, and accurate measurements of bone health. In this review, we have described bone remodeling processes and common bone disorders. We have also compiled information on the bone turnover markers for their use as biomarkers in biosensing devices to monitor bone health. Second, this review details biosensing technology for bone health assessment, including the latest developments in various non-invasive techniques, including dual-energy X-ray absorptiometry, magnetic resonance imaging, computed tomography, and biosensors. Further, we have also discussed the potential of emerging technologies, such as biosensors based on nano- and micro-electromechanical systems and application of artificial intelligence in noninvasive techniques for improving bone health assessment. Finally, we have summarized the advantages and limitations of each technology and described clinical applications for detecting bone disorders and monitoring treatment outcomes. Overall, this review highlights the potential of emerging technologies for improving bone health assessment with the potential to revolutionize clinical practice and improve patient outcomes. The review highlights key challenges and future directions for biosensor research that pave the way for continued innovations to improve diagnosis, monitoring, and treatment of bone-related diseases.
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TI Development of AAV-Mediated Gene Therapy Approaches to Treat Skeletal Diseases
SO HUMAN GENE THERAPY
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DT Review
DE AAV; Skeletal Diseases; Gene Therapy
ID fibrodysplasia ossificans progressiva; recombinant adenoassociated vector; enzyme replacement therapy; postmenopausal women; factor-ix; directed evolution; antagonist gene; bone-formation; mouse model; stem-cells
AB Adeno-associated viral (AAV) vectors have emerged as crucial tools in advancing gene therapy for skeletal diseases, offering the potential for sustained expression with low postinfection immunogenicity and pathogenicity. Preclinical studies support both the therapeutic efficacy and safety of these vectors, illustrating the promise of AAV-mediated gene therapy. Emerging technologies and innovations in AAV-mediated gene therapy strategies, such as gene addition, gene replacement, gene silencing, and gene editing, offer new approaches to clinical application. Recently, the increasing preclinical applications of AAV to rare skeletal diseases, such as fibrodysplasia ossificans progressiva (FOP) and osteogenesis imperfecta (OI), and prevalent bone diseases, such as osteoporosis, bone fracture, critical-sized bone defects, and osteoarthritis, have been reported. Despite existing limitations in clinical use, such as high cost and safety, the AAV-mediated gene transfer platform is a promising approach to deliver therapeutic gene(s) to the skeleton to treat skeletal disorders, including those otherwise intractable by other therapeutic approaches. This review provides a comprehensive overview of the therapeutic advancements, challenges, limitations, and solutions within AAV-based gene therapy for prevalent and rare skeletal diseases.
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TI Factors associated with cam deformity in Japanese local residents
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ID inflammatory-bowel-disease; c-reactive protein; active ulcerative-colitis; fecal calprotectin; crohns-disease; intraindividual variability; endoscopic activity; metaanalysis; biomarkers; utility
AB Femoroacetabular impingement has increasingly been recognized as a cause of primary hip osteoarthritis; however, its epidemiological indications remain unclear. We aimed to clarify the epidemiological indications and factors associated with cam deformity in a large-scale population-based cohort in Japan. Overall, 1480 participants (2960 hips) (491 men, 989 women; mean age, 65.3 years) analyzed in the third survey of the Research on Osteoarthritis/Osteoporosis Against Disability study were included. The alpha angle and spinopelvic parameters (lumbar lordosis, sacral slope, pelvic tilt, and pelvic incidence) were radiographically measured. Cam deformity was defined as alpha angle >= 60 degrees. Overall, the cam deformity prevalence was 147/2960 (5.0%). Cam deformity prevalence tended to increase with age; in the univariate analysis, a higher percentage of men was observed in the group with cam deformity than in the group without it. No relationship was observed between cam deformity and hip pain. Factors associated with alpha angle were examined via multiple regression analysis for each gender; alpha angle was

significantly associated with age and BMI in each gender. The alpha angle and PT were correlated in women. Thus, alpha angle and cam deformity prevalence increase with age in Japanese individuals. Accordingly, cam deformity can be considered a developmental disease.
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TI Gold nanoparticles exhibit anti-osteoarthritic effects via modulating interaction of the "microbiota-gut-joint" axis
SO JOURNAL OF NANOBIOTECHNOLOGY
LA English
DT Article
DE Osteoarthritis (OA); Gold nanoparticles (GNPs); Gut microbiota; Short-chain fatty acid (SCFA) metabolism; Anti-inflammatory effects
ID lactobacillus-salivarius li01; m2 macrophage polarization; chain fatty-acids; osteoarthritis development; intestinal barrier; ii collagen; stem-cells; tgf-beta; in-vitro; bone
AB Osteoarthritis (OA) is a common degenerative joint disease that can cause

severe pain, motor dysfunction, and even disability. A growing body of research indicates that gut microbiota and their associated metabolites are key players in maintaining bone health and in the progression of OA. Short-chain fatty acids (SCFAs) are a series of active metabolites that widely participate in bone homeostasis. Gold nanoparticles (GNPs) with outstanding anti-bacterial and anti-inflammatory properties, have been demonstrated to ameliorate excessive bone loss during the progression of osteoporosis (OP) and rheumatoid arthritis (RA). However, the protective effects of GNPs on OA progression are not clear. Here, we observed that GNPs significantly alleviated anterior cruciate ligament transection (ACLT)-induced OA in a gut microbiota-dependent manner. 16S rDNA gene sequencing showed that GNPs changed gut microbial diversity and structure, which manifested as an increase in the abundance of Akkermansia and Lactobacillus. Additionally, GNPs increased levels of SCFAs (such as butyric acid), which could have improved bone destruction by reducing the inflammatory response. Notably, GNPs modulated the dynamic balance of M1/M2 macrophages, and increased the serum levels of anti-inflammatory cytokines such as IL-10. To sum up, our study indicated that GNPs exhibited anti-osteoarthritis effects via modulating the interaction of "microbiota-gut-joint" axis, which might provide promising therapeutic strategies for OA.
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TI IGF signaling pathway in bone and cartilage development, homeostasis, and disease
SO FASEB JOURNAL
LA English
DT Review
DE bone development; dwarfism; gene regulatory network; insulin-like growth factor; osteoarthritis; osteoblast differentiation; osteoporosis; skeletal homeostasis
ID growth-factor-i; binding-protein expression; serum response factor; osteoblast differentiation; tgf-beta; articular-cartilage; parathyroid-hormone; osteogenic differentiation; conditional deletion; plate chondrocytes
AB The skeleton plays a fundamental role in the maintenance of organ function and daily activities. The insulin-like growth factor (IGF) family is a group of polypeptide substances with a pronounced role in osteoblast differentiation, bone development, and metabolism. Disturbance of the IGFs and the IGF signaling pathway is inextricably linked with assorted developmental defects, growth irregularities, and jeopardized skeletal structure. Recent findings have illustrated the significance of the action of the IGF signaling pathway via growth factors and receptors and its interactions with dissimilar signaling pathways (Wnt/beta-catenin, BMP, TGF-beta, and Hh/PTH signaling pathways) in promoting the growth, survival, and differentiation of osteoblasts. IGF signaling also exhibits profound influences on cartilage and bone development and skeletal homeostasis via versatile cell-cell interactions in an autocrine, paracrine, and endocrine manner systemically and locally. Our review summarizes the role and regulatory function as well as a potentially integrated gene network of the IGF signaling pathway with other signaling pathways in bone and cartilage development and skeletal homeostasis, which in turn provides an enlightening insight into visualizing bright molecular targets to be eligible for designing effective drugs to handle bone diseases and maladies, such as osteoporosis, osteoarthritis, and dwarfism.
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TI Carboxypeptidase M modulates BMSCs osteogenesis-adipogenesis via the MAPK/ERK pathway: An integrated single-cell and bulk transcriptomic study
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DT Article
DE adipogenesis; BMSCs; osteogenesis; osteoporosis; scRNA-seq
ID mesenchymal stem-cells; bone-marrow; adipocyte differentiation; gene-expression; activation; culture; gamma; c3a
AB The pathogenesis of osteoporosis (OP) is closely associated with the disrupted balance between osteogenesis and adipogenesis in bone marrow-derived mesenchymal stem cells (BMSCs). We analyzed published single-cell RNA sequencing (scRNA-seq) data to dissect the transcriptomic profiles of bone marrow-derived cells in OP, reviewing 56 377 cells across eight scRNA-seq datasets from femoral heads (osteoporosis or osteopenia n = 5, osteoarthritis n = 3). Seventeen genes, including carboxypeptidase M (CPM), were identified as key osteogenesis-adipogenesis regulators through comprehensive gene set enrichment, differential expression, regulon activity, and pseudotime analyses. In vitro, CPM knockdown reduced osteogenesis and promoted adipogenesis in BMSCs, while adenovirus-mediated CPM overexpression had the reverse effects. In vivo, intraosseous injection of CPM-overexpressing BMSCs mitigated bone loss in ovariectomized mice. Integrated scRNA-seq and bulk RNA sequencing analyses provided insight into the MAPK/ERK pathway's role in the CPM-mediated regulation of BMSC osteogenesis and adipogenesis; specifically, CPM overexpression enhanced MAPK/ERK signaling and osteogenesis. In contrast, the

ERK1/2 inhibitor binimetinib negated the effects of CPM overexpression. Overall, our findings identify CPM as a pivotal regulator of BMSC differentiation, which provides new clues for the mechanistic study of OP.
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NR 49
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TI Local and Systemic Side Effects of Corticosteroid Injections for Musculoskeletal Indications
SO AMERICAN JOURNAL OF ROENTGENOLOGY
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DT Review
DE corticosteroid; hyperglycemia; musculoskeletal injection; skin atrophy; tendon weakening
ID steroid injection; intraarticular injection; lateral epicondylitis; methylprednisolone acetate; triamcinolone acetonide; adrenal insufficiency; joint injections; association; management; pain
AB Corticosteroid injections can be associated with a range of potential side effects, which may be classified as local or systemic and further stratified as immediate or delayed in onset. Radiologists performing image-guided musculoskeletal injections should recognize the potential side effects of corticosteroid medication when counseling patients before injection and consider such side effects in planning individual injections. This Review summarizes the available evidence regarding the local and systemic side effects of corticosteroid injections performed for musculoskeletal indications. Local side effects include postinjection flare, skin hypopigmentation and atrophy, infection, tendon rupture,

accelerated progression of osteoarthritis, and osseous injury. Systemic side effects include adrenal suppression or insufficiency, facial flushing, hypertension, hyperglycemia, and osteoporosis. Additional targeted counseling is warranted regarding side effects that are specific to certain patient populations (i.e., premenopausal women, patients with diabetes, athletes, and pediatric patients). Corticosteroid injections are contraindicated in the presence of superficial or deep infection, fracture, or a prosthetic joint. Guidelines on the frequency, duration, and maximal lifetime use of corticosteroid injections are currently lacking. Further research is needed regarding the long-term complications of continuous corticosteroid use, particularly with regard to osseous effects.
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TI Incidence of Total Knee Arthroplasty in Older Females with Knee Osteoarthritis and Osteoporosis Treated with Denosumab Compared with Those Treated Using Bisphosphonates: A Population-Based Cohort Study
SO LIFE-BASEL
LA English
DT Article
DE bisphosphonates; older patients; denosumab
ID bone; risk
AB This study aimed to evaluate the incidence of total knee arthroplasty (TKA), a marker of severe knee osteoarthritis (OA), among older females with concurrent knee OA and osteoporosis (OP) who were treated with denosumab or bisphosphonates. By analyzing a large population-based cohort, we sought to clarify how these treatments influence the progression of knee OA to the point of

requiring surgical intervention. We used data from the Taiwan National Health Insurance Research Database, including data from females aged >= 50 years diagnosed with knee OA and OP who initiated treatment between 2012 and 2019. Propensity score matching (1:1) resulted in the selection of 13,774 patients (6897 per group). The TKA incidence was analyzed using Cox proportional hazards models. Patients treated with denosumab had a lower TKA incidence than those treated with bisphosphonates (6.9 vs. 8.5 per 1000 person-years). The adjusted hazard ratio (aHR) for TKA in the denosumab group was 0.77 (95% CI: 0.62-0.97; p = 0.024), with the most pronounced effect observed in patients aged >= 80 years (aHR = 0.39, 95% CI: 0.20-0.77; p = 0.007). These findings suggest that denosumab reduces TKA risk more effectively than bisphosphonates and may serve as a superior treatment option for mitigating severe knee OA progression, especially in older adults.
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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AF Nair, Abhinav
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TI Assessing the Value of Imaging Data in Machine Learning Models to Predict Patient-Reported Outcome Measures in Knee Osteoarthritis Patients
SO BIOENGINEERING-BASEL
LA English
DT Article
DE knee osteoarthritis; WOMAC; machine learning; imaging; radiograph; MRI
AB Knee osteoarthritis (OA) affects over 650 million patients worldwide. Total knee replacement is aimed at end-stage OA to relieve symptoms of pain, stiffness and reduced mobility. However, the role of imaging modalities in monitoring symptomatic disease progression remains unclear. This study aimed to compare machine learning (ML) models, with and without imaging features, in predicting the two-year Western Ontario and McMaster Universities Arthritis Index (WOMAC) score for knee OA patients. We included 2408 patients from the Osteoarthritis

Initiative (OAI) database, with 629 patients from the Multicenter Osteoarthritis Study (MOST) database. The clinical dataset included 18 clinical features, while the imaging dataset contained an additional 10 imaging features. Minimal Clinically Important Difference (MCID) was set to 24, reflecting meaningful physical impairment. Clinical and imaging dataset models produced similar area under curve (AUC) scores, highlighting low differences in performance AUC < 0.025). For both clinical and imaging datasets, Gradient Boosting Machine (GBM) models performed the best in the external validation, with a clinically acceptable AUC of 0.734 (95% CI 0.687-0.781) and 0.747 (95% CI 0.701-0.792), respectively. The five features identified included educational background, family history of osteoarthritis, co-morbidities, use of osteoporosis medications and previous knee procedures. This is the first study to demonstrate that ML models achieve comparable performance with and without imaging features.
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NR 64
TC 3
Z9 3
U1 1
U2 2
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AU Batoon, L
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TI Efferocytosis and Bone Dynamics
SO CURRENT OSTEOPOROSIS REPORTS
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DT Review
DE Efferocytosis; Bone phagocytes; Efferocytes; Efferocytosis in bone; Macrophages
ID estrogen-receptor-beta; macrophage efferocytosis; parathyroid-hormone; tissue macrophages; osteal macrophages; cross-presentation; immune cells; marrow; osteoclasts; homeostasis
AB Purpose of Review This review summarizes the recently published scientific evidence regarding the role of efferocytosis in bone dynamics and skeletal health. Recent Findings Several types of efferocytes have been identified within the skeleton, with macrophages being the most extensively studied. Efferocytosis is not merely a 'clean-up' process vital for maintaining skeletal homeostasis; it also plays a crucial role in promoting resolution pathways and orchestrating bone dynamics, such as osteoblast-osteoclast coupling during bone remodeling. Impaired efferocytosis has been associated with aging-related bone loss and various skeletal pathologies, including osteoporosis, osteoarthritis, rheumatoid arthritis, and

metastatic bone diseases. Accordingly, emerging evidence suggests that targeting efferocytic mechanisms has the potential to alleviate these conditions. Summary While efferocytosis remains underexplored in the skeleton, recent discoveries have shed light on its pivotal role in bone dynamics, with important implications for skeletal health and pathology. However, there are several knowledge gaps and persisting technical limitations that must be addressed to fully unveil the contributions of efferocytosis in bone.
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U1 3
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Salla, M
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AF Al Hajj, Walaa
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TI Hydrolyzed collagen: Exploring its applications in the food and beverage industries and assessing its impact on human health - A comprehensive review
SO HELIYON
LA English
DT Review
DE Hydrolyzed collagen; Hydrolysates; Peptides; Denaturation; Antioxidant activity; Osteoarthritis
ID physicochemical property; antioxidant activity; skin; tripeptide; peptides; gelatin; protein; atherosclerosis; supplementation; fabrication
AB Hydrolyzed collagen (HC) consists of many small and low-molecular-weight amino acid chains (3-6 kDa) that can be produced either in basic or acidic media through enzymatic activity. This review details the sources of hydrolyzed collagen, its biosynthesis and its uses in the food industry, as well as its production process and beneficial health effects. HC can be extracted from a variety of sources, during which acetic acid is used for the extraction of collagen type I from bovine, porcine, marine, chicken, and fish cartilage. An enzymatic treatment combined with an acidic treatment has shown more efficient extraction results. Because of its properties, it is frequently employed in the food industry since it improves sensorial qualities, as well as in the cosmetic industry as a functional component in face and body cream because of its moisturizing properties. It is also used in the pharmaceutical development of antioxidant supplements often combined with hyaluronic acid and vitamin C. HC has an excellent therapeutic effect on osteoporosis and osteoarthritis, where a daily dose of 12 g enhances pain symptoms and contributes to bone health. It also increases mineral density and protects articular cartilage. This review presents the structure and properties of hydrolyzed collagen, which mainly consists of the amino acids glycine, proline and hydroxyproline in a triple helix, its extraction process and its sources, as well as its applications. In particular, the creation of Enzymatic Membrane Reactor allows the production of HC with different molecular weight distributions, allowing wider application.
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NR 71
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PU CELL PRESS
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AU Shibata, S
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AF Shibata, Sachi
Kon, Shigeyuki
TI Functional Ingredients Associated with the Prevention and Suppression of Locomotive Syndrome: A Review
SO BIOLOGICAL & PHARMACEUTICAL BULLETIN
LA English
DT Review
DE Key words locomotive syndrome; functional ingredient; osteoarthritis; osteoporosis; rheumatoid arthritis
ID nf-kappa-b; inhibits interleukin-1-beta-induced expression; arthritis synovial fibroblasts; human articular chondrocytes; collagen-induced arthritis; green tea catechins; ellagic acid; in-vitro; oxidative stress; carnosic acid
AB In 2007, the Japanese Orthopaedic Association proposed the concept of locomotive syndrome, a comprehensive description of conditions involving the functional decline of the locomotor system. Locomotive syndrome includes bone-related diseases such as osteoporosis, joint cartilage and disc-related diseases such as osteoarthritis and lumbar spondylosis, and sarcopenia and locomotive syndrome-related diseases. If left untreated, these diseases are likely to reduce mobility, necessitating nursing care. To prevent the progression of locomotive syndrome, a daily exercise routine and well-balanced diet are important, in addition to recognizing one's own decline in mobility. Therefore, research on the effectiveness of functional ingredients in the prevention and suppression of locomotive syndrome progression is ongoing. In this review, we summarize the latest reports on the effectiveness of five functional ingredients, namely, epigallocatechin gallate, resveratrol, curcumin, ellagic acid, and carnosic acid, in the treatment of osteoarthritis, osteoporosis, and rheumatoid arthritis, which are considered representative diseases of the locomotive syndrome.
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FU Japan Society for the Promotion of Science (JSPS) KAKENHI [21K17672]; Tojuro Iijima Foundation for Food Science and Technology; Public Foundation of Elizabeth Arnold-Fuji; Koyanagi Foundation; Kanamori Foundation
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TI Associations between condylar height relative to occlusal plane and condylar osseous condition and TMJ loading based on 3D measurements and finite element analysis
SO SCIENTIFIC REPORTS
LA English
DT Article
DE Condylar height; Temporomandibular point; Three-dimensional measurement; Three-dimensional finite element
ID temporomandibular-joint disorders; diagnostic-criteria; osteoarthritis; stress
AB To investigate the relationship between condylar height relative to occlusal plane (CHO) and condylar osseous condition and the changes of condylar stress loading before and after CHO modifications. The condylar osseous conditions of 434 temporomandibular joints (TMJ) were assessed and grouped. Measurements of anatomical parameters were performed on CT-based reconstructed 3D stomatognathic models. Differences in anatomical parameters of the jaws in the different groups were compared, and the correlation between the Angle alpha (representing the CHO ratio) and related parameters was investigated. A finite element model (FEM) was constructed using 3D finite element analysis (FEA). The Angle alpha was altered by modifying condylar position and the inclination of mandibular plane (MP) and occlusal plane (OP) based on the FEM to analyze condylar stress loading under different working conditions. There were differences in anatomical parameters among the different groups, with the smaller Angle alpha in the osseous destruction group. Angle alpha was negatively correlated with the inclination of MP and OP. The FEA illustrated condylar stress loading changed after modifying the Angle alpha by both two modalities. After modifying condylar position, the stress increased with the proximal movement of the condyle toward

the OP. After changing the inclination of MP and OP, the stress increased with increasing inclinations. Changes in CHO correlate with condylar osseous condition, and distal movement of the condyle to the OP and reduction of MP and OP inclination may reduce TMJ stress overload. In clinical practice, it is advisable to assess patients for sufficient CHO ratio, as insufficiency in CHO may elevate the risk of TMJ stress overload. The CHO ratio could be modulated by changing the inclination of the OP.
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SC Science & Technology - Other Topics
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PT J
AU Hu, YC
Huang, TC
Huang, LW
Cheng, HL
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AF Hu, Yu-Chen
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TI S-Equol Ameliorates Menopausal Osteoarthritis in Rats through Reducing Oxidative Stress and Cartilage Degradation
SO NUTRIENTS
LA English

DT Article
DE S-equol; isoflavones; osteoarthritis; degenerative joint disease; menopause
ID ii collagen degradation; knee osteoarthritis; subchondral bone; ovariectomized rats; metabolic syndrome; risk-factors; postmenopausal women; hand osteoarthritis; articular-cartilage; estrogen therapy
AB Osteoarthritis (OA) is a chronic degenerative disease leading to articular cartilage destruction. Menopausal and postmenopausal women are susceptible to both OA and osteoporosis. S-equol, a soy isoflavone-derived molecule, is known to reduce osteoporosis in estrogen-deficient mice, but its role in OA remains unknown. This study aimed to explore the effect of S-equol on different degrees of menopausal OA in female Sprague-Dawley (SD) rats induced by estrogen deficiency caused by bilateral ovariectomy (OVX) combined with intra-articular injection of mono-iodoacetate (MIA). Knee joint histopathological change; serum biomarkers of bone turnover, including N-terminal propeptide of type I procollagen (PINP), C-terminal telopeptide of type I collagen (CTX-I) and N-terminal telopeptide of type I collagen (NTX-I); the cartilage degradation biomarkers hyaluronic acid (HA) and N-terminal propeptide of type II procollagen (PIINP); and the matrix-degrading enzymes matrix metalloproteinases (MMP)-1, MMP-3 and MMP-13, as well as the oxidative stress-inducing molecules nitric oxide (NO) and hydrogen peroxide (H2O2), were assessed for evaluation of OA progression after S-equol supplementation for 8 weeks. The results showed that OVX without or with MIA injection induced various severity levels of menopausal OA by increasing pathological damage, oxidative stress, and cartilage matrix degradation to various degrees. Moreover, S-equol supplementation could significantly reduce these increased biomarkers in different severity levels of OA. This indicates that S-equol can lessen menopausal OA progression by reducing oxidative stress and the matrix-degrading enzymes involved in cartilage degradation.
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NR 81
TC 6
Z9 8
U1 4
U2 6
PU MDPI
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JI Nutrients
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PT J
AU Fu, LX
Zhang, PL
Wang, YC
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AF Fu, Liangxuan
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TI Microbiota-bone axis in ageing-related bone diseases
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE aging; skeletal degenerative diseases; bone metabolism; gut microbiota; bone
ID gut microbiota; t-cells; metabolites; differentiation; senescence; arthritis; hormone; mass
AB Bone homeostasis in physiology depends on the balance between bone formation and resorption, and in pathology, this homeostasis is susceptible to disruption by different influences, especially under ageing condition. Gut microbiota has been recognized as a crucial factor in regulating host health. Numerous studies have demonstrated a significant association between gut microbiota and bone metabolism through host-microbiota crosstalk, and gut microbiota is even an important factor in the pathogenesis of bone metabolism-related diseases that cannot be ignored. This review explores the interplay between gut microbiota and bone metabolism, focusing on the roles of gut microbiota in bone ageing and aging-related bone diseases, including osteoporosis, fragility fracture repair, osteoarthritis, and spinal degeneration from different perspectives. The impact of gut microbiota on bone metabolism during aging through modification of endocrinology system, immune system and gut microbiota metabolites are summarized, facilitating a better grasp of the pathogenesis of aging-related bone metabolic diseases. This review offers innovative insights into targeting the gut microbiota for the treatment of bone ageing-related diseases as a clinical therapeutic strategy.
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Zou NY, 2024, BONE RES, V12, P0, DOI 10.1038/s41413-023-00309-1
NR 77
TC 11
Z9 11
U1 10
U2 27
PU FRONTIERS MEDIA SA
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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PT J
AU Wang, YXJ
Guglielmi, G
Guermazi, A
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Griffith, JF
AF Wang, Yi Xiang J.
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Kwok, Timothy C. Y.
Griffith, James F.
TI Much lower prevalence and severity of spine degenerative changes among older Chinese women than among older Caucasian women and its implication for the interpretation of lumbar spine BMD T-score for Chinese women
SO SKELETAL RADIOLOGY
LA English
DT Article
DE Bone mineral density; Osteoporosis; Spine; Degeneration; Chinese women
ID bone-mineral density; united-states; disc degeneration; back-pain; osteoarthritis; hip; epidemiology; fracture; japanese
AB The prevalence and severity of spine degenerative changes have been noted to be lower among older Chinese women than among older Caucasian women. Spine degenerative changes associated with marginal osteophytosis, trabecular thickening, subchondral sclerosis, facet joint arthrosis, and disc space narrowing can all lead to artificially higher spine areal bone mineral density (BMD). The lower prevalence and severity of spine degeneration have important implications for the interpretation of spine areal BMD reading for Chinese women. With fewer contributions from spine degenerative changes, following natural aging, the declines of population group means of spine BMD and T-score are faster for Chinese women than for Caucasian women. While a cutpoint T-score & LE; -2.5 for defining spine densitometric osteoporosis is recommended for Caucasian women, for Chinese women the same cutpoint T-score of & LE; -2.5 inflates the estimated osteoporosis prevalence based on spine BMD measure. In addition to the use of an ethnicity-specific BMD reference database, a stricter cutpoint T-score for defining spine densitometric osteoporosis among older Chinese women should be applied.
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AU Hong, MP
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AF Hong, Minping
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TI The impact of creatine levels on musculoskeletal health in the elderly: a mendelian randomization analysis
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Creatine levels; Elderly musculoskeletal health; Hand grip strength; Mendelian randomization; Nutritional supplements
ID skeletal-muscle; supplementation; strength
AB BackgroundMusculoskeletal health among the elderly emerges as a pivotal public health concern against the backdrop of a globally aging population. Creatine, popular within fitness circles, has emerged as a subject of scientific inquiry for its potential benefits on elderly' musculoskeletal well-being. Despite extensive documentation of its effects on athletic performance, investigations into creatine's long-term contributions to the musculoskeletal health of the elderly are comparatively limited. Utilizing publicly accessible genetic datasets, this study aimed to explore the potential causal link between creatine levels and a variety of musculoskeletal health markers in the elderly population, such as osteoarthritis (OA), rheumatoid arthritis (RA), osteoporosis (OP), bone-specific alkaline

phosphatase, bone mineral density(BMD), serum calcium levels, and reduced hand grip strength in individuals aged 60 and above.MethodsOur methodological approach was grounded in Mendelian Randomization (MR) analysis, with a primary emphasis on the Inverse Variance Weighted (IVW) technique, to explore potential causal links under specific assumptions and limitations inherent to MR analysis.ResultsA significant inverse relationship was observed between creatine levels and reduced hand grip strength in individuals aged 60 and above (OR = 0.64, b=-0.44, p = 0.01), suggesting higher creatine levels might be beneficial in maintaining hand grip strength. Conversely, analysis of other bone health parameters, including bone-specific alkaline phosphatase, bone mineral density, serum calcium levels, and conditions such as osteoarthritis, rheumatoid arthritis, and osteoporosis, yielded p-values exceeding 0.05, denoting no statistically significant associations.ConclusionsThis study provides preliminary evidence indicating a link between creatine levels and decreased hand grip strength among the elderly, notably in individuals aged 60 and older. This finding is significant for understanding the potential impact of creatine supplementation on elderly Musculoskeletal health and underscores the need for evidence-based decision-making in nutritional supplementation. To robustly validate these observations, it is essential to conduct future randomized controlled trials with large sample sizes.
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Z9 6
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TI NRF2 in age-related musculoskeletal diseases: Role and treatment prospects
SO GENES & DISEASES
LA English
DT Review
DE Intervertebral disc degeneration; NRF2; Osteoarthritis; Osteoporosis; Sarcopenia
ID intervertebral disc degeneration; transcription factor nrf2; kappa-b activation; oxidative stress; skeletal-muscle; stem-cells; mitochondrial biogenesis; signaling pathway; osteoarthritis chondrocytes; osteoclast differentiation
AB The NRF2 pathway is a metabolic- and redox-sensitive signaling axis in which the transcription factor controls the expression of a multitude of genes that enable cells to survive environmental stressors, such as oxidative stress, mainly by inducing the expression of cytoprotective genes. Basal NRF2 levels are maintained under normal physiological conditions, but when exposed to oxidative stress, cells activate the NRF2 pathway, which is crucial for supporting cell survival. Recently, the NRF2 pathway has been found to have novel functions in metabolic regulation and interplay with other signaling pathways, offering novel insights into the treatment of various diseases. Numerous studies have shown that targeting its pathway can effectively investigate the development and progression of age-related musculoskeletal diseases, such as sarcopenia, osteoporosis, osteoarthritis, and intervertebral disc degeneration. Appropriate regulation of the NRF2 pathway flux holds promise as a means to improve musculoskeletal function, thereby providing a new avenue for drug treatment of age-related musculoskeletal diseases in clinical settings. The review summarized an overview of the relationship between NRF2 and cellular processes such as oxidative stress, apoptosis, inflammation, mitochondrial dysfunction, ferroptosis, and autophagy, and explores

the potential of targeted NRF2 regulation in the treatment of age-related musculoskeletal diseases. (c) 2023 The Authors. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co., Ltd. This is an open access article under the CC BY license (http://creativecommons.org/ licenses/by/4.0/).
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TI Screening of active components of melastoma dodecandrum lour. against diabetic osteoporosis using cell membrane chromatography-mass spectrometry
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE melastoma dodecandrum lour.; isovitexin; RAGE pathway; diabetic osteoporosis; cell membrane chromatography
ID glycation end-products; tnf-alpha
AB Background Melastoma dodecandrum Lour. (MD), a traditional botanical drug known for its hypoglycemic, antioxidant, and anti-inflammatory properties, is commonly used to treat diabetes, osteoarthritis, and osteoporosis. However, its specific active components against diabetic osteoporosis remain unclear.Purpose This study aimed to identify the key active components in MD using cell membrane chromatography coupled with mass spectrometry and validate their effects in vitro.Methods An AGEs-induced osteoblast injury model was established. MTT assays measured cell viability, and ALP activity was assessed using a biochemical kit. Western blotting was employed to detect the expression levels of osteoblast-related proteins OCN and RUNX2 and the AGE receptor protein RAGE. ELISA was used to determine the levels of SOD, MDA, CAT, and GPx. PCR quantified TNF-alpha expression to evaluate the protective effects and potential mechanisms of MD. The AGEs-induced osteoblast cell membrane chromatography-mass spectrometry method facilitated the rapid identification of potentially active compounds based on their affinity for the osteoblast cell membrane. Cell experiments further validated the activity of the characteristic component isovitexin.Results MD significantly improved cell viability in AGEs-damaged osteoblasts, enhanced ALP, SOD, CAT, and GPx activities, reduced MDA levels, increased OCN and RUNX2 protein expression, and decreased TNF-alpha mRNA and RAGE protein expression. Cell membrane chromatography identified 20 chemical constituents, including 13 flavonoids, 4 organic acids, 1 phenylpropanoids, 1 terpenoids, and 1 alkaloid. Cell experiments have confirmed that isovitexin has significant protective activity against osteoblasts and can inhibit the expression of specific receptor RAGE on the osteoblast membrane, consistent with the effect of MD.Conclusion MD and its active component, isovitexin, provide protective effects against AGEs-induced osteoblast injury, offering a basis for subsequent drug development.
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TI Multi-omics Analysis to Identify Key Immune Genes for Osteoporosis based on Machine Learning and Single-cell Analysis
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE Bioinformatics; Immunology; Machine learning; Osteoporosis; Single cells analysis

ID genome-wide expression; bone loss; induction; network
AB ObjectiveOsteoporosis is a severe bone disease with a complex pathogenesis involving various immune processes. With the in-depth understanding of bone immune mechanisms, discovering new therapeutic targets is crucial for the prevention and treatment of osteoporosis. This study aims to explore novel bone immune markers related to osteoporosis based on single-cell and transcriptome data, utilizing bioinformatics and machine learning methods, in order to provide novel strategies for the diagnosis and treatment of the disease.MethodsSingle cell and transcriptome data sets were acquired from Gene Expression Omnibus (GEO). The data was then subjected to cell communication analysis, pseudotime analysis, and high dimensional WGCNA (hdWGCNA) analysis to identify key immune cell subpopulations and module genes. Subsequently, ConsensusClusterPlus analysis was performed on the key module genes to identify different diseased subgroups in the osteoporosis (OP) training set samples. The immune characteristics between subgroups were evaluated using Cibersort, EPIC, and MCP counter algorithms. OP's hub genes were screened using 10 machine learning algorithms and 113 algorithm combinations. The relationship between hub genes and immunity and pathways was established by evaluating the immune and pathway scores of the training set samples through the ESTIMATE, MCP-counter, and ssGSEA algorithms. Real-time fluorescence quantitative PCR (RT-qPCR) testing was conducted on serum samples collected from osteoporosis patients and healthy adults.ResultsIn OP samples, the proportions of bone marrow-derived mesenchymal stem cells (BM-MSCs) and neutrophils increased significantly by 6.73% (from 24.01% to 30.74%) and 6.36% (from 26.82% to 33.18%), respectively. We found 16 intersection genes and four hub genes (DND1, HIRA, SH3GLB2, and F7). RT-qPCR results showed reduced expression levels of DND1, HIRA, and SH3GLB2 in clinical blood samples of OP patients. Moreover, the four hub genes showed positive correlations with neutrophils (0.65-0.90), immature B cells (0.76-0.92), and endothelial cells (0.79-0.87), while showing negative correlations with myeloid-derived suppressor cells (negative 0.54-0.73), T follicular helper cells (negative 0.71-0.86), and natural killer T cells (negative 0.75-0.85).ConclusionNeutrophils play a crucial role in the occurrence and development of osteoporosis. The four hub genes potentially inhibit metabolic activities and trigger inflammation by interacting with other immune cells, thereby significantly contributing to the onset and diagnosis of OP. (A, B) Annotation of single-cell datasets (GSE147287) via dimensionality reduction, based on key marker genes of each cell type (A), yielded a total of six distinct cell populations (B). (C) Utilizing the Find All Markers function, the top three genes with the highest expression levels in each cell type were calculated and visualized. (D, E) Analysis of the cellular proportions in samples with high bone density (osteoarthritis) and low bone density (osteoporosis) revealed a significant increase in the proportions of BM-MSCs and neutrophils in the low bone density samples.image
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NR 64
TC 4
Z9 4
U1 3
U2 17
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 ORTHOP SURG
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BP 2803
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PT J
AU Lozano, D
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AF Lozano, Daniel
Gortazar, Arancha R.
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TI Osteostatin, a peptide for the future treatment of musculoskeletal diseases
SO BIOCHEMICAL PHARMACOLOGY
LA English
DT Review
DE Bone anabolism; Osteoporosis; Fracture; Aging; PTHrP; Osteostatin
ID hormone-related protein; nuclear-localization signal; inhibits bone-resorption; si-doped hydroxyapatite; c-terminal fragments; parathyroid-hormone; pthrp 107-139; humoral hypercalcemia; postmenopausal women; osteoblastic cells
AB Nowadays, the treatment of musculoskeletal diseases represents a major challenge in the developed world. Diseases such as osteoporosis, osteoarthritis and arthritis have a high incidence and prevalence as a consequence of population aging, and they are also associated with a socioeconomic burden. Many efforts have been made to find a treatment for these diseases with various levels of success, but new approaches are still needed to deal with these pathologies. In this context, one peptide derived for the C-terminal extreme of the Parathormone related Peptide (PTHrP) called Osteostatin can be useful to treat musculoskeletal diseases. This pentapeptide (TRSAW) has demonstrated both in different in vitro and in vivo models, its role as a molecule with anti-resorptive, anabolic, anti-inflammatory, and anti-antioxidant properties. Our aim with this work is to review the Osteostatin main features, the knowledge of its mechanisms of action as well as its possible use for the treatment of osteoporosis, bone regeneration and fractures and against arthritis given its anti-inflammatory properties.
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NR 85
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PU PERGAMON-ELSEVIER SCIENCE LTD
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PT J
AU Yang, S
Liu, PC
Deng, S
Wang, YW
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Liu, Pengcheng
Deng, Song
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TI Oil Detachment Mechanism in Natural Surfactant Flooding from Silica Surface Molecular Dynamics Simulation
SO SPE JOURNAL
LA English
DT Article
ID behavior; dust; face
AB International regulations have compelled Europe and the United States to phase out certain traditional surfactants to mitigate the use of toxic and nonbiodegradable chemicals. Sodium cocoyl propionate (SCA), as a natural surfactant with high performance, has been proved to have the potential to replace traditional surfactants in previous studies. However, its performance has not fully met practical application requirements. Therefore, in this paper, molecular dynamics (MD) simulation was used to study the detachment behavior and mechanism of SCA, lauryl dimethylamine oxide (OA-12), emulsifier OP-10, and SOO (combination of SCA, OA-12, and OP-10) on crude oil (dodecane, C-12) at different temperatures (80-120 degrees C) and salinities (20 000-200 000 mg/L). The complex interaction mechanism between surfactant molecules and C-12 molecules was revealed by analyzing the simulated snapshot, radial distribution function (RDF), mean square displacement (MSD), and interaction energy. The simulated snapshot captures the conformational evolution of surfactant molecules at different time points, emphasizing the spatiotemporal and spatial changes of their dynamic behavior. A comparison of two desorption modes reveals that dispersive adsorption displacement and concentrated adsorption displacement are two possible desorption mechanisms. RDF analysis shows that the probability of SOO

molecules near C-12 remains high even at high-salinity and -temperature conditions. MSD analysis showed that the diffusion capacity of SOO was the highest at 100 degrees C, reaching 1.52867x10 (-5) cm(2)/ps. The calculation of interaction energy results reveals that SOO has a strong adsorption capacity for C-12, which is mainly due to the effect of van der Waals (vdW) force. This is because the C-12 molecules are inert, and their molecular movement is mainly determined by the polar groups of the surfactant. The main contribution of this study is to provide a natural surfactant with superior performance as a viable alternative, offering experimental settings for further improvement in SCA performance. This research provides theoretical guidance for on-site applications of SCA and SOO to enhance oil recovery.
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U2 10
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AU Lu, ZJ
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TI Genetic evidence of the causal relationship between chronic liver diseases and musculoskeletal disorders
SO JOURNAL OF TRANSLATIONAL MEDICINE
LA English
DT Article
DE Chronic liver disease; Musculoskeletal disorder; Mendelian randomization; Causal relationship; Primary sclerosing cholangitis; Hepatocellular carcinoma
ID genome-wide association; primary biliary cholangitis; mendelian randomization; risk loci; osteoporosis; instruments; sarcopenia; metaanalysis; cirrhosis; bias
AB BackgroundChronic liver diseases constitute a major global public health burden, posing a substantial threat to patients' daily lives and even survival due to the potential development of musculoskeletal disorders. Although the relationship between chronic liver diseases and musculoskeletal disorders has received extensive attention, their causal relationship has not been comprehensively and systematically investigated.MethodsThis study aimed to assess the causal relationships between viral hepatitis, primary biliary cholangitis, primary sclerosing cholangitis (PSC), liver cirrhosis, and hepatocellular carcinoma (HCC) with osteoporosis, osteoarthritis, and sarcopenia through bidirectional Mendelian randomization (MR) research. The traits related to osteoporosis and osteoarthritis included both overall and site-specific phenotypes, and the traits linked to

sarcopenia involved indicators of muscle mass and function. Random-effect inverse-variance weighted (IVW), weighted median, MR-Egger, and Causal Analysis Using the Summary Effect Estimates were used to evaluate causal effects, with IVW being the main analysis method. To enhance robustness, sensitivity analyses were performed using Cochran's Q test, MR-Egger intercept, MR-PRESSO global test, funnel plots, leave-one-out analyses, and latent causal variable model.ResultsThe forward MR analysis indicated that PSC can reduce forearm bone mineral density (beta = - 0.0454, 95% CI - 0.0798 to - 0.0110; P = 0.0098) and increase the risk of overall osteoarthritis (OR = 1.012, 95% CI 1.002-1.022; P = 0.0247), while HCC can decrease grip strength (beta = - 0.0053, 95% CI - 0.008 to - 0.0025; P = 0.0002). The reverse MR analysis did not find significant causal effects of musculoskeletal disorders on chronic liver diseases. Additionally, no heterogeneity or pleiotropy was detected.ConclusionsThese findings corroborate the causal effects of PSC on osteoporosis and osteoarthritis, as well as the causal impact of HCC on sarcopenia. Thus, the implementation of comprehensive preventive measures is imperative for PSC and HCC patients to mitigate the risk of musculoskeletal disorders, ultimately improving their quality of life.
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AU Tang, JD
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AF Tang, Jiandong
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TI Mesenchymal stem cell-derived extracellular vesicles: a regulator and carrier for targeting bone-related diseases
SO CELL DEATH DISCOVERY
LA English
DT Review
ID rheumatoid-arthritis; surface functionalization; tnf-alpha; in-vitro; exosm; osteoporosis; doxorubicin; delivery; angiogenesis; therapy
AB The escalating threat of bone-related diseases poses a significant challenge to human health. Mesenchymal stem cell (MSC)-derived extracellular vesicles (MSC-EVs), as inherent cell-secreted natural products, have emerged as promising treatments for bone-related diseases. Leveraging outstanding features such as high biocompatibility, low immunogenicity, superior biological barrier penetration, and extended circulating half-life, MSC-EVs serve as potent carriers for microRNAs (miRNAs), long no-code RNAs (lncRNAs), and other biomolecules. These cargo molecules play pivotal roles in orchestrating bone metabolism and vascularity through diverse mechanisms, thereby contributing to the amelioration of bone diseases. Additionally, engineering modifications enhance the bone-targeting ability of MSC-EVs, mitigating systemic side effects and bolstering their clinical translational potential. This review comprehensively explores the mechanisms through which MSC-EVs regulate bone-related disease progression. It delves into

the therapeutic potential of MSC-EVs as adept drug carriers, augmented by engineered modification strategies tailored for osteoarthritis (OA), rheumatoid arthritis (RA), osteoporosis, and osteosarcoma. In conclusion, the exceptional promise exhibited by MSC-EVs positions them as an excellent solution with considerable translational applications in clinical orthopedics.
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NR 176
TC 35
Z9 36
U1 4
U2 19
PU SPRINGERNATURE
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON, N1 9XW, ENGLAND
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EI 2058-7716
J9 CELL DEATH DISCOV
JI Cell Death Discov.
PD MAY 2
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VL 10
IS 1
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DI 10.1038/s41420-024-01973-w
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WC Cell Biology
SC Cell Biology
GA RE2V2
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PT J
AU Liu, QL
Zhao, YT
Shi, HB
Xiang, DW
Wu, CY
Song, LA
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AF Liu, Qilin
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TI Long-term haplodeficency of DSPP causes temporomandibular joint osteoarthritis in mice
SO BMC ORAL HEALTH
LA English
DT Article
DE Temporomandibular joint; Osteoarthritis; Mandibular condylar cartilage; Subchondral bone; Dentin sialophosphoprotein; Knockout mice
ID articular-cartilage; dentin phosphoprotein; subchondral bone; model; gene; deficient; chondrogenesis; mineralization; sialoprotein; fibromodulin
AB Background Extracellular matrix (ECM) protein malfunction or defect may lead to temporomandibular joint osteoarthritis (TMJ OA). Dentin sialophophoprotein (DSPP) is a mandibular condylar cartilage ECM protein, and its deletion impacted cell proliferation and other extracellular matrix alterations of postnatal condylar cartilage. However, it remains unclear if long-term loss of function of DSPP leads to TMJ OA. The study aimed to test the hypothesis that long-term haploinsufficiency of DSPP causes TMJ OA.Materials and methods To determine whether Dspp +/- mice exhibit TMJ OA but no severe tooth defects, mandibles of wild-type (WT), Dspp +/-, and Dspp homozygous (Dspp -/-) mice were analyzed by Micro-computed tomography (micro-CT). To characterize the progression and possible mechanisms of osteoarthritic degeneration over time in Dspp +/- mice over time, condyles of Dspp +/- and WT mice were analyzed radiologically, histologically, and immunohistochemically.Results Micro-CT and histomorphometric analyses revealed that Dspp +/- and Dspp -/- mice had significantly lower subchondral bone mass, bone volume fraction, bone mineral density, and trabecular thickness compared to WT mice at 12 months. Interestingly, in contrast to Dspp -/- mice which exhibited tooth loss, Dspp +/- mice had minor tooth defects. RNA sequencing data showed that haplodeficency of DSPP affects the biological process of ossification and osteoclast differentiation. Additionally, histological analysis showed that Dspp +/- mice had condylar cartilage fissures, reduced cartilage thickness, decreased articular cell numbers and severe subchondral bone cavities, and with signs that were exaggerated with age. Radiographic data showed an increase in subchondral osteoporosis up to 18 months and osteophyte formation at 21 months. Moreover, Dspp +/- mice showed increased distribution of osteoclasts in the subchondral bone and increased expression of MMP2, IL-6, FN-1, and TLR4 in the mandibular condylar cartilage.Conclusions Dspp +/- mice exhibit TMJ OA in a time-dependent manner,

with lesions in the mandibular condyle attributed to hypomineralization of subchondral bone and breakdown of the mandibular condylar cartilage, accompanied by upregulation of inflammatory markers.
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NR 40
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Z9 1
U1 2
U2 11
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN 1472-6831
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J9 BMC ORAL HEALTH
JI BMC Oral Health
PD MAY 14
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IS 1
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DI 10.1186/s12903-024-04320-8
PG 13
WC Dentistry, Oral Surgery & Medicine

SC Dentistry, Oral Surgery & Medicine
GA QS0W8
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PT J
AU Kuroda, T
Shiraki, M
Saito, M
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AF Kuroda, Tatsuhiko
Shiraki, Masataka
Saito, Mitsuru
Urano, Tomohiko
TI Spinal osteoarthritis is a risk of vertebral fractures in postmenopausal women
SO SCIENTIFIC REPORTS
LA English
DT Article
DE Osteoarthritis; Fracture risk; Bone mineral density
ID bone-mineral density; quality-of-life; knee osteoarthritis; co-morbidity; hip fracture; older-adults; elderly-men; osteoporosis; homocysteine; arthritis
AB Recent studies have revealed that despite high bone mineral density (BMD), osteoarthritis (OA) is a risk factor for osteoporotic fractures. However, the relationship between spinal OA and vertebral fractures has not yet been fully investigated. This longitudinal analysis used a subset of ongoing cohort study consist with Japanese postmenopausal women. The prevalence of spinal OA was determined using Kellgren-Lawrence grading method. The incidence of vertebral fractures were determined by semiquantitative analysis of spinal X-ray films. The relationship between the presence of spinal OA and incidence of vertebral fractures was evaluated using the Cox regression analysis. In total, 1480 women were followed up for 8.1 +/- 6.4 years. Among them, 923 were diagnosed with spinal OA, and incident vertebral fractures were observed in 473 participants. After adjusting for confounding variables, the spinal OA (>= grade 2) was a significant predictor of incident vertebral fractures (hazard ratio, 1.52; 95% confidence interval: 1.19-1.93, p = 0.001). Using ROC analysis, the thresholds of lumbar BMD for incident vertebral fractures were 0.952 g/cm2 for patients with spinal OA and 0.753 g/cm2 for patients without spinal OA. The presence of spinal OA is a risk factor for incident vertebral fractures despite high lumbar BMD.
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NR 38
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Z9 3
U1 0
U2 2
PU NATURE PORTFOLIO
PI BERLIN
PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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J9 SCI REP-UK
JI Sci Rep
PD FEB 12
PY 2024
VL 14
IS 1
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DI 10.1038/s41598-024-53994-1
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
GA HT1E1
UT WOS:001161656900022
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PT J
AU Magnusson, K
Turkiewicz, A
Rydén, M
Englund, M
AF Magnusson, Karin
Turkiewicz, Aleksandra
Ryden, Martin
Englund, Martin
TI Genetic Influence on Osteoarthritis Versus Other Rheumatic Diseases
SO ARTHRITIS & RHEUMATOLOGY
LA English
DT Article
ID ankylosing-spondylitis; osteoporotic fractures; elderly-people; classical twin; arthritis; joint; pain; heritability; association; prevalence
AB Objective. We aimed to compare the genetic contribution to osteoarthritis (OA) versus other rheumatic/ musculoskeletal diseases (RMDs) in the same population and to explore the role for any shared genetics between OA and other RMDs. Methods. In 59,970 Swedish twins aged 35 years or older, we estimated the heritability (the variance explained by genetic factors) of OA in peripheral joints, back and neck pain, shoulder pain (adhesive capsulitis, impingement syndrome, etc), rheumatoid arthritis, spondyloarthritis (SpA) and psoriatic arthritis, myalgia, and osteoporosis diagnosed in specialist and inpatient care. We also studied how much covariance between OA and each of the RMDs could be explained by genetics by studying phenotypic correlations in bivariate classical twin models. Results. Any-site OA and hip OA (50% and 64%) were among the most heritable RMDs (as compared with 23% for fibromyalgia [lowest] and 63% for SpA [highest]). The highest phenotypic correlations were between OA (any joint site) and shoulder pain in the same individual (r = 0.33, 95% confidence interval 0.31-0.35), of which 70% (95% confidence interval 52-88) could be explained by shared genetics. The phenotypic correlation between OA and back/neck pain was r = 0.25, with 25% to 75% explained by genetics. Phenotypic correlations between OA and each of the other RMDs were lower (r similar to 0.1 to r similar to 0.2), with inconclusive sources of variation. Conclusion. OA has relatively large heritability as compared with other RMDs. The coexistence of OA and shoulder pain, as well as back pain, was common and could often be explained by genetic factors. Findings imply similar etiologies of OA and several pain conditions.
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TI Perspectives on Osteoarthritis Treatment with Mesenchymal Stem Cells and Radix Achyranthis Bidentatae
SO AGING AND DISEASE
LA English
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DE mesenchymal stem cells; Radix Achyranthis Bidentatae; osteoarthritis; estrogen; intestinal flora
ID regulatory dendritic cells; osteogenic differentiation; induce; bone; chondrogenesis; osteoporosis; chondrocytes; generation; mechanism; apoptosis
AB Knee osteoarthritis, a widespread degenerative condition, impacts a younger population and leads to high disability rates. Nature often provides solutions for aging and disease prevention. Mesenchymal stem cells (MSCs) and Radix Achyranthis Bidentatae (AB) are natural substances with potential. MSCs can transform into various tissues, alleviating symptoms by releasing factors and miRNA, potentially slowing osteoarthritis progression. AB's compositions target knee joint cells, enhancing internal conditions and joint function. Both MSCs and AB share mechanisms for immune regulation, reducing cartilage apoptosis,

promoting chondrocyte formation, and addressing osteoporosis. They also influence estrogen and gut flora. This article reviews their roles in treating osteoarthritis, discussing apoptosis reduction, chondrocyte growth, bone enhancement, angiogenesis, and regulation of estrogen and intestinal flora. It explores their relationship and suggests AB's potential in stimulating mesenchymal stem cell repair for knee osteoarthritis treatment.
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TI A trend of Tai Chi in osteoporosis research: A bibliometric analysis
SO COMPLEMENTARY THERAPIES IN MEDICINE
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DT Article
DE Osteoporosis; Tai Chi; Bibliometric analysis; CiteSpace
ID bone-mineral density; randomized controlled-trial; muscle strength; exercise; balance; health; women; osteoarthritis
AB Background: Tai chi has been used to treat different forms of osteoporosis and increase bone density without the use of pharmaceuticals. Objective: The purpose

of this study was to use bibliometric analysis to methodically examine trends and hotspots of tai chi treatment for osteoporosis in order to generate references for further investigation. Methods: The articles on Tai Chi to treat osteoporosis was obtained from China National Knowledge Infrastructure (CNKI), Wan Fang, Web of Science (WOS) and PubMed between inception and November 8,2023. The annual publication volume, authors, institutions, and keywords, along with co-citation, clustering, and burst analysis, were analyzed using CiteSpace. Results: Totally, 328 publications were included. The number of annual publications has been rising rapidly in recent years. Beijing University of Chinese Medicine and Shanghai University of Sport are two of the best universities for Tai Chi treatment in osteoporosis. This area of research is dominated by Zhou, Y; Yu, DH; Pence, BC and Qin,L. Core authors and core institutions having a relatively low level of collaboration indicates that there may be limited interaction and cooperation between these key players in the field. China had the highest volume of publications, followed by the United States. Furthermore, the majority of the study subjects and influence mechanism are the focus of current research in this field. Conclusion: Tai Chi in osteoporosis research field is in a stage of stable development. Universities and higher education institutions are the leading institutions in this field. China and the United States emerging as high productivity nations. The study of Tai Chi in osteoporosis not only focuses on the applicable population, effects and intervention methods, but also gradually shifts to the mechanism study such as "secretion of beneficial factors", "physical exercise load" and "oxidative stress status".
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Z9 5
U1 7
U2 28
PU CHURCHILL LIVINGSTONE
PI EDINBURGH
PA JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND
SN 0965-2299
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J9 COMPLEMENT THER MED
JI Complement. Ther. Med.
PD NOV 15
PY 2024
VL 86
IS
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DI 10.1016/j.ctim.2024.103083
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WC Integrative & Complementary Medicine
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PT J
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Liu, XM
Wang, GD
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AF Wang, Wei
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Qian, Shenglong
TI Special contoured pelvic brim reconstruction titanium plate combined with trans-plate buttress screws (quadrilateral screws) for acetabular fractures with quadrilateral plate involvement through the anterior ilioinguinal approach
SO FRONTIERS IN SURGERY
LA English
DT Article
DE acetabulum; acetabular fracture fixation; quadrilateral plate; ilioinguinal approach; technique
ID biomechanical analysis; stoppa approach; dome impaction; fixation; reduction; exposure; column
AB Background Managing complicated acetabular fractures involving the quadrilateral plate (QLP) can be challenging for surgeons, especially when complicated by comminution and osteoporosis. Traditional implants do not provide sufficient fixed strength or a proper match. The new-type pre-contoured infrapectineal buttress plates may have drawbacks, such as inaccurate fitting on the medial surface of QLP and an inability to apply reversed compression force to resist medial displacement of femoral head. Therefore, the primary purpose of this study is to introduce a novel technique that utilizes a special contoured pelvic brim reconstruction titanium plate combined with quadrilateral screws to reduce and stabilize acetabular fractures involving the QLP through the ilioinguinal approach. Additionally, the secondary purpose is to evaluate both clinical effectiveness and radiological outcomes of this technique for QLP fractures.Methods We conducted a retrospective analysis of prospectively collected data from 48 patients (31 males and 17 females) who suffered from acute displaced fractures of the QLP and were treated between January 2012 and December 2019 using a special contoured plate combined with quadrilateral screws. The patients' mean age was 47.56 +/- 11.31 years (range: 19-73 years). Fracture patterns included 20 both-column fractures, 12

anterior column and posterior hemitransverse fractures, eight T-type fractures, five transverse fractures and three anterior column fractures with the QLP affected, all of which had femoral head protrusion. Immediate postoperative reduction quality was evaluated according to Matta's criteria. Final clinical functions were assessed during follow-up using the modified Merle d'Aubign & eacute; and Harris Hip scores (HHS).Results The patients were followed up for an average of 48.36 +/- 12.94 months (ranging from 24 to 84 months). The mean operative time was 246.08 +/- 54.30 min (ranging from 178 to 397 min), and the average blood loss was 715.16 +/- 263.84 ml (ranging from 400 to 2000ml). The radiological grading at postoperative stage showed anatomical reduction in 30 patients (62.50%), satisfactory reduction in 14 patients (29.17%), and poor reduction in four patients (8.33%). At the final follow-up, no re-protrusion of the femoral head was observed. In terms of functional outcome, the mean modified Merle d'Aubign & eacute;-Postel score was excellent in 26 patients (54.17%), good in 17 patients (35.42%), fair in four patients (8.33%), and poor in one patient (2.08%). The HHS was excellent in 23 patients (47.92%), good in 20 patients (41.67%), fair in four patients (8.33%), and poor in one patient (2.08%). The average HHS was 87.38 +/- 7.86 (ranging from 52 to 98). Postoperative complications included lateral femoral cutaneous nerve injury in two patients, delayed wound healing and subsequent development of an inguinal hernia in one patient. Late complications were observed in two patients, with one case of heterotopic ossification and another case of post-traumatic osteoarthritis underwent hip arthroplasty within two years after surgery.Conclusion Our results indicate that employing the contoured plate specifically designed for QLP injuries, in conjunction with quadrilateral screws through the ilioinguinal approach, can lead to positive outcomes in the treatment of displaced acetabular fractures involving the QLP. This straightforward and efficient technique offers a viable option for surgeons who are managing complex acetabular fractures.
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PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
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WC Surgery
SC Surgery
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PT J
AU Zhou, HJ
Chen, L
Su, H
Chen, GQ
Tong, PJ
AF Zhou, Haojing
Chen, Lei
Su, Hai
Chen, Guoqian
Tong, Peijian
TI Risk of low bone mineral density in patients with haemophilia: a systematic review and meta-analysis
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Review
DE Bone density; Haemophilia; Meta-analysis; Osteopenia; Osteoporosis
ID international-society; children; osteoporosis; experience; individuals; outcm; markers; adult; boys; mass
AB IntroductionPatients with haemophilia (PWH) may have lower bone mineral density (BMD). The risk of low BMD in PWH has not been comprehensively analysed. This study aimed to examine the risk of low BMD and changes in BMD in PWH.MethodsA comprehensive systematic search was performed in 4 databases: PubMed, Embase, Web of Science, and Cochrane Library. The last search was carried out on 11 December 2022. Review Manager 5.4 and Stata 16 were used for meta-analysis. Odds ratios were calculated by the incidence of low BMD between the haemophilia and control groups in each study. A meta-analysis of the odds ratios for each study was performed to estimate pooled odds ratios. Fixed effects models or random effects models were used to assess outcomes. Heterogeneity was evaluated using Higgins' I2. Subgroup analysis and sensitivity analysis were performed to interpret the potential source of heterogeneity. A funnel plot, Egger's regression test, and the trim-and-fill method were used to assess publication bias.Results19 of 793 studies, published between 2004 and 2022, that were identified by search strategy were included in this meta-analysis. The risk for low

BMD was approximately four times higher compared to controls. PWH have significantly lower lumbar spine, femoral neck, and total hip BMD. Subgroup analysis showed that the risk of low BMD did not increase significantly in developed countries. Very low heterogeneity was observed in the meta-analysis of the risk of low BMD. The result from Egger's regression test suggested that there may be publication bias. However, the meta-analysis results did not alter after the trim-and-fill correction and the findings were robust.ConclusionHaemophilia was associated with an increased risk of low BMD. However, the risk of low BMD did not increase significantly in developed countries. And BMD was reduced in PWH, regardless of age, region, or economic ability. For PWH, our concerns should extend beyond bleeding and osteoarthritis to encompass BMD starting at a young age.
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FU National Natural Science Foundation of China
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NR 57
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PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 J ORTHOP SURG RES
JI J. Orthop. Surg. Res.
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WC Orthopedics
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PT J
AU Yang, K
Wu, ZS
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AF Yang, Ke
Wu, Zhuoshu
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Xu, Hockin H. K.
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Huang, Xiaojing
Zhou, Wen
TI Unlocking the potential of stimuli-responsive biomaterials for bone regeneration
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE bone regeneration; stimuli-responsive biomaterials; scaffolds; implants; composites; hydrogels
ID intensity pulsed ultrasound; drug-delivery; osteogenic differentiation; smart biomaterials; current progress; click chemistry; powerful tool; stem-cells; scaffold; hydrogels
AB Bone defects caused by tumors, osteoarthritis, and osteoporosis attract great attention. Because of outstanding biocompatibility, osteogenesis promotion, and less secondary infection incidence ratio, stimuli-responsive biomaterials are increasingly used to manage this issue. These biomaterials respond to certain stimuli, changing their mechanical properties, shape, or drug release rate accordingly. Thereafter, the activated materials exert instructive or triggering effects on cells and tissues, match the properties of the original bone tissues, establish tight connection with ambient hard tissue, and provide suitable mechanical strength. In this review, basic definitions of different categories of stimuli-responsive biomaterials are presented. Moreover, possible mechanisms, advanced studies, and pros and cons of each classification are discussed and analyzed. This review aims to provide an outlook on the future developments in stimuli-responsive biomaterials.

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TI Diabetes Mellitus Should Be Considered While Analysing Sarcopenia-Related Biomarkers
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DT Review
DE sarcopenia; type 2 diabetes mellitus; biomarkers; inflammatory markers; myokines; adipokines; hormones; aging; older people
ID serum dehydroepiandrosterone-sulfate; growth-factor-i; skeletal-muscle mass; asian working group; cystatin c ratio; leptin levels; older-adults; inflammatory markers; glycemic control; blood leptin
AB Sarcopenia is a chronic, progressive skeletal muscle disease characterised by low muscle strength and quantity or quality, leading to low physical performance. Patients with type 2 diabetes mellitus (T2DM) are more at risk of sarcopenia than euglycemic individuals. Because of several shared pathways between the two diseases, sarcopenia is also a risk factor for developing T2DM in older patients. Various biomarkers are under investigation as potentially valuable for sarcopenia diagnosis and treatment monitoring. Biomarkers related to sarcopenia can be divided into markers evaluating musculoskeletal status (biomarkers specific to muscle mass, markers of the neuromuscular junction, or myokines) and markers assuming causal factors (adipokines, hormones, and inflammatory markers). This paper reviews the current knowledge about how diabetes and T2DM complications affect potential sarcopenia biomarker concentrations. This review includes markers recently proposed by the expert group of the European Society for the Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) as those that may currently be useful in phase II and III clinical trials of sarcopenia: myostatin (MSTN); follistatin (FST); irisin; brain-derived neurotrophic factor (BDNF); procollagen type III N-terminal peptide (PIIINP; P3NP); sarcopenia index (serum creatinine to serum cystatin C ratio); adiponectin; leptin; insulin-like growth factor-1 (IGF-1); dehydroepiandrosterone sulphate (DHEAS); C-reactive protein (CRP); interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-alpha). A better understanding of factors influencing these biomarkers' levels, including diabetes and diabetic complications, may lead to designing future studies and implementing results in clinical practice.
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TI Bone density in postmenopausal women with scoliosis is associated with markers of degenerative joint disease
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DT Article
ID mineral density; end-plate; marrow changes; lumbar spine; osteoporosis; osteoarthritis; age; hip
AB PurposeBone mineral density (BMD) measured with dual x-ray absorptiometry (DXA) is the clinical standard for the diagnosis of osteoporosis and prediction of bone fracture risk. In the aging skeleton, osteoporosis is often concomitantly present with degenerative joint disease (DJD).MethodsIn this study, we evaluated tissue-level changes in the differentially loaded concave (CC) and convex (CV) sides of the lumbar spine in a sample of postmenopausal women with scoliosis. We used a cumulative degeneration score to assess osteophyte formation, the severity of sclerotic morphology, and marrow changes as markers of DJD in the lumbar spine and examined the correlation between markers of DJD and BMD.ResultsMore severe osteophyte growth and sclerosis were present on the CC side of the spine. The degenerative score (DS) was higher on the CC side of the lumbar spine compared with the CV side. While CC BMD was positively correlated with CC DS and marrow, CV DS was not correlated with CV BMD. Marrow changes were correlated with DS on the CC lumbar spine.ConclusionThese results highlight the importance of mechanoadaptive as well as broader inflammatory processes in the manifestation of degenerative changes and local mineral deposition at the lumbar spine. DXA-based BMD measurement of osteoporosis need to be contextualized within the biomechanical and degenerative conditions of a joint rather than using a strict threshold cutoff.
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NR 32
TC 0
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U1 0
U2 0
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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PT J
AU Farooq, HMU
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Dang, K
AF Farooq, Hafiz Muhammad Umer
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TI Recent Progress in the Research on RNA-Binding Proteins in Bone Development and Diseases
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE RNA-binding proteins; osteoblastogenesis; osteoclastogenesis; osteoporosis; osteoarthritis
ID stem-cells; expression; rankl; osteoblasts; opg
AB RNA-binding proteins (RBPs), which regulate gene expression through post-transcriptional modifications of RNAs, play a role in diverse biological processes that include bone cell development and bone tissue formation. RBP dysregulation may result in aberrant bone homeostasis and contribute to various bone diseases. The function of RBPs in bone physiology and pathophysiology and

the underlying molecular mechanisms have been extensively studied in recent years. This article provides a review of such studies, highlighting the potential of RBPs as pivotal targets for therapeutic intervention.
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NR 64
TC 2
Z9 2
U1 3
U2 6
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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SC Biochemistry & Molecular Biology; Chemistry
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AU Matsumoto, T
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Nakamura, Kozo
Tanaka, Sakae
Yoshimura, Noriko
TI Impact of lumbar spine pathology on asymmetrical hallux valgus in a population-based cohort study
SO SCIENTIFIC REPORTS
LA English
DT Article
ID muscle
AB This study aims to investigate the influence of lumbar spine disorders on the development of asymmetric hallux valgus (HV). Data from the fifth survey of the Osteoarthritis/Osteoporosis Against Disability (ROAD) study, a nationwide prospective study in Japan, were analyzed. HV severity was categorized into 4 grades based on the radiographic HV angle, and asymmetric HV was defined as having at least one HV on either side, with a difference of two or more severity grades between the left and right. Controls were matched from both the Normal group (without HV on both sides) and the Symmetric group (HV on at least one side with a difference of one or less severity grades). Univariate analysis assessed lumbar conditions, and multinomial logistic regression analysis explored the association between lumbar spine disorders and asymmetric HV. Among 1997 participants, 27 had asymmetric HV. Univariate analysis revealed a higher incidence of L5 spondylolisthesis and scoliosis in the Asymmetric group. Multinomial logistic regression analysis revealed that scoliosis independently increased the likelihood of asymmetrical HV (Odds ratio [OR] = 3.586, 95%Confidence interval [CI] 1.111-11.582), but showed no significant impact on symmetrical HV (OR 0.910, 95% CI 0.355-2.334). Asymmetric HV is rare but may be associated with lumbar spine disorders, particularly scoliosis.
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NR 28
TC 0
Z9 0
U1 0
U2 1
PU NATURE PORTFOLIO
PI BERLIN
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TI Therapeutic Potential of Ginsenosides on Bone Metabolism: A Review of Osteoporosis, Periodontal Disease and Osteoarthritis
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE ginsenoside; ginseng; osteoporosis; periodontal disease; osteoarthritis; osteoblast; osteoclast; periodontal ligament fibroblast; chondrocyte
ID korean red ginseng; nf-kappa-b; inhibits osteoclast differentiation; glucocorticoid-induced osteoporosis; panax-ginseng; osteogenic differentiation; inflammatory caspases; articular-cartilage; induced osteolysis; mc3t3-e1 cells
AB Ginsenosides, bioactive compounds from the genus Panax, have potential therapeutic effects on diverse ailments, including diabetes. Emerging evidence suggests their involvement in bone metabolism. The present review summarizes the current understanding of the effects of ginsenosides on osteoporosis, periodontal disease, and osteoarthritis. Their mechanisms of action include effects on osteoblasts, osteoclasts, periodontal ligament fibroblasts (PDLFs), and chondrocytes, which are pivotal in maintaining bone, periodontal tissue, and cartilage homeostasis. Ginsenosides may exert their beneficial effects by enhancing PDLF and osteoblast activity, suppressing osteoclast function, augmenting chondrocyte synthesis in the cartilage matrix, and mitigating connective tissue degradation. Moreover, they possess antioxidant, anti-inflammatory, antimicrobial, and anti-pyroptotic properties. Their efficacy in increasing bone density, ameliorating periodontitis, and alleviating osteoarthritis symptoms has been demonstrated in preclinical studies using animal models. In terms of their mechanism of action, ginsenosides modulate cellular differentiation, activity, and key signaling pathway molecules, such as mitogen-activated protein kinases (MAPKs), while also regulating various mediators. Furthermore, the symptomatic relief observed in animal models lends further credence to their therapeutic utility. However, to translate these preclinical findings into clinical practice, rigorous animal and clinical investigations are imperative to ascertain the safety, efficacy, and optimal dosing regimens in human subjects.
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TC 16
Z9 17
U1 2
U2 13
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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TI Associations of parecoxib and other variables with recovery and safety outcomes in total knee arthroplasty: insights from a retrospective cohort study
SO FRONTIERS IN SURGERY
LA English
DT Article
DE total knee arthroplasty; analgesia; parecoxib; mobilization; postoperative pain; rehabilitation
ID length-of-stay; nonsteroidal antiinflammatory drugs; total hip; early ambulation; pain management; sodium; analgesia; nsaids; replacement; inhibitors
AB Background Early mobilization post-total knee arthroplasty (TKA) significantly affects patient outcomes. While parecoxib is known to reduce postoperative pain and morphine use with a favorable safety profile, its impact on mobilization timing post-TKA remains uncertain. This retrospective study aims to assess parecoxib's influence on postoperative mobilization timing in TKA patients without compromising safety.Methods This study included unilateral TKA patients treated for primary knee osteoarthritis under general anesthesia. We divided the study period into two intervals, 2007-2012 and 2013-2018, to evaluate temporal differences. Both the control group and parecoxib group received standard postoperative oral analgesics and as-needed intramuscular morphine. The control group did not receive parecoxib, while the parecoxib group did. Primary outcomes compared postoperative complications and mobilization timing between groups, with secondary outcomes including length of hospital stay (LOS), Visual Analog Scale (VAS) scores for pain, as-needed morphine use, and postoperative nausea/vomiting.Results Parecoxib did not increase postoperative complications. Unmatched comparison with patients in controlled group found that patients in

parecoxib group had significantly shortened mobilization time (2.2 +/- 1.1 vs. 2.7 +/- 1.6 days, P < 0.001) and LOS (6.7 +/- 2.5 vs. 7.2 +/- 2.1 days, P = 0.01). Multivariate analysis linked parecoxib use with faster mobilization (beta = -0.365, P < 0.001) but not LOS. Males showed increased mobilization time and LOS compared to females during the period of 2007-2018, but gender had no significant association with LOS during the period of 2013-2018. The 2013-2018 period saw significant reductions in both mobilization time and LOS. Use of a tourniquet and local infiltration analgesia showed no significant impact. ASA classification 1-2 was positively associated with faster mobilization but not LOS. Longer operation times were linked to delayed mobilization and increased LOS.Conclusion In this study, intravenous parecoxib injection, female gender, and shorter OP time had consistent positive association with shorter time to mobilization after individual multivariate analysis in 2 different period. The use of parecoxib had consistent no significant association with LOS. Only shorter OP time was consistent positive associated with shorter LOS.
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NR 49
TC 0
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PT J
AU Zhang, F
Zhang, W
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Zhang, Wei
TI Research progress in Alzheimer's disease and bone-brain axis
SO AGEING RESEARCH REVIEWS
LA English
DT Review

DE Alzheimer's disease; Orthopedic diseases; Bone-brain axis; Research progress
ID mild cognitive impairment; extracellular vesicles; rheumatoid-arthritis; osteoarthritis; pathogenesis; osteopontin; association; osteocalcin; damage; dkk1
AB Alzheimer's disease (AD) is the most common type of cognitive impairment. AD is closely related to orthopedic diseases, such as osteoporosis and osteoarthritis, in terms of epidemiology and pathogenesis. Brain and bone tissues can regulate each other in different manners through bone-brain axis. This article reviews the research progress of the relationship between AD and orthopedic diseases, bone-brain axis mechanisms of AD, and AD therapy by targeting bone-brain axis, in order to deepen the understanding of bone-brain communication, promote early diagnosis and explore new therapy for AD patients.
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NR 119
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Z9 35
U1 53
U2 83
PU ELSEVIER IRELAND LTD
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J9 AGEING RES REV
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PT J
AU Urano, T
Kuroda, T
Shiraki, M
AF Urano, Tomohiko
Kuroda, Tatsuhiko

Shiraki, Masataka
TI Nutritional and inflammation factors associated with current frailty level and effect of co-morbidities on the progression of frailty
SO GERIATRICS & GERONTOLOGY INTERNATIONAL
LA English
DT Article
DE chronic inflammatory process; co-morbidities; frailty; nutrition; risk factor
ID 25-hydroxyvitamin d; adiponectin levels; physical function; older women; interleukin-6; osteoarthritis; metabolism; mortality; risk
AB AimFrailty is defined as extreme vulnerability, a syndrome that exposes the individual to a higher risk of disability. While risk factors for frailty have been gradually uncovered, the full identification of biochemical factors and co-morbidities influencing frailty remains incomplete.MethodsCross-sectional and longitudinal analyses were performed to elucidate the risk factors for the prevalence and progression of frailty. The study included 1035 Japanese female outpatients. At baseline, biochemical markers were measured. Co-morbidities included diabetes mellitus, dyslipidemia, hypertension, vertebral osteoarthritis, and osteoporosis. Frailty levels were assessed using frailty scores ranging from 0 to 5. Prevalence of frailty was judged by a score of 3 or above, and progression was judged by an increase in the frailty score during the observation period. Multiple regression analysis was used for the cross-sectional analysis, and the Cox hazard model was used for the longitudinal analysis.ResultsOf the 1035 selected participants, 212 were diagnosed with frailty. Advanced age and log IL-6 and branched-chain amino acids (BCAA) levels were significant independent risk factors for frailty. Subjects were followed for 7.7 +/- 5.9 years and progression was observed in 130 subjects. Older age, the absence of hyperlipidemia, the presence of osteoporosis, and lower frailty scores were identified as significant risk factors for frailty progression.ConclusionsInflammatory and nutritional markers exhibited significant associations with the current frailty status, whereas co-morbidities such as osteoporosis or hyperlipidemia emerged as independent risk or protective factors of future frailty progression. Geriatr Gerontol Int 2024; center dot center dot: center dot center dot-center dot center dot. We searched for the biochemical factors and co-morbidities influencing frailty. Serum IL-6 and branched-chain amino acids (BCAA) levels exhibited significant associations with the current frailty status, whereas the presence of osteoporosis was identified as a significant risk factor for frailty progression. image
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Li, Xihai
TI Potential mechanism of tea for treating osteoporosis, osteoarthritis, and rheumatoid arthritis
SO FRONTIERS IN MEDICINE
LA English
DT Review
DE Camellia sinensis; osteoporosis; osteoarthritis; rheumatoid arthritis; cyberpharmacology; molecular docking
ID inhibits interleukin-1-beta-induced expression; ovariectomy-induced osteoporosis; mesenchymal stem-cells; green tea; knee osteoarthritis; camellia-sinensis; osteoblast differentiation; synovial fibroblasts; adipose-tissue; nitric-oxide
AB Osteoporosis (OP), osteoarthritis (OA), and rheumatoid arthritis (RA) are common bone and joint diseases with a high incidence and long duration. Thus, these conditions can affect the lives of middle-aged and elderly people. Tea drinking is a traditional lifestyle in China, and the long-term intake of tea and its active ingredients is beneficial to human health. However, the mechanisms of action of tea and its active ingredients against OP, OA, and RA are not completely elucidated. This study aimed to assess the therapeutic role and related mechanisms of tea and its active ingredients in OP, OA, and RA. Moreover, it expanded the potential mechanisms of tea efficacy based on network pharmacology and molecular docking. Results showed that tea has potential anti-COX properties and hormone-like effects. Compared with a single component, different tea components synergize or antagonize each other, thereby resulting in a more evident dual effect. In conclusion, tea has great potential in the medical and healthcare fields. Nevertheless, further research on the composition, proportion, and synergistic mechanism of several tea components should be performed.
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FU National Natural Science Foundation of China [82374495]; Science and Technology Programs Pilot Project of Fujian Province [2021Y0032]; Major Project for Young and Middle-aged Fund of Fujian Provincial Health Commission [2023ZQNZD016]
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NR 124
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Z9 6
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PT J
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TI Preparation and evaluation of injectable sustained-release Alendronate-loaded lipid liquid crystal on ovariectomy-induced osteoporosis in rats
SO JOURNAL OF DRUG DELIVERY SCIENCE AND TECHNOLOGY
LA English
DT Article
DE Lipid liquid crystal; Sustained release; Alendronate; Ovariectomy-induced osteoporosis; In-situ gel
ID delivery; mechanisms; system; women
AB Alendronate, a bisphosphonate compound, is used to treat osteoporosis by inhibiting bone resorption. However, oral consumption of Alendronate can cause severe gastrointestinal side effects, such as heartburn, difficulty swallowing, constipation or diarrhea, flatulence, and esophageal irritation or pain. To overcome this problem, an injectable sustained-release formulation of alendronate based on

lipid liquid crystal (LLC) using phosphatidylcholine (PC), sorbitan monooleate (SMO), glycerol di-oleate (GDO), and N-methyl-2-pyrrolidone (NMP) or ethanol solvents was recommended. This compound was added as a base to one side of a coupling syringe, while alendronate powder was added to the other. After combining the two syringes, the resulting formulations were transferred into tubes containing PBS for in-vitro evaluation. In formulations containing ethanol, the cumulative percentage of drug release, water content, and degradation were higher than in those with NMP. Furthermore, LLC gel formulations with ethanol solvent had lower viscosity and a cubic structure, whereas LLC containing NMP had a hexagonal structure, indicating slower and longer release of alendronate in LLC-NMP formulations. In-vivo evaluations of subcutaneous injections of alendronate based on LLC formulation in rats with ovariectomyinduced osteoporosis showed significant advancements in osteogenesis markers, including RUNX2, OPG, VEGF, and Type 1 Collagen, according to Western blot analysis. These finding highlight alendronate's potential not only as a bone resorption inhibitor but also as a bone formation stimulator. Additionally, histopathology results revealed no osteoclast activity or osteoarthritis reactions in the LLC formulation group. Hence, an injectable LLC formulation containing PC, SMO and NMP could be a suitable option for developing a sustained-release LLC formulation of alendronate for osteoporosis treatment.
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PT J
AU Lamo-Espinosa, JM
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TI Femoroacetabular Impingement and the Effect of Osteochondroplasty on Hip Osteoarthritis Prevention: The Pandora's Box Opening Process
SO CARTILAGE
LA English
DT Article
DE femoroacetabular impingement; hip arthroscopy; osteochondroplasty; osteoarthritis; hip preservation surgery
ID cam-type deformity; acetabular dysplasia; articular-cartilage; prevalence; features; inflammation; association; arthroscopy; cohort; index
AB Objective. This study was conducted to assess the effect of osteochondroplasty on osteoarthritis (OA) prevention, comparing radiological evolution between identical hips from the same patient who had undergone unilateral surgery. Design. We retrospectively reviewed radiological evolution between hips with similar shape from the same patient who had undergone unilateral surgery. In all, 56 FAI patients

(112 hips) with a mean age of 42.18 +/- 9.16 years and had undergone unilateral arthroscopy treatment have been included. Four independent researchers measured Wiberg, Acetabular and Alpha angles, Extrusion index, and Tonnis classification preoperatively to verify that operated and non-operated hips had the same shape. OA evolution was assessed by joint space width (JSW) in 3 different articular points and Tonnis classification. Results. No preoperative anatomical differences were present between groups (P > 0.05). At the end of follow-up (31.9 months), a decrease of JSW in the 3 points measured was found in OP hips (OP vs. N-OP; P < 0.01). These results were correlated with changes in the proportion of patients who progressed to grade III in Tonnis classification (from 1.3% preoperative to 23.2% at the end of follow-up). Conclusions. Osteochondroplasty and labrum procedures were not associated with OA prevention. The OP hips showed a faster OA degeneration, which was not seen in the N-OP. These results will encourage hip surgeons to perform further investigations to avoid the "Pandora's Box Opening Process."
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Prevot, Andre S. H.
TI Local incomplete combustion emissions define the PM2.5 oxidative potential in Northern India
SO NATURE COMMUNICATIONS
LA English
DT Article
ID positive matrix factorization; source apportionment; organic aerosol; multilinear engine; air-pollution; mass; radiocarbon; matter; trends; delhi
AB The oxidative potential (OP) of particulate matter (PM) is a major driver of PM-associated health effects. In India, the emission sources defining PM-OP, and their local/regional nature, are yet to be established. Here, to address this gap we determine the geographical origin, sources of PM, and its OP at five Indo-Gangetic Plain sites inside and outside Delhi. Our findings reveal that although uniformly high PM concentrations are recorded across the entire region, local emission sources and formation processes dominate PM pollution. Specifically, ammonium chloride, and organic aerosols (OA) from traffic exhaust, residential heating, and oxidation of unsaturated vapors from fossil fuels are the dominant PM sources inside Delhi. Ammonium sulfate and nitrate, and secondary OA from biomass burning vapors, are produced outside Delhi. Nevertheless, PM-OP is overwhelmingly driven by OA from incomplete combustion of biomass and fossil fuels, including traffic. These findings suggest that addressing local inefficient combustion processes can effectively mitigate PM health exposure in northern India.
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TI Evidence map of traditional Chinese exercises
SO FRONTIERS IN PUBLIC HEALTH

LA English
DT Review
DE traditional Chinese exercises; evidence map; randomized controlled trials; systematic reviews; Tai Chi
ID quality-of-life; tai chi; protocol; liuzijue; disease; balance; wuqinxi; design; gait
AB Objective: This study aimed to assess and visually depict the clinical evidence landscape of traditional Chinese exercises and identify any research gaps and future research needs. Methods: We comprehensively searched seven Chinese and English databases to identify randomized controlled trials (RCTs) and systematic reviews (SRs) evaluating the effects of traditional Chinese exercises from their inception until May 2023. The quality of evidence was assessed via the GRADE approach, and the research topics, intervention effects, and strength of evidence were graphically displayed. Results: This evidence map includes 2,017 studies, comprising 1,822 RCTs and 195 SRs. These studies were conducted globally in various countries. Among the traditional Chinese exercises, Tai Chi and Baduanjin have received the most research attention, with a growing number of publications. When traditional Chinese exercises were compared with the control groups, 88.2% of the included SRs reported significantly positive effects, 4.1% reported unclear effects, and 7.7% reported no significant differences. The findings suggested that traditional Chinese exercises could benefit patients with osteoarthritis, osteoporosis, hypertension, coronary heart disease, diabetes, chronic obstructive pulmonary disease, stroke, Parkinson's disease, anxiety, and depression. However, the overall quality of the evidence was suboptimal, with 11.3% rated as moderate, 45.6% as low, and 43.1% as critically low. Conclusion: This evidence map visually represents valuable information on traditional Chinese exercises. While most studies have reported significant benefits, the overall quality of evidence is low.
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TI Functional Imaging in Musculoskeletal Disorders in Menopause
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LA English
DT Review
DE Menopause; Functional imaging; SPECT/CT; PET/CT; 18F-fluoride; FDG
ID knee osteoarthritis; metabolic-activity; body-composition; hybrid camera; tc-99m mdp; osteoporosis; spect/ct; sarcopenia; pet; mri
AB Menopause -related musculoskeletal (MSK) disorders include osteoporosis, osteoarthritis (OA), sarcopenia and sarco-obesity. This review focuses on the applications of nuclear medicine for the functional imaging of the aforementioned clinical conditions. Bone Scan (BS) with 99mTc-labeled phosphonates, alone or in combination with MRI, can identify "fresh" vertebral collapse due to age -associated osteoporosis and provides quantitative parameters characterized by a good correlation with radiological indices in patients with OA. 18F-NaF PET, particularly when performed by dynamic scan, has given encouraging results for measuring bone turnover in osteoporosis and allows the evaluation of subchondral bone metabolic activity in OA. FDG PET can help discriminate between pathological and nonpathological vertebral fractures, especially by applying appropriate SUVbased thresholds. In OA, it can effectively image inflamed joints and support appropriate clinical management. Preliminary evidences suggest a possible application of FDG in sarco-obesity for the detection and quantification of visceral adipose tissue (VAT). Further studies are needed to better define the role of nuclear medicine in menopause -related MSK disease, especially as regards the possible impact of new radiopharmaceuticals (ie, FAPI and RGD peptides) and recent technological advances (eg, total -body PET/CT scanners). Semin Nucl Med 54:206-218 (c) 2023 Elsevier Inc. All rights reserved.
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TI A size-switchable microsphere loaded with salmon calcitonin as two-weekly dosing for osteoporosis therapy
SO EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS
LA English
DT Article
DE Drug delivery; Osteoporosis; Salmon calcitonin; Nano-carrier for peptides; Size-switchable microspheres
ID in-vitro; release; formulation; delivery; osteoarthritis; nanoparticles; peptides
AB Osteoporosis is a disease with an increased incidence of fractures due to decreased bone mass and destruction of the microstructure of bone tissue. Salmon calcitonin (sCT), as a peptide, possesses the ability to inhibit osteoclast activity and thus regulate bone metabolism in clinical. However, short half-life and unstable physicochemical properties leading to rapid degradation of sCT have severely limited its clinical application. In this study, a sizeswitchable microsphere was developed to solve the problem of frequent administration and poor stability of sCT. sCT was encapsulated into Egg PC to form anhydrous reverse micelles (ARM) and then ARM was encapsulated into microspheres (MS@ARM). The degradable composite microspheres were utilized to provide a drug reservoir for sustained release of ARM encapsulated with sCT to reduce the frequency of drug

administration, while the released ARM encapsulated with sCT entered the blood circulation to further protect sCT. In vitro release experiments demonstrated that the microspheres could sustain the release of sCT for at least 16 days. The microspheres MS@ARM showed the advanced therapeutic effect on the mouse model of glucocorticoid-induced osteoporosis (GIOP) at a low dosing frequency. The size-switchable microsphere is expected to be a new strategy for delivering sCT for osteoporosis treatment.
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TI Prevalence of complications and co-morbidities in males and females with obesity: Real-world insights from claims data analysis
SO DIABETES OBESITY & METABOLISM
LA English
DT Article
DE cardiometabolic disorder; hypertension; obesity
ID coronary-heart-disease; body-mass index; pooled analysis; depression; overweight; adults; metaanalysis; mortality; cohorts; women
AB Aim:To comprehensively examine the range of co-morbidities among males andfemales with a diagnosis of obesity. Materials and Methods:This cross-sectional retrospective study used US commercialand Medicare claims data from Merative MarketScan Research Databases to identifyadults (age >= 18 years) with a diagnosis of obesity with continuous insurance cover-age from 2018 to 2020. Co-morbidities were tabulated based on coded diagnoses,and prevalences were calculated in males and females across age groups. Age-adjusted odds ratios (ORs) determined differences in co-morbidities between thesexes. Results:Of an eligible sample of 6.9 million, we identified 2 028 273 individuals withat least one obesity-related International Classification of Diseases, 10th Revision,Clinical Modification code. The proportions of males and females with obesity were43.0% versus 57.0%. The most prevalent co-morbidities among males and femaleswere hypertension (62.8% vs. 52.2%), dyslipidaemia (63.3% vs. 50.3%) and depres-sion and/or anxiety (D/A; 29.7% vs. 48.5%). The prevalence of D/A was high in theyounger age group, but steadily decreased with age in both sexes; however,

hyper-tension and dyslipidaemia continued to increase with age. The presence of diagnosisof hypertension and dyslipidaemia was 6-8 years earlier in males than in females.Females had higher odds than males for osteoarthritis (OR 1.33), depression(OR 2.22) or osteoporosis (OR 7.10); allP< .0001. Conclusions:Males with obesity received a diagnosis of cardiovascular risk factors atan earlier age than females, which may have contributed to the higher prevalence ofcoronary heart disease. Understanding sex-specific variations in co-morbidities acrossages can support early screening and diagnosis of risk clusters for optimal obesitymanagement.
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TI Age-related bone diseases: Role of inflammaging
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DT Article
DE Aging; Bone; Inflammaging; Cell senescence; Aging-related diseases
ID gingival crevicular fluid; c-reactive protein; cellular senescence; dna-damage; secretory phenotype; oxidative stress; metabolic syndrome; diabetes-mellitus; immune-system; older-adults
AB Bone aging is characterized by an imbalance in the physiological and pathological processes of osteogenesis, osteoclastogenesis, adipogenesis, and chondrogenesis, resulting in exacerbated bone loss and the development of age-related bone diseases, including osteoporosis, osteoarthritis, rheumatoid arthritis, and periodontitis. Inflammaging, a novel concept in the field of aging research, pertains to the persistent and gradual escalation of pro-inflammatory reactions during the aging process. This phenomenon is distinguished by its low

intensity, systemic nature, absence of symptoms, and potential for management. The mechanisms by which inflammaging contribute to age-related chronic diseases, particularly in the context of age-related bone diseases, remain unclear. The precise manner in which systemic inflammation induces bone aging and consequently contributes to the development of age-related bone diseases has yet to be fully elucidated. This article primarily examines the mechanisms underlying inflammaging and its association with age-related bone diseases, to elucidate the potential mechanisms of inflammaging in age-related bone diseases and offer insights for developing preventive and therapeutic strategies for such conditions.
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ID periprosthetic joint infection; nmda glutamate receptors; gamma-aminobutyric-acid; d-aspartate receptors; primary total hip; plg-r-kt; urokinase receptor; cardiac-surgery; trauma patients; synaptic-transmission
AB The worldwide burden of skeletal diseases such as osteoporosis, degenerative joint disease and impaired fracture healing is steadily increasing. Tranexamic acid (TXA), a plasminogen inhibitor and anti-fibrinolytic agent, is used to reduce bleeding with high effectiveness and safety in major surgical procedures. With its widespread clinical application, the effects of TXA beyond anti-fibrinolysis have been noticed and prompted renewed interest in its use. Some clinical trials have characterized the effects of TXA on reducing postoperative infection rates and regulating immune responses in patients undergoing surgery. Also, several animal studies suggest potential therapeutic effects of TXA on skeletal diseases such as osteoporosis and fracture healing. Although a direct effect of TXA on the differentiation and function of bone cells in vitro was shown, few mechanisms of action have been reported. Here, we summarize recent findings of the effects of TXA on skeletal diseases and discuss the underlying plasminogen-dependent and-independent mechanisms related to bone metabolism and the immune response. We furthermore discuss potential novel indications for TXA application as a treatment strategy for skeletal diseases. (c) 2024 The Authors. Published by Elsevier B.V. on behalf of Chinese Pharmaceutical Association and Institute of Materia Medica, Chinese Academy of Medical Sciences. This is an open access article under the CC BY-NCND license

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TI Effects of emulsified and non-emulsified palm tocotrienol on bone and joint health in ovariectomised rats with monosodium iodoacetate-induced osteoarthritis
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Arthritis; Bone; Joint; Oestrogen; Tocochromanols; Vitamin E
ID bixa-orellana annatto; histomorphometric parameters; postmenopausal women; estrogen deficiency; articular-cartilage; delta-tocotrienol; mineral density; model; calcium; osteoporosis
AB Postmenopausal women are susceptible to osteoporosis and osteoarthritis. Tocotrienol, a bone-protective nutraceutical, is reported to prevent osteoarthritis in male rats. However, its efficacy on joint health in oestrogen deficiency has not been validated. Besides, data on the use of emulsification systems in enhancing bioavailability and protective effects of tocotrienol are limited. Ovariectomised adult female Sprague-Dawley rats (3 months old) were treated with refined olive oil, emulsified (EPT, 100 mg/kg/day with 25% vitamin E content), non emulsified palm tocotrienol (NEPT, 100 mg/kg/day with 50% vitamin E content) and calcium carbonate (1% w/v in drinking water) plus glucosamine sulphate (250 mg/kg/day) for 10 weeks. Osteoarthritis was induced with monosodium iodoacetate four weeks after ovariectomy. Baseline control was sacrificed upon receipt, while the sham group was not ovariectomised and treated with refined olive oil. EPT and NEPT prevented femoral metaphyseal and subchondral bone volume decline caused by ovariectomy. EPT decreased subchondral trabecular separation compared to the negative control. EPT preserved stiffness and Young's Modulus at the femoral mid-shaft of the rats. Circulating RANKL was reduced post-treatment in the EPT group. Joint width was reduced in all the treatment groups vs the negative control. The EPT group's grip strength was significantly improved over the negative control and NEPT group. EPT also preserved cartilage histology based on several Mankin's subscores. EPT performed as effectively as NEPT in preventing osteoporosis and osteoarthritis in ovariectomised rats despite containing less vitamin E content. This study justifies clinical trials for the use of EPT in postmenopausal women with both conditions.
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TI What Gets Measured Gets Managed
SO AMERICAN JOURNAL OF PHYSICAL MEDICINE & REHABILITATION
LA English
DT Article
DE Musculoskeletal; Practice-Based Research Network; Primary Care; Review

ID low-back-pain; primary-care management; research networks pbrns; attending primary-care; australian osteopaths; chiropractic patients; hip fracture; neck pain; outcm; osteoporosis
AB Musculoskeletal conditions are often managed in primary care settings. To facilitate research and healthcare quality, practice-based research networks offer sustained collaborations between clinicians and researchers. A scoping review was conducted to describe characteristics of practice-based research networks used for musculoskeletal research and musculoskeletal research conducted through practice-based research networks. Practice-based research networks were identified from 1) musculoskeletal-studies identified in OVID Medline, CINAHL, and Embase databases from inception to 5 February 2023 and in ClinicalTrials.gov and 2) from practice-based research network registries and websites. Among active musculoskeletal-focused practice-based research networks (i.e., currently recruiting and conducting research), an assessment of practice-based research network research good practices was performed. After screening 3025 records, 85 studies from 46 unique practice-based research networks met our eligibility criteria. Common conditions studied were low back pain (28%), musculoskeletal conditions not otherwise specified (25%), and osteoarthritis (19%). Thirty-two practice-based research networks (70%) were deemed to be active. Among active musculoskeletal-focused practice-based research networks, best practice data management information was retrievable for most (53%). Because of the scarcity of publicly available information, a large proportion of practice-based research network research good practice items was not assessable. Practice-based research networks have provided an avenue to assess clinical practice and patient outcomes related to musculoskeletal conditions. Further work to increase the transparency of musculoskeletal practice-based research network research practices is warranted.
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TI Ferroptosis: Regulatory mechanisms and potential targets for bone metabolism: A review
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DT Article
DE bone homeostasis; ferroptosis; iron; organelles; signal pathway
ID cell-death; molecular control; iron-metabolism; hepcidin; osteoarthritis; apoptosis; protects; element; binding; rna
AB Bone homeostasis is a homeostasis process constructed by osteoblast bone formation and osteoclast bone resorption. Bone homeostasis imbalance and dysfunction are the basis for the development of various orthopedic diseases such

as osteoporosis, osteoarthritis, and steroid-induced avascular necrosis of femoral head. Previous studies have demonstrated that ferroptosis can induce lipid peroxidation through the generation of reactive oxygen species, activate a number of signaling pathways, and participate in the regulation of osteoblast bone formation and osteoclast bone resorption, resulting in bone homeostasis imbalance, which is an important factor in the pathogenesis of many orthopedic diseases, but the mechanism of ferroptosis is still unknown. In recent years, it has been found that, in addition to iron metabolism and intracellular antioxidant system imbalance, organelle dysfunction is also a key factor affecting ferroptosis. This paper takes this as the starting point, reviews the latest literature reports at home and abroad, elaborates the pathogenesis and regulatory pathways of ferroptosis and the relationship between ferroptosis and various organelles, and summarizes the mechanism by which ferroptosis mediates bone homeostasis imbalance, with the aim of providing new directions for the research related to ferroptosis and new ideas for the prevention and treatment of bone and joint diseases.

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TI Research progress of the mechanisms and applications of ginsenosides in promoting bone formation
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LA English

DT Article
DE Ginsenoside; Herbal medicine; Bone formation; Bone microenvironment; Bone deficiency-related diseases; Bone tissue engineering
ID stem-cells; panax-ginseng; rg1; differentiation; pharmacokinetics; mineralization; regeneration; osteoporosis; growth; roles
AB Background: Bone deficiency-related diseases caused by various factors have disrupted the normal function of the skeleton and imposed a heavy burden globally, urgently requiring potential new treatments. The multi-faceted role of compounds like ginsenosides and their interaction with the bone microenvironment, particularly osteoblasts can promote bone formation and exhibit anti-inflammatory, vascular remodeling, and antibacterial properties, holding potential value in the treatment of bone deficiency-related diseases and bone tissue engineering. Purpose: This review summarizes the interaction between ginsenosides and osteoblasts and the bone microenvironment in bone formation, including vascular remodeling and immune regulation, as well as their therapeutic potential and toxicity in the broad treatment applications of bone deficiency-related diseases and bone tissue engineering, to provide novel insights and treatment strategies. Methods: The literature focusing on the mechanisms and applications of ginsenosides in promoting bone formation before March 2024 was searched in PubMed, Web of Science, Google Scholar, Scopus, and Science Direct databases. Keywords such as "phytochemicals", "ginsenosides", "biomaterials", "bone", "diseases", "bone formation", "microenvironment", "bone tissue engineering", "rheumatoid arthritis", "periodontitis", "osteoarthritis", "osteoporosis", "fracture", "toxicology", "pharmacology", and combinations of these keywords were used. Results: Ginsenoside monomers regulate signaling pathways such as WNT/beta-catenin, FGF, and BMP/TGF-beta, stimulating osteoblast generation and differentiation. It exerts angiogenic and anti-inflammatory effects by regulating the bone surrounding microenvironment through signaling such as WNT/beta-catenin, NF-kappa B, MAPK, PI3K/Akt, and Notch. It shows therapeutic effects and biological safety in the treatment of bone deficiencyrelated diseases, including rheumatoid arthritis, osteoarthritis, periodontitis, osteoporosis, and fractures, and bone tissue engineering by promoting osteogenesis and improving the microenvironment of bone formation. Conclusion: The functions of ginsenosides are diverse and promising in treating bone deficiency-related diseases and bone tissue engineering. Moreover, potential exists in regulating the bone microenvironment, modifying biomaterials, and treating inflammatory-related bone diseases and dental material applications. However, the mechanisms and effects of some ginsenoside monomers are still unclear, and the lack of clinical research limits their clinical application. Further exploration and evaluation of the potential of ginsenosides in these areas are expected to provide more effective methods for treating bone defects.
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TI Lumbar spine densitometry in people with spinal cord injury: Investigation of potential sources of errors
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DT Article

DE Densitometry; Lumbar spine; DEXA; Spinal cord injury; Bone mineral density; Artifacts.
ID bone-mineral density; x-ray absorptiometry; lower-extremity; osteoporosis; hip; osteoarthritis; calcification
AB Purpose: People with spinal cord injury (SCI) experience a considerable loss of bone after the injury. Lumbar spine (LS) bone mineral density (BMD) has been reported to be within the normal range, or even higher when assessed with DXA, in people with SCI; hence, it has been hypothesized that sources of error may spuriously increase LS BMD. The aim of this study was to describe the frequency of potential sources of error that may alter LS BMD measurement in a cohort of individuals with chronic SCI at baseline and over a 2-year period. Methods: We analyzed baseline and 2-year follow up DXA scans (Hologic Discovery QDR 4500, Hologic Inc., MA, USA) previously performed from a cohort of males and females with chronic SCI. Two physicians independently reviewed each scan, commented on whether the scan was appropriate for BMD analysis, should be reanalyzed, or be removed from the dataset, and reported on the presence of potential sources of error in LS BMD measurement. Results: We reviewed 115 lumbar spine DXA scans from 58 participants, and 107 (93.0 %) scans from 52 participants presented at least one potential source of error. At baseline, the average number of potential sources of error per scan was 5.5 f 1.7 and 5.7 f 1.5 according to rater 1 and rater 2, respectively. Follow-up scans presented an average of 5.6 f 1.6 and 5.7 f 1.4 potential sources of error according to rater 1 and rater 2, respectively. Facet sclerosis, osteophytes and difficulty in detecting bone edges were the most prevalent sources of error. Conclusion: The high frequency of potential sources of error is consistent with current recommendations against the use of LS BMD for fracture risk assessment in people with SCI.
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PT J
AU Kim, T
AF Kim, Taewook
TI Factors associated with predicting knee pain using knee X-ray and personal factors: A multivariate logistic regression and XGBoost model analysis from the Nationwide Korean Database (KNHANES)
SO PLOS ONE
LA English
DT Article
ID symptomatic knee; body-composition; osteoarthritis; prevalence; health; hand; hip; progression; weight; index
AB With increasing life expectancy, knee pain has become more prevalent, highlighting the need for early prediction. Although X-rays are commonly used for diagnosis, knee pain and X-ray findings do not always match. This study aims to identify factors contributing to knee pain in individuals with both normal and abnormal knee X-ray results to bridge the gap between X-ray findings and knee pain. Data from the fifth Korea National Health and Nutrition Examination Survey

(KNHANES), collected from 2010 to 2012, including data from 5,191 participants, were analyzed. The focus was on epidemiological characteristics, medical histories, knee pain, and X-ray grades. Multivariate logistic regression and extreme gradient boosting (XGBoost) models were used to predict knee pain in individuals with normal and abnormal knee X-rays, categorized by Kellgren-Lawrence grades. For normal X-rays, the logistic regression model identified aging, being female, higher BMI, lower fat percentage, osteoporosis, depression, and rural living as factors associated with knee pain. The XGBoost model highlighted BMI, age, and sex as key predictors, with a feature importance >0.1. For abnormal X-rays, logistic regression indicated that aging, being female, higher BMI, osteoporosis, depression, and rural living were associated with knee pain. The XGBoost model highlighted age, BMI, sex, and osteoporosis as key predictors, with a feature importance >0.1. Aging and being female were associated with knee pain due to hormonal changes in women, as well as cartilage and bone deterioration. Lower fat percentage was significantly associated with increased pain, which might be attributable to higher activity levels. Higher BMI and osteoporosis were significantly associated with knee pain, possibly due to increased stress and reduced resistance on knee structures, respectively. Depression was identified as a key predictor of knee pain in patients with normal X-rays, potentially attributable to psychosomatic factors. The study's limitations include its cross-sectional nature, which does not allow for the establishment of causal relationships, the lack of detailed medical history such as trauma history, and recall bias due to self-reported questionnaires. Future research should address these limitations to support our hypothesis.

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Wu, Decheng
TI Hyaluronic Acid-Based Microparticles with Lubrication and Anti-Inflammation for Alleviating Temporomandibular Joint Osteoarthritis
SO BIOMATERIALS RESEARCH
LA English
DT Article
ID histopathology
AB The pathogenesis of temporomandibular joint osteoarthritis (TMJOA) is closely associated with mechanical friction, which leads to the up-regulation of inflammatory mediators and the degradation of articular cartilage. Injectable drug-loaded microparticles have attracted widespread interest in intra-articular treatment of TMJOA by providing lubrication and facilitating localized drug delivery. Herein, a hyaluronic acid-based microparticle is developed with excellent lubrication properties, drug loading capacity, antioxidant activity, and anti-inflammatory effect for the treatment of TMJOA. The microparticles are facilely prepared by the self-assembly of 3-aminophenylboronic acid-modified hyaluronic acid (HP) through hydrophobic interaction in an aqueous solution, which can further encapsulate diol-containing drugs through dynamic boronate ester bonds. The resulting microparticles demonstrate excellent injectability, lubrication properties, radical scavenging efficiency, and antibacterial activity. Additionally, the drug-loaded microparticles exhibit a favorable cytoprotective effect on chondrocyte cells in vitro under an oxidative stress microenvironment. In vivo experiments validate that intra-articular injection of drug-loaded microparticles effectively alleviates osteoporosis-like damage, suppresses inflammatory response, and facilitates matrix regeneration in the treatment of TMJOA. The HP microparticles demonstrate excellent injectability and encapsulation capacity for diol-containing drugs, highlighting its potential as a versatile drug delivery vehicle in the intra-articular treatment of TMJOA.
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AF Cheng, Bizhen
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Hassan, Muhammad Jawad
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TI Foliar Application of Chitosan (CTS), γ-Aminobutyric Acid (GABA), or Sodium Chloride (NaCl) Mitigates Summer Bentgrass Decline in the Subtropical Zone
SO PLANTS-BASEL
LA English
DT Article
DE high temperature; photosynthesis; oxidative damage; osmotic adjustment; photochemical efficiency
ID heat-stress injury; creeping bentgrass; osmotic adjustment; lipid-peroxidation; high-temperature; root-growth; drought; tolerance; soil; metabolism
AB Creeping bentgrass (Agrostis stolonifera) is an excellent cool-season turfgrass that is widely used in urban gardening, landscaping, and golf turf. Triennial field experiments from 2017 to 2019 were conducted to investigate effects of the foliar application of chitosan (CTS), gamma-aminobutyric acid (GABA), or sodium chloride (NaCl) on mitigating summer bentgrass decline (SBD) and exploring the CTS, GABA, or NaCl regulatory mechanism of tolerance to summer heat stress associated with changes in chlorophyll (Chl) loss and photosynthetic capacity, osmotic adjustment (OA), oxidative damage, and cell membrane stability. The findings demonstrated that persistent ambient high temperatures above 30 degrees C during the summer months of 2017, 2018, and 2019 significantly reduced the turf quality (TQ), Chl content, photochemical efficiency of PSII (Fv/Fm and PIABS), leaf relative water content, and osmotic potential (OP) but significantly increased electrolyte leakage (EL) and the accumulations of free proline, water-soluble carbohydrate (WSC), hydrogen peroxide (H_2O_2), and malondialdehyde (MDA). The foliar application of CTS, GABA, or NaCl could significantly alleviate SBD, as reflected by improved TQ and delayed Chl loss during hot summer months. Heat-induced declines in Fv/Fm, PIABS, the net photosynthetic rate (Pn), the transpiration rate (Tr), and water use efficiency (WUE)

could be significantly mitigated by the exogenous application of CTS, GABA, or NaCl. In addition, the foliar application of CTS, GABA, or NaCl also significantly improved the accumulations of free proline and WSC but reduced the EL, OP, and H2O2 content and the MDA content in leaves of creeping bentgrass in favor of water and redox homeostasis in summer. Based on the comprehensive evaluation of the subordinate function value analysis (SFVA), the CTS had the best effect on the mitigation of SBD, followed by GABA and NaCl in 2017, 2018, and 2019. The current study indicates that the foliar application of an appropriate dose of GABA, CTS, or NaCl provides a cost-effective strategy for mitigating SBD.
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TI Attenuative effects of collagen peptide from milkfish (Chanos chanos) scales on ovariectomy-induced osteoporosis
SO FOOD SCIENCE & NUTRITION
LA English
DT Article
DE milkfish scales; osteoblast; osteoclast; osteoporosis; ovariectomized
ID ii collagen; bone; rankl; raw264.7; efficacy; cells; osteoclastogenesis; osteoarthritis; osteoblasts; hydrolysate
AB Osteoporosis is characterized by low bone mass, bone microarchitecture disruption, and collagen loss, leading to increased fracture risk. In the current study, collagen peptides were extracted from milkfish scales (MS) to develop potential therapeutic candidates for osteoporosis. MS was used to synthesize a crude extract of fish scales (FS), collagen liquid (COL), and hydroxyapatite powder (HA). COL samples were further categorized according to the peptide size of total COL (0.1 mg/mL), COL < 1 kDa (0.1 mg/mL), COL: 1-10 kDa (0.1 mg/mL), and COL > 10 kDa (0.1 mg/mL) to determine it. Semi-quantitative reverse transcription polymerase chain reaction (sqRT-PCR) and immunofluorescence labeling were used to assess the expression levels of specific mRNA and proteins in vitro. For in vivo studies, mice ovariectomy (OVX)-induced postmenopausal osteoporosis were developed, while the sham surgery (Sham) group was treated as a control. Collagen peptides (CP) from MS inhibited osteoclast differentiation in RAW264.7 cells following an insult with nuclear factor kappa-B ligand (RANKL). CP also enhanced osteoblast proliferation in MG-63 cells, possibly through downregulating NFATc1 and TRAP mRNA expression and upregulating ALP and OPG mRNA levels. Furthermore, COL1 kDa also inhibited bone density loss in osteoporotic mice. Taken together, CP may reduce RANKL-induced osteoclast activity while promoting osteoblast synthesis, and therefore may act as a potential therapeutic agent for the prevention and control of osteoporosis.
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TI Associations between fetal position at delivery and duration of active phase of labor: A historical cohort study
SO ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA
LA English
DT Article
DE Apgar score; cesarean section; instrumental delivery; labor duration; occiput posterior position
ID occiput posterior position; head position; intrapartum sonography; 2nd-stage; classification; stage
AB IntroductionIn clinical experience, occiput posterior (OP) position is associated with longer labor duration than occiput anterior (OA) position, but few studies have investigated the association between labor duration and fetal position. We aimed to compare duration of the active phase of labor in OP deliveries with OA deliveries in a contemporary population using survival methods. Secondary aims were to compare the frequencies of operative interventions, obstetric anal sphincter injuries (OASIS), postpartum hemorrhage, and newborn outcomes in OP with OA deliveries.Material and MethodsWe did a historical cohort study in three university hospitals in Norway from 2012 to 2022. Women with a single fetus in cephalic presentation, no previous cesarean section and gestational age >= 37 weeks were eligible and stratified into the first four groups of the Robson ten-group classification system (TGCS). We estimated the mean duration and calculated the hazard ratio (HR) for delivery using survival analyses. Cesarean sections and instrumental vaginal deliveries were censored.ResultsThe study population comprised 112 019 women, 105 571 (94.2%) were delivered in OA and 6448 (5.8%) in OP position. The estimated mean duration of the active phase of labor was longer in women with the fetus in OP position in all four TGCS groups. The estimated duration was longer in the OP groups in analyses stratified with respect to epidural analgesia and oxytocin augmentation. The graphical abstract illustrates the probability of delivery in OP compared with OA position in merged TGCS groups 1 and 2a, as a function of time. The unadjusted HR was 0.33 (95% CI 0.31-0.36) for fetuses delivered in OP position compared with OA position in TGCS

group 1, 0.25 (95% CI 0.21-0.27) in group 2a, 0.70 (95% CI 0.67-0.73) in group 3, and 0.61 (95% CI 0.55-0.67) in group 4a, respectively. Neither maternal age, gestational age, BMI nor birthweight had confounding effect. Operative delivery rates and OASIS rates were higher in OP position in all four groups.ConclusionsWe found longer duration of the active phase of labor in women with the fetus delivered in OP position in all four TGCS groups. One-minus survival plots showing the probability for delivery of fetus if in occiput posterior (OP) versus occiput anterior (OA) position during the active phase of labor for Robson ten-group classification system group 1 and 2a (nulliparous women). The red line represents OP deliveries, and the blue line represents OA deliveries.image
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Zheng, Chen-Xi
TI AMPK, a hub for the microenvironmental regulation of bone homeostasis and diseases
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Review
DE AMPK; bone; bone marrow mesenchymal stem cells; microenvironmental modulation
ID activated protein-kinase; mesenchymal stem-cells; oxidative stress; therapeutic target; energy sensor; differentiation; inflammation; apoptosis; pathway; complex
AB AMP-activated protein kinase (AMPK), a crucial regulatory kinase, monitors energy levels, conserving ATP and boosting synthesis in low-nutrition, low-energy states. Its sensitivity links microenvironmental changes to cellular responses. As the primary support structure and endocrine organ, the maintenance, and repair of bones are closely associated with the microenvironment. While a series of studies have explored the effects of specific microenvironments on bone, there is lack of angles to comprehensively evaluate the interactions between microenvironment and bone cells, especially for bone marrow mesenchymal stem cells (BMMSCs) which mediate the differentiation of osteogenic lineage. It is noteworthy that accumulating evidence has indicated that AMPK may serve as a hub between BMMSCs and microenvironment factors, thus providing a new perspective for us to understand the biology and pathophysiology of stem cells and bone. In this review, we emphasize AMPK's pivotal role in bone microenvironment modulation via ATP, inflammation, reactive oxygen species (ROS), calcium, and glucose, particularly in BMMSCs. We further explore the use of AMPK-activating drugs in the context of osteoarthritis and osteoporosis. Moreover, building upon the foundation of AMPK, we elucidate a viewpoint that facilitates a comprehensive understanding of the dynamic relationship between the microenvironment and bone homeostasis, offering valuable insights for prospective investigations into stem cell biology and the treatment of bone diseases. The hub status of AMP-activated protein kinase (AMPK) in the interplay between the bone microenvironment and cellular behaviors. AMPK in bone links BMMSCs with the microenvironment, responding to ATP, inflammation, ROS, calcium, and glucose changes. It regulates organelles and BMMSCs behavior, impacting proliferation, differentiation, factor secretion, and cell regulation. image
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TI Oxidative potential apportionment of atmospheric PM1: a new approach combining high-sensitive online analysers for chemical composition and offline OP measurement technique
SO ATMOSPHERIC CHEMISTRY AND PHYSICS
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DT Article
ID positive matrix factorization; aerosol source apportionment; airborne particulate matter; resolved trace-elements; water-soluble pm2.5; organic aerosol; air-pollution; ultrafine particles; multilinear engine; speciation monitor
AB Source apportionment models were widely used to successfully assign highly time-resolved aerosol data to specific emissions and/or atmospheric chemical processes. These techniques are necessary for targeting the sources affecting air quality and for designing effective mitigation strategies. Moreover, evaluation of the toxicity of airborne particulate matter is important since the classically measured particulate matter (PM) concentrations appear insufficient for characterizing the impact on human health. Oxidative potential (OP) measurement has recently been developed to quantify the capability of PM to induce an oxidative imbalance in the lungs. As a result, this measurement unit could be a better proxy than PM mass concentration to represent PM toxicity. In the present study, two source apportionment analyses were performed using positive matrix factorization (PMF) from organic aerosol (OA) mass spectra measured at a 15 min time resolution using a time-of-flight aerosol chemical speciation monitor (ToF-ACSM) and from 19 trace elements measured on an hourly basis using an online metal analyser (Xact 625i). The field measurements were carried out in summer 2018. While it is common to perform PMF studies individually on ACSMs and more recently on Xact datasets, here we used a two-step methodology leading to a complete PM 1 source apportionment. The outputs from both OA PMF and Xact PMF, the inorganic species concentrations from the ACSM, and the black carbon (BC) fractions (fossil fuel and wood burning) measured using an Aethalometer (AE33) were gathered into a single dataset and subjected to a combined PMF analysis. Overall, eight factors were identified, each of them corresponding to a more precise source than performing single PMF analyses. The results show that besides the high contribution of secondary ammonium sulfate

(28 %) and organic nitrate (19 %), about 50 % of PM 1 originated from distinct combustion sources, including emissions from traffic, shipping, industrial activities, cooking, and biomass burning. Simultaneously, PM 1 filters were collected during the experimental period on a 4 h sampling basis. On these filters, two acellular OP assays were performed (dithiothreitol; OP DTT and ascorbic acid; OP AA) and an inversion method was applied on factors issued from all PMFs to assess the contribution of the PM sources to the OP. This work highlights the sensitivity of OP AA to industrial and dust resuspension sources and those of OP DTT to secondary ammonium sulfate, shipping, and biomass burning.
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NR 129
TC 10
Z9 11
U1 8
U2 42
PU COPERNICUS GESELLSCHAFT MBH
PI GOTTINGEN
PA BAHNHOFSALLEE 1E, GOTTINGEN, 37081, GERMANY
SN 1680-7316
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J9 ATMOS CHEM PHYS
JI Atmos. Chem. Phys.
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DI 10.5194/acp-24-3257-2024
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WC Environmental Sciences; Meteorology & Atmospheric Sciences
SC Environmental Sciences & Ecology; Meteorology & Atmospheric Sciences
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PT J
AU Azari, F
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Quintiens, J
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AF Azari, Fahimeh
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TI Accuracy of photon-counting computed tomography for the measurement of bone quality in the knee
SO BONE
LA English
DT Article
DE Photon counting computed tomography; High-resolution peripheral quantitative; computed tomography; Micro-computed tomography; Subchondral trabecular bone; Subchondral bone plate; Micro-finite element
ID joint space width
AB Visualization and quantification of bone microarchitecture in the human knee allows gaining insight into normal bone structure, and into the structural changes occurring in the onset and progression of bone diseases such as osteoporosis and osteoarthritis. However, current imaging modalities have limitations in capturing the intricacies of bone microarchitecture. Photon counting computed tomography (PCCT) is a promising imaging modality that presents high-resolution three-dimensional visualization of bone with a large field of view. However, the potential of PCCT in assessing trabecular microstructure has not been investigated yet. Therefore, this study aimed to evaluate the accuracy of PCCT in quantifying bone microstructure and bone mechanics in the knee. Five human cadaveric knees were scanned ex vivo using a PCCT scanner (Naetom alpha, Siemens, Germany) with an in-plane resolution of 146.5 mu m and slice thickness of 100 mu m. To assess accuracy, the specimens were also scanned with a high-resolution peripheral quantitative computed tomography (HR-pQCT; XtremeCT II, Scanco Medical, Switzerland) with a nominal isotropic voxel size of 60.7 mu m as well as with micro-computed tomography (micro-CT; TESCAN UniTOM XL, Czech Republic) with a nominal isotropic voxel size of 25 mu m which can be considered gold standards for in vivo and ex vivo scanning, respectively. The thickness and porosity of the subchondral bone and the microstructure of the underlying trabecular bone were assessed in the load bearing regions of the proximal tibia and distal femur. The apparent Young's modulus was determined by micro-finite element (mu FE) analysis of subchondral trabecular bone (STB) in the load bearing regions of the proximal tibia using PCCT, HR-pQCT and micro-CT images. The correlation between PCCT measurements and micro-CT and HR-pQCT, respectively, was calculated. The coefficients of determination (R2) between PCCT and micro-CT based parameters, ranged from 0.69 to 0.87. The coefficients of determination between PCCT and HR-pQCT were slightly higher and ranged from 0.71 to 0.91. Apparent Young's modulus, assessed by mu FE analysis of PCCT images, correlated well with that of micro-CT (R2 = 0.80, mean relative difference = 19 %). However, PCCT overestimated the apparent Young's modulus by 47 %, but the correlation (R2 = 0.84) remained strong when compared to HR-pQCT. The results of this study suggest that PCCT can be used to quantify bone microstructure in the knee.
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NR 27
TC 12
Z9 13
U1 1
U2 8
PU ELSEVIER SCIENCE INC
PI NEW YORK
PA STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA
SN 8756-3282
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J9 BONE
JI Bone
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA KR6H0
UT WOS:001181727300001
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PT J
AU Shariatzadeh, H
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AF Shariatzadeh, Hooman
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TI Association of distal radial fracture with comorbidities: model development and validation

SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE Distal radial fracture; Model; Risk assessment; Comorbidities; Screening; General Population
ID bone-mineral density; body-mass index; fragility fractures; united-kingdom; epidemiology; risk; cohort; health
AB Background: To better assess the risk of distal radial fracture in the general population, we need models that take into account a wide range of risk factors other than osteoporosis. The objective was to develop and validate a model for association of patients' characteristics with distal radial fracture that effectively incorporates multifactorial aspects and includes comorbidities. Method: We analyzed data from a large Longitudinal Health Insurance Database between 2000 and 2013. The outcome of the study was the occurrence of distal radial fracture and the predictors were demographic and comorbidity data. Two machine learning models were developed and validated for patients >= 50 (N = 2745) and <50 (N = 1587) years of age. Results: For patients aged >= 50 years, selected characteristics included sex, age, urbanization level, osteoarthritis, carpal tunnel syndrome, obesity, hyperlipidemia, trigger finger, hypertension, hypothyroidism, diabetes, hyperthyroidism, and rheumatoid arthritis. For patients <50 years old, selected characteristics included age, sex, diabetes mellitus, urbanization level, carpal tunnel syndrome, hyperlipidemia, osteoarthritis, obesity, and hypertension. Accuracy, sensitivity, specificity, area under the curve, and likelihood ratio were 0.77, 0.83, 0.72, 0.77, and 2.92 for age >= 50 years and 0.73, 0.79, 0.67, 0.73, and 2.41 for age <50 years. Conclusion: The study models can serve as reliable screening tools to assess the risk of distal radial fracture in the general population before bone mineral density testing. In addition, they can be integrated into decision support systems to help healthcare providers identify high-risk patients for additional evaluation and education, ultimately improving the quality of care.
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CR Aalaie B, 2023, MOD RHEUMATOL, V0, P0, DOI DOI 10.1093/mr/road076
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NR 36
TC 2
Z9 2
U1 0
U2 2
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 0020-1383
EI 1879-0267
J9 INJURY
JI Injury-Int. J. Care Inj.
PD JUL 15
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VL 55
IS 7
BP
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DI 10.1016/j.injury.2024.111607
EA MAY 2024
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WC Critical Care Medicine; Emergency Medicine; Orthopedics; Surgery
SC General & Internal Medicine; Emergency Medicine; Orthopedics; Surgery
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UT WOS:001292987000001
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PT J
AU Wojdasiewicz, P
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Purrahman, D
Mahmoudian-Sani, MR
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AF Wojdasiewicz, Piotr
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Poniatowski, Lukasz A.
Purrahman, Daryush
Mahmoudian-Sani, Mohammad-Reza
Szukiewicz, Dariusz
TI The Role of Rosavin in the Pathophysiology of Bone Metabolism
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE rosavin; adaptogens; bone metabolism; osteoblasts; osteoporosis; Rhodiola rosea; bone loss; osteoclastogenesis; osteogenesis
ID osteoporosis-related fractures; histone deacetylases; costs; differentiation; osteoarthritis
AB Rosavin, a phenylpropanoid in Rhodiola rosea's rhizome, and an adaptogen, is known for enhancing the body's response to environmental stress. It significantly affects cellular metabolism in health and many diseases, particularly influencing bone tissue metabolism. In vitro, rosavin inhibits osteoclastogenesis, disrupts F-actin ring formation, and reduces the expression of osteoclastogenesis-related genes such as cathepsin K, calcitonin receptor (CTR), tumor necrosis factor receptor-associated factor 6 (TRAF6), tartrate-resistant acid phosphatase (TRAP), and matrix metallopeptidase 9 (MMP-9). It also impedes the nuclear factor of activated T-cell cytoplasmic 1 (NFATc1), c-Fos, the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kappa B), and mitogen-activated protein kinase (MAPK) signaling pathways and blocks phosphorylation processes crucial for bone resorption. Moreover, rosavin promotes osteogenesis and osteoblast differentiation and increases mouse runt-related transcription factor 2 (Runx2) and osteocalcin (OCN) expression. In vivo studies show its effectiveness in enhancing bone mineral density (BMD) in postmenopausal osteoporosis (PMOP) mice, restraining osteoclast maturation, and increasing the active osteoblast percentage in bone tissue. It modulates mRNA expressions by increasing eukaryotic translation elongation factor 2 (EEF2) and decreasing histone deacetylase 1 (HDAC1), thereby activating osteoprotective epigenetic mechanisms, and alters many serum markers, including decreasing cross-linked C-telopeptide of type I collagen (CTX-1), tartrate-resistant acid phosphatase 5b (TRACP5b), receptor activator for nuclear factor kappa B ligand (RANKL), macrophage-colony-stimulating factor (M-CSF), and TRAP, while increasing alkaline phosphatase (ALP) and OCN. Additionally, when combined with zinc and probiotics, it reduces pro-osteoporotic matrix metallopeptidase 3 (MMP-3), interleukin 6 (IL-6), and tumor necrosis factor alpha (TNF-alpha), and enhances anti-osteoporotic interleukin 10 (IL-10) and tissue inhibitor of metalloproteinase 3 (TIMP3) expressions. This paper aims to systematically review rosavin's impact on bone tissue metabolism, exploring its potential in osteoporosis prevention and treatment, and suggesting future research directions.
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TI Mapping knowledge landscapes and research frontiers of gastrointestinal microbiota and bone metabolism: a text-mining study
SO FRONTIERS IN CELLULAR AND INFECTION MICROBIOLOGY
LA English
DT Article
DE bibliometrics; hotspots; gastrointestinal microbiota; bone metabolism; CiteSpace; VOSviewer
ID gut microbiota; calcium-absorption; oxidative stress; short-chain; gen. nov.; osteoarthritis; butyrate; inflammation; association
AB Introduction Extensive research efforts have been dedicated to elucidating the intricate pathways by which gastrointestinal microbiota and their metabolites exert influence on the processes of bone formation. Nonetheless, a notable gap exists in the literature concerning a bibliometric analysis of research trends at the nexus of gastrointestinal microbiota and bone metabolism.Methods To address this scholarly void, the present study employs a suite of bibliometric tools including online platforms, CiteSpace and VOSviewer to scrutinize the pertinent literature in the realm of gastrointestinal microbiota and bone metabolism.Results and discussion Examination of the temporal distribution of publications spanning from 2000 to 2023 reveals a discernible upward trajectory in research output, characterized by an average annual growth rate of 19.2%. Notably, China and the United States emerge as primary contributors. Predominant among contributing institutions are Emory University, Harvard University, and the University of California. Pacifici R from Emory University contributed the most research with 15 publications. In the realm of academic journals, Nutrients emerges as the foremost publisher, followed closely by Frontiers in Microbiology and PLOS One. And PLOS One attains the highest average citations of 32.48. Analysis of highly cited papers underscores a burgeoning interest in the therapeutic potential of probiotics or probiotic blends in modulating bone metabolism by augmenting host immune responses. Notably, significant research attention has coalesced around the therapeutic interventions of probiotics, particularly Lactobacillus reuteri, in osteoporosis, as well as the role of gastrointestinal microbiota in the etiology and progression of osteoarthritis. Keyword analysis reveals prevalent terms including gut microbiota, osteoporosis, bone density, probiotics, inflammation, SCFAs, metabolism, osteoarthritis, calcium absorption, obesity, double-blind, prebiotics, mechanisms, postmenopausal women, supplementation, risk factors, oxidative stress, and immune system. Future research endeavors warrant a nuanced exploration of topics such as inflammation, obesity, SCFAs, postmenopausal osteoporosis, skeletal muscle, oxidative stress, double-blind trials, and pathogenic mechanisms. In summary, this study presents a comprehensive bibliometric analysis of global research on the interplay between gastrointestinal microbiota and bone metabolism, offering valuable insights for scholars, particularly nascent researchers, embarking on analogous investigations within this domain.

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TI Cellular Senescence: The Driving Force of Musculoskeletal Diseases
SO BIOMEDICINES
LA English
DT Review
DE cellular senescence; musculoskeletal diseases; osteoporosis; sarcopenia; osteoarthritis; SASP; physiology; exercise; nutrition; prevention

ID osteoarthritis; cells; knee; osteoporosis; activation; management; sarcopenia; exercise; life; hip
AB The aging of the world population is closely associated with an increased prevalence of musculoskeletal disorders, such as osteoporosis, sarcopenia, and osteoarthritis, due to common genetic, endocrine, and mechanical risk factors. These conditions are characterized by degeneration of bone, muscle, and cartilage tissue, resulting in an increased risk of fractures and reduced mobility. Importantly, a crucial role in the pathophysiology of these diseases has been proposed for cellular senescence, a state of irreversible cell cycle arrest induced by factors such as DNA damage, telomere shortening, and mitochondrial dysfunction. In addition, senescent cells secrete pro-inflammatory molecules, called senescence-associated secretory phenotype (SASP), which can alter tissue homeostasis and promote disease progression. Undoubtedly, targeting senescent cells and their secretory profiles could promote the development of integrated strategies, including regular exercise and a balanced diet or the use of senolytics and senomorphs, to improve the quality of life of the aging population. Therefore, our review aimed to highlight the role of cellular senescence in age-related musculoskeletal diseases, summarizing the main underlying mechanisms and potential anti-senescence strategies for the treatment of osteoporosis, sarcopenia, and osteoarthritis.
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TI Therapeutic potential of mesenchymal stem cell-derived exosomes in skeletal diseases
SO FRONTIERS IN MOLECULAR BIOSCIENCES
LA English
DT Review
DE MSC-exosomes; skeletal disease; osteoarthritis; osteoporosis; fracture
ID osteoarthritis; osteoporosis; inflammation; apoptosis; protect; rats
AB Skeletal diseases impose a considerable burden on society. The clinical and tissue-engineering therapies applied to alleviate such diseases frequently result in complications and are inadequately effective. Research has shifted from conventional therapies based on mesenchymal stem cells (MSCs) to exosomes derived from MSCs. Exosomes are natural nanocarriers of endogenous DNA, RNA, proteins, and lipids and have a low immune clearance rate and good barrier penetration and allow targeted delivery of therapeutics. MSC-derived exosomes (MSC-exosomes) have the characteristics of both MSCs and exosomes, and so they can have both immunosuppressive and tissue-regenerative effects. Despite advances in our knowledge of MSC-exosomes, their regulatory mechanisms and functionalities are unclear. Here we review the therapeutic potential of MSC-exosomes for skeletal diseases.
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NR 137
TC 10
Z9 11
U1 7
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TI Gender and age differences in the associations between cortical thickness and hand osteoarthritis severity: data from the Osteoarthritis Initiative
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Hand osteoarthritis; Radiography; Cortical thickness; Gender
ID bone-mineral density; rheumatoid-arthritis; postmenopausal women;

clinical-relevance; joint damage; knee; osteoporosis; progression; mass; population
AB Objective To evaluate gender differences in the association between metacarpal cortical thickness (T-cort)-a surrogate for bone density-and severity of radiographic hand osteoarthritis (HOA) in a longitudinal observational study. Method Hand radiographs of 3575 participants (2039 F/1536 M) from the Osteoarthritis Initiative were assessed at baseline and 48 months. A reader used a semi-automated software tool to calculate T-cort, a measurement of the cortical thickness, for metacarpals 2-4. Average T-cort at baseline and change in T-cort from baseline to 48 months was determined and stratified by gender and age for 7 5-year age groups. Spearman's rank correlation coefficients were calculated for the association of baseline T-cort and 2 measures of baseline HOA severity: the sum of Kellgren-Lawrence (KL) grade and total number of joints with radiographic HOA. Longitudinally, logistic regression was used to assess the relationship of T-cort loss to new finger joint radiographic HOA, increase in KL grades, and incident hand pain. Results Male T-cort was higher than females. Significant correlations between T-cort and radiographic severity were noted for women but not men, with stronger associations among women >60 years (rho = -0.25; 95% confidence interval (CI) = -0.31 to -0.19). Statistically significant associations were seen between T-cort change and radiographic osteoarthritis change among women but not men, with substantial gender differences for T-cort change, particularly ages 50 to 70 years ($p < 0.01$; e.g., T-cort change ages 55 to <60: males = -0.182 (0.118), females = -0.219 (0.124)). Conclusion We found significant HOA-related gender differences in T-cort, suggesting the involvement of female bone loss during and after menopause.
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NR 44
TC 1
Z9 1
U1 1
U2 6
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
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Xiao, Wen-feng
TI Irisin in degenerative musculoskeletal diseases: Functions in system and potential in therapy
SO PHARMACOLOGICAL RESEARCH
LA English
DT Article
DE Irisin; Degenerative musculoskeletal diseases; Bone-muscle-adipose crosstalk; Inflammation; Senescence; Cell death
ID ameliorates bone loss; alpha-v integrin; quality-of-life; postmenopausal women; skeletal-muscle; myokine irisin; oxidative stress; mitochondrial biogenesis; osteoporotic fractures; circulating irisin
AB Degenerative musculoskeletal diseases are a class of diseases related to the gradual structural and functional deterioration of muscles, joints, and bones, including osteoarthritis (OA), osteoporosis (OP), sarcopenia (SP), and intervertebral disc degeneration (IDD). As the proportion of aging people around the world increases, degenerative musculoskeletal diseases not only have a multifaceted impact on patients, but also impose a huge burden on the medical industry in various countries. Therefore, it is crucial to find key regulatory factors and potential therapeutic targets. Recent studies have shown that irisin plays an important role in degenerative musculoskeletal diseases, suggesting that it may become a key

molecule in the prevention and treatment of degenerative diseases of the musculoskeletal system. Therefore, this review provides a comprehensive description of the release and basic functions of irisin, and summarizes the role of irisin in OA, OP, SP, and IDD from a cellular and tissue perspective, providing comprehensive basis for clinical application. In addition, we summarized the many roles of irisin as a key information molecule in bone-muscle-adipose crosstalk and a regulatory molecule involved in inflammation, senescence, and cell death, and proposed the interesting possibility of irisin in degenerative musculoskeletal diseases.
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TI Outcome after total ankle replacement or ankle arthrodesis in end-stage ankle osteoarthritis on the basis of german-wide data: a retrospective comparative study over 10 years
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Ankle arthrodesis; Total ankle replacement; Ankle fusion; Revision rate; Unplanned surgery
ID long-term outcm; survivorship analysis; controlled-trial; risk-factors; arthroplasty; intermediate; experience; arthritis; survival; failures
AB Background In symptomatic end-stage osteoarthritis of the ankle joint, total ankle replacement and ankle arthrodesis are the two primary surgical options for patients for whom conservative treatment fails. Published revision rates are often biased and difficult to compare. In this study, unplanned reoperation rates and

revision rates were determined for both surgical interventions based on a large dataset, and risk factors for unplanned reoperations were identified. Methods German-wide health data of the largest German health-care insurance carrier between 2001 and 2012 were retrospectively analyzed, and unplanned reoperation rates within 10 years were determined for index surgeries conducted in 2001 and 2002. Unplanned reoperation rates within 5 years for index surgeries conducted in 2001/2002 were compared to index surgeries conducted in 2006/2007. Multivariate logistic regression was used to identify risk factors for unplanned reoperations. Results After ankle arthrodesis, 19% (95% confidence interval [CI], 16-22%) of 741 patients needed to undergo an unplanned reoperation within ten years. After total ankle replacement, the unplanned reoperation rate was 38% [95% CI, 29-48%] among 172 patients. For initial surgeries conducted at a later date, unplanned reoperation rates within five years were 21% [95% CI, 19-24%] for 1,168 ankle arthrodesis patients and 23% [95% CI, 19-28%] for 561 total ankle replacement patients. Significant risk factors for unplanned reoperations after ankle arthrodesis in the initial cohort were age < 50 years (odds ratio [OR] = 4.65 [95% CI 1.10;19.56]) and osteoporosis (OR = 3.72 [95% CI, 1.06;13.11]); after total ankle replacement, they were osteoporosis (OR = 2.96 [95% CI, 1.65;5.31]), Patient Clinical Complexity Level (PCCL) grade 3 (OR = 2.19 [95% CI, 1.19;4.03]), PCCL grade 4 (OR = 2.51 [95% CI, 1.22;5.17]) and diabetes mellitus (OR = 2.48 [95% CI, 1.33;4.66]). Kaplan-Meier analyses including 1,525 ankle arthrodesis patients and 644 total ankle replacement patients revealed an average unplanned reoperation-free time of approximately 17 years for both procedures. Conclusions Similar revision rates and unplanned reoperation rates for both procedures in the later-date cohort can likely be attributed to a learning curve for surgeons as well as advances in implant design. This analysis of billing health insurance data supports an increase in total ankle replacement surgeries.
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NR 69
TC 0
Z9 1
U1 0
U2 1
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD JUN 25
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IS 1
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DI 10.1186/s12891-024-07612-w
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA WK6N0
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PT J
AU Gula, Z
Losinska, K
Kuszmiersz, P
Strach, M
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AF Gula, Zofia
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Zimba, Olena
Dyczek, Lukasz
Haugeberg, Glenn
Korkosz, Mariusz
TI A comparison of comorbidities and their risk factors prevalence across rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis with focus on cardiovascular diseases: data from a single center real-world cohort
SO RHEUMATOLOGY INTERNATIONAL
LA English
DT Article
DE Rheumatoid arthritis; Psoriatic arthritis; Axial spondyloarthritis; Comorbidities; Cardiovascular diseases; Risk factors; Hypertension; Dyslipidemia; Obesity; Osteoporosis; Depression; Inflammatory arthritis; Real-world data.comorbidities; Real-world evidence; Cardiovascular risk
ID classification criteria; validation; burden
AB Management of comorbidities is essential to a patient-centered approach to the treatment of chronic inflammatory arthritis. The aim of this study was to compare the prevalence of comorbidities and their risk factors in rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) in a single center outpatient cohort. This cross-sectional study included adult patients diagnosed with RA, PsA, and axSpA from a single rheumatology outpatient center. Comorbidities were documented by physicians, and patients were categorized into two age groups, younger (< 45 years) and older (>= 45 years), with age- and gender-based comparisons. Disease activity, comorbidities, and cardiovascular (CV) risk factors were analyzed using chi-squared tests for categorical variables and independent samples t-tests for continuous variables, with p values < 0.05 considered statistically significant. Comorbidities were registered by physicians using GoTreatIt (R) Rheuma software. Among 508 RA, 267 PsA, and 285 axSpA patients, the four most common comorbidities were hypertension (36.4%, 25.1%, and 19.7%, respectively), dyslipidemia (19.5%, 15.4%, 14.7% respectively), obesity (16.9%, 22.5%, 14% respectively) and thyroid disease (21.5%, 13.9%, 11.2% respectively). Other comorbidities differed among the diseases and included osteoporosis, osteoarthritis, diabetes mellitus, arrhythmia, and asthma in RA, diabetes mellitus, depression and asthma in PsA, osteoporosis and serious infection in axSpA. RA patients, compared to axSpA had a higher prevalence of coronary artery disease (4.1% vs. 0.7%, p = 0.006), arrhythmia (6.9% vs. 2.5%, p = 0.008) and

major adverse cardiac events (2.6% vs. 0.4%, p = 0.024) compared to axSpA. Osteoporosis was more frequent in RA (19.1%) and axSpA (8.4%) than in PsA (2.3%; p < 0.001) and was frequently diagnosed in patients aged < 45. Depression prevalence was surprisingly low (1.6%, 5.2%, and 1.8%, respectively). RA patients had the highest multimorbidity rate, with 26.6% reporting three or more comorbidities, compared to 16.8% in PsA and 10.6% in axSpA (p < 0.001). Health status was poorest in RA and worse in women compared to men for all diseases. RA, PsA, and axSpA share the same four most common comorbidities: hypertension, dyslipidemia, obesity, and thyroid disease but have different prevalence of other disorders and CV risk factors, indicating the need for an individual screening and prevention approach. The possible unrecognition of depression should be evaluated.
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FU National Center for Research and Development (NCBiR) [0026/2019-00]
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NR 30
TC 6
Z9 7
U1 0
U2 1
PU SPRINGER HEIDELBERG
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J9 RHEUMATOL INT
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BP 2817
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WC Rheumatology
SC Rheumatology
GA O7A2N
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PT J
AU Al-Saleh, J
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TI Prevalence of comorbidities among patients with rheumatoid arthritis in the UAE: a case-control study
SO BMJ OPEN
LA English
DT Article
DE RHEUMATOLOGY; Cardiovascular Disease; EPIDEMIOLOGY; Musculoskeletal disorders; Overweight
ID ischemic-heart-disease; risk-factors; association; fibromyalgia; depression; severity; duration; impact
AB Objectives Data on the rate of comorbidities in Arab patients with rheumatoid arthritis (RA) are limited, and extrapolating the prevalence of comorbidities from international studies is challenging. This study aimed to investigate the prevalence

of comorbidities in patients with RA, compare it with that in non-RA controls and explore the association between the body mass index of patients with RA and comorbidities. Design This is a retrospective, case-control study. Setting This study included patients receiving secondary care at the Rheumatology Department of a public hospital in the Emirate of Dubai. The controls were recruited from patients receiving primary and secondary care at the Dubai Academic Health Corporation in the fourth quarter of 2022. Participants This study included all consecutive UAE national patients with RA who visited the rheumatology clinic. The study included 1756 participants in an age-matched and sex-matched control group and 439 patients with RA. Of these, 88.6% were female, and the median age was 55 years. Each RA case was randomly matched with four controls of the same age and sex. All relevant information, including case and control demographics and comorbidities, was retrieved from the electronic medical record. Primary and secondary outcome measures The relative risk of comorbidities was compared between patients with RA and age-matched controls. The relationship between obesity in RA and the frequency of comorbidities was determined. Results This study revealed that 188 (42.8%) patients with RA had at least one comorbidity, whereas only 636 (36.2%) individuals in the control group had at least one comorbidity (OR 1.3; 95% CI 1.1 to 1.6, p<0.01). Patients with RA were more likely to have ischaemic heart disease (OR 3.9; 95% CI 2.3 to 6.6, p<0.0001), fibromyalgia (OR 25; 95% CI 13 to 34, p<0.0001), cataract (OR 5.8; 95% CI 4 to 8.5, p<0.0001), osteoporosis (OR 6.8; 95% CI 4.6 to 10, p<0.0001) and knee osteoarthritis (OR 6.1; 95% CI 4.8 to 7.8, p<0.0001). Conclusions Patients with RA were more likely to have cardiovascular, pulmonary and musculoskeletal comorbidities compared with the control group. Obese patients with RA had a higher incidence of comorbidity than non-obese patients with RA.
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FU Sheikh Hamdan Medical Science Award, non-profitable agency.; Sheikh Hamdan Medical Science Award
CR Ajeganova S, 2013, ARTHRIT CARE RES, V65, P78, DOI 10.1002/acr.21710
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NR 60
TC 2
Z9 2
U1 0
U2 1
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PA BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND
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WC Medicine, General & Internal
SC General & Internal Medicine
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UT WOS:001353889400001
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PT J
AU Heinz, T
Hoxha, M
Anderson, PM
Jakuscheit, A
Weissenberger, M
Luedemann, M
Rak, D
Rudert, M
Horas, K
AF Heinz, Tizian
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Weissenberger, Manuel
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Horas, Konstantin
TI Prevalence and Associated Risk Factors for Hypovitaminosis D in Patients Scheduled for Primary Total Knee Arthroplasty in Germany
SO NUTRIENTS
LA English
DT Article
DE total knee arthroplasty; vitamin D insufficiency; osteoporosis; hypovitaminosis D; Germany; prevalence
ID vitamin-d deficiency; geographic-variation; orthopedic patients; joint arthroplasty; united-states; osteoarthritis; cancer; us
AB Objective: Several studies have reported a high prevalence of hypovitaminosis D

in orthopedic patients. The purpose of this prospective observational study was to report on the prevalence of hypovitaminosis D in patients scheduled for elective primary total knee arthroplasty (TKA) and its associated risk factors. Methods: In this monocentric cohort study, 25(OH) vitamin D serum levels were measured in 687 consecutive patients undergoing primary total knee arthroplasty (TKA) over a period of twelve months. Vitamin D levels were classified into deficiency (<20 ng/mL), insufficiency (20-29 ng/mL), and sufficiency (>= 30 ng/mL). The study assessed the association of vitamin D levels with demographic and clinical factors, including age, sex, BMI, smoking status, and season of measurement. Statistical analyses included chi-square tests, correlation analyses, and multiple linear regression to identify significant predictors of vitamin D levels. Results: The cohort had a mean age of 67.70 +/- 8.95 years and a mean BMI of 31.00 +/- 5.71 kg/m(2). Collectively, 33.9% of patients were vitamin D deficient, a further 32.9% were insufficient, and only 33.2% were sufficient. Vitamin D levels varied significantly with the season and were associated with obesity and smoking. Specifically, there was a small significant inverse correlation between BMI and vitamin D levels ($r = -0.17$, $p < 0.01$). Furthermore, regular nicotine abuse was linked to lower vitamin D levels ($r = 0.14$, $p < 0.01$). Multiple linear regression analysis reveals that age, BMI, nicotine abuse, and season were small significant predictors of preoperative vitamin D levels (R-2 = 0.15, adjusted R-2 = 0.12). A total of 121 (17.61%) patients reported routine vitamin D intake prior to surgery. Supplementing patients had a significantly higher mean serum vitamin D level and a significant reduction in the mean length of in-hospital stay ($p < 0.01$). Conclusions: The prevalence of vitamin D insufficiency and deficiency in patients undergoing elective primary TKA is alarmingly high. In ongoing efforts to optimize the efficacy and outcome of the TKA procedure, orthopedic surgeons should be advised to strongly implement the role of perioperative vitamin D levels in their routine practice.
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CR Alzohily B, 2024, SCI REP-UK, V14, P0, DOI 10.1038/s41598-024-58154-z
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NR 40
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PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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WC Nutrition & Dietetics
SC Nutrition & Dietetics
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UT WOS:001377252100001
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PT J
AU Liu, MF
Jiang, K
Ju, XC
AF Liu, Mengfei
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TI Biomechanical effects of femoral prosthesis misalignment on the structure of the lateral compartment during medial unicompartmental knee arthroplasty in osteoporotic patients
SO JOURNAL OF ORTHOPAEDIC SURGERY
LA English
DT Article

DE finite element analysis; knee; osteoporosis; unicompartmental knee arthroplasty
ID finite-element-analysis; proximal tibial strain; articular-cartilage; survivorship; outcm; stress; depth; joint; leads
AB BackgroundThis study aims to investigate the impact of varying coronal alignments of femoral prostheses on stress and strain distributions within the lateral compartment following unicompartmental knee arthroplasty (UKA) in patients with normal bone density and osteoporosis using finite element analysis. Additionally, it examines the relationship between osteoporosis and the progression of osteoarthritis in the lateral compartment postoperatively.MethodsUKA models were developed for both normal bone and osteoporotic conditions using a validated finite element model of the knee. Seven alignment conditions for the femoral prosthesis were simulated: 0 degrees (neutral alignment), varus angles of 3 degrees, 6 degrees, and 9 degrees, and valgus angles of 3 degrees, 6 degrees, and 9 degrees, resulting in a total of 14 scenarios. Stress and strain distributions in the meniscus, tibial cartilage, and femoral cartilage of the lateral compartment were evaluated.ResultsThe results indicated that stress and strain in the meniscus, tibial cartilage, and femoral cartilage of the lateral compartment increased with greater varus alignment and decreased with greater valgus alignment in both normal and osteoporotic models. At equivalent alignment angles, stress and strain were consistently higher in the osteoporotic model (M2) compared to the normal bone model (M1), although the peak equivalent stress in the tibial cartilage was lower in the M2 model than in the M1 model.ConclusionsIn patients with osteoporosis undergoing fixed-bearing medial UKA, varus malalignment of the femoral prosthesis can lead to increased stress and strain in the lateral compartment's meniscus, tibial cartilage, and femoral cartilage. These findings suggest that osteoporosis may contribute to abnormal stress and strain distributions in the lateral compartment following UKA, potentially accelerating the progression of osteoarthritis in this region postoperatively.
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NR 32
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Z9 3
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JI J. Orthop. Surg.
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WC Orthopedics; Surgery
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PT J
AU Wei, YB
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AF Wei, Yibao
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TI Protective effects of emodin on subchondral bone and articular cartilage in osteoporotic osteoarthritis rats: A preclinical study
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Article

DE Knee osteoarthritis; Osteoporosis; Subchondral bone; Emodin; Articular cartilage; OP-OA
ID mesenchymal stem-cells; differentiation
AB Background: Osteoporotic osteoarthritis (OP-OA) is a severe pathological form of OA, urgently requiring precise management strategies and more efficient interventions. Emodin (Emo), an effective ingredient found in the traditional Chinese medicine rhubarb, has been dEmonstrated to promote osteogenesis and inhibit extracellular matrix degradation. In this study, we aimed to investigate the interventional effects of Emo on the subchondral bone and cartilage of the knee joints in OP-OA model rats. Methods: Thirty-two SD rats were randomly and equally divided into sham, OP-OA, Emo low-dose, and Emo highdose groups. Micro-CT scanning was conducted to examine the bone microstructure of the rat knee joints. H&E and Safranin O and Fast Green staining (SO&FG) were performed for the pathomorphological evaluation of the rat cartilage tissues. ELISA was used to estimate the rat serum expression levels of inflammatory factors, including interleukin-1 beta (IL-1 beta) and tumor necrosis factor-alpha (TNF-alpha). Additionally, the CCK-8 assay was utilized for determining the viability of Emo-treated BMSCs. Western blot and real-time PCR analyses were also employed to measure the bone formation indexes and cartilage synthesis and decomposition indexes. Lastly, the osteogenic and chondrogenic differentiation efficiency of the BMSCs was investigated via Alizarin Red and Alcian Blue staining. Results: Emo intervention alleviated the bone microstructural disruption of the subchondral bone and articular cartilage in the OP-OA rats and up-regulated the expression of bone and cartilage anabolic metabolism indicators, decreased the expression of cartilage catabolism indicators, and diminished the expression of inflammatory factors in the rat serum ($P<0.05$). Furthermore, Emo reversed the decline in the osteogenic and chondrogenic differentiation ability of the BMSCs ($P<0.05$). Conclusion: Emo intervention mitigates bone loss and cartilage damage in OP-OA rats and promotes the osteogenic and chondrogenic differentiation of BMSCs.
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NR 40
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PU PERGAMON-ELSEVIER SCIENCE LTD
PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND
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WC Geriatrics & Gerontology
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PT J
AU Kong, YJ
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Hou, Y
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Li, WJ
Song, YZ
AF Kong, Yajie
Yang, Yujia
Hou, Yu
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TI Advance in the application of organoids in bone diseases
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE bone diseases; bone organoids; stem cells; regenerative medicine; biomaterials
ID stem-cells; in-vitro; differentiation; cartilage
AB Bone diseases such as osteoporosis and osteoarthritis have become important human health problems, requiring a deeper understanding of the pathogenesis of related diseases and the development of more effective treatments. Bone organoids are three-dimensional tissue masses that are useful for drug screening, regenerative medicine, and disease modeling because they may mimic the structure and physiological activities of organs. Here, we describe various potential methods for culturing bone-related organoids from different stem cells, detailing the construction processes and highlighting the main applications of these bone organoid models. The application of bone organoids in different skeletal diseases is highlighted, and current and promising bone organoids for drug screening and regenerative medicine as well as the latest technological advancements in bone organoids are discussed, while the future development of bone organoids is discussed. Looking forward, it will provide a reference for constructing bone organoids with more complete structures and functions and applying them to biomedical research. The graphical abstract was created with BioRender (www.biorender.com).
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TI A review of the sources and pharmacological research of morroniside
SO FRONTIERS IN PHARMACOLOGY
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DT Review
DE morroniside; sources; pharmacology; distribution; detection
ID attenuates neuropathic pain; liuwei dihuang pill; fructus-corni; bioactive constituents; cerebral-ischemia; oxidative stress; inflammatory response; cell-proliferation; iridoid glycosides; protects
AB Introduction Morroniside (Mor) is a bioactive compound found in Corni Fructus (CF) [Cornaceae; Cornus officinalis Siebold & Zucc.], which has been used as medicine and food in China, Korea, and Japan for over 2,000 years. This review summarizes recent progress on Mor, specifically focusing on its distribution, isolation, detection, and various pharmacological effects.Methods A literature survey on Mor was conducted using electronic databases such as PubMed, ScienceDirect, CNKI, and Google Scholar. After removing TCM prescription-related standards, medicinal herb processing-related research, and other irrelevant works of literature, we obtained relevant information on Mor's biological and pharmacological properties.Results The main conclusions are as follows: Mor is widely distributed in the plant kingdom; the methods for extracting and isolating Mor are well established; and the technology for detecting it is accurate. Mor exhibits numerous pharmacological effects. Along with CF, Mor has shown renoprotective effects against diabetes, hepatoprotective effects against diabetes, triptolide, and nonalcoholic steatohepatitis, and boneprotective effects against osteoporosis and osteoarthritis. In addition, researchers have also explored other pharmacological effects of Mor, including neuroprotective effects against focal cerebral ischemia, spinal cord injury, and Alzheimer's disease; cardioprotective effects against acute myocardial infarction; protection of the digestive system from gastritis, inflammatory bowel disease, and colitis; protection of the skin by promoting hair growth, wound healing, and flap survival; and protection of the lungs from acute lung injury and pulmonary fibrosis. Moreover, Mor has anti-obesity effects, anti-inflammatory effects in the eye, and improves follicular development.Discussion Overall, this review provides a comprehensive understanding of the pharmacological effects of Mor, from which the limitations of the current research can be understood, which will help facilitate future research.
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TI Increased bone resorption that outpaces increased bone formation: An important pathology of rapidly destructive coxarthrosis
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE homocysteine; rapidly destructive coxarthrosis; total P1NP; TRACP-5b
ID collagen c-telopeptide; total hip-arthroplasty; early mri findings; osteoarthritis;

quality; prevalence; serum
AB Rapid joint destruction caused by rapidly destructive coxarthrosis (RDC) can increase surgical complexity and intraoperative blood loss. This single-center retrospective study investigates osteoporosis-related biomarkers for early RDC diagnosis and explores new treatment targets. We included 398 hip joints from patients who underwent total hip arthroplasty, examining medical records for preoperative patient demographics, bone mineral density of the hip and lumbar spine from dual-energy X-ray absorptiometry scans, and osteoporosis-related biomarkers including TRACP-5b, total P1NP, intact parathyroid hormone, and homocysteine. We compared RDC and osteoarthritis (OA) patients, and univariate analysis showed that RDC patients were older ($p < 0.001$) and had lower serum levels of albumin ($p < 0.001$) and higher serum levels of TRACP-5b, total P1NP ($p < 0.001$), and homocysteine ($p = 0.006$). Multivariable analysis showed that the ratio of serum TRACP-5b to total P1NP had a more significant difference in RDC patients than in OA patients ($p = 0.04$). Serum TRACP-5b levels were negatively correlated with the time between RDC onset and blood collection, and Japanese Orthopedic Association pain score. Receiver operating characteristic curve analysis revealed that the ratio of serum TRACP-5b to total P1NP had the highest area under the curve value. This study is the first to demonstrate that the ratio of serum TRACP-5b to total P1NP-increased bone resorption that outpaces increased bone formation-is significantly elevated in patients with RDC and that TRACP-5b is higher in the early stages of RDC. Inhibiting serum levels of TRACP-5b, activated osteoclasts, during early RDC may suppress disease progression.
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NR 30
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TI Impact of patient education by nurse case managers on decision making for out-of-pocket anti-osteoporotic pharmaceutical therapy: a single-center retrospective study
SO BMC NURSING
LA English
DT Article
DE Case managers; Osteoporosis; Patient education; Decision making; Out-of-pocket cost
ID hip fracture; care; probability; position; taiwan
AB Background Osteoporosis is a common condition that increases the risk of fracture and mortality. In Taiwan, clinical guidelines recommend pharmaceutical therapy for patients with a T-score of <= - 2.5; however, Taiwan's National Health Insurance (NHI) only covers these medications for those with a history of fragility fractures. This gap in coverage necessitates a discussion of out-of-pocket treatment options. To address this, we provided an integrated care program with patient

education and shared decision-making by nurse case managers specializing in osteoporosis. We evaluated whether education by nurse case managers influences patients with a T-score <= - 2.5, who are not covered by the NHI, to choose out-of-pocket pharmaceutical therapy. Methods We retrospectively reviewed medical records of patients who underwent bone density scanning at our hospital between January 2014 and December 2021. We identified 4,462 patients with a T-score of <= - 2.5 who were ineligible for NHI-covered anti-osteoporotic therapy and analyzed trends in out-of-pocket medication use. Since the integrated care program began in 2018, we evaluated whether education by nurse case managers between 2018 and 2021 influenced patients' decisions to pay out-of-pocket for therapy. After the implementation of the integrated care program, we identified 2,910 patients with a T-score <= -2.5 who were ineligible for NHI-covered anti-osteoporotic therapy. Of these, 640 opted for out-of-pocket treatment, while 2,270 chose conservative care. After a 1:1 propensity score match based on age and sex, logistic regression was used to analyze the impact of nurse case manager education on these decisions. Results Between 2014 and 2021, 888 of the 4,462 patients chose out-of-pocket pharmaceutical therapy. Before the implementation of the integrated care program and patient education by nurse case managers (2014-2017), 16% of the patients opted to pay out-of-pocket for anti-osteoporotic therapy. After the program was implemented (2018-2021), the rate increased significantly to 22% (P < 0.001). A multivariate logistic regression model showed that a history of osteoarthritis (adjusted odds ratio = 1.576; P = 0.009) and education provided by the nurse case managers (adjusted odds ratio = 5.044; P < 0.001) were significantly associated with choosing out-of-pocket therapy. Conclusions Education from nurse case managers significantly increased the likelihood of patients choosing out-of-pocket anti-osteoporotic therapy in our hospital, thereby bridging the gap between clinical guidelines and NHI reimbursement criteria.

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TI Polysaccharides to postbiotics: Nurturing bone health via modulating "gut-immune axis"
SO INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES
LA English
DT Review
DE Gut microbiome; Gut-associated metabolites; Immune cells; Osteoimmune system; Immunoporosis; Bone pathologies; Polysaccharides; Postbiotics
ID chain fatty-acids; trimethylamine-n-oxide; histone deacetylase inhibitors; sodium-butyrate; bile-acid; microbial metabolites; intestinal-absorption; tryptophan-metabolism; rheumatoid-arthritis; gene identification
AB The increasing prevalence of individuals affected by bone pathologies globally has sparked catastrophic concerns. Ankylosing spondylitis, osteoporosis, rheumatoid arthritis, osteoarthritis, and fractures alone impact an estimated 1.71 billion people worldwide. The gut microbiota plays a crucial role in interacting with the host through the synthesis of a diverse range of metabolites called gut-associated metabolites (GAMs), which originate from external dietary substrates or endogenous host compounds. Many metabolic disorders have been linked to alterations in the gut microbiota's activity and composition. The

development of metabolic illnesses has been linked to certain microbiota-derived metabolites, such as branched-chain amino acids, bile acids, short-chain fatty acids, tryptophan, trimethylamine N-oxide, and indole derivatives. Moreover, the modulation of gut microbiota through biotics (prebiotics, probiotics and postbiotics) presents a promising avenue for therapeutic intervention. Biotics selectively promote the growth of beneficial gut bacteria, thereby enhancing the production of GAMs with potential beneficial effects on bone metabolism. Understanding the intricate interplay between GAMs, and bone-associated genes through molecular informatics holds significant promise for early diagnosis, prognosis, and novel treatment strategies for various bone disorders.

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DT Review
DE pathogenic microbiome; orthopedic; machine learning; deep learning; applications; individuation; osteoporosis; arthritis
ID osteoporosis; osteoarthritis
AB Osteoporosis, arthritis, and fractures are examples of orthopedic illnesses that not only significantly impair patients' quality of life but also complicate and raise the expense of therapy. It has been discovered in recent years that the pathophysiology of orthopedic disorders is significantly influenced by the microbiota. By employing machine learning and deep learning techniques to conduct a thorough analysis of the disease-causing microbiome, we can enhance our comprehension of the pathophysiology of many illnesses and expedite the creation of novel treatment approaches. Today's science is undergoing a revolution because to the introduction of machine learning and deep learning technologies, and the field of biomedical research is no exception. The genesis, course, and management of orthopedic disorders are significantly influenced by pathogenic microbes. Orthopedic infection diagnosis and treatment are made more difficult by the lengthy and imprecise nature of traditional microbial detection and characterization techniques. These cutting-edge analytical techniques are offering previously unheard-of insights into the intricate relationships between orthopedic health and pathogenic microbes, opening up previously unimaginable possibilities for illness diagnosis, treatment, and prevention. The goal of biomedical research has always been to improve diagnostic and treatment methods while also gaining a deeper knowledge of the processes behind the onset and development of disease. Although traditional biomedical research methodologies have demonstrated certain limits throughout time, they nevertheless rely heavily on experimental data and expertise. This is the area in which deep learning and machine learning approaches excel. The advancements in machine learning (ML) and deep learning (DL) methodologies have enabled us to examine vast quantities of data and unveil intricate connections between microorganisms and orthopedic disorders. The

importance of ML and DL in detecting, categorizing, and forecasting harmful microorganisms in orthopedic infectious illnesses is reviewed in this work.
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NR 48
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PU FRONTIERS MEDIA SA
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TI Links between three chronic and age-related diseases, osteoarthritis, periodontitis, and osteoporosis, in a wild mammal (moose) population
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Alces alces; Periodontal disease; Arthritis; Chronic diseases; Age -related diseases; Isle Royale
ID sex-differences; prevalence; burden; hip
AB Objective: Osteoarthritis, periodontitis and osteoporosis are chronic, age-related diseases which adversely impact millions of people worldwide. Because these diseases pose a major global public health challenge, there is an urgent need to better understand how these diseases are interrelated. Our objective was to

document the age and sex-specific prevalence of each disease and assess interrelationships among the three diseases in a wild mammal (moose, Alces alces) population. Methods: We examined the bones of moose dying from natural causes and recorded the severity of osteoarthritis (typically observed on the hip and lowest vertebrae), osteoporosis (osteoporotic lesions observed on the skull) and periodontitis (observed on maxilla and mandibles). Results: Periodontitis was associated with a greater prevalence of both severe osteoarthritis and osteoporotic lesions in moose. We found no evidence to suggest that moose with osteoporotic lesions were more or less likely to exhibit signs of osteoarthritis or severe osteoarthritis. The prevalence of osteoarthritis, periodontitis and osteoporotic lesions was greater among males than for females. Conclusions: Our results were consistent with the hypothesis that bacterial pathogens causing periodontitis are a risk factor for osteoarthritis and osteoporosis. They are also consistent with the hypothesis that the inverse association between osteoarthritis and osteoporosis sometimes observed in humans may be influenced by shared risk factors, such as obesity, smoking or alcohol consumption, which are absent in moose. Together these results provide insights about three diseases which are expected to become more prevalent in the future and that cause substantial socio-economic burdens.
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NR 15
TC 1
Z9 1
U1 1
U2 3
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
PD MAR 15
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AU Rosenberg, J
Sundaresh, V
Gililland, J

Osman, A
Woolley, W
Acevedo, C
AF Rosenberg, James
Sundaresh, Vishnu
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TI Glycemic Marker Correlation with Collagen Denaturation and Non-Enzymatic Collagen Cross-Linking in Age-Associated Bone Resistance
SO JOM
LA English
DT Article
ID glycation end-products; human cortical bone; hip fracture; density; osteoarthritis; polymorphism; endproducts; morphology; mortality; toughness
AB The primary clinical indicator of fracture risk among the elderly is low bone mass, yet it accounts for less than half of fractures in individuals over 50 years. Age is recognized to influence bone quality, affecting bone structure and properties. Previous research indicates that age diminishes tissue plasticity and toughness conferred by collagen, suggesting that age-related changes in the collagen environment may contribute to bone fragility. This study explores the relationship between age-related collagen impairment, specifically the accumulation of non-enzymatic collagen cross-linking and molecular collagen denaturation, and bone toughness in middle-aged and older patients (postmenopausal 50-70 years old and senile osteoporosis age > 70 years old). Additionally, it examines the influence of blood glucose and HbA1c levels, as well as body mass index (BMI), on these factors. Despite not finding any differences in fracture toughness between groups, we found a significant correlation between hemoglobin A1c and collagen integrity (collagen denaturation and non-enzymatic cross-linking).
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NR 61
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PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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WC Materials Science, Multidisciplinary; Metallurgy & Metallurgical Engineering; Mineralogy; Mining & Mineral Processing
SC Materials Science; Metallurgy & Metallurgical Engineering; Mineralogy; Mining & Mineral Processing
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AU Hiltzik, DM
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TI The Role of the Gut Microbiome in Orthopedic Surgery-a Narrative Review
SO CURRENT REVIEWS IN MUSCULOSKELETAL MEDICINE
LA English

DT Review
DE Gut microbiome; Dysbiosis; Gut flora; Commensal bacteria; Orthopedic surgery; Osteoarthritis; Osteoporosis; Osteomyelitis; Fracture healing; Degenerative disc disease; Spinal cord injury; Athletics; Probiotic
ID disease; risk
AB Purpose of ReviewThe importance of the gut microbiome has received increasing attention in recent years. New literature has revealed significant associations between gut health and various orthopedic disorders, as well as the potential for interventions targeting the gut microbiome to prevent disease and improve musculoskeletal outcomes. We provide a broad overview of available literature discussing the links between the gut microbiome and pathogenesis and management of orthopedic disorders.Recent FindingsHuman and animal models have characterized the associations between gut microbiome dysregulation and diseases of the joints, spine, nerves, and muscle, as well as the physiology of bone formation and fracture healing. Interventions such as probiotic supplementation and fecal transplant have shown some promise in ameliorating the symptoms or slowing the progression of these disorders.SummaryWe aim to aid discussions regarding optimization of patient outcomes in the field of orthopedic surgery by providing a narrative review of the available evidence-based literature involving gut microbiome dysregulation and its effects on orthopedic disease. In general, we believe that the gut microbiome is a viable target for interventions that can augment current management models and lead to significantly improved outcomes for patients under the care of orthopedic surgeons.
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TI Osteoporosis, Osteoarthritis, and Subchondral Insufficiency Fracture: Recent Insights
SO BIOMEDICINES
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DE osteoarthritis; osteoporosis; subchondral insufficiency fracture; bone mineral density; osteoporotic fracture
ID bone-mineral density; vitamin-d supplementation; medial femoral condyle; spontaneous osteonecrosis; knee osteoarthritis; strontium ranelate; hip osteoarthritis; cartilage volume; marrow lesions; radiographic osteoarthritis
AB The increased incidence of osteoarthritis (OA), particularly knee and hip OA, and osteoporosis (OP), owing to population aging, have escalated the medical expense burden. Osteoarthritis is more prevalent in older women, and the involvement of subchondral bone fragility spotlights its association with OP. Notably, subchondral insufficiency fracture (SIF) may represent a more pronounced condition of OA pathophysiology. This review summarizes the relationship between OA and OP, incorporating recent insights into SIF. Progressive SIF leads to joint collapse and secondary OA and is associated with OP. Furthermore, the thinning and fragility of subchondral bone in early-stage OA suggest that SIF may be a subtype of OA (osteoporosis-related OA, OPOA) characterized by significant subchondral bone damage. The high bone mineral density observed in OA may be overestimated due to osteophytes and sclerosis and can potentially contribute to OPOA. The incidence of OPOA is expected to increase along with population aging. Therefore, prioritizing OP screening, early interventions for patients with early-stage OA, and fracture prevention measures such as rehabilitation, fracture liaison services, nutritional management, and medication guidance are essential.
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NR 219
TC 29
Z9 32
U1 7
U2 54
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WC Biochemistry & Molecular Biology; Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Biochemistry & Molecular Biology; Research & Experimental Medicine; Pharmacology & Pharmacy
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PT J
AU Kok, YE
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AF Kok, Yong En
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Venkateswaran, Seshasailam
Oreffo, Richard
Mahajan, Sumeet
Pound, Michael
TI Classification of osteoarthritic and healthy cartilage using deep learning with Raman spectra
SO SCIENTIFIC REPORTS
LA English
DT Article
DE Raman spectra; Osteoarthritis; Deep learning; Convolutional neural network; Classification
ID convolutional neural-networks; base-line-correction; background subtraction; spectroscopy; recognition; algorithm; disease
AB Raman spectroscopy is a rapid method for analysing the molecular composition of biological material. However, noise contamination in the spectral data necessitates careful pre-processing prior to analysis. Here we propose an end-to-end Convolutional Neural Network to automatically learn an optimal combination of pre-processing strategies, for the classification of Raman spectra of superficial and deep layers of cartilage harvested from 45 Osteoarthritis and 19 Osteoporosis (Healthy controls) patients. Using 6-fold cross-validation, the Multi-Convolutional Neural Network achieves comparable or improved classification accuracy against the best-performing Convolutional Neural Network applied to either the raw or pre-processed spectra. We utilised Integrated Gradients to identify the contributing features (Raman signatures) in the network decision process, showing they are biologically relevant. Using these features, we compared Artificial Neural Networks, Decision Trees and Support Vector Machines for the feature selection task. Results show that training on fewer than 3 and 300 features, respectively, for the disease classification and layer assignment task provide performance comparable to the best-performing CNN-based network applied to the full dataset. Our approach, incorporating multi-channel input and Integrated Gradients, can potentially facilitate the clinical translation of Raman spectroscopy-based diagnosis without the need for laborious manual

pre-processing and feature selection.
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Bennett, Alexander N.
TI Developing an exercise intervention to minimise hip bone mineral density loss following traumatic lower limb amputation: a Delphi study
SO BRITISH JOURNAL OF SPORTS MEDICINE
LA English
DT Article
DE Exercise; Exercise Therapy; Bone density; Bone; Lower limb
ID postmenopausal women; erlangen fitness; osteoporosis; recommendations; osteoarthritis; epidemiology; prevalence; pain
AB Objective To elicit expert opinion and gain consensus on specific exercise intervention parameters to minimise hip bone mineral density (BMD) loss following traumatic lower limb amputation. Methods In three Delphi rounds, statements were presented to a panel of 13 experts from six countries. Experts were identified through publications or clinical expertise. Round 1 involved participants rating their agreement with 22 exercise prescription statements regarding BMD loss post amputation using a 5-point Likert scale. Agreement was deemed as 3-4 on the scale (agree/strongly agree). Statements of <50% agreement were excluded. Round 2 repeated remaining statements alongside round 1 feedback. Round 3 allowed reflection on round 2 responses considering group findings and the chance to change or maintain the resp onse. Round 3 statements reaching >= 70% agreement were defined as consensus. Results All 13 experts completed rounds 1, 2 and 3 (100% completion). Round 1 excluded 12 statements and added 1 statement (11 statements for rounds 2-3). Round 3 reached consensus on nine statements to guide future exercise interventions. Experts agreed that exercise interventions should be performed at least 2days per week for a minimum of 6 months, including at least three different resistance exercises at an intensity of 8-12 repetitions. Interventions should include weight-bearing and multiplanar exercises, involve high-impact activities and be supervised initially. Conclusion This expert Delphi process achieved consensus on nine items related to exercise prescription to minimise hip BMD loss following traumatic lower limb amputation. These recommendations should be tested in future interventional trials.
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Wang, Yufeng
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TI Role of oxytocin in bone
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE bone metabolism; oxytocin; BMSC; osteoblast; osteoclast; chondrocyte; estrogen; osteoporosis
ID mesenchymal stem-cells; receptor; differentiation; osteoarthritis; proliferation; expression; female; model; body
AB Oxytocin (OT) is a posterior pituitary hormone that, in addition to its role in regulating childbirth and lactation, also exerts direct regulatory effects on the skeleton through peripheral OT and oxytocin receptor (OTR). Bone marrow mesenchymal stem cells (BMSCs), osteoblasts (OB), osteoclasts (OC), chondrocytes, and adipocytes all express OT and OTR. OT upregulates RUNX2, BMP2, ALP, and OCN, thereby enhancing the activity of BMSCs and promoting their differentiation towards OB rather than adipocytes. OT also directly regulates OPG/RANKL to inhibit adipocyte generation, increase the expression of SOX9 and COMP, and enhance chondrocyte differentiation. OB can secrete OT, exerting influence on the surrounding environment through autocrine and paracrine mechanisms. OT directly increases OC formation through the N kappa B/MAP kinase signaling pathway, inhibits osteoclast proliferation by triggering cytoplasmic Ca2+ release and nitric oxide synthesis, and has a dual regulatory effect on OCs. Under the stimulation of estrogen, OB synthesizes OT, amplifying the biological effects of estrogen and OT. Mediated by estrogen, the OT/OTR forms a feedforward loop with OB. Apart from estrogen, OT also interacts with arginine vasopressin (AVP), prostaglandins (PGE2), leptin, and adiponectin to regulate bone metabolism. This review summarizes recent research on the regulation of bone metabolism by OT and OTR, aiming to provide insights into their clinical applications and further research.
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TI Steroids and Malignancy Increase Local Heparanase and Decrease Markers of Osteoblast Activity in Bone Tissue Microcirculation
SO BIOMOLECULES
LA English
DT Article
DE bone; microcirculation; thrombosis; heparanase; steroids; malignancy

ID cancer metastasis; activation; involvement; hemostasis; expression; marrow; cells
AB Bone metastasis and steroids are known to activate the coagulation system and induce osteoporosis, pathological bone fractures, and bone pain. Heparanase is a protein known to enhance the hemostatic system and to promote angiogenesis, metastasis, and inflammation. The objective of the present study was to evaluate the effects of steroids and malignancy on the coagulation factors and osteoblast activity in the bone tissue. The effects of dexacort and malignant medium were evaluated in osteoblasts derived from human bone marrow mesenchymal stem cells and human umbilical vein endothelial cells (HUVECs). The bones of mice treated with dexacort for 1 month were studied. Bone biopsies of ten patients with bone metastasis, ten with steroid-induced avascular necrosis (AVN), and ten with osteoarthritis were compared to ten controls. We found that dexacort and malignant medium significantly increased the heparanase levels in osteoblasts and HUVECs and decreased the levels of alkaline phosphatase (ALKP). Peptide 16AC, derived from heparanase, which interacts with tissue factor (TF), further increased the effect, while peptide 6, which inhibits interactions between heparanase and TF, reversed the effect in these cells. The bone microcirculation of mice treated with dexacort exhibited significantly higher levels of heparanase, TF, TF pathway inhibitor (TFPI), TFPI-2, thrombin, and syndecan-1, but reduced levels of osteocalcin and ALKP. The pathological human bone biopsies' microcirculation exhibited significantly dilated blood vessels and higher levels of heparanase, TF, TFPI, TFPI-2, and fibrin. In summary, steroids and malignancy increased the activation of the coagulation system in the bone microcirculation and reduced the osteoblast activity. Heparanase inhibitors should be further investigated to attenuate bone fractures and pain.
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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JI Biomolecules
PD DEC 15
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VL 14
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DI 10.3390/biom14121506
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WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
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Ward, Kate A.
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TI General self-efficacy, not musculoskeletal health, was associated with social isolation and loneliness in older adults during the COVID-19 pandemic: findings from the Hertfordshire Cohort Study
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Social isolation; Loneliness; Self-efficacy; Ageing; COVID-19 pandemic; Musculoskeletal conditions
ID risk-factors; depressive symptoms; mortality; individuals; performance
AB Background Social isolation and loneliness are prevalent among older adults. This study investigated factors influencing worsening social isolation and loneliness in community-dwelling older adults during the COVID-19 pandemic, focusing on musculoskeletal conditions, falls, and fractures. Methods We studied 153 participants from the Hertfordshire Cohort Study. Baseline assessments (2019-20) included osteoporosis, clinical osteoarthritis, fractures after age 45 years, falls in previous year, and lifestyle factors. Self-efficacy was assessed using a shortened General Self-Efficacy Scale. Social isolation was assessed using the 6-item Lubben Social Network Scale. Follow-up (2020-21) assessments included social isolation and loneliness using the 6-item De Jong-Gierveld scale for emotional, social, and overall loneliness. Results Baseline median age was 83.1 years. A history of smoking predicted worsening social isolation ($p = 0.046$). Being married ($p = 0.026$) and higher self-efficacy scores ($p = 0.03$) predicted reduced social isolation at follow-up. Greater alcohol consumption was associated with higher overall loneliness ($p = 0.026$). Being married was related to a 36% (95% CI: 3%, 58%) reduction in emotional loneliness ($p = 0.037$). No musculoskeletal condition was associated with social isolation or loneliness. However, we observed a 22% (14%, 30%; $p < 0.001$) reduction in emotional loneliness and a 12% (4%, 20%; $p = 0.003$) reduction in overall loneliness per unit increase in self-efficacy score. Conclusions No musculoskeletal condition was associated with increased social isolation or loneliness, but longitudinal studies in larger samples are required. Greater self-efficacy was associated with reduced social isolation and reduced loneliness. Interventions promoting self-efficacy in older adults may reduce isolation and loneliness in this age group.
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TI Exosomal communication: a pivotal regulator of bone homeostasis and a potential therapeutic target
SO FRONTIERS IN PHARMACOLOGY
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DT Review
DE exosome; extracellular vesicle; bone homeostasis; osteoporosis; osteoarthritis
ID mesenchymal stem-cells; macrophage-derived exosm; extracellular vesicles; osteogenic differentiation; osteoblastic differentiation; osteoarthritis; osteoporosis; cartilage; expression; osteoclastogenesis
AB Bone homeostasis encompasses two interrelated aspects: bone remodeling and cartilage metabolism. Disruption of bone homeostasis can lead to the development of metabolic bone diseases such as osteoporosis and osteoarthritis. The maintenance of bone homeostasis is a complex process that does not solely rely on the functions of the bone tissue itself. In fact, bone tissue is not an isolated entity; it is closely connected to other tissues in the body via exosomes. Within this interconnectivity, exosomes derived from both bone and non-bone cells interfere with each other, forming a complex regulatory network. Therefore, with cell origin as the guiding principle, we have delineated the bone regulatory network of exosomes, elaborated on the specific roles and regulatory mechanisms of exosomes derived from common cell types (cells within the skeletal microenvironment, stem cells from extra-osseous tissues, vascular-derived cells, muscle-derived cells, and neurogenic cells) in bone formation, bone resorption, and cartilage metabolism. We have also discussed the challenges faced in the field of exosome research related to bone homeostasis, unveiled the critical role of exosomes in maintaining bone homeostasis, and proposed that exosomes could serve as highly valuable therapeutic targets for metabolic bone diseases.
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TI The specificities, influencing factors, and medical implications of bone circadian rhythms
SO FASEB JOURNAL
LA English
DT Review
DE BMAL1; bone development; bone diseases; bone mineralization; bone remodeling; chronotherapy; circadian rhythm; melatonin
ID mesenchymal stem-cells; sympathetic-nervous-system; clock gene-expression; mineral density; osteoblast differentiation; parathyroid-hormone; constant light; melatonin production; peripheral clocks; diurnal-variation
AB Physiological processes within the human body are regulated in approximately 24-h cycles known as circadian rhythms, serving to adapt to environmental changes. Bone rhythms play pivotal roles in bone development, metabolism, mineralization, and remodeling processes. Bone rhythms exhibit cell specificity, and different cells in bone display various expressions of clock genes. Multiple environmental factors, including light, feeding, exercise, and temperature, affect bone diurnal rhythms through the sympathetic nervous system and various hormones. Disruptions in bone diurnal rhythms contribute to the onset of skeletal disorders such as osteoporosis, osteoarthritis and skeletal hypoplasia. Conversely, these bone diseases can be effectively treated when aimed at the circadian clock in bone cells, including the rhythmic expressions of clock genes and drug targets. In this review, we describe the unique circadian rhythms in physiological activities of various bone cells. Then we summarize the factors synchronizing the diurnal

rhythms of bone with the underlying mechanisms. Based on the review, we aim to build an overall understanding of the diurnal rhythms in bone and summarize the new preventive and therapeutic strategies for bone disorders. Bone diurnal rhythms exhibit cell specificity, and different cells in bone display various expressions of clock genes. Multiple environmental factors, including light, feeding, exercise, and temperature, affect bone rhythms through the sympathetic nervous system and various hormones. Disruptions in circadian rhythms contribute to the onset of skeletal disorders such as osteoporosis, osteoarthritis and skeletal hypoplasia. Conversely, these bone diseases can be effectively treated when aimed at the circadian rhythms.image
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TI The glucocorticoid receptor in skeletal health and disease: insights from targeted knockout mice
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LA English
DT Review
DE glucocorticoid receptor; glucocorticoids; knockout mice; skeletal disease; skeletal development; bone loss; fracture; arthritis
ID 11-beta-hydroxysteroid dehydrogenase type-1; suppress bone-formation; osteoblast differentiation; transgenic disruption; mature osteoblasts; binding; arthritis; therapy; mechanisms; expression
AB Glucocorticoids are steroid hormones, secreted by the adrenals to regulate a range of metabolic, immunologic, and homeostatic functions. Due to their potent anti-inflammatory effects, synthetic glucocorticoids are widely used to treat inflammatory disorders. However, their use especially at high doses and over the long-term is associated with several unwanted side effects that compromises their intended use (e.g. glucocorticoid-induced osteoporosis and/or diabetes, myopathy, and skin atrophy). Both endogenous and synthetic glucocorticoids exert their effects through the glucocorticoid receptor, a transcription factor present in nearly all nucleated cells. Glucocorticoid receptor knockout mouse models have proved to be valuable tools in understanding how glucocorticoids contribute to skeletal health and disease. These models, described in this review, have helped to establish that the effects of glucocorticoids on the skeleton are multifaceted, cell specific and concentration dependent. Intriguingly, while endogenous glucocorticoids are essential for bone formation, high-dose exogenous glucocorticoids may induce bone loss. Additionally, the actions of endogenous glucocorticoids vary greatly depending on the disease microenvironment. For example, endogenous glucocorticoids have predominately beneficial anti-inflammatory effects in rheumatoid arthritis, but detrimental actions in osteoarthritis by driving cartilage loss and abnormal bone formation. Studies in tissue-specific knockout models provide important insights that will aid the development of new glucocorticoid therapeutics that can specifically target certain cell types to minimise unwanted effects from current glucocorticoid therapy.
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TI Fostering tissue engineering and regenerative medicine to treat musculoskeletal disorders in bone and muscle
SO BIOACTIVE MATERIALS
LA English
DT Review
DE Musculoskeletal disorders; Tissue engineering; Regenerative medicine; Bone; Muscle
ID mesenchymal stem-cells; growth-factors; satellite cells; in-vitro; scaffold; differentiation; proliferation; promotes; osteoarthritis; stimulation
AB The musculoskeletal system, which is vital for movement, support, and protection, can be impaired by disorders such as osteoporosis, osteoarthritis, and muscular dystrophy. This review focuses on the advances in tissue engineering and regenerative medicine, specifically aimed at alleviating these disorders. It explores the roles of cell therapy, particularly Mesenchymal Stem Cells (MSCs) and Adipose-Derived Stem Cells (ADSCs), biomaterials, and biomolecules/external stimulations in fostering bone and muscle regeneration. The current research underscores the potential of MSCs and ADSCs despite the persistent challenges of cell scarcity, inconsistent outcomes, and safety concerns. Moreover, integrating exogenous materials such as scaffolds and external stimuli like electrical stimulation and growth factors shows promise in enhancing musculoskeletal regeneration. This review emphasizes the need for comprehensive studies and adopting innovative techniques together to refine and advance these multi-therapeutic strategies, ultimately benefiting patients with musculoskeletal disorders.
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DE traditional Chinese rehabilitation exercise; pain; myofascial chain; rehabilitation
ID quality-of-life; low-back-pain; knee osteoarthritis; primary osteoporosis; wuqinxi exercise; trigger points; tai chi; qigong; covid-19; stroke
AB Myofascial as a holistic structure emphasizes a holistic approach to intervention and treatment of fascial-related disorders such as neck pain (NP), low back pain (LBP), and knee pain. There are currently adverse effects of medication for diseases related to myofascial. Traditional Chinese rehabilitation exercise (TCRE) is a practical approach to traditional Chinese medicine and is a valuable option for intervening in myofascial-related pain. This article found some research evidence for Baduanjin, Wuqinxi, and Yijinjing in clinical studies of myofascial chain-related

pain. The article summarizes the current evidence and finds that TCRE can enhance limb movement function through breathing and slow movements, increase joint movement and flexibility, and reduce joint pathology and stress-induced pain. As for future directions, focus on TCRE in improving the health of older adults and treating longCOVID syndrome, and integrate robotic and TCRE training to frame safe and effective exercise models. Relevant studies have already been registered in the Clinical Trials Registry, and some clinical study protocols have been published. TCRE can be an alternative nonpharmacological rehabilitation therapy to alleviate chronic rheumatic pain symptoms and augment public health management.
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SC Neurosciences & Neurology
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TI Femoral Component Design Is Associated With the Risk of Periprosthetic Femur Fracture After Cementless THA in Patients 65 Years or Older
SO CLINICAL ORTHOPAEDICS AND RELATED RESEARCH
LA English
DT Article

ID total hip-arthroplasty; collar; stems
AB Background Periprosthetic femur fracture is a known complication after THA. The associated risk of cementless femoral component design for periprosthetic femur fracture in a registry population of patients older than 65 years has yet to be clearly identified. Questions/purposes(1) Is femoral stem geometry associated with the risk of periprosthetic femur fracture after cementless THA? (2) Is the presence or absence of a collar on cementless femoral implant designs associated with the risk of periprosthetic femur fracture after THA? Methods We analyzed American Joint Replacement Registry data from 2012 to March 2020. Unique to this registry is the high use of cementless femoral stems in patients 65 years and older. We identified 266,040 primary cementless THAs during the study period in patients with a diagnosis of osteoarthritis and surgeries linked to supplemental Centers for Medicare and Medicaid data where available. Patient demographics, procedure dates, and reoperation for periprosthetic femur fracture with revision or open reduction and internal fixation were recorded. The main analysis was performed comparing the Kheir and Chen classification: 42% (112,231 of 266,040) were single-wedge, 22% (57,758 of 266,040) were double-wedge, and 24% (62,983 of 266,040) were gradual taper/metadiaphyseal-filling cementless femoral components, which yielded a total of 232,972 primary cementless THAs. An additional analysis compared cementless stems with collars (20% [47,376 of 232,972]) with those with collarless designs (80% [185,596 of 232,972]). A Cox proportional hazard regression analysis with the competing risk of death was used to evaluate the association of design and fracture risk while adjusting for potential confounders. Results After controlling for the potentially confounding variables of age, sex, geographic region, osteoporosis or osteopenia diagnosis, hospital volume, and the competing risk of death, we found that compared with gradual taper/metadiaphyseal-filling stems, single-wedge designs were associated with a greater risk of periprosthetic femur fracture (HR 2.9 [95% confidence interval (CI) 2.2 to 3.9]; p < 0. 001). Compared with gradual taper/metadiaphyseal-filling stems, double-wedge designs showed an increased risk of periprosthetic femur fracture (HR 3.0 [95% CI 2.2 to 4.0]; p < 0. 001). Collarless stems showed an increased risk of periprosthetic fracture compared with collared stems (HR 7.8 [95% CI 4.1 to 15]; p < 0. 001). Conclusion If cementless femoral fixation is used for THA in patients 65 years or older, surgeons should consider using gradual taper/metadiaphyseal-filling and collared stem designs because they are associated with a lower risk of periprosthetic femur fracture. Future investigations should compare gradual taper/metadiaphyseal-filling and collared cementless designs with cemented fixation in this population.
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TI Exposure to per- and polyfluoroalkyl substances and bone health: a systematic review and meta-analysis
SO INTERNATIONAL JOURNAL OF ENVIRONMENTAL HEALTH RESEARCH
LA English
DT Review
DE Per- and polyfluoroalkyl substances; bone mineral density; bone mineral content; fracture; osteoporosis
ID perfluorooctane sulfonate; perfluoroalkyl substances; mineral density; us population; association; nhanes; osteoarthritis
AB Perfluoroalkyl substances (PFAS) as a large group of synthetic compounds widely contaminated the environment and lead to health problems. However, the correlation between PFAS exposure, bone health parameters and osteoporosis

remains controversial. Therefore, we conducted a systematic review and meta-analysis of published literature to evaluate the effects of PFAS on human bone health. All observational studies were collected up to 2 December 2023. A total of 2096 articles were retrieved. Of these, 21 articles investigated the association between PFAS exposure and human bone health. However, only 10 studies were included in the final meta-analysis. Doubling of serum perfluorooctanoic acid (PFOA) (beta = -0.11, 95% confidence interval (CI): -0.18, -0.05) and perfluorooctane sulfonic acid (PFOS) (beta = -0.06, 95% CI: -0.11, -0.01) levels showed significant negative correlations with total body less head bone mineral density (TBLH-BMD). Subgrouping showed that only perfluorohexane sulfonate (PFHxS) (odds ratio [OR] = 1.37, 95% CI: 1.12, 1.68) was correlated with osteoporosis.
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PT J
AU Zhou, Y
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TI Prediction of the Molecular Mechanism of Corni Fructus-Epimedii Folium-Rehmanniae Radix Praeparata in the Treatment of Postmenopausal Osteoporosis based on Network Pharmacology and Molecular Docking
SO CURRENT COMPUTER-AIDED DRUG DESIGN
LA English
DT Article
DE Corni fructus; epimedii folium; rehmanniae radix praeparata; data mining; network pharmacology; postmenopausal osteoporosis
ID growth-factor receptor; osteoclast differentiation; thyroid-hormone; bone-formation; big data; akt1; transactivation; osteoarthritis; osteogenesis; association
AB Introduction: In this study, core drugs of clinical postmenopausal osteoporosis were retrieved using data mining, the drug molecular action target was predicted through network pharmacology, the key nodes of interaction were identified by combining postmenopausal osteoporosis-related targets, and the pharmacological mechanism of Traditional Chinese Medicine (TCM) against postmenopausal osteoporosis and other action mechanisms was explored.Methods: TCMISS V2.5 was used to collect TCM prescriptions of postmenopausal osteoporosis from databases, including Zhiwang, Wanfang, PubMed, etc., for selecting the highest confidence drugs. TCMSP and SwissTargetPrediction databases were selected to screen the main active ingredients of the highest confidence drugs and their targets. Relevant targets for postmenopausal osteoporosis were retrieved from GeneCards and GEO databases, PPI network diagrams construction and selection of core nodes in the network, GO and KEGG enrichment analysis, and molecular docking validation.Results: Correlation analysis identified core drug pairs as 'Corni

Fructus-Epimedii Folium-Rehmanniae Radix Praeparata' (SZY-YYH-SDH). After TCMSP co-screening and de-weighting, 36 major active ingredients and 305 potential targets were selected. PPI network graph was built from the 153 disease targets and 24 TCM disease intersection targets obtained. GO, KEGG enrichment results showed that the intersectional targets were enriched in the PI3K-Akt signalling pathway, etc. The target organs were mainly distributed in the thyroid, liver, CD33+_Myeloid, etc. Molecular docking results showed that the core active ingredients of the 'SZY-YYH-SDH' were able to bind to the pair core nodes and PTEN and EGFR.Conclusion: The results showed that 'SZY-YYH-SDH' can provide the basis for clinical application and treat postmenopausal osteoporosis through multi-component, multi-pathway, and multi-target effects.
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TI The role of bDMARDs in the prevention and treatment of inflammatory-related comorbidities in Psoriatic Arthritis
SO EXPERT OPINION ON BIOLOGICAL THERAPY
LA English
DT Review
DE Psoriatic arthritis; bDMARDs; comorbidities; obesity; metabolic syndrome; depression; osteoporosis; NASH
ID platelet-rich plasma; position statement; knee arthroplasty; total hip; society; osteoarthritis; management; recommendations; rheumatology; replacement
AB IntroductionPsoriatic arthritis (PsA) is an immune-inflammatory disease that affects both joints and entheses, and with diverse extra-articular manifestations (psoriasis, inflammatory bowel disease (IBD), and uveitis). A wide range of comorbid conditions, including cardiovascular diseases, obesity, metabolic syndrome (MetS), nonalcoholic fatty liver disease (NAFLD), mental health disorders (depression/anxiety), and osteoporosis are highly prevalent in course of PsA.Biological DMARDs (bDMARD), including TNF-inhibitors (TNFi), Interleukin (IL-17i) and IL-23i represent the cornerstone of the management of active disease. The use of these therapies obviously requires considering comorbidities presence, safety aspects and contraindications.IntroductionPsoriatic arthritis (PsA) is an immune-inflammatory disease that affects both joints and entheses, and with diverse extra-articular manifestations (psoriasis, inflammatory bowel disease (IBD), and uveitis). A wide range of comorbid conditions, including cardiovascular diseases, obesity, metabolic syndrome (MetS), nonalcoholic fatty liver disease (NAFLD), mental health disorders (depression/anxiety), and osteoporosis are highly prevalent in course of PsA.Biological DMARDs (bDMARD), including TNF-inhibitors

(TNFi), Interleukin (IL-17i) and IL-23i represent the cornerstone of the management of active disease. The use of these therapies obviously requires considering comorbidities presence, safety aspects and contraindications.Areas coveredThe aim of this review is to describe the inflammatory mechanisms behind PsA comorbidities, and the role of bDMARDs in the prevention and treatment of these conditions in course of PsA.Expert opinionTailoring therapeutic strategies to the individual characteristics of each PsA patient can be an effective approach to manage comorbidities, maximizing the efficacy of bDMARDs, and reducing the incidence of AEs. Identifying targets within disease pathways can guide research into therapeutics that address both PsA and comorbidities simultaneously, but more studies are advocated for clarifying the potential prevention and management of bDMARDs used for PsA.
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JI Expert Opin. Biol. Ther.
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WC Biotechnology & Applied Microbiology; Medicine, Research & Experimental
SC Biotechnology & Applied Microbiology; Research & Experimental Medicine
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UT WOS:001276945200001
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TI Mechanism exploration of Osteoking in the treatment of lumbar disc herniation based on network pharmacology and molecular docking
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Osteoking; Lumbar disc herniation; Network pharmacology; Molecular docking
ID human intervertebral disc; nucleus pulposus; tnf-alpha; cells; expression; injection
AB ObjectiveLumbar disc herniation (LDH) is a common spinal surgical disease. Low back and leg pain caused by LDH is the main factor leading to functional disability, which has caused a serious burden to patients and society. Osteoking can delay the progression of osteoporosis and osteoarthritis, and even has a significant effect on the prevention of deep vein thrombosis after fracture surgery. In recent years, it has been gradually used in the treatment of LDH and has received significant results. However, the underlying mechanism remains unclear. The aim of this study was to predict the mechanism of Osteoking in the treatment of LDH through network pharmacology and verify it by molecular docking method.MethodsThe TCMSP database was used to collect the relevant active components and targets of Osteoking, while the GeneCards, OMIM and DisGeNET databases were utilized to collect the relevant disease targets of LDH. The Venny 2.1.0 software was employed to obtain the intersecting gene targets of Osteoking and LDH. PPI network construction and core target selection were performed using Cytoscape 3.9.0 software. The Metascape database was used for GO and KEGG enrichment analysis of the relevant targets. Finally, molecular docking was conducted using AutoDock software.ResultsThe study identified 116 potential targets and 26 core targets for the treatment of LDH with Osteoking. Pathways in cancer, Alzheimer's disease, microRNAs in cancer and the IL-17 signalling pathway were among the main involved signalling pathways. Molecular docking results demonstrated that the key targets AKT1, IL-6, ALB, TNF and IL-1 beta exhibited relatively stable binding activities with the main active components of Osteoking.ConclusionsOsteoking can alleviate the symptoms of lumbar disc herniation through the modulation of multiple targets and signalling pathways.

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JI J. Orthop. Surg. Res.
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WC Orthopedics
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AF Wu, Yan
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Ji, Hong
TI Knowledge, Attitudes, and Practices of Patients with Knee Osteoarthritis Regarding Osteoporosis and Its Prevention: A Cross-Sectional Study in China
SO INTERNATIONAL JOURNAL OF GENERAL MEDICINE
LA English
DT Article
DE osteoarthritis of the knee; osteoporosis; disease prevention; surveys and questionnaires; health knowledge; attitudes; practice
ID management; diagnosis; fractures; women; hip
AB Background: Older age and female sex are risk factors for osteoarthritis and

osteoporosis (OP). This study evaluated the knowledge, attitudes, and practices of patients with knee osteoarthritis (KOA) in China regarding OP and its prevention. This cross-sectional, questionnaire-based study enrolled patients with KOA at four grade-A tertiary hospitals in Shandong Province between 1st September and 20th November 2022. Methods: The administered questionnaire contained 55 items across four dimensions (demographic information, knowledge, attitude, and practice). Logistic regression analyses were performed to identify factors associated with an overall questionnaire score >= 70% of the maximum possible score. SPSS 26.0 was used for the analyses; P<0.05 was considered significant. Results: The analysis included 434 participants (261 females). The median knowledge, attitude, and practice scores were 7 (interquartile range: 5-10) (possible range, 0-17 points), 44 (interquartile range: 42-49) (possible range, 11-55 points), and 43 (interquartile range: 38- 47) (possible range, 13-65 points), respectively. Multivariable logistic regression indicated that female sex (odds ratio [OR], 2.421; 95% confidence interval [95% CI] 1.558-3.762; P<0.001), age 56-65 years-old (OR, 4.222; 95% CI, 1.763-10.109; P=0.001 vs <= 55 years-old), age >65 years-old (OR, 4.358; 95% CI, 1.863-10.195; P=0.001 vs <= 55 years-old), middle/high/technical secondary school education (OR, 1.853; 95% CI, 1.002-3.428; P=0.049 vs primary school or below), and having KOA for 4-5 years (OR, 2.682; 95% CI, 1.412-5.094; P=0.003 vs <= 3 years) were independently associated with a high KAP score. Conclusion: There is room for improvement in the knowledge and practices of patients with osteoarthritis in China regarding OP. The findings of this study may facilitate the design and implementation of education programs to increase awareness about OP prevention among patients with KOA.
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JI Int. J. Gen. Med.
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WC Medicine, General & Internal
SC General & Internal Medicine
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AU Chen, HP
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AF Chen, Haiperng
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Zheng, Zhihui
Xuzhou, Hengte
Wang, Qinglai
TI Effect of Bone Marrow Stromal Cells Derived miR-26b on Chondrocytes of Osteoporosis Rats
SO ANNALS OF CLINICAL AND LABORATORY SCIENCE
LA English
DT Article
DE mir-26b; sirt2; osteoporosis
ID mesenchymal stem-cells; osteogenic differentiation; microrna expression; management; prevention; endocrine; diagnosis; sirtuins
AB Objective. Osteoporosis is a common bone disease. miR-26b regulates OA-induced osteogenesis and induces osteoporosis. miR-26b is elevated in bone marrow stromal cells (BMSCs) during bone formation; however, we haven't fully revealed whether it is directly involved in this process, which was the aim of this study. Methods. An oophorectomized rat model of osteoporosis was used. BMSCs were detected by electron microscopy of exosomes, and mir-26b levels were detected by RT-PCR. The correlation between mir-26b and sirt2 was detected by bioinformatics and luciferase activity analysis. Bone microstructure and cartilage moisture content were also measured. The proliferation ability of mir-26b and sirt2 on chondrocytes was detected by cell viability test and flow cytometry. Results. Western blotting further proved that the surface markers of isolated granular exosomes were positive for CD63 and CD81. Further analysis showed that exosomes' diameters ranged from 50 to 150 nm. Mir-26b is elevated in BMSC, and its mimics can promote proliferation. Luciferase showed that mir-26b targets sirt2 and the effect of elevated mir-26b on chondrocytes was completely reversed by silencing sirt2. The proliferation ability of C28/12 chondrocytes in Mir MICs group was lower than other two groups, while that in Mir inhibition group had stronger proliferation ability than in the Mir NC group. mir-26b was highly expressed in BMSC, indicating that mir-26b comes from secretion of BMSC. Conclusion. Mir-26 is highly expressed in OP. mir-26b can therefore target sirt2 to promote proliferation and inhibit apoptosis of OP chondrocytes. It may offer a possibility of a treatment of OP in the future.
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NR 24
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U2 1
PU ASSOC CLINICAL SCIENTISTS
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J9 ANN CLIN LAB SCI
JI Ann. Clin. Lab. Sci.
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WC Medical Laboratory Technology
SC Medical Laboratory Technology
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PT J
AU Xin, L
Tan, GY
Zhang, Q
Zhang, Q
AF Xin, Li
Tan, Guo-yao
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TI Protective Effects of Phellodendron Species on Bone Health: A Novel Perspective on Their Potentials in Treating Osteoporosis and Osteoarthritis
SO CHINESE JOURNAL OF INTEGRATIVE MEDICINE
LA English
DT Review
DE Phellodendron species; bone health; osteoporosis; osteoarthritis; review
ID metabolism; berberine; palmatine; mice
AB Phellodendron (PN) species, traditionally used in Chinese medicine for centuries, hold promise as a potential treatment for osteoporosis (OP) and osteoarthritis (OA) due to their bioactive compounds. The bioactive compounds, including berberine and palmatine, exhibit anti-inflammatory, antioxidant, and bone-protective properties, contributing to their potential therapeutic benefits in promoting bone health and preventing bone loss. However, challenges such as the need for standardized preparation and dosing, limited clinical studies, and potential interactions with other medications hinder their clinical use. Nonetheless, the rich history of PN species in Chinese medicine provides a promising foundation for future investigation into their potential as alternative treatments for OP and OA. Further research is needed to fully understand the underlying mechanisms of action and explore the clinical implications of PN for bone health.
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NR 49
TC 2
Z9 4
U1 0
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PT J
AU Kogan, F
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TI Multimodal positron emission tomography (PET) imaging in non-oncologic musculoskeletal radiology
SO SKELETAL RADIOLOGY
LA English
DT Review
DE PET; Metabolic imaging; Quantitative imaging; Musculoskeletal
ID early-stage osteoarthritis; regional bone metabolism; rheumatoid-arthritis; fluoride pet; joint infection; lumbar spine; f-18-fluoride; pet/mri; knee; localization
AB Musculoskeletal (MSK) disorders are associated with large impacts on patient's pain and quality of life. Conventional morphological imaging of tissue structure is limited in its ability to detect pain generators, early MSK disease, and rapidly assess treatment efficacy. Positron emission tomography (PET), which offers unique capabilities to evaluate molecular and metabolic processes, can provide novel information about early pathophysiologic changes that occur before structural or

even microstructural changes can be detected. This sensitivity not only makes it a powerful tool for detection and characterization of disease, but also a tool able to rapidly assess the efficacy of therapies. These benefits have garnered more attention to PET imaging of MSK disorders in recent years. In this narrative review, we discuss several applications of multimodal PET imaging in non-oncologic MSK diseases including arthritis, osteoporosis, and sources of pain and inflammation. We also describe technical considerations and recent advancements in technology and radiotracers as well as areas of emerging interest for future applications of multimodal PET imaging of MSK conditions. Overall, we present evidence that the incorporation of PET through multimodal imaging offers an exciting addition to the field of MSK radiology and will likely prove valuable in the transition to an era of precision medicine.
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NR 96
TC 3
Z9 3
U1 0
U2 1
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WC Orthopedics; Radiology, Nuclear Medicine & Medical Imaging
SC Orthopedics; Radiology, Nuclear Medicine & Medical Imaging
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AF Hol, Caroline
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TI Temporomandibular Joint Discectomy in Patients With Disc Displacement: Assessment of Osteoarthritis at 10-and 30-Year Follow-Up
SO JOURNAL OF ORAL REHABILITATION
LA English
DT Article
DE DC-TMD; discectomy; follow-up; osteoarthritis; radiography; temporomandibular joint
ID long-term evaluation; chronic closed lock; internal derangement; surgical-treatment; diagnostic-criteria; clicking
AB Background: Few >= 10-year follow-up studies of temporomandibular joint (TMJ) discectomy without replacement in patients with disc displacement (DD) analyse the relationship between the surgery and osteoarthritis (OA) exist. Objectives: To radiologically evaluate bony joint changes and OA development 10 and 30 years after TMJ discectomy as well as 30-year clinical outcome. Methods: Twenty-two discectomy patients at the University of Oslo, Norway, with records confirming initial TMJ diagnosis and attendance of 10-year radiological follow-up were evaluated and eligible for 30-year follow-up. Primary variables: discectomy

and CT-/CBCT-diagnosed OA at follow-ups. Secondary variables: perioperative TMJ diagnoses and remodelling at follow-up. Unoperated TMJs (Unop-TMJs) in unilaterally operated patients were controls. Statistical association and correlation analyses were performed for the 10-year follow-up (significance level $p < 0.05$). Results: Twenty-two patients attended the 10-year follow-up (mean follow-up 11 years) with 27 operated TMJs (Op-TMJs) and 17 Unop-TMJs. OA perioperatively was associated with DD without reduction ($p = 0.001$) and additional disc abnormalities ($p = 0.016$). Although statistically non-significant, the number of TMJs with OA had increased at 10-year follow-up ($p = 0.114$, Op-TMJs: 14 to 20 joints; Unop-TMJs: 2 to 5 joints). Remodelling was correlated with discectomy ($p = 0.003$) and to OA ($p = 0.006$). Nine patients attended the 30-year follow-up (mean follow-up 32 years, 11 Op-TMJs). All TMJs with OA at 30-year follow-up had OA at 10-year follow-up. Mean maximal interincisal opening was 39 mm. No DC-TMD-diagnosed arthralgia was found. Conclusion: Osteoarthritis developed similarly between Op- and Unop-TMJs. Only remodelling, not OA, was correlated to the surgery. The clinical results were still favourable at final follow-up.
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NR 41
TC 3
Z9 2
U1 0
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BP 2643
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PT J
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TI Flap-Based Lower Extremity Reconstruction in the Elderly-Is It Safe and Does Age Impact Ambulation?
SO MICROSURGERY
LA English
DT Article
DE ambulation; free flap; local flap; lower extremity; outcomes
ID quality-of-life; microsurgical reconstruction; lower leg; amputation; thickness; mortality; defects; older
AB Introduction: Lower extremity (LE) reconstruction in the elderly population presents a multifaceted challenge, primarily due to age-related degenerative changes, comorbidities, and functional decline. Elderly individuals often encounter conditions such as osteoarthritis, osteoporosis, and cardiovascular and peripheral artery disease (PAD), which can severely compromise the structural integrity and function of the lower limbs. As such, we aim to assess postoperative complications and functional recovery following LE reconstruction in elderly patients. Methods: Patients >= 18 years who underwent post-traumatic LE reconstruction with flap reconstruction at a Level 1 trauma center between 2007 and 2022 were included. Patient demographics, flap/wound characteristics, complications, and ambulation for the elderly (>= 60 years old) and the control (< 60 years old) cohorts were recorded. The primary outcome was final ambulation status, modeled with logistic regression. Secondary outcomes included postoperative complications. Results: The mean ages of the control (n = 374) and elderly (n = 49) groups were 37.4 +/- 12.6 and 65.8 +/- 5.1 years, respectively. Elderly patients more frequently required amputation after flap surgery (p = 0.002). There was no significant difference between the two cohorts in preoperative ambulation status (p = 0.053). Postoperatively, 22.4% of elderly patients were independently ambulatory at final follow-up, compared to 49.5% of patients < 60. Of the elderly, 14.3% could ambulate with an assistance device (cane, walker, etc.), compared to 26.5% in the control group. A wheelchair was required for 46.9% of elderly patients, significantly higher than the 22.7% of those < 60 years of age (p < 0.001). Multivariate regression confirmed an association between older age and nonambulatory final status (p = 0.033). Conclusion: LE reconstruction can likely be performed safely in patients 60 years of age or older. However, older age is independently associated with significantly worse postoperative ambulation. Preoperative assessment, including gait and muscle strength, and early initiation of postoperative rehabilitation can potentially improve ambulation in elderly individuals undergoing LE reconstruction.
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TI The current insights of mitochondrial hormesis in the occurrence and treatment of bone and cartilage degeneration
SO BIOLOGICAL RESEARCH
LA English
DT Review
DE Mitochondrial hormesis; Senescence; Osteoarthritis; Intervertebral disc degeneration; Osteoporosis
ID intervertebral disc; oxidative stress; osteoarthritis implications; cellular senescence; kinase-activity; life-span; mitohormesis; ros; promotes; exercise
AB It is widely acknowledged that aging, mitochondrial dysfunction, and cellular phenotypic abnormalities are intricately associated with the degeneration of bone and cartilage. Consequently, gaining a comprehensive understanding of the regulatory patterns governing mitochondrial function and its underlying mechanisms holds promise for mitigating the progression of osteoarthritis, intervertebral disc degeneration, and osteoporosis. Mitochondrial hormesis, referred to as mitohormesis, represents a cellular adaptive stress response mechanism wherein mitochondria restore homeostasis and augment resistance capabilities against stimuli by generating reactive oxygen species (ROS), orchestrating unfolded protein reactions (UPRmt), inducing mitochondrial-derived peptides (MDP), instigating mitochondrial dynamic changes, and activating mitophagy, all prompted by low doses of stressors. The varying nature, intensity, and duration of stimulus sources elicit divergent degrees of mitochondrial stress responses, subsequently activating one or more signaling pathways to initiate mitohormesis. This review focuses specifically on the effector molecules and regulatory networks associated with mitohormesis, while also scrutinizing extant mechanisms of mitochondrial dysfunction contributing to bone and cartilage degeneration through oxidative stress damage. Additionally, it underscores the potential of mechanical stimulation, intermittent dietary restrictions, hypoxic preconditioning, and low-dose toxic compounds to trigger mitohormesis, thereby alleviating bone and cartilage degeneration.
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TC 13
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TI Long-term results after medial patellotibial ligament reconstruction for the treatment of patellofemoral instability
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article
DE MPTL reconstruction; Patellar dislocation; Patellar instability; Knee reconstructive surgery
ID primary patellar dislocation; mpfl reconstruction; clinical-outcm; follow-up; children
AB Purpose To evaluate long-term clinical outcomes and redislocation rate after medial patellotibial ligament reconstruction. Materials and methods A total of 26 knees with mean age 26.3 +/- 10.6 years (25 patients, 7 males and 18 females) treated for patellar instability (at least two objective dislocations) with medialization of the patellar tendon medial third were evaluated with an intermediate clinical follow-up (FU) at a mean of 6.5 +/- 2.1 years and with a final telephone interview follow-up at mean of 15.6 +/- 2.5 years (11.4-20.1). Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC), Kujala, Visual Analog Scale (VAS) for pain and Tegner activity scores were used. Information about further redislocation and knee surgery was also collected. Results All the clinical scores had a significant improvement compared to preoperative status (WOMAC pre-op 55.9 +/- 27.2 vs. WOMAC final FU 80.8 +/- 22.2; KUJALA pre-op 41.0 +/- 24.0 vs. KUJALA final FU 77.2 +/- 24.1; VAS pre-op 6.0 +/- 3.1 vs. VAS final FU 3.44 +/- 2.35; TEGNER pre-op 2.1 +/- 2.0 vs. TEGNER final FU 3.6 +/- 1.8; $p < 0.001$), and the outcomes remained stable at the final follow-up compared to the intermediate follow-up ($p > 0.05$). A total of 4 knees had at least one redislocation at the final follow-up, while 3 knees underwent total knee replacement surgery. The redislocation-survival rate at 5 years is 92%, meanwhile is 84% at 10 and 15 years. Conclusions MPTL reconstruction produced good clinical results and a survival rate of 84% at a mean of 16 years follow-up and could be considered as associated procedure in case of patellofemoral instability. Level of evidenceLevel IV.
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NR 28
TC 1
Z9 1
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PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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SC Orthopedics; Surgery
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TI Prevention of obstetric anal sphincter injuries with perineal support and lateral episiotomy: A historical cohort study
SO ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA
LA English
DT Article
DE delivery mode; episiotomy; fetal position; OASIS; parity
ID operative vaginal delivery; fetal head position; risk-factors; mediolateral episiotomy; routine; reduce; tears
AB IntroductionThere are many risk factors for obstetric anal sphincter injury (OASIS) and the interaction between these risk factors is complex and understudied. The many observational studies that have shown a reduction of OASIS rates after implementation of perineal support have short follow-up time. We aimed to study the effect of integration of active perineal support and lateral episiotomy on OASIS rates over a 15-year period and to study interactions between risk factors known before delivery.Material and methodsWe performed a historical cohort study over the periods 1999-2006 and 2007-2021 at Stavanger University Hospital, Norway. The main outcome was OASIS rates. Women without a previous cesarean section and a live singleton fetus in cephalic presentation at term were eligible. The department implemented in 2007 the Finnish concept of active perineal protection, which includes support of perineum, control of fetal expulsion, good communication with the mother and observation of perineal stretching. The practice of mediolateral episiotomy was replaced with lateral episiotomy when indicated. We analyzed the OASIS rates in groups with and without episiotomy stratified for delivery mode, fetal position at delivery and for parity, and adjusted for possible confounders (maternal age, gestational age, oxytocin augmentation and epidural analgesia).ResultsWe observed a long-lasting reduction in OASIS rates from 4.9% to 1.9% and an increase in episiotomy rates from 14.4% to 21.8%. Lateral episiotomy was associated with lower OASIS rates in nulliparous women with instrumental vaginal deliveries and occiput anterior (OA) position; 3.4% versus 10.1% (OR 0.31; 95% CI: 0.24-0.40) and 6.1 versus 13.9% (OR 0.40; 95% CI: 0.19-0.82) in women with occiput posterior (OP) position. Lateral episiotomy was also associated with lower OASIS rates in nulliparous women with spontaneous deliveries and OA position; 2.1% versus 3.2% (OR 0.62; 95% CI: 0.49-0.80). The possible confounders had little confounding effects on the risk of OASIS in groups with and without episiotomy.ConclusionsWe observed a long-lasting reduction in OASIS rates after implementation of preventive procedures. Lateral episiotomy was associated with lower OASIS rates in nulliparous women with an instrumental delivery. Special attention should be paid to deliveries with persistent OP position. Obstetric anal sphincter injuries rates during the study period differentiated in accordance with the Robson ten-group classification system. Blue line represents Robson ten-group classification system group 1, green line group 2, brown line

group 3 and red line group 4.image
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TI Multiple applications of metal-organic frameworks (MOFs) in the treatment of orthopedic diseases
SO FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY
LA English
DT Review
DE metal-organic frameworks; MOFs; tumor; osteoporosis; osteoarthritis
ID delivery; osteoarthritis; nanoparticles; hydroxyapatite; osteosarcoma; hif-2-alpha; osteogenesis; prevalence; stability; chemistry
AB Pharmacologic treatment of orthopedic diseases is a common challenge for clinical orthopedic surgeons, and as an important step in the stepwise treatment of orthopedic diseases, it is often difficult to achieve satisfactory results with existing pharmacologic treatments. Therefore, it is increasingly important to find new ways to effectively improve the treatment pattern of orthopedic diseases as well as to enhance the therapeutic efficacy. It has been found that metal-organic frameworks (MOFs) possess the advantages of high specific surface area, high porosity, chemical stability, tunability of structure and biocompatibility. Therefore, MOFs are expected to improve the conventional traditional treatment modality for bone diseases. This manuscript reviewed the applications of MOFs in the treatment of common clinical bone diseases and look forward to its future development.
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TI Sphingolipid-Induced Bone Regulation and Its Emerging Role in Dysfunction Due to Disease and Infection

SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE sphingolipids; bone; infection; disease; osteoporosis
ID mesenchymal stem-cells; necrosis-factor-alpha; staphylococcus-aureus infections; sphingosine 1-phosphate levels; collagen-induced arthritis; neutral sphingomyelinase 2; novo ceramide synthesis; acid sphingomyelinase; pseudomonas-aeruginosa; induced apoptosis
AB The human skeleton is a metabolically active system that is constantly regenerating via the tightly regulated and highly coordinated processes of bone resorption and formation. Emerging evidence reveals fascinating new insights into the role of sphingolipids, including sphingomyelin, sphingosine, ceramide, and sphingosine-1-phosphate, in bone homeostasis. Sphingolipids are a major class of highly bioactive lipids able to activate distinct protein targets including, lipases, phosphatases, and kinases, thereby conferring distinct cellular functions beyond energy metabolism. Lipids are known to contribute to the progression of chronic inflammation, and notably, an increase in bone marrow adiposity parallel to elevated bone loss is observed in most pathological bone conditions, including aging, rheumatoid arthritis, osteoarthritis, and osteomyelitis. Of the numerous classes of lipids that form, sphingolipids are considered among the most deleterious. This review highlights the important primary role of sphingolipids in bone homeostasis and how dysregulation of these bioactive metabolites appears central to many chronic bone-related diseases. Further, their contribution to the invasion, virulence, and colonization of both viral and bacterial host cell infections is also discussed. Many unmet clinical needs remain, and data to date suggest the future use of sphingolipid-targeted therapy to regulate bone dysfunction due to a variety of diseases or infection are highly promising. However, deciphering the biochemical and molecular mechanisms of this diverse and extremely complex sphingolipidome, both in terms of bone health and disease, is considered the next frontier in the field.
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TI Two Decades of High-Resolution Peripheral Quantitative Computed Tomography: Present and Future Clinical Perspectives
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DE bone microarchitecture; fracture risk assessment; osteoporosis; osteoarthritis; high-resolution peripheral quantitative computed tomography
ID in-vivo assessment; trabecular bone score; fracture risk-assessment; 2nd-generation hr-pqct; distal radius; cortical bone; subject motion; mass measurements; mineral density; microarchitecture
AB Twenty years have passed since the introduction of high-resolution peripheral quantitative computed tomography (HR-pQCT) to assess human bone microarchitecture. During that time, the technique has emerged as an important research tool used by clinicians and scientists to learn about the pathophysiology of bone adaptation in the context of osteoporosis and many other bone-affected conditions. Its rich three-dimensional data is well suited for precise longitudinal monitoring of bone microarchitecture and associated patient-specific estimated bone strength. However, uptake of HR-pQCT as a clinical diagnostic tool has been limited, in part due to challenges such as availability, regulatory approvals, and demonstrated cost effectiveness. New research suggests fracture risk assessment using HR-pQCT is comparable with current standards based on traditional bone densitometry, but its contribution to clinical care is best suited to two areas: (1) leveraging microarchitectural information to assist in treatment decisions for the large subset of patients who lie in the so-called gray zone by current fracture risk assessment, and (2) longitudinal monitoring that establishes highly refined trajectories of bone adaptation and can inform decisions to initiate treatment, monitor treatment effects, and inform cessation.
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TI Prediction of Multiple Degenerative Diseases Based on DNA Methylation in a Co-Physiology Mechanisms Perspective
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
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DT Article
DE DNA methylation; epigenetic clock; degenerative diseases; deep learning
ID biomarker
AB Degenerative diseases oftentimes occur within the continuous process of aging, and the corresponding clinical manifestations may be neurodegeneration, neoplastic diseases, or various human complex diseases. DNA methylation provides the opportunity to explore aging and degenerative diseases as epigenetic traits. It

has already been applied to age prediction and disease diagnosis. It has been shown that various degenerative diseases share co-physiology mechanisms with each other, clues of which may be gained from studying the aging process. Here, we endeavor to predict the risk of degenerative diseases in an aging-relevant comorbid mechanism perspective. Firstly, an epigenetic clock method was implemented based on a multi-scale convolutional neural network, and a Shapley feature attribution analysis was applied to discover the aging-related CpG sites. Then, these sites were further screened to a smaller subset composed of 196 sites by using biomics analysis according to their biological functions and mechanisms. Finally, we constructed a multilayer perceptron (MLP)-based degenerative disease risk prediction model, Mlp-DDR, which was well trained and tested to accurately classify nine degenerative diseases. Recent studies also suggest that DNA methylation plays a significant role in conditions like osteoporosis and osteoarthritis, broadening the potential applications of our model. This approach significantly advances the ability to understand degenerative diseases and represents a substantial shift from traditional diagnostic methods. Despite the promising results, limitations regarding model complexity and dataset diversity suggest directions for future research, including the development of tissue-specific epigenetic clocks and the inclusion of a wider range of diseases.
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TI 3D printing technology and its combination with nanotechnology in bone tissue engineering
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DT Review
DE Bone tissue engineering; Nanotechnology; 3D printing technology; Bioactive scaffold
ID calcium-phosphate ceramics; silver nanoparticles; tricalcium phosphate; in-vitro; scaffolds; proliferation; biomaterials; regeneration; fabrication; design
AB With the graying of the world's population, the morbidity of age-related chronic degenerative bone diseases, such as osteoporosis and osteoarthritis, is increasing yearly, leading to an increased risk of bone defects, while current treatment methods face many problems, such as shortage of grafts and an incomplete repair. Therefore, bone tissue engineering offers an alternative solution for regenerating and repairing bone tissues by constructing bioactive scaffolds with porous structures that provide mechanical support to damaged bone tissue while promoting angiogenesis and cell adhesion, proliferation, and activity. 3D printing technology has become the primary scaffold manufacturing method due to its ability to precisely control the internal pore structure and complex spatial shape of bone scaffolds. In contrast, the fast development of nanotechnology has provided more possibilities for the internal structure and biological function of scaffolds. This review focuses on the application of 3D printing technology in bone tissue engineering and nanotechnology in the field of bone tissue regeneration and repair, and explores the prospects for the integration of the two technologies.
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ID articular-cartilage; raman-spectroscopy; nir spectroscopy; disease

AB Osteoarthritis (OA) is the most common degenerative joint disease, presented as wearing down of articular cartilage and resulting in pain and limited mobility for 1 in 10 adults in the UK [Osteoarthr. Cartil. 28(6), 792 (2020)]. There is an unmet need for patient friendly paradigms for clinical assessment that do not use ionizing radiation (CT), exogenous contrast enhancing dyes (MRI), and biopsy. Hence, techniques that use non-destructive, near- and shortwave infrared light (NIR, SWIR) may be ideal for providing label-free, deep tissue interrogation. This study demonstrates multimodal "spectromics", low-level abstraction data fusion of non-destructive NIR Raman scattering spectroscopy and NIR-SWIR absorption spectroscopy, providing an enhanced, interpretable "fingerprint" for diagnosis of OA in human cartilage. This is proposed as method level innovation applicable to both arthro- or endoscopic (minimally invasive) or potential exoscopic (non-invasive) optical approaches. Samples were excised from femoral heads post hip arthroplasty from OA patients (n =13) and age-matched control (osteoporosis) patients (n = 14). Under multivariate statistical analysis and supervised machine learning, tissue was classified to high precision: 100% segregation of tissue classes (using 10 principal components), and a classification accuracy of 95% (control) and 80% (OA), using the combined vibrational data. There was a marked performance improvement (5 to 6-fold for multivariate analysis) using the spectromics fingerprint compared to results obtained from solely Raman or NIR-SWIR data. Furthermore, clinically relevant tissue components were identified through discriminatory spectral features - spectromics biomarkers - allowing interpretable feedback from the enhanced fingerprint. In summary, spectromics provides comprehensive information for early OA detection and disease stratification, imperative for effective intervention in treating the degenerative onset disease for an aging demographic. This novel and elegant approach for data fusion is compatible with various NIR-SWIR optical devices that will allow deep non-destructive penetration.
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TI Relationship between DXA measured systemic bone mineral density and subchondral bone cysts in postmenopausal female patients with knee osteoarthritis: a cross-sectional study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Bone mineral density; Osteoarthritis; Subchondral bone cyst; Vitamin D
ID synovial-fluid macrophages; vitamin-d; resorption; hip; 1,25-dihydroxyvitamin-d3; association; progression; prevalence; expression; cartilage
AB BackgroundIndividuals with high systemic bone mineral density (BMD) may have an increased risk of incident knee osteoarthritis (OA). Besides that, radiographic osteophytes are strongly associated with BMD. Because of these

reasons, the aim of the study was to investigate the possible association between radiological subchondral bone cyst (SBC) grade and systemic BMD and vitamin D status in the postmenopausal female patients with knee OA in a crosss-sectional study.MethodsThis study included of 48 osteoporosis treatment-free postmenopausal patients diagnosed with symptomatic medial compartment knee OA. BMD analysis was performed using dual-energy X-ray absorptiometry (DXA) and serum vitamin D levels were measured after recording patients' findings. Each knee was scanned using computed tomography (CT), and categorical SBC scores were graded for the medial and lateral tibiofemoral (TF) and patellofemoral (PF) compartments and further calculated as compartmental total, total TF and grand total of both TF compartments. SBC scores were analysed with correlation analysis.ResultsThe patient population was characterized by radiographic joint space narrowing, obesity and low vitamin D status. Median medial total and grand total TF SBC scores were significantly different between the patient groups according to the Kellgren-Lawrence (KL) radiographic grading ($p = 0.006$ and $p = 0.007$, respectively). There were no correlations between femoral BMD values and SBC scores. However, positive correlations were detected significantly between L1 - 4 DXA values and TF SBC scores, but not with PF SBC scores ($p = 0.005$ for the correlation between L1 - 4 BMD and medial compartments total TF SBC score, $p = 0.021$ for the correlation between L1 - 4 BMD and grand total TF SBC score). No significant correlations were found with Vitamin D levels.ConclusionsDevelopment of TF OA high-grade SBCs may be linked to systemic bone mass as represented by trabecular bone-rich lumbar vertebrae. The relationship might point to the importance of bone stiffness as an acting factor in knee OA possibly with mechanical energy transfer to the joint.
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TI Exploring the pharmacological mechanism of Xianlingubao against diabetic osteoporosis based on network pharmacology and molecular docking: An observational study
SO MEDICINE

LA English
DT Article
DE diabetes mellitus; drug repurposing; osteoporosis; pharmacology; traditional Chinese medicine
ID bone-mineral density; differentiation; adipocytes; quercetin; osteoblast; pathways; resource
AB Xianlinggubao formula (XLGB), is a traditional Chinese compound Medicine that has been extensively used in osteoarthritis and aseptic osteonecrosis, but its curative effect on diabetic osteoporosis (DOP) and its pharmacological mechanisms remains not clear. The aim of the present study was to investigate the possible mechanism of drug repurposing of XLGB in DOP therapy. We acquired XLGB active compounds from the traditional Chinese medicine systems pharmacology and traditional Chinese medicines integrated databases and discovered potential targets for these compounds by conducting target fishing using the traditional Chinese medicine systems pharmacology and Swiss Target Prediction databases. Gene Cards and Online Mendelian Inheritance in Man (R) database were used to identify the DOP targets. Overlapping related targets between XLGB and DOP was selected to build a protein-protein interaction network. Next, the Metascape database was utilized to enrich the Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathways. In addition, Auto-Dock Vina software was used to verify drug and target binding. In total, 48 hub targets were obtained as the candidate targets responsible for DOP therapy. The anti-DOP effect mediated by XLGB was primarily centralized on the advanced glycation end products (AGEs)-receptor for AGE signaling pathway in diabetic complications and osteoclast differentiation. In addition, AKT serine/threonine kinase 1, tumor necrosis factor, Interleukin-6, vascular endothelial growth factor A and peroxisome proliferator activated receptor gamma, which were considered as potential therapeutic targets. Furthermore, molecular docking results confirm the credibility of the predicted therapeutic targets. This study elucidates that XLGB may through regulating AGEs formation and osteoclast differentiation as well as angiogenesis and adipogenesis against DOP. And this study provides new promising points to find the exact regulatory mechanisms of XLGB mediated anti-DOP effect.
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NR 61
TC 3
Z9 3
U1 3
U2 8
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0025-7974
EI 1536-5964
J9 MEDICINE

JI Medicine (Baltimore)
PD AUG 2
PY 2024
VL 103
IS 31
BP
EP
DI 10.1097/MD.0000000000039138
PG 10
WC Medicine, General & Internal
SC General & Internal Medicine
GA A5T5Y
UT WOS:001283157500043
PM 39093780
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ER

PT J
AU Ho, TJ
Tsai, WT
Wu, JR
Chen, HP
AF Ho, Tsung-Jung
Tsai, Wan-Ting
Wu, Jia-Ru
Chen, Hao-Ping
TI Biological Activities of Deer Antler-Derived Peptides on Human Chondrocyte and Bone Metabolism
SO PHARMACEUTICALS
LA English
DT Article
DE chondrocyte; deer antler; Guilu erxian jiao; kyotorphin; osteoblast; osteoclast differentiation
ID expression; rankl; kyotorphin; cells; calcium; culture; brain
AB Orally administered "tortoiseshell and deer antler gelatin" is a common traditional medicine for patients with osteoporosis or osteoarthritis. From the pepsin-digested gelatin, we previously isolated and identified the osteoblast-stimulating pentapeptide, TSKYR. Its trypsin digestion products include the dipeptide YR, enhancing calcium ion uptake, and tripeptide TSK, resulting in remarkable 30- and 50-fold increases in mineralized nodule area and density in human osteoblast cells. These peptides were chemically synthesized in this study. The composition of deer antler preparations comprises not only proteins and peptides but also a significant quantity of metal ion salts. By analyzing osteoblast growth in the presence of peptide YR and various metal ions, we observed a

synergistic effect of calcium and strontium on the effects of YR. Those peptides could also stimulate the growth of C2C12 skeletal muscle cells and human chondrocytes, increasing collagen and glycosaminoglycan content in a three-dimensional environment. The maintenance of bone homeostasis relies on a balance between osteoclasts and osteoblasts. Deer antler peptides were observed to inhibit osteoclast differentiation, as evidenced by ROS generation, tartrate-resistant acid phosphatase (TRACP) activity assays, and gene expression in RAW264.7 cells. In summary, our findings provide a deep understanding of the efficacy of this folk medicine.
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NR 43
TC 4
Z9 7
U1 3
U2 26
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 1424-8247
J9 PHARMACEUTICALS-BASE

JI Pharmaceuticals
PD APR 15
PY 2024
VL 17
IS 4
BP
EP
DI 10.3390/ph17040434
PG 13
WC Chemistry, Medicinal; Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
GA OY0E6
UT WOS:001210712100001
PM 38675396
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ER

PT J
AU Alidina, S
Luxenburg, D
Castro, A
Subhawong, TK
de Souza, FF
AF Alidina, Sameer
Luxenburg, Dylan
Castro, Athena
Subhawong, Ty K.
de Souza, Felipe Ferreira
TI Imaging Review of Different Subchondral Insufficiency Fractures
SO JOURNAL OF COMPUTER ASSISTED TOMOGRAPHY
LA English
DT Article
DE subchondral fractures; joint arthropathy; osteoarthritis
ID bone-marrow edema; dual-energy ct; osteochondritis-dissecans; transient osteoporosis; mri
AB Subchondral fractures are a common cause of joint pain that may ultimately lead to articular collapse and the need for arthroplasty. This type of fracture has been reported at multiple joints throughout the body. While clinical and radiographic resolution can be achieved, progressive bone collapse can occur and lead to a variety of complications. Understanding the pertinent imaging findings can aid in the early evaluation of subchondral fractures and in the prevention of their associated complications.
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NR 35
TC 0
Z9 0
U1 0
U2 1
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 0363-8715
EI 1532-3145
J9 J COMPUT ASSIST TOMO
JI J. Comput. Assist. Tomogr.
PD JUL-AUG 15
PY 2024
VL 48
IS 4
BP 663
EP 668
DI 10.1097/RCT.0000000000001628
PG 6
WC Radiology, Nuclear Medicine & Medical Imaging
SC Radiology, Nuclear Medicine & Medical Imaging
GA YE2H3
UT WOS:001266739100003
PM 38834938
DA 2026-02-10
ER

PT J
AU Szala, D
Kopanska, M
Trojniak, J
Jablonski, J
Hanf-Osetek, D
Snela, S
Zawlik, I
AF Szala, Dariusz
Kopanska, Marta

Trojniak, Julia
Jablonski, Jaroslaw
Hanf-Osetek, Dorota
Snela, Slawomir
Zawlik, Izabela
TI The Role of MicroRNAs in the Pathophysiology of Osteoarthritis
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE microRNA; osteoarthritis; OA; osteoarthrosis; miRNA; pathophysiology
ID affects chondrocyte proliferation; risk-factors; knee osteoarthritis; articular-cartilage; double-blind; tnf-alpha; expression; targets; pathogenesis; diagnosis
AB Worldwide, osteoarthritis (OA) is the most common cause of joint pain in older people. Many factors contribute to osteoarthritis' development and progression, including secondary osteoarthritis' underlying causes. It is important to note that osteoarthritis affects all four tissues: cartilage, bone, joint capsule, and articular apparatus. An increasingly prominent area of research in osteoarthritis regulation is microRNAs (miRNAs), a small, single-stranded RNA molecule that controls gene expression in eukaryotes. We aimed to assess and summarize current knowledge about the mechanisms of the action of miRNAs and their clinical significance. Osteoarthritis (OA) is affected by the interaction between miRNAs and inflammatory processes, as well as cartilage metabolism. MiRNAs also influence cartilage cell apoptosis, contributing to the degradation of the cartilage in OA. Studies have shown that miRNAs may have both an inhibitory and promoting effect on osteoporosis progression through their influence on molecular mechanisms. By identifying these regulators, targeted treatments for osteoarthritis may be developed. In addition, microRNA may also serve as a biomarker for osteoarthritis. By using these biomarkers, the disease could be detected faster, and early intervention can be instituted to prevent mobility loss and slow deterioration.
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PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
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AU Wittoek, R
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TI RANKL blockade for erosive hand osteoarthritis: a randomized placebo-controlled phase 2a trial
SO NATURE MEDICINE
LA English
DT Article
ID interphalangeal finger joints; radiographic progression; postmenopausal women; denosumab treatment; general-population; pain; prevalence; index

AB Erosive hand osteoarthritis (OA) is a prevalent and disabling disease with limited treatment options. Here we present the results of a monocentric, placebo-controlled, double-blind, randomized phase 2a clinical trial with denosumab, a receptor activator of nuclear factor-kappa B ligand inhibitor, evaluating the effects on structure modification in erosive hand OA. Patients were randomized to 48 weeks treatment with denosumab 60 mg every 3 months (n = 51, 41 females) or placebo (n = 49, 37 females). The primary (radiographic) endpoint was the change in the total Ghent University Scoring System (GUSS) at week 24, where positive changes correspond to remodeling and negative changes to erosive progression. Secondary endpoints were the change in the GUSS at week 48 and the number of new erosive joints at week 48 by the anatomical phase scoring system. Baseline mean GUSS (standard deviation) of target joints was 155.9 (69.3) in the denosumab group and 158.7 (46.8) in the placebo group. The primary endpoint was met with an estimated difference between groups of 8.9 (95% confidence interval (CI) 1.0 to 16.9; P = 0.024) at week 24. This effect was confirmed at week 48 (baseline adjusted GUSS (standard error of the mean) denosumab and placebo were 163.5 (2.9) and 149.2 (3.9), respectively; with an estimated difference between groups of 14.3 (95% CI 4.6 to 24.0; P = 0.003)). At patient level, more new erosive joints were developed in the placebo group compared with denosumab at week 48 (odds ratio 0.24 (95% CI 0.08 to 0.72); P = 0.009). More adverse events occurred in the placebo group (125 events in 44 patients (90%)) compared with the denosumab group (97 events in 41 patients (80%)). These results demonstrate that denosumab has structure modifying effects in erosive hand OA by inducing remodeling and preventing new erosive joints. EU Clinical Trials Register identifier 2015-003223-53. Denosumab, a receptor activator of nuclear factor-kappa B ligand inhibitor, previously developed for osteoporosis, was shown to be effective at inducing structural modification in patients with erosive hand osteoarthritis after 24 weeks.
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TI Immunosenescence: A new direction in anti-aging research
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Review
DE Immune system; Immunosenescence; Aging; Anti-aging; Age-related diseases
ID alzheimers association guidelines; immune-system; t-cells; posttraumatic osteoarthritis; neuropathologic assessment; streptococcus-pneumoniae; parkinsons-disease; therapeutic target; national institute; senescent cells
AB The immune system is a major regulatory system of the body, that is composed of immune cells, immune organs, and related signaling factors. As an organism ages, observable age-related changes in the function of the immune system accumulate in a process described as 'immune aging. Research has shown that the impact of aging on immunity is detrimental, with various dysregulated responses that affect the function of immune cells at the cellular level. For example, increased aging has been shown to result in the abnormal chemotaxis of neutrophils and decreased phagocytosis of macrophages. Age-related diminished functionality of immune cell types has direct effects on host fitness, leading to poorer responses to vaccination, more inflammation and tissue damage, as well as autoimmune disorders and the inability to control infections. Similarly, age impacts the function of the immune system at the organ level, resulting in decreased hematopoietic function in the bone marrow, a gradual deficiency of catalase in the thymus, and thymic atrophy, resulting in reduced production of related immune cells such as B cells and T cells, further increasing the risk of autoimmune disorders in the elderly. As the immune function of the body weakens, aging cells and inflammatory factors cannot be cleared, resulting in a cycle of increased inflammation that accumulates over time. Cumulatively, the consequences of immune aging increase the likelihood of developing age-related diseases, such as Alzheimer's disease, atherosclerosis, and osteoporosis, among others. Therefore, targeting the age-related changes that occur within cells of the immune system might be an effective anti-aging strategy. In this article, we summarize the relevant literature on immune aging research, focusing on its impact on aging, in hopes of providing new directions for anti-aging research.
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TI The burden of knee osteoarthritis worldwide, regionally, and nationally from 1990 to 2019, along with an analysis of cross-national inequalities
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DE Knee osteoarthritis; Global burden of disease; Joinpoint analysis; Cross-national inequality
ID patient-reported outcm; body-mass index; total hip-arthroplasty; income inequality; global burden; obesity; health; disease; risk; osteoporosis
AB ObjectiveTo describe the disease burden of knee osteoarthritis (KOA) globally, regionally, and in 204 countries by age, sex, and sociodemographic index (SDI) from 1990 to 2019, and to explore cross-national inequalities across SDI.MethodsThe Global Burden of Disease (GBD) 2019 database collected data on KOA worldwide from 1990 to 2019, including prevalence, incidence, years lived with disability (YLDs). The average annual percentage change (AAPC) was used to measure temporal trends. In addition, the inequality slope index and the health concentration index were calculated to quantify the unequal distribution of the burden of KOA across 204 countries worldwide.ResultsIn 2019, the global age-standardized prevalence rate increased by 7.5% compared with 1990, and the age-standardized incidence rate increased by about 6.2%; The age-standardized YLDs rate increased by about 7.8%. In addition to the Republic of Korea and the United States of America, the disease burden of KOA has increased year by year in other countries around the world. The incidence of KOA was highest at ages 50-59, while the prevalence and rates of YLDs were highest at ages 75-84. The burden of KOA was higher in women than in men. Cross-country inequality suggests that the inequality in the burden of KOA between high SDI and low SDI countries becomes greater, and that countries with high SDI bear a disproportionately high burden.ConclusionThe global KOA burden has risen steadily between 1990 and 2019, and cross-national inequality gaps remain large. Targeted measures must therefore be taken to address this inequality and the increasing global KOA disease burden.
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AU Lin, ZD
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TI Chondrocyte-targeted exosome-mediated delivery of Nrf2 alleviates cartilaginous endplate degeneration by modulating mitochondrial fission
SO JOURNAL OF NANOBIOTECHNOLOGY
LA English
DT Article
DE Cartilaginous endplate degeneration; Engineered exosome; Nrf2; Drp1; Mitochondrial fission; Apoptosis
ID inflammation

AB Background Cartilaginous endplate (CEP) degeneration, which is an important contributor to intervertebral disc degeneration (IVDD), is characterized by chondrocyte death. Accumulating evidence has revealed that dynamin-related protein 1 (Drp1)-mediated mitochondrial fission and dysfunction lead to apoptosis during CEP degeneration and IVDD. Exosomes are promising agents for the treatment of many diseases, including osteoporosis, osteosarcoma, osteoarthritis and IVDD. Despite their major success in drug delivery, the full potential of exosomes remains untapped.Materials and methods In vitro and in vivo models of CEP degeneration were established by using lipopolysaccharide (LPS). We designed genetically engineered exosomes (CAP-Nrf2-Exos) expressing chondrocyte-affinity peptide (CAP) on the surface and carrying the antioxidant transcription factor nuclear factor E2-related factor 2 (Nrf2). The affinity between CAP-Nrf2-Exos and CEP was evaluated by in vitro internalization assays and in vivo imaging assays. qRT-PCR, Western blotting and immunofluorescence assays were performed to examine the expression level of Nrf2 and the subcellular localization of Nrf2 and Drp1. Mitochondrial function was measured by the JC-1 probe and MitoSOX Red. Mitochondrial morphology was visualized by MitoTracker staining and transmission electron microscopy (TEM). After subendplate injection of the engineered exosomes, the degree of CEP degeneration and IVDD was validated radiologically and histologically.Results We found that the cargo delivery efficiency of exosomes after cargo packaging was increased by surface modification. CAP-Nrf2-Exos facilitated chondrocyte-targeted delivery of Nrf2 and activated the endogenous antioxidant defence system in CEP cells. The engineered exosomes inhibited Drp1 S616 phosphorylation and mitochondrial translocation, thereby preventing mitochondrial fragmentation and dysfunction. LPS-induced CEP cell apoptosis was alleviated by CAP-Nrf2-Exo treatment. In a rat model of CEP degeneration, the engineered exosomes successfully attenuated CEP degeneration and IVDD and exhibited better repair capacity than natural exosomes.Conclusion Collectively, our findings showed that exosome-mediated chondrocyte-targeted delivery of Nrf2 was an effective strategy for treating CEP degeneration.
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TI The osteocytic actions of glucocorticoids on bone mass, mechanical properties, or perilacunar remodeling outcomes are not rescued by PTH(1-34)
SO FRONTIERS IN ENDOCRINOLOGY
LA English

DT Article
DE osteocyte; glucocorticoids; prednisolone; parathyroid hormone (PTH); PTH (1-34); perilacunar canalicular remodeling; osteocytic osteolysis; bone
ID parathyroid-hormone; induced osteoporosis; gene-expression; articular-cartilage; subchondral bone; femoral-head; mice; pth; gender; osteoarthritis
AB Glucocorticoids (GC) and parathyroid hormone (PTH) are widely used therapeutic endocrine hormones where their effects on bone and joint arise from actions on multiple skeletal cell types. In osteocytes, GC and PTH exert opposing effects on perilacunar canalicular remodeling (PLR). Suppressed PLR can impair bone quality and joint homeostasis, including in GC-induced osteonecrosis. However, combined effects of GC and PTH on PLR are unknown. Given the untapped potential to target osteocytes to improve skeletal health, this study sought to test the feasibility of therapeutically mitigating PLR suppression. Focusing on subchondral bone and joint homeostasis, we hypothesize that PTH(1-34), a PLR agonist, could rescue GC-suppressed PLR. The skeletal effects of GC and PTH(1-34), alone or combined, were examined in male and female mice by micro-computed tomography, mechanical testing, histology, and gene expression analysis. For each outcome, females were more responsive to GC and PTH(1-34) than males. GC and PTH(1-34) exerted regional differences, with GC increasing trabecular bone volume but reducing cortical bone thickness, stiffness, and ultimate force. Despite PTH(1-34)'s anabolic effects on trabecular bone, it did not rescue GC's catabolic effects on cortical bone. Likewise, cartilage integrity and subchondral bone apoptosis, tartrate-resistant acid phosphatase (TRAP) activity, and osteocyte lacunocanalicular networks showed no evidence that PTH(1-34) could offset GC-dependent effects. Rather, GC and PTH(1-34) each increased cortical bone gene expression implicated in bone resorption by osteoclasts and osteocytes, including Acp5, Mmp13, Atp6v0d2, Ctsk, differences maintained when GC and PTH(1-34) were combined. Since PTH(1-34) is insufficient to rescue GC's effects on young female mouse bone, future studies are needed to determine if osteocyte PLR suppression, due to GC, aging, or other factors, can be offset by a PLR agonist.
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AU Yin, Q
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TI Microbiome dysbiosis by antibiotics protects cartilage degradation in OAOP mice
SO JOURNAL OF ENDOCRINOLOGY
LA English
DT Article
DE gut microbiota; osteoarthritis; osteoporosis; LPS
ID nf-kappa-b; gut microbiota; bone mass; osteoarthritis; osteoporosis; model; severity; fracture; density; impact
AB The role of this study was to evaluate the impact of gut microbiota depletion on the progression of osteoarthritis (OA) and osteoporosis (OP). We conducted an experimental mouse model of OA and OP over an 8-week period. The model involved destabilization of the medial meniscus and bilateral ovariectomy (OVX). To deplete the gut microbiota, we administered a course of antibiotics for 8 weeks. The severity of OA was assessed through micro-CT scanning, X-rays, and immunohistochemical staining. Microbiome analysis was performed using PCR of 16S DNA on fecal samples, and the levels of serum lipopolysaccharide, interleukin 6, tumor necrosis factor-alpha (TNF-alpha), osteocalcin, and estrogen were measured using enzyme-linked immunosorbent assay. We found that in comparison to the OVX+OA group, the OVX+OA+ABT group exhibited increased bone mineral density ($P < 0.0001$), bone volume fraction ($P = 0.0051$), and trabecular number ($P = 0.0023$) in the metaphyseal bone. Additionally, cartilage injury and levels of matrix metalloproteinase 13 were reduced in the OVX+OA+ABT group compared to the OVX+OA group. Moreover, the OVX+OA+ABT group demonstrated decreased relative abundance of Bacteroidetes, serum lipopolysaccharide ($P = 0.0005$), TNF-alpha ($P < 0.0001$), CTX-1 ($P = 0.0002$), and increased expression of bone formation markers. These findings were further supported by correlation network analyses. Depletion of gut microbiota was shown to protect against bone loss and cartilage degradation by modulating the composition of the gut microbiota in osteoporosis and osteoarthritis.
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TI Ten-Year Incidence of Sarcopenia in a Population-Based Cohort: Results from the Research on Osteoarthritis/Osteoporosis Against Disability Study
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DT Article
DE Sarcopenia; incidence; cohort study; AWGS 2019
ID asian working group; bioelectrical-impedance analysis; dwelling elderly subjects; skeletal-muscle mass; older men; prevalence; consensus; adults; epidemiology; association
AB Objectives: To investigate the prevalence and incidence rates of sarcopenia in Japanese communitydwelling people according to the criteria of the Asian Working Group for Sarcopenia 2019 recommendations, using a large-scale

population-based cohort over a 10-year follow-up period. Design: Prospective cohort study. Setting and Participants: This study was conducted using data from the Research on Osteoarthritis/ Osteoporosis Against Disability (ROAD) study. In total, 1551 participants (521 men and 1030 women; mean age, 65.8 years) from the second ROAD survey (2008-2-10) were included in this study. Methods: The participants from the second survey were followed-up at 4, 7, and 10 years. Skeletal muscle mass, handgrip strength, and walking speed were assessed. Sarcopenia was defined according to the Asian Working Group for Sarcopenia 2019 criteria. The incidence of sarcopenia was calculated using the person-year method. Cox proportional hazard model was used to assess risk factors for incident sarcopenia. Results: The prevalence of sarcopenia was 8.1% (8.8% in men and 7.7% in women), and the prevalence of severe sarcopenia was 2.9% (2.7% in men and 3.1% in women). The incidence rates of sarcopenia were 17.8 per 1000 and 14.5 per 1000 person-years in men and women, respectively. Additionally, the incidence rates of severe sarcopenia were 6.4 per 1000 and 4.2 per 1000 person-years in men and women, respectively. The significant risk factors for the incidence of sarcopenia were age [+1 year; hazard ratio risk factors for the incidence of severe sarcopenia were age (+1 year; HR, 1.18; 95% CI, 1.14-1.22) and body Conclusions and Implications: The prevalence and incidence rates of sarcopenia in Japan were clarified in (c) 2024 The Author(s). Published by Elsevier Inc. on behalf of Post-Acute and Long-Term Care Medical Association. This is an open access article under the CC BY license (http://creativecommons.org/licenses/
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Li, Chengen
Lv, Naishan
TI Exploration beyond osteoarthritis: the association and mechanism of its related comorbidities
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE osteoarthritis; osteoporosis; sarcopenia; cardiovascular diseases; diabetes mellitus; dementia; Parkinson's disease; mental disease
ID knee osteoarthritis; cardiovascular-disease; risk-factors; depressive symptoms; physical function; muscle strength; vitamin-d; inflammation; epidemiology; prevalence
AB Osteoarthritis is the most prevalent age-related degenerative joint disease and a leading cause of pain and disability in aged people. Its etiology is multifaceted, involving factors such as biomechanics, pro-inflammatory mediators, genetics, and metabolism. Beyond its evident impact on joint functionality and the erosion of patients' quality of life, OA exhibits symbiotic relationships with various systemic diseases, giving rise to various complications. This review reveals OA's extensive impact, encompassing osteoporosis, sarcopenia, cardiovascular diseases, diabetes mellitus, neurological disorders, mental health, and even cancer. Shared inflammatory processes, genetic factors, and lifestyle elements link OA to these systemic conditions. Consequently, recognizing these connections and addressing them offers opportunities to enhance patient care and reduce the burden of

associated diseases, emphasizing the need for a holistic approach to managing OA and its complications.
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ID suppresses osteoclast differentiation; mesenchymal stem-cells; osteogenic differentiation; epigenetic regulation; gene-expression; transcriptional repression; chromatin modifications; lineage commitment; stromal cells; osteoblast
AB Bone metabolism plays a crucial role in maintaining normal bone tissue homeostasis and function. Imbalances between bone formation and resorption can lead to osteoporosis, osteoarthritis, and other bone diseases. The dynamic and complex process of bone remodeling is driven by various factors, including epigenetics. Histone modification, one of the most important and well-studied components of epigenetic regulation, has emerged as a promising area of research in bone metabolism. Different histone proteins and modification sites exert diverse effects on osteogenesis and osteoclastogenesis. In this review, we summarize recent progress in understanding histone modifications in bone metabolism, including specific modification sites and potential regulatory enzymes. Comprehensive knowledge of histone modifications in bone metabolism could reveal new therapeutic targets and treatment strategies for bone diseases. (c) 2024 Published by Elsevier B.V.
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AU Mejia, AC
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TI A clinical application of gait quality patterns in osteoarthritis
SO GAIT & POSTURE
LA English
DT Article
DE Gait Analysis; Smartphone; Primary Health Care; Osteoarthrosis
ID reliability
AB Aim: To investigate whether a smartphone-based gait analysis tool can reliably output gait quality parameters that can be cross-analyzed to establish individual & disease-based changes in gait quality patterns. Methods: A cross-sectional study made up of a 48-patients undergoing disability certification at the "Dr. Jose<acute accent> Castro Villagrana" or the "Dr. David Fragoso Lizalde" Health Centers in Mexico City, Mexico. Their sensorimotor performance was evaluated through an in-house smartphone/IMU based digital tool. Gait was analyzed by means of frequency analysis of the acceleration of the body mass measured at the sternum. A composite gait quality score was determined through principal component analysis based primarily on the explainability and uniformity of gait. Quality independence against demographic variables (age & weight) was tested through

ANCOVA. The association between gait quality and gait parameters was analyzed by using multiple linear regression. Results: A multiple regression model developed with a limited set of gait quality parameters successfully predicted gait smoothness with a 97.05% accuracy with a mean square error of 0.085 between predicted and actual quality scores. The model demonstrates different predictive capacities across disease groups, with Osteoarthrosis + Osteoporosis having the highest R2 at 0.98 ($p < 0.001$) and Coxarthrosis having the lowest explained R2 at 0.79 ($p < 0.001$). Conclusions: The assessment of gait quality, in family medicine, with low-cost digital tools is an area of opportunity yet to be explored. This tool can potentially disrupt the current disability workflow between primary and specialty care to have an objective method of assessing gait within a clinical consult. Individual patient-level benchmarking can give us insights into the patient's disease status, develop practical intervention strategies, and control the cost and quality of medical care by predicting an individualized course of disability or rehabilitation. Further studies are needed to validate digital gait assessments as clinical decision support tools for day-to-day clinical operations. MeSH: Gait Analysis, Smartphone, Primary Health Care, Osteoarthrosis
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TI Unlocking the potential of exosomes: a breakthrough in the theranosis of degenerative orthopaedic diseases
SO FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY
LA English
DT Review
DE exosomes; osteoarthritis; osteoporosis; intervertebral disc degeneration; treatment
ID mesenchymal stem-cells; suppress cartilage degradation; extracellular vesicles; membrane-vesicles; drug-delivery; disc degeneration; rat model; in-vitro; osteoarthritis; inflammation
AB Degenerative orthopaedic diseases pose a notable worldwide public health issue attributable to the global aging population. Conventional medical approaches, encompassing physical therapy, pharmaceutical interventions, and surgical methods, face obstacles in halting or reversing the degenerative process. In recent times, exosome-based therapy has gained widespread acceptance and popularity as an effective treatment for degenerative orthopaedic diseases. This therapeutic approach holds the potential for "cell-free" tissue regeneration. Exosomes, membranous vesicles resulting from the fusion of intracellular multivesicles with the cell membrane, are released into the extracellular matrix. Addressing challenges such as the rapid elimination of natural exosomes in vivo and the limitation of drug concentration can be effectively achieved through various strategies, including engineering modification, gene overexpression modification, and biomaterial binding. This review provides a concise overview of the source, classification, and preparation methods of exosomes, followed by an in-depth analysis of their functions and potential applications. Furthermore, the review explores various strategies for utilizing exosomes in the treatment of degenerative orthopaedic diseases, encompassing engineering modification, gene overexpression, and biomaterial binding. The primary objective is to provide a fresh viewpoint on the utilization of exosomes in addressing bone degenerative conditions and to support the practical application of exosomes in the theranosis of degenerative orthopaedic diseases.
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TI Incidence and Progression of Foot Osteoarthritis in a Longitudinal Cohort: The Johnston County Osteoarthritis Project
SO GERONTOLOGY
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DT Article
DE Foot; Osteoarthritis; Pain; Cohort; Epidemiology
ID knee osteoarthritis; outcome score; association; ankle; population; prevalence; epidemiology; arthritis; gout; pain

AB Introduction: The aim of this study was to examine the incidence and progression of foot osteoarthritis (OA), as well as associated factors, in a community-based cohort. Methods: Baseline (2013-2015) and follow-up (2016-2018) foot radiographs were available for 541 participants (71% women, mean age 69 years; 35% black, 53% with obesity). The LaTrobe Foot Atlas was used to examine osteophytes (OPs, score 0-3) and joint space narrowing (JSN, score 0-3) at 5 joint sites. Incident foot radiographic OA (rOA) was a baseline score < 2 OP and JSN in all 5 joints with >= 2 OP or JSN at follow-up in any of the joints. Progression was a worsening OP or JSN score in a joint with baseline foot rOA. At baseline and follow-up, participants reported the presence/ absence of foot symptoms and completed the Foot and Ankle Outcome Score (FAOS) for each foot. Joint-based logistic regression models with generalized estimating equations were used to examine associations (adjusted odds ratio [aOR], 95% confidence interval [CI]) of foot rOA incidence and progression and with covariates. Results: Among 928 feet without baseline rOA, 4% developed incident foot rOA (2% of those developed symptoms). Among 154 feet with baseline foot rOA, 55% had radiographic progression (16% of those had symptoms). Women and those with higher body mass index (BMI) were more likely to have incident foot rOA (aOR [95% CI] = 4.10 [1.22, 13.8] and 1.60 [1.31, 1.97], respectively); history of gout was associated with incidence or progression of foot rOA (2.75 [1.24, 6.07]). BMI was associated with worse scores on all FAOS subscales (aORs range 1.21-1.40). Conclusion: Progression of foot rOA is common but not necessarily related to worsening symptoms. BMI may be a modifiable risk factor for foot OA. (c) 2024 S. Karger AG, Basel
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TI Novel Risk Factors for Cervical Facet Joint Degeneration in the Subaxial Cervical Spine: Correlation with Cervical Sagittal Alignment and Bone Mineral Density
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LA English
DT Article
DE Bone mineral density; Disc degeneration; Modic change; Sagittal alignment; Zygapophyseal joint
ID osteoarthritis; osteoporosis; balance
AB Objective: The impact of cervical sagittal alignment on cervical facet joint degeneration (CFD) and the risk factors for CFD in patients with degenerative cervical myelopathy (DCM) were investigated in the current study. Methods: A total of 250 surgical patients with DCM were recruited. The clinical data and radiographical characteristics, including CFD, cervical sagittal balance parameters, Hounsfield unit (HU) values, disc degeneration (DD), and modic change, were collected. The detailed correlation between these characteristics and CFD was analyzed. Characteristics, including CFD, were compared among the various cervical alignment types and different CFD groups. Finally, the risk factors for CFD were revealed via logistic regression. Results: CFD was prevalent in DCM patients. Age, cervical sagittal vertical axis (cSVA), range of motion, T1 slope, thoracic inlet angle, DD, HU value, and modic change correlated with CFD segmentally and globally (P

< 0.05). The lordosis and sigmoid types had a significantly higher CFD prevalence (P < 0.05). Furthermore, the average CFD threshold for the severe CFD group was 1.625 (area under the curve, 0.958). Additionally, 167 patients with average CFD <1.625 and 83 patients with CFD of >= 1.625 were classified into the mild CFD group and severe CFD group, respectively. Finally, multivariate analysis was performed, and age, cSVA, HU value, modic change, and DD were determined to be independent risk factors for CFD. Conclusions: The load distribution tends to shift to a more shear-like pattern in the sigmoid and kyphosis types and in those with a higher cSVA, thereby promoting CFD. Aging, cervical malalignment, low bone mineral density, DD, and modic change were revealed to result in high risks of CFD.
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SC Neurosciences & Neurology; Surgery
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PT J
AU Zeng, JW
Li, C
Gu, ZC
AF Zeng, Jianwei
Li, Cheng
Gu, Zuchao
TI A network pharmacological study to unveil the mechanisms of xianlinggubao capsule in the treatment of osteoarthritis and osteoporosis
SO ARCHIVES OF MEDICAL SCIENCE
LA English
DT Article
DE network pharmacology; traditional Chinese medicine; osteoarthritis; osteoporosis; KEGG
ID estrogen-receptor modulator; bone mass; osteoblast; cells; kinase; endometrium; inhibition; pathway; drugs; trial
AB Introduction: Xianlinggubao (XLGB) capsule is a traditional Chinese medicine, which is approved by the Chinese State Food and Drug Administration (CFDA) for osteoarthritis (OA) and osteoporosis (OP). However, as a capsule with complex ingredients, the molecular mechanisms supporting the therapeutic effects have not been explored. Material and methods: A network pharmacology -based approach was conducted to explore the complex interactome among the targets of the XLGB active compounds. Results: The herbs in the capsule contain 41 compounds with 246 high score targets, which cover four known OA targets (PTGS1, PTGS2, PTGER4 and TNF) and six known OP targets (AR, ESR1, PGR, PTGER2, TNFSF11 and VDR) of FDA -approved drugs or drugs undergoing clinical trials. The protein -protein interaction (PPI) network of the 246 targets had six key modules. Among the six modules, neuroactive ligand-receptor interaction, cAMP signaling pathway and calcium signaling pathway are the key pathways, which are all closely associated with the degeneration of joint cartilage and bone formation and resorption. Conclusions: Neuroactive ligand-receptor interaction, cAMP signaling pathway, and calcium signaling pathway might be the critical pathways upon which the capsule

might act. The present study laid down a foundation to understand the molecular mechanisms of the XLGB capsule and also provided fundamental information for better improvement of the drug with the concept "less herbal materials for achieving equal treatment efficacy".
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AU Milone, D
Longo, F
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AF Milone, Dario
Longo, Francesco
Merlino, Giovanni
De Marchis, Cristiano
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D'Agati, Luca
TI MocapMe: DeepLabCut-Enhanced Neural Network for Enhanced Markerless Stability in Sit-to-Stand Motion Capture
SO SENSORS
LA English
DT Article
DE human movement analysis; motion tracking; neural network; markerless pose estimation; sit-to-stand analysis
ID osteoarthritis; predict
AB This study examined the efficacy of an optimized DeepLabCut (DLC) model in motion capture, with a particular focus on the sit-to-stand (STS) movement, which is crucial for assessing the functional capacity in elderly and postoperative patients. This research uniquely compared the performance of this optimized DLC model, which was trained using 'filtered' estimates from the widely used OpenPose (OP) model, thereby emphasizing computational effectiveness, motion-tracking precision, and enhanced stability in data capture. Utilizing a combination of smartphone-captured videos and specifically curated datasets, our methodological approach included data preparation, keypoint annotation, and extensive model training, with an emphasis on the flow of the optimized model. The findings demonstrate the superiority of the optimized DLC model in various aspects. It exhibited not only higher computational efficiency, with reduced processing times, but also greater precision and consistency in motion tracking thanks to the stability brought about by the meticulous selection of the OP data. This precision is vital for developing accurate biomechanical models for clinical interventions. Moreover, this study revealed that the optimized DLC maintained higher average confidence levels across datasets, indicating more reliable and accurate detection capabilities compared with standalone OP. The clinical relevance of these findings is profound. The optimized DLC model's efficiency and enhanced point estimation stability make it an invaluable tool in rehabilitation monitoring and patient assessments,

potentially streamlining clinical workflows. This study suggests future research directions, including integrating the optimized DLC model with virtual reality environments for enhanced patient engagement and leveraging its improved data quality for predictive analytics in healthcare. Overall, the optimized DLC model emerged as a transformative tool for biomechanical analysis and physical rehabilitation, promising to enhance the quality of patient care and healthcare delivery efficiency.
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Xia, TT
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TI Targeting type H vessels in bone-related diseases
SO JOURNAL OF CELLULAR AND MOLECULAR MEDICINE
LA English
DT Review
DE angiogenesis; osteoarthritis; osteogenesis; osteoporosis; type H vessels
ID attenuates osteoarthritis; angiogenesis; regeneration; osteogenesis; metastasis; subtype
AB Blood vessels are essential for bone development and metabolism. Type H vessels in bone, named after their high expression of CD31 and Endomucin (Emcn), have recently been reported to locate mainly in the metaphysis, exhibit different molecular properties and couple osteogenesis and angiogenesis. A strong correlation between type H vessels and bone metabolism is now well-recognized. The crosstalk between type H vessels and osteoprogenitor cells is also involved in bone metabolism-related diseases such as osteoporosis, osteoarthritis, fracture healing and bone defects. Targeting the type H vessel formation may become a new approach for managing a variety of bone diseases. This review highlighted the roles of type H vessels in bone-related diseases and summarized the research attempts to develop targeted intervention, which will help us gain a better understanding of their potential value in clinical application.

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TC 12
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TI Investigate the Therapeutic Effect of Ibandronate Sodium on Knee Osteoarthritis Based on TLRs/MyD88/NF-κB Signaling Pathway in Vitro and in Vivo
SO DISCOVERY MEDICINE
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DE ibandronate sodium; knee osteoarthritis; TLRs/MyD88/NF-B-K; articular chondrocyte
ID chondrocytes; resveratrol
AB Background: For decades, bisphosphonates have primarily found application in clinical practice for the treatment and pre-vention of bone metastases associated with malignant tumors and various bone metabolic disorders. However, third-generation bisphosphonates like ibandronate have demonstrated significant utility in addressing conditions like osteoporosis (OA) and other bone metabolism-related ailments. Ibandronate, distinguished by its high effectiveness, low toxicity, and ease of administration, has garnered attention for its potential applications in the treatment of rheumatoid arthritis, OA, and orthopedic concerns. In recent years, the utilization of ibandronate sodium in these contexts has sparked considerable interest. Research has pointed to a possible connection between ibandronate and the Toll-like receptors (TLRs), myeloid differentiation factor 88 (MyD88), and nuclear factor -KB (NF -KB) signaling pathway, particularly in the context of inflammation and immunological regulation. Consequently, this study is designed to investigate the therapeutic impact of ibandronate on in vitro and in vivo models of knee osteoarthritis, while also delving into its influence on the TLRs/MyD88/NF-KB pathway. Method: Various dosages of ibandronate sodium, including low (10 g/kg), medium (20 g/kg), and high (30 g/kg), were administered following the establishment of both in vivo and in vitro models of knee osteoarthritis (KOA). Post-intervention, an in-depth quantitative analysis of bone tissue microstructure was conducted. The morphology of articular cartilage tissue was observed in vivo, and the modified Mankin score was subsequently calculated. In the in vitro setting, cartilage was entirely isolated, and mRNA and total protein were extracted to measure the expression levels of TLR4, MyD88, and NF -KB at both the mRNA and protein levels. Furthermore, the study explored the effects of Interleukin-1 beta (IL-1 beta) on cell proliferation, apoptosis, stromal

decomposition enzyme activity, ossification, and the expression of TLR4, MyD88, and NF -KB. Result: In the results of the in vivo experiments, several noteworthy findings emerged. The knee curvature, gait score, Mankin score, pathological knee joint injury degree, cartilage protein loss, and trabecular separation within the model group exhibited significant elevations compared to both the sham operation group and the blank control group ($p < 0.05$). Conversely, bone density, bone volume fraction, and trabecular thickness in the model group displayed lower values in comparison to the sham operation and blank control groups ($p < 0.05$). Following the administration of ibandronate sodium, there was a progressive improvement in these parameters, with the medium and high-dose groups demonstrating the most favorable outcomes ($p < 0.05$). Additionally, the model group exhibited the highest expression levels of TLR4, MyD88, and NF -KB, while the ibandronate sodium intervention group displayed reduced expression levels of these markers, with the high-dose group registering the most significant changes ($p < 0.05$). Turning to the in vitro experiments, it was observed that the cell proliferation capacity and ossification degree of the IL-1 beta-induced group experienced declines, concomitant with an increase in stromal decomposition enzyme activity and cell apoptosis rate ($p < 0.05$). However, post-intervention with ibandronate sodium, all these indicators gradually returned to normal, with the medium-dose group exhibiting the most notable improvements. The expression levels of TLR4, MyD88, and NF -KB in the IL-1 beta-induced group showed an increase, while the expression levels in the ibandronate sodium intervention group displayed a decrease, particularly in the high-dose group ($p < 0.05$). Conclusions: Ibandronate sodium demonstrates a protective effect on articular chondrocytes and exhibits the potential to decelerate the pathological progression of knee osteoarthritis (KOA) in rats. This mechanism is likely achieved through the inhibition of the TLRs/MyD88/NF-KB signaling pathway.
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TI A monoallelic variant in CCN2 causes an autosomal dominant spondyloepimetaphyseal dysplasia with low bone mass
SO BONE RESEARCH
LA English
DT Article
ID tissue-growth-factor; monoclonal-antibody; family proteins; signal peptide; in-vitro; gene; mutations; differentiation; expression; ctgf
AB Cellular communication network factor 2 (CCN2) is a secreted extracellular matrix-associated protein, and its aberrantly increased expression has been implicated in a diversity of diseases involving pathological processes of fibrosis, chronic inflammation, or tissue injury, which has promoted the evaluation of CCN2 as therapeutic targets for multiple disorders. However, human phenotypes associated with CCN2 deficiency have remained enigmatic; variants in CCN2 have not yet been associated with a human phenotype. Here, we collected families diagnosed with spondyloepimetaphyseal dysplasia (SEMD), and screened candidate pathogenic genes for families without known genetic causes using next-generation sequencing. We identified a monoallelic variant in signal peptide of CCN2 (NM_001901.2: c.65 G > C [p.Arg22Pro]) as the cause of SEMD in 14 subjects presenting with different degree of short stature, premature osteoarthritis, and osteoporosis. Affected subjects showed decreased serum CCN2 levels. Cell lines harboring the variant displayed decreased amount of CCN2 proteins in culture medium and an increased intracellular retention, indicating impaired protein secretion. And the variant weakened the stimulation effect of CCN2 on osteogenesis of bone marrow mesenchymal stem cells. Zebrafish ccn2a knockout model and osteoblast lineage-specific Ccn2-deficient mice (Ccn2(fl/fl);Prx1(Cre)) partially recapitulated the phenotypes including low bone mass observed in affected subjects. Pathological mechanism implicated in the skeletal abnormality in Ccn2(fl/fl);Prx1(Cre) mice involved decreased bone formation, increased bone resorption, and abnormal growth plate formation. Collectively, our study indicate that monoallelic variants in CCN2 lead to a human inherited skeletal dysplasia, and highlight the critical role of CCN2 in osteogenesis in human.
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TI Microbiome's role in musculoskeletal health through the gut-bone axis insights
SO GUT MICROBES
LA English
DT Review
DE Microbiome; musculoskeletal health; gut-bone axis; musculoskeletal disease; bone health
ID vitamin-d; dietary fiber; calcium; supplementation; osteoclastogenesis; inflammation; association; mechanisms; cells
AB The interplay between the human microbiome and the musculoskeletal system represents a burgeoning field of research with profound implications for understanding and treating musculoskeletal disorders. This review articulates the pivotal role of the microbiome in modulating bone health, highlighting the gut-bone axis as a critical nexus for potential therapeutic intervention. Through a meticulous analysis of recent clinical research, we underscore the microbiome's influence on osteoporosis, sarcopenia, osteoarthritis, and rheumatoid arthritis, delineating both the direct and indirect mechanisms by which microbiota could impact musculoskeletal integrity and function. Our investigation reveals novel insights into the microbiota's contribution to bone density regulation, hormone production, immune modulation, and nutrient absorption, laying the groundwork for innovative microbiome-based strategies in musculoskeletal disease management. Significantly, we identify the challenges hindering the translation of research into clinical practice, including the limitations of current microbial sequencing techniques and the need for standardized methodologies in microbiome studies. Furthermore, we highlight promising directions for future research, particularly in the realm of personalized medicine, where the

microbiome's variability offers unique opportunities for tailored treatment approaches. This review sets a new agenda for leveraging gut microbiota in the diagnosis, prevention, and treatment of musculoskeletal conditions, marking a pivotal step toward integrating microbiome science into clinical musculoskeletal care.
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PT J
AU Kuswanto, W
Baker, MC
AF Kuswanto, Wilson
Baker, Matthew C.
TI Repurposing drugs for the treatment of osteoarthritis
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Review
DE Osteoarthritis; Disease modification; DMOAD; Drug repurposing
ID bone-marrow lesions; vitamin-d supplementation; interleukin-1 receptor antagonist; radiographic knee osteoarthritis; cartilage volume; double-blind; structural progression; zoledronic acid; clinical-trial; pain
AB Objective: Currently, no disease-modifying therapies for osteoarthritis (OA) exist, and attempts to identify novel cellular targets have been challenging. Risk factors for OA include advanced age, obesity, and metabolic syndrome. This creates an attractive opportunity to repurpose existing drugs that are used to treat comorbidities commonly encountered in patients with OA, if those drugs possess OA disease modifying properties. Methods: This narrative review incorporates findings from knee or hand OA randomized clinical trials, posthoc clinical trial analyses, prospective cohort studies, and observational data. Results: Drugs used for the treatment of rheumatoid arthritis (methotrexate; TNFa, IL-1, and IL-6 pathway inhibitors; hydroxychloroquine), atopic/allergic disease (anti-histamines), osteoporosis (bisphosphonates and vitamin D), type 2 diabetes (metformin and GLP-1 agonists), and cardiovascular disease (atorvastatin, fish oil, and beta blockers) were reviewed for their potential benefit in OA. This review outlines the successful attributes of repurposed drugs, the challenges in repurposing drugs, and strategies for future clinical trials to support OA drug repurposing. Potential drug candidates for OA may be identified through the use of existing datasets and via collaborations with researchers in other fields to include OA endpoints in future clinical trials. Conclusion: Given the association of OA with several commonly treated comorbidities, drug repurposing is an appealing approach that could provide a favorable benefit-to-risk ratio for chronic OA treatment. (c) 2024 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies.
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NR 73
TC 17
Z9 18
U1 6
U2 21
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
PD AUG 15
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PT J
AU Sines, J
Cai, K
Cashman, B
Abbott, P
Zengin, A
Manolios, N
Wong, PKK
AF Sines, Jason
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Cashman, Belinda
Abbott, Penelope
Zengin, Ayse
Manolios, Nicholas
Wong, Peter K. K.
TI The burden of rheumatologic disease in Aboriginal and Torres Strait Islander Australians
SO INTERNAL MEDICINE JOURNAL
LA English
DT Review
DE rheumatology; indigenous health; epidemiology
ID systemic-lupus-erythematosus; low-back-pain; gouty-arthritis; indigenous australians; body-composition; high prevalence; people; care; health; impact
AB The objective of this article is to summarise the current knowledge regarding the prevalence of six rheumatological conditions in indigenous Australians - rheumatoid arthritis (RA), osteoarthritis (OA), osteoporosis (OSP), systemic lupus erythematosus (SLE), gout and musculoskeletal (MSK) pain. Online medical literature databases were searched for 'indigenous', 'Aboriginal' and 'Torres Strait Islander', as well as the names of the six conditions. Other included search terms were 'crystal', 'urate', 'arthritis' and 'arthropathy'. No limitations were placed on publication data or language. Forty-five articles examining the prevalence of the six conditions were identified. Based on the published literature, SLE appears to have a higher prevalence, while RA appears to have a lower prevalence in indigenous Australians compared to the non-indigenous community. MSK pain is prevalent, has a significant impact on indigenous people and is perceived as an important area of need. There is a paucity of data regarding these conditions in indigenous Australians. This may be impacted by the uncertainty of case ascertainment by self-report, differences in disease phenotypes and prevalence between the

metropolitan compared to the rural or remote indigenous population, and difficulty with access to healthcare. Further studies in conjunction with local indigenous communities are needed to accurately determine the burden of rheumatological disease in the indigenous population. This will assist with resource and workforce planning to deliver culturally appropriate interventions. Strategies for future clinical work and research include the development and dissemination of culturally safe rheumatology resources, rheumatology training of Aboriginal Health Workers and wider integration of rheumatology clinics into community-controlled Aboriginal Health Services.
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JI Intern. Med. J.
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BP 1603
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WC Medicine, General & Internal
SC General & Internal Medicine
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UT WOS:001289466700001
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PT J
AU Chen, QX
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Zhang, ZL
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AF Chen, Qiuxian
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Zhang, Yong
TI The effect of the Hippocampus erectus decoction on improving osteoporosis in zebrafish
SO AQUACULTURE REPORTS
LA English
DT Article
DE Osteoporosis; Zebrafish larvae; Seahorse decoction; Prednisolone
ID seahorse hippocampus; induced inhibition; osteoblast; model; expression; osteogenesis; extracts; taurine; peptide; cells
AB The seahorse is a traditional Chinese herbal medicine that has been utilized for the treatment of conditions such as osteoporosis, nonunion fractures, knee osteoarthritis, and herniated lumbar disks. Zebrafish is an excellent animal model to study the effects of herbal preparations on osteogenesis and bone metabolism, and bone biology is highly similar to that of mammals, so it has been used to develop multiple glucocorticoid-induced osteoporosis (GIOP) models. Our study aimed to explore whether the decoction of Hippocampus erectus (DHe) administered in zebrafish larvae promotes bone health under physiological and osteoporotic conditions. In zebrafish larvae, 25 mu M prednisolone solution was successfully used to induce the zebrafish osteoporosis model, which can significantly inhibit the mineralization area and degree of bone mineralization, reduce the activity of alkaline phosphatase, and increase tartrate-resistant acid phosphatase activity. The results showed that 0.3 g/L DHe had a significant improvement effect on osteoporosis in zebrafish by enhancing the mineralization degree and phosphatase activity of zebrafish, while also promoting the expression of genes associated with bone development. It can be considered a good candidate to develop new drugs against osteoporosis.
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C3 Sun Yat Sen University; Southern Marine Science & Engineering Guangdong Laboratory; Southern Marine Science & Engineering Guangdong Laboratory (Zhuhai); Sun Yat Sen University
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J9 AQUACULT REP
JI Aquacult. Rep.
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WC Fisheries
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AU Yoo, YS
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TI Additional effects of herbal medicine combined with bisphosphonates for primary osteoporosis: a systematic review and meta-analysis
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE primary osteoporosis; herbal medicines; bisphosphonates; combination therapy; bone mineral density
ID bone-resorption; in-vitro; differentiation; mechanisms; quality; capsule; osteoarthritis; prevention; diagnosis; luteolin
AB Background: Osteoporosis (OP) is a significant medical issue associated with population aging. Recent research on herbal medicines (HMs) for OP has been increasing, with these therapies sometimes used in conjunction with bisphosphonates (BPs), the standard treatment for OP. We conducted a systematic review and meta-analysis to evaluate the effects of combining HMs with BPs on improving bone mineral density (BMD) in patients with primary OP. Methods: We searched nine databases-PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure Wanfang, KISS, Kmbase, Science On, and Oasis-up to 31 August 2023. We selected randomized controlled trials (RCTs) comparing BMD between HMs plus BPs and BPs alone in primary OP. A meta-analysis with BMD as the primary outcome was performed using RevMan version 5.4. Study quality and evidence certainty were assessed through Cochrane's risk of bias2 and GRADE. Results: Out of 43 RCTs involving 4,470 participants (mean age 65.8 +/- 6.6 years), 35 RCTs with 3,693 participants were included in the meta-analysis. The combination of HMs and BPs was found to be more effective in improving BMD

compared to BPs alone, with improvements of 0.10 g/cm(2) at the lumbar spine (33 RCTs, 95% CI: 0.07-0.12, p < 0.001, I-2 = 93%) and 0.08 g/cm(2) at the femoral neck (20 RCTs, 95% CI: 0.05-0.12, p < 0.001, I-2 = 94%), though this result was associated with high heterogeneity, high risk of bias, and very low certainty of evidence. Conclusion: Our data suggest the possibility that combining HMs with BPs may improve BMD in primary OP more effectively than using BPs alone. However, the results should be interpreted with caution due to the high heterogeneity and low quality of the studies included in the review. Therefore, further well-designed RCTs are needed to confirm these findings.
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TI MicroRNA-877-5p promotes osteoblast differentiation by targeting EIF4G2 expression
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE miR-877-5p; Osteoblast differentiation
ID mc3t3-e1 cells; translation; phosphorylation; osteoarthritis; proliferation; osteoporosis; initiation; migration; model
AB Stimulating bone formation potentially suggests therapeutics for orthopedic diseases including osteoporosis and osteoarthritis. Osteoblasts are key to bone remodeling because they act as the only bone-forming cells. miR-877-5p has a chondrocyte-improving function in osteoarthritis, but its effect on osteoblast differentiation is unknown. Here, miR-877-5p-mediated osteoblast differentiation was studied. Real-time reverse transcriptase-polymerase chain reaction was performed to measure miR-877-5p expression during the osteogenic differentiation of MC3T3-E1 cells. Osteoblast markers, including alkaline phosphatase (ALP), collagen type I a1 chain, and osteopontin, were measured and detected by alizarin red staining and ALP staining. Potential targets of miR-877-5p were predicted from three different algorithms: starBase (http://starbase.sysu.edu.cn/), PITA (http://genie.weizmann.ac.il/pubs/mir07/mir07_data.html), and miRanda (http://www.microrna.org/microrna/home.do). It was further verified by dual luciferase reporter gene assay. The experimental results found that miR-877-5p was upregulated during the osteogenic differentiation of MC3T3-E1 cells. Overexpression of miR-877-5p promoted osteogenic differentiation, which was characterized by increased cell mineralization, ALP activity, and osteogenesis-related gene expression. Knockdown of miR-877-5p produced the opposite result. Dual luciferase reporter gene assay showed that miR-877-5p directly targeted eukaryotic translation initiation factor 4 gamma 2 (EIF4G2). Overexpression of EIF4G2 inhibited osteogenic differentiation and reversed the promoting effect of overexpression of miR-135-5p on osteogenic differentiation. These results indicate that miR-877-5p might have a therapeutic application related to its promotion of bone formation through targeting EIF4G2.
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TI Noncoding RNAs in skeletal development and disorders
SO BIOLOGICAL RESEARCH
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ID pulposus cell apoptosis; circular rnas; nuclear export; osteoblast differentiation; dendritic cells; tnf-alpha; expression; cartilage; dicer; mouse
AB Protein-encoding genes only constitute less than 2% of total human genomic sequences, and 98% of genetic information was previously referred to as "junk DNA". Meanwhile, non-coding RNAs (ncRNAs) consist of approximately 60% of the transcriptional output of human cells. Thousands of ncRNAs have been identified in recent decades, and their essential roles in the regulation of gene expression in diverse cellular pathways associated with fundamental cell processes, including proliferation, differentiation, apoptosis, and metabolism, have been extensively investigated. Furthermore, the gene regulation networks they form modulate gene expression in normal development and under pathological conditions. In this review, we integrate current information about the classification, biogenesis, and function of ncRNAs and how these ncRNAs support skeletal development through their regulation of critical genes and signaling pathways in vivo. We also summarize the updated knowledge of ncRNAs involved in common skeletal diseases and disorders, including but not limited to osteoporosis, osteoarthritis, rheumatoid arthritis, scoliosis, and intervertebral disc degeneration, by highlighting their roles established from in vivo, in vitro, and ex vivo studies.
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TI Radiofrequency Echographic Multispectrometry (REMS) can Overcome the Effects of Structural Internal Artifacts and Evaluate Bone Fragility Accurately
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DT Article
DE Abdominal aortic calcification; Bone mineral density; Dual-energy X-ray absorptiometry; REMS; Semi-quantitative grading of vertebral fractures
ID abdominal aortic calcification; hip osteoarthritis; mineral density; osteoporosis; prevention; fracture; mass
AB PurposeThis study measured bone mineral density (BMD) in a Japanese population using the novel non-ionizing system using radiofrequency echographic multispectrometry (REMS) and compared the results with those obtained using traditional dual-energy X-ray absorptiometry (DXA). We aimed to identify any discrepancies between measurements obtained using these instruments and identify the influencing factors.MethodsThis cross-sectional study examined patients with osteoporosis treated at a single center from April to August 2023. We examined BMD assessment by DXA and REMS in lumbar spine and proximal femur. Patients were categorized into two groups: those with discrepancies between lumbar spine BMD measured by DXA and REMS, and those without. Semiquantitative evaluation of vertebral fractures and abdominal aortic

calcification scoring were also performed and compared between the two groups, along with various patient characteristics.ResultsA total of 70 patients (88.6% female; mean age 78.39 +/- 9.50 years) undergoing osteoporosis treatment were included in the study. A significant difference was noted between DXA and REMS measurement of BMD and T-scores, with REMS recording consistently lower values. The discrepancy group exhibited a higher incidence of multiple vertebral fractures and increased vascular calcification than the non-discrepancy group. Multivariate analysis indicated that diabetes mellitus, severe vertebral fractures, and increased abdominal aortic calcification scores were significantly associated with discrepancies in lumbar spine T-scores.ConclusionThis study suggests that REMS may offer a more accurate measurement of BMD, overcoming the overestimation of BMD by DXA owing to factors such as vertebral deformities, abdominal aortic calcification, and diabetes mellitus.
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TI Mesenchymal stem cell-derived extracellular vesicles: A novel nanoimmunoregulatory tool in musculoskeletal diseases
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DE Mesenchymal stem cell extracellular vesicles; Osteoimmunology; Nanoparticles; Exosomes; Musculoskeletal disorders
ID regulatory t-cells; stromal cells; tnf-alpha; macrophage polarization; rheumatoid-arthritis; vertebral fractures; cartilage repair; bone-resorption; exosm; osteoarthritis
AB The musculoskeletal system involves various cell types that participate in maintaining bone homeostasis, which is crucial for balancing osteogenesis and osteoclastogenesis. Imbalances in bone homeostasis can lead to numerous musculoskeletal disorders, including osteoarthritis (OA) and osteoporosis (OP). In recent years, there has been growing interest in osteoimmunity due to its significant regulatory impact on bone homeostasis. Various cell types, including macrophages, T cells, and B cells, participate in osteoimmunology and regulate bone homeostasis. Currently, extracellular vesicles (EVs) play crucial roles in cell -to -cell communication. In particular, mesenchymal stem cell (MSC) -derived EVs have been reported as potential immunoregulators in certain immune -related diseases. This comprehensive review aims to present recent advancements in the understanding of the immunoregulatory effects of MSC -derived EVs in musculoskeletal diseases. In addition, we discuss the immunoregulatory effects of MSC-EVs on programed cell death in osteoblasts, osteoclasts, and chondrocytes, and the effect of this modulation on bone homeostasis. Moreover, we provide insights into the potential applications of MSC-EVs in the management of prevalent musculoskeletal disorders, including OP, OA, and bone fractures. In conclusion, this review emphasizes current advancements in research and future directions in MSC-EV-based therapies for musculoskeletal disorders.
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TI Sensory nerve regulation of bone homeostasis: Emerging therapeutic opportunities for bone-related diseases
SO AGEING RESEARCH REVIEWS
LA English
DT Review
DE Sensory nerves; Neuropeptides; Bone homeostasis; Bone tissue cells; Bone-related diseases; Therapeutic targets
ID gene-related peptide; substance-p; growth-factor; osteochondral junction; semaphorin 3a; calcitonin; marrow; innervation; neurons; differentiation
AB Understanding the intricate interplay between sensory nerves and bone tissue cells is of paramount significance in the field of bone biology and clinical medicine. The regulatory role of sensory nerves in bone homeostasis offers a novel perspective for the development of targeted therapeutic interventions for a spectrum of bonerelated diseases, including osteoarthritis, osteoporosis, and intervertebral disc degeneration. By elucidating the mechanisms through which sensory nerves and their neuropeptides influence the differentiation and function of bone tissue cells, this review aims to shed light on emerging therapeutic targets that harness the neuro-skeletal axis for the treatment and management of debilitating bone disorders. Moreover, a comprehensive understanding of sensory nerve -mediated bone regulation may pave the way for the development of innovative strategies to promote bone health and mitigate the burden of skeletal pathologies in clinical practice.
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AU Wu, ZP
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TI The role of neuropilin in bone/cartilage diseases
SO LIFE SCIENCES
LA English
DT Article
DE Neuropilin; Osteoblast; Osteoclast; Osteoimmunology; Cartilage
ID mesenchymal stem-cells; growth-factor isoforms; rheumatoid-arthritis; polysialylated neuropilin-2; osteogenic differentiation; dendritic cells; semaphorin 3a; expression; bone; receptors
AB Bone remodeling is the balance between osteoblasts and osteoclasts. Bone diseases such as osteoporosis and osteoarthritis are associated with imbalanced bone remodeling. Skeletal injury leads to limited motor function and pain. Neurophilin was initially identified in axons, and its various ligands and roles in bone remodeling, angiogenesis, neuropathic pain and immune regulation were later discovered. Neurophilin promotes osteoblast mineralization and inhibits osteoclast differentiation and its function. Neuropolin-1 provides channels for immune cell chemotaxis and cytokine diffusion and leads to pain. Neuropolin-1 regulates the proportion of T helper type 17 (Th17) and regulatory T cells (Treg cells), and affects bone immunity. Vascular endothelial growth factors (VEGF) combine with neuropilin and promote angiogenesis. Class 3 semaphorins (Sema3a) compete with VEGF to bind neuropilin, which reduces angiogenesis and rejects sympathetic nerves. This review elaborates on the structure and general physiological functions of neuropilin and summarizes the role of neuropilin and its ligands in bone and cartilage diseases. Finally, treatment strategies and future research directions based on neuropilin are proposed.
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TI A systematic review and cross-database analysis of single nucleotide polymorphisms underlying hip morphology and osteoarthritis reveals shared mechanisms
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Review
DE SNP; GWAS; Hip; Morphology; Gene Ontology
ID genome-wide association; alpha gene polymorphisms; bone-mineral density; femoral-neck; body-composition; fracture risk; geometry; osteoporosis; parameters; variants
AB Objective: Understanding the mechanisms of hip disease, such as osteoarthritis (OA), is crucial to advance their treatment. Such hip diseases often involve specific morphological changes. Genetic variations, called single nucleotide polymorphisms (SNPs), influence various hip morphological parameters. This study investigated the biological relevance of SNPs correlated to hip morphology in genome-wide association studies (GWAS). The SNP-associated genes were compared to genes associated with OA in other joints, aiming to see if the same genes play a role in both hip development and the risk of OA in other lower limb joints. Methodology: A systematic literature review was conducted to identify SNPs correlated with hip morphology, based on the Population, Intervention, Comparison, Outcome, and Study (PICOS) framework. Afterwards, Gene Ontology (GO) analysis was performed, using EnrichR, on the SNP-associated genes and compared with non-hip OA-associated genes, across different databases. Results: Reviewing 49 GWAS identified 436 SNPs associated with hip joint morphology, encompassing variance in bone size, structure and shape. Among the SNP-associated genes, SOX9 plays a pivotal role in size, GDF5 impacts bone structure, and BMP7 affects shape. Overall, skeletal system development, regulation of cell differentiation, and chondrocyte differentiation emerged as crucial processes influencing hip morphology. Eighteen percent of GWAS-identified genes related to hip morphology were also associated with non-hip OA. Conclusion: Our findings indicate the existence of multiple shared genetic mechanisms across hip morphology and OA, highlighting the necessity for more extensive research in this area, as in contrast to the hip, the genetic background on knee or foot morphology remains largely understudied. (c) 2024 The Author(s). Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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TI Risk and Epidemiology of Periprosthetic Knee Fractures After Primary Total Knee Arthroplasty: A Nationwide Cohort Study
SO JOURNAL OF ARTHROPLASTY
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DT Article
DE periprosthetic knee fracture; epidemiology; total knee arthroplasty; risk; risk factors
AB Background: Periprosthetic knee fractures (PPKFs) following total knee arthroplasty (TKA) are uncommon, but potentially serious injuries. We analyze the risk and risk factors for a PPKF in standard primary TKA patients who have osteoarthritis and a minimally (cruciate-retaining TKAs without a femoral box cut) or posterior-stabilized TKA. In addition, we report the risk for patients who have other underlying knee disorders and/or a higher level of TKA constraint. Methods: All primary TKAs were identified from the Danish National Patient Register and the Danish Knee Arthroplasty Register using data between 1997 and 2022. Subsequent fractures were identified through the International Classification of Diseases diagnosis code, Nordic Medico-Statistical Committee procedure code, or indication for revision TKA. Results: We included 120,642 standard primary TKA patients who had 1,659 PPKFs. The cumulated proportions were 0.4% (95% confidence interval (CI) 0.3 to 0.4) at 2 years 0.8% (0.7 to 0.8) at 5 years. At 10 years, the cumulated proportion was 1.7% (1.6 to 1.8), with 1.3% in the femur, 0.2% in the patella, and 0.2% in the tibia. Significant risk factors were (hazard ratio [HR] [95% CI]); ipsilateral hip arthroplasty (2.3 [2.0 to 2.6]); women (2.1 [1.8 to 2.4]), osteoporosis (1.4 [1.2 to 1.7]); age 80+ (1.4 [1.3 to 1.6]), uncemented TKA (1.3 (1.1 to 1.5) and Charlson Comorbidity Index score 3+ (1.4 [1.1 to 1.8]). An additional 22,624 primary TKA patients who had other underlying knee disorders and/or a higher level of implant constraint were included with 633 PPKFs. The 10-year cumulated proportions were 8.3% (95% CI 6.9 to 9.8) when the underlying disorder was a previous fracture, 2.8% (2.2 to 3.5) for rheumatic disorders, and 5.2% (2.6 to 10.6) for osteonecrosis. In patients who had condylar constrained knees, it was 6.9% (5.1 to 9.4), and 12.4%

(8.0 to 16.04) for hinges. Conclusions: In standard primary TKA patients, the 10-year cumulated proportion of PPKFs was 1.7%, and ipsilateral hip arthroplasty, women, osteoporosis, advanced age, uncemented TKA and higher Charlson Comorbidity Index increased the risk. Higher risks were observed in non-osteoarthritis patients and/or patients who had a higher level of TKA constraint. (c) 2024 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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PU CHURCHILL LIVINGSTONE INC MEDICAL PUBLISHERS
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J9 J ARTHROPLASTY
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WC Orthopedics
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PT J
AU Li, MD
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AF Li, Mingdong
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TI Multi-omics Data Integration Analysis Identified Therapeutic Targets and Potential Reuse Drugs for Osteoporosis
SO CURRENT MEDICINAL CHEMISTRY
LA English
DT Article
DE Osteoporosis; BM-MSCs; therapeutic target; drug reuse; network proximity; molecular docking
AB Aims To facilitate drug discovery and development for the treatment of osteoporosis.Background With global aging, osteoporosis has become a common problem threatening the health of the elderly. It is of important clinical value to explore new targets for drug intervention and develop promising drugs for the treatment of osteoporosis.Objective To understand the major molecules that mediate the communication between the cell populations of bone marrow-derived mesenchymal stem cells (BM-MSCs) in osteoporosis and osteoarthritis patients and identify potential reusable drugs for the treatment of osteoporosis.Methods Single-cell RNA sequencing (scRNA-seq) data of BM-MSCs in GSE147287 dataset were classified using the Seurat package. CellChat was devoted to analyzing the ligand-receptor pairs (LR pairs) contributing to the communication between BM-MSCs subsets. The LR pairs that were differentially expressed between osteoporosis samples and control samples and significantly correlated with immune score were screened in the GSE35959 dataset, and the differentially expressed gene in both GSE35959 and GSE13850 data sets were identified as targets from a single ligand or receptor. The therapeutic drugs for osteoporosis were screened by network proximity method, and the top-ranked drugs were selected for molecular docking and molecular dynamics simulation with the target targets.Results Twelve subsets of BM-MSCs were identified, of which CD45-BM-MSCS_4, CD45-BM-MSCS_5, and CD45+ BM-MSCs_5 subsets showed significantly different distributions between osteoporosis samples and osteoarthritis samples. Six LR pairs were identified in the bidirectional communication between these three BM-MSCs subsets and other BM-MSCs subsets. Among them, MIF-CD74 and ITGB2-ICAM2 were significantly correlated with the immune score. CD74 was identified as the target, and a total of 48 drugs targeting CD47 protein were identified. Among them, DB01940 had the lowest free energy binding score with CD74 protein and the binding state was very stable.Conclusion This study provided a new network-based framework for drug reuse and identified initial insights into therapeutic agents targeting CD74 in osteoporosis, which may be meaningful for promoting the development of osteoporosis treatment.
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AF Mills, Emily S.
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TI Patients with Hip Osteoarthritis Have a Higher Rate of Spinal Reoperation Following Lumbar Spinal Fusion
SO JOURNAL OF BONE AND JOINT SURGERY-AMERICAN VOLUME
LA English
DT Article
ID stand-alone cages; arthroplasty; dislocation; risk; instrumentation; revision
AB Background: Lumbar spinal pathology is known to affect outcomes following total hip arthroplasty (THA). However, the effect of hip osteoarthritis (OA) on outcomes following lumbar fusion has not been well studied. The purpose of this study was to determine the association between hip OA and spinal reoperation following lumbar spinal fusion. Methods: The 5% Medicare Part B claims database was queried for all patients who underwent primary elective lumbar fusion from 2005 to 2019. Patients were divided into 2 groups: those who underwent elective THA within 1 year after primary lumbar fusion, indicating that they had severe hip OA at the time of lumbar fusion, and those who underwent lumbar fusion with no

diagnosed hip OA and no THA during the study period. Exclusion criteria included THA as a result of trauma, revision THA or primary THA in the 5-year period before primary lumbar fusion, <65 years of age, and no enrollment in the database for 5 years before and 1 year after primary lumbar fusion. The primary outcome was spinal reoperation within 1, 3, and 5 years. Multivariable Cox regression was performed with age, sex, diabetes, heart disease, obesity, smoking status, osteoporosis, number of levels fused, use of posterior instrumentation, use of an interbody device, use of bone graft, and surgical approach as covariates. Results: Overall, 1,123 patients (63.4% female; 91.3% White; mean age, 76.8 +/- 4.1 years) were included in the hip OA group and 8,893 patients (56.2% female; 91.3% White; mean age, 74.8 +/- 4.9 years) were included in the control group. After multivariable analysis, patients with severe hip OA had significantly greater rates of revision surgery at 3 years (odds ratio [OR], 1.61; $p < 0.001$) and 5 years (OR, 1.87; $p < 0.001$) after the index lumbar fusion. Conclusions: Patients with severe hip OA at the time of primary lumbar fusion had a significantly increased risk of spinal reoperation at 3 and 5 years postoperatively. These data provide further evidence to support performing THA prior to lumbar fusion in the unsettled debate regarding which surgery should be prioritized for patients with simultaneous degenerative diseases of the hip and lumbar spine. Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

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NR 27
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PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
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JI J. Bone Joint Surg.-Am. Vol.

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TI The Advantages of Radiofrequency Echographic MultiSpectrometry in the Evaluation of Bone Mineral Density in a Population with Osteoarthritis at the Lumbar Spine
SO DIAGNOSTICS
LA English
DT Article
DE osteoarthritis; bone mineral density (BMD); dual-energy X-ray absorptiometry (DXA); radiofrequency echographic multispectrometry (REMS); osteoporosis; Kellgren/Lawrence grading score

ID osteoporosis; association; fractures; society; health; risk; tbs
AB Background: Osteoarthritis (OA) in the lumbar spine can potentially lead to an overestimation of bone mineral density (BMD), and this can be a challenge in accurately diagnosing conditions like osteoporosis, where precise measurement of BMD is crucial. Radiofrequency Echographic Multi Spectrometry (REMS) is being recognized as an innovative diagnostic tool for assessing bone status. The purpose of this study was to evaluate whether the use of REMS may enhance the identification of osteoporosis in patients with osteoarthritis. Methods: A cohort of 500 patients (mean age: 63.9 +/- 11.2 years) diagnosed with osteoarthritis and having a medical prescription for dual-energy X-ray absorptiometry (DXA) were recruited for the study. All patients underwent BMD measurements at lumbar spine and femoral sites by both DXA and REMS techniques. Results: The T-score values for BMD at the lumbar spine (BMD-LS) by DXA were significantly higher with respect to BMD-LS by REMS across all OA severity scores, and the differences were more pronounced in patients with a higher degree of OA severity ($p < 0.001$). Furthermore, the percentage of subjects classified as "osteoporotic", on the basis of BMD by REMS was markedly higher than those classified by DXA, both when considering all skeletal sites (39.4% vs. 15.1%, respectively) and the lumbar spine alone (30.5% vs. 6.0%, respectively). A similar pattern was observed when OA patients were grouped according to the Kellgren-Lawrence grading score. Conclusions: The findings from our study indicate that, in a population with varying severity levels of osteoarthritis, REMS demonstrated a higher capability to diagnose osteoporosis compared to DXA, and this could lead to earlier intervention and improved outcomes for patients with bone fragility, reducing the likelihood of fractures and associated complications.
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NR 30
TC 11
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SC General & Internal Medicine
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TI Modulation of Carnitine Palmitoyl Transferase 1b Expression and Activity in

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LA English
DT Article
DE osteoporosis; osteoarthritis; muscle atrophy; energy metabolism; oxidative stress; mitochondria biogenesis; myoblast regeneration
ID oxidative stress; sarcopenia; apoptosis
AB In the pathophysiology of osteoarthritis and osteoporosis, articular cartilage and bone represent the target tissues, respectively, but muscle is also involved. Since many changes in energy metabolism occur in muscle with aging, the aim of the present work was to investigate the involvement of carnitine palmitoyl transferase 1b (Cpt1b) in the muscle pathophysiology of the two diseases. Healthy subjects (CTR, n = 5), osteoarthritic (OA, n = 10), and osteoporotic (OP, n = 10) patients were enrolled. Gene expression analysis conducted on muscle and myoblasts showed up-regulation of CPT1B in OA patients; this result was confirmed by immunohistochemical and immunofluorescence analyses and enzyme activity assay, which showed increased Cpt1b activity in OA muscle. In addition, CPT1B expression resulted down-regulated in cultured OP myoblasts. Given the potential involvement of Cpt1b in the modulation of oxidative stress, we investigated ROS levels, which were found to be lower in OA myoblasts, and gene expression of nicotinamide adenine dinucleotide phosphate hydrogen oxidase 4 (Nox4), which resulted up-regulated in OA cells. Finally, the immunofluorescence of BCL2/adenovirus E1B 19 kDa protein-interacting protein 3 (Bnip3) showed a decreased expression in OP myoblasts, with respect to CTR and OA. Contextually, through an ultrastructural analysis conducted by Transmission Electron Microscopy (TEM), the presence of aberrant mitochondria was observed in OP muscle. This study highlights the potential role of Cpt1b in the regulation of muscle homeostasis in both osteoarthritis and osteoporosis, allowing for the expansion of the current knowledge of what are the molecular biological pathways involved in the regulation of muscle physiology in both diseases.
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TI Investigating and Practicing Orthopedics at the Intersection of Sex and Gender: Understanding the Physiological Basis, Pathology, and Treatment Response of Orthopedic Conditions by Adopting a Gender Lens: A Narrative Overview
SO BIOMEDICINES
LA English
DT Review
DE sex and gender; orthopedics; personalized medicine
ID degenerative lumbar scoliosis; calve-perthes disease; clinical-features; bone-formation; hip fracture; dimorphism; epidemiology; prevalence; mortality; estrogens
AB In the biomedical field, the differentiation between sex and gender is crucial for enhancing the understanding of human health and personalizing medical treatments, particularly within the domain of orthopedics. This distinction, often overlooked or misunderstood, is vital for dissecting and treating musculoskeletal conditions effectively. This review delves into the sex- and gender-specific physiology of bones, cartilage, ligaments, and tendons, highlighting how hormonal differences impact the musculoskeletal system's structure and function, and exploring the physiopathology of orthopedic conditions from an epidemiological, molecular, and clinical perspective, shedding light on the discrepancies in disease manifestation across sexes. Examples such as the higher rates of deformities (adolescent idiopathic and adult degenerative scoliosis and hallux valgus) in females and osteoporosis in postmenopausal women illustrate the critical role of sex and gender in orthopedic health. Additionally, the review addresses the morbidity-mortality paradox, where women, despite appearing less healthy on frailty indexes, show lower mortality rates, highlighting the complex interplay between biological and social determinants of health. Injuries and chronic orthopedic conditions such osteoarthritis exhibit gender- and sex-specific prevalence and progression patterns, necessitating a nuanced approach to treatment that considers these differences to optimize outcomes. Moreover, the review underscores the importance of recognizing the unique needs of sexual minority and gender-diverse individuals in orthopedic care, emphasizing the impact of gender-affirming hormone therapy on aspects like bone health and perioperative risks. To foster advancements in sex- and gender-specific orthopedics, we advocate for the strategic disaggregation of data by sex and gender and the inclusion of "Sexual Orientation and Gender Identity" (SOGI) data in research and clinical practice. Such measures can enrich clinical insights, ensure

tailored patient care, and promote inclusivity within orthopedic treatments, ultimately enhancing the precision and effectiveness of care for diverse patient populations. Integrating sex and gender considerations into orthopedic research and practice is paramount for addressing the complex and varied needs of patients. By embracing this comprehensive approach, orthopedic medicine can move towards more personalized, effective, and inclusive treatment strategies, thereby improving patient outcomes and advancing the field.
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WC Biochemistry & Molecular Biology; Medicine, Research & Experimental; Pharmacology & Pharmacy
SC Biochemistry & Molecular Biology; Research & Experimental Medicine; Pharmacology & Pharmacy
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TI Novel Insights into the Links between N6-Methyladenosine and Regulated Cell Death in Musculoskeletal Diseases
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LA English
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DE regulated cell death; musculoskeletal diseases; m6A; apoptosis; autophagy-dependent cell death; ferroptosis; pyroptosis
ID messenger-rna; proliferation; osteosarcoma; promotes; mettl3; recommendations; methylation; ferroptosis; progression; apoptosis
AB Musculoskeletal diseases (MSDs), including osteoarthritis (OA), osteosarcoma (OS), multiple myeloma (MM), intervertebral disc degeneration (IDD), osteoporosis (OP), and rheumatoid arthritis (RA), present noteworthy obstacles associated with pain, disability, and impaired quality of life on a global scale. In recent years, it has become increasingly apparent that N6-methyladenosine (m6A) is a key regulator in the expression of genes in a multitude of biological processes. m6A is composed of 0.1-0.4% adenylate residues, especially at the beginning of 3 '-UTR near the translation stop codon. The m6A regulator can be classified into three types, namely the "writer", "reader", and "eraser". Studies have shown that the epigenetic modulation of m6A influences mRNA processing, nuclear export, translation, and splicing. Regulated cell death (RCD) is the autonomous and orderly death of cells under genetic control to maintain the stability of the internal environment. Moreover, distorted RCDs are widely used to influence the course of various diseases and receiving increasing attention from researchers. In the past few years, increasing evidence has indicated that m6A can regulate gene expression and thus influence different RCD processes, which has a central role in the etiology and evolution of MSDs. The RCDs currently confirmed to be associated with m6A are autophagy-dependent cell death, apoptosis, necroptosis, pyroptosis, ferroptosis, immunogenic cell death, NETotic cell death and oxeiptosis. The m6A-RCD axis can regulate the inflammatory response in chondrocytes and the invasive and migratory of MM cells to bone remodeling capacity, thereby influencing the development of MSDs. This review gives a complete overview of the regulatory functions on the m6A-RCD axis across muscle, bone, and cartilage. In addition, we also discuss recent advances in the control of RCD by m6A-targeted factors and explore the clinical application prospects of therapies targeting the m6A-RCD in MSD prevention and treatment. These may provide new ideas and directions for understanding the pathophysiological mechanism of MSDs and the clinical prevention and treatment of these diseases.
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TI Family History of Arthritis, Osteoporosis, and Carpal Tunnel Syndrome and Risk

of These Conditions Among US Adults
SO ARTHRITIS CARE & RESEARCH
LA English
DT Article
ID systemic-lupus-erythematosus; rheumatoid-arthritis; united-states; diagnosed arthritis; body-mass; osteoarthritis; prevalence; population; prevention; metaanalysis
AB ObjectiveThe aim was to estimate odds ratios (ORs) of associations between family history of arthritis, osteoporosis, and carpal tunnel syndrome and prevalence in a real-world population, uncovering family histories of related conditions that may increase risk because of shared heritability, condition pathophysiology, or social/environmental factors.MethodsUsing data from 156,307 participants in the All of Us (AoU) Research Program, we examined associations between self-reported first-degree family history of five common types of arthritis (fibromyalgia, gout, osteoarthritis [OA], rheumatoid arthritis, and systemic lupus erythematosus [SLE]), osteoporosis, and carpal tunnel syndrome and prevalence. We evaluate associations across seven conditions and performed stratified analyses by race and ethnicity, sex, socioeconomic differences, body mass index, and type of affected relative.ResultsMore than 38% of AoU participants reported a family history of any arthritis, osteoporosis, or carpal tunnel syndrome. Adults with a family history of any arthritis, osteoporosis, and carpal tunnel syndrome exhibited 3.68 to 7.59 (4.90, on average) odds of having the same condition and 0.70 to 2.10 (1.24, on average) odds of having a different condition. The strongest associations observed were between family history of OA and prevalence of OA (OR 7.59; 95% confidence interval [95% CI] 7.32-7.88) and family history of SLE and prevalence of SLE (OR 6.34; 95% CI 5.17-7.74). We additionally uncover race and ethnicity and sex disparities in family history associations.ConclusionFamily history of several related conditions was associated with increased risk for arthritis, osteoporosis, and carpal tunnel syndrome, underscoring the importance of family history of related conditions for primary prevention. imageConclusionFamily history of several related conditions was associated with increased risk for arthritis, osteoporosis, and carpal tunnel syndrome, underscoring the importance of family history of related conditions for primary prevention. image
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NR 76
TC 0
Z9 1
U1 0
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PU WILEY
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J9 ARTHRIT CARE RES
JI Arthritis Care Res.
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TI Opportunistic Screening of Low Bone Mineral Density From Standard X-Rays
SO JOURNAL OF THE AMERICAN COLLEGE OF RADIOLOGY
LA English
DT Article
DE Bone mineral density; machine learning; opportunistic screen; x-ray
ID osteoporosis; rationale
AB Background: Osteoporosis, characterized by loss of bone mineral density (BMD), is underscreened. Osteoporosis and low bone mass are diagnosed by a BMD T-score <= -2.5, and between -1.0 and -2.5, respectively, at the femoral neck or lumbar vertebrae (L1-4), using dual energy x-ray absorptiometry (DXA). The ability to estimate BMD at those anatomic sites from standard radiographs would enable opportunistic screening of low BMD (T-score < -1) in individuals undergoing x-ray for any clinical indication. Methods: Radiographs of the lumbar spine, thoracic spine, chest, pelvis, hand, and knee, with a paired DXA acquired within 1 year, were obtained from community imaging centers (62,023 x-ray-DXA pairs of patients). A software program called Rho was developed that uses x-ray, age, and sex as inputs, and outputs a score of 1 to 10 that corresponds with the likelihood of low BMD. The program's performance was assessed using receiver-operating characteristic analyses in three independent test sets, as follows: patients from community imaging centers (n = 3,729; 83% female); patients in the Canadian Multicentre Osteoporosis Study (n = 1,780; 71% female); and patients in the Osteoarthritis Initiative (n = 591; 50% female). Results: The areas under the receiver-operating characteristic curves were 0.89 (0.87-0.90), 0.87 (0.85-0.88), and 0.82 (0.79-0.85), respectively, and subset analyses showed similar results for each sex, body part, and race. Conclusion: Rho can opportunistically screen patients at risk of low BMD (at femoral neck or L1-4) from radiographs of the lumbar spine, thoracic spine, chest, pelvis, hand, or knee.
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AU Van Overschelde, P
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TI A single-centre RetrospeCtive sTudy Investigating patient-reported outcomeS of extended dressing wear time for incisional healing following orthopaedic surgery: the ARCTIS study
SO JOURNAL OF WOUND CARE
LA English
DT Article
DE incision care; PROMS; sustainability; telemedicine; undisturbed wound healing (UWH); UNSDG 12; wound care; wound dressing; wound healing
ID surgical site infection; hospital readmission; wound dehiscence; care; hip;

reasons; score
AB Objective: Orthopaedic surgery is an effective intervention for treating the symptoms of degenerative joint disease or osteoarthritis (OA). Frequent wound dressing changes, unless clinically indicated, can disrupt the healing process and increase the occurrence of incision site contamination. Protection from contamination is critical for surgical incisions and, therefore, undisturbed wound healing (UWH) in surgical wound management is vital. This article describes a retrospective study reporting the clinical performance of a self-adherent, absorbent postoperative dressing, with a focus on dressing wear time. Method: A single-centre, retrospective electronic medical record review of a convenience sample of adult patients treated with a dressing (Mepilex Border Post Op; M ölnlycke, Sweden) following elective hip or knee replacement was undertaken. Data relating to dressing wear time, rationale for dressing changes and patient-reported outcomes were extracted from a mobile health application moveUP Therapy (moveUP NV, Belgium). Health-related quality of life assessment was conducted using the EQ-5D-5L questionnaire and orthopaedic-specific quality of life (QoL) indicator tools. Results: Of the 558 records reviewed, 151 respondents (27.1%) reported outcomes relating to dressing wear time and frequency of dressing change. The average wear time of the first dressing was 13.6 days (second dressing: 5.3 days). The proportion of patients who wore the first dressing for 1-7 days, 8-13 days and for >= 14 days was 17.2%, 13.2% and 69.5%, respectively. Data from the completed questionnaires revealed improvement in QoL over time. Conclusion: The results of this study are a good indicator of the suitability of the postoperative dressing for a 14-day wear time, in line with the principles of UWH.
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NR 54
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TI What do osteoporosis and osteoarthritis have in common? An integrated study of overlapping differentially expressed genes in bone mesenchymal stem cells of osteoporosis and osteoarthritis
SO GENE
LA English
DT Article
DE Mesenchymal stem cells; Osteoarthritis; Osteoporosis; Treatment ingredients; Bioinformatics
AB Objective: For identification of aberrantly expressed genes in mesenchymal stem cells of osteoporosis (OP) and osteoarthritis (OA), Gene Expression Omnibus

(GEO) datasets were integrated to investigate the intersection point.Methods: GSE35958 (osteoporosis) and GSE19664 (osteoarthritis) datasets were obtained from GEO database. The abnormally expressed genes were analyzed by GEO2R. Functional enrichment was explored by Metascape database and R software. The String database and Cytoscape software were used to build the protein-protein interaction network and identify hub genes. GSE35957 and GSE116925 were used as verification datasets. Single-cell analysis and pseudotime analysis were undertaken. CTDbase, Network Analyst, HPA database, HERB database and MIRW database were used to research the information, tissue and cell distribution, regulation, interaction and ingredients targeting the hub genes. Additionally, in vitro experiments such as RT-PCR, ALP staining and immunofluorescence were undertaken as verification tests.Results: Ten hub genes were identified in this study. All these genes play an important role in bone or cartilage generation. They have diagnostic values and therapeutic potential for OA and OP. Single-cell analysis visualized the cell distribution and pseudotime distribution of these genes. Some potential therapeutic ingredients of these genes were identified, such as curcumin, wogonin and glycerin. In vitro experiments, RT-PCR results showed that COL9A3 and MMP3 were downregulated and PTH1R was upregulated during osteogenic induction of BMSC. Immunohistochemical results showed the expression trend of MMP3 and COL2A1.Conclusion: Ten abnormal hub genes of osteoporosis and osteoarthritis were identified successfully by this study. They were important regulatory genes for healthy bone and cartilage. These genes could be the common con-nections between osteoporosis and osteoarthritis as well as treatment targets. Further study of the regulatory mechanism and treatment effects of these genes would be valuable. The results of this study could contribute to further research.
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TI Mesenchymal stem cells and their extracellular vesicles in bone and joint diseases: targeting the NLRP3 inflammasome
SO HUMAN CELL
LA English
DT Review
DE Mesenchymal stem cells; Extracellular vesicles; NLRP3 inflammasome; Bone and joint diseases; Inflammation
ID activation; exosm; transplantation; osteoarthritis; mechanisms; receptor; repair; rats; rna
AB The nucleotide-binding oligomerization domain-like-receptor family pyrin domain-containing 3 (NLRP3) inflammasome is a cytosolic multi-subunit protein complex, and recent studies have demonstrated the vital role of the NLRP3 inflammasome in the pathological and physiological conditions, which cleaves gasdermin D to induce inflammatory cell death called pyroptosis and mediates the release of interleukin-1 beta and interleukin-18 in response to microbial infection or cellular injury. Over-activation of the NLRP3 inflammasome is associated with the pathogenesis of many disorders affecting bone and joints, including gouty arthritis, osteoarthritis, rheumatoid arthritis, osteoporosis, and periodontitis. Moreover, mesenchymal stem cells (MSCs) have been discovered to facilitate the inhibition of NLRP3 and maybe ideal for treating bone and joint diseases. In this review, we implicate the structure and activation of the NLRP3 inflammasome along with the detail on the involvement of NLRP3 inflammasome in bone and joint diseases pathology. In addition, we focused on MSCs and MSC-extracellular vesicles targeting NLRP3 inflammasomes in bone and joint diseases. Finally, the existing problems and future direction are also discussed.
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AU Chen, YR
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Zhou, HL
AF Chen, Yue-Ru
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TI Achyranthes bidentata Blume (Amaranthaceae): a review of its botany, traditional uses, phytochemistry, pharmacology, and toxicology
SO JOURNAL OF PHARMACY AND PHARMACOLOGY
LA English
DT Review
DE Achyranthes bidentata Blume; botany; traditional uses; phytochemistry; pharmacology
ID osteogenic differentiation; root extract; polysaccharides; saponins; osteoporosis; apoptosis; neurons; growth; cells
AB Objectives Achyranthes bidentata Blume (A. bidentata) is a plant of Amaranthaceae family, and its root is the main medicinal part, named "Huai-Niu-Xi." It is used to expel blood stasis through menstruation, tonify liver and kidney, strengthen muscles and bones, and induce diuresis. This review aimed to provide a systematic summary of botany, traditional uses, phytochemistry, pharmacology, and toxicology of A. bidentata.Methods The present review covers the literature survey. The data have been collected from various journals, books, and some of the electronic search via Internet-based information such as Web of Science, PubMed, Google Scholar, Google patents, CNKI, SpringerLink, online

electronic journals, and ScienceDirect.Key findings So far, more than 270 metabolites have been isolated from A. bidentata, including terpenoids, steroids, alkaloids, flavonoids, and so on. Among them, terpenoids and steroids are the main metabolites. The extract and metabolites exert multiple pharmacological activities such as alleviating osteoarthritis effect, antiosteoporosis activity, neuroprotective effect, antidiabetic activity-associated complications, immunoregulatory activity, and so on.Summary Some traditional uses of A. bidentata need further in-depth studies to confirm. Similarly, the separation and screening of active compounds, as well as the corresponding molecular mechanisms of action of compounds, are also needed to be studied.
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TI Adipose Mesenchymal Stem Cell-Derived Exosomes as Nanocarriers for Treating Musculoskeletal Disorders
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DT Review
DE exosomes; adipose mesenchymal stem cells; musculoskeletal disorders; regenerative medicine
ID bone-fat balance; extracellular vesicles; signaling pathways; tendon injury; cartilage; osteoporosis; biology; matrix; roles; differentiation
AB Musculoskeletal disorders are a series of diseases involving bone, muscle,

cartilage, and tendon, mainly caused by chronic strain, degenerative changes, and structural damage due to trauma. The disorders limit the function of patients due to pain and significantly reduce their quality of life. In recent years, adipose-derived mesenchymal stem cells have been extensively applied in regeneration medicine research due to their particular abilities of self-renewal, differentiation, and targeted homing and are more easily accessed compared with other sources. The paracrine effect of ADSCs plays a crucial role in intercellular communication by releasing mass mediators, including cytokines and growth factors, particularly the exosomes they secrete. Not only do these exosomes possess low immunogenicity, low toxicity, and an enhanced ability to penetrate a bio-barrier, but they also inherit their parent cells' characteristics and carry various bioactive molecules to release to targeted cells, modulating their biological process. Meanwhile, these characteristics also make exosomes a natural nanocarrier capable of targeted drug delivery to specific sites, enhancing the bioavailability of drugs within the body and achieving precision therapy with fewer toxic side effects. Furthermore, the integration of exosomes with tissue engineering and chemical modification strategies can also significantly enhance their efficacy in facilitating tissue repair. However, the current research on ADSC-Exos for improving MSDs remains at an early stage and needs further exploration. Therefore, this review summarized the ADSC-Exo as a nanodrug carrier characteristics and mechanism in the treatment of fracture, osteoporosis, osteoarthritis, intervertebral disc degeneration, and tendon injury, which push forward the research progress of ADSC-Exo therapy for MSDs.
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TI Former Olympians had remained on high bone mineral density for a long period: Consecutive checkup of the 1964 Tokyo Olympic Japanese contestants for over 50

years
SO BONE
LA English
DT Article
DE Aging; Bone mineral density; Exercise; Osteoporosis; Olympians; Former elite athletes
ID provides lifelong benefits; physical-activity; strength; geometry; osteoarthritis; young; size; risk; exercise; girls
AB Introduction: We performed consecutive checkups of the 1964 Tokyo Olympic contestants every 4 years for 50 years. This study evaluated bone mineral density (BMD) and its related factors in former Tokyo Olympic athletes. Objectives: The study population comprised 181 former Olympians (141 men and 40 women) who had undergone BMD measurement in at least one of the four checkups performed every 4 years since 2005. The mean age of the 104 subjects who participated in the last checkup in 2016 was 76.1 years for men and 74.0 years for women. Methods: Health-related information regarding medical history, regular physical activity, alcohol consumption, and smoking was obtained using questionnaires. The areal BMD of the total body was measured using dualenergy X-ray absorptiometry (DXA). The relationship between BMD and anthropometric measurements, medical history, and health behaviors was examined. Furthermore, we assessed the influence of the mode and magnitude of weight-bearing and impact loading during athletic events during their active careers on BMD. Results: The mean Z-scores of BMD of the total body, lumbar spine, pelvis, and upper and lower limbs were > 0 in both male and female subjects at each checkup. The subjects had a higher mean height and weight than the Japanese age- and sex-matched individuals. Furthermore, the subjects had higher grip strength than the age- and sex-matched individuals. BMD showed a positive correlation with body weight, lean body mass (LBM), muscle mass, and grip strength, with higher correlation coefficients found between BMD of the pelvis or lower limbs and LBM or muscle mass volume. When the association with current participation in sports activities was examined, male subjects who exercised weekly had significantly higher grip strength and greater muscle mass volume; however, no significant differences were observed among female subjects. After adjusting for age and LMB, BMD was significantly higher in both the lumbar spine and lower limbs of male subjects with relatively more impact loading in sports events during their active careers. Conclusion: The Tokyo Olympic contestants maintained a high muscle mass even at an older age, regardless of their medical history, which may be one of the reasons for their ability to maintain a high BMD.
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PT J
AU Wu, CS
Hsu, LY
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Chen, WJ
Lin, MC
Fan, CC
Wang, SH
AF Wu, Chi-Shin
Hsu, Le-Yin
Shen, Chen-Yang
Chen, Wei J.
Lin, Mei-Chen
Fan, Chun Chieh
Wang, Shi-Heng
TI Comparison of Demographic and Clinical Characteristics of Taiwan Biobank Participants with Nonparticipants
SO JOURNAL OF EPIDEMIOLOGY
LA English
DT Article
DE healthy volunteer effect; biobank; Taiwan biobank; representativeness; sociodemographic characteristics; clnical characteristics
ID population; mortality; risk
AB Background: This study investigated fundamental demographic variables within the Taiwan Biobank (TWBB) and compared them with national demographic statistics. Additionally, a matched cohort analysis compared TWBB participants with nonparticipants to uncover disparities in sociodemographic and clinical characteristics. Methods: A total of 128,663 individuals aged 30 to 70 without cancer were recruited within the TWBB, and 514,652 nonparticipants matched by age and sex were randomly selected from the National Health Insurance claims database. Sociodemographic variables, healthcare utilization metrics, underlying medical conditions, and subsequent mortality and cancer risk were analyzed. Results: TWBB participants were more likely to be female, older, married, higher educated, with higher incomes, and urban residency. Healthcare utilization metrics showed minimal differences. Pre-cohort entry, TWBB participants had a higher prevalence of certain medical conditions, such as peptic ulcer disease, osteoarthritis, osteoporosis, and uterine leiomyoma in females. During follow-up periods, elevated mortality rates were observed among TWBB participants but decreased cancer risk. Conclusion: The TWBB cohort exhibits disparities in sociodemographic and healthrelated attributes compared to the general population, comprising older, females, married, higher educated, higher income, and predominantly in urban areas. While mortality rates are slightly elevated within the TWBB cohort, cancer incidence rates are lower. Despite limitations in representativeness, the TWBB's size and exposure measures offer valuable insights into associations between exposures and health conditions.
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TI Unravelling the Relacatib activity against the CTSK proteins causing pycnodysostosis: a molecular docking and dynamics approach
SO JOURNAL OF BIOMOLECULAR STRUCTURE & DYNAMICS
LA English
DT Article
DE Pycnodysostosis; CTSK protein; Relacatib; molecular docking; molecular dynamics; MMPBSA
ID cell lung-cancer; tyrosine kinases; mutant p53; expression; overexpression; therapy; complex; egfr; stem
AB Pycnodysostosis is an atypical autosomal recessive condition of Lysosomal storage disorder that originated due to the deficit of the enzyme Cathepsin K which is vital for normal osteoclast action in bone resorption. Abnormal degradation of type 1 collagen and accumulation of toxic undigested collagen fibers in lysosomes of the osteoclast cells resulting in high bone density, brittle bones, and a short stature is caused in CTSK protein-carrying individuals. The broad aim of this study is to identify the most significant variant through various computational pipelines. This study was initiated by retrieving a total number of thirty-six variants from NCBI, HGMD, and UniProt databases, and the Y283C variant was found to be more significant by various standard computational tools. A structural investigation was performed to understand and gain a better knowledge about the interaction profile for the native (1BY8) and variant (Y283C) with Relacatib (a small-molecule drug that blocks the function of Cathepsin K, an enzyme that has been linked to osteoporosis, osteoarthritis, and other bone-degrading diseases). The interaction profile was analyzed using molecular docking. Relacatib (ligand) had an average binding affinity for both native (-7.16 kcal/mol) and Y283C (-6.76 kcal/mol). Finally, Molecular dynamics simulations were done in duplicates to recognize the variant (Y283C) activity of the protein structure against Relacatib for 100 ns. This study assists in comprehending the most pathogenic amino-acid variant, the ligand interaction with the protein structure, and paves the way for understanding the steadiness of the ligand with the native and selected significant amino-acid variant.Communicated by Ramaswamy H. Sarma
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AU Stellpflug, A
   Walls, J
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AF Stellpflug, Austin
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TI From bone to nanoparticles: development of a novel generation of bone derived nanoparticles for image guided orthopedic regeneration
SO BIOMATERIALS SCIENCE
LA English
DT Article

ID controlled drug-release; extracellular-matrix; indocyanine green; delivery systems; aspect ratio; in-vivo; size; cell; fluorescence; medicine
AB Bone related diseases such as osteoporosis, osteoarthritis, metastatic bone cancer, osteogenesis imperfecta, and Paget's disease, are primarily treated with pharmacologic therapies that often exhibit limited efficacy and substantial side effects. Bone injuries or fractures are primarily repaired with biocompatible materials that produce mixed results in sufficiently regenerating healthy and homogenous bone tissue. Each of these bone conditions, both localized and systemic, use different strategies with the same goal of achieving a healthy and homeostatic bone environment. In this study, we developed a new type of bone-based nanoparticle (BPs) using the entire organic extracellular matrix (ECM) of decellularized porcine bone, additionally encapsulating indocyanine green dye (ICG) for an in vivo monitoring capability. Utilizing the regenerative capability of bone ECM and the functionality of nanoparticles, the ICG encapsulated BPs (ICG/BPs) have been demonstrated to be utilized as a therapeutic option for localized and systemic orthopedic conditions. Additionally, ICG enables an in situ monitoring capability in the Short-Wave Infrared (SWIR) spectrum, capturing the degradation or the biodistribution of the ICG/BPs after both local implantation and intravenous administration, respectively. The efficacy and safety of the ICG/BPs shown within this study lay the foundation for future investigations, which will delve into optimization for clinical translation. This study developed a new type of bone-based nanoparticle (BPs) directly from the entire decellularized porcine bone, additionally encapsulating indocyanine green dye (ICG) for an in vivo monitoring capability.
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PU ROYAL SOC CHEMISTRY
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PT J
AU Delsmann, J
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TI Alterations in compositional and cellular properties of the subchondral bone are linked to cartilage degeneration in hip osteoarthritis
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Subchondral bone; Osteocyte; Matrix mineralization; Biomechanics
ID trabecular bone; marrow lesions; zoledronic acid; femoral-head; knee; osteoporosis; sclerostin; turnover; quality; volume
AB Objective: The subchondral bone is an emerging regulator of osteoarthritis (OA). However, knowledge of how specific subchondral alterations relate to cartilage degeneration remains incomplete. Method: Femoral heads were obtained from 44 patients with primary OA during total hip arthroplasty and from 30 non-OA controls during autopsy. A multiscale assessment of the central subchondral bone region comprising histomorphometry, quantitative backscattered electron imaging, nanoindentation, and osteocyte lacunocanalicular network characterization was employed. Results: In hip OA, thickening of the subchondral bone coincided with a higher number of osteoblasts (controls: 3.7 +/- 4.5 mm(-1), OA: 16.4 +/- 10.2 mm(-1), age-adjusted mean difference 10.5 mm(-1) [95% CI 4.7 to 16.4], p < 0.001) but a similar number of osteoclasts compared to controls (p = 0.150). Furthermore, higher matrix mineralization heterogeneity (CaWidth, controls: 2.8 +/- 0.2 wt%, OA: 3.1 +/- 0.3 wt%, age-adjusted mean difference 0.2 wt% [95% CI 0.1 to 0.4], p = 0.011) and lower tissue hardness (controls: 0.69 +/- 0.06 GPa, OA: 0.67 +/- 0.06 GPa, age-adjusted mean difference -0.05 GPa [95% CI -0.09 to -0.01], p = 0.032) were detected. While no evidence of altered osteocytic perilacunar/canalicular remodeling in terms of fewer osteocyte canaliculi was found in OA, specimens with advanced cartilage degeneration showed a higher number of osteocyte canaliculi and larger lacunocanalicular network area compared to those with low-grade cartilage degeneration. Multiple linear regression models indicated that several subchondral bone properties, especially osteoblast and osteocyte parameters, were closely related to cartilage degeneration (R-2 adjusted = 0.561, p < 0.001). Conclusion: Subchondral bone properties in OA are affected at the compositional, mechanical, and cellular levels. Based on their strong interaction with cartilage degeneration, targeting osteoblasts/osteocytes may be a promising therapeutic OA approach. Data and materials availability: All data are available in the main text or the supplementary materials. (c) 2024 The Author(s). Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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FU Else Kro ner-Fresenius foundation [2021_EKEA.23]
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NR 57
TC 9
Z9 10
U1 2
U2 6
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
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JI Osteoarthritis Cartilage
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TI Novel heart valve leaflet designs with stiff polymeric materials and biomimetic kinematics

SO BIO-DESIGN AND MANUFACTURING
LA English
DT Article
DE Fully polymeric heart valve; Parametric leaflet design; Finite element analysis; Leaflet kinematics; In vitro testing
ID in-vitro; hydrodynamic function; behavior
AB Despite continuous efforts to improve the robustness of cardiac valve implants, neither bioprosthetic nor mechanical valves fulfill both hemodynamic and durability requirements. This study discussed novel flexible leaflet designs, focusing on polymeric materials with proven hemocompatibility, such as polyether ether ketone, of much higher stiffness than native tissue, aiming at optimal valve implants. A biomimetic valve with a single-curvature belly-curve (B-C) was used as a reference for new design variants with a double-curvature B-C with varying radii. Soft (13.2 MPa) and stiff (2.4 GPa) leaflet materials and different thicknesses were studied using lean simulations and in vitro experiments under physiologic hemodynamic conditions. The performance was assessed using opening pressure (OP) and orifice area (OA). The latter was determined by a newly developed automatized image processing tool. Experimental trends are in agreement with simulations and demonstrated that a buckling-inspired double-curvature leaflet design significantly enhances the trileaflet valve opening behavior, which is particularly advantageous for stiffer leaflet materials. Compared to the reference, the best-performing variant showed an OP improvement of 47% and 44% based on simulations and experiments, respectively. In contrast, the achieved mean pressure differential was directly comparable to state-of-the-art bioprosthetic valves. The OA was slightly reduced for new variants but still in the satisfying range.
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AU Yu, JC
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TI Unraveling the potential of nanozymes in the tapestry of orthopedic healing
SO MATERIALS & DESIGN
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DT Article

DE Nanozymes; Bone-related Disorders; Nanoparticles; Oxidative Stress; Biomedical Applications
ID intervertebral disc degeneration; oxidative stress; cerium oxide; femoral-head; bone; angiogenesis; nanoparticles; microenvironment; osteosarcoma; osteoarthritis
AB Bone-related disorders, such as osteoporosis, osteoarthritis, and osteosarcoma, have complex origins. Genetic, environmental factors, and significantly, oxidative stress due to Reactive Oxygen Species (ROS) play pivotal roles in these disorders. With their profound implications on global health, it becomes imperative to seek innovative therapeutic solutions. Nanozymes, known for their superior stability, cost-effectiveness, and tunable properties, present themselves as a prospective answer in mitigating ROS-driven bone ailments. This review explores the diverse applications and mechanisms of nanozymes in the context of bone health. They show potential in not only counteracting ROS-induced oxidative stress but also in modulating angiogenesis and showcasing antibacterial effects. We systematically analyze the effects of nanozymes on conditions such as osteonecrosis of the femoral head, skin flap transplantation, osteomyelitis, osteoarthritis, intervertebral disc disease, osteoporosis, and osteosarcoma, highlighting their potential roles in modulating disease processes. In addition, we discuss the challenges of applying nanozymes to orthopedic diseases. It offers insights into the transformative potential of nanozymes in bone therapeutics, underscoring the need to address challenges and capitalize on opportunities for their broader application in orthopedics.
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TI Icariin promotes bone marrow mesenchymal stem cells osteogenic differentiation via the mTOR/autophagy pathway to improve ketogenic diet-associated osteoporosis
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Icariin; mTOR; Ketogenic diet; Osteoporosis; Autophagy
ID turnover markers; animal-model; autophagy; osteoarthritis; management; metabolism; mechanisms; therapy; rat
AB BackgroundIcariin, a traditional Chinese medicine, has demonstrated anti-osteoporotic properties in ovariectomized mice. However, its effectiveness in preventing bone loss induced by ketogenic diet (KD), which mimics osteoporosis in human, remains unexplored. This study aims to investigate icariin's impact on KD-induced bone loss in mice.MethodsThirty mice were divided into: sham, KD, and KD + icariin groups. Post a 12-week intervention, evaluation including bone microstructures, serum concentrations of tartrate-resistant acid phosphatase (TRAP) and bone-specific alkaline phosphatase (ALP), and femoral tissue expression levels of osteocalcin (OCN) and TRAP. The expression levels of mammalian target of rapamycin (mTOR), ALP, peroxisome proliferator-activated receptor gamma (PPAR-gamma), phosphorylated mTOR (p-mTOR), and the autophagy adaptor protein (p62) were also analyzed. Alizarin granule deposition and cellular ALP levels were measured following the induction of bone marrow mesenchymal stem cells (BMSCs) into osteogenesis.ResultsThe study found that KD significantly impaired BMSCs' osteogenic differentiation, leading to bone loss. Icariin notably increased bone mass, stimulated osteogenesis, and reduced cancellous bone loss. In the KD + icariin group, measures such as bone tissue density (TMD), bone volume fraction (BV/TV), trabecular number (Tb.N), and trabecular thickness (Tb.Th) were significantly higher than in the KD group. Additionally, bone trabecular separation (Tb.Sp) was markedly lower in the KD + icariin group. Moreover, icariin increased OCN and ALP levels while suppressing PPAR-gamma, TRAP, p62, and p-mTOR. In cellular studies, icariin encouraged osteogenic development in BMSCs under KD conditions.ConclusionsIcariin effectively counteracts bone thinning and improves bone microstructure. Its mechanism likely involves stimulating BMSCs osteogenic differentiation and inhibiting bone resorption, potentially through mTOR downregulation. These findings suggest icariin's potential as an alternative treatment for KD-induced bone loss.

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NR 37
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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ER

PT J
AU Yang, YJ
Zhou, XC
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AF Yang, Yajing
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TI The role of O-GlcNAcylation in bone metabolic diseases
SO FRONTIERS IN PHYSIOLOGY
LA English
DT Review
DE O-GlcNAcylation; bone; cartilage; osteoporosis; osteoarthritis; osteosarcoma
ID n-acetylglucosamine modification; glcnac transferase; osteoclast differentiation; protein modification; mineral density; in-vitro; glucosamine; expression; osteoblast; growth
AB O-GlcNAcylation, as a post-translational modification, can modulate cellular activities such as kinase activity, transcription-translation, protein degradation, and insulin signaling by affecting the function of the protein substrate, including cellular localization of proteins, protein stability, and protein/protein interactions. Accumulating evidence suggests that dysregulation of O-GlcNAcylation is associated with disease progression such as cancer, neurodegeneration, and diabetes. Recent studies suggest that O-GlcNAcylation is also involved in the regulation of osteoblast, osteoclast and chondrocyte differentiation, which is closely related to the initiation and development of bone metabolic diseases such as osteoporosis, arthritis and osteosarcoma. However, the potential mechanisms by which O-GlcNAcylation regulates bone metabolism are not fully understood. In this paper, the literature related to the regulation of bone metabolism by O-GlcNAcylation was summarized to provide new potential therapeutic strategies for the treatment of orthopedic diseases such as arthritis and osteoporosis.
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TI Subchondral insufficiency fractures: overview of MRI findings from hip to ankle joint
SO ROFO-FORTSCHRITTE AUF DEM GEBIET DER RONTGENSTRAHLEN UND DER BILDGEBENDEN VERFAHREN
LA English
DT Review
DE Subchondral insufficiency fracture; Hip; Knee; ankle; Magnetic resonance imaging
ID bone-marrow edema; spontaneous osteonecrosis; transient osteoporosis; femoral-head; early-stage; knee; lesions; tear
AB Background Subchondral insufficiency fracture (SIF) represents a potentially severe condition that can advance to osteoarthritis, with collapse of the articular surface. SIF manifests as a fracture in bone weakened by non-tumorous disease, precipitated by repetitive physiological stress, without a clear history of major trauma. It is observed along the central weight-bearing region of the femoral condyle, with a higher incidence in the medial femoral condyle, but also in other large weight-bearing synovial joints, such as the femoral head, tibial plateau, or talus. Method A review of the literature from the past six years was performed by searching PubMed and ScienceDirect databases, using the keywords "subchondral insufficiency fracture" and "spontaneous osteonecrosis of the knee". The inclusion criteria were scientific papers presented in the English language that reported on the magnetic resonance imaging (MRI) aspects of SIF of the lower limb. Results and Conclusion Detecting SIF at the level of the hip, knee, and ankle may present challenges both clinically and radiologically. The MRI appearance is dominated by a bone marrow edema-like signal and subchondral bone changes that can sometimes be subtle. Subchondral abnormalities are more specific than the pattern of bone marrow edema-like signal and are best shown on T2-weighted and proton-density-weighted MR images. MRI plays an important role in accurately depicting even subtle subchondral fractures at the onset of the disease and proves valuable in follow-up, prognosis, and the differentiation of SIF from other conditions. Key Points center dot Subchondral insufficiency fractures may affect the hip, knee, and ankle. center dot Subchondral insufficiency fractures may heal spontaneously or progress to collapse. center dot MRI is important for the detection, follow-up, and prognosis of subchondral insufficiency fractures. center dot Differential diagnosis may include transient osteoporosis and osteonecrosis of systemic origin.
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TI The emerging role of Piezo1 in the musculoskeletal system and disease
SO THERANOSTICS
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DT Review
DE Piezo1; bone; muscle; cartilage; intervertebral disc
ID mechanosensitive ion channels; duchenne muscular-dystrophy; stem-cell; skeletal-muscle; nucleus pulposus; satellite cells; blood-pressure; tendon injury; flow; transduction
AB Piezo1, a mechanosensitive ion channel, has emerged as a key player in translating mechanical stimuli into biological signaling. Its involvement extends beyond physiological and pathological processes such as lymphatic vessel development, axon growth, vascular development, immunoregulation, and blood pressure regulation. The musculoskeletal system, responsible for structural support, movement, and homeostasis, has recently attracted attention regarding the significance of Piezo1. This review aims to provide a comprehensive summary of the current research on Piezo1 in the musculoskeletal system, highlighting its impact on bone formation, myogenesis, chondrogenesis, intervertebral disc homeostasis, tendon matrix cross -linking, and physical activity. Additionally, we explore the potential of targeting Piezo1 as a therapeutic approach for musculoskeletal disorders, including osteoporosis, muscle atrophy, intervertebral

disc degeneration, and osteoarthritis.
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AU Kiliç, SC
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AF Kilic, Songul Comert
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TI Correlations with clinical and radiologic findings and prevalence of

osteopenia/osteoporosis in the patients with bilateral temporomandibular joint osteoarthritis
SO JOURNAL OF STOMATOLOGY ORAL AND MAXILLOFACIAL SURGERY
LA English
DT Article
DE Cone-beam computed tomography; Absorptiometry; Photon; Bone density; Osteoarthritis; Bone diseases; Metabolic; Osteoporosis; Temporomandibular joint
ID osteoporosis
AB This study aimed to evaluate the prevalence of osteopenia/osteoporosis in patients with bilateral temporomandibular joint osteoarthritis (TMJ-OA) and its correlations with clinical and radiological findings. A total of 95 patients with bilateral TMJ-OA diagnosed by CBCT were included in the study. Clinical and radiological findings and bone mineral density (BMD) scores were recorded. Descriptive statistics and the Spearman rho correlation tests were performed. Osteopenia/osteoporosis was found in 44 of 95 patients (46.32 %) (30, osteopenia; 14 osteoporosis). Osteopenia/osteoporosis is significantly associated with postmenopausal status and age over 40 years, but it is not associated with clinical and radiological findings of TMJ-OA. Patients with bilateral TMJ-OA have a high prevalence of osteopenia/osteoporosis. (c) 2024 Published by Elsevier Masson SAS.
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JI J. Stomatol. Oral Maxillofac. Surg.
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TI Air pollution and risk of 32 health conditions: outcome-wide analyses in a population-based prospective cohort in Southwest China
SO BMC MEDICINE
LA English
DT Article
DE Air pollution; Fine particulate matter components; Prospective cohort study; Multiple exposure analysis; Outcome-wide analysis
ID fine particulate matter; chemical-composition; hospital admissions; inflammation; disease; dysfunction; exposure; aerosol; coarse
AB Background Uncertainty remains about the long-term effects of air pollutants (AP) on multiple diseases, especially subtypes of cardiovascular disease (CVD). We aimed to assess the individual and joint associations of fine particulate matter (PM2.5), along with its chemical components, nitrogen dioxide (NO2) and ozone (O-3), with risks of 32 health conditions. Methods A total of 17,566 participants in Sichuan Province, China, were included in 2018 and followed until 2022, with an average follow-up period of 4.2 years. The concentrations of AP were measured using a machine-learning approach. The Cox proportional hazards model and quantile g-computation were applied to assess the associations between AP and CVD. Results Per interquartile range (IQR) increase in PM2.5 mass, NO2, O-3, nitrate, ammonium, organic matter (OM), black carbon (BC), chloride, and sulfate were significantly associated with increased risks of various conditions, with hazard ratios (HRs) ranging from 1.06 to 2.48. Exposure to multiple air pollutants was associated with total cardiovascular disease (HR 1.75, 95% confidence intervals (CIs) 1.62-1.89), hypertensive diseases (1.49, 1.38-1.62), cardiac arrests (1.52, 1.30-1.77), arrhythmia (1.76, 1.44-2.15), cerebrovascular diseases (1.86, 1.65-2.10), stroke (1.77, 1.54-2.03), ischemic stroke (1.85, 1.61-2.12), atherosclerosis (1.77, 1.57-1.99),

diseases of veins, lymphatic vessels, and lymph nodes (1.32, 1.15-1.51), pneumonia (1.37, 1.16-1.61), inflammatory bowel diseases (1.34, 1.16-1.55), liver diseases (1.59, 1.43-1.77), type 2 diabetes (1.48, 1.26-1.73), lipoprotein metabolism disorders (2.20, 1.96-2.47), purine metabolism disorders (1.61, 1.38-1.88), anemia (1.29, 1.15-1.45), sleep disorders (1.54, 1.33-1.78), renal failure (1.44, 1.21-1.72), kidney stone (1.27, 1.13-1.43), osteoarthritis (2.18, 2.00-2.39), osteoporosis (1.36, 1.14-1.61). OM had max weights for joint effects of AP on many conditions. Conclusions Long-term exposure to increased levels of multiple air pollutants was associated with risks of multiple health conditions. OM accounted for substantial weight for these increased risks, suggesting it may play an important role in these associations.
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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TI Oroxylin A suppresses breast cancer-induced osteoclastogenesis and osteolysis as a natural RON inhibitor
SO PHYTOMEDICINE
LA English
DT Article
DE Oroxylin A; RON; Osteoclast; Breast cancer; MDA-MB-231
ID receptor tyrosine kinase; bone metastases; mechanisms; osteoporosis; pathogenesis; activation
AB Background: Malignant breast cancer cells trigger the over-activation of osteoclast precursor cells, leading to bone loss and severe pain. Targeted inhibition of osteoclast differentiation has emerged as an important strategy for treating bone syndromes induced by breast cancer. Purpose: The objective is to discover natural osteoclast inhibitor to treat osteoclastogenesis and bone destruction induced by breast cancer, and clarify the specific mechanisms. Methods: Recepteur d'origine Nantais (RON) protein was employed to search the natural osteoclast inhibitor for breast cancer-induced osteoclastogenesis by molecular docking, molecular dynamics simulation and cellular thermal shift assay (CETSA). In the in vitro experiment, breast cancer MDA-MB-231 cell-conditioned medium (MDA-MB-231 CM) was used to induce osteoclastogenesis in murine bone marrow-derived macrophages (BMMs), aiming to elucidate the effects and mechanisms of the natural osteoclast inhibitor. In the in vivo model, MDA-MB-231 cells was injected into the mouse tibia to evaluate the therapeutic effect of drug on

breast cancerinduced bone destruction. Results: We discovered a significant increase in the expression of RON during MDA-MB-231 CM-induced osteoclast differentiation in vitro. Molecular docking analysis found that oroxylin A (OA), a flavonoid derived from the Chinese medicine Scutellaria baicalensis Georgi, showed binding ability with RON, while its impact and mechanism on breast cancer-induced osteoclastogenesis and osteolysis remains unclear. Molecular dynamics simulation and CETSA further revealed that OA bound directly to the RON protein, and it also decreased RON expression in breast cancer CM-induced osteoclastogenesis. Correspondingly, OA suppressed the MDA-MB-231 CM-induced osteoclastogenesis and bone resorption in vitro. The downstream signals of RON including Src and NFATc1, as well as the osteoclast-specific genes, were downregulated by OA. Of interesting, the suppressive effect of OA on osteoclastogenesis induced by MDA-MB-231 CM was abolished after RON was knocked down by the specific RON-siRNA, this further confirmed that OA showed inhibitory effects on osteoclasts through targeting RON. In addition, we found that OA attenuated MDA-MB-231 cell-induced osteolysis and reduced the number of osteoclasts in vivo. Conclusion: Our results indicate that OA acts as a natural RON inhibitor to suppress breast cancer-induced osteoclastogenesis and osteolysis. This provides new strategy for treating breast cancer-induced bone destruction and related syndromes.
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AF Chaiyavech, Napat
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TI Prevalence of Common Metabolic Bone Diseases Diagnosed by Dual-Energy

X-Ray Absorptiometry Scanning and Blood Test in Outpatients With Osteoarthritis the Knee
SO GERIATRIC ORTHOPAEDIC SURGERY & REHABILITATION
LA English
DT Article
DE metabolic bone diseases; vitamin D; osteoarthritis of the knee
ID mineral density; kidney-disease; osteoporosis; hip; population; fractures; femur; women
AB Introduction: Osteoarthritis of the knee (OA knee) is a common geriatric disease that require total knee arthroplasty. Periprosthetic fracture is one of the common complications, which is strongly related to metabolic bone disease. Materials and methods: We conducted a prospective study on 291 outpatients with OA knee between November 2020 and April 2021. Baseline characteristics, dual-energy X-ray absorptiometry and blood test results were analysed using logistic regression analysis and expressed as odds ratio, 95% confidence intervals and P-values. Results: Overall metabolic bone diseases were found in 82.91% of patients. Vitamin D insufficiency (53.38%) was the most prevalent, followed by osteopenia (44.38%), impaired renal function (26.69%), and osteoporosis (17.45%). Risk factors of vitamin D insufficiency are age >= 71 years (OR 0.33, P = 0.003) and bilateral affected side (OR 1.99, P = 0.007). For osteopenia and osteoporosis, risk factors were age, body mass index, affected side, and chronic kidney disease (P < 0.05). Discussion: In the aspect of Vit D insufficiency, age>70 and bilateral OA knee were significantly related in many ways, such as reduction in cutaneous synthesis and daily exposure to sunlight and various diseases, including CKD and GI malabsorption. The risk factors of osteopenia and osteoporosis can be explained throughout several mechanisms. For instance, abnormality in hormone and cytokines metabolism will lead to the increase in adipocyte differentiation and fat accumulation. And that situation may lead to the decrease in osteoblast differentiation and increased osteoclast activity which could lead to negative impact on bone strength. Conclusions: Metabolic bone diseases were common in most patients with OA knee, and the insufficiency in amount of vitamin D(serum 25-hydroxyvitamin D), osteoporosis, and osteopenia conditions were mainly identified. These preventable conditions have risk factors that are mostly correctable These preventable conditions have risk factors that are mostly correctable, for example gain more outdoor activities, consume vitamin D supplement or start osteoporosis treatment program. Further analysis is necessary to establish solid evidence in the comparison of risk factors between the OA and non-OA groups.
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AU Hwang, JM
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TI In Vitro and In Vivo Bone-Forming Effect of a Low-Molecular-Weight Collagen Peptide
SO JOURNAL OF MICROBIOLOGY AND BIOTECHNOLOGY

LA English
DT Article
DE collagen hydrolysate; Gly-Pro-Hyp; bone remodeling; Sprague-Dawley rats
ID pro-hyp; differentiation; tripeptide; microarchitecture; osteoarthritis; mineralization; proliferation; hydrolysate; metabolism; blood
AB This study reveals that low -molecular -weight collagen peptide (LMWCP) can stimulate the differentiation and the mineralization of MC3T3-E1 cells in vitro and attenuate the bone remodeling process in ovariectomized (OVX) Sprague-Dawley rats in vivo. Moreover, the assessed LMWCP increased the activity of alkaline phosphatase (ALP), synthesis of collagen, and mineralization in MC3T3-E1 cells. Additionally, mRNA levels of bone metabolism -related factors such as the collagen type I alpha 1 chain, osteocalcin (OCN), osterix, bone sialoprotein, and the Runt family -associated transcription factor 2 were increased in cells treated with 1,000 mu g/ml of LMWCP. Furthermore, we demonstrated that critical bone morphometric parameters exhibited significant differences between the LMWCP (400 mg/kg)-receiving and vehicle -treated rat groups. Moreover, the expression of type I collagen and the activity of ALP were found to be higher in both the femur and lumbar vertebrae of OVX rats treated with LMWCP. Finally, the administration of LMWCP managed to alleviate osteogenic parameters such as the ALP activity and the levels of the bone alkaline phosphatase, the OCN, and the procollagen type 1 N -terminal propeptide in OVX rats. Thus, our findings suggest that LMWCP is a promising candidate for the development of food -based prevention strategies against osteoporosis.
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TI The biomedical applications of nanozymes in orthopaedics based on regulating reactive oxygen species
SO JOURNAL OF NANOBIOTECHNOLOGY
LA English
DT Review
DE Bone tissue engineering; Biomedical applications; Nanozymes; Orthopaedics; Reactive oxygen species
ID glutathione-peroxidase; nanoparticles; inflammation; mechanism; horizons; catalase; stress; enzyme; ros
AB Nanozymes, a category of nanomaterials with enzyme-like activity, have

garnered growing interest in various biomedical contexts. Notably, nanozymes that are capable of regulating reactive oxygen species levels by emulating antioxidant or prooxidant enzymes within cells hold significant therapeutic potential for a range of disorders. Herein, we overview the catalytic mechanisms of four exemplary nanozymes within the orthopedic domain. Subsequently, we emphasize recent groundbreaking advancements in nanozyme applications in orthopaedics, encompassing osteoarthritis, osteoporosis, intervertebral disc degeneration, bone defects, spinal cord injury, gout, rheumatoid arthritis, osteosarcoma and bone infection. Furthermore, we discuss the emerging area's future prospects and several noteworthy challenges in biomedical application. This review not only fosters the ongoing development of nanozyme research but also fosters the emergence of more potent nanozymes for the treatment of orthopaedical diseases in the future.
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TI Oleanolic acid exerts bone anabolic effects via activation of osteoblastic 25-hydroxyvitamin D 1-alpha hydroxylase
SO BIOMEDICINE & PHARMACOTHERAPY
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DT Article
DE 25-Hydroxyvitamin D 3 1-alpha-hydroxylase; Vitamin D; Osteoporosis; Oleanolic acid; Aging
ID vitamin-d-receptor; messenger-rna expression; parathyroid-hormone; gene-expression; cells; cyp27b1; differentiation; osteoporosis; d-3
AB Oleanolic acid (OA) is previously shown to exert bone protective effects in aged animals. However, its role in regulating osteoblastic vitamin D bioactivation, which is one of major causes of age-related bone loss, remains unclear. Our results revealed that treatment of OA significantly increased skeletal CYP27B1 expression and circulating 1,25(OH)(2)D-3 in ovariectomized mice ($p < 0.01$). Moreover, OA upregulated CYP27B1 protein expression and activity, as well as the vitamin D-responsive bone markers alkaline phosphatase (ALP) activity and osteopontin (OPN) protein expression, in human osteoblast-like MG-63 cells ($p<0.05$). CYP27B1 expression increased along with the osteoblastic differentiation of human bone marrow derived mesenchymal stem cells (hMSCs). CYP27B1 expression and cellular 1,25(OH)(2)D-3 production were further potentiated by OA in cells at mature osteogenic stages. Notably, our study suggested that the osteogenic actions of OA were CYP27B1 dependent. In summary, the bone protective effects of OA were associated with the induction of CYP27B1 activity and expression in bone tissues and osteoblastic lineages. Hence, OA might be a potential approach for management of age-related bone loss.
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DE bone targeting; receptor mediation; glycobiology; bone and cartilage development
ID enzyme replacement therapy; mesenchymal stem-cells; osteogenic differentiation; delivery-system; receptor; matrix; osteopontin; expression; binding; channels
AB Bone development is characterized by complex regulation mechanisms, including signal transduction and transcription factor-related pathways, glycobiological processes, cellular interactions, transportation mechanisms, and,

importantly, chemical formation resulting from hydroxyapatite. Any abnormal regulation in the bone development processes causes skeletal system-related problems. To some extent, the avascularity of cartilage and bone makes drug delivery more challenging than that of soft tissues. Recent studies have implemented many novel bone-targeting approaches to overcome drawbacks. However, none of these strategies fully corrects skeletal dysfunction, particularly in growth plate-related ones. Although direct recombinant enzymes (e.g., Vimizim for Morquio, Cerezyme for Gaucher, Elaprase for Hunter, Mepsevii for Sly diseases) or hormone infusions (estrogen for osteoporosis and osteoarthritis), traditional gene delivery (e.g., direct infusion of viral or non-viral vectors with no modifications on capsid, envelope, or nanoparticles), and cell therapy strategies (healthy bone marrow or hematopoietic stem cell transplantation) partially improve bone lesions, novel delivery methods must be addressed regarding target specificity, less immunogenicity, and duration in circulation. In addition to improvements in bone delivery, potential regulation of bone development mechanisms involving receptor-regulated pathways has also been utilized. Targeted drug delivery using organic and inorganic compounds is a promising approach in mostly preclinical settings and future clinical translation. This review comprehensively summarizes the current bone-targeting strategies based on bone structure and remodeling concepts while emphasizing potential approaches for future bone-targeting systems.

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AF Ho, Wang-Chun
Chang, Chung-Chih
Wu, Wen-Tien
Lee, Ru-Ping
Yao, Ting-Kuo
Peng, Cheng-Huan
Yeh, Kuang-Ting
TI Effect of Osteoporosis Treatments on Osteoarthritis Progression in Postmenopausal Women: A Review of the Literature
SO CURRENT RHEUMATOLOGY REPORTS
LA English
DT Review
DE Osteoporosis; Osteoarthritis (OA); Bisphosphonate; Selective estrogen receptor modulators (SERMs); Parathyroid hormone (PTH); Denosumab
ID parathyroid-hormone 1-34; knee osteoarthritis; bisphosphonate use; rat model; denosumab; estrogen; bone; cartilage; metaanalysis; association
AB Purpose of ReviewThe purpose of this literature review was to determine if medications used to treat osteoporosis are also effective for treating osteoarthritis (OA).Recent FindingsA total of 40 relevant articles were identified. Studies were categorized into those (1) discussing estrogen and selective estrogen receptor modulators (SERMs), (2) bisphosphonates, (3) parathyroid hormone (PTH) analogs, and (4) denosumab, and (5) prior review articles. A large amount of evidence suggests that estrogen and SERMs are effective at reducing OA symptoms and disease progression. Evidence suggests that bisphosphonates, the most common medications used to treat osteoporosis, can reduce OA symptoms and disease progression. In vivo studies suggest that PTH analogs may improve the cartilage destruction associated with OA; however, few human trials have examined its use for OA. Denosumab is approved to treat osteoporosis, bone metastases, and certain types of breast cancer, but little study has been done with respect to its effect on OA.SummaryThe current evidence indicates that medications used to treat osteoporosis are also effective for treating OA. Estrogen, SERMs, and bisphosphonates have the most potential as OA therapies. Less is known regarding the effectiveness of PTH analogs and denosumab in OA, and more research is needed.
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NR 41
TC 15
Z9 15
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U2 10
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WC Rheumatology
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TI Influence of Sex and Gender on Musculoskeletal Conditions and How They Are Reported
SO JOURNAL OF BONE AND JOINT SURGERY-AMERICAN VOLUME
LA English
DT Review
ID 17-beta-estradiol; risk; testosterone; chondrocytes; responses; severity; exhibit
AB There is increasing evidence that musculoskeletal tissues are differentially regulated by sex hormones in males and females. The influence of sex hormones, in addition to other sex-based differences such as in anatomical alignment and immune-system function, impact the prevalence and severity of disease as well as the types of injuries that affect the musculoskeletal system and the outcomes of prevention measures and treatment. Literature specifically addressing sex differences related to the musculoskeletal system is limited, underscoring the imperative for both basic and clinical research on this topic. This review highlights areas of research that have implications for bone and cartilage health, including growth and development, sports injuries, osteoarthritis, osteoporosis, and bone frailty. It is clear that important aspects of the musculoskeletal system have been understudied. Consideration of how sex hormone therapy will affect musculoskeletal tissues in prepuberty, during puberty, and in adults is vital, yet little is known. The purpose of this article is to foster awareness and interest in advancing our understanding of how sex differences influence orthopaedic practice.
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NR 76
TC 10
Z9 12
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U2 3
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PT J
AU Li, Y
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AF Li, Ying
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TI Development and validation of a three-dimensional nomogram prediction model for knee osteoarthritis in middle-aged population
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Knee osteoarthritis; Middle-aged; Risk factor; Uncomfortable symptom; Nomogram
ID risk-factors; prevalence; management
AB ObjectivesThis study aims to identify predictors of knee osteoarthritis (KOA) risk in middle-aged population, construct and validate a nomogram for KOA in this demographic.MethodsFrom June to December 2020, we conducted a cross-sectional survey on 5,527 middle-aged individuals from Changsha and Zhangjiajie cities in Hunan Province, selected using a stratified multi-stage random sampling method. Data collection involved a structured questionnaire

encompassing general demographic, physical condition, and lifestyle behaviors dimensions. The dataset was randomly split into a training set (n = 3868) and a validation set (n = 1659) at a 7:3 ratio via computerized randomization. We analyzed the prevalence of self-reported KOA and identified its influencing factors using logistic regression. A nomogram was constructed based on these "three-dimensional" factors. Subsequent validation was conducted, and the nomogram's performance was further evaluated through ROC curves, C-index, Hosmer-Lemeshow test, and calibration curves.ResultsThe self-reported prevalence of KOA in the middle-aged population was 11.4% (632/5527). The risk factor with the greatest impact is: diagnosed with osteoporosis(95% CI 2.269-3.568, OR = 2.845), followed by age between 51 to 60 years (95% CI 2.176-3.151, OR = 2.619), diagnosed with hypertension(95% CI 1.633-2.499, OR = 2.02), diagnosed with diabetes (OR = 1.689), ethnic Han Chinese (OR = 1.673), exercise according to physical condition (OR = 1.643), pay attention to keeping the knee joint warm (OR = 1.535), eating habits are mainly light vegetables (OR = 1.374), male gender (OR = 1.343), drink occasionally in small amounts (OR = 1.286); a higher level of education (OR = 0.477) and frequently or always apply an external or plaster to relieve symptoms after knee discomfort (OR = 0.377; OR = 0.385) are protective factors.The C-index of the training set model was 0.8107 (95% CI: 0.8102-0.8111), with a statistically significant area under the ROC curve (AUC = 0.818), and the calibration curve showed a good fit. The C-index for the validation set was 0.8124 (95% CI: 0.8109-0.8140), with an AUC of 0.812. The Hosmer-Lemeshow test resulted in a P-value of 0.46 (P >= 0.05)indicating good calibration of the model.ResultsThe self-reported prevalence of KOA in the middle-aged population was 11.4% (632/5527). The risk factor with the greatest impact is: diagnosed with osteoporosis(95% CI 2.269-3.568, OR = 2.845), followed by age between 51 to 60 years (95% CI 2.176-3.151, OR = 2.619), diagnosed with hypertension(95% CI 1.633-2.499, OR = 2.02), diagnosed with diabetes (OR = 1.689), ethnic Han Chinese (OR = 1.673), exercise according to physical condition (OR = 1.643), pay attention to keeping the knee joint warm (OR = 1.535), eating habits are mainly light vegetables (OR = 1.374), male gender (OR = 1.343), drink occasionally in small amounts (OR = 1.286); a higher level of education (OR = 0.477) and frequently or always apply an external or plaster to relieve symptoms after knee discomfort (OR = 0.377; OR = 0.385) are protective factors.The C-index of the training set model was 0.8107 (95% CI: 0.8102-0.8111), with a statistically significant area under the ROC curve (AUC = 0.818), and the calibration curve showed a good fit. The C-index for the validation set was 0.8124 (95% CI: 0.8109-0.8140), with an AUC of 0.812. The Hosmer-Lemeshow test resulted in a P-value of 0.46 (P >= 0.05)indicating good calibration of the model. ConclusionThe three dimensions nomogram generated in this study was a valid and easy-to-use tool for assessing the risk of KOA in middle-aged population, and helped healthcare professionals to screen the high-risk population.
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TC 0
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PT J
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TI Lumbar Osteoarthritis in Patients with Osteoporosis Evaluated with the Lane and Wilke Scale and its Effect on Dexa Scores
SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE Dexa; Lane and Wilke Scale; Lumbar osteoarthritis; Osteoporosis
ID bone-mineral density; radiographic osteoarthritis; hand osteoarthritis; association; knee; hip; population; turnover; fracture; women
AB Objective: This study aimed to compare bone mineral density (BMD) values in patients with lumbar osteoarthritis (OA) with and without osteoporosis (OP). This study evaluated the effect of lumbar osteoarthritis in patients with osteoporosis on Dexa scores using the Lane and Wilke scale. Methods: A total of 51 individuals with OA, 20 with OP, and 31 without OP were included in the study. Lumbar osteoarthritis was assessed and recorded using the Lane and Wilke scale. BMD was measured by dual-energy X-ray absorptiometry (DEXA) at the waist and hip (femoral neck, lumbar vertebrae). Frax assessed the risk of osteoporosis and fracture risk. Results: The mean age of patients with OP was 68.1 +/- 8.2 years, and the mean age of patients without OP was 68.6 +/- 9.4 years. There was a significant decrease between the lumbar vertebrae and femoral neck BMD values of the two groups in favor of the osteoporosis group. The t-scores of the OP group were significantly lower ($p = 0.045$). All variables showed a statistically significant difference between the group with OP and those without OP ($p<0.05$). The median values of L1-L2, L2-L3, L3-L4, and total L1-L4 were higher in absolute value in the group with OP. In frax hip and frax primary osteoporosis, the median values were higher in the group with OP than in the group without OP ($p = 0.023/p = 0.020$). All L1-L2, L2-L3, and L3-L4 dexa parameters with and without OP were not significantly different between the groups according to the Lane and Wilke classification ($p> 0.05$). Conclusion: There was no statistically significant difference between DEXA parameters in osteoporosis and non-osteoporosis patients with low back osteoarthritis (according to the Lane and Wilke classification).
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AU Di, JK
Bai, J
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AF Di, Jingkai
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Hao, Yuxuan
Bai, Jiaqi
Xiang, Chuan

TI Regional disparities, age-related changes and sex-related differences in knee osteoarthritis
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Knee osteoarthritis; Age-standardized rates; Incidence; Sex-Related Differences; Risk factors
ID body-mass index; risk; hip; osteoporosis; association; prevention; injury; obesity; level; women
AB BackgroundThe objective of the study is to analyse the regions, age and sex differences in the incidence of knee osteoarthritis (KOA).MethodsData were extracted from the global burden of diseases (GBD) 2019 study, including incidence, years lived with disability (YLD), disability-adjusted life-years (DALYs) and risk factors. Estimated annual percentage changes (EAPCs) were calculated to quantify the temporal trends in age standardized rate (ASR) of KOA. Paired t-test, paired Wilcoxon signed-rank test and spearman correlation were performed to analyze the association of sex disparity in KOA and socio-demographic index (SDI).ResultsThere were significant regional differences in the incidence of knee osteoarthritis. In 2019, South Korea had the highest incidence of knee osteoarthritis (474.85,95%UI:413.34-539.64) and Thailand had the highest increase in incidence of knee osteoarthritis (EAPC = 0.56, 95%CI = 0.54-0.58). Notably, higher incidence, YLD and DALYs of knee osteoarthritis were associated with areas with a high socio-demographic index ($r = 0.336$, $p < 0.001$; $r = 0.324$, $p < 0.001$; $r = 0.324$, $p < 0.001$). In terms of age differences, the greatest increase in the incidence of knee osteoarthritis was between the 35-39 and 40-44 age groups. (EAPC = 0.52, 95%CI = 0.40-0.63; 0.47, 95%CI = 0.36-0.58). In addition, there were significant sex differences in the disease burden of knee osteoarthritis ($P < 0.001$).ConclusionsThe incidence of knee osteoarthritis is significantly different with regions, age and sex.
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U1 26
U2 83
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PI LONDON
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AU Lee, C
Park, YH
Cho, B
Lee, HA
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Cho, Belong
Lee, Hye Ah
TI A network-based approach to explore comorbidity patterns among community-dwelling older adults living alone
SO GEROSCIENCE
LA English
DT Article
DE Aged; Comorbidity; Chronic disease; Network analysis
ID urinary-incontinence; peptic-ulcer; otitis-media; depression; association; regulator; women
AB The detailed comorbidity patterns of community-dwelling older adults have not yet been explored. This study employed a network-based approach to investigate the comorbidity patterns of community-dwelling older adults living alone. The sample comprised a cross-sectional cohort of adults 65 or older living alone in a Korean city (n = 1041; mean age = 77.7 years, 77.6% women). A comorbidity network analysis that estimates networks aggregated from measures of significant co-occurrence between pairs of diseases was employed to investigate comorbid associations between 31 chronic conditions. A cluster detection algorithm was employed to identify specific clusters of comorbidities. The association strength was expressed as the observed-to-expected ratio (OER). As a result, fifteen diseases were interconnected within the network (OER > 1, p-value < .05). While hypertension had a high prevalence, osteoporosis was the most central disease, co-occurring with numerous other diseases. The strongest associations among comorbidities were found between thyroid disease and urinary incontinence, chronic otitis media and osteoporosis, gastric duodenal ulcer/gastritis and anemia, and depression and gastric duodenal ulcer/gastritis (OER > 1.85). Three distinct clusters were identified as follows: (a) cataracts, osteoporosis, chronic otitis media, osteoarthritis/rheumatism, low back pain/sciatica, urinary incontinence, post-accident sequelae, and thyroid diseases; (b) hyperlipidemia, diabetes mellitus, and hypertension; and (c) depression, skin disease, gastric duodenal ulcer/gastritis, and anemia. The results may prove valuable in guiding the early diagnosis, management, and treatment of comorbidities in older adults living alone.
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NR 46
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PU SPRINGER
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AU Zhang, T
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   Barlow, JW
AF Zhang, Tao
   OConnor, Christine
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TI Vitamin K2 in Health and Disease: A Clinical Perspective
SO FOODS
LA English
DT Review
DE vitamin K2; VK2; menaquinone; health; therapeutic potential
ID matrix gla protein; hepatocellular-carcinoma; k intake; gamma-carboxylation; growth-inhibition; kappa-b; monocytic differentiation; dietary phylloquinone; insulin-resistance; metabolic syndrome
AB Vitamins are essential organic compounds that vary widely in chemical structure

and are vital in small quantities for numerous biochemical and biological functions. They are critical for metabolism, growth, development and maintaining overall health. Vitamins are categorised into two groups: hydrophilic and lipophilic. Vitamin K (VK), a lipophilic vitamin, occurs naturally in two primary forms: phylloquinone (VK1), found in green leafy vegetables and algae, and Menaquinones (VK2), present in certain fermented and animal foods and widely formulated in VK supplements. This review explores the possible factors contributing to VK deficiency, including dietary influences, and discusses the pharmacological and therapeutic potential of supplementary VK2, examining recent global clinical studies on its role in treating diseases such as osteoporosis, osteoarthritis, rheumatoid arthritis, cardiovascular disease, chronic kidney disease, diabetes, neurodegenerative disorders and cancers. The analysis includes a review of published articles from multiple databases, including Scopus, PubMed, Google Scholar, ISI Web of Science and CNKI, focusing on human studies. The findings indicate that VK2 is a versatile vitamin essential for human health and that a broadly positive correlation exists between VK2 supplementation and improved health outcomes. However, clinical data are somewhat inconsistent, highlighting the need for further detailed research into VK2 ' s metabolic processes, biomarker validation, dose-response relationships, bioavailability and safety. Establishing a Recommended Daily Intake for VK2 could significantly enhance global health.
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TI Current knowledge of bone-derived factor osteocalcin: its role in the management and treatment of diabetes mellitus, osteoporosis, osteopetrosis and inflammatory joint diseases
SO JOURNAL OF MOLECULAR MEDICINE-JMM
LA English
DT Review
DE Osteocalcin; Preclinical and clinical studies; Diabetes mellitus; Osteoporosis; Osteopetrosis; Inflammatory joint diseases
ID serum undercarboxylated osteocalcin; glucocorticoid-induced osteoporosis; endoplasmic-reticulum stress; diet-induced obesity; mineral density; turnover markers; postmenopausal women; glucose-metabolism; alkaline-phosphatase; biochemical markers
AB Osteocalcin (OC) is the most abundant non-collagenous and osteoblast-secreted protein in bone. It consists of two forms such as carboxylated OC (cOC) and undercarboxylated OC (ucOC). While cOC promotes bone mineralization and increases bone strength, ucOC is regarded an endocrinologically active form that may have several functions in multiple end organs and tissues. Total OC (tOC) includes both of these forms (cOC and ucOC) and is considered a marker of bone turnover in clinical settings. Most of the data on OC is limited to

preclinical studies and therefore may not accurately reflect the situation in clinical conditions. For the stated reason, the aim of this review was not only to summarize current knowledge of all forms of OC and characterize its role in diabetes mellitus, osteoporosis, osteopetrosis, inflammatory joint diseases, but also to provide new interpretations of its involvement in the management and treatment of aforementioned diseases. In this context, special emphasis was placed on available clinical trials. Significantly lower levels of tOC and ucOC could be associated with the risk of type 2 diabetes mellitus. On the contrary, tOC level does not seem to be a good indicator of high bone turnover status in postmenopausal osteoporosis, osteoarthritis and rheumatoid arthritis. The associations between several pharmacological drugs used to treat all disorders mentioned above and OC levels have also been provided. From this perspective, OC may serve as a medium through which certain medications can influence glucose metabolism, body weight, adiponectin secretion, and synovial inflammation.
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TI Resolving Organic Aerosol Components Contributing to the Oxidative Potential of PM2.5 in the North China Plain
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ID ambient particulate matter; mass spectrometers ams; air-pollution; severe haze; humic-like; oxygen; dithiothreitol; particles; dtt; generation
AB The oxidative potential (OP) of ambient particulate matter (PM) is a common metric for estimating PM toxicity and linking PM exposure to adverse health effects. Organic aerosol (OA), a dominant fraction of ambient PM worldwide, may significantly contribute to PM toxicity. Here, we investigated the source-based OA components contributing to the OP of PM in the urban (Beijing, summer and winter) and rural (Gucheng, winter) environments of the North China Plain (NCP). Various OA components as identified by the aerosol mass spectrometer/aerosol chemical speciation monitor (AMS/ACSM), transition metals, and black carbon were compared with the OP of PM measured by dithiothreitol assays. The results consistently demonstrate the importance of OA as a contributor to PM's OP in both urban and rural NCP environments. Higher intrinsic OP was observed in winter Beijing than in summer, possibly due to OA being predominantly from anthropogenic sources in winter. Furthermore, different OA components were

found to drive the response of OP in the two environments. More-oxidized oxygenated OA (MO-OOA), cooking OA, and oxidized primary OA (during winter) are the OA contributors to OP in the urban environment, with a dominant contribution from MO-OOA. In contrast, biomass burning OA (BBOA) and OOA play a major role in the OP in the rural environment, with BBOA making the largest contribution. Overall, this work highlights the significance of OA in determining PM's OP and calls for more work to reveal the sources and characteristics of OA components contributing to OP across different regions.
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NR 87
TC 2
Z9 2
U1 12
U2 83
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SN 2169-897X
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J9 J GEOPHYS RES-ATMOS
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WC Meteorology & Atmospheric Sciences
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PT J
AU Mathieu, S
Fayet, F
Salembien, MH
Rodere, M
Soubrier, M
Tournadre, A
AF Mathieu, Sylvain
Fayet, Francoise
Salembien, Marie-Helene
Rodere, Malory
Soubrier, Martin
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TI Prevalence of comorbidities and cardiovascular risk factor management in hand osteoarthritis: a cross-sectional study
SO RHEUMATOLOGY INTERNATIONAL
LA English
DT Article
DE Hand osteoarthritis; Cardiovascular risk profile; Comorbidities
ID population; disease; events
AB ObjectivesTo assess the prevalence of comorbidities and management of cardiovascular risk factors according to established guidelines for patients with hand osteoarthritis.MethodsA cross-sectional study was conducted that included 110 hand osteoarthritis patients. The clinical parameters (pain, function, grip strength, quality of life, sarcopenia, and comorbidities) were assessed along with cardiovascular (CV) risk factors (blood pressure, body mass index, and dyslipidaemia). CV risk was assessed using SCORE2 or SCORE2-OP algorithms. Comparisons of patient characteristics were performed using Student's or chi-squared tests.ResultsTwenty-eight patients were identified with comorbidities, and they tended to be older, male, and with a lower quality of life. The median SCORE2 was 5.1%. SCORE2 was negatively associated with grip strength (r=-0.27, p = 0.02). There was no difference in SCORE2 between hand osteoarthritis patients with (n = 60) and without (n = 50) neuropathic-like pain (5.6 +/- 3.7 versus 6.2 +/- 3.3%; p = 0.38). Among the 40 patients with an intermediate or high CV risk, 33 (82.5%) were off target for low-density lipoproteins (LDL) level with no lipid-lowering treatment (n = 29) or an insufficient statin treatment (n = 4). Obesity

was observed in 24 patients (21.8%) and 30 (27.3%) were overweight. Forty-two patients (41.2%) had blood hypertension (41 systolic and one diastolic patient) despite treatment for 9 patients.ConclusionsWe found an increased CV risk in hand osteoarthritis patients who had an insufficient LDL cholesterol target achievement. Hand osteoarthritis patients appear to have a pro-atherogenic profile. These results suggest that CV risk factors should be assessed in patients with hand osteoarthritis and managed according to recommended guidelines.
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NR 31
TC 3
Z9 3
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PU SPRINGER HEIDELBERG
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PT J
AU Huang, K
Cai, HL
AF Huang, Kai
Cai, Haili
TI The interplay between osteoarthritis and osteoporosis: Mechanisms, implications, and treatment considerations - A narrative review
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Review
DE Osteoarthritis; Osteoporosis; Pathophysiological mechanisms
ID foxo transcription factors; bone-mineral density; articular-cartilage; osteopontin; association; pathogenesis; polymorphism; progression; severity; mediator
AB This comprehensive review examines the relationship between osteoarthritis (OA) and osteoporosis (OP), two common disorders in the elderly. OA involves joint cartilage degeneration and pain, while OP leads to fractures due to reduced bone mass. Despite different pathologies, both conditions share risk factors such as age and genetics. Studies reveal mixed results: some show higher bone mineral density (BMD) in OA patients, suggesting an inverse relationship, while others find no significant link. Proposed mechanisms include mechanical loading, bone remodeling, and inflammation. Clinical strategies focus on maintaining bone health in OA and monitoring joint health in OP, with treatments like bisphosphonates and exercise. Understanding these interactions is crucial for developing integrated treatments to improve patient outcomes and quality of life. Further research is needed to clarify these complex mechanisms.
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TI Evidence-Based Guideline for the management of osteoporosis in men
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DT Article
ID trabecular bone score; fracture risk reduction; cost-utility analysis; hip fracture; older men; postmenopausal women; parathyroid-hormone; zoledronic acid; mineral density; european-society
AB Historically, osteoporosis has been viewed as a disease of women, with research, trials of interventions and guidelines predominantly focused as such. It is apparent, however, that this condition causes a substantial health burden in men also, and that its assessment and management must ultimately be addressed across both sexes. In this article, an international multidisciplinary working group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases presents GRADE-assessed recommendations for the diagnosis, monitoring and treatment of osteoporosis in men. The recommendations are based on a comprehensive review of the latest research related to diagnostic and screening approaches for osteoporosis and its associated high fracture risk in men, covering disease burden, appropriate interpretation of bone densitometry (including the use of a female reference database for densitometric diagnosis in men) and absolute fracture risk, thresholds for treatment, and interventions that can be used therapeutically and their health economic evaluation. Future work should specifically address the efficacy of anti-osteoporosis medications, including denosumab and bone-forming therapies.

In this Evidence-Based Guideline article, an international multidisciplinary working group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases presents recommendations for the diagnosis, monitoring and treatment of osteoporosis in men.
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AU Lee, JM
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AF Lee, Jung-Min
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TI Prediction of prognosis in supramalleolar osteotomy with or without additional fibula osteotomy by approaching a biomechanical study: a finite element analysis
SO BIOMEDICAL ENGINEERING LETTERS
LA English
DT Review
DE Supramalleolar osteotomy; Fibular osteotomy; Osteoarthritis; Finite element analysis; Ankle joint
ID low tibial osteotomy; ankle osteoarthritis; wedge osteotomy; varus deformity; opening wedge; arthritis; joint; foot
AB Supramalleolar osteotomy (SMO) is a representative procedure to restore a malalignment in the varus ankle deformity by shifting the concentrated pressure on the medial ankle joint to the lateral area. Additionally, fibula osteotomy (FO) is selectively selected and performed according to the surgeon's preference. However, it is controversial whether FO is effective in shifting the abnormal

pressure from the medial to the lateral area on the ankle joint. Some cadaveric studies have been performed to prove this. However, it is difficult to consistently reconstruct amount of the varus ankle deformities angle in cadavers and to guarantee reliable contact pressure between the ankle joint. Thus, the aim of this study was predicted and quantitatively compared a peak pressure between single SMO and SMO with FO procedure by using a finite element analysis as a powerful biomechanical tool to those limitations of cadaveric study. This study reconstructed total 4 3D foot and ankle models including a normal and pre-op model and 2 post-op models. The pre-op model was modified by assigning 10 degrees varus tilting corresponding to stage 3b in the classification of varus ankle osteoarthritis based on the validated normal model. Also, the post-op models were reconstructed by applying single SMO and SMO with FO, respectively. All of the models were assumed as one-leg standing position and to mimic smooth ankle joint motion. Peak contact pressure change was predicted at the medial ankle joint by using computational simulation. As a result, 2 post-op models showed a remarkably peak pressure reduction by up to 5.5 times on the medial tibiotalar joint. However, a comparison between single SMO and SMO with FO model showed no appreciable differences. In conclusion, this study predicted that single SMO may be as effective as SMO with FO in reducing peak contact pressure on the medial tibiotalar joint in varus ankle osteoarthritis.
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TI Euthanasia and Physician-Assisted Suicide in People With an Accumulation of Health Problems Related to Old Age: A Cross-Sectional Questionnaire Study Among Physicians in the Netherlands
SO INTERNATIONAL JOURNAL OF PUBLIC HEALTH
LA English
DT Article
DE accumulation of health problems related to old age; euthanasia; physician-assisted suicide; end-of-life care; medical decision-making
ID requests
AB Objectives: We explored characteristics of people with an accumulation of health problems related to old age requesting euthanasia or physician-assisted suicide (EAS) and identified characteristics associated with granting EAS requests.

Methods: We conducted a cross-sectional questionnaire study among Dutch physicians on characteristics of these people requesting EAS (n = 123). Associations between characteristics and granting a request were assessed using logistic regression analyses. Results: People requesting EAS were predominantly >80 years old (82.4%), female (70.0%), widow/widower (71.7%), (partially) care-dependent (76.7%), and had a life expectancy >12 months (68.6%). The most prevalent health problems were osteoarthritis (70.4%) and impaired vision and hearing (53.0% and 40.9%). The most cited reasons to request EAS were physical deterioration (68.6%) and dependence (61.2%). 44.7% of requests were granted. Granting a request was positively associated with care dependence, disability/immobility, impaired vision, osteoporosis, loss of control, suffering without prospect of improvement and a treatment relationship with the physician >12 months. Conclusion: Enhanced understanding of people with an accumulation of health problems related to old age requesting EAS can contribute to the ongoing debate on the permissibility of EAS in people without life-threatening conditions.
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AF Dash, Subhransu
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TI Why Pharmacovigilance of Non-steroidal Anti-inflammatory Drugs is Important in India?
SO ENDOCRINE METABOLIC & IMMUNE DISORDERS-DRUG TARGETS
LA English
DT Review
DE Adverse drug reaction; drug safety design; NSAIDS; patient safety; pharmacovigilance; regulatory affairs
ID cancer pain management; low-dose aspirin; adverse-reactions; rheumatoid-arthritis; gastrointestinal toxicity; current perspectives; cardiovascular risk; human pharmacology; nsaids; barriers
AB Background Non-steroidal Anti-Inflammatory Drugs (NSAIDs) are among the drugs that are most regularly administered to manage inflammation and pain. Over-the-Counter (OTC) NSAIDs are widely accessible, particularly in developing countries like India. This casual approach to using NSAIDs may operate as a magnet for NSAID-related adverse drug reactions (ADRs) among

patients.Objectives As patients in India are less informed about the appropriate use of NSAIDs and consumption patttern, adverse drug reactions, and the importance of reporting ADRs, the current study's objective is to promote patient safety by using pharmacovigilance as a tool to educate patients.Methods A targeted literature methodology was utilized to gather the data pertaining to NSAIDs, their ADRs and their pharmacovigilance. Different scientific databases, such as Science Direct, PubMed, Wiley Online Library, Springer, and Google Scholar, along with authentic textbooks, were explored as reference literature.Results In general, NSAIDs consumption pattern depends upon the different age groups. Around 1.6 billion tablets of NSAIDs are consumed in India for ailments, such as headaches, arthritis, menstrual cramps, osteoarthritis, back pain, rheumatoid arthritis, gout, osteoporosis, tendinitis, cancer pain and chronic pain. Common ADRs of NSAIDs include nausea, vomiting, headache, gastritis, abdominal pain, and diarrhoea. Also, they can cause renal damage and cardiovascular problems if not consumed in a dose-dependent manner. However, Diclofenac and Ibuprofen have both been linked to depression and dementia. There have been reports of aplastic anaemia, agranulocytosis linked to phenylbutazone, Stevens-Johnson, and Lyell's syndrome linked to isoxicam and piroxicam, as well as the vulnerability of new-borns to Reye's syndrome after aspirin use. Lack of awareness, time constraints and unpredictability, poor training in ADRs identification, etc., are some of the reasons for the under-reporting of ADR of NSAIDs in India.Conclusion In order to rationally prescribe NSAIDs, it is essential to be aware of probable ADR's and establish prescription guidelines. Prescribers' behaviour can be changed toward excellent prescribing practices by conducting routine prescription assessments dealing with NSAIDs and providing feedback. In the near future, it will be critical to strengthen ADR data management and expand the reach of pharmacovigilance programs, ADR monitoring centers, and healthcare professionals' especially pharmacists' training in rural locations.
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TI Parathyroid hormone (1-34) retards the lumbar facet joint degeneration and activates Wnt/β-catenin signaling pathway in ovariectomized rats
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Joint degeneration; Lumbar facet joint; Parathyroid hormone; Wnt/beta-catenin signaling; Cartilage; Subchondral bone; Ovariectomized rat model
ID subchondral bone; differentiated osteoblasts; terminal differentiation; articular chondrocytes; disc degeneration; back-pain; osteoarthritis; cartilage; estrogen; model
AB Purpose Facet joint degeneration (FJD) is a major cause of low back pain. Parathyroid hormone (PTH) (1-34) is commonly used to treat osteoporosis. However, little is known about its effects on FJD induced by estrogen deficiency.

This study aims to investigate the effects of PTH (1-34) on FJD induced by estrogen deficiency and the underlying pathogenesis of the disease.Methods Forty 3-month-old female Sprague-Dawley rats were randomly divided into four groups: 30 received bilateral ovariectomy (OVX) followed by 12 weeks of treatment with normal saline, PTH (1-34) or 17 beta-estradiol (E2), and 10 received sham surgery followed by administration of normal saline. Status and Wnt/beta-catenin signaling activity in the cartilage and subchondral bone of the L4-L5 FJs and serum biomarkers were analyzed.Results Administration of PTH (1-34) and E2 ameliorated cartilage lesions, and significantly decreased MMP-13 and caspase-3 levels and chondrocyte apoptosis. PTH (1-34) but not E2 significantly increased cartilage thickness, number of chondrocytes, and the expression of aggrecan. PTH (1-34) significantly improved microarchitecture parameters of subchondral bone, increased the expression of collagen I and osteocalcin, and decreased RANKL/OPG ratio. E2 treatment significantly increased the OPG level and decreased the RANKL/OPG ratio in the subchondral bone of ovariectomized rats, but it did not significantly improve the microarchitecture parameters of subchondral bone. Wnt3a and beta-catenin expression was significantly reduced in the articular cartilage and subchondral bone in OVX rats, but PTH (1-34) could increase the expression of these proteins. E2 significantly increased the activity of Wnt/beta-catenin pathway only in cartilage, but not in subchondral bone. The restoration of Wnt/beta-catenin signaling had an obvious correlation with the improvement of some parameters associated with the FJs status.Conclusion Wnt/beta-catenin signaling may be a potential therapeutic target for FJD induced by estrogen deficiency. PTH (1-34) is effective in treating this disease with better efficacy than 17 beta-estradiol, and the efficacy may be attributed to its restoration of Wnt/beta-catenin signaling.
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TI Well-known polypeptides of deer antler velvet with key actives: modern pharmacological advances
SO NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY
LA English
DT Review
DE Deer antler polypeptides; System-related diseases; Pharmacology; Review
ID negative breast-cancer; neural stem-cells; pilose-antler; osteoblast differentiation; oxidative stress; gut microbiota; peptide; proliferation; injury; prevents
AB Deer antler velvet, with kidney tonifying, promoting the production of essence and blood, strengthening tendons and bones, not only has a thousand-year medicinal history but also its modern pharmacology mainly focuses on its active polypeptides on motor, nerve, and immune systems. The purpose of this report is to fill the gap in the comprehensive, systematic, and detailed review of polypeptides during the recent 30 years (1992-2023). The research method was to review 53 pharmacological articles from the Public Medicine, Web of science, ACS, and Science Direct database sources by searching the keywords " pilose antler," "deer velvet," "Pilose Antler Peptide (PAP) and Velvet Antler Polypeptide (VAP)." The results showed that deer antler polypeptides (DAPs), by regulating EGF, EGFR, MAPK, P38, ERK, NF-.B, Wnt, PI3K, Akt, MMP, AMPK, Stir1, NLRP3, HO-1, Nrf, Rho, TLR, TGF-beta, Smad, Ang II, etc., revealed their effects on seven system-related diseases and their mechanisms, including osteoarthritis, intervertebral disc degeneration, osteoporosis, Alzheimer's, Parkinson's, triplenegative breast cancer, liver injury, liver fibrosis, cardiovascular disease, acute lung injury, and late-onset hypogonadism. In conclusion, DAPs have good effects on motor and other system-related diseases, but the secondary and tertiary structures of DAPs (0.5-1800 KDa) need to be further elucidated, and the structure-activity relationship study is still unavailable and needs to be covered. It is expected that this review may provide

the necessary literature support for further research.
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TI Does Chronic Pancreatitis in Growing Pigs Lead to Articular Cartilage Degradation and Alterations in Subchondral Bone?
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE pig; chronic pancreatitis; articular cartilage; cytokines
ID c-reactive protein; tumor-necrosis-factor; mmp-13 expression; tnf-alpha; osteoarthritis; osteoporosis; interleukin-1; inflammation; inhibition; predictor
AB Chronic pancreatitis (CP), a progressive inflammatory disease, poses diagnostic challenges due to its initially asymptomatic nature. While CP's impact on exocrine and endocrine functions is well-recognized, its potential influence on other body systems, particularly in young individuals, remains underexplored. This study investigates the hypothesis that CP in growing pigs leads to alterations in articular cartilage and subchondral bone, potentially contributing to osteoarthritis (OA) development. Utilizing a pig model of cerulein-induced CP, we examined the structural and compositional changes in subchondral bone, articular cartilage, and synovial fluid. Histological analyses, including Picrosirius Red and Safranin-O staining, were employed alongside immuno-histochemistry and Western blotting techniques. Our findings reveal significant changes in the subchondral bone, including reduced bone volume and alterations in collagen fiber composition. Articular cartilage in CP pigs exhibited decreased proteoglycan content and alterations in key proteins such as MMP-13 and TGF-beta 1, indicative of early cartilage degradation. These changes suggest a link between CP and musculoskeletal alterations, underscoring the need for further research into CP's systemic effects. Our study provides foundational insights into the relationship

between CP and skeletal health, potentially guiding future pediatric healthcare strategies for early CP diagnosis and management.
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TI Work intensity and fat mass percentage are associated with asymptomatic morphometric vertebral fractures in knee osteoarthritis patients: A cross-sectional study
SO PLOS ONE
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DT Article
ID risk; osteoporosis; prevalence; men; index; women; pain
AB Knee osteoarthritis (OA) is a common condition with a prevalence of 365 million individuals globally, and it is an independent risk factor for falls and fractures, notably asymptomatic morphometric vertebral fractures (AMVF). The high prevalence of knee OA, the severity of AMVF, and their combined impacts on quality of life underscore the need for early detection, appropriate treatment and management. To address this, our cross-sectional study aims to identify potential predictive factors associated with AMVF in knee OA patients. Our cohort consisted of 76 patients diagnosed with knee OA, predominantly female (84.2%), of Malay ethnicity (84.2%), and obese (55.3%). In univariable analysis, significant association was found between occupation (moderate or heavy work) and AMVF ($p<0.001$). Diabetes mellitus comorbidity ($p = 0.016$) and fat mass percentage ($p = 0.027$) also demonstrated a significant association with AMVF in knee OA patients. Multivariable logistic regression analysis revealed that an increase in fat mass percentage resulted in decreased AMVF incidence (HR: 0.83, 95% CI: 0.70-0.97; $p = 0.018$), while occupation (moderate or heavy work) remained a highly significant predictor (HR: 57.76, 95% CI: 4.23-788.57; $p = 0.002$). These findings support the potential importance of considering occupational activities and body fat composition in managing AMVF among knee OA patients, but further research is required to establish causal relationships.
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PA 1160 BATTERY STREET, STE 100, SAN FRANCISCO, CA 94111 USA
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WC Multidisciplinary Sciences
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PT J
AU Cardín-Pereda, A
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TI Diagnostic Reliability of Plain Radiography in Osteonecrosis of the Femoral Head: General Radiological Features Revised
SO CURRENT MEDICAL IMAGING
LA English
DT Article
DE Osteonecrosis of the femoral head; Avascular necrosis of the hip; Radiological diagnosis; Radiograph; Reliability; Ficat and Arlet classification
ID total hip-arthroplasty; avascular necrosis; interobserver; reproducibility; classification; ficat; ct
AB Background and Objectives: Osteonecrosis of the femoral head (ONFH) is an incapacitating disease that frequently results in the collapse of the femoral head and secondary osteoarthritis. The diagnosis and staging of this pathology, which usually rely on imaging studies, are challenging. Currently, conventional radiography is the basis of the initial diagnostic assessment. In recent decades, however, radiographs have been considered insensitive to early changes in ONFH and thus, a suboptimal diagnostic tool. Paradoxically, the imaging features of radiographs are often profuse, substantial, and characteristic. This study aimed to elucidate the real limitations of this radiologic tool by assessing the diagnostic reliability of the key radiologic features and staging.Methods: This was a retrospective study in which radiographs from 28 idiopathic ONFH confirmed cases who underwent hip arthroplasty were analyzed by eight observers who were asked to identify the presence or absence of ONFH universally reported imaging features in AP hip radiographs.Results: Concordance analysis revealed a poor agreement between observers for most of the assessed imaging features. Only the identification of femoral head flattening and osteoarthritis signs exhibited moderate agreement with statistical significance. In contrast, the detection of radiological osteoporosis and the loss of trabeculation showed the lowest reliability, with negative kappa coefficients.Conclusion: There is a lack of agreement between qualified observers, even for the identification of the most characteristic ONFH radiographic features. The reliability of plain radiography for the detection

of basic radiological elements is even weaker in the early stages of the disease.
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SC Radiology, Nuclear Medicine & Medical Imaging
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AF Mallik, Abhijit
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TI Length-Weight Relationship, Condition Factor and Otolith Shape Indices of Four Creek-Associated Fish of the Northeastern Arabian Sea
SO ACTA ZOOLOGICA BULGARICA
LA English
DT Article
DE Otolith; condition factor; mean area; marine fish
ID size; river; morphology; basin; history; growth; north; bay
AB This study aimed to estimate the relationship between fish size and otolith size of four creek-associated fishes (Anodontostoma chacunda, Epinephelus diacanthus, Johnius glaucus and Mugil cephalus) collected from the north-eastern Arabian Sea from November 2021 to November 2022. The numerical relations were established using regression between fish size (Total length-TL and Body weight-BW) and otolith dimensions (Length-OL, Weight-Owt, Area-OA, Width-OW and Perimeter-OP). All regressions between the fish size and otolith morphometric measurements were highly correlated (R-2 > 0.8), which indicates the robustness of the model. Taxonomists can use findings from this study for species confirmation and reconstruction of past species assemblages. These findings might provide insight into predicting the prey size in food and feeding studies to explore the food web dynamics.
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SC Zoology
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AU Toya, M
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Zhang, N.
Goodman, S. B.
TI Sex differences of NF-KB-targeted therapy for mitigating osteoporosis associated with chronic inflammation of bone
SO BONE & JOINT RESEARCH
LA English
DT Article
ID kappa-b kinase; rheumatoid-arthritis; resorption; female; osteoarthritis; osteonecrosis; prevention; inhibitor; particles; mediator
AB Aims Transcription factor nuclear factor kappa B (NF -KB) plays a major role in the pathogenesis of chronic inflammatory diseases in all organ systems. Despite its importance, NF -KB targeted drug therapy to mitigate chronic inflammation has had limited success in preclinical studies. We hypothesized that sex differences affect the response to NF -KB treatment during chronic inflammation in bone. This study investigated the therapeutic effects of NF -KB decoy oligodeoxynucleotides (ODN) during chronic inflammation in male and female mice. Methods We used a murine model of chronic inflammation induced by continuous intramedullary delivery of lipopolysaccharide-contaminated polyethylene particles (cPE) using an osmotic pump. Specimens were evaluated using micro-CT and histomorphometric analyses. Sex-specific osteogenic and osteoclastic differentiation potentials were also investigated in vitro, including alkaline phosphatase, Alizarin Red, tartrate-resistant acid phosphatase staining, and gene expression using reverse transcription polymerase chain reaction (RT-PCR). Results Local delivery of NF -KB decoy ODN in vivo increased osteogenesis in males, but not females, in the presence of chronic inflammation induced by cPE. Bone resorption activity was decreased in both sexes. In vitro osteogenic and osteoclastic differentiation assays during inflammatory conditions did not reveal differences among the groups. Receptor activator of nuclear factor kappa B ligand (Rankl) gene expression by osteoblasts was significantly decreased only in males when treated with ODN. Conclusion We demonstrated that NF -KB decoy ODN increased osteogenesis in male mice and decreased bone resorption activity in both sexes in preclinical models of chronic inflammation. NF -KB signalling could be a therapeutic target for chronic inflammatory diseases involving bone, especially in males.
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TI Contribution of macrophage polarization in bone metabolism: A literature review
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AB Macrophage polarization divides macrophages into two main cell subpopulations, classically and alternatively activated macrophages (M1 and M2, respectively). M1 polarization promotes osteoclastogenesis, while M2 polarization promotes osteogenesis. The physiological homeostasis of bone metabolism involves a high dynamic balance between osteoclastic-mediated bone resorption and formation. Reportedly, M1/M2 imbalance causes the onset and persistence of inflammation-related bone diseases. Therefore, understanding the research advances in functions and roles of macrophages in such diseases will provide substantial guidance for improved treatment of bone diseases. In this review, we underscore and summarize the research advances in macrophage polarization, and bone-related diseases, such as rheumatoid arthritis, osteoarthritis, and osteoporosis, over the last 5 years. Our findings showed that targeting macrophages and balancing macrophage polarization can effectively reduce inflammation and decrease bone destruction while promoting bone formation and vascular repair. These results indicate that regulating macrophage and macrophage polarization to restore homeostasis is a prospective approach for curing bone-related diseases.
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TI Role of signaling pathways in age-related orthopedic diseases: focus on the fibroblast growth factor family
SO MILITARY MEDICAL RESEARCH
LA English
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DE Fibroblast growth factor (FGF); Fibroblast growth factor receptor (FGFR); Osteoarthritis (OA); Intervertebral disc degeneration (IVDD); Orthopedic degeneration; Osteoporosis (OP); Sarcopenia
ID factor receptor 1; skeletal-muscle mass; protein-kinase-c; articular-cartilage; knee osteoarthritis; intraarticular sprifermin; chondrocyte proliferation; heparan-sulfate; fgf receptor-3; high-affinity
AB Fibroblast growth factor (FGF) signaling encompasses a multitude of functions, including regulation of cell proliferation, differentiation, morphogenesis, and patterning. FGFs and their receptors (FGFR) are crucial for adult tissue repair processes. Aberrant FGF signal transduction is associated with various pathological conditions such as cartilage damage, bone loss, muscle reduction, and other core pathological changes observed in orthopedic degenerative diseases like osteoarthritis (OA), intervertebral disc degeneration (IVDD), osteoporosis (OP), and sarcopenia. In OA and IVDD pathologies specifically, FGF1, FGF2, FGF8, FGF9, FGF18, FGF21, and FGF23 regulate the synthesis, catabolism, and ossification of cartilage tissue. Additionally, the dysregulation of FGFR expression (FGFR1 and FGFR3) promotes the pathological process of cartilage degradation. In OP and sarcopenia, endocrine-derived FGFs (FGF19, FGF21, and FGF23) modulate bone mineral synthesis and decomposition as well as muscle tissues. FGF2 and other FGFs also exert regulatory roles. A growing body of research has focused on understanding the implications of FGF signaling in orthopedic degeneration.

Moreover, an increasing number of potential targets within the FGF signaling have been identified, such as FGF9, FGF18, and FGF23. However, it should be noted that most of these discoveries are still in the experimental stage, and further studies are needed before clinical application can be considered. Presently, this review aims to document the association between the FGF signaling pathway and the development and progression of orthopedic diseases. Besides, current therapeutic strategies targeting the FGF signaling pathway to prevent and treat orthopedic degeneration will be evaluated.
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AU Lei, SG
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TI Denosumab ameliorates osteoarthritis by protecting cartilage against degradation and modulating subchondral bone remodeling
SO REGENERATIVE THERAPY
LA English
DT Article
DE Osteoarthritis; Denosumab; Osteoclast; Chondrocyte
ID chondrocyte apoptosis; differentiation; osteoporosis; pathogenesis; teriparatide; mice
AB Osteoarthritis (OA) is the most prevalent degenerative joint disease worldwide. Effective management for early-stage OA is crucial. Denosumab (DS) has been widely used to treat osteoporosis (OP) and rheumatoid arthritis, but its potential for managing OA remains clear. We assessed the effects of DS on osteoclast activity and chondrocyte apoptosis using tartrate-resistant acid phosphatase (TRAP) assay, quantitative real-time polymerase chain reaction (qRT-PCR), flow cytometry, and TUNEL staining. To assess the impact of DS on the NF-kB pathway, we performed Western blot and immunofluorescence staining. Additionally, we used an OA model to explore the influence of DS on subchondral bone remodeling and cartilage degeneration in vivo. We found that DS hindered receptor activator of nuclear factor kappa B ligand (RANKL)-induced osteoclastogenesis by inhibiting the activity of the NF-kB pathway. Besides, DS alleviated reactive oxygen species (ROS)-induced apoptosis in chondrocytes by regulating the expression of genes related to apoptosis. Moreover, we observed an attenuation of OArelated subchondral bone remodeling and cartilage degeneration in vivo. Our findings indicate that DS could effectively suppress osteoclast activity and chondrocyte apoptosis, thereby mitigating OA-related subchondral bone remodeling and cartilage degeneration. These results provide a mechanistic basis for using DS to treat OA. (c) 2024, The Japanese Society for Regenerative Medicine. Production and hosting by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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AU Choi, YS
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AF Choi, Yun Seong
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TI The difference in bone mineral density between femur and tibia is related to tibia deformation in endstage knee osteoarthritis
SO KNEE
LA English
DT Article
DE Osteoporosis; Knee osteoarthritis; Varus alignment
ID varus osteoarthritis; proximal tibia; alignment; osteoporosis; progression; women; risk
AB Background: This study investigated bone mineral density (BMD) around the knee joint to clarify the mechanism by which tibia deformation exceeds that of the femur in patients with end-stage knee osteoarthritis (KOA). Methods: We retrospectively analyzed 193 patients who underwent total knee arthroplasty for end-stage KOA with varus alignment. Preoperative T-score of the femur neck and femur total using dual-energy X-ray absorptiometry (DXA) and hounsfield units (HU) of the distal femur and proximal tibia using computed tomography (CT) were measured to asess the BMD. HU was measured by dividing the femur and tibia into medial, lateral, and total parts, respectively. Patients with medial proximal tibial angle (MPTA) < 85 degrees were considered 'group 1 , and MPTA < 85 degrees were 'group 2 . The HU between femur and tibia were compared in group 1. T-score, HU, and HU difference between group 1 and group 2 were compared. Results: The HU of the proximal tibia was lower than that of the distal femur (femur lateral > femur medial > tibia medial > tibia lateral). T-score (femur neck, femur total) and HU (femur lateral, femur total, tibia lateral) were lower in group 2 than in group 1. There was no difference in femur-tibia HU difference between groups. Conclusion: The medial tibia collapse more than the medial femur in varus endstage KOA was associated with the lower BMD of the proximal tibia than that of the distal femur, and the MPTA collapse was affected by the absolute value of BMD rather than by the femur-tibia BMD difference. (c) 2024 Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.
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NR 17
TC 1
Z9 2
U1 0
U2 3
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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WC Orthopedics; Sport Sciences; Surgery
SC Orthopedics; Sport Sciences; Surgery
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PT J
AU He, Q
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Chen, BH
Chen, CY
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Dou, XY
Cai, DL
Zhou, C
Wang, HB
AF He, Qi
Lin, Yuewei
Chen, Baihao
Chen, Chuyi
Zeng, Jiaxu
Dou, Xiangyun
Cai, Dongling
Zhou, Chi
Wang, Haibin
TI Vitamin K2 ameliorates osteoarthritis by suppressing ferroptosis and extracellular matrix degradation through activation GPX4's dual functions
SO BIOMEDICINE & PHARMACOTHERAPY
LA English
DT Article
DE Vitamin K2; GPX4's dual functions; Knee osteoarthritis; Ferroptosis; Extracellular matrix degradation; MAPK/NF kappa B pathway
ID articular-cartilage; inactivation; regulator
AB Vitamin K2 (VK2) is an effective compound for anti-ferroptosis and anti-osteoporosis, and Semen sojae praeparatum (Dandouchi in Chinese) is the

main source of VK2. Chondrocyte ferroptosis and extracellular matrix (ECM) degradation playing a role in the pathogenesis of osteoarthritis (OA). Glutathione peroxidase 4 (GPX4) is the intersection of two mechanisms in regulating OA progression. But no studies have elucidated the therapeutic effects and mechanisms of VK2 on OA. This study utilized an in vivo rat OA model created via anterior cruciate ligament transection (ACLT) and an in vitro chondrocyte oxidative damage model induced by TBHP to investigate the protective effects and mechanisms of action of VK2 in OA. Knee joint pain in mice was evaluated using the Von Frey test. Micro-CT and Safranin O-Fast Green staining were employed to observe the extent of damage to the tibial cartilage and subchondral bone, while immunohistochemistry and PCR were used to examine GPX4 levels in joint cartilage. The effects of VK2 on rat chondrocyte viability were assessed using CCK-8 and flow cytometry assays, and chondrocyte morphology was observed with toluidine blue and alcian blue staining. The impact of VK2 on intracellular ferroptosis-related markers was observed using fluorescent staining and flow cytometry. Protein expression changes were detected by immunofluorescence and Western blot analysis. Furthermore, specific protein inhibitors were applied to confirm the dual-regulatory effects of VK2 on GPX4. VK2 can increase bone mass and cartilage thickness in the subchondral bone of the tibia, and reduce pain and the OARSI score induced by OA. Immunohistochemistry results indicate that VK2 exerts its anti-OA effects by regulating GPX4 to delay ECM degradation. VK2 can inhibit the activation of the MAPK/NF kappa B signaling pathway caused by reduced expression of intracellular GPX4, thereby decreasing ECM degradation. Additionally, VK2 can reverse the inhibitory effect of RSL3 on GPX4, increase intracellular GSH content and the GSH/GSSG ratio, reduce MDA content, and rescue chondrocyte ferroptosis. The protective mechanism of VK2 may involve its dualtarget regulation of GPX4, reducing chondrocyte ferroptosis and inhibiting the MAPK/NF kappa B signaling pathway to decelerate the degradation of the chondrocyte extracellular matrix.
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PU ELSEVIER FRANCE-EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER
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AU Caruso, G
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AF Caruso, Gaetano
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TI Pulsed Electromagnetic Field Stimulation in Bone Healing and Joint Preservation: A Narrative Review of the Literature
SO APPLIED SCIENCES-BASEL
LA English
DT Review
DE pulsed electromagnetic fields; PEMFs; capacitively coupled electric fields; CCEFs; bone healing; joint preservation; traumatology; sport medicine; hip and knee replacement; reverse shoulder arthroplasty
ID double-blind; biophysical stimulation; knee osteoarthritis; electrical-stimulation; adenosine receptors; therapy; cells; pain; osteonecrosis; osteoporosis
AB Background: Biophysical stimulation therapy, Pulsed Electromagnetic Fields (PEMFs) and Capacitively Coupled Electric Fields (CCEFs) have significantly increased in the last twenty years. Due to this, it is necessary to have clear information regarding their efficacy, therapeutic indications and expected objectives. Application fields: There is a unanimous opinion regarding the usefulness of applying biophysical therapy on the bone compartment both in

terms of the tissue-healing process and the symptoms associated with this situation. Differently, but no less important, positive results were observed in the joint compartment, especially with regard to the inhibition of the inflammatory process. Good results for chondroprotection were obtained in vitro and after a surgical procedure. New studies have shown the effectiveness also in cases of osteoporosis. Conclusions: The effectiveness of PEMFs and CCEFs on the bone-healing process and on joint preservation in the orthopedic and traumatology fields has consolidated evidence in the literature. We have also found positive results for symptoms and patient compliance with rehabilitation therapies. Therefore, their notable applications can be envisaged in the fields of prosthetic surgery and sports medicine.
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NR 62
TC 3
Z9 4
U1 1
U2 11
PU MDPI
PI BASEL
PA ST ALBAN-ANLAGE 66, CH-4052 BASEL, SWITZERLAND
SN
EI 2076-3417
J9 APPL SCI-BASEL
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PD MAR 15
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IS 5
BP
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WC Chemistry, Multidisciplinary; Engineering, Multidisciplinary; Materials Science, Multidisciplinary; Physics, Applied
SC Chemistry; Engineering; Materials Science; Physics
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PT J
AU Wan, XY
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Chen, L
AF Wan, Xinyue

Zhang, Wenjie
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Chen, Liang
TI The Role of Extracellular Vesicles in Bone Regeneration and Associated Bone Diseases
SO CURRENT ISSUES IN MOLECULAR BIOLOGY
LA English
DT Review
DE EVs; bone regeneration; mechanisms; diagnosis; treatment
ID mesenchymal stem-cells; promote angiogenesis; exosm; osteoarthritis; delivery; differentiation; microvesicles; osteoporosis; diagnosis; membrane
AB Extracellular vesicles (EVs) are nanoscale particles with a lipid bilayer membrane structure secreted by various cell types. Nearly all human cells secrete EVs, primarily mediating intercellular communication. In recent years, scientists have discovered that EVs can carry multiple biological cargos, such as DNA, non-coding RNAs (ncRNAs), proteins, cytokines, and lipids, and mediate intercellular signal transduction. Bone is a connective tissue with a nerve supply and high vascularization. The repair process after injury is highly complex, involving interactions among multiple cell types and biological signaling pathways. Bone regeneration consists of a series of coordinated osteoconductive and osteoinductive biological processes. As mediators of intercellular communication, EVs can promote bone regeneration by regulating osteoblast-mediated bone formation, osteoclast-mediated bone resorption, and other pathways. This review summarizes the biogenesis of EVs and the mechanisms by which EV-mediated intercellular communication promotes bone regeneration. Additionally, we focus on the research progress of EVs in various diseases related to bone regeneration. Finally, based on the above research, we explore the clinical applications of engineered EVs in the diagnosis and treatment of bone regeneration-related diseases.
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AU Steffann, F
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TI Should trochanteric fractures in elderly patients be treated by arthroplasty or internal fixation?
SO ORTHOPAEDICS & TRAUMATOLOGY-SURGERY & RESEARCH
LA English
DT Review
DE Trochanteric fractures; Arthroplasty; Internal fixation; Extramedullary fixation; Intramedullary fixation
ID unstable intertrochanteric fractures; cementless bipolar hemiarthroplasty; total hip-arthroplasty; proximal femoral nail; intramedullary fixation; femur fractures; replacement; complications; mortality; failure
AB Most trochanteric fractures are treated by fixation, most often intramedullary. Nevertheless, the desire to have patients walk as soon as possible and the fear of fixation failure has driven some surgeons to carry out an arthroplasty instead,

especially for unstable fractures and/or in patients with severe osteoporosis, in order to avoid the difficult conversion to arthroplasty later on if the fixation fails. The aim of this review was to specify the role, technique and results of performing arthroplasty in this context. In which fractures? Unstable fractures (A2.2, A2.3 and A3), especially in osteoporotic bone, which are the most difficult to reduce and fix, and in cases with associated osteoarthritis. For which patients? Arthroplasty should not be done in patients who have ASA = 3 due to greater blood loss and longer operative time. Since the postoperative Parker score often drops, arthroplasty should not be done in patients having a Parker score < 6. What are the technical problems? Arthroplasty must be done by an experienced surgeon because of the lack of anatomical landmarks, although fracture fixation has its own demands (satisfactory reduction, appropriate length and position of cervicocephalic screw). What are the results and complications? Despite several comparative studies (randomized trials, meta-analysis and prospective studies), it is difficult to draw any conclusions. These studies show worse performance of dynamic hip screws relative to intramedullary nails. The complication and revision rates were higher for nails than arthroplasty, but not in every study, while the functional outcomes with nails (with or without immediate weightbearing) were better than those of arthroplasty beyond 6 months. What is the mortality rate? It was lower after nailing in a few studies but was mainly determined by the patient's comorbidities and preoperative Parker score. The best indication for arthroplasty may be self-sufficient patients over 70 years of age who have an unstable fracture with severe osteoporosis. Nevertheless, new studies should be done to compare arthroplasty to nailing with immediate return to weightbearing in patients having the same type of fracture, defined using 3D CT scan. Level of evidence: Expert advice (c) 2023 Elsevier Masson SAS. All rights reserved.
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TI IVD fibrosis and disc collapse comprehensively aggravate vertebral body disuse osteoporosis and zygapophyseal joint osteoarthritis by posteriorly shifting the load transmission pattern
SO COMPUTERS IN BIOLOGY AND MEDICINE
LA English
DT Article
DE Intervertebral disc fibrosis; Disuse osteoporosis; Disc collapse; Load transmission pattern; Numerical models
ID finite-element-analysis; end-plate; clinical-applications; calibration method; hounsfield units; lumbar spine; degeneration; model; epidemiology; accuracy
AB Background: Disuse is a typical phenotype of osteoporosis, but the underlying mechanism has yet to be identified in elderly patients. Disc collapse and intervertebral disc (IVD) fibrosis are two main pathological changes in IVD degeneration (IDD) progression, given that these changes affect load transmission patterns, which may lead to disuse osteoporosis of vertebral bodies and zygapophyseal joint (ZJ) osteoarthritis (ZJOA) biomechanically. Methods: Clinical data from 59 patients were collected retrospectively. Patient vertebral bony density, ZJOA grade, and disc collapse status were judged via CT. The IVD fibrosis grade was determined based on the FA measurements. Regression analyses identified

potential independent risk factors for osteoporosis and ZJOA. L4L5 numerical models with and without disc collapse and IVD fibrosis were constructed; stress distributions on the bony endplate (BEP) and zygapophyseal joint (ZJ) cartilages were computed in models with and without disc collapse and IVD fibrosis. Results: A significantly lower disc height ratio and significantly greater FA were recorded in patients with ZJOA. A significant correlation was observed between lower HU values and two parameters related to IDD progression. These factors were also proven to be independent risk factors for both osteoporosis and ZJOA. Correspondingly, compared to the intact model without IDD. Lower stress on vertebral bodies and greater stress on ZJOA can be simultaneously recorded in models of disc collapse and IVD fibrosis. Conclusions: IVD fibrosis and disc collapse simultaneously aggravate vertebral body disuse osteoporosis and ZJOA by posteriorly shifting the load transmission pattern.
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NR 66
TC 22
Z9 22
U1 0
U2 10
PU PERGAMON-ELSEVIER SCIENCE LTD
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WC Biology; Computer Science, Interdisciplinary Applications; Engineering, Biomedical; Mathematical & Computational Biology
SC Life Sciences & Biomedicine - Other Topics; Computer Science; Engineering; Mathematical & Computational Biology
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PT J
AU Zhang, W
Sun, D
Zhang, XL
Wu, G
AF Zhang, Wei
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Zhang, Xiaoli
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TI The Value of Computer Vision in Identifying the Bone of Dialysis Patients
SO CURRENT MEDICAL IMAGING
LA English
DT Article
DE Dialysis; Osteoporosis; Computer vision; Convolution neural networks; ResNet; Kidney disease
ID osteoporosis; management
AB Background: In the end stage of kidney disease, abnormal levels of blood calcium, phosphorus, and parathyroid hormone lead to bone metabolism disorders, manifesting as osteoporosis or fibrocystic osteoarthritis. X-ray, CT, and MR are useful for detecting bone lesions in dialysis patients, but currently, computer vision has not yet been used for this purpose. Methods: ResNet is a powerful deep CNN model, which has not yet been used to distinguish between the bones of dialysis patients and healthy people. Therefore, this study aimed to

investigate the ability of the Resnet50 model to identify the bone of dialysis patients from normal bone. Results: CT images of 200 cases (100 dialysis patients and 100 healthy people aged 31-72 years with male:female ratio of 51:49) were randomly divided into the training and testing groups at the ratio of 8:2. The module of 'torch' was used to train the model of Resnet50 for the current task of image classification. In the test cohort, the accuracy, sensitivity, and specificity with hyper-parameter=0 were 60%, 65%, and 55%, respectively. When the hyper-parameter was 0.6 or 0.7 versus 0, the accuracy was significantly higher ($P<0.05$). When the hyper-parameter was another number, the accuracy was not significantly different from that with no hyper-parameter ($P>0.05$). Conclusion: This study has indicated computer vision to be suitable for identifying bone changes caused by dialysis; a hyper-parameter has been found necessary for improving model accuracy. The ResNet50 model with hyper-parameter = 0.7 has exhibited 90% sensitivity in identifying the bone of dialysis patients.
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NR 24
TC 1
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SC Radiology, Nuclear Medicine & Medical Imaging
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UT WOS:001440462100001
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PT J
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TI Similarities and differences between European guidelines for the management of postmenopausal osteoporosis
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE European guidelines; Postmenopausal osteoporosis; Fracture risk
ID risk; denosumab; fracture
AB We conducted a review of 10 national guidelines from five EU countries to identify similarities or differences in recommendations for the management of patients with osteoporosis. We found general alignment of key recommendations; however, there are notable differences, largely attributed to country-specific approaches to risk assessment and reimbursement conditions. Introduction The classification of fracture risk is critical for informing treatment decisions for post-menopausal osteoporosis. The aim of this review was to summarise 10 national guidelines from five European countries, with a focus on identifying similarities or differences in recommendations for the management of patients with osteoporosis. Methods We summarised the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Disease-International Osteoporosis Foundation guidelines and reviewed guidelines from France, Germany, Italy, Spain and the UK. Results The approach to risk assessment differed across the guidelines. In France, and Spain, risk assessment was based on DXA scans and presence of prior fractures, whereas UK, German and Italian guidelines recommended use of a validated risk tool. These differences led to distinct definitions of very high and high-risk patients. Guidelines aligned in recommending antiresorptive and anabolic agents as pharmacologic options for the management of osteoporosis, with sequential treatment recommended. There was agreement that patients at high or very high risk of fracture or with severe osteoporosis should receive anabolic agents first, followed by antiresorptive drugs. Variations were identified in recommendations for follow up of patients on anti-osteoporosis therapies. Reimbursement conditions in each country were a key difference identified. Conclusions Criteria for risk assessment of fractures differ across European guidelines which may impact treatment and access to anabolic agents. Harmonisation across EU guidelines may help identify patients eligible for treatment and impact treatment uptake. However, country-specific reimbursement and prescribing processes may present a challenge to achieving a consistent approach across Europe.
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NR 33
TC 14
Z9 14
U1 3
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PU SPRINGER LONDON LTD
PI LONDON
PA 236 GRAYS INN RD, 6TH FLOOR, LONDON WC1X 8HL, ENGLAND
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WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
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TI Controlled mechanical loading affects the osteocyte transcriptome in porcine trabecular bone in situ
SO BONE
LA English
DT Article
DE Trabecular bone; Mechanobiology; Transcriptomics; Bioreactor; Organ culture
ID endothelial growth-factor; nf-kappa-b; differential gene; fluid-flow; rna; expression; strength; tnf; osteoblasts; adaptation
AB Introduction: Osteocytes modulate bone adaptation in response to mechanical stimuli imparted by the deforming bone tissue in which they are encased by communicating with osteoclasts and osteoblasts as well as other osteocytes in the lacuna-canalicular network through secreted cytokines and chemokines. Understanding the transcriptional response of osteocytes to mechanical stimulation in situ could identify new targets to inhibit bone loss or enhance bone formation in the presence of diseases like osteoporosis or metastatic cancer. We compared the mechanically regulated transcriptional response of osteocytes in trabecular bone following one or three days of controlled mechanical loading. Methods: Porcine trabecular bone explants were cultured in a bioreactor for 48 h and subsequently loaded twice a day for one day or 3 days. RNA was isolated and sequenced, and the Tuxedo suite was used to identify differentially expressed genes and pathway analysis was conducted using Ingenuity Pathway Analysis (IPA). Results: There were about 4000 differentially expressed genes following in situ culture relative to fresh bone. One hundred six genes were differentially expressed between the loaded and non-loaded groups following one day of loading compared to 913 genes after 3 d of loading. Only 45 of these were coincident between the two time points, indicating an evolving transcriptome. Clustering and principal component analysis indicated differences between the loaded and non-loaded groups after 3 d of loading. Discussion: With sustained loading, there was a nine-fold increase in the number of differentially expressed genes, suggesting that osteocytes respond to loading through sequential activation of downstream genes in the same pathways. The differentially expressed genes were related to osteoarthritis, osteocyte, and chondrocyte signaling pathways. We noted that NFkB and TNF signaling are affected by early loading and this may drive downstream effects on the mechanobiological response. Moreover, these genes may regulate catabolic effects of mechanical disuse through their actions on pre-osteoclasts in the bone marrow niche.
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TI Investigating mechanical and inflammatory pathological mechanisms in osteoarthritis using MSC-derived osteocyte-like cells in 3D
SO FRONTIERS IN ENDOCRINOLOGY

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DT Article
DE osteocyte; mechanical load; osteoarthritis; inflammation; 3D model; RNAseq analysis
ID excitatory amino-acids; bone-marrow lesions; glutamate receptors; synovial-fluids; tnf-alpha; knee pain; expression; interleukin-6; differentiation; association
AB Introduction Changes to bone physiology play a central role in the development of osteoarthritis with the mechanosensing osteocyte releasing factors that drive disease progression. This study developed a humanised in vitro model to detect osteocyte responses to either interleukin-6, a driver of degeneration and bone remodelling in animal and human joint injury, or mechanical loading, to mimic osteoarthritis stimuli in joints. Methods Human MSC cells (Y201) were differentiated in 3-dimensional type I collagen gels in osteogenic media and osteocyte phenotype assessed by RTqPCR and immunostaining. Gels were subjected to a single pathophysiological load or stimulated with interleukin-6 with unloaded or unstimulated cells as controls. RNA was extracted 1-hour post-load and assessed by RNAseq. Markers of pain, bone remodelling, and inflammation were quantified by RT-qPCR and ELISA. Results Y201 cells embedded within 3D collagen gels assumed dendritic morphology and expressed mature osteocytes markers. Mechanical loading of the osteocyte model regulated 7564 genes (Padj $p<0.05$, 3026 down, 4538 up). 93% of the osteocyte transcriptome signature was expressed in the model with 38% of these genes mechanically regulated. Mechanically loaded osteocytes regulated 26% of gene ontology pathways linked to OA pain, 40% reflecting bone remodelling and 27% representing inflammation. Load regulated genes associated with osteopetrosis, osteoporosis and osteoarthritis. 42% of effector genes in a genome-wide association study meta-analysis were mechanically regulated by osteocytes with 10 genes representing potential druggable targets. Interleukin-6 stimulation of osteocytes at concentrations reported in human synovial fluids from patients with OA or following knee injury, regulated similar readouts to mechanical loading including markers of pain, bone remodelling, and inflammation. Discussion We have developed a reproducible model of human osteocyte like cells that express >90% of the genes in the osteocyte transcriptome signature. Mechanical loading and inflammatory stimulation regulated genes and proteins implicated in osteoarthritis symptoms of pain as well as inflammation and degeneration underlying disease progression. Nearly half of the genes classified as 'effectors' in GWAS were mechanically regulated in this model. This model will be useful in identifying new mechanisms underlying bone and joint pathologies and testing drugs targeting those mechanisms.
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TI The role of WWP1 and WWP2 in bone/cartilage development and diseases
SO MOLECULAR AND CELLULAR BIOCHEMISTRY
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DT Review
DE WWP1; WWP2; Bone; Cartilage
ID regulates craniofacial development; c2 domain; bone; protein; expression; cancer; ubiquitination; proliferation; mir-140; pten
AB Bone and cartilage diseases are often associated with trauma and senescence, manifested as pain and limited mobility. The repair of bone and cartilage lesion by mesenchymal stem cells is regulated by various transcription factors. WW domain-containing protein 1 (WWP1) and WW domain-containing protein 2 (WWP2) are named for WW domain which recognizes PPXY (phono Ser Pro and Pro Arg) motifs of substrate. WWP1and WWP2 are prominent components of the homologous to the E6-AP carboxyl terminus (HECT) subfamily, a group of the ubiquitin ligase. Recently, some studies have found that WWP1 and WWP2 play an important role in the pathogenesis of bone and cartilage diseases and regulate the level and the transactivation of various transcription factors through ubiquitination. Therefore, this review summarizes the distribution and effects of WWP1 and WWP2 in the development of bone and cartilage, discusses the potential mechanism and therapeutic drugs in bone and cartilage diseases such as osteoarthritis, fracture, and osteoporosis.
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TI Pyroptosis in Skeleton Diseases: A Potential Therapeutic Target Based on

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SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
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DT Review
DE pyroptosis; inflammation; skeleton diseases; treatment; cell death
ID intervertebral disc degeneration; spinal-cord-injury; nlrp3 inflammasome; gasdermin-d; rheumatoid-arthritis; propionibacterium-acnes; metformin protects; caspase activation; aim2 inflammasome; pore formation
AB Skeletal disorders, including fractures, osteoporosis, osteoarthritis, rheumatoid arthritis, and spinal degenerative conditions, along with associated spinal cord injuries, significantly impair daily life and impose a substantial burden. Many of these conditions are notably linked to inflammation, with some classified as inflammatory diseases. Pyroptosis, a newly recognized form of inflammatory cell death, is primarily triggered by inflammasomes and executed by caspases, leading to inflammation and cell death through gasdermin proteins. Emerging research underscores the pivotal role of pyroptosis in skeletal disorders. This review explores the pyroptosis signaling pathways and their involvement in skeletal diseases, the modulation of pyroptosis by other signals in these conditions, and the current evidence supporting the therapeutic potential of targeting pyroptosis in treating skeletal disorders, aiming to offer novel insights for their management.
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TI Advancements in deep learning-based image screening for orthopedic conditions: Emphasis on osteoporosis, osteoarthritis, and bone tumors
SO AGEING RESEARCH REVIEWS
LA English
DT Review
DE Deep learning; Osteoporosis; Osteoarthritis; Bone tumor; Imaging screening
ID artificial-intelligence; spinal metastases; mineral density; prediction; classification; sacroiliitis; diagnosis; model
AB Artificial intelligence (AI) has garnered increasing attention in the medical field. As the core technology of AI, deep learning (DL) has been extensively applied to the imaging-based screening of orthopedic diseases, primarily including image classification, segmentation, and risk prediction. This review systematically summarizes recent research advances, methodologies, and clinical applications of AI-assisted diagnostic technologies in orthopedic imaging, highlighting the practical value and development trends of DL in this field. By retrieving literature published over the past five years in PubMed and the Web of Science Core Collection, this study emphasizes the application of DL-based techniques in the screening of orthopedic conditions, such as osteoarthritis (OA), osteoporosis (OP), and bone tumors. The results demonstrate that DL-based methods exhibit excellent diagnostic performance and considerable clinical potential. However, despite the rapid increase in research output, there are still several challenges in this field, including the lack of high-quality datasets, the limited cross-institutional generalizability of models, the absence of standardized quality control protocols, and the urgent demand for multicenter clinical validation. Overall, DL holds great promise for enhancing diagnostic accuracy and improving patient outcomes in

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TI Proximal tibial stress fracture in patients with advanced knee osteoarthritis: a narrative review
SO EFORT OPEN REVIEWS
LA English
DT Review
DE knee; osteoarthritis; stress fracture; total knee arthroplasty
ID arthritic knees; arthroplasty; management
AB In patients with knee osteoarthritis, tibial stress fractures are mostly associated with osteoporosis and lower limb malalignment. Nonoperative management may lead to knee stiffness (due to prolonged immobilization), persistence of pain (due to the underlying knee osteoarthritis), and fracture nonunion. Acute unstable tibial

stress fractures can be managed with long-stem total knee arthroplasty. Exposing the fracture site should be avoided as much as possible because it may be associated with skin necrosis and delayed union. In irreducible cases or fractures with persistent gaps, fibular osteotomy, by increasing the mobility and compression across the fracture site, may help with fracture reduction and decrease the rate of nonunion.
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TI Preoperative Osteoporosis Is Associated With Increased Health Care Utilization and Compromised Pain and Function Improvement After Primary Total Hip Arthroplasty: A Prospective Cohort Analysis
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE THA; osteoporosis; imaging; patient oriented outcomes; total hip arthroplasty
ID patient-reported outcm; acceptable symptom state; osteoarthritis; diagnosis; tha; responsiveness; replacement; management; fractures; index
AB Background: Osteoporosis (OP) has been linked to complications after total hip arthroplasty (THA), but its impact on health care utilization and patient-reported outcomes remains unclear. This study aimed to evaluate the association between: 1) pre-THA OP and health care utilization as well as patient-reported pain and function outcome measures; and 2) dual energy X-ray absorptiometry (DEXA) scan-based Tscores and the aforementioned outcomes. Methods: A retrospective analysis of prospectively collected data of primary THA (2015 to 2018) was performed (n 1/4 5,321) from a validated academic institutional database of a large North American tertiary health care system; of which 4,074 (76.6%) completed 1-year follow-up. Outcomes included prolonged length of stay [LOS] > three days, discharge disposition, 90-day readmission, and 1-year reoperation, as well as Hip Disability and Osteoarthritis Outcome Score (HOOS]) Pain, HOOS-function (PS), and minimal clinically important difference thresholds (MCID), and satisfaction. Results: The prevalence of OP pre-THA was 56.9%, of which 39.8% were not prescribed OP medications and 15.3% had a DEXA scan. Compared to those who did not have OP, those who had OP were independently associated with higher odds of prolonged LOS, nonhome discharge, 90-day readmission, and 1-year reoperation ($P < 0.005$). Furthermore, they had significantly higher odds of failing to achieve MCID (odds ratio: 1.41 (95% confidence interval: 1.06 to 1.89)) for HOOS-PS and satisfaction (odds ratio: 1.5 (95% confidence interval: 1.16 to 1.93)) at one year. Higher T-scores were associated with lower odds of prolonged LOS, nonhome discharge, failure to achieve MCID in HOOS-Pain, and HOOS-PS. Conclusions: Over half of patients had OP; however, only 15.3% of patients had a DEXA scan before THA. Patients who had OP were at higher risk of prolonged LOS, nonhome discharge, 90-day readmission, and 1-year reoperation in addition to poor pain/function improvement and dissatisfaction one year after THA. (c) 2024 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

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AU Shinohara, I
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TI Pathophysiology of the Effects of Oxidative Stress on the Skeletal System
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English

DT Review
DE osteoarthritis; osteonecrosis; osteoporosis; oxidative stress; reactive oxidative species
ID induced apoptosis; osteonecrosis; inflammation; osteoarthritis; inhibition; activation; cells
AB Reactive oxygen species (ROS) are molecules that are generated primarily during energy production in cells. ROS are involved in critical biological functions such as signal transduction; when the production of ROS is imbalanced, excessive ROS causes oxidative stress, and subsequent cellular damage. Oxidative stress is linked to numerous pathological disorders in major organs including the skeletal system. In an aging society, understanding the role of ROS in skeletal health is critical to developing preventative and therapeutic interventions. Oxidative stress causes defects in cellular differentiation, apoptosis, mitochondrial dysfunction, and inflammation. The effects of oxidative stress on the skeletal system have been implicated in the development of osteoporosis, knee osteoarthritis, and osteonecrosis by inhibiting bone remodeling, increasing osteoclast activity, and decreasing osteoblast function. ROS are also involved in many signaling pathways that regulate immune defense, cell proliferation, and inflammation. This underscores the importance of maintaining a balance between ROS and antioxidants to prevent oxidative stress and related diseases. Targeting ROS and oxidative stress mechanisms may offer new treatments for diseases affecting the skeletal system and other organs, potentially improving health outcomes, and extending healthy lifespans. This review highlights the significant impact of oxidative stress on skeletal health and explores potential preventative and therapeutic strategies to mitigate the adverse effects of ROS.
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SO INFLAMMOPHARMACOLOGY
LA English
DT Article
DE Statin; Osteoporosis; Osteoarthritis; Mendelian randomization; Causality
ID mendelian randomization; mechanisms; instruments; population; expression; diagnosis; bias
AB BackgroundObservational studies suggest that statins may be protective against osteoporosis and osteoarthritis. However, the association between statins and the risk of osteoporosis and osteoarthritis has not been fully clarified.ObjectiveThe association between statins and the risk of osteoporosis and osteoarthritis was explored by Mendelian randomization analyses using pooled data from a large population-based genome-wide association study (GWAS).MethodsData on statin-associated single-nucleotide polymorphisms were obtained from version 10 of the FinnGen database, while information regarding osteoporosis and osteoarthritis was sourced from IEU Open GWAS and UK Biobank, database. The primary analytical method employed was inverse variance weighting to assess causal effects. Additional methods including weighted median, simple median, weighted mode, and MR-Egger regression were utilized for further clarification. Odds ratios along with 95% confidence intervals were calculated to evaluate the causal relationship between statins and the risks associated with osteoarthritis and osteoporosis. Subsequently, sensitivity analyses were conducted to verify result reliability by employing Cochran's Q test for heterogeneity assessment, MR-Egger intercept for detecting horizontal pleiotropy presence, as well as leave-one-out analysis to identify potentially influential single nucleotide polymorphisms.Results(1) The results of the inverse variance weighting method showed a negative causal relationship between genetically predicted statins and osteoporosis (OR = 0.998, 95% CI 0.996-0.999, P = 0.01) risk; and a negative causal relationship between statins and osteoarthritis (OR = 0.974, 95% CI 0.951-0.998, P = 0.037) risk; (2) MR-Egger-intercept analysis did not detect potential horizontal

pleiotropy (osteoporosis: P = 0.848; osteoarthritis: P = 0.483); and (3) the findings provide favorable evidence that statins reduce the risk of osteoporosis and osteoarthritis as described in the observational study, but further research is needed on the specific mechanisms of statins for osteoporosis and osteoarthritis.ConclusionStatins reduce the risk of osteoporosis and osteoarthritis, which is consistent with the results of observational studies. Further studies are essential to validate these results and explore the underlying mechanisms in detail.
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J9 INFLAMMOPHARMACOLOGY
JI Inflammopharmacology
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PY 2025
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IS 8
BP 4659
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EA JUL 2025
PG 11
WC Immunology; Pharmacology & Pharmacy; Toxicology
SC Immunology; Pharmacology & Pharmacy; Toxicology
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PT J
AU Wang, JT
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AF Wang, Junting
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TI Mechanical robust, pH responsive hemicellulose-based PVA film with barrier performance for fruit preservation and monitoring
SO FOOD CHEMISTRY
LA English
DT Article
DE Barrier film; PVA; Fruit preservation; Hemicellulose; Blueberry anthocyanins
ID antibacterial activity; anthocyanins; cellulose; nmr
AB Barrier films are essential for food packaging, but conventional solutions hinder the circular economy. This study introduces hemicellulose-based antioxidant crosslinked composite films as a sustainable alternative. We develop pH-responsive films (K-B/PVA/OA) using polyvinyl alcohol (PVA), silanized hemicellulose (KHC), blueberry anthocyanin (BA) as a pH indicator, and oxalic acid (OA) as a crosslinker. The films exhibit excellent oxygen and water vapor barrier properties and can be easily fabricated via solution casting with food-safe dispersions. The oxygen permeability (OP) decreases from 13.22 f 0.65 x 10-14 to 3.24 f 0.98 x 10- 14 cm3 center dot mu m/(m2 center dot d center dot Pa), and the water vapor permeability coefficient (Pv) drops from 15.43 f 0.85 x 10-13 to 7.27 f 0.46 x 10-13 g center dot cm/ (cm2 center dot s center dot Pa). Tensile strength and modulus increase from 32.63 MPa and 765.80 MPa to 41.24 MPa and 1281.39 MPa. Esterification between PVA and hemicellulose raises surface energy, increasing the contact angle from 39.4 degrees to 78.34 degrees. Strawberries packaged in these films maintain their structure and exhibit a visible color change after 7 days, offering sustainable, real-time monitoring packaging.
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PA 125 London Wall, London, ENGLAND
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J9 FOOD CHEM
JI Food Chem.
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VL 481
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DI 10.1016/j.foodchem.2025.144028
EA APR 2025
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WC Chemistry, Applied; Food Science & Technology; Nutrition & Dietetics
SC Chemistry; Food Science & Technology; Nutrition & Dietetics
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AU Zhou, J
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AF Zhou, Jian
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Dong, Yanan
Liu, Ziyu
Fan, Yubo
TI Personalized Design of 3D-Printed Osteochondral Scaffold for Osteoarthritis Patients with Different Bone Conditions and Mechanical Evaluation
SO BIOENGINEERING-BASEL
LA English
DT Article
DE scaffold structure; 3D printing; knee joint bioreactor; mechanical simulation; osteoarthritis
AB As osteoarthritis is a common disease in elderly people and large cartilage defects can only be treated by joint replacement surgery, a scaffold is seen as a potential treatment that could help patients to delay or avoid surgery. An ideal scaffold should have similar properties to the surrounding tissues. Thus, for different levels of OA, patients with different bone properties should use different scaffold structures with different mechanical or biological properties. In this paper five structures (A-E) are designed for young OA patients or patients with good bone mechanical properties, middle-age OA patients with weak bone mechanical properties or patients with little osteoporosis, and elderly OA patients who have severer OA and osteoporosis who are not able to perform normal activities. And these five scaffold structures are 3D-printed by an EOS machine with Ti6Al4V powder and evaluated by experiments based on a biomechanical bioreactor simulating the human knee joint and simulation through ANSYS. Structure D with a solid thick beam in the middle has the highest loading force, which is 3707.835 N, and structure E, composed of the polyhedron with the highest specific surface area, has the lowest loading force, which is 1837.402 N. Structures A, B, and C are intended for young OA patients or patients with good bone mechanical properties. Structures D and E are designed for patients who need to avoid or delay joint replacement surgery.
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PY 2025
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PT J
AU Shao, CW
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Liu, Tingting
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TI The Hippo pathway in bone and cartilage: implications for development and disease
SO PEERJ
LA English
DT Article
DE Hippo; Bone; RANKL; Yes; TAZ
ID signaling pathway; cell-proliferation; regulating osteoclast; rheumatoid-arthritis; global burden; osteosarcoma; yap/taz; yap1; osteoarthritis; osteoporosis
AB Bone is the main structure of the human body; it mainly plays a supporting role and participates in metabolic processes. The Hippo signaling pathway is composed of a series of protein kinases, including the mammalian STE20-like kinase MST1/2 and the large tumor suppressor LATS1/2, which are widely involved in pathophysiological processes, including cell proliferation, differentiation, apoptosis and death, especially those related to biomechanical transduction in vivo. However, the role of it in regulating skeletal system development and the evolution of bone-related diseases remains poorly understood. The pathway can intervene in and regulate the physiological activities of bone-related cells such as osteoclasts and chondrocytes through its own or other bone-related signaling pathways, such as the Wnt pathway, the Notch pathway, and receptor activator of nuclear factor-kappa B ligand (RANKL), thereby affecting the occurrence and development of bone diseases. This article discusses the role of the Hippo signaling pathway in bone development and disease to provide new insights into the treatment of bone-related diseases by targeting the Hippo signaling pathway.
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TI pH-dependent Osteoimmunomodulation: Molecular mechanisms and therapeutic targeting in bone disorders
SO PHARMACOLOGICAL RESEARCH
LA English
DT Article
DE Bone microenvironment; Osteoimmunology; Acid-base balance; Bone homeostasis; Immune cells; Therapeutic strategies
ID v-h+-atpase; in-vitro; slc4a2-mediated cl-/hco3; selective inhibitor; acid; nanoparticles; exchange; cells; differentiation; methotrexate
AB The bone microenvironment represents a highly sophisticated ecosystem comprising diverse cellular components-including osteoblasts, osteoclasts, immune cells, endothelial cells, and mesenchymal stem cells-that interact dynamically to maintain skeletal homeostasis and facilitate repair. Emerging insights from osteoimmunology have revealed that acid-base balance serves as a central regulatory node in bone remodeling, working synergistically with other physiological signals to fine-tune osteoclast/osteoblast activity through intricate molecular crosstalk. Notably, even subtle pH fluctuations within this microenvironment can exert profound effects on both bone and immune cell function. This review provides a comprehensive examination of: (1) the physiological principles governing acid-base balance in bone, (2) the pathological consequences of its dysregulation on bone remodeling via osteoimmune networks, and (3) the therapeutic promise of pH-modulating strategies for bone disorders such as osteoporosis and osteoarthritis. Our synthesis positions bone as a precision

acid-base regulatory organ while establishing a mechanistic framework for developing targeted therapies that restore pH equilibrium in skeletal tissues.
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Tanaka, Sakae
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TI Investigation of brain volume changes associated with aging: Results from the fourth research on osteoarthritis/osteoporosis against disability survey
SO GERIATRICS & GERONTOLOGY INTERNATIONAL
LA English
DT Article
DE aging; brain volume; gray matter volume; magnetic resonance imaging; voxel-based morphometry
ID functional connectivity; alzheimers-disease; sex-differences; amygdala; age; morphometry; adults; hippocampus; somatotopy; movement
AB AimThis study aims to investigate the impact of aging on brain volume among community residents in Japan, focusing on trends over time and specific brain structures.MethodsWe analyzed data from the fourth survey (2015-2016) of the Research on Osteoarthritis/Osteoporosis Against Disability project, encompassing 2146 community residents from Japan's mountainous and coastal regions. A total of 1755 participants (81.8% of the baseline population) underwent extensive data collection including lifestyle and health questionnaires, anthropometric measurements and brain magnetic resonance imaging. The imaging data were

processed to examine correlations between total brain volume, gray matter volume (GMV), white matter volume (WMV), cerebrospinal fluid volume and participant age.ResultsAnalysis showed significant sex differences in total brain volume, with GMV demonstrating a strong negative correlation with age - more pronounced than the moderate negative correlation seen in WMV. Cerebrospinal fluid volume exhibited a strong positive correlation with age. Notably, specific brain regions such as the bilateral amygdala, hippocampus, thalamus and primary motor cortex showed significant age-related volume reductions.ConclusionThis study confirms that GMV and WMV are smaller in older individuals in the Japanese population, with more pronounced differences in GMV. The amygdala, hippocampus, thalamus and primary motor cortex were particularly affected. Geriatr Gerontol Int 2025; center dot center dot: center dot center dot-center dot center dot.
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NR 45
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WC Geriatrics & Gerontology; Gerontology
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TI Liver injury severity determines skeletal deterioration: a shared pathophysiological axis between MASLD and osteoarthritis
SO GEROSCIENCE
LA English
DT Article
DE MASH; Fibrosis; Osteoarthritis; Osteoporosis
ID articular chondrocytes; synovial inflammation; gene-regulation; diet; fructose; resistin; disease; nash
AB Nonalcoholic fatty liver disease (NAFLD) and metabolic syndrome (MetS) have been linked to osteoporosis and osteoarthritis (OA), where the prevalence of all increase with age. Many individuals with NAFLD also exhibit MetS, a condition that is now termed metabolic dysfunction-associated steatotic liver disease (MASLD). MASLD spans from simple hepatic steatosis to hepatocyte ballooning and inflammation, termed metabolic dysfunction-associated steatohepatitis (MASH), which may occur with or without fibrosis. To delineate the contribution of liver injury to skeletal deterioration within the context of metabolic syndrome (MetS), we fed male mice a high-fat, cholesterol, and fructose (HFCF) diet that induces metabolic syndrome-associated steatohepatitis (MASH) and liver fibrosis, associated with moderate obesity but without profound insulin resistance. A nutrient-matched diet with high carbohydrates but low in fat, cholesterol, and fructose (LFCF), which induced steatosis in adult mice, served as the control. Micro-CT analysis of the femur of HFCF-fed mice that developed MASH with fibrosis revealed significant cortical thinning (reduced bone area and thickness),

decreased trabecular thickness, and lower bone mineral density compared to LFCF-fed mice, with no liver fibrosis. In the knee joint, MASH with fibrosis was associated with subchondral bone loss, medial cartilage erosion, and elevated chondrocyte expression of iNOS, NLRP3, and beta-galactosidase. Bulk RNA-seq of knee tissue identified 152 differentially expressed genes: interferon-related (Oas3, Nlrc5, Zbp1) and stress-response (Slc6a4, Alox12, Cirbp, Trpc6, Tap1, Ubash3, Nrg1) pathways were upregulated, while extracellular matrix organization pathways were downregulated. Our findings reveal a mechanistic connection between the degree of liver injury and deterioration of bone and joint integrity, pointing to a shared pathophysiological axis in MASLD and OA. Clinically, this raises the prospect that a single therapeutic, designed to modulate inflammation, or hepatic lipid metabolism, could be repurposed or developed to concurrently treat both steatohepatitis and osteoarthritic degeneration.
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NR 66
TC 1
Z9 1
U1 6
U2 6
PU SPRINGER
PI DORDRECHT
PA VAN GODEWIJCKSTRAAT 30, 3311 GZ DORDRECHT, NETHERLANDS
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
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PT J
AU Yang, MY
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TI Genetic causality between insomnia and specific orthopedic conditions: Insights from a two-sample Mendelian randomization study
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Article
DE Insomnia; rheumatoid arthritis; Ankylosing spondylitis; Osteoporosis; Gout; Genetic

ID necrosis-factor-alpha; ankylosing-spondylitis; risk-factors; sleep; osteoporosis; prevalence; gout; osteoarthritis; frailty; epidemiology
AB Objective: To investigate the genetic causality for the insomnia and common orthopedic diseases, such as rheumatoid arthritis (RA), ankylosing spondylitis (AS), osteoporosis (OP), and gout (GT). Methods: The genome-wide association study (GWAS) summary data on insomnia were obtained from a published study, while the GWAS summary data on RA, AS, OP, and GT were sourced from the FinnGen consortium. We utilized the TwoSampleMR package of the R software (version 4.1.2) to conduct a two-sample Mendelian randomization (MR) analysis. Our primary method of analysis was the random-effects inverse variance weighted (IVW) approach. Subsequently, we conducted a series of sensitivity analyses for the MR analysis. Results: The MR analysis revealed a positive genetic causal relationship between insomnia and RA (P = 0.016, odds ratio [OR] 95 % confidence interval [CI] = 1.112 [1.020-1.212]). However, no significant genetic causal relationship was observed between insomnia and AS (P = 0.194, OR 95 % CI = 1.121 [0.944-1.331]), OP (P = 0.788, OR 95 % CI = 1.016 [0.904-1.142]), and GT (P = 0.757, OR 95 % CI = 1.018 [0.912-1.136]). The MR analysis did not exhibit heterogeneity, horizontal pleiotropy, outlier effects, or dependence on a single SNP, and demonstrated normal distribution, which guaranteed the robustness of the results. Conclusion: The results of this study suggest that insomnia may be a significant risk factor for RA, and controlling insomnia may represent a promising strategy for preventing RA. While insomnia was not observed to be associated with AS, OP, and GT at the genetic level, other levels of association cannot be excluded.
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NR 81
TC 0
Z9 0
U1 1
U2 3
PU PERGAMON-ELSEVIER SCIENCE LTD
PI OXFORD
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J9 EXP GERONTOL
JI Exp. Gerontol.
PD FEB 15
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IS
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DI 10.1016/j.exger.2025.112682
EA JAN 2025
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA S5N5S
UT WOS:001398687200001
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PT J
AU Li, JC
Huang, WS
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Sun, W
AF Li, Jia-Chen

Huang, Wei-Sheng
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Sun, Wei
TI Assessing causality between mitochondrial-associated proteins with musculoskeletal diseases: A Mendelian randomization study
SO MEDICINE
LA English
DT Article
DE ankylosing spondylitis; Mendelian randomization; mitochondria; musculoskeletal disease; osteoarthritis; osteoporosis; rheumatoid arthritis
ID variance weighted estimator; transporter family slc25; identification; dysfunction; robust; genes
AB Musculoskeletal diseases are the leading cause of disability-adjusted life years. Mitochondria, often referred to as the "powerhouses" of cells, are believed to play a role in regulating cellular metabolism and differentiation, potentially influencing the occurrence and progression of musculoskeletal diseases. However, the exact causal relationships remain to be defined. This study aimed to investigate the causal relationships between mitochondrial biological functions and musculoskeletal diseases (including osteoarthritis (OA), osteoporosis, rheumatoid arthritis (RA), and ankylosing spondylitis through Mendelian randomization (MR) analysis). We systematically summarized data related to mitochondrial functional proteins and musculoskeletal diseases from the IEU OpenGWAS and UK Biobank databases. We used single nucleotide polymorphisms significantly associated with musculoskeletal diseases as instrumental variables. The inverse variance weighting method performed the main MR analysis. We used Mendelian randomized residual sum of pleiotropy and outliers, MR-Egger regression, Cochran Q statistic, Rucker Q statistic, Radial-MR, weighted median, simple mode, weighted mode, and leave-one-out analysis methods as supplementary analyses. First, 14 positive mitochondrial functional proteins were screened out. After Bonferroni correction, COA3 and COX4I2 were found to be causally related to OA and act as protective factors. We identified a causal relationship between SLC25A18 and RA as a risk factor. This study provides genetic support and offers new evidence regarding the roles of COA3, COX4I2, and SLC25A18 in the pathophysiology of OA and RA. This study paves the way for a deeper understanding of the pathological mechanisms of musculoskeletal diseases and provides information for their prevention strategies and treatments.
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NR 58
TC 1
Z9 1
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U2 8
PU LIPPINCOTT WILLIAMS & WILKINS
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JI Medicine (Baltimore)
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WC Medicine, General & Internal
SC General & Internal Medicine
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PT J
AU Leal, AF
Pachajoa, H
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AF Leal, Andres Felipe
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Tomatsu, Shunji
TI Mesenchymal Stem Cell-Derived Extracellular Vesicles: Seeking into Cell-Free Therapies for Bone-Affected Lysosomal Storage Disorders
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE extracellular vesicles; lysosomal storage disorders; mesenchymal stem cells; microenvironment
ID mucopolysaccharidosis type-i; enzyme replacement therapy; gene-therapy; ex-vivo; exosm; mouse; promote; growth; transplantation; osteogenesis
AB Lysosomal storage disorders (LSDs) constitute a group of monogenic systemic diseases resulting from deficiencies in specific lysosomal enzymes that cause the intralysosomal accumulation of non- or partially degraded substrates, leading to lysosomal dysfunction. In some cases of LSDs, the bone is more severely affected, thus producing skeletal manifestations in patients. Current therapies, such as enzyme replacement therapy (ERT) and gene therapy (GT), show limited efficacy in correcting skeletal abnormalities. Increasing evidence suggests that microenvironmental disturbances also contribute significantly to disease pathogenesis. Therefore, therapeutic strategies targeting lysosomal dysfunction and microenvironmental dysregulation are needed. Mesenchymal stem-cell-derived extracellular vesicles (MSC-EVs) are emerging as promising candidates in regenerative medicine due to their immunomodulatory, pro-regenerative, and paracrine properties. MSC-EVs have shown potential to

modulate the microenvironment and favor tissue repair in bone-related disorders such as osteoarthritis and osteoporosis. Interestingly, MSC-EVs can be engineered to reach the bone and carry therapeutics, including ERT- and GT-related molecules, enabling targeted delivery to hard-to-reach bone regions. This review describes the main features of MSC-EVs and discusses the therapeutic potential of MSC-EVs as a potential cell-free strategy for bone-affected LSDs.
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TI High Prevalence of Osteopenia and Osteoporosis in Total Hip and Total Knee Arthroplasty Patients and Effects of Anti-Resorptive Agents on Bone Health Optimization: A Systematic Review and Meta-Analysis

SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Review
DE arthroplasty; bone health optimization; osteoporosis; periprosthetic fracture; revision surgery
ID prior fragility fractures; mineral density loss; periprosthetic fractures; bisphosphonate use; risk; replacement; alendronate; revision; association; therapy
AB Background: Osteoarthritis is a leading cause of chronic pain and long-term disability in adults, which commonly affects the hip and knee joints. Joint arthroplasties are one of the management strategies for end-stage osteoarthritis. Periprosthetic fractures after hip or knee arthroplasties have mortality rates comparable to hip fractures. Recent studies assessed bone health optimization and the use of anti-osteoporotic agents in elective hip and knee arthroplasty surgeries. This systematic review and meta-analysis aimed to determine the prevalence of osteoporosis before surgery and the effect of bone health optimization on periprosthetic fractures and revisions. Methods: A systematic search was carried out on three databases, including PubMed, Embase, and Web of Science. The keywords used were (Revision or Periprosthetic fracture) AND (osteop*) and (Total Knee* or Total Hip*). Studies that included subjects aged >50 years with investigated outcomes were included in the review. The quality of selected randomized controlled trials was assessed using the Cochrane Collaboration tool, and non-randomized studies were assessed using the Newcastle-Ottawa Scale. The review was not registered with the International Prospective Register of Systematic Reviews (PROSPERO). Results: A total of 2482 records were identified. Twenty-three studies were included, and eighteen were used for quantitative analysis. Pooled overall prevalence of osteopenia in patients undergoing total knee arthroplasty (TKA)/total hip arthroplasty (THA) surgery was 42.87% (95% confidence interval (CI) 32.65 to 53.09). Pooled overall prevalence of osteoporosis in patients undergoing TKA/THA surgery was 23.99% (95% CI 15.72 to 32.26). The overall mean difference was in favor of anti-resorptive treatment on periprosthetic BMD of the medial calcar region (Gruen zone 7) after THA (12.16% (95% CI 8.78 to 15.53, $p < 0.00001$). Pooled odds ratio of periprosthetic fracture was 1.27 (95% CI 1.08 to 1.48, $p = 0.003$) in favor of the control group compared to bisphosphonate treatment. The pooled hazard ratio for all-cause revisions after TKA/THA for both osteopenia and osteoporotic patients was 0.26 (95% CI 0.13 to 0.51, $p = 0.0001$, I-2 76%), signifying an improvement with bisphosphonates. Limitations of this study include the heterogeneity and retrospective nature of the included studies, with the average level of evidence subject to bias. Conclusions: There was a high prevalence of osteopenia/osteoporosis amongst patients undergoing total knee and total hip arthroplasty at 66.86%. Whilst bone health optimization with bisphosphonates may decrease the risk of revisions, the risk of periprosthetic fracture appeared to increase. Further research will be required to evaluate the effects of bone health optimization on the risk of periprosthetic fracture and revisions, and the effects of anabolic agents on periprosthetic fractures.

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TI From Development, Disease, and Decline: A Review of What Defines an Osteoclast Progenitor
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE RANKL; RANK; M-CSF; CSF1; CSF1R; bone remodeling; osteoporosis; surface marker; osteomorph; osteomac; bone healing; fracture; periodontitis; arthritis

ID bone-marrow-transplantation; necrosis-factor-alpha; receptor activator; titanium implants; peripheral-blood; suppressor-cells; dendritic cells; tissue-response; precursor cells; hip-fractures
AB Our understanding of the different developmental origins of osteoclast progenitors and their respective roles during homeostatic bone remodeling at different skeletal sites as well as their roles within bone regeneration and degenerative conditions is evolving. In this narrative review article, we summarize what is known about the developmental origins, anatomical sources, and markers of osteoclast progenitors. We touch on how osteoclast progenitors vary during different disease contexts, including periodontitis, rheumatoid arthritis, and osteoarthritis. In addition, we also characterize osteoclast progenitors that contribute to bone healing and define changes observed with advancing age. In this regard, we offer a critical review of gaps within our understanding and opportunities for future development within the field. Because of their diverse nature under different contexts, identifying and characterizing osteoclast progenitors may help to advance condition-specific therapies.
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TI Rheumatoid arthritis and subsequent fracture risk: an individual person meta-analysis to update FRAX
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DE Epidemiology; Fracture risk; FRAX; Glucocorticoids; Hip fracture; Major osteoporotic fracture; Meta-analysis; Osteoporosis; Rheumatoid arthritis; Risk factors
ID modifying antirheumatic drugs; bone-mineral density; osteoporosis; prediction; women; score
AB The relationship between rheumatoid arthritis (RA) and fracture risk was estimated in an international meta-analysis of individual-level data from 29 prospective cohorts. RA was associated with an increased fracture risk in men and women, and these data will be used to update FRAX (R). Introduction RA is a well-documented risk factor for subsequent fracture that is incorporated into the FRAX algorithm. The aim of this study was to evaluate, in an international meta-analysis, the association between rheumatoid arthritis and subsequent fracture risk and its relation to sex, age, duration of follow-up, and bone mineral density (BMD) with a view to updating FRAX. Methods The resource comprised 1,909,896 men and women, aged 20-116 years, from 29 prospective cohorts in which the prevalence of RA was 3% or less (primary analysis) and an additional 17 cohorts with a prevalence greater than 3% (supplementary analysis). The association between RA and fracture risk (any clinical fracture, osteoporotic fracture, major osteoporotic fracture (MOF), and hip fracture) was examined using an extension of the Poisson regression model in each cohort and each sex, followed by random-effects meta-analyses of the weighted beta coefficients. Results In the primary analysis, RA was reported in 1.3% of individuals. During 15,683,133 person-years of follow-up, 139,002 fractures occurred, of which 27,518 were hip fractures. RA was associated with an increased risk of any clinical fracture (hazard ratio [HR] 1.49, 95% confidence interval [CI] 1.35-1.65). The HRs were of similar magnitude for osteoporotic fracture and MOF but higher for hip fracture

(HR=2.23; 95% CI 1.85-2.69). For hip fracture, there was a significant interaction with age with higher HRs at younger ages. HRs did not differ between men and women and were independent of exposure to glucocorticoids and femoral neck BMD. Lower HRs were observed in the supplementary analysis cohorts, particularly in those with a high apparent prevalence of RA, possibly from conflation of RA with osteoarthritis. Conclusions A diagnosis of RA confers an increased risk of fracture that is largely independent of BMD, sex, and corticosteroids. RA should be retained as a risk factor in future iterations of FRAX with updated risk functions to improve fracture risk prediction.

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TI More severe microdamage and micromechanical alterations: altered subchondral bone remodeling in varus knee osteoarthritis with osteoporosis
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Bone remodeling; Knee osteoarthritis; Osteoporosis; Subchondral bone; Tibial varus
ID cancellous bone; mineral density; postmenopausal women; articular-cartilage; axial alignment; lower-extremity; microarchitecture; microcracks; morphology; damage
AB Previous studies show osteoporosis causes tibial varus in knee osteoarthritis patients. Our analysis of tibial plateau specimens from osteoarthritic patients reveals that osteoporosis accelerates the deterioration of the subchondral microstructure of the tibial plateau, exacerbating tibial varus. Introduction The relationship between osteoporosis (OP) and knee osteoarthritis (OA) has garnered

significant clinical interest, particularly regarding the prevelence of tibial varus in patients suffering from both conditions. This study aimed to elucidate the association between OP and knee OA by examining bone remodeling and microstructural parameters of cartilage and subchondral bone. Methods We analyzed tibial plateau specimens from 50 patients, with 25 in the OA group and 25 in the OP-OA group. These specimens were further categorized into four subgroups: OA medial plateau, OA lateral plateau, OP-OA medial plateau, and OP-OA lateral plateau. Comprehensive analyses, including cartilage histology, micro-CT, immunohistochemical techniques, basic fuchsin histological analysis, and micro-finite elements, revealed significant microstructural differences and aberrant bone remodeling processes between the groups. Results The OARSI cartilage score of the medial tibial plateau was 13.71% higher in the OP-OA group compared to the OA group ($P < 0.05$), indicating more severe cartilage degeneration. Micro-CT analysis revealed a lower BV/TV in the subchondral bone of the medial tibial plateau in the OP-OA group (0.58 +/- 0.02) compared to the OA group (0.68 +/- 0.02) ($P < 0.05$). Additionally, significant decreases were observed in Tb.N and Tb.Th, while Tb.Sp and SMI increased. The number of osteoblasts in the subchondral bone of the medial tibial plateau was lower in the OP-OA group than in the OA group, while the number of osteoclasts was 55.90% higher ($P < 0.05$). Result of basic fuchsin staining showed that the CrDn in the subchondral bone of the medial tibial plateau was 69.01% higher in the OP-OA group ($P < 0.05$), with greater microdamage severity. Micro-finite element analysis showed that subchondral bone stresses in the OP-OA group were higher and more localized to the medial side compared to the OA group. Conclusions Our findings indicate that osteoporosis significantly intensifies cartilage degeneration in the medial tibial plateau of patients with knee osteoarthritis. It aggravates aberrant subchondral bone remodeling, increases microdamage, impairs mechanical structure, and accelerates tibial varus.
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TI Influence of Comorbidities on Health-Related Quality of Life in Alcohol-Related Liver Disease: A Population-Based Survey
SO CLINICAL GASTROENTEROLOGY AND HEPATOLOGY
LA English
DT Article
DE Health-Related Quality Of Life; Alcohol-Related Liver Disease; Cirrhosis; Comorbidities; Patient-Reported Outcomes
AB BACKGROUND AND AIMS: Extrahepatic comorbidities are common in alcohol-related liver disease (ALD). We examined associations between burden of comorbidities, alcohol, and smoking with low health-related quality of life (HRQoL) among patients with ALD. METHODS: Patients with ALD and matched comparators were identified among respondents of the Danish National Health Survey waves in 2010-2017. Survey data included generic measures of physical and mental HRQoL (12-Item Short Form Health Survey), comorbidities, alcohol and smoking. Low HRQoL in ALD was defined as >= 1.5 SD worse than the average HRQoL in the comparators. Odds ratios (ORs) of low HRQoL were estimated with multivariable logistic regression, adjusting for potential confounders. RESULTS: We included 772 ALD patients, 53% of whom had cirrhosis; 37% had low physical HRQoL and 22% had low mental HRQoL. Disc herniation (found in 21%), osteoarthritis (36%), chronic obstructive pulmonary disease (11%), cancer (6%), stroke (1%), and psychiatric disease (9%) were associated with low physical and/or mental HRQoL, whereas alcohol use disorder (24%), diabetes (19%), acute myocardial infarction (1%), hypertension (34%), and osteoporosis (12%) were not. For example, osteoarthritis was associated with low physical (OR, 2.17; 95% confidence interval, 1.54-3.05) and low mental (OR, 1.91; 95% confidence interval, 1.27-2.88) HRQoL. For lifestyle factors, drinking >= 20 units/week was associated with low physical and smoking >= 20 cigarettes/day with low mental HRQoL when compared with abstainers and nonsmokers, respectively. CONCLUSIONS: Common comorbidities including chronic obstructive pulmonary disease, musculoskeletal disease, and psychiatric disease are associated with low HRQoL in ALD, independent of liver

disease severity, and so are alcohol consumption and smoking. These findings highlight the importance of multidisciplinary management of patients with ALD.
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TI Treatment with a superoxide dismutase mimetic for joint preservation during 35 and 75 days in orbit aboard the international space station, and after 120 days recovery on Earth
SO LIFE SCIENCES IN SPACE RESEARCH
LA English
DT Article
DE International space station; Rodent spaceflight; Osteoarthritis; Osteoporosis; Antioxidant; Countermeasure
ID cartilage atrophy; down-regulation; osteoarthritis; progression; stress; antioxidants; knees
AB Reduced weight-bearing during spaceflight has been associated with musculoskeletal degradation that risks astronaut health and performance in transit and upon reaching deep space destinations. Previous rodent experiments aboard the international space station (ISS) have identified that the spaceflight-induced

molecular arthritic phenotype was characterized with an increase in oxidative stress. This study evaluated if treatment with a superoxide dismutase (SOD) mimetic on orbit could prevent spaceflight-induced damage to the knee and hip articular cartilage, and the menisci in rodents. Cartilage and meniscal degradation in mice were measured via microCT, histology, and transcriptomics after: (1) similar to 35 days on the ISS, (2) similar to 35 days on the ISS followed by 120 days weight-bearing readaptation on Earth or (3) similar to 75 days on the ISS. The study had a limited sample size, so both significant effects and generalized patterns are reported. After 35 days aboard the ISS, cartilage volume at the tibial-femoral cartilage-cartilage contact point decreased, meniscal volume decreased concurrent with an increase in pro-osteoarthritic signaling in the joint soft tissue. Similarly, a decrease in cortical and trabecular bone volume of the tibia was observed. Treatment with the SOD mimetic preserved the trabecular bone, articular cartilage and the menisci after 35 days aboard the ISS, but had limited efficacy retaining that recovery after 120 days of weight bearing, and after 75 days on orbit. Antioxidants including BuOE may serve as a potential countermeasure option to protect musculoskeletal health during spaceflight missions, and continued use may be necessary upon reaching a destination.
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TI Update on the correlation between mitochondrial function and osteonecrosis of the femoral head osteocytes
SO REDOX REPORT
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DT Review
DE Mitochondria; mitochondrial physiological function; osteocyte; bone disease
ID steroid-induced osteonecrosis; endothelial progenitor cells; mesenchymal stem-cells; oxidative stress; energy-metabolism; activation; antioxidants; dysfunction; receptors; mitophagy
AB Mitochondrial health is maintained in a steady state through mitochondrial dynamics and autophagy processes. Recent studies have identified healthy mitochondria as crucial regulators of cellular function and survival. This process involves adenosine triphosphate (ATP) synthesis by mitochondrial oxidative phosphorylation (OXPHOS), regulation of calcium metabolism and inflammatory responses, and intracellular oxidative stress management. In the skeletal system, they participate in the regulation of cellular behaviors and the responses of osteoblasts, osteoclasts, chondrocytes, and osteocytes to external stimuli. Indeed, mitochondrial damage or dysfunction occurs in the development of a few bone diseases. For example, mitochondrial damage may lead to an imbalance in osteoblasts and osteoclasts, resulting in osteoporosis, osteomalacia, or poor bone production, and chondrocyte death and inflammatory infiltration in osteoarthritis are the main causes of cartilage degeneration due to mitochondrial damage.

However, the opposite exists for osteosarcoma, where overactive mitochondrial metabolism is able to accelerate the proliferation and migration of osteosarcoma cells, which is a major disease feature. Bone is a dynamic organ and osteocytes play a fundamental role in all regions of bone tissue and are involved in regulating bone integrity. This review examines the impact of mitochondrial physiological function on osteocyte health and summarizes the microscopic molecular mechanisms underlying its effects. It highlights that targeted therapies focusing on osteocyte mitochondria may be beneficial for osteocyte survival, providing a new insight for the diagnosis, prevention, and treatment of diseases associated with osteocyte death.
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TI Genomic structural equation modeling decodes skeletal aging: novel loci discovery and multisystem genetic crosstalk
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DE Skeletal aging; Genomic structural equation modeling (Genomic SEM); Genome-wide association study (GWAS); Multi-system crosstalk; Wnt signaling
ID causal relationship; bone; osteoarthritis; risk; prioritization; mechanisms; stress
AB Objective Skeletal aging, a core determinant of systemic aging, poses a global public health challenge due to its association with chronic diseases and functional decline. This study aimed to decode the genetic architecture of skeletal aging by identifying novel loci and multi-system crosstalk using genomic structural equation modeling (Genomic SEM). Methods We integrated genome-wide association study (GWAS) data from five musculoskeletal-related traits (osteoporosis [OP], osteoarthritis [OA], lumbar spinal stenosis [LSS], telomere length [TL], and low back pain [LBP]) across 462,933 to 472,174 European individuals. Genomic SEM, FUMA, FUSION, and fine-mapping tools (SuSIE/FINEMAP) were applied to model latent skeletal aging ("mvSAge") and identify causal variants, enriched pathways, and tissue-specific gene expression. Results The latent factor model (CFI = 0.993, SRMR = 0.065) revealed shared genetic architecture among OP, OA, LSS, TL, and LBP. We identified 514 lead SNPs (P < 5 x 10(-)(12)), including 136 novel loci enriched in

regulatory regions (e.g., brain putamen, frontal cortex). Fine-mapping prioritized causal variants (posterior probability > 0.95) near MTPAP, GRAMD4, and DPP8, implicating mitochondrial function and immune regulation. Transcriptome-wide analyses highlighted PPP6R3 (bone mineral density) and SLC33A1 (anticancer target) as key genes. Enrichment analyses linked mvSAge to Wnt signaling, ER stress, and Mendelian disorders (e.g., ALS). Chromosomes 1, 2, and 4 showed elevated heritability contributions, driven by conserved regulatory elements (RUNX2, SP7) and chromatin accessibility hotspots. Conclusion This study establishes mvSAge as a genetically cohesive construct and uncovers novel loci, pathways, and multi-system interactions underlying skeletal aging. These findings advance precision medicine strategies for aging-related musculoskeletal disorders.
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TI Femoral neck shape and trabecular bone microarchitecture association with hip osteoarthritis - Results from the QUALYOR study
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DE Hip osteoarthritis; Subchondral bone; Microarchitecture; QCT

ID subchondral bone; osteoporosis; fracture; geometry; density
AB Objectives: Hip osteoarthritis (OA) is a major public health concern. The determinants of hip OA, however, are not as well understood as those of other OA sites, such as the knee. In recent years, the role of subchondral bone in the pathogenesis of OA has been emphasized but data are lacking for hip OA. Therefore, we aimed to determine which bone characteristics were associated to hip OA. Methods: We made a cross-sectional analysis of 1537 postmenopausal women included in the QUALYOR prospective cohort. At baseline, we measured areal BMD by DXA at the lumbar spine and the hip, volumetric BMD and geometry by hip quantitative computerized tomography (QCT) using the Bone Investigational Toolkit (BIT) software, as well as microarchitecture at the distal radius and tibia by high-resolution peripheral quantitative tomography (HR-pQCT). We built a hip OA score (CT OA score) with images from the hip QCT, based on the depiction of the four major signs of osteoarthritis: subchondral bone sclerosis, joint space narrowing, osteophytes and subchondral cysts. The severity of each of these four signs was graded as absent, mild, moderate or severe (semi-quantitative score ranging from 0 to 3 for each sign). The absence of hip OA was defined as CT score equal to 0, mild hip OA as CT score between 1 and 4 and moderate to severe hip OA as CT score>4. Women with and without hip OA were compared using t tests and multivariable modeling. Results: The mean age was 65.9 (+/- 6.7) years and the mean body mass index was 24.6 (+/- 3.6) kg/m(2). Among these 1537 women, 601 had an OA score of 0, 756 between 1 and 4 (mild OA) and 180 greater than 4 (severe OA). Women with hip osteoarthritis had lower trabecular total hip vBMD (125 vs. 129mg/cm(3), P<0.01). Cortical hip vBMD did not differ between women with and without hip OA (966.5 vs. 963.5mg/cm(3), P n.s). Patients with hip OA also had larger femoral neck volume (11.55 vs. 11.27mm(3), P<0.001). The BIT analysis showed greater bone resistance to bending (cross-sectional moment of inertia [CSMI] min with 6.03 vs. 5.6cm(4) and section modulus [Z] polar with 7.98 vs. 7.59cm(3), P<0.05) at the femoral neck in patients with mild hip OA and even greater in women with severe hip OA. Patients with hip OA had significantly higher trabecular area measured at the radius by HR-pQCT (205.11 vs. 192.61mm(2), between group difference 12.50 95% CI [8.15-16.86] P<0.01), lower trabecular number at the tibia (1.57/mu m vs. 1.63/mu m, between group difference -0.06 95% CI [-0.09 to -0.03] P<0.001) and higher trabecular spacing at the tibia (0.58 vs. 0.56 mu m, between group difference 0.02 95% CI [0.011-0.038] P<0.005). Cortical parameters were not different in patients with hip OA compared to controls. Conclusion: Women with hip OA have larger femoral neck and lower trabecular bone parameters, suggesting a sizeable role of hip bone geometry and remodeling in the pathophysiology of hip OA. (c) 2025 The Authors. Published by Elsevier Masson SAS on behalf of Soci o<acute accent>t o<acute accent> Fran o<acute accent>aise de Rhumatologie. This is an open access article under the CC BY license (http://creativecommons.org/ licenses/by/4.0/).
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TI Role of YAP/TAZ in bone diseases: A transductor from mechanics to biology
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
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DT Review
DE Bone diseases; Mechanoresponse; Mechanosensing; Mechanotransduction; TAZ; YAP
ID yes-associated protein; hippo signaling pathway; mesenchymal stem-cells; smooth muscle actin; organ size control; osteogenic differentiation; regulating osteoclast; yap pathway; growth; taz
AB Wolff's Law and the Mechanostat Theory elucidate how bone tissues detect and convert mechanical stimuli into biological signals, crucial for maintaining bone equilibrium. Abnormal mechanics can lead to diseases such as osteoporosis, osteoarthritis, and nonunion fractures. However, the detailed molecular mechanisms by which mechanical cues are transformed into biological responses in

bone remain underexplored. Yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ), key regulators of bone homeostasis, are instrumental in this process. Emerging research highlights bone cells' ability to sense various mechanical stimuli and relay these signals intracellularly. YAP/TAZ are central in receiving these mechanical cues and converting them into signals that influence bone cell behavior. Abnormal YAP/TAZ activity is linked to several bone pathologies, positioning these proteins as promising targets for new treatments. Thus, this review aims to provide an in-depth examination of YAP/TAZ's critical role in the interpretation of mechanical stimuli to biological signals, with a special emphasis on their involvement in bone cell mechanosensing, mechanotransduction, and mechanoresponse. The translational potential of this article: Clinically, appropriate stress stimulation promotes fracture healing, while bed rest can lead to disuse osteoporosis and excessive stress can cause osteoarthritis or bone spurs. Recent advancements in the understanding of YAP/TAZ-mediated mechanobiological signal transduction in bone diseases have been significant, yet many aspects remain unknown. This systematic review summarizes current research progress, identifies unaddressed areas, and highlights potential future research directions. Advancements in this field facilitate a deeper understanding of the molecular mechanisms underlying bone mechanics regulation and underscore the potential of YAP/TAZ as therapeutic targets for bone diseases such as fractures, osteoporosis, and osteoarthritis.
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TI Direct lateral vs. posterior-lateral approach in robotic-assisted total hip arthroplasty: clinical and radiographic comparison
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article
DE Lateral approach; Posterior approach; Robotic THA; Mako; WOMAC; HHS
ID surgical approach; anteversion; quality; offset
AB IntroductionThe main goal of this study was to compare patient outcomes following robotic-arm assisted THA (RTHA) using the direct lateral approach (DLA) and the posterior-lateral approach (PLA) by analysing the clinical and radiographical data.Materials and Methods203 consecutive patients diagnosed with end stage hip osteoarthritis underwent RTHA at the same orthopaedic centre between 2015 and 2019. Patients were divided in two groups based on the surgical approach where 95 patients received PLA and 108 received DLA. All patients were assessed pre-operatively and at minimum 3-year follow-up using Harris Hip Score (HHS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). A radiographic evaluation was performed for every patient to assess the incidence of heterotopic ossification (HO).ResultsPatients in the PLA cohort had higher scores in the post-operative WOMAC when compared to the DLA group (PLA: 96.2 +/- 8.2 vs. DLA: 93.6 +/- 10.3, p = 0.05). There was no statistical difference in the post-op HHS (PLA 86.3 +/- 7 vs. DLA: 86.3 +/- 9.5, p = 0.97).

Accurate component positioning was achieved according to the pre-operative planning in both groups. There were no cases of dislocation. We found a significantly higher incidence of HO in the DLA group (59.3%) compared to the PLA group (12.6%). However, this difference was not associated with a poorer clinical outcome.ConclusionsCurrent controversy still persists regarding the surgical approach without clear evidence about which one is more appropriate. Nowadays, it seems that surgeons' skill and experience to perform an approach are still more relevant than the choice of the approach. Both PLA and DLA represent valid surgical options for performing RTHA, yielding excellent clinical outcomes without clear evidence of superiority of one approach over the other.
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TI Alternative Splicing: A Critical Regulator in Human Bone Biology and Tumor Progression
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DT Review
ID prostate-cancer cells; mechano-growth-factor; messenger-rna; differential expression; dna-damage; sr proteins; recessive osteopetrosis; transcriptional control; isoform expression; variant expression
AB Alternative splicing (AS) is the central mechanism of transcriptional regulation and generates diverse splice variants that influence protein structure, function, and intracellular activity. AS plays critical roles in tissue differentiation, organ development, and disease progression. This review focuses on the pivotal roles of AS in bone biology, highlighting its regulatory effects on osteoblasts, osteoclasts, chondrocytes, bone matrix remodeling, and bone remodeling, as well as the involvement of AS-related RNA-binding proteins in these processes. We also emphasize bone-specific AS events and their physiological importance in skeletal development and maintenance. Furthermore, the pathological role of AS is emphasized in bone-related tumors such as osteosarcoma, Ewing sarcoma, and

chondrosarcoma. This review also explores aberrant AS mechanisms in bone metastatic cancers, including prostate, bladder, and breast cancers, with an in-depth analysis of their roles in tumor progression and alterations in the bone microenvironment. This review provides a comprehensive perspective on how AS factors, signaling pathways, and mechanical stimulation collaboratively regulate bone cells under both physiological and pathological conditions, paving the way for identifying potential intervention strategies. The mechanisms of AS in other pathological bone conditions, such as osteoporosis, osteoarthritis, and hereditary bone disorders, are also summarized. The potential applications of targeting AS in the diagnosis and treatment of bone diseases are discussed, offering insights into the underlying mechanisms and clinical translational potential.
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TI The Role of Adipokines in Spinal Disease: A Narrative Review
SO JOR SPINE
LA English
DT Review
DE adipokines; degeneration; intervertebral disc; leptin; spinal pathology
ID posterior longitudinal ligament; adipose-tissue; oxidative stress; messenger-rna; skeletal-muscle; gene-expression; cord-injury; tnf-alpha; leptin; resistin
AB BackgroundAdipokines are bioactive molecules secreted by adipose tissue that influence both local and systemic physiological processes. Although adipokine dysregulation has been widely implicated in the pathogenesis of cardiovascular, gastrointestinal, nervous, immune, and musculoskeletal disorders- especially osteoarthritis, rheumatoid arthritis, and osteoporosis- their involvement in spinal pathology remains comparatively underinvestigated. Recent evidence indicates that

certain adipokines may influence spinal disease progression by affecting bone, intervertebral discs, musculature, and neural structures.MethodsA comprehensive literature review was conducted to evaluate preclinical and clinical studies investigating the role of adipokines in spinal pathology. PubMed and related databases were searched for studies reporting associations between adipokine expression and structural or functional changes in spinal tissues, including vertebral bone, intervertebral discs, paraspinal muscles, spinal ligaments, and the spinal cord. Particular attention was given to mechanistic insights and translational relevance.ResultsThe review identified emerging evidence implicating several adipokines, including leptin, adiponectin, resistin, and visfatin, in degenerative and inflammatory changes across various spinal structures. Adipokines were found to influence matrix degradation, bone turnover, muscle atrophy, and neural inflammation through cytokine signaling, oxidative stress, and metabolic dysregulation. However, findings are often heterogeneous and context-dependent, with limited longitudinal or interventional data.ConclusionsAdipokines represent a promising yet underexplored avenue in spinal disease research. Their diverse functions in both structural and metabolic regulation highlight their potential as both biomarkers and therapeutic targets. Further mechanistic and clinical studies are needed to elucidate causal relationships and therapeutic efficacy, particularly in degenerative spine disorders.
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TI Uncemented reverse total shoulder arthroplasty: is it a safe option for elderly patients with proximal humerus fractures?
SO INTERNATIONAL ORTHOPAEDICS
LA English
DT Article
DE Reverse shoulder arthroplasty; Proximal humerus fracture; Osteoporosis; Uncemented stem; Stem loosening; Tuberosity healing
ID 4-part fractures; fixation; hemiarthroplasty; osteoarthritis; outcm; quality; stem
AB PurposeReverse shoulder arthroplasty (RSA) is a common surgical procedure for elderly patients with proximal humerus fractures. Cement fixation of the humeral stem is considered the gold standard for this procedure. Due to the high prevalence of osteoporosis in this patient population, the risk of intraoperative fractures is increased when uncemented stems are used. Stem loosening is another concern of uncemented stems. However, the use of cement is associated with the risk of cement embolisation, impairment of tuberosity healing, and technical difficulties for later revisions. This study aimed (i) to evaluate the clinical and

radiological outcomes of patients treated with uncemented RSA for proximal humerus fractures at two years postoperatively, and (ii) to compare these outcomes between patients with and without decreased low bone quality as measured by the deltoid tuberosity index.MethodsThe single-centre prospective study included 54 shoulders (52 patients) with a proximal humerus fracture between 2019 and 2022. Enrolled were patients aged 65 and older with acute or secondary displaced three- or four-part fractures or head-split fractures treated with RSA using the same uncemented system and tubercula refixation. At 24 months post-surgery, clinical evaluations included range of motion (ROM), Constant-Murley Score (CS), Subjective Shoulder Value (SSV), and American Shoulder and Elbow Surgeons (ASES) Score. Radiological assessments evaluated scapular notching, radiolucent lines, and greater tuberosity healing.ResultsThe mean age was 79 years (+/- 8), 87% were female, and 69% had osteoporotic fractures. At the two-year follow-up, the median SSV was 90% (IQR 80-95), the median CS Score was 76.5 (IQR 72-81), and the median ASES Score was 89.9 (IQR 82-93). The ROM measurements were: median active forward flexion 140 degrees (IQR 120-160), median external rotation 30 degrees (IQR 20-40), and median active internal rotation 6 (IQR 4-8). The greater tuberosity healing rate was 94.5%. Although osteoporotic fractures occurred more often in older patients (mean 81 vs. 72 years, respectively), no other significant differences were detected between the groups. One case of aseptic stem loosening occurred in the non-osteoporotic group.ConclusionEven in osteoporotic proximal humerus fractures, cementless stems combined with tubercula refixation resulted in favourable outcomes and were not associated with increased complications.
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TI Osteosarcopenia, osteoarthritis and frailty: a two-sample Mendelian

randomization study
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE Osteosarcopenia; Osteoarthritis; Frailty; Mendelian randomization
ID c-reactive protein; older-adults; association; risk; bone; knee; interleukin-6; metaanalysis; population; prevalence
AB Background Musculoskeletal disease, which has a complicated relationship with frailty, is a common clinical problem among elderly individuals. AimsThis study evaluated the potential causal relationships between osteosarcopenia, osteoarthritis and frailty by Mendelian Randomization (MR) analysis. Methods This study employed a two-sample MR approach to investigate the causal relationships among osteosarcopenia, osteoarthritis and frailty. Published summary statistics were used to obtain instrumental variables at the genome-wide significance level. Results Among the age groups with osteoporosis, high total bone mineral density (TBMD) (45-60, OR = 0.966, 95% CI 0.940-0.993, P = 0.013) and TBMD (over 60, OR = 0.974, 95% CI 0.954-0.994, P = 0.011) reduced the risk of frailty. Similarly, high forearm BMD (FA-BMD), high ultradistal forearm BMD (UFA-BMD), and high Heel-BMD at different sites also reduced the risk of frailty (OR = 0.966, 95% CI 0.936-0.996, P = 0.028; OR = 0.975, 95% CI 0.953-0.997, P = 0.029; OR = 0.981, 95% CI 0.967-0.995, P = 0.008). Among the characteristics related to sarcopenia, grip strength in the left hand, grip strength in the right hand, appendicular lean mass, and walking pace were all protective factors for frailty (OR = 0.788, 95% CI 0.721-0.862, P < 0.001; OR = 0.800, 95% CI 0.737-0.869, P < 0.001; OR = 0.955, 95% CI 0.937-0.974, P = 0.000; OR = 0.480, 95% CI 0.388-0.593, P < 0.001), with low grip strength in those over 60 years of age significantly positively correlated with frailty (OR = 1.168, 95% CI 1.059-1.289, P = 0.002). The MR results of osteoarthritis and frailty revealed a causal relationship between specific joint sites and frailty, including KOA (OR = 1.086, 95% CI 1.017-1.160, P = 0.014), HOA (OR = 1.028, 95% CI 1.007-1.049, P = 0.009), and KOA/HOA (OR = 1.082, 95% CI 1.053-1.113, P = 0.000), increasing the risk of frailty. Conclusion Osteosarcopenia, osteoarthritis and frailty exhibit significant causal effects, rendering them risk factors for frailty. Therefore, in clinical practice, patients with osteosarcopenia and osteoarthritis should be required to undergo relevant interventions to reduce the risk of frailty.
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TI Nanozymes in Bone Regeneration: Mechanistic Insights and Therapeutic Applications
SO ACS APPLIED MATERIALS & INTERFACES
LA English
DT Review
DE nanozymes; bone regeneration; enzyme-like activity; mechanism; therapeutic applications
ID cerium oxide; stem-cells; nanoparticles; gold; hydrogel; nanomaterials; platinum; repair; silver
AB Nanozymes, an emerging class of nanomaterials, demonstrate enzyme-like activities and have significantly broadened the enzyme mimicry field by extending it from organic to inorganic materials. Their affordability, multifunctionality, and enhanced stability under harsh conditions position them as potential replacements for natural enzymes in various applications. Nanozymes have demonstrated tremendous application potential in orthopedic diseases including osteoarthritis, osteoporosis, bone regeneration, bacteria-related infections, rheumatoid arthritis, and osteosarcoma. The regenerative repair of bone defects is a critical research direction in modern medicine, where bone remodeling and regeneration are essential for maintaining skeletal integrity and mineral homeostasis. Nanozymes play a significant role in bone regeneration and repair by regulating the balance between osteoblasts and osteoclasts, promoting vascular and neural regeneration, controlling infections, and modulating cellular immune functions. This article discusses the latest advancements in applying nanozymes in bone tissue regenerative medicine. It reviews the mechanisms through which nanozymes facilitate osteogenesis and enhance bone regeneration. Additionally, this review examines the current uses of various nanozymes in bone regeneration and explores

both the prospects and the challenges of nanozymes in clinical therapies.
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TI Nutrition supplementation combined with exercise versus exercise alone in treating knee osteoarthritis: a double-blinded, randomised, placebo-controlled trial
SO AGE AND AGEING
LA English
DT Article
DE knee osteoarthritis; nutrition supplementation; exercise; older people
ID glucosamine sulfate; chondroitin sulfate; obese adults; therapy; pain; osteoporosis; combination; outcm; womac; hip

AB Objective: To investigate the effectiveness of formula nutrition supplementation (mainly containing glucosamine sulphate, chondroitin sulphate and rhizoma drynariae) plus supervised exercise versus exercise alone for the treatment of knee osteoarthritis (OA). Methods: This was a double-blinded, single-centre, randomised, placebo-controlled trial. The study recruited 65 participants (40-75 years) with knee OA. Participants were randomly allocated to nutrition supplementation plus exercise (N + E) group or placebo plus exercise (P + E) group. The intervention lasted for 6 months. The primary outcome was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. Secondary outcomes included physical function and performance scores, lower extremity strength and serum biomarkers. Results: Among the 65 randomised patients, 56 (86%) completed the trial. At 3 months, more participants in the N + E group than in the P + E group achieved minimum clinically important difference (MCID) in WOMAC total score (19/30 [63.3%] vs 8/26 [30.8%]; P < .01). At 6 months, more participants in the N + E group than in the P + E group achieved MCID in WOMAC stiffness score (19/30 [63.3%] vs 10/26 [38.5%]; P < .05). Meanwhile, at 6 months the decreased percentages of WOMAC stiffness score in the N + E group was greater than in the P + E group (P < .05). The flexor peak torque at 120 degrees/s and 180 degrees/s in the N + E group were significantly higher than those in the P + E group at 3 months (P < .05). Moreover, compared with baseline, improvements in the WOMAC overall and pain score, visual analogue scale pain and 30-second chair stand test were observed in both groups at 6 months. However, these indicators in the N + E group were improved as early as 3 months (P < .05). Conclusions: The improvement effects of nutrition supplementation plus exercise were superior to those of exercise alone, and the improvement occurred earlier. Nutrition supplementation plus exercise would be a more efficient strategy for knee OA.
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
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TI Locomotive syndrome and increased musculoskeletal disorder incidence in older adults: a prospective study
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Locomotion Disorders; Musculoskeletal Diseases; Incidence; Prospective Studies; Geriatric Assessment
ID quality-of-life; knee osteoarthritis; risk; pain; epidemiology; prevalence; disability; decrease; diseases; people
AB Introduction With the population aging, musculoskeletal disorders increasingly impair older adults' quality of life and escalating healthcare costs, necessitating effective prevention strategies. Locomotive syndrome (LS), characterized by mobility decline due to musculoskeletal dysfunction, is closely linked to these disorders. However, its role in predicting future musculoskeletal conditions remains unclear. This study examined the association between LS and the incidence of newly diagnosed musculoskeletal disorders. Material and Methods This prospective study included 367 community-dwelling adults aged >= 40 years who were independent in daily activities. LS was assessed using the five-question Geriatric Locomotive Function Scale (GLFS-5). The primary outcome was the incidence of musculoskeletal disorders, including osteoarthritis, lumbar spinal stenosis, and osteoporosis. Cox proportional hazards regression analyzed associations between LS and future diagnoses, while receiver operating characteristic (ROC) analysis determined the GLFS-5 cutoff score for risk prediction. Results At baseline, 19.1% of participants had LS. Over four years, musculoskeletal disorders occurred more frequently in participants with LS than in those without (22.2 vs. 8.8 per 100 person-years, $p < 0.001$). After adjusting for covariates, LS remained a significant risk factor (hazard ratio 1.98, 95% confidence interval 1.16-3.36, $p = 0.011$). ROC analysis identified a GLFS-5 cutoff score of 2 (sensitivity: 62.0%, specificity: 62.0%). Conclusions LS nearly doubled the risk of musculoskeletal disorders, with a GLFS-5 score >= 2 serving as an early risk indicator. Proactive screening and targeted interventions may mitigate this risk in aging populations.

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TI Statins and long-term risk of revision surgery after total hip arthroplasty in osteoarthritis: a multi-source data linkage study
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE osteoarthritis; statins; orthopedic surgery; total hip arthroplasty; prosthesis outcomes
ID knee arthroplasty; simvastatin; gender; differentiation; osteoporosis; disease
AB Background Statins, widely used lipid lowering drugs, have been associated with pleiotropic beneficial effects. Notably, studies conducted in vitro and in vivo suggest a link between statins and bone metabolism. Observational data in humans also hint at a decreased fracture rate among statin users. Revision of total hip arthroplasty (THA) is a serious and costly medical event. Whether statins might influence THA failure is not clear. Aim of the current study is to assess how the preoperative use of statins may influence the risk of THA revision in patients with hip osteoarthritis (OA). Methods We performed a retrospective analysis of patients

who underwent THA for OA in the Italian RIPO registry of Emilia-Romagna. Electronic health records were scrutinized to gather information regarding comorbidities and statin prescriptions. We employed propensity score (PS) matching to pair 1:1 statin users (SU) with statin non-users (SNU), considering factors such as age, sex, and the duration of follow-up. Survival of THA was compared between the two groups; secondary analyses were performed to ascertain the role of mortality, sex, indication for statin treatment, and statin potency or lipophilicity. Results 10,927 patients were classified as SU and PS-matched with SNU. SU showed a reduced risk of THA revision over a 15-year period (adjHR 0.76, 95% CI: 0.67-0.88; p < 0.001). Notably, this observation remained consistent regardless of the indication for statin therapy or the specific characteristics of the statin medications prescribed, and it was more pronounced among male patients (adjHR 0.64, 95% CI: 0.52-0.80, p < 0.001). Conclusion Our findings suggest that statin treatment is associated with a decreased risk of long-term THA revision in patients with OA, irrespective of the original indication for statin therapy.
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TC 0
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PU FRONTIERS MEDIA SA
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AU Zhang, X
Huang, L
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AF Zhang, Xu
Huang, Ling
Feng, Wenjun
Xu, Danghan
Zeng, Yirong
TI Salidroside ameliorates lipopolysaccharide-induced ferroptosis in chondrocytes via regulation of the sirt1/foxo1 axis
SO MOLECULAR MEDICINE REPORTS
LA English
DT Article
DE salidroside; osteoarthritis; sirt1/foxo1 signaling; ferroptosis
ID osteoarthritis; osteoporosis; cartilage; cancer
AB Salidroside (SAL) is a bioactive constituent extracted from Rhodiola rosea plant and exerts antioxidant and anti-inflammatory properties. However, understanding of SAL for the treatment of arthritis is limited. The aim of the present study was to investigate whether SAL treats lipopolysaccharide (LPS)-induced chondrocyte injury by modulating the sirt1 silent information regulator 1)/FoxO1 (forkhead transcription factors O1) signaling pathway. Network pharmacology was used to screen the potential pathway of SAL for the treatment of osteoarthritis via the ferroptosis pathway. Subsequently, a chondrocyte inflammation model was established in vitro using LPS and SAL was used as a drug treatment. Effects of SAL treatment of chondrocytes was evaluated by western blot analysis, fluorescence, cell viability and oxidative assay. Analysis revealed that SAL significantly attenuated

LPS-induced apoptosis and accumulation of oxides in chondrocytes, thereby protecting the integrity of cartilage extracellular matrix. In addition, SAL promoted the activation of the sirt1/foxo1 signaling cascade, which alleviated LPS-induced ferroptosis in chondrocytes. The present study demonstrated that SAL attenuated LPS-induced chondrocyte ferroptosis by regulating the sirt1/foxo1 pathway. This may provide a potential therapeutic avenue for cartilage damage in osteoarthritis.
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Chen, SL
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Chen, Y
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AF Hu, Weiqi
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Ma, Dandan
TI Oral microbiome, periodontal disease and systemic bone-related diseases in the era of homeostatic medicine
SO JOURNAL OF ADVANCED RESEARCH
LA English
DT Article
DE Oral microbiome; Homeostatic medicine; Dysbiosis; Periodontal disease; Bone-related diseases; Targeted therapies
ID tumor-necrosis-factor; porphyromonas-gingivalis; rheumatoid-arthritis; osteoclast differentiation; gut microbiota; synovial-fluid; bacterial-dna; factor-alpha; stem-cells; lipopolysaccharide
AB Background: Homeostasis is a state of self-regulation and dynamic equilibrium, maintaining the good physiological functions of each system in living organisms. In the oral cavity, the interaction between the host and the oral microbiome forms oral microbial homeostasis. Physiological bone remodeling and renewal can occur under the maintenance of oral microbial homeostasis. The imbalance of bone homeostasis is a key mechanism leading to the occurrence of systemic bone-related diseases. Considering the importance of oral microbial homeostasis in the maintenance of bone homeostasis, it still lacks a complete understanding of the relationship between oral microbiome, periodontal disease and systemic bone-related diseases. Aim of review: This review focuses on the homeostatic changes, pathogenic routes and potential mechanisms in the oral microbiome in periodontal disease and systemic bone-related diseases such as rheumatoid arthritis, osteoarthritis, osteoporosis and osteomyelitis. Additionally, this review discusses oral microbiome-based diagnostic approaches and explores probiotics, mesenchymal stem cells, and oral microbiome transplantation as promising treatment strategies. Key scientific concepts of review: This review highlights the association between oral microbial homeostasis imbalance and systemic bone-related diseases, and highlights the possibility of remodeling oral microbial homeostasis for the prevention and treatment of systemic bone-related diseases.
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TI A development of machine learning models to preoperatively predict insufficient clinical improvement after total knee arthroplasty
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DT Article
DE Total knee arthroplasty; Insufficient clinical improvement prediction; WOMAC; Minimal clinically important difference; Machine learning

ID reported outcome measures; patient satisfaction; risk-factor; total hip; pain; quality; comorbidity; replacement; algorithms; health
AB BackgroundIdentifying patients unlikely to achieve meaningful improvement following total knee arthroplasty (TKA) supports more effective shared decision-making (SDM). This study aimed to develop and validate machine learning (ML) models that preoperatively predict insufficient clinical improvement one year after TKA using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscales and total scores, and to assess the important predictive variables.MethodsA retrospective analysis was performed on consecutive primary TKA patients from 2004 to 2022 at a single tertiary hospital was conducted. Insufficient clinical improvement was defined as not achieving the minimal clinically important difference (MCID) for each WOMAC subscale and total. Candidate preoperative variables included demographics, comorbidities, knee range of motion, radiologic variables, and WOMAC scores. A variety of ML models were evaluated using performance metrics for calibration and discrimination, as well as decision curve analysis and Shapley additive explanations.ResultsAmong the 3,810 TKAs included, the ExtraTrees model performed best for WOMAC pain, stiffness, function, and total scores, achieving AUCs of 0.92, 0.90, 0.87, and 0.89; recall rates of 0.79, 0.86, 0.70, and 0.83; and Brier scores of 0.09, 0.10, 0.11, and 0.06, respectively, along with demonstrating good calibration curves and net clinical benefit. Shapley additive explanations identified better preoperative WOMAC scores, osteoporosis, diabetes mellitus, older age, malignancy, and coronary artery disease as important predictors of insufficient clinical improvement.ConclusionsThe ML models demonstrated good performance in preoperatively predicting insufficient clinical improvement at 1 year after TKA based on WOMAC. These models have the potential to enhance SDM and perioperative patient management by preoperatively identifying approximately 70% to over 80% of patients likely to experience insufficient clinical improvement, with a specificity of about 80%, and by providing explanations regarding associated factors.
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Zhang, XD
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Chen, Qian
Xiao, Zhuojie
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Wang, Yuyi
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Liu, Limin
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Zhu, Xiangdong
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TI Shockwave-driven activation of endoplasmic reticulum stress in osteoblasts to enhance bone formation under osteoporotic conditions
SO REGENERATIVE BIOMATERIALS

LA English
DT Article
DE extracorporeal shockwave; osteoporosis; endoplasmic reticulum stress; cellular senescence; osteogenesis
ID er stress; therapy; waves; nanoparticles; apoptosis; autophagy; fracture
AB Extracorporeal shockwave (ESW) therapy is a noninvasive physical intervention widely applied in orthopedics for the treatment of musculoskeletal disorders such as plantar fasciitis, osteoarthritis, delayed fracture healing and tendinopathies. In recent years, accumulating evidence has suggested that ESW may also have beneficial effects on bone regeneration and local bone mineral density, particularly under osteoporotic conditions. However, the precise biological mechanisms underlying these effects remain incompletely elucidated. In this study, we systematically investigated the effects of different radial extracorporeal shockwave (r-ESW) intensities on osteoblasts derived from osteoporotic bone (OPOB), with a specific focus on osteogenic activity and the involvement of endoplasmic reticulum (ER) stress. Our in vitro results demonstrated that moderate-intensity r-ESW (3 bar) significantly enhanced osteoblast proliferation, upregulated the expression of osteogenic markers including Runx2, Col I, OPN and OCN and promoted matrix mineralization. Mechanistically, this was accompanied by mild ER stress and activation of the PERK-eIF2 alpha-ATF4 signaling pathway, which contributed to improved osteogenic differentiation and alleviated cellular senescence. In contrast, high-intensity stimulation (5 bar) induced excessive ER stress, calcium overload and subsequent apoptosis and necrosis, ultimately impairing osteogenesis. Furthermore, in an ovariectomy (OVX)-induced osteoporotic rat model, 3 bar r-ESW treatment effectively increased bone mass, stimulated new bone formation and decreased osteoclast activity and senescence-associated markers in vivo. These findings collectively highlight the potential of moderate-intensity r-ESW as a promising nonpharmacological strategy for osteoporosis management, providing novel insights into the modulation of ER stress as a therapeutic target in OPOB remodeling.
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NR 50
TC 0
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PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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WC Materials Science, Biomaterials
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TI Evaluation of Vitamin E in Trauma and Orthopaedics: A Narrative Synthesis
SO INDIAN JOURNAL OF ORTHOPAEDICS
LA English
DT Review
DE Vitamin E; Antioxidant; Anti-inflammatory; Oxidative stress; Arthroplasty; Orthopaedic surgery; Osteoporosis
ID cross-linked polyethylene; total hip-arthroplasty; e supplementation; alpha-tocopherol; spinal-cord; bone mass; cells; wear; differentiation; tocotrienols
AB BackgroundThere is an emerging role for vitamin E in orthopaedics due to its antioxidant, immunomodulation and anti-inflammatory effects. The current review aims to comprehensively evaluate evidence regarding the use, benefits, pitfalls and future implications of vitamin E in diverse subspecialties of orthopaedics.Materials and MethodologyA comprehensive search of literature was performed on 5 databases on January 5, 2025. The manuscripts, which pertain to examining the role of vitamin E in orthopaedics, were considered. Among them, opinions, editorials, letters, case reports and non-English manuscripts were excluded.Results19 manuscripts were selected for our review. Vitamin E is utilised in diverse forms in orthopaedic patients: administered systemically, intraarticularly or locally. Systemically-administered vitamin E can mitigate osteoarthritis progression through strengthening of adjoining musculature, gene regulation, protection of subchondral vasculature, and anti-inflammatory properties. Vitamin E incorporation has been demonstrated to improve the wear characteristics of highly crosslinked polyethylene and metal alloys in arthroplasty through its antioxidant and osteointegrative abilities. Antioxidant vitamin E has been shown to mitigate postoperative arthrofibrosis and septic loosening. Vitamin E can positively

influence late callus formation during secondary fracture healing. Through its effects on osteoblastic cells, proinflammatory cytokines, growth factors, antioxidant mechanism, hormones and micro-RNA, systemic vitamin E administration can meliorate osteoporosis and mitigate fractures.ConclusionThere is emerging evidence regarding the roles of vitamin E in diverse orthopaedic conditions like osteoarthritis, osteoporosis, fracture healing, osteomyelitis and arthroplasty. These actions are attributed to its antioxidant, anti-inflammatory, and immunomodulatory functions. Large-scale trials are needed to ascertain its safety and future prospects.
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TC 0
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PT J
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TI Role of leptin as a factor regulating bone metabolism
SO MEDYCYNA WETERYNARYJNA-VETERINARY MEDICINE-SCIENCE AND PRACTICE
LA English
DT Review
DE adipokines; leptin; bone; health; animals
ID mineral density; growth-hormone; mass; physiology; serotonin; cells; body; deficiency; expression; endocrine
AB Discovered in 1994, leptin is one of the most important anorexigenic factors in the body. This hormone is synthesized and released mainly by white adipose tissue, but could also be released by other tissues. Its main function is suppressing the feeling of hunger by interacting with LEPRs receptors located in the hypothalamus, which makes it one of the main factors regulating the food intake. Appetite regulation is not the only function of leptin in the organism. By interacting with LEPRs, it can also influence the metabolism of various body tissues and organs, such as gonads, immune system cells, bone marrow, and bones. A very important aspect of leptin activity, though seldom discussed in the literature, is its impact on bone tissue metabolism. Leptin can affect bone cells through two different pathways: a peripheral one and a central one. The peripheral pathway involves a direct interaction of leptin with LEPRs located on the surface of bone cell. The central pathway, on the other hand, involves the interaction of leptin with structures of the central nervous system, which regulates the secretion of many hormones, such as serotonin, growth hormone, and thyroid hormones, directly affecting the metabolic activity of bone cells. Determining the overall effect of leptin on bone metabolism is not an easy task. This is due to significant differences in the way individual leptin activity pathways may affect bone metabolism. Indirect pathways stimulate bone tissue in bone anabolic or bone katabolic processes, leading to an increase or a decrease in bone mass, depending on the hormone

through which bone metabolism is regulated. However, most of the literature data suggest that the leptin regulation of bone turnover is determined mainly by the direct pathway, and the overall effect of its activity is an increase in bone tissue mechanical parameters. Nevertheless, a complete understanding of these mechanisms requires further research. It is worth mentioning that this hormone is also involved in the development of several disorders of the skeletal system, such as osteoarthritis, osteoporosis, and rheumatoid arthritis, but the exact impact of leptin on the course of these diseases is still not fully understood.
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TI Altered Expression of Cell Cycle Regulators and Factors Released by Aged Cells in Skeletal Muscle of Patients with Bone Fragility: A Pilot Study on the Potential Role of SIRT1 in Muscle Atrophy
SO BIOMEDICINES
LA English
DT Article
DE cellular aging; senescence; physiology; SIRT1; muscle atrophy; bone fragility; osteoporosis; fragility fractures
ID senescence; sarcopenia; interleukin-1-beta
AB Background/Objectives: Cellular aging represents a crucial element in the progression of musculoskeletal diseases, contributing to muscle atrophy, functional decline, and alterations in bone turnover, which promote fragility fractures. However, knowledge about expression patterns of factors potentially involved in aging and senescence at the tissue level remains limited. Our pilot study aimed to characterize the expression profile of cell cycle regulators, factors released by aged cells, and sirtuin 1 (SIRT1) in the muscle tissue of 26 elderly patients undergoing hip arthroplasty, including 13 with low-energy fracture and 13 with osteoarthritis (OA). Methods: The mRNA expression levels of cyclin-dependent kinase inhibitor 1A (CDKN1A), cyclin-dependent kinase inhibitor 1B (CDKN1B), cyclin-dependent kinase inhibitor 2A (CDKN2A), p53, tumor necrosis factor alpha (TNF-alpha), interleukin-1 beta (IL-1 beta), interleukin-6 (IL-6), interleukin-15 (IL-15), chemokine (C-C motif) ligand 2 (CCL2), chemokine (C-C motif) ligand 3 (CCL3), growth differentiation factor 15 (GDF15), and SIRT1 were evaluated in muscle tissue by qRT-PCR. In addition, immunohistochemistry and Western blotting analysis were conducted to measure the protein levels of SIRT1. Results: A marked muscle atrophy was observed in fractured patients compared to the OA group, in association with an up-regulation of cell cycle regulators and factors released by the aged cells. The expression of matrix metallopeptidase 3 (MMP3), plasminogen

activator inhibitor 1 (PAI-1), and fas cell surface death receptor (FAS) was also investigated, although no significant differences were observed between the two experimental groups. Notably, SIRT1 expression was significantly higher in OA patients, confirming its role in maintaining muscle health during aging. Conclusions: Further studies will be needed to clarify the role of SIRT1 in the senescence characteristic of age-related musculoskeletal disorders, counteracting the muscle atrophy that predisposes to fragility fractures.
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TI From bone marrow mesenchymal stem cells to diseases: the crucial role of m6A methylation in orthopedics
SO STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE BMSCs; m(6)A methylation; Epitranscriptomic regulation; Signal transduction pathways; Orthopedic diseases; Regenerative medicine
ID pre-messenger-rnas; osteogenic differentiation; regulates adipogenesis; comprehensive analysis; intervertebral disc; gene-expression; fat mass; methyltransferase; promotes; progression
AB Elucidating the molecular mechanisms underlying orthopedic diseases is crucial for guiding therapeutic strategies and developing innovative interventions. N6-methyladenosine (m(6)A)-an epitranscriptomic modification-has emerged as a key regulator of cellular fate and tissue homeostasis. Specifically, m(6)A plays a pivotal role in several RNA biological processes such as precursor RNA splicing, 3'-end processing, nuclear export, translation, and stability. Recent advancements indicate that m(6)A methylation regulates stem cell proliferation and osteogenic differentiation by modulating various signaling pathways. Extensive research has shown that abnormalities in m(6)A methylation contribute significantly to the onset and progression of various orthopedic diseases such as osteoporosis (OP), osteoarthritis (OA), rheumatoid arthritis (RA), and bone tumors. This review aims to

summarize the key proteases involved in m(6)A methylation and their functions. The detailed mechanisms by which m(6)A methylation regulates osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) through direct and indirect ways are also discussed, with a focus on specific molecular pathways. Finally, this review analyzes the roles and mechanisms of m(6)A modification in the development and progression of multiple orthopedic diseases, offering a comprehensive understanding of the pathophysiology of these conditions and proposing new directions and molecular targets for innovative treatment strategies.
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TI A comprehensive review of Drynariae rhizoma: botany, traditional applications, and active flavonoid components
SO JOURNAL OF PHARMACY AND PHARMACOLOGY
LA English
DT Review
DE Drynariae rhizoma; traditional applications; flavonoid components; extraction methods; analytical characterization; biological activities; quality control
ID osteoprotective fraction; flavan-3-ols; fortunei; expression; naringin
AB Objectives Drynaria fortunei, a species within the Drynaria genus, is a widely distributed medicinal plant with abundant resources. Its rhizome, Drynariae rhizoma, has been extensively utilized in traditional Chinese medicine for its therapeutic efficacy in promoting wound healing, alleviating pain, tonifying the kidneys, and strengthening bones. With a well-documented historical presence in classical texts, Drynariae rhizoma has played a significant role in traditional medical systems across various cultures. Recent phytochemical investigations have identified a diverse array of compounds in Drynariae rhizoma, including flavonoids, phenolic acids, lignans, steroids, and glycosides. Among these, flavonoids represent the principal active constituents, attracting considerable research attention due to their extensive pharmacological activities. This review systematically integrates and critically analyzes the recent research progress in this field,providing a comprehensive overview of the current research landscape,with the aim of identifying promising future directions for Drynariae rhizome.Methods This review leveraged a wide range of online databases, including SciFinder, PubMed, SpringerLink, Baidu Scholar, Google Scholar, ScienceDirect, American Chemical Society (ACS) Publications, Web of Science, and China National Knowledge Infrastructure (CNKI), to collect relevant literature. Comprehensive searches were

conducted using keywords such as "Drynariae Rhizoma", "flavonoids", "extraction", "chemical constituents", "analytical characterization". To ensure the scientific accuracy of this study, the botanical name of the plant was meticulously cross-verified using authoritative platforms such as "World Flora Online" and "The Plant List."Key findings This article provides a comprehensive overview of the botany (including characteristics, distribution, and origin) and traditional applications (such as its historical evolution, botanical sources, and multi-ethnic as well as cross-national therapeutic practices) of Drynariae rhizoma. Additionally, it highlights the latest research advancements on its flavonoid compounds, encompassing extraction methods (e.g. solvent extraction, ultrasound-assisted extraction, and microwave-assisted extraction), analytical characterization (e.g. ultraviolet spectroscopy, high-performance liquid chromatography, and nuclear magnetic resonance), chemical constituents (with 60 flavonoid compounds identified to date), biological activities (e.g. anti-osteoporosis, anti-osteoarthritis, renal protection, dental health promotion, neuroprotection, lipid-lowering, and immunomodulation), and clinical applications. Furthermore, the review discusses current quality control strategies, highlighting the impact of geographical origin and processing methods on flavonoid content. Further in-depth studies are essential to comprehensively explore these areas, paving the way for enhanced understanding and application of Drynariae rhizoma in both traditional and modern medicines.Conclusions A comprehensive analysis of existing literature reveals that the flavonoid constituents of Drynariae rhizoma exhibit remarkable therapeutic potential owing to their structural diversity and extensive pharmacological properties. Nevertheless, current understanding of its pharmacodynamic material basis and quality control parameters remains inadequate, highlighting the urgent need for more rigorous investigations to facilitate its broader applications in both traditional and contemporary medical practices. This review is anticipated to provide a rigorous scientific basis for subsequent investigations and clinical translation of therapies based on Drynariae rhizoma.
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Livshits, G
AF Kalinkovich, Alexander
Livshits, Gregory
TI The cross-talk between the cGAS-STING signaling pathway and chronic inflammation in the development of musculoskeletal disorders
SO AGEING RESEARCH REVIEWS
LA English

DT Review
DE Sarcopenia; Osteoarthritis; Osteoporosis; Disk degeneration; cGAS-STING; Rheumatoid arthritis
ID polyunsaturated fatty-acids; pro-resolving mediators; gmp-amp synthase; factor-kappa-b; dna-damage; myocardial-infarction; estrogen deficiency; knee osteoarthritis; metabolic diseases; senescent cells
AB Musculoskeletal disorders (MSDs) comprise diverse conditions affecting bones, joints, and muscles, leading to pain and loss of function, and are one of the most prevalent and major global health concerns. One of the hallmarks of MSDs is DNA damage. Once accumulated in the cytoplasm, the damaged DNA is sensed by the cyclic GMP-AMP synthase (cGAS)/stimulator of interferon genes (STING) pathway, which triggers the induction of type I interferons and inflammatory cytokines. Thus, this pathway connects the musculoskeletal and immune systems. Inhibitors of cGAS or STING have shown promising therapeutic effects in the pre-clinical models of several MSDs. Systemic, chronic, low-grade inflammation (SCLGI) underlies the development and maintenance of many MSDs. Failure to resolve SCLGI has been hypothesized to play a critical role in the development of chronic diseases, suggesting that the successful resolution of SCLGI will result in the alleviation of their related symptomatology. The process of inflammation resolution is feasible by specialized pro-resolving mediators (SPMs), which are enzymatically generated from dietary essential polyunsaturated fatty acids (PUFAs). The supplementation of SPMs or their stable, small-molecule mimetics and receptor agonists has revealed beneficial effects in inflammation-related animal models, including arthropathies, osteoporosis, and muscle dystrophy, suggesting a translational potential in MSDs. In this review, we substantiate the hypothesis that the use of cGAS-STING signaling pathway inhibitors together with SCLG-resolving compounds may serve as a promising new therapeutic approach for MSDs.
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TI Beyond Bone Remodeling: Denosumab's Multisystemic Benefits in Musculoskeletal Health, Metabolism, and Age-Related Diseases-A Narrative Review
SO BIOMEDICINES
LA English
DT Review
DE osteoporosis; sarcopenia; osteosarcopenia denosumab; RANKL inhibitor; RANK/RANKL/OPG pathway (RRO pathway)

ID smooth-muscle-cells; postmenopausal women; vertebral fractures; insulin-resistance; receptor activator; osteoporosis; osteoprotegerin; management; beta
AB Background: Denosumab, a receptor activator of nuclear factor kappa-Beta ligand (RANKL) inhibitor, demonstrates therapeutic effects beyond traditional osteoporosis management through the RANK/RANKL/osteoprotegerin pathway. Methods: This narrative review analyzed 37 studies (2018-2024) examining denosumab's broader physiological effects and clinical applications. Results: Long-term safety data spanning 10 years showed sustained fracture prevention efficacy with a favorable benefit/risk profile. Compared to bisphosphonates, denosumab demonstrated superior outcomes in bone mineral density improvement and fracture risk reduction, particularly in elderly and frail populations. It enhanced muscular function by improving appendicular lean mass and grip strength while reducing fall risk. The drug showed potential cardiovascular benefits through its effects on cardiac and smooth muscle function. Notably, denosumab use was associated with reduced Type II diabetes mellitus risk through improved glucose metabolism. Additionally, it demonstrated promise in osteoarthritis treatment by suppressing osteoclast activity and chondrocyte apoptosis. While there are multisystem benefits, vigilance is required regarding adverse events, including hypocalcemia, infection risk, cutaneous reactions, and osteonecrosis of the jaw. Conclusions: Denosumab exhibits potential benefits in bone and systemic metabolism. Further research is needed to fully understand its therapeutic potential beyond osteoporosis and optimize clinical applications across different populations.
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TI Nanomaterial-mediated multidimensional regulation of the bone microenvironment: a precise therapeutic strategy for bone metabolic imbalance

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AB With the advancement of global population aging, the incidence of skeletal diseases (e.g. osteoporosis, fractures, and osteoarthritis) in clinical diagnosis increases and poses a serious threat to human health. Skeletal diseases usually occur as a result of disturbed cellular metabolism in a specific period or environment. The bone microenvironment, as an important physiological environment of bone tissue, consists of various cell types, and cell-cell interactions play a decisive role in the biological behavior and metabolic regulation of bone cells. Disorders of the bone microenvironment can exacerbate bone diseases. Conventional therapeutic for skeletal diseases often suffer from poor efficacy, low targeting, and side effects. Therefore, a new therapeutic strategy should be developed urgently to improve the existing deficiencies. With the continuous advancement of nanomedicine, the application of nanomaterials provides new research perspectives and application value for the treatment of skeletal diseases. With their unique physicochemical properties, nanomaterials can directly or indirectly mediate the bone microenvironment to regulate the bone metabolic process through self-regulation, drug carriers, and in vivo scaffolds. All the above strategies are extensively explored in this study. In this paper, we systematically summarize the nanomaterials currently used in the clinical treatment of bone diseases and discuss the application strategies of nanomaterials to regulate the bone microenvironment and thus bone metabolism. Moreover, we evaluated the challenges faced by nanomaterials in the clinical treatment of bone diseases. We aim to provide basic theories and new perspectives for the design and development of novel nanomaterials for improved clinical applications.
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NR 206
TC 0
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U2 7
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PT J
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TI Subchondral insufficiency fractures of the medial tibial condyle are associated with medial meniscus extrusion: A retrospective observational study
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English
DT Article
DE Medial tibial condyle; Subchondral insufficiency fracture; Medial meniscus extrusion; Lower extremity alignment
ID spontaneous osteonecrosis; knee; tear; osteoarthritis; subluxation; mri
AB Background: To the best of our knowledge, no prior studies have identified any risk factors for subchondral insufficiency fractures of the medial tibial condyle. This study aimed to explain relationships between subchondral insufficiency fractures of the medial tibial condyle and the meniscus status, lower extremity alignment, or osteoporosis. Methods: This retrospective study included 325 consecutive patients whose chief complaint is knee joint pain and who had visited one institution between April 2016 and March 2021, of which 70 patients (8 men and 62 women) who had suspected subchondral insufficiency fractures of the medial tibial condyle had undergone magnetic resonance imaging and radiographic examination. These patients were divided into two groups based on the results of their magnetic resonance imaging: the insufficiency fracture group included 46 patients who had subchondral insufficiency fractures of the medial tibial condyle and the nonfracture group included 24 patients without fractures. The meniscus injury and medial meniscus extrusion (MME) were evaluated by using magnetic resonance imaging. The Kellgren-Lawrence grade, the femorotibial angle, and the percent mechanical axis (%MA) were evaluated with the use of knee radiographs. T-scores were also measured by using dual-energy X-ray absorptiometry with a bone densitometer. Results: MME were significantly larger and the %MA was significantly smaller in the insufficiency fracture group than that in the nonfracture group. The prevalence of medial meniscus injuries and pathological MME were higher in the insufficiency fracture group than those in the nonfracture group. The prevalence of varus knee and osteoporosis did not vary remarkably different between the two groups. Conclusion: The patients who had insufficiency fractures of the medial tibial condyle tended to have medial meniscus extrusion. (c) 2024 The Authors. Published by Elsevier B.V. on behalf of The Japanese Orthopaedic Association. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/ 4.0/).
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NR 21
TC 0
Z9 1
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U2 1
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PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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AU Azzam, W
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TI Salvage tibiotarsal arthrodesis with circular external fixator for end-stage posttraumatic ankle arthritis, infection, and bone loss
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE Ankle arthrodesis; Ankle fusion; Ilizarov external fixator; Tibiotalar arthrodesis; Tibiocalcaneal arthrodesis
ID gait analysis; arthroplasty; metaanalysis; foot
AB Background: Chronic posttraumatic sequelae, such as chronic ankle joint

infection with loss of the articular cartilage, significant ankle deformities with advanced osteoarthritis, or significant bone loss of the distal tibia or talus, cause chronic ankle pain and functional impairment. Arthrodesis is usually required to relieve pain and improve function. These disabling conditions cannot be treated with ordinary arthrodesis methods, particularly if they are associated with severe osteoporosis and/or poor soft-tissue coverage. The present study aimed to report the outcomes and complications of ankle arthrodesis with circular external fixators in patients with end-stage, posttraumatic ankle arthritis, infection, and/or bone loss. Methods: Patients treated with tibiotalar and tibiocalcaneal fusion for posttraumatic sequelae using the circular external fixator between January 2001 and January 2022 were retrospectively reviewed. The outcomes were evaluated using the Catagni tibiotarsal fusion score, and the complications were recorded. Results: The study included 81 consecutive patients; 58 were males, and 23 were females. The mean age of the patients was 41.52 years (range, 18-75). Successful arthrodesis was obtained in 73 patients (90.1 %). Twenty-four patients (29.6 %) developed complications. Most complications were minor except for unacceptable deformity in four patients, refracture of the arthrodesis site in one patient, and failure of arthrodesis in seven patients. At the final evaluation, the mean Catagni Score was 85.4 (range, 52-96). Fifty-eight patients achieved excellent results, 13 patients achieved good results, two patients achieved fair results, and eight patients achieved poor results. Higher Catagni scores were associated with patients without pre-operative infection, with union, without unplanned additional surgical procedures, without complications, and with better final results (all $p < 0.001$). In the multivariate regression analyses, we observed that the Catagni score tends to decrease as patient age increases ($p = 0.010$). Catagni scores of the anterior arthrodesis position were higher than the cases of the sinus tarsi position ($p < 0.001$). Conclusion: Tibiotarsal arthrodesis with the circular external fixator can effectively treat complex ankle joint problems resulting from severe injuries. The Catagni score is a simple and reliable evaluation score after tibiotarsal arthrodesis surgeries.
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NR 24
TC 0
Z9 0
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PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
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WC Critical Care Medicine; Emergency Medicine; Orthopedics; Surgery
SC General & Internal Medicine; Emergency Medicine; Orthopedics; Surgery
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TI Tree shrew as a new animal model for musculoskeletal disorders and aging
SO BONE RESEARCH
LA English
DT Article
ID intervertebral disc degeneration; articular-cartilage; mouse models; osteoarthritis; age; depression
AB Intervertebral disc degeneration (IDD), osteoarthritis (OA), and osteoporosis (OP) are common musculoskeletal disorders (MSDs) with similar age-related risk factors, representing the leading causes of disability. However, successful therapeutic development and translation have been hampered by the lack of clinically-relevant animal models. In this study, we investigated the potential suitability of the tree shrew, a small mammal with a close genetic relationship to primates, as a new animal model for MSDs. Age-related spontaneous IDD in parallel with a gradual disappearance of notochordal cells were commonly observed in tree shrews upon skeletal maturity with no sex differences, while age-related osteoporotic changes including bone loss in the metaphyses were primarily presented in aged females, similar to observations in humans. Moreover, in the osteochondral defect model, tree shrew cartilage exhibited behavior similar to that of humans, characterized by a more restricted self-healing capacity compared to the rapid spontaneous healing of joint surfaces observed in rats. The

induced OA model in tree shrews was highly efficient and reproducible, characterized by gradual deterioration of articular cartilage, recapitulating the human OA phenotype to some degree. Surgery-induced IDD models were successfully established in tree shrews, in which the lumbar spine instability model developed slow progressive disc degeneration with more similarity to the clinical state, whereas the needle puncture model led to the rapid development of IDD with more severe symptoms. Taken together, our findings pave the way for the development of the tree shrew as a new animal model for the study of MSDs and aging.
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TI A randomized controlled trial comparing romosozumab and denosumab in elderly women with primary osteoporosis and knee osteoarthritis
SO SCIENTIFIC REPORTS
LA English
DT Article
DE Denosumab; Knee osteoarthritis; Osteophyte; Osteoporosis; Romosozumab
ID postmenopausal women; prevention; fractures; alendronate; risk
AB We compared the efficacy of romosozumab and denosumab in elderly women with primary osteoporosis and knee osteoarthritis in a randomized controlled trial. A total of 112 participants aged 75-90 years were randomized equally into the romosozumab and denosumab groups. Among these, 49 and 52 participants, respectively, who received their initial dose were included in the analysis. The primary outcome was change in lumbar spine (LS)-bone mineral density (BMD) at 12 months in the romosozumab group versus the denosumab group. Secondary outcomes were changes in knee osteophyte development, patient-reported outcomes (PROs), and the incidence of serious adverse events. Mean age of participants was 80.9 years. There was no difference in baseline LS-BMD between the two groups, with a T-score of -2.6. The mean percentage change in LS-BMD at 12 months was significantly higher in the romosozumab group (13.7%) than in the denosumab group (8.5%; p = 0.0035). No significant differences were observed in knee osteophyte development and PROs between the two groups. Serious adverse events included a case of mitral regurgitation in the romosozumab group. These findings emphasize the need for refined treatment strategies in high-risk populations, highlighting romosozumab's benefits and the need to monitor cardiovascular risks.
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TI Peptide-Oligonucleotide Nanohybrids Designed for Precise Gene Therapy of Rheumatoid Arthritis
SO ADVANCED MATERIALS
LA English
DT Article

DE bioorthogonal click reaction; cell-penetrating peptide; gene therapy; oligonucleotide; rheumatoid arthritis
ID cathepsin-k activity; delivery; osteoarthritis; mechanisms; defense
AB Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by excessive inflammation, pathological bone resorption, and systemic osteoporosis. It lacks effective treatment due to the complex pathogenesis. Gene therapy, especially targeted oligonucleotide (ON) delivery therapy, offers a new prospect for the precise treatment of RA. Nevertheless, the clinical application of ON delivery therapy still faces various challenges such as the rapid enzymolysis by RNAse, the lack of tissue targeting ability, difficulty in cell membrane penetration, and the incapability of endolysosomal escape. To address these issues, a novel kind of engineered peptide and oligonucleotide (PON) nanohybrids are designed and fabricated, which provide various advantages including good biosafety, inflammatory region-targeted delivery, cell membrane penetration, reactive oxygen species (ROS) scavenging, and endolysosomal escape. The PON nanohybrids produce promising effects in suppressing inflammatory responses and osteoclastogenesis of macrophages via multiple signaling pathways. In vivo administration of PON nanohybrids not only ameliorates local joint bone destruction and systemic osteoporosis in the pathological state, but also demonstrates good prophylactic effects against the rapid progression of RA disease. In conclusion, the study presents a promising strategy for precise RA treatment and broadens the biomedical applications of gene therapy based on delivery system.
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TI FOXC1 and FOXC2 in Osteogenesis: Emerging roles and therapeutic potential in bone regeneration and remodeling
SO EXPERIMENTAL CELL RESEARCH
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DT Review
DE FOXC1; FOXC2; Bone fracture; Osteoporosis; Osteoarthritis
ID mesenchymal stem-cells; hematopoietic stem; osteoblast differentiation; transcription factors; stromal cells; up-regulation; expression; growth; gene; naringin
AB Bone is a remarkable dynamic tissue, continually undergoing intricate processes of development, repair, and lifelong remodeling, all vital for maintaining skeletal integrity, facilitating injury recovery, and preserving overall health. Mesenchymal stem cells (MSCs) are central to these processes, characterized by their self-renewal capacity, multipotent differentiation (including osteoblasts), and crucial roles in secreting growth factors and remodeling the extracellular matrix. The highly conserved transcription factors FOXC1 and FOXC2 are crucial for correct skeletal development, profoundly influencing both intramembranous and endochondral ossification. Beyond these established developmental functions, recent evidence illuminates their critical emerging roles in actively regulating MSC osteogenic commitment and promoting osteoblastic differentiation, particularly in early cellular stages. FOXC1, for instance, orchestrates the expression of key osteogenic and chondrogenic transcription factors such as SOX9 (vital for endochondral ossification) and MSX2 (paramount in intramembranous bone formation). FOXC2, in turn, significantly contributes to osteoblast maturation through robust activation of the WNT/beta-catenin signaling pathway. Furthermore, compelling experimental studies now directly implicate FOXC1 and FOXC2 in adult bone repair, the

maintenance of bone mineral density (BMD), and the modulation of joint health. This bridges their developmental significance to substantial therapeutic potential in adult skeletal pathologies. This review comprehensively synthesizes current understanding of the developmental and emerging adult roles of FOXC1 and FOXC2 in bone biology, with a focused exploration of their underlying molecular and cellular mechanisms in osteogenesis. We also critically discuss their promising therapeutic potential in prevalent skeletal conditions such as fractures, osteoporosis, and osteoarthritis, illustrating how insights from embryonic bone formation can directly inform novel strategies for enhancing adult bone regeneration and remodeling.

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TI Skeletal progenitor LRP1 deficiency causes severe and persistent skeletal defects with Wnt pathway dysregulation
SO BONE RESEARCH
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ID receptor-related protein; planar cell polarity; growth-factor; chondrocyte differentiation; tyrosine phosphorylation; expression; catenin; degradation; cartilage; roles
AB Low-density lipoprotein receptor-related protein 1 (LRP1) is a multifunctional endocytic receptor whose dysfunction is linked to developmental dysplasia of the hip, osteoporosis and osteoarthritis. Our work addresses the critical question of how these skeletal pathologies emerge. Here, we show the abundant expression of LRP1 in skeletal progenitor cells at mouse embryonic stage E10.5 and onwards, especially in the perichondrium, the stem cell layer surrounding developing limbs essential for bone formation. Lrp1 deficiency in these stem cells causes joint fusion,

malformation of cartilage/bone template and markedly delayed or lack of primary ossification. These abnormalities, which resemble phenotypes associated with Wnt signalling pathways, result in severe and persistent skeletal defects including a severe deficit in hip joint and patella, and markedly deformed and low-density long bones leading to dwarfism and impaired mobility. Mechanistically, we show that LRP1 regulates core non-canonical Wnt/planar cell polarity (PCP) components that may explain the malformation of long bones. LRP1 directly binds to Wnt5a, facilitates its cell-association and endocytic degradation and recycling. In the developing limbs, LRP1 partially colocalises with Wnt5a and its deficiency alters abundance and distribution of Wnt5a and Vangl2. Finally, using Xenopus as a model system, we show the regulatory role for LRP1 in Wnt/PCP signalling. We propose that in skeletal progenitors, LRP1 plays a critical role in formation and maturity of multiple bones and joints by regulating Wnt signalling, providing novel insights into the fundamental processes of morphogenesis and the emergence of skeletal pathologies.

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TI Metabolic, skeletal, and cartilage effects of a high-fat diet and the therapeutic impact of MGL3196 are age- and sex-dependent in mice
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DE Type 2 diabetes; Osteoarthritis; Osteoporosis; Cortical bone; Aging; High fat diet
ID articular-cartilage; adipose-tissue; bone-marrow; obesity; fracture; mouse; osteoporosis; androgens; estrogen; mgl-3196
AB Aged individuals with type 2 diabetes (T2D) may suffer from complications of common comorbid conditions like osteoporosis or osteoarthritis. MGL3196 (MGL) is a therapeutic thyroid hormone receptor beta (TR beta) agonist that has been shown to rescue non-alcoholic steatohepatitis by enhancing lipid metabolism. In a previous study, we demonstrated that MGL treatment protected against high-fat diet (HFD)-induced adiposity but increased HFDinduced trabecular bone loss in male mice. In this study, we explored the impact of MGL treatment on adiposity, bone, and cartilage in aged-21-month-old C57BL/6J mice after a 12-week HFD regimen. Our results show that MGL reduced body weight as well as adverse effects caused by HFD adiposity, in male mice only. Aged HFD-fed male mice experienced cortical bone loss, in contrast to the trabecular bone loss observed in adult male mice. Notably, MGL treatment further exacerbated the cortical bone loss. Mechanical testing of tibias from aged male mice by 3-point bending revealed a reduced maximum load and tibia stiffness with HFD and MGL treatment. Transcriptome analyses for cortical bone formation regulators unveiled a decreased expression of Wnt16 and increased expression of the Wnt inhibitor, Sost, in the bones of HFD-fed male mice. Additionally, measurements of articular cartilage indicated that MGL treatment reduced articular cartilage degradation in both sexes, which was attributed to aging and a HFD. Our findings suggest tailored therapies are necessary to address the adverse effects of a HFD on fat, bone, and cartilage metabolism, specifically considering factors such as age and sex.
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TI Effect of Ag Nanoparticles Containing Ocimum basilicum Leaf Extract on Complete Freund Adjuvant-Induced Arthritis and Methyl Prednisolone Sodium Succinate-Induced Osteoporosis in Rats
SO APPLIED ORGANOMETALLIC CHEMISTRY
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DE Ag nanoparticles; anti-arthritis; anti-osteoporosis; <fixed-case><italic>Ocimum

basilicum</italic></fixed-case>; therapeutic supplements
ID medicinal-plants
AB In the current research, we developed and formulated an innovative therapeutic agent utilizing silver nanoparticles infused with the Ocimum basilicum leaves, aimed at addressing arthritis and osteoporosis. The AgNPs characterization was conducted using techniques such as field emission-scanning electron microscopy (FE-SEM), X-ray diffraction (XRD), ultraviolet-visible spectroscopy (UV-Vis), and transmission electron microscopy (TEM). The distinct peak observed at 448 nm in the UV-Vis spectrum indicated the successful formation of silver nanoparticles. Furthermore, the TEM and FE-SEM images revealed that these NPs were predominantly spherical (10-50 nm). The potential for anti-osteoarthritic activity was assessed in vitro through protein denaturation methods involving egg albumin and bovine serum albumin, as well as membrane stabilization techniques, utilizing several concentrations (1-1000 mu g/mL). In vivo evaluations were conducted using formaldehyde, CFA, and turpentine oil models at several doses. Additionally, the in vitro antioxidant capacity was evaluated through a reducing power assay. The findings demonstrated concentration-dependent inhibition of albumin denaturation, along with significant stabilization of RBC membranes, with optimal results achieved at 1000 mu g/mL. Similarly, the nanoparticles demonstrated the anti-osteoarthritic effect with the highest activity noted at 1 mg/kg. The CFA model findings indicated a more pronounced protective efficacy against osteoarthritic lesions and changes in body weight. Furthermore, silver NPs reduced significantly rheumatoid parameters levels, ameliorated the altered hematological factors, and positively influenced both histopathological and radiographic alterations. Additionally, silver nanoparticles showed strong antioxidant qualities. In Wistar rats, osteoporosis was induced by the combination of MPSC (10 mg/kg, subcutaneously, three times a week for 4 weeks) and silver nanoparticles (5 mu g/kg/day, oral, for 30 days). This treatment led to an elevation in serum levels of markers associated with bone mineral content, while simultaneously causing a reduction in both urinary and serum levels of bone resorption markers indicative. An increase in the tibia and femur strength was reported, especially at 5 mu g/kg of silver NPs. The mechanisms by which silver nanoparticles may counteract glucocorticoid-induced osteoporosis likely include calcium homeostasis regulation, collagen synthesis, and free radicals neutralization. Collectively, these findings endorse the conventional application of silver nanoparticles as effective agents against osteoarthritis and osteoporosis in humans.
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0268-2605
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J9 APPL ORGANOMET CHEM
JI Appl. Organomet. Chem.
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WC Chemistry, Applied; Chemistry, Inorganic & Nuclear
SC Chemistry
GA 1LD2F
UT WOS:001467614800001
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ER

PT J
AU Li, Y
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AF Li, Yan
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TI Metabolites mediate the effects of healthy lifestyles on the risks of common age-related diseases
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Article
DE healthy lifestyle; metabolites; age-related disease; diabetes; chronic diseases
ID cardiovascular-disease; diet quality; inflammation; insights; albumin; burden; score
AB Background Limited research is available on the associations between healthy lifestyles and age-related diseases, particularly those involving multiple diseases and their underlying mechanisms. We aimed to determine whether healthy lifestyles are associated with a lower likelihood of age-related diseases, and whether metabolites mediate these associations.Methods The UK Biobank data cohort was used in this study. Five lifestyle factors (diet, physical activity, sedentary behavior, sleep duration, and alcohol consumption) were combined to determine that composite lifestyle scores. Lifestyle-related metabolic signatures were analyzed using Cox proportional hazards models. We then conducted sequential analyses combining Cox regression, linear regression, extreme gradient boosting (XGBoost), and Shapley additive explanation (SHAP) values to identify metabolites associated with age-related diseases and healthy lifestyle scores. Mediation analysis was performed to investigate the potential mediating effects of the identified metabolites on age-related diseases.Results Healthy lifestyle scores contributed the most to prevention of chronic obstructive pulmonary disease (COPD) (hazard ratio [HR] [95% confidence interval (CI): 0.72 (0.71, 0.74)], followed by emphysema [HR

(95% CI): 0.75 (0.71, 0.78)]. Furthermore, intermediate or healthy lifestyles significantly decreased the age-related risk of stroke, chronic liver disease, chronic kidney disease (CKD), osteoporosis, osteoarthritis, and hypertension. Age-related diseases were associated with the top 10 metabolites, and these associations were individually or jointly mediated. For example, glycoprotein acetylation contributed 14.43% to the overall association between healthy lifestyle scores and inflammatory bowel disease (IBD), whereas low-density lipoprotein (LDL) cholesterol level attenuated this association by 2.92%, the fatty acid content based on the degree of unsaturation showed a 21.64% contribution to the association between the healthy lifestyle score and type 2 diabetes, whereas cholesterol esters in large high-density lipoproteins (HDLs) accounted for 4.57%. Sensitivity analyses verified the robustness and validity of these findings.Conclusions These findings provide a deeper understanding of the intricate relationships among lifestyle and metabolites and the development of age-related diseases.
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NR 62
TC 0
Z9 0
U1 1
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J9 FRONT ENDOCRINOL
JI Front. Endocrinol.
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
GA 9FC8Y
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Chen, Tien-Yu
TI Association between sleep duration, sleep apnea risk, and osteoporosis in older adults: a cross-sectional study in elder care institutions in Taiwan
SO BMC GERIATRICS
LA English
DT Article
DE Sleep duration; Sleep apnea; Osteoporosis; Older adults; Heart rate variability
ID heart-rate-variability; population; health; impact; women; bone
AB Background This study investigated the relationship between sleep disturbance, obstructive sleep apnea (OSA), and osteoporosis in older adults. Methods This cross-sectional study involved 326 older adults (mean age: 83.46 years) in elder care institutions in Taiwan. The presence of osteoporosis was assessed using dual-energy X-ray absorptiometry, while sleep quality and OSA risk were evaluated using the Pittsburgh Sleep Quality Index and STOP-Bang questionnaire, respectively. Heart rate variability (HRV) was measured to assess autonomic function. Logistic regression models, adjusted for age, body mass index (BMI), and comorbidities, were used to examine the associations among sleep duration, OSA risk, and osteoporosis. Results Osteoporosis was more prevalent in females and those with lower BMI and neck circumference, and less common in individuals with knee osteoarthritis. Intermediate-to-high OSA risk was associated with the male sex, higher BMI, higher neck circumference, and cardiovascular comorbidities. Short sleep duration (< 4 h) was initially correlated with a higher osteoporosis risk, but this association disappeared after adjusting for covariates. However, after adjusting for covariates, intermediate-to-high OSA risk was significantly associated with osteoporosis. HRV showed no significant difference in assessing osteoporosis or OSA risk in this study. Conclusion Short sleep duration (< 4 h) and intermediate-to-high OSA risk were associated with a higher prevalence of

osteoporosis among older adult participants, compared to those with 6-7 h of sleep or low OSA risk. Further research is required to explore the relationship between sleep and osteoporosis in older adults.
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NR 30
TC 0
Z9 0
U1 0
U2 0
PU BMC
PI LONDON
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EI 1471-2318
J9 BMC GERIATR
JI BMC Geriatr.
PD NOV 6
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WC Geriatrics & Gerontology; Gerontology
SC Geriatrics & Gerontology
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PT J
AU Li, XY
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AF Li, Xiaoying
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TI Role and mechanism of Integrin α5β1 in bone formation and disease
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE integrin alpha 5 beta 1; bone formation; osteoporosis; osteoarthritis; bone metastasis
ID peptide atn-161 ac-phscn-nh2; mesenchymal stromal cells; skeletal development; stem-cells; cancer; adhesion; metastasis; expression; cartilage; binding
AB Integrin alpha 5 beta 1 is a key signaling protein between cells and the extracellular matrix. It plays crucial roles in biological processes such as cell adhesion, migration, and differentiation. Recent studies have shown that integrin alpha 5 beta 1 is significantly involved in bone formation and related diseases. Integrin alpha 5 beta 1 participates in the differentiation of mesenchymal stem cells into osteoblasts. It interacts with the CCN family and the bone morphogenetic protein pathway to upregulate the expression of osteogenic markers, promoting the formation of mineralization nodules. Additionally, it can mediate mechanical force stimulation to upregulate osteogenic gene expression and promote bone formation. In diseases such as osteoporosis, osteoarthritis, and bone metastasis, integrin alpha 5 beta 1 mediates abnormal cell-matrix adhesion and migration, promoting pathological bone resorption and inhibiting bone formation, thereby exacerbating bone loss. Therefore, integrin alpha 5 beta 1 may be a potential therapeutic target for these bone diseases. Elucidating its mechanism of action will

help understand the homeostatic regulation of bone metabolism and provide ideas for the development of novel therapeutic strategies for skeletal diseases.
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TI Lactylation Dynamics and Its Regulatory Roles in Orthopedic Pathologies: A Research Update
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DT Review
DE lactylation; intervertebral disc degeneration; osteoporosis; osteoarthritis; spinal cord injury
ID activation; lactate; promotes; differentiation; osteoblast; cells; rat
AB Post-translational modifications (PTMs) dynamically regulate cellular processes by modifying protein function. Among these, lactylation, a modification derived from lactate, functions through direct or indirect modification of histones or

nonhistone proteins. While glycosylation and phosphorylation have established roles in bone metabolism and joint disorders, the biological significance of lactylation in musculoskeletal diseases remains underexplored. This study synthesizes current evidence investigating lactylation in four major orthopedic diseases: intervertebral disc degeneration (IVDD), osteoporosis (OP), osteoarthritis (OA), and spinal cord injury (SCI). The evidence indicates that lactylation modulates disease progression through dual mechanisms: coordinating cellular metabolism with extracellular matrix remodeling in IVDD and OA and regulating neuroimmune responses during SCI recovery. Notably, lactylation's regulatory patterns differ from classical PTMs by serving as a molecular bridge linking metabolic reprogramming to pathological tissue remodeling. This contrasts with phosphorylation, which primarily dominates signal transduction pathways. These insights reposition lactate from a metabolic byproduct to a disease-modifying signaling molecule, suggesting lactylation could inform therapeutic strategies for inflammatory, degenerative, and regenerative musculoskeletal disorders.
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NR 97
TC 0
Z9 0
U1 6
U2 6
PU AMER CHEMICAL SOC
PI WASHINGTON
PA 1155 16TH ST, NW, WASHINGTON, DC 20036 USA
SN 1535-3893
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J9 J PROTEOME RES
JI J. Proteome Res.
PD NOV 7
PY 2025
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IS 11
BP 5319
EP 5328
DI 10.1021/acs.jproteome.5c00714
EA OCT 2025
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WC Biochemical Research Methods
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UT WOS:001596006700001
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ER

PT J
AU Ma, J
Gong, D
Chen, XT
AF Ma, Jun
Gong, Dong
Chen, Xiaotao
TI Ophiopogonin D Attenuates Mitochondrial Dysfunction in Chondrocytes via Nrf2

Signaling to Ameliorate Osteoarthritis
SO JOURNAL OF HARD TISSUE BIOLOGY
LA English
DT Article
DE Ophiopogonin D; Osteoarthritis; Chondrocytes; Mitochondrial dysfunction; Nrf2 signaling
AB Osteoarthritis (OA) is a progressive joint disorder characterized by cartilage degradation, inflammation, and chondrocyte dysfunction, with mitochondrial dysfunction and oxidative stress being central to its pathogenesis. The Nrf2 pathway is vital for maintaining redox homeostasis and mitochondrial integrity. This study investigated the protective effects of Ophiopogonin D (OP-D), a natural saponin compound, on IL-1(3-induced chondrocyte injury in vitro. Using C28/I2 cells, we demonstrated that OP-D restored cell viability and reduced the secretion of proinflammatory cytokines following IL-1(3 exposure. OP-D also alleviated mitochondrial dysfunction by decreasing mitochondrial ROS production and preserving mitochondrial membrane potential. Furthermore, OP-D mitigated extracellular matrix degradation. Mechanistically, OP-D activated the Keap1/Nrf2 pathway. These findings suggest that OP-D exerts chondroprotective effects by improving mitochondrial function and maintaining ECM integrity via Nrf2 pathway activation, highlighting its therapeutic potential for the treatment of osteoarthritis.
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NR 19
TC 0
Z9 0
U1 0
U2 0
PU JOURNAL HARD TISSUE BIOLOGY
PI MINATO KU
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SC Engineering
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PT J
AU Jiang, ZQ
Wang, KX
Zhang, HD
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Liu, XN
AF Jiang, Ziqi
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Weng, Yuanzhi
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Liu, Xiaoning
TI Correlation between paraspinal muscle fat infiltration and thoracic vertebral degeneration based on phantom-less QCT: a novel insight into thoracic vertebral degeneration
SO EUROPEAN SPINE JOURNAL
LA English
DT Article
DE Fat infiltration; Bone mineral density; Phantom-less quantitative computed tomography; Thoracic vertebral degeneration; Paraspinal muscles
ID lumbar; tomography; herniations; pain
AB Purpose This study aimed to elucidate the correlation between the degree of fat infiltration (FI) in thoracic paraspinal muscles and thoracic vertebral degeneration (TVD). Methods This cross-sectional study comprised 474 patients who underwent standard thoracic computed tomography (CT) scans. The FI was quantified as the percentage of adipose tissues within the cross-sectional area of thoracic paraspinal muscles. Thoracic vertebra was assessed in terms of osteoporosis, ossification of the anterior longitudinal ligament (OALL), ossification of the posterior longitudinal ligament (OPLL), intervertebral disc calcification, intervertebral disc cavity, and facet joint osteoarthritis (FJO). Logistic regression, linear regression, subgroup, and receiver operating characteristic (ROC) analyses were assessed to evaluate the association between FI and TVD. Results Multivariate logistic regression revealed that more severe FI was closely associated with more serious osteoporosis ($P < 0.001$). Furthermore, after adjusting for only age, higher FI was significantly associated with nastier FJO ($P < 0.05$). In male patients, severe FI was greatly associated with worse osteoporosis ($P < 0.05$). In female patients, severe FI maintained close correlations with more severe osteoporosis and FJO ($P < 0.05$). Furthermore, in patients aged < 60 or >= 60 years, higher FI had a strong correlation with more severe osteoporosis ($P < 0.001$). In patients aged < 60 years, higher FI was associated with worse intervertebral disc calcification, OALL, and FJO ($P < 0.05$). Meanwhile, in patients aged >= 60 years, increased FI was only associated with severe OPLL ($P < 0.05$). Multivariate linear regression showed that FI negatively correlated with bone mineral density in the general population and different sex and age groups ($P < 0.001$). ROC analysis indicated that FI could predict the occurrence of TVD ($P < 0.05$). Conclusion Higher FI is associated with more severe TVD. Studies on TVD are currently limited; therefore, this study enriches the related research on TVD, and our findings would facilitate the early prediction and diagnosis of TVD in clinical practice. Furthermore, our findings indicate that thoracic spine pain (TSP) caused by TVD can be prevented, potentially improving the prognosis of patients with TSP.

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NR 44
TC 4
Z9 6
U1 6
U2 13
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 EUR SPINE J

JI Eur. Spine J.
PD MAR 15
PY 2025
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IS 3
BP 837
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DI 10.1007/s00586-025-08645-y
EA JAN 2025
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WC Clinical Neurology; Orthopedics
SC Neurosciences & Neurology; Orthopedics
GA 0DP3C
UT WOS:001396490200001
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PT J
AU Li, ZC
Cheng, WX
Gao, KH
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AF Li, Zhichao
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Gao, Kuanhui
Liang, Songlin
Ke, Liqing
Wang, Mengjie
Fan, Jilin
Li, Dandan
Zhang, Peng
Xu, Zhanwang
Li, Nianhu
TI Pyroptosis: A spoiler of peaceful coexistence between cells in degenerative bone and joint diseases
SO JOURNAL OF ADVANCED RESEARCH

LA English
DT Article
DE Pyroptosis; Bone and joint diseases; Osteoporosis; Osteoarthritis; Intervertebral disc degeneration
ID intervertebral disc degeneration; nucleus pulposus cells; nlrp3 inflammasome activation; mesenchymal stem-cells; tumor-necrosis-factor; nerve growth-factor; interleukin-1 receptor antagonist; stimulates osteoclast formation; vertebral end-plates; kappa-b pathway
AB Background: As people age, degenerative bone and joint diseases (DBJDs) become more prevalent. When middle-aged and elderly people are diagnosed with one or more disorders such as osteoporosis (OP), osteoarthritis (OA), and intervertebral disc degeneration (IVDD), it often signals the onset of prolonged pain and reduced functionality. Chronic inflammation has been identified as the underlying cause of various degenerative diseases, including DBJDs. Recently, excessive activation of pyroptosis, a form of programed cell death (PCD) mediated by inflammasomes, has emerged as a primary driver of harmful chronic inflammation. Consequently, pyroptosis has become a potential target for preventing and treating DBJDs. Aim of Review: This review explored the physiological and pathological roles of the pyroptosis pathway in bone and joint development and its relation to DBJDs. Meanwhile, it elaborated the molecular mechanisms of pyroptosis within individual cell types in the bone marrow and joints, as well as the interplay among different cell types in the context of DBJDs. Furthermore, this review presented the latest compelling evidence supporting the idea of regulating the pyroptosis pathway for DBJDs treatment, and discussed the potential, limitations, and challenges of various therapeutic strategies involving pyroptosis regulation. Key Scientific Concepts of Review: In summary, an interesting identity for the unregulated pyroptosis path-way in the context of DBJDs was proposed in this review, which was undertaken as a spoiler of peaceful coexistence between cells in a degenerative environment. Over the extended course of DBJDs, pyroptosis pathway perpetuated its activity through crosstalk among pyroptosis cascades in different cell types, thus exacerbating the inflammatory environment throughout the entire bone marrow and joint degeneration environment. Correspondingly, pyroptosis regulation therapy emerged as a promising option for clinical treatment of DBJDs. (c) 2024 The Authors. Published by Elsevier B.V. on behalf of Cairo University This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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TI Beyond Structure: The Interplay of Bone and Brain During Alzheimer's Disease
SO COMPREHENSIVE PHYSIOLOGY
LA English
DT Review
DE Alzheimer's disease; dementia; osteoarthritis; osteoporosis
ID hip fracture risk; vitamin-d; cognitive impairment; mineral density; transgenic mice; cigarette-smoking; dementia; association; metaanalysis; increases
AB Alzheimer's disease (AD), a leading cause of dementia in the elderly, is traditionally characterized by neurodegeneration driven by amyloid-beta plaques and tau tangles. However, emerging evidence reveals that AD's impact extends beyond the brain, significantly affecting skeletal health. This review integrates clinical and transgenic mouse model data to elucidate the mechanistic interplay between AD pathology and bone metabolism. AD patients exhibit increased risk for hip fractures and low bone mineral density (BMD), independent of cognitive impairment severity. We found altered calcium and alkaline phosphate levels in the blood of patients with mild cognitive impairment and AD, as assessed from the Alzheimer's Disease Neuroimaging Initiative data. Convergent risk factors-age, sex, APOE4 genotype, smoking, and vitamin D deficiency-contribute to both neurodegeneration and bone fragility. Key molecular pathways, such as Wnt/beta-catenin signaling and TREM2-mediated osteoclast regulation, underscore shared mechanisms driving disease pathology in both systems. Mouse models of AD consistently demonstrate disrupted bone remodeling, impaired osteoblast

function, and heightened osteoclast activity. Therapeutic strategies targeting overlapping pathways, including lithium, anti-FSH antibodies, and NF-kappa B inhibitors, show promise in mitigating both cognitive decline and bone loss. Collectively, these insights advocate for a more integrated view of AD that includes skeletal comorbidities, potentially guiding the development of dual-purpose interventions.
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TI The research progress and potential applications of n-3 fatty acids in orthopaedics: a narrative review
SO BRITISH JOURNAL OF NUTRITION
LA English
DT Review
DE <italic>n</italic>-3 PUFA; Nutrition; Orthopaedics; Health benefits; Anti-inflammatory
ID alpha-linolenic acid; docosahexaenoic acid; omega-3 supplementation; cardiovascular-disease; eicosapentaenoic acid; rheumatoid-arthritis; omega-3-fatty-acids; management; oil; fish
AB n-3 PUFA, including ALA, EPA and DHA, are widely found in plant oils and marine organisms. These fatty acids demonstrate significant biological effects, and their adequate intake is essential for maintaining health. However, modern diets often lack sufficient n-3 PUFA, especially among populations that consume little fish or seafood, leading to a growing interest in n-3 PUFA supplementation in nutrition and health research. In recent decades, the role of n-3 PUFA in preventing and treating various diseases has gained increasing attention, particularly in cardiovascular, neurological, ophthalmic, allergic, hepatic and oncological fields. In

orthopaedics, n-3 PUFA exert beneficial effects through several mechanisms, including modulation of inflammatory responses, enhancement of cartilage repair and regulation of bone metabolism. These effects demonstrate potential for the treatment of conditions such as osteoarthritis, rheumatoid arthritis, gout, osteoporosis, fractures, sarcopenia and spinal degenerative diseases. This review summarises the clinical applications of n-3 PUFA, with a focus on their research progress in the field of orthopaedics, and explores their potential in the treatment of orthopaedic diseases.
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TI 3D bioprinting bone/cartilage organoids: construction, applications, and challenges
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DE 3D bioprinting; Bone/cartilage organoids; Regenerative medicine
ID therapeutic targets; bone; bioinks; systems; niche
AB Orthopaedic disorders, such as osteoporosis and osteoarthritis, impose

substantial suffering upon an increasing population, driving demand for accurate disease models. Bone/cartilage organoids offer a promising solution by replicating complex 3D microstructures and multi-cellular niches, overcoming limitations of 2D models and animal experiments. 3D bioprinting, an additive manufacturing technology, enables the spatially precise deposition of cells and bioactive materials, facilitating efficient construction of organoids with enhanced structural fidelity. Therefore, this review specifically focuses on bone and cartilage organoids constructed using 3D bioprinting technologies. We summarize the prevailing 3D bioprinting techniques and biomaterials employed, critically analyze the unique advantages of bioprinting for creating these organoids, explore current technical challenges, such as standardization and scalability, and discuss future research directions. By addressing current progress and key issues in bioprinting bone/cartilage organoids, this review aims to accelerate their standardization and application as powerful platforms for multiscale disease modeling, drug screening, and regenerative medicine strategies. The translational potential of this article: Bone/cartilage organoids constructed via 3D bioprinting, through precise recapitulation of bone and cartilage tissue microenvironment and physiology, enable multiscale disease modeling from localized pathologies to systemic responses, despite persisting unresolved challenges in reproducibility and stability. This review highlights their clinical translational value and elucidates the driven role of 3D bioprinting in accelerating their clinical adoption, particularly in regenerative medicine.
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PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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JI J. ORTHOP. TRANSL.
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AU Zhou, HL
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AF Zhou, Hao-long
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TI Unhealthy lifestyles accelerated aging and consequential musculoskeletal morbidity
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Composite unhealthy lifestyle; Aging acceleration; Musculoskeletal disorders; Mediation
ID osteoporosis; metaanalysis; smoking; fruit; risk
AB IntroductionFew studies assessed comprehensive effects of composite unhealthy lifestyles on aging and musculoskeletal health. This study aimed to address such issues with the UK Biobank datasets.Materials and methodsAn unhealthy lifestyle score (UHLS) was constructed based on 9 lifestyle behaviors. Aging indicators were calculated from 18 clinical traits. General linear and Cox proportional hazards regression models were used to analyze associations between UHLS, aging, and musculoskeletal morbidity. Mendelian randomization (MR) analysis was performed for causal relationship exploration.ResultsAmong 396,037 participants, 54.5% and 3.3% of them were designated to the low (scored 0-2) and high UHLS (scored 6-9) groups, respectively. Increasing UHLS was associated with elevated aging acceleration (AA) based on biological age (0.343 per unit; 95% CI: 0.331, 0.355) and phenotypic age (AA_PA) (0.408 per unit; 95% CI: 0.394, 0.422), and higher morbidity of low grip strength (HR = 1.025; 95% CI: 1.001, 1.050), slow walking pace (HR = 1.134; 95% CI: 1.074, 1.198), osteoporosis (HR = 1.077; 95% CI: 1.063, 1.091), fracture (HR = 1.059; 95% CI: 1.048, 1.069) and osteoarthritis (HR = 1.036; 95% CI: 1.030, 1.042). Unhealthy lifestyles in conjunction with AA jointly increased musculoskeletal morbidity. Besides, AA mediated UHLS effects on slow walking pace, osteoporosis and fracture, with mediating proportion of 4.85%-12.79%. MR analyses revealed causal relationships between UHLS and low grip strength, osteoarthritis, and reduced femoral neck bone mineral density. In addition, AA_PA suggestively mediated the UHLS-osteoarthritis association.ConclusionsComposite unhealthy lifestyles accelerate aging and impair musculoskeletal health. Both mediating and joint effects of AA showed unhealthy lifestyle-associated musculoskeletal morbidity.
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SC Endocrinology & Metabolism; Research & Experimental Medicine
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AU Liu, Y
Wang, W
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AF Liu, Yu
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Yang, Yusheng
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TI Vitamin D and bone health: from physiological function to disease association
SO NUTRITION & METABOLISM
LA English
DT Review
DE Vitamin D; Bone destruction diseases; Immunoregulation
ID d deficiency; mineral density; mendelian randomization; rheumatoid-arthritis; knee osteoarthritis; 25-hydroxyvitamin d; d supplementation; polymorphisms; metaanalysis; calcium
AB Vitamin D (VD) is a pleiotropic secosteroid hormone with well-established roles in calcium homeostasis, bone metabolism, and emerging functions in immune regulation, inflammation, and chronic disease modulation. In this paper, we provide a comprehensive summary of the current research on the significance of VD for bone health, with emphasis on its mechanism of action and its clinical significance in bone health. This review starts with an overview of VD metabolism, with emphasis on the enzyme transformation of vitamin D3 (VD3) and vitamin D2 (VD2) into the active 1,25-dihydroxyvitamin D (1 alpha,25(OH)2D) and their genomic and non-genomic signaling pathways through the Vitamin D receptor (VDR). Then, we

discuss how VDR polymorphisms affect disease susceptibility and the dual role of VD in promoting innate immunity as well as inhibiting over-adaptive immunity. Our main focus is placed on VD's involvement in bone destruction diseases, including osteoarthritis (OA), osteoporosis (OP), rheumatoid arthritis (RA), and bone tuberculosis. For OA, there is conflicting evidence on whether VD supplementation reduces cartilage degradation or pain. In OP, vitamin D deficiency aggravates bone loss, but the effectiveness of supplementation is dependent on baseline and calcium supplementation. For RA, the immunomodulatory effects of VD may decrease the activity of the disease, whereas in tuberculosis, VD increases the clearance of macrophage-mediated mycobacterial clearance, although the clinical study data are still inconclusive. This review underscores VD as a critical mediator of bone-immune crosstalk while calling for rigorous translational research to clarify its therapeutic potential across diverse diseases.
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TI Maternal high-fat high-sugar diet impairs bone quality and strength but not cartilage in aging mice
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article
DE developmental origins of health and disease (DOHaD); developmental programming; intergenerational; musculoskeletal; osteoporosis
ID pericellular matrix; birth-weight; micromechanical property; mitochondrial dysfunction; primordial follicles; oocyte quality; obesity; mouse; mass; osteoarthritis
AB Osteoarthritis (OA) is a prevalent aging disorder of synovial joints and recent work suggests that a parental high-fat diet increases OA severity following joint injury in offspring. We hypothesized that a maternal high-fat high-sugar (HFHS) diet would promote spontaneous osteoarthritis-related cartilage and bone changes in 1-year-old offspring. Female C57BL/6 J mice were placed on either a chow control or HFHS diet for 6 weeks before mating to a chow-fed C57BL/6 J male and maintained on their assigned diets throughout pregnancy and lactation. Male and female offspring were weaned onto a chow diet, raised to 1 year of age, and evaluated for cartilage and bone changes indicative of OA. However, offspring did not show early signs of OA as measured by histological Mankin scoring, mechanical testing of the pericellular matrix, histological synovitis scoring, or subchondral bone thickening as measured by microcomputed Tomography. On the other hand, male offspring from HFHS-fed dams had reduced trabecular bone quality in the tibial metaphysis and decreased cortical thickness. Although maternal HFHS diet did not impact trabecular or cortical bone quality in tibias of female offspring, the radii of these animals had decreased cortical thickness, increased medullary area, and impaired breaking strength compared to those of control-fed dams. Finally, we evaluated bone quality and strength in male and female F2 offspring and found that the grandmaternal diet modestly impacted radial bone geometry but not strength. Together these results suggest that maternal HFHS diet impairs F1 offspring skeletal integrity in a sex and bone site-specific manner.
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TI Additional cartilage treatment for small defects in chronic ankle instability shows no mid-term benefit and delays recovery: a randomized controlled trial
SO JOURNAL OF ORTHOPAEDICS AND TRAUMATOLOGY
LA English
DT Article
DE Ankle joint; Ankle injuries; Lateral ligament; Ankle; Subchondral; Osteoarthritis; Randomized controlled trial; Cartilage diseases; Arthroscopy; Joint instability
ID lateral ligament injury; quality-of-life; osteochondral lesions; arthroscopic findings; follow-up; physical-activity; repair; talus; health; reconstruction
AB Background The presence of chondral lesions in patients with chronic ankle instability is common and has been suggested as a possible cause of persistent pain in some cases, even after successful ligament reconstruction. For this reason, some authors have proposed combining ankle stabilization with cartilage microfracture; however, the results reported in literature are contradictory. Materials and methods The study was designed as a prospective randomized clinical study with two parallel arms. Patients with an anterior talofibular ligament tear causing pain and instability, associated with a Berndt-Harty stage I-IIb talar osteochondral lesion of < 150 mm2 that had not responded to conservative treatment, were blindly assigned to either isolated ligament reconstruction (REC) or reconstruction plus microfracture (REC +MIC). Evaluators were also blinded. Results A total of 71 patients were included in the study, with 36 in the REC group and 35 in the REC +MIC group. The groups were comparable in terms of anthropometry and pathology. The operating time was significantly longer in the REC +MIC group (48.0 +/- 4.5 min) compared with the REC group (24.9 +/- 3.9 min; p < 0.001). At the end of follow- up, both patient groups showed similar results on the American Orthopaedic Foot and Ankle Society (AOFAS) score (p = 0.755), Self-Reported Foot and Ankle Score (SEFAS) (p = 0.862), Karlsson score (p = 0.993), and visual analog scale (VAS) (p = 0.870). However, the time to recovery differed between the groups, with patients in the REC group recover- ing faster from before the operation (pre-op) through the third month after the operation (post-op).The difference in recovery at 3 months post-op was statistically significant on the AOFAS (p < 0.001),

SEFAS ($p < 0.001$), and Karls- son ($p < 0.001$) scores. No statistically significant difference was observed in terms of pain ($p = 0.342$).The failure rate was also comparable between the groups, with four (11.1%) reoperations in the REC group and five (14.3%) in the REC +MIC group ($p = 0.735$). Conclusions At 2 years post surgery, no differences were observed in function (according to the AOFAS, SEFAS, and Karlsson scores), pain, or complications in patients with ankle instability and associated chondral damage treated with or without microfractures. However, patients who underwent microfractures experienced a significantly slower recovery of function. Level of evidence: Level 1. Trial registration: ClinicalTrials.gov Identifier NCT06947317 (retrospectively registered). Date: 1 May 2025. (https:// clini caltrials.gov/study/NCT06947317).

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TI Denosumab attenuates knee osteoarthritis progression by inhibiting synovial inflammation via the RANK/TRAF6/FSTL1 signalling
SO NATURE COMMUNICATIONS
LA English
DT Article
ID cartilage degradation; biochemical markers; bone; arthritis; cells; model; pathophysiology; histopathology; identification; risedronate
AB Synovitis has recently been shown to be a critical early stage in development of osteoarthritis (OA), and inhibiting synovitis significantly alleviates OA symptoms. Denosumab, a monoclonal antibody targeting RANKL, previously developed for osteoporosis. Here, we report the effect of denosumab on fibroblast-like synoviocytes (FLSs), attenuating synovitis and consequently OA progression. We first demonstrate that RANKL is highly expressed in the knee synovium of OA mice, as well as in patients. Next, we show that denosumab, injected systemically, accumulates in the synovium and effectively reduces synovitis through RANK/TRAF6/FSTL1 signalling in post-traumatic, inflammatory, and aged OA murine models and a beagle dog OA model, delaying OA progression. Finally, a single-arm clinical trial with primary endpoints of VAS and OKS scores, and secondary endpoints of WOMAC score and adverse events rate, shows that denosumab alleviates synovitis and pain, improving joint function in knee OA patients. These findings provide a translational basis for using denosumab to treat knee OA in the clinic.
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TI Osteoarthritis risk associated with romosozumab compared with teriparatide in individuals with osteoporosis: a target trial emulation study
SO ANNALS OF THE RHEUMATIC DISEASES
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DT Article
ID postmenopausal women; subchondral bone; sclerostin; cartilage; knee; hip; outcm; spine; oa
AB Objectives: To compare osteoarthritis among individuals with osteoporosis initiating romosozumab vs an active comparator. Methods: This new user comparative effectiveness study, emulating a target trial, included individuals aged >= 50 years in the administrative claims database from 2019 to 2022. Individuals who initiated romosozumab were compared with those who initiated teriparatide. The primary outcome was the incidence of osteoarthritis, while secondary outcomes included joint-specific osteoarthritis (knee, hip, and hand) at 1 year. Inverse probability of treatment weighting (IPTW) was applied to balance baseline characteristics between romosozumab and teriparatide users, and inverse probability of censoring weighting (IPCW) was employed to account for informative censoring. Absolute risk reduction (ARR) and relative risk (RR) at 1 year were estimated using a weighted Kaplan-Meier estimator. Results: A total of 22,145 individuals were included in the study (87% female; mean age, 80 years). After IPTW-IPCW adjustment, romosozumab was associated with a lower risk of osteoarthritis compared with teriparatide (ARR, 1.1% [95% CI, 0.5%-1.8%]; RR, 0.79 [0.66, 0.89]). Joint-specific analyses showed the following results: knee osteoarthritis: ARR, 0.8% (95% CI, 0.3%-1.5%), RR, 0.79 (0.66, 0.92); hip osteoarthritis: ARR, 0.2% (95% CI, 0.0%0.5%), RR, 0.68 (0.37, 1.05); and hand osteoarthritis: ARR, 0.2% (95% CI, 0.0%-0.4%), RR, 0.61 (0.35, 1.06). Conclusions: Romosozumab was associated with a lower risk of osteoarthritis than teriparatide among individuals with osteoporosis, particularly for knee osteoarthritis. Similar trends were observed for hip and hand osteoarthritis; however, the differences were not significant.

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TI Progress in the application of epimedium and its major bioactive components in the treatment of orthopedic diseases
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE epimedium; orthopedic diseases; target; enrichment analysis; pathway
ID herba-epimedii; neuromuscular-junction; inflammatory markers; osteoclast formation; signaling pathway; muscle atrophy; bone loss; in-vivo; osteoporosis;

icariin
AB Epimedium brevicornu (Yin Yang Huo), a widely used traditional Chinese medicinal ingredient, has garnered significant attention for its role in treating orthopedic diseases such as osteoporosis. Our work through network pharmacology and bioinformatics analysis, we identified that out of 27 major active components in Epimedium brevicornu, 8 key components have therapeutic effects on 11 types of diseases related to orthopedic conditions. The disease-target association analysis indicated that Osteoarthritis, Osteoporosis, Muscle Spasm and Myopathy have relatively clear targets for disease treatment. The KEGG enrichment analysis results indicate that the signaling pathway of Epimedium treatment in Osteoarthritis may be closely related to the Lipid and atherosclerosis pathway, PPAR signaling pathway and Arachidonic acid metabolism. Epimedium may treat osteoporosis with Nitrogen metabolism, GABAergic synapse, and Pathways in cancer. Epimedium may affect muscle spasticity through Neuroactive ligand-receptor interaction, Serotonergic synapse and Cholinergic synapse closely related to nervous system function; Additionally, our analysis suggests that Epimedium may treat myopathy through Nitrogen metabolism and GABAergic synapse pathways. These studies have not only provided a molecular mechanism-based explanation for the pharmacological effects of Epimedium, but also laid a theoretical foundation for the development of Epimedium-based precision therapeutic regimens.
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TI Immunotherapies for Aging and Age-Related Diseases: Advances, Pitfalls, and Prospects
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AB Aging is characterized by a gradual decline in the functionality of all the organs and tissues, leading to various diseases. As the global population ages, the urgency to develop effective anti-aging strategies becomes increasingly critical due to the growing severity of associated health problems. Immunotherapy offers novel and promising approaches to combat aging by utilizing approaches including vaccines,

antibodies, and cytokines to target specific aging-related molecules and pathways. In this review, we summarize the recent advancements of immunotherapies to eliminate senescence cells and senescence-associated secretory phenotypes (SASPs). Next, we describe immunotherapies against age-related diseases containing neurodegenerative diseases, vascular pathologies, type 2 diabetes (T2D), arthritis, osteoporosis, chronic obstructive pulmonary disease (COPD), fibrosis, skin aging, and cancer, detailing the targets, corresponding manipulations, and clinical trials. Related problems including immunosenescence, serious adverse effects, the duality of function of senescent cells and SASPs, and inherent problems of immunotherapy are also discussed, suggesting directions for improvement. In addition to recent development and challenges in the field, we describe a blueprint of personalized aging immunotherapy by multi-omics, Big Data, artificial intelligence (AI), and nanobots in the future, aiming to inspire the development of novel strategies for healthy aging.
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TI Automated Fast Prediction of Bone Mineral Density From Low-dose Computed Tomography
SO ACADEMIC RADIOLOGY
LA English
DT Article
DE Bone mineral density; Convolutional neural network; Osteoporosis
ID osteoporosis
AB Background: Low-dose chest CT (LDCT) is commonly employed for the early screening of lung cancer. However, it has rarely been utilized in the assessment of volumetric bone mineral density (vBMD) and the diagnosis of osteoporosis (OP). Purpose: This study investigated the feasibility of using deep learning to establish a system for vBMD prediction and OP classification based on LDCT scans. Methods: This study included 551 subjects who underwent both LDCT and QCT examinations. First, the U-net was developed to automatically segment lumbar vertebrae from single 2D LDCT slices near the mid-vertebral level. Then, a prediction model was proposed to estimate vBMD, which was subsequently employed for detecting OP and osteopenia (OA). Specifically, two input modalities were constructed for the prediction model. The performance metrics of the models were calculated and evaluated. Results: The segmentation model exhibited a strong correlation with manual segmentation, achieving a mean Dice similarity coefficient (DSC) of 0.974, sensitivity of 0.964, positive predictive value (PPV) of 0.985, and Hausdorff distance of 3.261 in the test set. Linear regression and Bland-Altman analysis demonstrated strong agreement between the predicted vBMD from two-channel inputs and

QCTderived vBMD, with a root mean square error of 8.958 mg/mm3 and an R2 of 0.944. The areas under the curve for detecting OP and OA were 0.800 and 0.878, respectively, with an overall accuracy of 94.2%. The average processing time for this system was 1.5 s. Conclusion: This prediction system could automatically estimate vBMD and detect OP and OA on LDCT scans, providing great potential for the osteoporosis screening.
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AU Li, ZH
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AF Li, Zihan
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TI Role of NEL-like molecule-1 in osteogenesis/chondrogenesis (Review)
SO INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE
LA English
DT Review
DE NELL-1; bone diseases; osteogenesis; bone tissue engineering
ID perivascular stem-cells; craniosynostosis-associated gene; marrow stromal cells; spinal-fusion; bone regeneration; osteogenic differentiation; pegylated nell-1; chondrogenic differentiation; controlled-release; protein-1 nell-1
AB A dynamic balance exists between osteogenesis and osteoclastogenesis in bone tissue, which can lead to several bone diseases, such as osteoporosis, osteoarthritis, bone necrosis and bone defects, in cases of insufficient osteogenesis or excessive osteoclastogenesis. NEL-like molecule-1 (NELL-1) was first discovered in 1999 as an osteogenic factor that can prevent or treat bone diseases by increasing osteogenic levels. To date, research has identified multiple signaling pathways involved in improving osteogenic levels. Furthermore, to apply NELL-1 in clinical practice, researchers have optimized its osteogenic effect by combining it with other molecules, changing its molecular structure and performing bone tissue engineering. Currently, research on NELL-1 is gaining increasing attention. In the near future, it will definitely be applied in clinical practice to eliminate diseases. Thus, the present study provides a comprehensive review of NELL-1 in enhancing osteogenic levels from the perspectives of the molecular mechanism, interactions with other molecules/cells, molecular-level changes, applications in bone tissue engineering and its expression in tumors, providing a solid theoretical basis for its clinical application.
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TI Risk factors for non-union in foot and ankle arthrodesis: a population-based case-control study using registry data
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Ankle arthrodesis; Foot arthrodesis; Risk factor; Nonunion
ID bone; osteoporosis
AB BackgroundNonunion is a common complication following foot and ankle arthrodesis. This study endeavoured to determine the risk factors for nonunion in foot and ankle arthrodesis.MethodsThis was a retrospective case-control study using the National Health Insurance Research Database. Patients who underwent foot and ankle arthrodesis with a minimum follow-up duration of 6 months were included. International Classification of Diseases codes were used to identify diagnoses and treatment. Patients with nonunion were matched by age and sex with patients with union at a ratio of 1:4. Logistic regression was performed to compare between patients with nonunion and controls with union to ascertain the effects of various risk factors.ResultsA total of 107 joints were identified as nonunion, and 428 age- and sex-matched controls were selected. Patients with

diabetes mellitus had a 1.710 times (95% CI = 1.060 - 2.756, p = 0.0278) higher risk of nonunion than those without. No significant differences were observed in the risk of nonunion in relation to which joint was treated; the presence of osteoarthritis, traumatic osteoarthritis, rheumatoid arthritis, osteoporosis, or open/arthroscopic arthrodesis; internal or external fixation; or the usage of a bone graft. For patients without diabetes mellitus, those who underwent arthrodesis in the tarsometatarsal joint had a 6.507 times (95% CI: 1.045 - 40.522, p = 0.0256) higher risk of nonunion compared to those who underwent arthrodesis in the ankle joint.ConclusionDiabetes mellitus increases the risk of nonunion among patients with and without diabetes mellitus. For those without diabetes mellitus, arthrodesis in the tarsometatarsal joint is associated with the highest risk of nonunion.
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NR 19
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Z9 1
U1 0
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JI BMC Musculoskelet. Disord.
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TI Bidirectional Regulatory Mechanisms of Disulfidptosis Govern Precision Targeting in Degenerative Bone Diseases and Osteosarcoma
SO JOURNAL OF CELLULAR PHYSIOLOGY
LA English
DT Review
DE disulfidptosis; immunometabolism; orthopedic degenerative diseases; osteosarcoma; targeted therapy
ID osteoarthritis; apoptosis; cells; microenvironment; prognosis
AB Disulfidptosis is a newly identified form of programmed cell death closely associated with cystine metabolism abnormalities and cytoskeletal damage. Orthopedic diseases, such as degenerative conditions including intervertebral disc degeneration, osteoporosis, osteoarthritis, and malignant bone tumors like osteosarcoma, all involve imbalances in the immunometabolic microenvironment. The triggering conditions for disulfidptosis, such as high expression of SLC7A11 and glucose deprivation, are highly correlated with the pathaological features of orthopedic diseases and associated immune dysregulation. However, there is currently a lack of systematic understanding regarding the regulatory networks, molecular markers, and intervention strategies of disulfidptosis in orthopedic diseases, and the specific mechanisms by which it contributes to disease onset and progression remain unclear. This review systematically summarizes the bidirectional immunometabolic regulatory molecular mechanisms, pathological associations, and potential therapeutic strategies of disulfidptosis in orthopedic degenerative diseases and bone tumors. By analyzing the immunometabolic regulatory networks of key molecules such as SLC7A11, TXNRD1, and RPN1, we propose immune-aware precision strategies combining disulfidptosis-targeted metabolic intervention with checkpoint blockade immunotherapy. This review fills the gap in the research of disulfidptosis in orthopedic diseases, providing new insights for a deeper understanding of the molecular mechanisms underlying these conditions, while establishing a theoretical framework for developing precise therapeutic strategies based on the regulation of disulfidptosis.
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PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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JI J. Cell. Physiol.
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WC Cell Biology; Physiology
SC Cell Biology; Physiology
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AU Wang, XY
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TI Quantitative computed tomography provides improved accuracy for diagnosis of lumbar osteoporosis in patients with facet joint osteoarthritis: a cross-sectional study
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Bone mineral density; Dual-energy X-ray absorptiometry; Facet joint osteoarthritis; Quantitative computed tomography
ID bone-mineral density; spine; calcification; physiology; strength; men
AB This study employed both QCT and DXA to assess BMD in the same cohort and investigated the influence of FJOA on BMD measurements and the detection rates of osteoporosis. The results indicate that QCT is more accurate for assessing regional BMD in patients with FJOA.PurposeThis study aimed to compare the detection rates of lumbar osteoporosis in patients with FJOA between QCT and DXA and to analyze the impact of FJOA on regional BMD measurement using each method.MethodsThis single-center, retrospective, cross-sectional study included participants without a history of spinal instrumentation surgery, spinal fractures of > 2 levels, spinal tumors or infections, and sacralization of lumbar spine. The detection rates of lumbar osteoporosis between QCT and DXA in patients with FJOA were compared using McNemar's test. Associations between BMDs and FJOA severity were assessed using linear mixed models. Discordance in BMD classification between DXA and QCT was categorized as minor or major according to Woodson's definition.ResultsThe 219 study participants had a mean age of 65.0 +/- 10.7 years and included 155 (70.8%) women. The rate of lumbar osteoporosis identification with QCT was noticeably greater than that with DXA (58% vs 34.2%, p < 0.0001). Severe FJOA was independently associated with lower vBMD (multivariable beta = - 4.23 (95% confidence interval (CI), - 7.68 to - 0.77); p = 0.17), while both slight-to-moderate and severe FJOA were independently

associated with higher areal BMD (aBMD). With increasing FJOA severity, the aBMD measured by DXA also increased (slight-to-moderate, beta = 0.31 (95% CI, 0.16-0.46), p < 0.001; severe FJOA, beta = 1.03 (95% CI, 0.79-1.27), p < 0.001).ConclusionsMore severe FJOA was associated with higher aBMD on DXA and a lower vBMD on QCT. Additionally, the rate of lumbar osteoporosis detection was significantly higher with QCT than with DXA. These findings indicate that QCT is more accurate for assessing regional BMD in patients with FJOA, supporting the need for caution when using DXA to evaluate BMD in clinical practice.
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U2 20
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J9 OSTEOPOROSIS INT
JI Osteoporosis Int.
PD SEP 15
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VL 36
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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TI Assessing the effects of immune checkpoint inhibitors on bone utilizing machine learning-assisted opportunistic quantitative computed tomography
SO JOURNAL OF BONE AND MINERAL RESEARCH
LA English
DT Article
DE immune checkpoint inhibitors; immune related adverse events; cancer; melanoma; BMD; osteoporosis; osteoarthritis; opportunistic computed tomography
ID mineral density; osteoporosis; dxa; osteoarthritis; calibration; attenuation; qct
AB Immune checkpoint inhibitors (ICIs) are widely used in cancer treatment, yet their impact on bone health remains unclear. This study aimed to perform a retrospective cohort study utilizing routine CT scans from patients with melanoma to perform opportunistic QCT analysis to investigate the effects of ICI treatment on skeletal health, including volumetric BMD (vBMD) measurements and osteoarthritis (OA) parameters. A previously established machine learning-assisted opportunistic QCT pipeline was used to estimate lumbar spine vBMD from baseline and 12-mo follow-up CT scans in patients with melanoma treated with ICI therapy and those not treated with ICI therapy. Facet joint OA, osteophyte formation, and endplate sclerosis were also graded. Independent and paired t tests were used to determine any differences in vBMD and OA parameters between ICI users and non-ICI users. Multivariable linear regression models were used to control for confounding variables. Non-ICI users had a significant decrease in vBMD of -6.96 mg/cm3 from baseline to follow-up, whereas the ICI users had no significant change. There was a significant difference in change in vBMD from baseline to follow-up between the 2 groups, with the non-ICI users experiencing a 11.22 mg/cm3 larger decrease in

vBMD. After adjusting for baseline age, sex, baseline vBMD, and change in OA parameters, this difference remained significant at -13.04 mg/cm3. Among the ICI users, those who had a decline in vBMD had a lower baseline vBMD compared with those who had increased vBMD. Neither group showed a significant change in OA parameters over the follow-up period, nor a difference in change between ICI and non-ICI users, even after adjusting for sex, age, and baseline OA parameters. While the effects of ICI treatment on vBMD may vary based on baseline bone health, ICIs do not significantly impact OA parameters in the short term. The effects of immune checkpoint inhibitors (ICIs) on BMD and degenerative spine changes are not well understood, despite the plausible relationship between ICI treatment and bone health. These findings demonstrate that depending on baseline bone health, ICI treatment may have varying effects on bone health and may even be protective against bone loss in some ICI users. ICIs appear to have no effect on osteoarthritis parameters such as osteophyte formation. This is the first study to investigate changes in bone health in humans after ICI treatment.
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JI J. Bone Miner. Res.
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SC Endocrinology & Metabolism
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TI Cellular senescence in skeletal diseases: A bibliometric analysis from 2007 to 2024
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Article
DE Cellular senescence; Skeletal diseases; Bibliometric; Visualized analysis
ID cells; osteoarthritis
AB Background: Cellular senescence is a state of permanent cell cycle arrest. Numerous studies have highlighted the significant role of cellular senescence in age-related skeletal diseases, including intervertebral disc degeneration (IDD), osteoporosis, and osteoarthritis (OA). This article aims to review the current research landscape and identify emerging trends. Methods: Literature concerning cellular senescence and skeletal disease was obtained from the Web of Science Core Collection database, covering publications from 2007 to 2024. The Bibliometrix R package, VOSviewer, and CiteSpace were employed to perform the bibliometric analysis. Results: A total of 2653 publications were analyzed, revealing a rapid growth trend. China emerged as the dominant contributor, with the highest publication volume (n = 1148), while the United States led in citation impact (total citations = 50,420). Key journals, such as Osteoarthritis and Cartilage and Aging Cell, served as primary platforms for high-impact studies. The most influential author was James L. Kirkland, followed by Richard F. Loeser. Keyword clustering identified cellular senescence in intervertebral disc degeneration, osteoporosis, and osteoarthritis as core research domains, while current frontiers focus on the senescence-associated secretory phenotype (SASP), mitochondrial dysfunction, extracellular vesicles, and immune infiltration. Conclusion: Research in this field has garnered substantial attention in recent years. This bibliometric analysis not only underscores the correlation between cellular senescence and skeletal diseases, but also highlights that targeting cellular senescence and the SASP may offer potential therapeutic strategies. These findings can inform future research directions and the development of targeted interventions for age-related skeletal conditions.
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TI Sheep Models in Translational Surgery
SO EUROPEAN SURGICAL RESEARCH
LA English
DT Review
DE Sheep model; Surgical research; Cardiothoracic surgery; Neonatal surgery; Orthopaedic surgery; Osteoarthritis; Spinal surgery; Anaesthesia
ID animal-models; ovine model; fusion; vertebroplasty; management; stifle
AB Background: The selection of an animal model is tedious. One must consider

several factors; one of these, of utmost importance, is the translational value of the animal model. The sheep, as a translational surgical model, possesses a multiple of advantages that makes it one of the preferred models in several research domains. Summary: Sheep are the state-of-the-art test models for cardiovascular research and safety studies required for approval of cardiovascular implantable devices; the sheep's heart size, cardiac muscle, heart valves, and the mechanical, haemodynamic, and coagulation parameters are very similar to humans. Furthermore, the pregnant sheep/lamb are robust models for studying neonatal adaptation and placental physiology due to its physiological similarities with humans. Its placental structure supports efficient gas exchange, resembling human oxygen transfer mechanisms. The ovine model is mainly used in studies of adaptation at birth, foetal physiology during labour, and congenital diaphragmatic hernia. The sheep model is also used in several orthopaedic preclinical models, mainly in the study of critical bone defects, cancellous bone healing, osteomyelitis, and joint replacement surgeries. It is also a preferred model of bone healing in osteoporosis. Moreover, the sheep has gained popularity as a model of osteoarthritis (OA); it is a validated model of surgically induced OA. Several therapeutic modalities can be evaluated using validated outcome measures such as, kinetics, kinematics, imaging, repeated arthroscopic grading, synovial fluid analysis, and biomarkers. The ovine model, because of its size, is the closest to humans for the evaluation of spinal surgery techniques, devices, and spinal fusion biological enhancers/cancellous graft replacement. Finally, we will outline the different specificities of sheep analgesia and anaesthesia. Challenges encountered in ruminant anaesthesia are mainly in relation with their digestive physiology that creates a high risk of regurgitation during anaesthesia and a hindrance of diaphragm/respiratory movements due to rumen repletion and meteorism. Fasting regimen and management of recovery should encompass strategies that limit the starving sensation and allow for reduced social isolation. Clarification of the interactions between scientific objectives and anaesthesia-analgesia protocols prevents conflicts between the ethics and the purpose of the experiment while allowing for development of model-specific anaesthesia and pain management protocols. Key Messages: The sheep has become a popular model because of its size, availability, robustness, cost, and ease of handling. Furthermore, as a preclinical model, the same validated objective outcome measures used to measure success in humans can apply to sheep.

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TI Mechanical complications and revision following total joint arthroplasty in acromegalic patients: A nationwide US-based study
SO BONE
LA English
DT Article
DE Total joint arthroplasty; Revision; Mechanical complication; Acromegaly; Outcome
ID osteoarthritis; arthropathy; outcm; burden
AB Background: Acromegaly is associated with significant osteoarthritis (OA) and increased risk of vertebral and hip fractures. There is limited data on total joint arthroplasty (TJA) outcomes in patients with acromegaly. Methods: In this retrospective study, we identified patients with acromegaly who underwent total hip arthroplasty (THA), total knee arthroplasty (TKA), and total shoulder arthroplasty (TSA) between 2010 and 2022 using the PearlDiver national database. Patients with a prior history of osteoporosis and follow-up duration of less than one year were excluded. Non-acromegalic control groups were selected through matching based on confounding factors. We compared all-cause revision and implant-related complications between the groups using R software integrated with the PearlDiver database. Results: We identified 1440 patients with acromegaly: 665 underwent THA, 618 underwent TKA, and 157 underwent TSA. Compared to the control group (2634 THA, 2445 TKA, and 600 TSA), there was no significant association with post-op revision following THA (OR(1-year) = 0.76[0.42-1.28], OR(5-year) = 0.68 [0.42-1.06]), TKA (OR(1-year) = 0.89[0.48-1.55], OR(5-year) = 0.78[0.49-1.17]), and TSA (OR(1-year) = 0.19 [0.02-1.40], OR(5-year) = 0.32[0.10-1.07]). Additionally, the risk of mechanical complications did not significantly increase in patients with acromegaly, either one year or five years post-operation. Conclusion: The study showed no significant increase in risk of revisions or mechanical complications in patients with acromegaly compared to controls. These findings bridge an important gap in the understanding of postarthroplasty complications in patients with acromegaly and offer valuable insights into surgical expectations.
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TI Pharmacological landscape of linarin: From benchside mechanisms to potential bedside applications
SO FITOTERAPIA
LA English
DT Review
DE Linarin; Flavonoids; Medicinal plants; Anti-inflammatory; Antioxidant
ID in-vitro; inhibitory-activity; flavonoids; apoptosis; acacetin; injury; glioma; cells
AB Linarin, a glycosylated flavonoid derived from medicinal plants such as Buddleja and Chrysanthemum species, has emerged as a bioactive compound with significant pharmacological potential. This review provides a comprehensive overview of linarin's chemical structure, extraction methods, pharmacokinetics, and therapeutic applications. Linarin exhibits diverse biological activities, including anti-inflammatory, antioxidant, neuroprotective, and anticancer effects, making it a promising candidate for drug development. The flavonoid demonstrates protective effects against hyperuricemia, acute kidney injury, spinal cord injury, ischemic stroke, diabetes, osteoporosis, and inflammatory bowel disease, primarily through modulation of signaling pathways such as Nrf2/Keap1, NF-kappa B, and MAPK. Additionally, linarin has shown potential in managing neurodegenerative disorders, including Alzheimer's disease, through its acetylcholinesterase inhibitory activity. Its anti-cancer effects have been linked to the inhibition of proliferation, apoptosis induction, and suppression of metastasisrelated pathways in lung, prostate, and brain cancers. Moreover, recent studies highlight its potential for ameliorating osteoarthritis, liver injury, and infectious diseases. The mechanisms underlying linarin's therapeutic effects involve its ability to modulate oxidative stress, inflammation, apoptosis, and metabolic pathways. Given its low toxicity, bioavailability, and structural versatility, linarin represents a compelling natural compound for future pharmaceutical applications. However, further preclinical and clinical investigations are warranted to fully elucidate its pharmacokinetics, optimize its bioavailability, and establish its clinical efficacy. This review advances a systems-level perspective that unifies linarin's pleiotropic mechanisms across several diseases. By linking structure-activity relationships with translational bottlenecks such as poor bioavailability and limited clinical validation, we outline a forward-looking roadmap for its development as a multi-target therapeutic scaffold.

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NR 50
TC 2
Z9 2
U1 8
U2 8
PU ELSEVIER
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 0367-326X
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J9 FITOTERAPIA
JI Fitoterapia
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PT J
AU Zhang, XQ
Wei, XD
Gu, ZX
Zhou, GH
Huang, CJ

Luo, MH
Zeng, LF
Yang, WY
AF Zhang, Xian-Quan
Wei, Xing-De
Gu, Zhuo-Xu
Zhou, Guang-Hui
Huang, Chu-Jia
Luo, Ming-Hui
Zeng, Ling-Feng
Yang, Wei-Yi
TI Application of artificial intelligence-assisted Traditional Chinese medicine formula granules in bone and joint degenerative diseases in the field of holistic health
SO FRONTIERS IN MEDICINE
LA English
DT Review
DE artificial intelligence; AI assisted; TCM formula granules; plant-based natural products; bone and joint degenerative diseases; bone aging and osteoporosis
AB As global aging intensifies, the incidence of degenerative bone and joint diseases such as osteoarthritis bone aging and osteoporosis continues to rise. Traditional treatment methods face bottlenecks in long-term management, including drug side effects and low patient compliance. Traditional Chinese medicine (TCM) formula granules, which utilize plant-based natural products, show excellent clinical efficacy in managing these conditions. With the development of technology, artificial intelligence (AI) technology has enhanced the clinical efficacy of TCM formula granules through multiple approaches such as intelligent syndrome differentiation and formula optimization, drug efficacy prediction and mechanism analysis, as well as patient management and therapeutic effect monitoring, providing a new approach for the prevention and treatment of complex degenerative diseases. This paper systematically reviews the core advantages of TCM formula granules and their suitability for orthopedic diseases such as bone aging and osteoporosis. It analyzes the application models of AI technology in optimizing TCM formula granules, predicting drug efficacy, and personalized treatment. The main research results show that the artificial intelligence-driven TCM formula granule system is beneficial for promoting the full-cycle integration of "prevention - treatment - rehabilitation" in the chronic disease management of bone and joint degenerative diseases. However, challenges persist in clinical evidence standardization, algorithm interpretability, and ethical frameworks. Future directions require interdisciplinary technological innovation, policy-industrial synergy, and global collaboration to advance intelligent TCM transformation for degenerative disease management.
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NR 29
TC 1
Z9 1
U1 17
U2 18
PU FRONTIERS MEDIA SA
PI LAUSANNE
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J9 FRONT MED-LAUSANNE
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WC Medicine, General & Internal
SC General & Internal Medicine

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AU Li, SY
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Fan, YH
Zhang, H
Guan, XF
AF Li, Siyu
Yang, Yongju
Zhang, Yu
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Fan, Yuanhe
Zhang, Hui
Guan, Xuefeng
TI Multi-omics joint analysis reveals the mechanism underlying Chinese herbal Yougui Pill in the treatment of knee osteoarthritis
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE Knee osteoarthritis; Yougui pill; Metabolomics; Transcriptomics
ID osteoporosis; chondrocytes; model
AB Ethnopharmacological relevance: Yougui Pill (YGP), originating from Jingyue Quanshu, comprises 10 traditional Chinese medicines (TCMs). This classic prescription is renowned for its ability to tonify the kidney, warm the kidney, promote yang, warm the interior, and dispel cold. YGP has proven effective in treating degenerative knee arthritis, osteoporosis, delayed fracture healing, and other orthopedic conditions, making it a widely used clinical prescription for knee osteoarthritis (KOA). Aim of the study: Although YGP is commonly used in clinical practice, its pharmacodynamic material basis and anti-arthritis mechanisms remain unclear. This study aims to comprehensively analyze the chemical constituents of YGP and elucidate its anti-arthritis mechanisms. Materials and methods: Ultra-high performance liquid chromatography coupled with electrospray ionizationtriple quadrupole-linear ion trap mass spectrometry(ESI-Q TRAP-MS/MS) was used to identify the chemical constituents of YGP. The Hulth method was utilized to establish KOA rat model, and pathological examinations were performed to assess

the anti-arthritis effects of YGP. Integrated metabolomics and transcriptomics analyses were conducted to explore the anti-arthritis mechanisms of YGP. Key targets were confirmed via immunohistochemistry. Results: A total of 1981 chemical components were identified in YGP, predominantly phenolic acids and flavonoids. Compared with the model group, 422 differentially expressed metabolites and 214 differentially expressed genes were identified, primarily involving the MAPK signaling pathway, FoxO signaling pathway, and PI3K-Akt pathway. YGP exerted an anti-osteoarthritis effect by inhibiting the excessive activation of the EGFR/ERT/FOS signaling pathway. Conclusions: TCM offers significant advantages in the treatment of KOA, addressing the shortcomings of current clinical medications. YGP displayed exceptional pharmacodynamic effects. This study elucidated its pharmacodynamic material basis and anti-osteoarthritis mechanisms, providing substantial support for its clinical application and the development of related drugs.
C1 [Li, Siyu; Yang, Yongju; Zhang, Yu; He, Fanyu; Chen, Jie; Fan, Yuanhe; Zhang, Hui; Guan, Xuefeng] Liaoning Univ Tradit Chinese Med, Shenyang 110000, Peoples R China.
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NR 42
TC 3
Z9 4
U1 5
U2 29
PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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J9 J ETHNOPHARMACOL
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SC Plant Sciences; Pharmacology & Pharmacy; Integrative & Complementary Medicine
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PT J
AU Ponich, B
Platt, A
Turk, M
Ramji, M
Knox, A
AF Ponich, Brett
Platt, Alexander
Turk, Madison
Ramji, Maleka
Knox, Aaron
TI WALANT Proximal Row Carpectomy Under Field Sterility: A Case Report and Description of Technique
SO PLASTIC SURGERY
LA English
DT Article
DE WALANT; field sterility; proximal row carpectomy; champ st & eacute;rile; carpectomie proximale
ID osteoarthritis; population
AB Field sterility and Wide Awake Local Anesthesia No Tourniquet (WALANT) technique is a commonly used operative technique for many hand and wrist pathologies. We present a case of a successful proximal row carpectomy using WALANT and field sterility in a minor surgery operating theatre setting. These techniques can be applied in appropriate patients to reduce the overall cost of surgery, anesthetic complications, and prolonged hospital stay. Le champ st & eacute;rile et l'anesth & eacute;sie locale sans garrot (WALANT, d'apr & egrave;s l'acronyme anglais) sont une technique op & eacute;ratoire courante pour de

nombreuses pathologies de la main et du poignet. Les chercheurs pr ésentent le cas d'une carpectomie proximale r éussie à l'aide de la technique de WALANT et du champ st érile dans un bloc op ératoire pour chirurgie mineure. Ces techniques peuvent être utilis ées aupr ès de patients bien choisis pour r éduire le co ût global de l'op ération et le risque de complications anesth ésiques et pour éviter un s éjour hospitalier prolong é.
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CR Avoricani A, 2022, PLAST SURG-CHIR PLAS, V30, P122, DOI 10.1177/22925503211003840
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NR 12
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JI Plast. Surg.
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SC Surgery
GA 7JI0E
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AU Zhang, Y
Wang, NN
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AF Zhang, Yan
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An, Wen-Na
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Chen, Fei
Zhang, Da-Jin
Wang, Si-Yue
Yang, Tie-Lin

Hu, Shou-Ye
Guo, Yan
TI The function of GPCRs in different bone cells
SO INTERNATIONAL JOURNAL OF BIOLOGICAL SCIENCES
LA English
DT Review
DE GPCR; MSC; osteoblast; osteoclast; chondrocyte
ID calcium-sensing receptor; prostaglandin ep2 receptor; protein-coupled receptors; mesenchymal stem-cells; beta-arrestin; osteoblast differentiation; osteoclast differentiation; osteogenic differentiation; chondrocyte hypertrophy; allosteric modulators
AB G protein-coupled receptors (GPCRs) are recognized as critical therapeutic targets in bone disorders, owing to their multifaceted regulatory roles across diverse bone cell lineages. This review systematically catalogs GPCR expression and functional heterogeneity in key bone cells: 12 GPCRs in mesenchymal stem cells (MSCs) orchestrate lineage specification; 21 GPCRs in osteoblasts/osteocytes mediate matrix mineralization and mechanotransduction; 23 GPCRs in macrophages/osteoclasts regulate inflammatory bone resorption; 31 GPCRs in chondrocytes govern endochondral ossification and osteoarthritis pathogenesis; and 8 GPCRs in other cell types modulate bone-related physiological processes. By integrating canonical signaling axes-cAMP/PKA-dependent transcriptional networks, PLC-beta/IP3-driven calcium signaling, and NF-kappa B-modulated immuno-skeletal interactions-we elucidate how GPCRs dynamically coordinate cellular plasticity to maintain skeletal homeostasis. This work establishes a multidimensional research framework integrating historical context, molecular mechanisms, and cutting-edge methodologies to advance GPCR-targeted therapies for bone-related diseases. Moreover, this review provides insights for clinical translation, including biased agonism and allosteric modulation precision strategies to restore skeletal equilibrium in osteoporosis, arthritis, and regenerative medicine.
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TI Role of Body Fat and Metabolic Rate in Site-Specific Fracture Risk: A 20-Year Taiwanese Cohort Study
SO MEDICAL SCIENCE MONITOR
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DT Article
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ID bone-mineral density; physical-activity; mass index; lean mass; strength
AB Background: Osteoporotic fractures are a significant public health problem, yet traditional risk assessment methods have limitations. This retrospective study used the integrated Healthcare information (iHi) Data Platform of China Medical University Hospital (CMUH) (2000-2020) to evaluate associations between body mass index (BMI), bone mineral density (BMD), body fat percentage (BFP), basal metabolic rate (BMR), and site-specific fracture risk in 9583 Taiwanese individuals. Material/Methods: We extracted DXA-measured BMD, BMI, BFP, and BMR data from CMUH's iHi Platform. Fracture events were identified using ICD-9/10 codes and verified through radiology reports. Cox proportional hazards regression models estimated fracture risk, adjusting for demographic and clinical factors. Mediation analysis quantified the contributions of BFP and BMR to the BMI-fracture relationship. Results: During median follow-up of 8.7 years, 1672 fractures (17.4%) occurred. Individuals with normal BMD showed an 82% lower fracture risk compared to those with osteoporosis (adjusted hazard ratio [aHR]=0.18, 95% CI: 0.15-0.22, p<0.001). Normal BFP significantly reduced fracture risk by 77% versus low BFP (aHR=0.23, 95% CI: 0.07-0.72, p=0.012). Higher BMR was consistently protective, with aHR=0.54 (95% CI: 0.36-0.82, p=0.004) for BMR >= 1500 versus BMR <1000. While underweight increased fracture risk (aHR=1.75, 95% CI: 1.29-2.36, p<0.001), obesity conferred no significant protection (aHR=1.04, 95% CI: 0.89-1.21, p=0.58). Conclusions: This study demonstrates that fracture risk assessment should incorporate BFP and BMR alongside BMD and BMI. The "BMI paradox" was explained through mediation analysis, revealing BFP and BMR as critical intermediaries accounting for 50% and 32% of the BMI-fracture relationship, respectively. These findings support stratification.
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AU Liu, XJ
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TI Dysregulation of miR-106a-5p/PTEN axis associated with progression and diagnostic of postmenopausal osteoporosis
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
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DT Article
DE miR-106a-5p; PTEN; Postmenopausal osteoporosis; Iron accumulation
ID iron-metabolism; serum ferritin; differentiation; osteoarthritis; microrna; health; stores; women
AB ObjectivePostmenopausal osteoporosis (PMOP) is a bone disorder in postmenopausal women and a significant risk factor for fragility fractures. This study aims to explore the role of miR-106a-5p in the pathogenesis of PMOP and its potential as a diagnostic biomarker.Methods220 postmenopausal women were recruited. The levels of miR-106a-5p, PTEN, and osteogenic-related genes were quantified using qRT-PCR. The relative protein of PTEN was detected using Western blotting. ROC curve and Pearson correlation were employed to evaluate the diagnostic value and relationships between variables. To model iron accumulation, hFOB1.19 osteoblasts were treated with ferric ammonium citrate (FAC). Cell proliferation and apoptosis were assessed using the CCK-8 and flow cytometry. The target relationship was verified using dual-luciferase assays.ResultsmiR-106a-5p levels were reduced, while PTEN levels were increased in PMOP. miR-106a-5p was positively correlated with bone mineral density and negatively correlated with ferritin. In the FAC-treated cells, miR-106a-5p decreased, and PTEN increased. Dual-luciferase assays confirmed that miR-106a-5p targets PTEN. Successful transfection was confirmed by observing the corresponding changes in miR-106a-5p and PTEN expression. Up-regulated miR-106a-5p increased the PTEN protein level, mRNA expression of RUNX2, OPN, and OCN, promoted cell proliferation, and decreased cell apoptosis under iron accumulation conditions. These effects were reversed by the upregulation of PTEN.ConclusionmiR-106a-5p has the potential to diagnose osteoporosis in postmenopausal women and is linked to ferritin levels. miR-106a-5p plays a protective role in PMOP by regulating PTEN under conditions of iron accumulation, suggesting its potential as a promising biomarker for PMOP.

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AU Abdelnabi, H
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TI Phytochemicals in Bone Therapy: Exploring Natural Alternatives for Bone Health
SO INTERNATIONAL JOURNAL OF NANOMEDICINE
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DT Review
DE phyto-nanomedicine; phytochemicals; bone; natural compounds; plant-based nanoparticles
ID osteoblast differentiation; in-vitro; phenolic-compounds; basic science; scaffolds; quercetin; nanoparticles; osteogenesis; berberine; repair
AB Bone diseases such as osteoporosis and osteoarthritis are increasingly prevalent, particularly in aging populations. While conventional treatments, including synthetic drugs and mineral supplements, are effective yet often associated with side effects and long-term economic burdens. Active compounds derived from nature, "Phytochemicals" have garnered attention due to their potential to provide safer and more sustainable alternative therapeutic options. However, due to their complex structure and poor pharmacokinetics, their clinical applications are limited. Nano-drug delivery systems address these limitations by developing phytochemicalbased nanocarriers, which enable targeted delivery,

protect active compounds, and enhance both pharmacokinetics and pharmacodynamics. Given the limitations of synthetic treatments, there is growing interest in exploring phytochemicals and plants and herbal extracts to support bone health. This review focuses on nano-phytochemical approaches for bone therapy, outlining key phytochemicals, their natural sources, nanoformulations, and mechanisms of action. It also evaluates current commercial supplements and highlights the challenges and future directions for clinical translation of nano-phytomedicine in bone health management.
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TI Prediction of Fractures After Open Wedge High Tibial Osteotomy Based on the Distance From the Tibial Osteotomy Point to the Medial Edge of the Tibia
SO JOURNAL OF ARTHROPLASTY
LA English
DT Article
DE high tibial osteotomy; lateral hinge fracture; preventive strategy; osteoarthritis; osteotomy position

ID lateral hinge fracture; unicompartmental knee arthroplasty; computed-tomography; safe zone; risk; osteoarthritis
AB Background: To investigate the relationship between the distance from the medial tibial osteotomy point to the medial tibial edge and the development of lateral tibial hinge fracture (type II) and intra-articular tibial plateau fracture (type III) in patients who have degenerative disease undergoing open wedge high tibial osteotomy (OWHTO). This information will aid surgeons in avoiding the occurrence of fractures. Methods: This retrospective study analyzed 304 patients who underwent OWHTO from January 2018 to January 2024 in the Affiliated Hospital of Qingdao University. The distance from the tibial osteotomy point to the medial tibial edge on imaging was analyzed to determine its association with fracture. A oneway analysis of variance was used to compare the differences in height, weight, body mass index, the distance from the medial tibial osteotomy point to the medial tibial edge, sex, left and right sides of the knee, and osteoporosis in the occurrence of types II and III fractures. Receiver operating characteristic curves were used to identify the critical distances associated with type II and type III fractures. Logistic regression analyses were used to obtain the OR of the critical distance adjusted for age, sex, left and right sides, body mass index, and T value. Results: There were 40 fractures (13.3%) in 304 patients after OWHTO, comprising 21 type II fractures (7.0%) and 19 type III fractures (6.3%). A single-factor variance analysis showed that the tibial bone cutting distance to the medial tibial edge (P = 0.02) and osteoporosis (P = 0.01) were significantly different from the fracture. Receiver operating characteristic curves showed that the critical distances for types II and III fractures were 40.5 and 47.1 mm, respectively. Logistic regression analysis showed that the ORs [odds ratios] of types II and III fractures were 1.061 (95% CI [confidence interval] = 1.010 to 1.115) and 1.064 (95% CI = 1.011 to 1.119), respectively. Conclusions: In patients undergoing OWHTO, the risk factors for type II and III fractures are osteoporosis and the distance from the tibial bone cutting point to the medial tibial edge. This distance should be minimized during OWHTO to avoid type II and III fractures. (c) 2024 Published by Elsevier Inc.
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AU Larsen, P
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AF Larsen, Peter
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TI The effect of medical comorbidity on HOOS/KOOS/FAOS: a national register-based cohort study of 7850 representative citizens
SO CLINICAL RHEUMATOLOGY
LA English
DT Article
DE Comorbidity; HOOS/KOOS/FAOS; Outcome; PROM
ID osteoarthritis outcome score; knee injury; health; koos
AB ObjectivesDespite extensive validation, the impact of medical comorbidities on the outcomes of the Hip Disability and Osteoarthritis Outcome Score (HOOS), Knee Injury Osteoarthritis Outcome Score (KOOS), and Foot and Ankle Outcome Score (FAOS) remains underexplored. This study aimed to evaluate the effect of medical comorbidities on HOOS, KOOS, and FAOS subscales using a large, nationally representative sample.MethodsThis national register-based cohort study invited 26,877 participants to complete HOOS, KOOS, or FAOS questionnaires. Medical comorbidities-including diabetes, chronic obstructive pulmonary disease/asthma, rheumatological diseases, osteoporosis, stroke, obesity, and heart disease-were identified through the Danish National Patient Register.ResultsA total of 7850 participants (29%) responded, with 1863 (24%) having medical comorbidities. HOOS/KOOS/FAOS subscale scores were significantly worse in patients with comorbidities, particularly in the Sport/Rec, ADL, and QOL subscales. Mean score differences between participants with and without comorbidities were pain (- 5.7, 95% CI - 6.6 to - 4.7), symptoms (- 4.6, 95% CI - 5.5 to - 3.6), ADL (- 7.1, 95% CI -

8.0 to - 6.1), Sport/Rec (- 10.4, 95% CI - 11.9 to - 8.9), and QOL (- 6.9, 95% CI - 8.2 to - 5.7). Diabetes, rheumatological diseases, and obesity were associated with the greatest complaints.ConclusionPatients with medical comorbidity reported significantly lower HOOS/KOOS/FAOS subscale scores compared to participants without medical comorbidity. Diabetes, chronic rheumatological diseases, and adiposities were observed with the most complaints.Key Points center dot Medical comorbidity predicts considerably lower HOOS/KOOS/FAOS subscale scores.center dot Diabetes, rheumatological diseases, and obesity exerted the most pronounced negative effects on the HOOS/KOOS/FAOS.center dot Findings underscore the importance of considering comorbidities when interpreting HOOS/KOOS/FOAS subscale scores.ConclusionPatients with medical comorbidity reported significantly lower HOOS/KOOS/FAOS subscale scores compared to participants without medical comorbidity. Diabetes, chronic rheumatological diseases, and adiposities were observed with the most complaints.Key Points center dot Medical comorbidity predicts considerably lower HOOS/KOOS/FAOS subscale scores.center dot Diabetes, rheumatological diseases, and obesity exerted the most pronounced negative effects on the HOOS/KOOS/FAOS.center dot Findings underscore the importance of considering comorbidities when interpreting HOOS/KOOS/FOAS subscale scores.
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TI Leveraging Proteomics and Proteogenomics for Understanding Osteoporosis and Other Musculoskeletal Diseases
SO CURRENT OSTEOPOROSIS REPORTS
LA English
DT Review
DE Genomics; Osteoarthritis; Osteoporosis; Proteomics; Proteogenomics; Sarcopenia
ID bone-mineral density; postmenopausal women; osteoarthritis; genetics; muscle; risk; romosozumab; prevention; biomarkers; sarcopenia
AB Purpose of ReviewOsteoporosis and musculoskeletal diseases, including osteoarthritis and sarcopenia, contribute substantially to global morbidity and healthcare costs. This review explores how proteogenomics integrates genomic and proteomic data to refine disease classification, identify causal pathways, and accelerate biomarker and drug target discovery.Recent FindingsLarge-scale proteomic studies, including UK Biobank-based research, have identified circulating proteins associated with musculoskeletal disease risk and progression. Proteomic risk models outperform conventional clinical metrics in predicting outcomes. Genomics, proteomics, and proteogenomics have facilitated the identification of causal markers through methods such as genome-wide association studies, effector gene mapping, and proteome-wide Mendelian randomization. Pathways implicated in disease mechanisms include extracellular matrix remodeling (e.g., COL6A3, COL9A1), metabolic regulation (e.g., IGFBP2, GDF15), inflammatory processes (e.g., TNF family ligands, CXCL17), and sex-hormone-related signaling (e.g., FSHB, SHBG). While these biological processes contribute across osteoporosis, osteoarthritis, and sarcopenia, distinct proteins have also been linked to disease-specific pathophysiology, offering potential therapeutic targets.SummaryGenomics, proteomics, and proteogenomics refine our understanding of musculoskeletal conditions and hold strong potential for improving early diagnosis, enhancing risk stratification, and advancing precision treatments.
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NR 99
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TI Prevalence, clinical characteristics, and biological markers of postmenopausal osteoporosis and knee osteoarthritis in Beijing: study protocol for a cross-sectional and prospective study
SO FRONTIERS IN MEDICINE
LA English
DT Article
DE postmenopausal osteoporosis; knee osteoarthritis; cross-sectional study; prospective; follow-up; risk factors
ID epidemiology
AB Background Postmenopausal osteoporosis (PMOP) and knee osteoarthritis (KOA) are common musculoskeletal disorders that share risk factors such as aging, hormonal changes, and inflammation. PMOP often remains asymptomatic until fractures occur, while KOA leads to pain and disability. Their comorbidity remains underexplored, particularly in community settings. This study aims to investigate the prevalence, risk factors, and clinical features of PMOP-KOA comorbidity among Beijing residents aged 45-80 years, providing evidence-based recommendations for early identification, prevention, and management. Methods Over 2 years, this study will conduct a PMOP-KOA screening and prospective follow-up in the Beijing community to investigate the incidence, risk factors, and clinical characteristics of PMOP-KOA. This study will undertake bone mineral density detection, collect biological samples, and record information via questionnaires. Discussion The study

aims to investigate the incidence, risk factors, and clinical characteristics of PMOP-KOA comorbidity and explore related traditional Chinese medicine syndromes based on large community-based samples in Beijing. Data on PMOP-KOA occurrence and associated risk factors over the 2 years follow-up will be available on the Chinese Clinical Trial Registry (ChiCTR2300073575).
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NR 29
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TI Trolox, r-irisin and resveratrol cocktail to counteract osteoblast metabolism alterations in osteoarthritis and osteoporosis
SO JOURNAL OF BONE AND MINERAL METABOLISM
LA English
DT Article
DE Osteoporosis; Osteoarthritis; Bone metabolism; Musculoskeletal aging; Physiology
ID oxidative stress; prevents; sirt1
AB IntroductionOsteoarthritis and osteoporosis are age-related musculoskeletal disorders characterized by increased oxidative stress and cellular senescence, which contribute to altered metabolism and disease progression. Although research in this field is constantly evolving, the discovery of new molecular targets and drug combinations to counteract musculoskeletal disorders remains a goal of great interest. This study aimed to evaluate the efficacy of a cocktail of trolox, recombinant irisin (r-irisin) and resveratrol in modulation of osteoblastic metabolism by investigating the expression of NADPH oxidase 4 (NOX4), sirtuin 1 (SIRT1) and pentraxin 3 (PTX3).Materials and methods20 male patients undergoing hip arthroplasty were enrolled, including ten patients with coxarthrosis and ten patients with osteoporosis. Femoral head biopsies were taken from each patient to isolate primary osteoblast cultures, which were treated with the cocktail for 6 days.ResultsThe cocktail of trolox, r-irisin and resveratrol increased cell viability, and

reduced ROS and senescence beta-galactosidase activity (SA-beta-Gal) levels. In addition, western blotting analysis showed reduced expression of NOX4 and increased expression of SIRT1 and PTX3 in both experimental groups, although with more pronounced effects in osteoarthritic patients, highlighting lower treatment efficacy in the presence of osteoporosis.ConclusionsThe improvement in cell viability and reduction in oxidative stress and cellular senescence observed through treatment-induced modulation of the NOX4-SIRT1 axis and PTX3 suggests a protective role for these biomarkers in bone metabolism. These findings could offer new perspectives in counteracting the effects of aging on the skeletal system by improving bone health and mitigating metabolic alterations.
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TI Senescence of bone marrow mesenchymal stromal cells: a narrative review of mechanisms, functional consequences, and rejuvenation strategies for age-related disorders
SO STEM CELL RESEARCH & THERAPY
LA English
DT Review

DE Bone marrow mesenchymal stromal cells; Cellular senescence; Telomere shortening; Oxidative stress; Senescence-associated secretory phenotype; Anti-Aging therapeutics
ID stem-cells; in-vitro; oxidative stress; telomerase; autophagy; survival; inhibit
AB With the intensification of global population aging, research on aging-related diseases has become increasingly critical. Bone marrow mesenchymal stromal cells (BMSCs), residing in bone marrow microvironment, serve as precursors for osteoblasts and adipocytes while playing unique roles in regulating hematopoietic and immune systems. However, BMSCs undergo progressive senescence during aging, characterized by diminished proliferative capacity, skewed differentiation potential, compromised immunomodulatory functions, and the development of a senescence-associated secretory phenotype (SASP). These age-related alterations exacerbate inflammatory responses within the bone marrow microenvironment, contributing to the pathogenesis of degenerative diseases such as osteoporosis and osteoarthritis, while potentially inducing hematopoietic dysfunction and oncogenic transformation. Notably, senescent BMSCs secrete pro-inflammatory cytokines that establish a chronic inflammatory milieu, which not only impairs hematopoietic stem cells (HSCs) functionality but also promotes bone marrow adipogenesis. Despite these insights, the intricate interplay between BMSC senescence and microenvironmental alterations remains incompletely understood. This narrative review Comprehensively synthesizes current knowledge on the molecular mechanisms underlying BMSCs senescence, with particular emphasis on telomere attrition, DNA damage accumulation, oxidative stress, epigenetic dysregulation, and bidirectional microenvironmental crosstalk. Furthermore, we critically evaluate emerging therapeutic strategies aimed at mitigating BMSCs senescence and optimizing their clinical applications in age-related disorders.
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TI Advances in 3D-Printed Drug Delivery and Screening Platforms for Bone Disease Therapy
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DT Review
DE 3D printing; drug delivery; drug screening; bone diseases; patient-specific; orthopedics; physiopathology
ID gaucher-disease; in-vitro; mechanical-property; composite scaffolds; regeneration; vancomycin; release; nanoparticles; ciprofloxacin; antibiotics
AB Bone diseases such as osteomyelitis, osteosarcoma, and osteoarthritis, as well as conditions caused by metabolic imbalances, including osteoporosis, require more efficient and optimized therapies. Systemic drug administration entails major disadvantages like cytotoxicity and adverse reactions, which can lead to serious complications or death. Therefore, local drug administration alternatives are currently under investigation for different pharmacological therapies. New vectors were created to improve control over administration, and 3D-printed and patient-specific drug delivery systems have been tested, revealing great potential. Moreover, 3D-printed platforms that mimic human tissues for drug testing are innovative solutions emerging for the pharmaceutical industry. Situated between in vitro and in vivo testing on human patients, they offer the advantage of reproducing functional architecture, providing results that are closer to those encountered in clinical trials performed on patients. In our article, we present the two categories of 3D systems, from the perspective of main drug groups (antibiotics, anticancer, and anti-inflammatory) as well as other categories, alongside their advantages, limitations, and their adaptations to 3D printing technologies. This article also highlights the technological drawbacks encountered in both delivery and screening systems, as well as the printing methods and materials used, including their physical and biological properties.

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NR 300
TC 0
Z9 0
U1 1
U2 1
PU MDPI
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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EI 1999-4923
J9 PHARMACEUTICS
JI Pharmaceutics
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TI Hip fractures and type 2 diabetes in the elderly: Risk factors analysis of the Nedices cohort

SO DIABETES & METABOLISM
LA English
DT Article
DE Elderly; Hip fracture; Risk factors; Type 2 diabetes
ID bone turnover; population; mellitus; women; health; metaanalysis; density
AB Aim:- To analyze the association between type 2 diabetes (T2D) and the incidence of hip fractures in the elderly, while also considering the influence of socioeconomic status (SES), and other risk factors (RFs). Methods:- Data were collected from 5278 participants aged >= 65 years. The study included a baseline and a follow-up survey 3 years later. Participants completed a questionnaire, anthropometric measurements, blood tests, and physical and cognitive tools. The research was conducted in three Spanish communities with different socioeconomic backgrounds. Results:- At baseline, there were 874 T2D and 4494 controls. Body mass index (BMI) was slightly higher in individuals with hip fractures. Significant differences were observed in BMI, education level, physical activity, osteoporosis, cataracts, and osteoarthritis. In the follow-up survey, 96 newly, 615 previously T2D, and 2985 controls were compared. Those with hip fractures were associated with lower educational attainment, sedentary life, and higher diagnoses of osteoporosis, cataracts, and osteoarthritis. Charlson index was higher in individuals with hip fractures. A higher proportion of fractures occurred in urban areas. The rate of incidence of T2D between individuals with and without fractures was not different. Conclusion:- RFs for hip fractures in T2D are similar to those in the general population. Osteoporosis, being female, and advancing age were independent RFs for hip fractures. There was an inverse association between educational level, community allocation, and physical activity which may further contribute to hip fracture risk. These highlights the need for research to better understand the role of T2D and these RFs in hip fracture incidence.
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NR 45
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Z9 2
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PU MASSON EDITEUR
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PA 21 STREET CAMILLE DESMOULINS, ISSY, 92789 MOULINEAUX CEDEX 9, FRANCE
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J9 DIABETES METAB
JI Diabetes Metab.
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IS 4
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WC Endocrinology & Metabolism
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PT J
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TI Study of rheumatoid arthritis in older patients: a cross-sectional study
SO BMC GERIATRICS
LA English
DT Article
DE Rheumatoid arthritis; Elderly-onset rheumatoid arthritis; Serum 14-3-3 eta
ID health-assessment questionnaire; population-based cohort; clinical-practice; indian version; joint damage; young-onset; disease; prevalence; validation; antibody
AB Background: Rheumatoid Arthritis (RA) in older adults is a chronic inflammatory condition causing severe disability and impacting patients' physical, psychological, and social health. It lowers productivity in society and puts pressure on healthcare systems. This study aims to explore the different aspects of RA and investigate the diagnostic potential of serum marker 14-3-3 eta. Method: This Cross-sectional study recruited 205 arthritis patients (63 RA and 142 OA) over sixty years old. The participants underwent a thorough clinical evaluation according to the established design. Anti-CCP and serum 14-3-3 eta levels were measured. Simple logistic regression was performed to identify significant predictors of RA. ROC curve determined optimal cut-off value for 14-3-3 eta. Results: This study reported an average age of 63.67 years with a high female-to-male ratio of 4:1 in the RA cohort, while in the OA cohort, the mean age was 65.5 years with a low female-to-male ratio of 2:1 overall. Symptomatically, RA patients exhibited earlier onset, pronounced early morning stiffness, fever, weight loss, myalgia, and fatigue, all with highly significant p-values (< 0.001). Comorbidities showed higher incidences of anemia, ILD, and osteoporosis in RA patients. Impaired ADL and IADL were noted in 17.5% and 73.2%, respectively. Impaired HMSE and GDS were found in 36.5% and 74.6%, respectively. Logistic regression analysis identified key predictors distinguishing RA from OA, including EMS (OR: 1.09, $p < 0.001$), fever (OR: 6.68, $p < 0.001$), weight loss (OR: 6.35, $p < 0.001$), myalgia (OR: 5.07, $p < 0.001$), osteoporosis (OR: 2.21, $p = 0.013$), ACCP levels (OR: 1.28, $p < 0.001$), and the novel marker 14-3-3 eta (OR: 2.87, $p = 0.047$). Using both ACCP and14-3-3 eta markers, 88.88% of RA patients were positive for at least one marker, enhancing its diagnostic coverage. Elderly onset RA (EORA) patients had a significantly higher age and shorter disease duration compared to those with young onset RA (YORA). The

female-to-male ratio in the YORA and EORA group were 6.97:1 and 1.66:1 respectively. PMR-like symptoms were more prevalent in the EORA group (31.25% vs.14.9%). Hypothyroidism was more frequent in the EORA group (31% vs. 17%). Sulfasalazine was more commonly prescribed in both EORA (100%) and YORA (89%) groups. Conclusion: This study contributes to a better understanding of distinguishing RA from OA. It also highlights the differences between young and elderly onset RA, and supports the diagnostic potential of the serum marker 14-3-3 eta.
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NR 55
TC 1
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PU BMC
PI LONDON
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J9 BMC GERIATR
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PD JUL 30
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VL 25
IS 1
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WC Geriatrics & Gerontology; Gerontology
SC Geriatrics & Gerontology
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AU Sgaglione, J
Neufeld, EV
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TI Clinical Status of Exosomes: A Review
SO HSS JOURNAL
LA English
DT Review
DE stem cells; extracellular vesicle; mesenchymal stem cells; regenerative medicine
ID mesenchymal stem-cells; intervertebral disc degeneration; extracellular vesicles; femoral-head; osteonecrosis
AB Nano-sized extracellular vesicles enclosed by a lipid bilayer and secreted by various cell types including mesenchymal stem cells, exosomes act as natural transporters, carrying bioactive molecules such as proteins, lipids, and nucleic acids that mediate intercellular communication. Exosomes influence a range of cellular processes, including immune modulation, tissue repair, and disease progression. Compared to whole-cell therapies, exosomes provide anti-inflammatory, immunosuppressive, and regenerative effects with reduced risks linked to cellular components, such as infusion toxicity, immunogenicity, and tumorigenic phenomena. This article reviews isolation, modification, characterization, and storage techniques, challenges in clinical translation, and innovative engineering strategies to enhance targeting and efficacy. It also examines preliminary evidence suggesting that exosomes may have potential in managing degenerative disorders such as osteoarthritis, intervertebral disc degeneration, osteoporosis, osteonecrosis, and tendinopathy, as well as non-degenerative disorders such as sciatic nerve injury, fractures, and soft tissue trauma.
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TI Causality between coffee intake and bone health: A Mendelian randomization study

SO MEDICINE
LA English
DT Article
DE coffee intake; Mendelian randomization; osteoarthritis; osteoporosis; rheumatoid arthritis
ID rheumatoid-arthritis; mineral density; caffeic acid; risk; consumption; cells; differentiation
AB Observational studies have reported associations between coffee intake and osteoarthritis (OA), rheumatoid arthritis (RA), and osteoporosis (OP). However, it remains unknown whether these relationships are causal. In this study, we applied a 2-sample bidirectional Mendelian randomization (MR) analysis to comprehensively evaluate the causal association between coffee intake and OA, RA, and OP. Genetic data for OA (40,425 controls and 10,083 cases), RA (22,350 controls and 74,823 cases), OP (476,847 controls and 7751 cases), and coffee intake (263,464 Europeans) were obtained from the UK Biobank. The causal relationship between coffee intake and OA-, RA-, and OP-related traits was investigated using 2-sample MR analysis with a pooled dataset from genome-wide association studies. Inverse variance weighting (IVW) was used as the main outcome, whereas MR-Egger and weighted median were used to supplement the IVW estimates. Heterogeneity was assessed using Cochran Q statistic. Confounding-related single-nucleotide polymorphisms and single-nucleotide polymorphisms with P < .05 in MR-PRESSO analysis were excluded. There was no evidence of a causal relationship between coffee intake and the risk of RA (odds ratio [OR]: 0.84; 95% confidence interval [CI]: 0.24-2.93) using the IVW with random effect. Genetic predisposition to coffee intake was not associated with OA (OR: 1.21; 95% CI: 1.01-1.45) and OP (OR: 1; 95% CI: 0.99-1.0) using the main IVW method. Reverse MR analysis did not reveal evidence of a significant causal effect of OA, RA, and OP on coffee intake. Our findings do not support a causal relationship between coffee intake and the risk of OA, RA, and OP.
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TI Network Toxicology and Molecular Docking Reveal the Toxicological Mechanisms of DEHP in Bone Diseases
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES

LA English
DT Article
DE Di(2-ethylhexyl) phthalate (DEHP); network toxicology; molecular docking; osteoporosis; osteoarthritis; osteonecrosis of the femoral head
ID osteogenic differentiation
AB Di(2-ethylhexyl) phthalate (DEHP), a widely employed exogenous plasticizer, has become pervasive in the environment and living organisms due to its extensive use in food packaging, medical devices, and daily consumer products, and is established as a typical endocrine-disrupting chemical. Growing evidence indicates a strong association between DEHP exposure and the incidence of chronic bone disorders, including osteoporosis (OP), osteoarthritis (OA), and osteonecrosis of the femoral head (ONFH). However, the molecular mechanisms underlying its pathogenic effects across these diseases remain poorly defined. In this study, we applied an environmental network toxicology approach to integrate predicted protein targets of DEHP with known disease-associated targets of the three bone disorders using multiple databases. Through Venn analysis, protein-protein interaction (PPI) network construction, and Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses, we identified core targets and key signaling pathways. Molecular docking and molecular dynamics (MD) simulations were further employed to validate the binding modes and stability between DEHP and the core targets, thereby elucidating common and distinct mechanisms of DEHP across these bone diseases. A total of 109 overlapping targets of DEHP and the three bone diseases were identified, among which 7 core targets-AKT1, SRC, ESR1, CASP3, MMP9, BCL2, and BCL2L1-were common to all three disorders. These are implicated in critical biological processes such as apoptosis regulation, inflammation, extracellular matrix degradation, and estrogen signaling. KEGG enrichment analysis revealed significant involvement of the PI3K-Akt, MAPK, Ras, TNF, and estrogen signaling pathways across all three diseases. Molecular docking and MD simulations confirmed stable binding of DEHP to key targets including AKT1, ESR1, and MMP9, supporting its potential to disrupt bone metabolic homeostasis via multi-target and multi-pathway mechanisms. Further analysis indicated that DEHP exerts both shared and disease-specific effects: it disrupts osteoblast/osteoclast balance in OP, amplifies inflammatory responses and matrix degradation in OA, and contributes to impaired angiogenesis and osteocyte necrosis in ONFH. This study systematically reveals how DEHP disrupts bone homeostasis through a multi-target and multi-pathway network, constructing a cross-disease osteotoxicity framework. It is the first to delineate the common and distinct molecular mechanisms of DEHP in OP, OA, and ONFH. Although these insights are derived from computational models and require further experimental validation, they provide a novel theoretical basis for combined intervention strategies targeting multiple bone diseases and for environmental health risk assessment.
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PT J
AU Allan, R
Dillon, S
Booth, N
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Hurst, H
Sinclair, J
AF Allan, Robert
Dillon, Stephanie
Booth, Nicole
Dickson, Joshua
Shadwell, Gareth
Hurst, Howard
Sinclair, Jonathan
TI Patient Perceptions, Beliefs, and Behaviors in Bone-Related Disease and Pain Management: A Cross-Sectional Study
SO JOURNAL OF MANIPULATIVE AND PHYSIOLOGICAL THERAPEUTICS
LA English
DT Article
DE Bone diseases; Osteoporosis; Osteoarthritis; Pain
ID therapy; calcium; osteoarthritis; menopause; benefits; knee
AB Objective: The purpose of this study was to examine methods of pharmacologic and nonpharmacological pain management for people with bone-related diseases. Methods: Bone-related disease incidence, treatment, and pain management strategies were assessed using an anonymous online survey in 2021. The survey included questions about demographics, disease characteristics, and pain coping. One-sample x2 goodness of fit tests, 2-way Pearson x2 tests of independence, and probability values were used for data analysis. Results: Respondents were primarily postmenopausal females, aged 55-60 years old, with moderate disease activity, with osteoporosis most commonly reported. Responses suggest medical professionals' advice for pain management included multiple medications, especially analgesics. Dietary interventions also played an important role with vitamin D and calcium supplementation regularly being reported. Patients seek to use alternative methods of pain relief and disease management, with many respondents reporting nonpharmacological pain relief treatments playing a significant role in coping with their bone disease. Although respondents aged 46 to 50 opted against nonpharmacological relief, those aged 56 to 60 years reported they were willing to try nonpharmacological interventions that reduced pain, with the choice of treatment based on "how it made me feel." Conclusion: A substantial number of respondents believed that more research is required into pain relief for bone-related diseases, with those affected by these conditions seeking a more acute and analgesic approach to managing pain. Most respondents answered "yes" when asked if nonpharmacological pain relief treatments play a sufficient role in

coping with their bone-related pain. (J Manipulative Physiol Ther 2025;48;365-372)
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TI NLRP3 Inflammasome-Mediated Pyroptosis in Osteoporosis: Osteoimmune Mechanisms and Therapeutic Targeting
SO JOURNAL OF CELLULAR AND MOLECULAR MEDICINE
LA English
DT Review
DE action mechanism; cell pyroptosis; intervention measures; NLRP3 inflammasome; osteoimmunology; osteoporosis
ID oxidative stress; in-vitro; activation; macrophages; inhibition; cells; osteoarthritis; progression; osteoblast; exosm
AB Osteoporosis (OP) is a chronic, age-related skeletal disorder characterised by progressive bone loss and microstructural deterioration, which increases bone fragility and fracture risk. The NOD-like receptor family pyrin domain-containing 3 (NLRP3) inflammasome, a multi-subunit protein complex involved in bone homeostasis, mediates inflammatory cascades in response to external stimuli and pathological conditions. This process triggers pyroptosis in various bone-related cells, disrupting bone repair and remodelling. Oestrogen deficiency and aging lead to the overactivation of the NLRP3 inflammasome, stimulate bone immunity, metabolism and other abnormalities and disrupt angiogenesis-osteogenesis coupling. These factors contribute significantly to the pathological progression of OP. However, the precise mechanisms remain poorly understood and are lacking clinical validation. Therefore, this review summarises the mechanisms of NLRP3 inflammasome in response to bone immune signals, external stress and intercellular communication, as well as its role in metabolic regulation, including reprogramming and post-translational modification, thereby influencing pyroptosis in macrophages, endothelial cells, mesenchymal stem cells and osteoblasts. It explores potential therapeutic strategies that target NLRP3 activation, including exosome (Exos)-based interventions and traditional Chinese medicine components, which may modulate its differential expression and affect angiogenesis-osteogenesis differentiation. These approaches offer promising avenues for the prevention and treatment of OP.
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TI Current cutting-edge omics techniques on musculoskeletal tissues and diseases
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DT Review
ID human articular-cartilage; muscle satellite cells; single-cell; proteomic analysis; stem-cells; transcriptome analysis; intervertebral discs; human osteoarthritis; dna methylation; gene-expression
AB Musculoskeletal disorders, including osteoarthritis, rheumatoid arthritis, osteoporosis, bone fracture, intervertebral disc degeneration, tendinopathy, and myopathy, are prevalent conditions that profoundly impact quality of life and place substantial economic burdens on healthcare systems. Traditional bulk transcriptomics, genomics, proteomics, and metabolomics have played a pivotal role in uncovering disease-associated alterations at the population level. However, these approaches are inherently limited in their ability to resolve cellular heterogeneity or to capture the spatial organization of cells within tissues, thus hindering a comprehensive understanding of the complex cellular and molecular mechanisms underlying these diseases. To address these limitations, advanced single-cell and spatial omics techniques have emerged in recent years, offering unparalleled resolution for investigating cellular diversity, tissue microenvironments, and biomolecular interactions within musculoskeletal tissues. These cutting-edge techniques enable the detailed mapping of the molecular landscapes in diseased tissues, providing transformative insights into pathophysiological processes at both the single-cell and spatial levels. This review presents a comprehensive overview of the latest omics technologies as applied to musculoskeletal research, with a particular focus on their potential to revolutionize our understanding of disease mechanisms. Additionally, we explore the power of multi-omics integration in identifying novel therapeutic targets and highlight key challenges that must be overcome to successfully translate these advancements into clinical applications.
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TI Prevalence, comorbidities, and disease-related complications of rheumatoid

arthritis in Colombia: a national cross-sectional study based on administrative claims data
SO ADVANCES IN RHEUMATOLOGY
LA English
DT Article
DE Latin America; Comorbidity; Complications; Prevalence; Rheumatoid arthritis
ID population; care
AB BackgroundTo date, there has been limited exploration, particularly on a national scale, of the prevalence patterns of comorbidities and complications associated with rheumatoid arthritis (RA) in Colombia. We aimed to analyze the prevalence patterns of comorbidities and disease-related complications of RA patients enrolled in Colombia's contributory healthcare regime.MethodsWe performed a nationwide observational descriptive cross-sectional study using administrative claims data. We used a set of sensitive and specific electronic algorithms (i.e., a set of rules) applied to linked data based on ICD-10 codes and unique medication use codes. We compared all those algorithms with several sources, including governmental agencies and scientific literature, to identify all the known adults treated for RA.ResultsA total of 123,080 RA cases for 2018 were identified, corresponding to a point prevalence of 0.86 (95% CI 0.86-0.87) per 100. Compared to a non-RA reference population, hypertension (68.2 vs. 20.0%), osteoarthritis (43.6 vs. 6.1%), and osteoporosis (18.6 vs. 1.1%) provided larger standardized mean differences. Lupus (30.04; 95%CI 29.3-30.8), multiple sclerosis (7.18; 95%CI 6.6-7.8), and osteoporosis (5.57; 95%CI 5.5-5.6) provided higher age- and sex-adjusted prevalence ratios. Disease-related complications were found in 62.2% of cases.ConclusionsWe describe the first comprehensive assessment of the prevalence patterns of disease-related complications and comorbidities that define the RA burden of disease within a multimorbidity profile. Also, our study provides a narrower and more reliable point prevalence estimate for RA in Colombia.
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TI Research advances in the study of traditional Chinese medicine formula granules on signaling pathway-mediated disease mechanisms
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE traditional Chinese medicine formula granules; signaling pathways; mechanisms of disease; secondary metabolites; orthopedic diseases; plant-based natural products
ID tgf-beta; decoction; injury
AB As a modern dosage form of traditional Chinese medicine, Traditional Chinese Medicine Formula Granules (TCMFG) maximally retains active metabolites through standardized production processes, including dynamic countercurrent extraction and low-temperature concentration. This serves as a critical material basis for elucidating its multi-target regulatory mechanisms. Recent studies have highlighted the significant potential of TCMFG in treating complex diseases, such as inflammation, tumors, metabolic disorders, fibrosis, and orthopedic conditions like osteoarthritis and osteoporosis, by modulating signaling pathways such as TLR4/NF-kappa B, MAPK, NLRP3 inflammasome, PI3K/Akt/mTOR, Wnt/beta-catenin, and TGF-beta/Smads. For example, berberine alleviates acute lung injury by inhibiting the TLR4/NF-kappa B pathway, while tetramethylpyrazine derived from Ligusticum chuanxiong Hort granules mitigate joint destruction in rheumatoid arthritis by suppressing MAPK signaling. Curcumin analogs inhibit tumor metabolic reprogramming via the PI3K/Akt pathway. Despite these advances, current research encounters challenges, such as single-component analysis, unclear synergistic mechanisms of compound mixtures, and insufficient clinical evidence for translational applications. In the future, integrating multi-omics technologies (e.g., metabolomics, spatial transcriptomics) will be crucial for exploring supramolecular synergistic effects of compound mixtures. Furthermore, large-scale clinical trials are necessary to validate its potential in precision medicine. This article systematically reviews the progress of TCMFG research in signaling pathway-mediated disease mechanisms and outlines future directions to enhance its application in modern precision medicine.
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TC 0
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PU FRONTIERS MEDIA SA
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WC Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
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PT J
AU Li, LC
Liu, L
Xu, F
Wang, YZ
Mao, KL
AF Li, Liu-Cheng
Liu, Lei
Xu, Feng
Wang, Yu-Zhen
Mao, Kai-Li
TI Unraveling the role of FGF7 in osteoarthritis and osteoporosis: Therapeutic implications and challenges
SO FASEB JOURNAL
LA English
DT Review
DE FGF7; osteoarthritis; osteoporosis
AB Fibroblast growth factors (FGF) are involved in the regulation of cellular and physiological processes. Recent findings indicate that FGF7 shields osteoblasts from oxidative stress, diminishes apoptosis, and maintains osteogenic differentiation, thereby offering protection against osteoporosis. In contrast, within the context of osteoarthritis (OA), FGF7 intensifies disease progression through the upregulation of matrix-degrading enzymes, erosion of articular cartilage, and remodeling of subchondral bone. This review underscores the necessity for further investigation into the mechanisms driving FGF7's dual roles and its potential as a therapeutic target. Future research should focus on validating FGF7-targeted therapies in clinical trials and assessing the effects of FGF7 modulators on skeletal health across various orthopedic conditions, including osteoporosis and OA. These efforts are crucial for unraveling the multifaceted nature of FGF7 in bone metabolism and advancing precision medicine approaches for skeletal disorders.
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NR 13
TC 2
Z9 2
U1 0
U2 3
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 0892-6638
EI 1530-6860
J9 FASEB J
JI Faseb J.
PD MAR 26
PY 2025
VL 39
IS 6
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DI 10.1096/fj.202500226R
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SC Biochemistry & Molecular Biology; Life Sciences & Biomedicine - Other Topics; Cell Biology
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PT J
AU Qiu, DD
Yan, BH
Xue, HP
Xu, ZW
Tan, GQ
Liu, YJ
AF Qiu, Daodi
Yan, Binghan
Xue, Haipeng
Xu, Zhanwang
Tan, Guoqing
Liu, Yajuan
TI Perspectives of exosomal ncRNAs in the treatment of bone metabolic diseases: Focusing on osteoporosis, osteoarthritis, and rheumatoid arthritis
SO EXPERIMENTAL CELL RESEARCH
LA English
DT Review
DE Exosome; ncRNA; Bone metabolism; Osteoporosis; Osteoarthritis; Rheumatoid arthritis
ID nf-kappa-b; pi3k/akt/mtor signaling pathway; osteoblast differentiation; chondrocyte proliferation; articular chondrocytes; down-regulation; cells; osteoclastogenesis; biogenesis; microrna
AB Bone metabolic disorders, constituting a group of prevalent and grave conditions, currently have a scarcity of therapeutic alternatives. Over the recent past, exosomes have been at the forefront of research interest, owing to their nanoparticulate nature and potential for therapeutic intervention. ncRNAs are a class of heterogeneous transcripts that they lack protein-encoding capacity, yet they can modulate the expression of other genes through multiple mechanisms. Mounting evidence underscores the intricate role of exosomes as ncRNAs couriers implicated in the pathogenesis of bone metabolic disorders. In this review, we endeavor to elucidate recent insights into the roles of three ncRNAs - miRNAs, lncRNAs, and circRNAs - in bone metabolic ailments such as osteoporosis, osteoarthritis, and rheumatoid arthritis. Additionally, we examine the viability of exosomal ncRNAs as innovative, cell-free modalities in the diagnosis and therapeutic management of bone metabolic disorders. We aim to uncover the critical function of exosomal ncRNAs within the context of bone metabolic diseases.
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AB Sarcopenia, a progressive and systemic skeletal muscle disorder marked by the accelerated deterioration of both muscle function and mass, is highly prevalent among the elderly population, significantly contributing to an elevated risk of adverse outcomes, including falls, fractures, and muscle weakness. Clinical investigations have identified a strong correlation between sarcopenia and several prevalent degenerative skeletal muscle disorders. This correlation is attributed to imbalances in joint mechanics resulting from localized muscle atrophy and the influence of musculoskeletal secretory factors. In this review, we discuss the broader implications of sarcopenia and critically evaluate the currently established assessment methods. Furthermore, the clinical significance of prevalent musculoskeletal disorders (including osteoporosis, osteoarthritis, and spinal pathologies) in relation to sarcopenia, alongside the underlying mechanisms influencing this relationship, is summarized. Additionally, the effects of sarcopenia on the therapeutic efficacy of medications and surgical interventions for musculoskeletal conditions are reviewed. Sarcopenia is intricately linked to the onset, progression, and prognosis of musculoskeletal disorders. Future research should prioritize elucidating the potential mechanisms that connect muscle loss with skeletal muscle diseases, and investigating whether mitigating sarcopenia symptoms could decelerate the progression of these disorders, thereby paving new pathways for therapeutic interventions.
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TI High Prevalence of Symptomatic Knee Osteoarthritis Among Patients Who Have Fragility Hip Fractures
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DE fall; fragility hip fracture; knee; osteoarthritis; osteoporosis; subsequent fracture
ID osteoporotic fractures; risk-factors; elderly-men; fall risk; women; pain; epidemiology; questionnaire; instability; mortality
AB Background: Knee osteoarthritis (OA) is a common degenerative musculoskeletal condition that impairs mobility and balance, increasing fall risk. When combined with osteoporosis, it further increases the risk of fragility fractures. Despite its prevalence, the frequency of knee OA in patients who have fragility hip fractures (FHFs) is not well established. This study aimed to determine the prevalence of knee OA among FHF patients. Methods: We conducted a cross-sectional analysis of patients who underwent surgical treatment for FHF. The knee OA diagnoses followed the American College of Rheumatology criteria, and severity was assessed via the Kellgren-Lawrence classification system. Bone mineral density (BMD) was evaluated at the lumbar spine and contralateral hip, and fall risk was assessed using a self-report questionnaire. Results: Among the 162 patients

who had FHF (mean age 79 +/- 8.1 years; 80.2% women), 66% had symptomatic knee osteoarthritis (SKOA). Of these, 21.0% were classified as end-stage knee osteoarthritis. Notably, 47.1% of these end-stage knee osteoarthritides were recommended for knee OA surgery before their hip fracture. The presence of SKOA was significantly associated with a history of multiple falls (P = 0.013) and a high fall risk (P = 0.020). Among the 120 patients who had BMD data, 68% had low BMD (T-score <-2.5) at the contralateral hip or lumbar spine. Almost half (45%) of the FHF patients had concurrent SKOA and low BMD, whereas approximately 20% had SKOA, low BMD, and a high fall risk. Conclusions: There is a high prevalence of SKOA among FHF patients. Comprehensive evaluation and management of knee OA and osteoporosis are essential to reduce the risk of subsequent fractures in this vulnerable population.
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TI Osteoporosis should be evaluated by bone mineral density at the combination of the lumbar spine and ipsilateral femoral neck in female patients with knee osteoarthritis scheduled for knee arthroplasty: A retrospective observational study
SO JOURNAL OF ORTHOPAEDIC SCIENCE
LA English
DT Article
DE Knee arthroplasty; Osteoporosis; Dual-energy X-ray absorptiometry; Bone mineral density; Lumbar spine; Ipsilateral femoral neck
ID prevalence; hip
AB Background: Knee arthroplasty is a well-established surgery with good clinical outcomes. However, periprosthetic fractures and aseptic loosening negatively impact clinical outcomes, and osteoporosis is one of the causes of such complication. Osteoporosis is usually evaluated by bone mineral density of the lumbar spine and hip using dual-energy X-ray absorptiometry (DXA). However, the prevalence of this disease in patients with knee osteoarthritis scheduled for knee arthroplasty may be underestimated due to differences in the measurement sites. This study aimed to determine the appropriate measurement site for DXA that would not miss osteoporosis in female patients with knee osteoarthritis undergoing knee arthroplasty. Methods: We measured bone mineral density preoperatively in the consecutive 50 female patients with knee osteoarthritis scheduled for knee arthroplasty by dual-energy X-ray absorptiometry at five sites: the lumbar spine, bilateral-total hip, and femoral neck. We then compared the prevalence of osteoporosis among the four combinations of the lumbar spine and single hip site (ipsilateral or contralateral total hip or femoral neck). Results: Osteoporosis prevalence in the combination of the lumbar spine and ipsilateral or contralateral total hip was 32%, and that in the combination of the lumbar spine and contralateral femoral neck was 44%. Notably, the disease's prevalence in the combination of the lumbar spine and ipsilateral femoral neck was 50%, which was significantly higher than that in the other combinations. Conclusion: Osteoporosis should be evaluated by bone mineral density in the combination of the lumbar spine and ipsilateral femoral neck in female patients with knee osteoarthritis scheduled for knee arthroplasty. (c) 2024 The Japanese Orthopaedic Association. Published by Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.
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TI Osteonecrosis: A disabling disease not to be ignored in asthma and atopic conditions
SO ANNALS OF ALLERGY ASTHMA & IMMUNOLOGY
LA English
DT Review
ID femoral-head; avascular necrosis; nontraumatic osteonecrosis; idiopathic osteonecrosis; aseptic necrosis; atraumatic osteonecrosis; natural-history; bone; risk; pathophysiology
AB Osteonecrosis, also referred to as avascular necrosis, is a disease characterized by necrosis or death of a bone secondary to impairment in blood supply. The condition affects the epiphyseal ends of the bones such as the femur and the humerus, but it can also involve the metacarpal and metatarsal bones, the patella, the knee, the vertebrae, and the jaw. A plethora of inflammatory, autoimmune, hematological, thrombotic, and vascular diseases can lead to osteonecrosis. Corticosteroids are intimately linked to the development of osteonecrosis. The frequent use of systemic corticosteroids in patients with asthma, eczema, nasal polyposis, sinusitis, urticaria and angioedema, or anaphylaxis makes this disease of great relevance to the practicing allergist and pulmonologist. Untreated, bone

necrosis leads to frustrated bone remodeling and angiogenesis, leading to subchondral fractures and collapse of the articular heads of the bones, and culminating in debilitating osteoarthritis, often requiring arthroplasty. Recent studies have shed light on the molecular mechanisms underlying osteonecrosis and on the role of glucocorticoids. The gold standard test in patients suspected of having the disease is magnetic resonance imaging scanning, with plain radiographs having a lower sensitivity and specificity. Early diagnosis and intervention are essential. The allergist should avoid the frequent use of glucocorticoids and consider early introduction of steroid-sparing alternatives for asthma or sinusitis. Smoking and alcohol ingestion need to be addressed, and the management of glucocorticoid-induced osteoporosis may be helpful. It is essential for allergists to familiarize themselves with the disease and its diagnosis and to consider early referral to an orthopedic surgeon for surgical intervention. (c) 2024 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.
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TI Further Evidence That Chondrocalcinosis 1 (CCAL1) is a Confirmed Mendelian Phenotype With a Known Molecular Basis
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DE c.1205A>T; calcium pyrophosphate dehydrate deposition disease; CCAL1; chondrocalcinosis 1; CPPDD; osteoarthritis; osteoprotegerin; TNFRSF11B
ID deposition disease; osteoarthritis; mutation
AB Chondrocalcinosis (CCAL), also known as calcium pyrophosphate dihydrate deposition disease (CPPDD), is a frequent multifactorial condition in the elderly, but there are two rare autosomal dominant Mendelian forms, CCAL1 (OMIM %600668) and CCAL2. Only three families with molecularly proven CCAL1 have been reported. Here, we describe an additional family from Germany (12 individuals, nine living) with CPPDD manifesting in the third decade of life, presenting with severe spinal problems and variable levels of disability, only two of them with hip problems. The mildly impaired growth in this family (median height at age 20: 10th percentile) may represent an as yet undescribed sign of CCAL1, or alternatively familial short stature. In all documented families and in this family, the disorder resulted from the recurrent heterozygous stop-loss variant NM_002546.4:c.1205A>T; p.(Ter402Leuext*19) in TNFRSB11B on chromosome 8q24, which predicts an extended osteoprotegerin protein with 19 additional amino acid residues. The pathomechanism of CCAL1 is not known. Biallelic TNFRSF11B loss-of-function variants cause autosomal recessive juvenile Paget's disease of bone (PDB5); shared features between CCAL1 and PDB5 include demineralization, osteoporosis, increased fractures, and a progressive height loss with age, but PDB5 and CCAL1 have very different phenotypes and heterozygous carriers of PDB5-associated variants are asymptomatic. Summing up, NM_002546.4:c.1205A>T represents a rare type of stop-lost variant, likely a gain-of-function variant, and to date no other variant is known to cause CCAL1. Our findings expand the phenotypic spectrum of CCAL1 and underscore that CCAL1 is a distinct rare Mendelian disorder for which the underlying molecular basis is now known.
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TI Lipid-Driven Immunometabolism in Mesenchymal Stromal Cells: A New Axis for Musculoskeletal Regeneration
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE lipids; immunometabolism; mesenchymal stromal cells; tissue regeneration; post-traumatic osteoarthritis; osteoporosis; inflammation
ID energy-metabolism; stem-cells; bioactive lipids; bone-resorption; inflammation; resolution; cartilage; gpr120; mechanisms; mediators
AB The immunosuppressive and anti-inflammatory potential of mesenchymal stromal cells (MSCs) underpins their therapeutic value in musculoskeletal disorders. However, the underlying mechanisms remain ill-defined. Traditionally associated with immune cells, immunometabolism (the cellular metabolism-immune system interplay) is now recognized as central in a broader range of processes, including tissue homeostasis, repair, and chronic inflammation. Depending on the context and cell type, distinct metabolic pathways (e.g., fatty acid oxidation, lipid mediator biosynthesis) can drive pro-inflammatory/pro-resolving immune phenotypes. This dynamic is salient in musculoskeletal tissues: macrophage polarization, T-cell activation, and MSC immunomodulation are governed by metabolic cues. Emerging evidence highlights lipid-driven immunometabolism as a key player in MSC function, particularly in post-traumatic osteoarthritis (PTOA) and osteoporosis (OP). Unlike immune cells, MSCs rely on distinct metabolic programs (e.g., lipid sensing, uptake, and signaling) to exert context-dependent immunoregulation. In PTOA, persistent inflammation triggers lipid-centric metabolic pathways, enhancing MSC-driven immunomodulation and therapeutic outcomes. In OP, low-grade inflammation and altered lipid metabolism impair bone regeneration, modulating lipid-driven routes that can restore MSC osteogenic function and influence osteoclast precursors. This review explores how lipid-derived mediators and signaling contribute to MSCs' immunosuppressive capacity, positioning lipid

immunometabolism as a novel axis for rebalancing the inflamed joint microenvironment and encouraging musculoskeletal regeneration.
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PT J
AU Yin, M
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AF Yin, Meng
Zheng, Xin
Shi, Liang
TI Targeting p38 MAPK: A potential bridge between ER stress and age-related bone loss
SO CELLULAR SIGNALLING
LA English
DT Article
DE Endoplasmic reticulum stress; p38 MAPK; Age-related bone loss; Therapeutic strategies
ID endoplasmic-reticulum stress; activated protein-kinase; osteoblast differentiation; regulates osteoclast; pathway; osteoarthritis; apoptosis; mechanisms; decreases; inhibitor
AB The endoplasmic reticulum (ER) is crucial in the development of numerous age-related bone disorders. Notably, ER stress can precipitate bone loss by orchestrating inflammatory responses, apoptosis, and autophagy through the activation of the p38 MAPK pathway. Age-related bone loss diseases pose a significant burden on society and healthcare as the global population ages. This review provides a comprehensive analysis of recent research advancements, delving into the critical role of ER stress-activated p38 MAPK in inflammation, apoptosis, and autophagy, as well as its impact on bone formation and bone resorption. This review elucidates the molecular mechanisms underlying the involvement of ER stress-activated p38 MAPK in osteoporosis, rheumatoid arthritis, periodontitis, and osteoarthritis and discusses the therapeutic potential of targeting p38 MAPK. Furthermore, this review provides a scientific foundation for new therapeutic strategies by highlighting prospective research directions.
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TI Extracellular vesicles from adipose-derived stem cells in bone regeneration: Mechanisms and therapeutic advances
SO WORLD JOURNAL OF STEM CELLS
LA English
DT Review
DE Adipose-derived stem cell; Extracellular vesicle; Bone regeneration; Fracture healing; Osteoarthritis; Osteoporosis; Therapeutic mechanism

ID exosm; osteoarthritis; osteoporosis; alleviate; diagnosis
AB Extracellular vesicles (EVs) secreted by adipose-derived stem cells (ADSCs) have emerged as a promising cell-free therapeutic tool for bone regeneration. These EVs deliver a diverse array of bioactive molecules, including proteins, lipids, and nucleic acids, thereby modulating the bone microenvironment, activating key signaling pathways, and promoting bone regeneration. Innovative strategies involving preconditioning, genetic modification, and biomaterial-assisted delivery have been explored, with preclinical studies demonstrating synergistic effects that enhance targeting specificity and therapeutic efficacy. Functionally, EVs derived from ADSCs promote osteogenesis by enhancing osteoblast and mesenchymal stem cell activity, support angiogenesis through vascular endothelial growth factor signaling, and modulate inflammation by shifting macrophages from pro-inflammatory to anti-inflammatory phenotypes. In disease-specific contexts, they reduce cartilage degradation and support subchondral bone restoration in osteoarthritis, while in osteoporosis, they help restore the balance between bone formation and resorption and mitigate bone loss. Despite these promising developments, challenges remain in standardizing production protocols, optimizing delivery systems, and confirming long-term safety and efficacy in clinical settings. This review summarizes current insights into the mechanisms of EVs derived from ADSCs in bone-related diseases and highlights recent innovations and future directions that may accelerate their clinical application as a regenerative therapy.
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TI Multivariate analysis of Raman spectra for discriminating human collagens: In vitro identification of extracellular matrix collagens produced by an osteosarcoma cell line
SO SPECTROCHIMICA ACTA PART A-MOLECULAR AND BIOMOLECULAR SPECTROSCOPY
LA English
DT Article
DE Collagen; Raman spectroscopy; Multivariate analysis; Extracellular matrix; Bone; Connective tissues
ID morphometric-analysis; bone; spectroscopy; biomarkers; mechanism
AB Background: The NHS spends 4.3 pound billion annually to address musculoskeletal conditions, encompassing age- related bone disorders like osteoarthritis and osteoporosis. Traditional X-ray diagnostic methods are commonly employed for bone disorder diagnosis, primarily assessing gross anatomical bone structure changes. However, these methods are unable to identify subtle biochemical alterations within the bone. More detailed information, particularly about protein changes, may lead to enhanced diagnostics and treatment. Raman spectroscopy is a non-invasive, laser-based technique capable of detecting changes in the collagen component of bone. Despite its long-standing application in discerning mineral and protein changes within bone, there is limited

evidence on Raman spectral signatures of purified human collagens and their differentiation. This study aimed to test the hypothesis that Raman spectroscopy could detect different types of collagen in the human body. Results: A Raman microspectrometer with a 785 nm laser was used to measure unmineralized human collagens types I - VI and collagenous extracellular matrix (ECM) secreted by MG63 osteoblast-like cells. The results demonstrated the efficacy of Raman spectroscopy and subsequent multivariate analysis in distinguishing human collagen types I - VI. This implies that Raman spectroscopy, coupled with multivariate analysis, can identify pure human collagens and offers reference spectra similar to natural human collagen in the bone extracellular matrix. Significance: This study establishes Raman spectroscopy as a tool for identifying and characterizing human collagens, aiding in the diagnosis of connective tissue disorders. The creation of a spectral reference library for pure human collagen types I - VI holds potential for medical diagnostics, analytical chemistry, and materials science applications.
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TI Tissue-specific roles of de novo DNA methyltransferases
SO EPIGENETICS & CHROMATIN
LA English
DT Review
DE DNA methylation; <italic>De novo</italic> methyltransferase; Dnmt3a; Dnmt3b; Knockout; Cre recombinase; LoxP; Tissue-specific; Development; Differentiation; Stem cells
ID embryonic stem-cells; hematopoietic stem; clinical-significance; synaptic

function; mammalian dna; dnmt3a; methylation; expression; deletion; gene
AB DNA methylation, catalyzed by DNA methyltransferases (DNMT), plays pivotal role in regulating embryonic development, gene expression, adaption to environmental stress, and maintaining genome integrity. DNMT family consists of DNMT1, DNMT3A, DNMT3B, and the enzymatically inactive DNMT3L. DNMT3A and DNMT3B establish novel methylation patterns maintained by DNMT1 during replication. Genetic variants of DNMT3A and DNMT3B cause rare diseases such as Tatton-Brown-Rahman and ICF syndromes. Additionally, somatic mutations cause common conditions such as osteoarthritis, osteoporosis, clonal hematopoiesis of indeterminate potential (CHIP), hematologic malignancies, and cancer. While DNMTs have been extensively studied in vitro, in early development and in disease, their detailed physiologic roles remain less understood as in vivo investigations are hindered by the embryonic or perinatal lethality of the knockout mice. To circumvent this problem, tissue-specific Dnmt3a and Dnmt3b knockouts were engineered. This review explores their diverse molecular roles across various organs and cell types and characterizes the phenotype of the knockout mice. We provide a comprehensive collection of over forty tissue-specific knockout models generated by cre recombinase. We highlight the distinct functions of DNMT3A and DNMT3B in germ cells, early development, uterus, hematopoietic differentiation, musculoskeletal development, visceral organs, and nervous system. Our findings indicate that DNMT3A primarily regulates hematopoietic differentiation, while DNMT3B is crucial for cartilage homeostasis and ossification. We emphasize the context-dependent roles of DNMT3A and DNMT3B and demonstrate that they also complement DNMT1 maintenance methyltransferase activity. Overall, the expression patterns of DNMTs across tissues provide insights into potential therapeutic applications for treating neurologic diseases, cancer, and osteoporosis.
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AF Lallemant, M.
   Ecoffet, R.
   Kadiake, T.
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   Mottet, N.
TI Perineal deformation during forceps, vacuum and OdonAssistTM assisted vaginal deliveries: A simulation study based on advanced image processing☆

SO EUROPEAN JOURNAL OF OBSTETRICS & GYNECOLOGY AND REPRODUCTIVE BIOLOGY
LA English
DT Article
DE Perineal strain; Biomechanic; Perineal trauma; OdonAssist; Vacuum; Forceps; Stereophotogrammetry
ID bd odon device(tm); fetal head; birth; lacerations; protection; risk
AB Objectives: The aim of this study was to analyse influence of the fetal head position and the type of instrument used (forceps, vacuum, OdonAssist (TM)) on perineal deformation, during simulated vaginal deliveries monitored by stereophotogrammetry. Methods: An exploratory study was conducted using mannequins simulating vaginal births. Fifty simulated deliveries were performed with different fetal head positions and instruments: Pajot's forceps, Kiwi-vacuum, and OdonAssist (TM). Stereophotogrammetry measured perineal deformations called equivalent strains E-eq. Results: E-eq during spontaneous deliveries were minimal, average, and maximal at 0.8 %, 5.8 %, and 11.6 %, respectively. Assisted vaginal births (AVB) showed slightly higher strains compared to spontaneous deliveries. In the occipito-posterior position (OP), strains were significantly higher ($p < 0.05$). Equivalent strain Eeq trend towards higher mean (6.7 f 0.6 %) and maximum (12.3 f 0.8 %) with forceps compared to other methods in the occiput anterior position (OA), especially against spontaneous (mean: 5.3 f 0.5 % and max: 9.9 f 0.6; $p = 0.06$), vacuum AVB (mean: 4.6 f 1.0 % and max: 9.4 f 0.1 %, $p = 0.06$) and OdonAssistTM AVB (mean: 3.8 f 0.9 % and max: 8.8 f 1.0 %, $p = 0.06$). Forceps induced greater strains compared to vacuum and OdonAssits (TM). In OP position, OdonAssistTM tend to lower mean equivalent strain Eeq compared to spontaneous vaginal deliveries (4.9 f 0.6 % vs 6.4 f 0.5 %, $p = 0.06$). Conclusion: Results confirmed increased mechanical perineal stress for OP fetal position and for forceps assisted deliveries compared to others devices. The OdonAssistTM may offer a less invasive alternative, reducing perineal strains. Stereophotogrammetry provides valuable data on the mechanical effects of childbirth.
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Kalinkovich, A
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TI The role of TRIM proteins in chronic inflammation-associated musculoskeletal diseases
SO AGEING RESEARCH REVIEWS
LA English
DT Review
DE TRIM proteins; Chronic inflammation; Musculoskeletal disorders
ID nf-kappa-b; drug-delivery systems; innate immune; artificial-intelligence; tnf-alpha; ubiquitin; degradation; osteoarthritis; cells; activation
AB Musculoskeletal disorders (MSDs), including osteoarthritis (OA), rheumatoid arthritis (RA), osteoporosis (OP), and intervertebral disc degenerative disease (IVDD), are among the most common and serious health problems worldwide. However, despite extensive research, drug therapy for these diseases remains a major challenge. This is likely due to a poor understanding of the underlying mechanisms. Recent evidence suggests that the development of these MSDs is associated with protein dysregulation and ongoing chronic inflammation. Protein turnover is controlled by the ubiquitin-proteasome system (UPS), in which E3 ubiquitin ligases, including tripartite motif proteins (TRIMs), are responsible for substrate specificity. Since multiple TRIMs are involved in the development of MSDs, their targeting may be used to correct impaired protein turnover. The recent development of targeted protein degradation technologies has revolutionized drug discovery by selectively degrading specific proteins using the UPS. It is hypothesized that failure to resolve chronic inflammation plays a critical role in the development of MSDs, suggesting that its successful resolution will result in the alleviation of MSD-related symptoms. The process of inflammation resolution is enabled by specialized pro-resolving mediators (SPMs), which are enzymatically generated from dietary essential polyunsaturated fatty acids. Supplementation with SPMs or their stable, small-molecule receptor mimetics and agonists has shown beneficial effects in MSD animal models. In this review, we substantiate the idea that the combined use of TRIM-targeting drugs and inflammation-resolving compounds represents a promising new therapeutic approach to mitigate OA, RA, OP, and IVDD manifestations and improve patient outcomes. Methods: Aligning with the primary objectives of this review, we used a narrative-style review design to explore and critically analyze the potential links between TRIMs, chronic inflammation, and musculoskeletal disorders. Articles included in this review were identified through literature searches using PubMed (English-language original and review articles published until May 2025). The following search terms were used considering all possible combinations: "TRIM proteins", "ubiquitin proteasome system", "ubiquitin ligases", "targeted protein degradation", "proteolytic targeting chimeras", "molecular glues", "musculoskeletal disorders", "osteoarthritis", "rheumatoid arthritis", "osteoporosis", "intervertebral disc degenerative disease", "chronic inflammation", "inflammation resolution", "specialized pro-resolving mediators". Search results were supplemented by reviewing reference citations from the articles identified in the initial searches and drawing on the authors' familiarity with the published literature.

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NR 331
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J9 AGEING RES REV
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WC Cell Biology; Geriatrics & Gerontology
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GA 5PD7J
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AF Wang, Diaodiao
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Liu, Yubo
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Ye, Peng
Sun, Wenqiang
Yao, Qi
TI Porous PLGA microspheres loaded with PTH1-34 peptide for long-term treatment of OA
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Article
DE Osteoarthritis; PTH1-34; Porous PLGA microspheres; Sustained release; Cartilage repair
ID osteoarthritis; teriparatide; diagnosis; osteoporosis; degradation; women
AB Background: Osteoarthritis (OA) is a chronic disease characterized by degeneration of articular cartilage, affecting over 530 million patients worldwide. Current oral medications such as non-steroidal anti-inflammatory drugs (NSAIDs) can only alleviate symptoms and are associated with numerous adverse effects. Although teriparatide (PTH1-34) exhibits dual functions of chondroprotection and osteogenic effects, its clinical application is significantly limited by its short biological half-life (30-60 min) and accelerated degradation within the inflammatory microenvironment of joint cavities. Methods: Porous sustained-release microspheres (M@PTH1-34) were fabricated using FDA-approved poly (lactic-co-glycolic acid) (PLGA) as the matrix, encapsulating PTH1-34 within their multi-channel porous structure. Uniform microsphere preparation and high-efficiency drug loading were achieved through membrane emulsification and temperature-controlled embedding techniques. To systematically evaluate the sustained-release profile and therapeutic outcomes, both in vitro and in vivo OA models were established, enabling comprehensive analysis of cartilage repair efficacy, anti-inflammatory regulation, and immunomodulatory effects. Results: PTH1-34 could be efficiently loaded into microspheres after self-healing and achieve consistent release over 30 days with biological activity being maintained. In OA model rats, M@PTH1-34 significantly improved behavioral and radiological outcomes, increased cartilage smoothness and thickness, and increased the expression of chondrogenic markers. Additionally, in vitro and in vivo safety tests revealed no significant safety issues. These findings indicate that M@PTH1-34 holds promise as a long-lasting, cost-effective, and safe therapeutic approach for OA. Conclusion: This study successfully developed a uniform-sized PLGA-based sustained-release microsphere system (M@PTH1-34) that enables continuous drug release for over 30 days following single intra-articular administration. M@PTH1-34

exerts its therapeutic effects on osteoarthritis through the following two ways: (1) Promoting cartilage repair by enhancing the chondrogenic differentiation ability of bone marrow mesenchymal stem cells (BMSCs); (2) Improve the inflammatory microenvironment of joints by inhibiting the expression of inflammatory factors (such as IL-1 beta) and regulating the polarization state of M1/M2 macrophages. The translation potential of this article: The system demonstrates prominent clinical translation advantages: (1) Innovative utilization of FDA-approved PLGA carrier combined with membrane emulsification technique ensures precise size control and standardized production; (2) Localized delivery strategy achieves targeted retention within articular cavity, validated by animal studies showing no systemic exposure risks; (3) Standardized preparation process demonstrates the feasibility of industrial-scale production.
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NR 41
TC 5
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PU ELSEVIER
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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J9 J ORTHOP TRANSL
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AU Xu, XR
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AF Xu, Xin-Rui
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Wang, Xing-Yu
Bi, Hai-Zheng

Bai, Qian-Xiang
Wang, Meng
TI Botany, traditional uses, phytochemistry, pharmacology, processing, and applications of Cibotium barometz (L.) J. Sm.: A review
SO FITOTERAPIA
LA English
DT Review
DE Traditional uses; Phytochemistry; Pharmacology; Processing; Applications; Cibotium barometz (L.) J. Sm
ID osteoporosis; polysaccharides; proliferation; glioblastoma; metabolism; extracts; rhizome; cells
AB Cibotium barometz (L.) J. Sm. (C. barometz), an ancient fern has a long history as a natural medicine in China, India, Vietnam, and other countries. In the traditional medical system, it is often used to treat bone pain, urinary system diseases, reproductive disorders, and so on. This paper aims to provide a comprehensive overview of current research on botany, traditional uses, phytochemistry, pharmacology, processing, and applications of C. barometz. In addition, resource conservation, quality control, and perspectives for future research on C. barometz are also discussed. Recent phytochemical studies of C. barometz have shown that over 100 compounds have been isolated from the plant, including phenylpropanoids, polyphenols, flavonoids, terpenoids, steroids, polysaccharides, and other compounds. Modern pharmacological studies have also confirmed that C. barometz has anti-osteoporosis activity, anti-microorganism activity, anti-osteoarthritis activity, anti-cancer activity, hepatoprotective activity, protective activity on muscle, alleviating Alzheimer's disease, and so on. As an important means of preclinical application, the type and content of the components contained in C. barometz changed significantly before and after processing, and the strength of its pharmacological activity also changed. Furthermore, it has many applications in the fields of compound preparations and biomedicine, which have great development potential. Nevertheless, there are also some research gaps in C. barometz. This review appeals for more studies on C. barometz to better understand its pharmacological mechanism and active substance basis. Besides, more research on resource conservation and quality control is also necessary to ensure its sustainable use and development.
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TI Histone modifications: Unveiling the epigenetic enigma of degenerative skeletal diseases
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DE Epigenetics; Histone modifications; Degenerative skeletal diseases; Small molecule inhibitors; Epigenetic therapy
ID intervertebral disc degeneration; inhibitor vorinostat saha; deacetylase inhibitor; gene-expression; bone-marrow; lysine 2-hydroxyisobutyrylation; osteogenic differentiation; clinical pharmacokinetics; metabolic-regulation; chromatin-structure
AB Degenerative skeletal diseases, including osteoporosis, osteoarthritis, and intervertebral disc degeneration, are prevalent age-related conditions characterized by progressive tissue degeneration and functional decline. Histone modifications are covalent modifications of histone residues, catalyzed by specific enzymes, that modulate chromatin architecture and transcriptional activity. Accumulating evidence highlights the critical involvement of histone modifications in orchestrating disease-associated transcriptional programs. In osteoporosis, histone modifications regulate osteoblast and osteoclast differentiation, thereby disrupting bone homeostasis. In osteoarthritis, they drive the expression of matrix-degrading enzymes in chondrocytes, contributing to cartilage degradation. In intervertebral disc degeneration, they are implicated in nucleus pulposus cell senescence, apoptosis, and extracellular matrix degradation. This review summarizes the distinct mechanistic roles of histone modifications across these conditions and explores the therapeutic potential of targeting histone-modifying enzymes, underscoring epigenetic regulation as a promising strategy for precision intervention in degenerative skeletal diseases. The translational potential of this article: This review comprehensively explores the role of histone modifications in degenerative skeletal diseases and evaluates the potential of histone-modifying enzyme inhibitors as therapeutic targets. These insights provide new strategies and directions for the treatment of degenerative skeletal diseases.
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TI Insights into the role of histone lysine demethylases in bone homeostasis and skeletal diseases: A review
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DT Review
DE Bone remodelling; Bone resorption; Bone formation; Histone demethylases; Osteoporosis; Osteoarthritis; Osteosarcoma
ID mesenchymal stem-cells; osteogenic differentiation; domain; osteosarcoma; hypertrophy; adipocyte; therapy; protein; target; growth
AB Histone lysine demethylases (KDMs), as important epigenetic regulators, are involved in various biological processes such as energy metabolism, apoptosis, and autophagy. Recent research shows that KDMs activate or silence downstream target genes by removing lysine residues from histone tails, and participate in the regulation of bone marrow mesenchymal stem cells (BM-MSCs), osteoblasts (OB), osteoclasts (OC), chondrocytes and other skeletal cell development, differentiation and formation. Moreover, several members of the KDM family affect the occurrence and development of bone diseases such as osteoporosis (OP), osteoarthritis (OA), osteosarcoma (OS), by regulating target genes. Specific regulation mechanisms of KDMs suggest new strategies for bone disease treatment and prevention. Despite the unique function and importance of KDMs in the skeletal system, previous studies have never systematically summarized their specific role, molecular mechanism, and clinical treatment in bone physiology and

pathology. Therefore, this review summarises the expression pattern, intracellular signal transduction, and mechanism of action of the KDM family in several bone physiological and pathological conditions, aiming to highlight the important role of KDMs in bone diseases and provide a reference for the future treatment of bone diseases.
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NR 92
TC 1
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PT J
AU Huang, JW
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TI The role of LGR4 in bone metabolism and tumor bone metastasis
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE LGR4; bone metabolism; bone metastasis; osteoclasts; osteoblasts
ID molecular-mechanisms; multiple-myeloma; cancer; differentiation; expression; receptor; cells; disease; gpr48; gene
AB The Leucine-rich repeat-containing G protein-coupled receptor 4 (LGR4) is a member of the G protein-coupled receptor family and plays an important role in bone metabolism and tumor bone metastasis. LGR4 affects bone metabolism by regulating the differentiation and activity of osteoblasts and osteoclasts, and is involved in the balance between bone resorption and bone formation. Deficiency of LGR4 leads to osteoporosis, whereas the up-regulation of LGR4 may help to alleviate the development of traumatic osteoarthritis. Furthermore, in breast cancer and multiple myeloma, LGR4 promotes tumor cell metastasis to bone tissue by activating related signaling pathways. Therefore, LGR4 may be a potential target for the treatment of bone metabolic diseases and tumor bone metastasis.
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NR 76
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TI Cumulative Burden of Digital Health Technologies for Patients With Multimorbidity: A Systematic Review
SO JAMA NETWORK OPEN
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ID care
AB Importance: Digital health technologies (DHTs) aiming to monitor, treat, and manage diseases can be prescribed for patients with multimorbidity; yet most DHTs are designed for individual conditions or problems, while approximately half of patients with chronic conditions have multiple chronic conditions. Objectives: To identify DHTs approved by the US Food and Drug Administration (FDA) or listed in the Organisation for the Review of Care and Health Apps (ORCHA) library and prescribable for a hypothetical patient with 5 conditions and to model the number of DHTs this patient should be prescribed to receive benefits health professionals considered important. Evidence review: The FDA databases (Premarket Notification 510(k), Premarket Approval, and De Novo) and the ORCHA App Library from National Health Service Somerset were systematically searched for DHTs registered or updated between January 1, 2019, and December 31, 2022, that could be prescribed to a hypothetical woman with 5 chronic conditions (type 2 diabetes, hypertension, chronic obstructive pulmonary disease, osteoporosis, and osteoarthritis). After abstracting each DHT's elementary functions (ie, simple and delineated features to monitor, treat, and/or manage conditions), an assessment was undertaken to determine the fewest DHTs this hypothetical patient should be prescribed to receive benefit from digital functions health professionals considered important. Findings: A total of 148 DHTs were identified (68 [46%] from FDA databases), of which 96 (65%) involved devices and 52 (35%) were standalone health apps. Only 5 DHTs (3.4%) were intended for 2 or more conditions. DHTs offered 140 elementary functions, ranging from recording, tracking, or visualizing health parameters to providing information to digital therapeutics with just-in-time interventions. The hypothetical patient would need to be prescribed up to 13 apps and 7 devices (a blood pressure monitor, a smartwatch, a pulse oximeter, a connected weight scale, a sensor-attached inhaler to monitor adherence, a lung function monitor, and a blood glucose sensor) to receive benefits from 28 functions at least 3 of 5 health professionals considered important. Conclusions and relevance: This systematic review found that almost all prescribable DHTs were developed for a single condition or problem. Thus, patients with multiple chronic conditions would have to routinize many DHTs concurrently in daily life to benefit from digital functions health professionals considered important.
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PA 330 N WABASH AVE, STE 39300, CHICAGO, IL 60611-5885 USA
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TI Antioxidative fullerol prevents bone loss due to its anti-osteoclastogenic and pro-osteogenic activities
SO NANOMEDICINE-NANOTECHNOLOGY BIOLOGY AND MEDICINE
LA English
DT Article
DE Fullerene derivative; Signal pathways; Osteoclast formation; Osteogenesis; Osteoporosis
ID oxidative stress; redox regulation; differentiation; osteoporosis; osteoarthritis; adipogenesis; activation; mechanisms; cells; foxo1
AB Purpose: Previous studies have demonstrated a role for oxidative stress in promoting osteoclastogenesis and bone loss. This study aimed to assess the ability of fullerol, a powerful nano-antioxidant, to prevent bone loss and promote osteogenesis, and additionally provide novel insight into mechanisms of action. Methods: Osteoclastogenesis assays were conducted in murine progenitor cells stimulated with receptor activator of nuclear factor kappa-B ligand (RANKL), with and without fullerol. The cells were stained to detect the presence of osteoclastic markers and RT-PCR was used to measure the expression of osteoclastic genes. To assess osteogenesis, stem cells were incubated in osteogenic medium with or without fullerol, as well as with an inhibitor of p38-MAPK, then stained to determine mineralization. RT-PCR was used to measure osteoblastic gene expression. In the animal model, rabbits were injected with methylprednisolone with or without fullerol, or a control. Animals were later euthanized and spine fragments underwent imaging assessment. Results: Fullerol prevented formation of osteoclasts in RAW264.7 cells exposed to RANKL as well as the expression of osteoclastic genes TRAP, CATK, and MMP9. D1 cells exposed to fullerol displayed an increase in extracellular matrix mineralization and expression of osteoblastic genes. However, when fullerol was added in the presence of a p38-MAPK inhibitor, its effects on mineralization were attenuated. In a rabbit model of steroid-induced osteoporosis, simultaneous injection of fullerol reduced vertebral bone loss, decreased trabecular separation, and increased trabecular number. Conclusion: Fullerol shows early potential for use in osteoporosis therapy, due to its ability to inhibit osteoclast formation and stimulate osteogenesis.
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TI Advances in 3D bioprinting to enhance translational applications in bone tissue engineering and regenerative medicine
SO HISTOLOGY AND HISTOPATHOLOGY
LA English
DT Review
DE 3D bioprinting; Bioink; TERM; Bone; Biomaterials; Hydrogel
ID cell; limitations; challenges; cellulose; glycol)
AB . Bone defects are due to trauma, infections, tumors, or aging, including bone fractures, bone metastases, osteoporosis, or osteoarthritis. The global burden of these demands research into innovative strategies that overcome the limitations of conventional autografts. In this sense, the development of threedimensional (3D) bioprinting has emerged as a promising approach in the field of tissue engineering and regenerative medicine (TERM) for the on-demand generation and transplantation of tissues and organs, including bone. It combines biological materials and living cells, which are precisely positioned layer by layer. Despite obtaining some promising results, 3D bioprinting of bone tissue still faces several challenges, such as generating an effective vascular network to increase tissue viability. In this review, we aim to collect the main knowledge on methods and techniques of 3D bioprinting. Then, we will review the main biomaterials, their composition, and the rationale for their application in 3D bioprinting for the TERM of bone.
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TI The Outcome of Post-Surgical Hip Prosthesis Rehabilitation: Results from a Monocentric Cohort Study
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DT Article
DE outcome; orthopedic rehabilitation; hip prothesis; post-surgical
ID total joint arthroplasty; total knee arthroplasty; body-mass-index; quality-of-life; screening tools; united-states; risk-factors; obesity; replacement; osteoarthritis
AB Background: With the increase in life expectancy, more patients are undergoing total hip arthroplasty, primarily due to the rising incidence of osteoarthritis. The outcomes of rehabilitation following these surgical interventions are influenced by various factors. This study aims to explore the impact of age, gender, and body mass index (BMI) on pain and functional and rehabilitative outcomes after surgical hip prosthesis rehabilitation. Methods: We enrolled all patients admitted to a private clinic from January 2021 to December 2023 for rehabilitation after unilateral hip arthroplasty. For each patient, we collected data of Barthel Index, Tinetti Scale, Numeric Rating Scale (NRS), and range of motion (ROM) at the beginning and end of the hospitalization. We assessed whether the evaluated outcomes differed based on gender, age, and BMI using the Mann-Whitney and Kruskal-Wallis tests. Results: A total of 2.167 patients were studied (56% female and 36.5% over 75 years old). Male patients, adults (18-64 years), and those with a BMI < 30 showed higher values of Barthel Index, Tinetti Scale, and ROM at both admission and discharge ($p < 0.05$), along with significantly lower NRS scores. Each subgroup based on age, gender, and BMI showed an improvement in NRS (difference between admission and discharge) of at least 40%, it was about 50% for men and adults. The improvement in ROM (difference between admission and discharge) was more than 10% in both active and passive flexion, around 20% for passive abduction, and 50% for active abduction, with no significant differences based on age, gender, or BMI. Conclusions: Despite the absence of specific contraindications for arthroplasty procedures, a high BMI, age over 75 years, and female gender are associated with slightly worse functional and rehabilitation outcomes compared to other patients undergoing the same procedures. A preoperative screening for the evaluation of osteopenia, osteoporosis, and BMI could be a valuable tool for studying and improving outcomes in these patients.
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TC 1
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PU MDPI
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J9 J CLIN MED
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WC Medicine, General & Internal
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TI Jiawei yanghe decoction alleviates osteoporotic osteoarthritis by promoting MSC osteogenic differentiation and homing via ITGB6/TGF-β/ CXCR4 pathway
SO PHYTOMEDICINE
LA English
DT Article
DE Osteoporotic Osteoarthritis; Jiawei Yanghe Decoction; Mesenchymal stem cell; Bone formation; Cell migration
ID subchondral bone; articular-cartilage; degeneration; inhibition; increases; migration; severity; model; axis
AB Background: Osteoporotic osteoarthritis (OPOA), a distinct subtype of osteoarthritis (OA), has imposed a significant health and economic burden

worldwide. However, mechanistic studies and therapeutic strategies for this disease remain in the exploratory stage. Purpose: This study aimed to investigate the specific molecular mechanisms by which osteoporosis (OP) exacerbates OA progression through accelerated subchondral bone (SB) sclerosis and the potential of Jiawei Yanghe Decoction (JWYHD) in treating OPOA. Methods: Key genes in the progression of OPOA were investigated through human clinical sample studies, GEO database analysis, and RNA-seq. The OPOA mouse model was established by a combination of OVX and DMM, with JWYHD administered at different concentrations. In vivo, the pathological status of OPOA and the therapeutic effects of JWYHD were evaluated using behavioral tests, micro-CT, and histopathological examinations. In vitro, the osteogenic differentiation and migration capabilities of mesenchymal stem cells (MSC) were assessed by WB, qRT-PCR, Transwell assays, wound healing assays, and IF co-staining. Results: ITGB6/TGF-(3 plays a vital role in the pathogenesis of OPOA. A novel concept, the 'Diaphysis-Epiphysis paradox', is hereby proposed, providing a new theoretical framework for research into the pathomechanisms of OPOA from the perspective of abnormal bone mass distribution. By protecting cartilage, regulating the balance of bone mass, and modulating the migration of MSC, JWYHD improves cartilage degeneration and bone mass distribution abnormalities caused by OPOA in an all-around manner. Conclusion: Abnormal migration and osteogenic differentiation disorders of MSC accelerate OPOA progression. JWYHD achieved bidirectional regulation of OPOA through ITGB6/TGF-(3/(3-catenin and CXCL12/CXCR4 multiple signaling pathways.
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EA SEP 2025
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WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy

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TI Immunometabolic regulation of disulfidptosis in orthopedic diseases: mechanistic heterogeneity and therapeutic targets
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE disulfidptosis; bone diseases; oxidative stress; immunometabolism; targeted therapy
ID osteoarthritis; apoptosis
AB Disulfidptosis is a novel form of programmed cell death triggered by cystine metabolic disorders and disulfide stress, initially studied primarily in the context of tumors. In recent years, its role in the occurrence and development of orthopedic diseases has gained increasing attention. This review systematically explores the dual regulatory mechanisms of disulfidptosis in degenerative orthopedic diseases, such as intervertebral disc degeneration, osteoporosis, and osteoarthritis, as well as in malignant bone tumors like osteosarcoma, along with their immunometabolic basis. The research findings indicate that in degenerative lesions, microenvironmental stresses such as ischemia and hypoxia exacerbate tissue degeneration by promoting abnormal accumulation of disulfide bonds and damaging the cytoskeleton. In osteosarcoma, tumor-associated oxidative stress can induce metabolism-dependent cell death, providing new opportunities for targeted therapy. The article further summarizes key signaling pathways and molecular

regulatory networks, discussing the potential value of targeted intervention strategies in slowing disease progression and achieving precision treatment.
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AU Sauhta, R
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AF Sauhta, Ravi
Makkar, Dheeraj
TI Proximal Tibia Fractures in Osteoporosis
SO INDIAN JOURNAL OF ORTHOPAEDICS
LA English
DT Review
DE Osteoporosis; Proximal tibia; ORIF; Osteoarthritis; Elderly
ID total knee arthroplasty; plateau fractures; internal-fixation; condylar fractures; surgical-treatment; trabecular bone; risk-factors; infection; microstructure; complications

AB BackgroundTibial plateau fractures are frequently observed in elderly patients, often resulting from low-energy trauma. The treatment of tibial plateau fractures in this population is further complicated by factors such as osteoporosis, osteoarthritis, and other medical comorbidities.ObjectiveThis article provides a comprehensive review of the different treatment strategies for proximal tibial fractures in the elderly. A variety of internal and external fixation techniques, medical management as well as acute arthroplasty, are discussed as potential approaches for achieving optimal reconstruction and functional recovery.What is already knownExisting literature emphasizes that osteoporotic bones, characterized by reduced bone density and compromised structural integrity, pose significant challenges to fracture fixation. These factors often diminish the efficacy of fixation devices in proximal tibial fractures, leading to an increased likelihood of fixation failure.Gap in literatureWhile the high failure rates associated with osteoporotic bone fixation are wellrecognized, there is a notable lack of comprehensive studies that integrate biomechanical, biological, and technological advancements to improve fixation outcomes, in proximal tibial fractures. This article aims to address this gap by reviewing current diagnostic approaches and exploring innovative strategies involving advanced materials and regenerative technologies designed to enhance fixation success.ConclusionThe management of proximal tibial fractures in the elderly requires a nuanced approach that integrates surgical intervention with medical management. A tailored treatment plan, based on specific fracture characteristics and overall health, is critical to optimizing postoperative functional outcomes. This article emphasizes the importance of a comprehensive, individualized treatment strategy to improve recovery and quality of life for elderly patients suffering from tibial plateau fractures.
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J9 INDIAN J ORTHOP
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WC Orthopedics
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AF de Siqueira, Lilian
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TI 3D-printed β-TCP/curcumin scaffolds as a local drug delivery system for bone tissue regeneration
SO BIOMEDICAL MATERIALS
LA English
DT Article
DE scaffolds; <italic>beta</italic>-tricalcium phosphate; curcumin; 3D printing; tissue engineering
ID in-vitro; curcumin; microstructure; complexes; silicate; release
AB The growing clinical need for filling defects and bone voids has led to the development of scaffolds that stimulate bone regeneration and serve as temporary models for vascularised bone growth. Additionally, these scaffolds can function as drug delivery systems to reduce inflammatory processes associated with diseases such as osteoarthritis, rheumatoid arthritis, osteoporosis, and bone cancer. Among the materials used to manufacture scaffolds, beta-tricalcium phosphate (beta-TCP, Ca3(PO4)2) stands out due to its excellent biocompatibility and chemical composition, closely resembling minerals from bone tissue. When combined with curcumin, calcium phosphate scaffolds offer a promising platform for drug delivery, as their tailored porous structure can provide controlled release. Curcumin enhances anti-inflammatory and antioxidant properties, thereby promoting tissue

regeneration. In this study, beta-TCP powders loaded with 5 and 10 mg ml-1 of curcumin (designated as beta-TCP/Curc 5 and beta-TCP/Curc 10) were successfully obtained via freeze-drying and characterised using x-ray diffraction and Fourier-transform infrared spectroscopy to assess their crystallinity and chemical composition. The beta-TCP/Curc powders were evaluated for their ability to load and release curcumin. Subsequently, beta-TCP and beta-TCP/Curc 5 scaffolds were prepared using 3D printing. The beta-TCP/Curc 5 scaffolds were assessed for curcumin release, cytotoxicity profile, and antimicrobial activity. The beta-TCP/Curc 5 powders exhibited significantly higher curcumin adsorption and good release capacity, whereas the beta-TCP/Curc 10 powders displayed reduced curcumin loading and limited release efficiency. The combination of beta-TCP/Curc 5 with sodium alginate produced a suitable paste for 3D printing scaffold fabrication, and the beta-TCP/Curc 5 scaffolds demonstrated high similarity to the computational model. Importantly, the beta-TCP scaffolds did not exhibit cytotoxicity in the MC3T3-E1 cell line, and after curcumin loading, there was no increase in cellular cytotoxicity observed. In fact, an increase in cell viability was noted compared to the control after three days of indirect assays, suggesting that this combination may be beneficial for promoting cell growth. However, the scaffolds did not show any antibacterial effects against S. aureus and E. coli under the tested conditions. This study demonstrates that adequate curcumin loading in 3D-printed beta-TCP scaffolds can facilitate curcumin release at the bone healing site, potentially influencing the cellular processes involved in bone regeneration and remodelling.
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NR 58
TC 0
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PA TEMPLE CIRCUS, TEMPLE WAY, BRISTOL BS1 6BE, ENGLAND
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TI Musculoskeletal disease in acromegaly-a population-based registry study
SO EUROPEAN JOURNAL OF ENDOCRINOLOGY
LA English

DT Article
DE acromegaly; musculoskeletal disease; osteoarthritis; osteoporosis; joint replacement surgery
ID quality-of-life; vertebral fractures; arthropathy; progression; prevalence; patient
AB Objective Acromegaly is associated with multiple musculoskeletal complications that affect the quality of life and work ability. We aimed to examine the risk of osteoarthritis, musculoskeletal surgery (including joint replacement), osteoporosis, fractures, and analgesic consumption in Danish acromegaly patients.Design National, registry-based cohort study.Methods All validated incidents and prevalent cases of acromegaly in the period 1977-2021 (n = 844) were included and matched 1:100 with healthy controls. Outcomes were identified using diagnosis, surgical procedure, and medication codes and analyzed using Cox regression and Kaplan-Meier plots.Results Patients were at significantly increased risk of osteoarthritis of the shoulder [hazard ratio (HR): 5.25 (3.05; 9.06)], hip [HR: 3.15 (2.57; 3.87)], and knee [HR: 2.25 (1.85; 2.72)], and medically treated osteoporosis [HR: 2.13 (1.64; 2.78)] even before acromegaly diagnosis. The risk of joint replacement surgery of the shoulder [HR: 4.60 (2.57; 8.25)], hip [HR: 3.32 (2.67; 4.12)], and knee [HR: 2.52 (1.89; 3.36)] was increased in acromegaly patients, as was the risk of being prescribed weak analgesics [HR: 1.22 (1.04; 1.44)] or opioids [HR: 1.58 (1.38; 1.82)]. Surgical complications [HR: 2.19 (1.59; 3.03)] and repeat hip surgery [HR: 3.64 (2.09; 6.34)] also exhibited increased risk in patients.Conclusion In acromegaly, severe osteoarthritis involving multiple joints develops even before acromegaly diagnosis and continues to progress over time after acromegaly treatment. Furthermore, acromegaly imposes an increased risk of medically treated osteoporosis, musculoskeletal surgery-particularly joint replacement surgery-, surgical complications, and the necessity of analgesic medication. Our findings warrant further research into the management of musculoskeletal disease in acromegaly.
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TI Diameter Control and Optical Properties of CsPbBr3 Nanowires Based on the Oleylamine-Octylamine System
SO JOURNAL OF PHYSICAL CHEMISTRY C
LA English
DT Article
ID halide; size; shape
AB Metal halide perovskites (MHPs) have emerged as prominent materials in optoelectronics due to their exceptional photoelectric conversion efficiency and tunable band structures. Traditional perovskite nanocrystal synthesis systems often employ oleic acid (OA) to accelerate the crystallization kinetics, which inadvertently hinders nanowire growth and morphology control. In this study, we adopted a dual-ligand system using oleylamine (OAm) and octylamine (OctAm) without preadding OA. By postinjecting a cesium oleate solution, we achieved precise control over Pb2+ ion release, enabling the controllable synthesis of cesium lead halide (CsPbBr3) nanowires (NWs) across 100-160 degrees C. This strategy yielded micrometer-scale NWs with tunable diameters (8.3-12.6 nm) and lengths reaching the microscale. Temperature-dependent optical studies revealed that elevated synthesis temperatures weakened quantum confinement effects, leading to systematic red-shifts in ultraviolet-visible (UV-vis) absorption (505-507 nm) and photoluminescence (PL) emission (516-518 nm) peaks. Concurrently, time-resolved PL measurements revealed a significant enhancement in carrier lifetime (24.72-91.99 ns), reflecting reduced nonradiative recombination pathways. Variable-temperature PL spectroscopy (80-300 K) demonstrates that CsPbBr3 NWs synthesized at 140 degrees C exhibit higher exciton binding energy (E b = 44.7 meV) and enhanced exciton-phonon coupling strength (Gamma OP = 46.48 meV) compared to samples prepared at 120 degrees C. These findings demonstrate that

high-temperature synthesis confers superior thermal stability on CsPbBr3 NWs. Our work not only clarifies the critical role of amine ligands in modulating NW growth dynamics but also provides a robust framework for designing stable, high-performance, one-dimensional perovskite optoelectronic materials.
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WC Chemistry, Physical; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary
SC Chemistry; Science & Technology - Other Topics; Materials Science
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TI Addressing the growing burden of musculoskeletal diseases in the ageing US population: challenges and innovations
SO LANCET HEALTHY LONGEVITY
LA English
DT Article
ID knee osteoarthritis; muscle mass; pain; management; sarcopenia; fracture; people; impact; injury; drugs
AB The prevalence of musculoskeletal diseases such as osteoarthritis, osteoporosis, sarcopenia, and rheumatoid arthritis is rising sharply with global ageing, increasing disability rates among older adults (aged >= 60 years), diminishing quality of life, and burdening health-care systems. Current musculoskeletal care for older adults faces multiple limitations, including comorbidities, frailty, and fragmented care. High osteoarthritis prevalence in individuals older than 55 years, the mounting

economic burden of osteoporotic fractures, the growing concern of muscle mass decline, and insufficient guideline implementation collectively underscore these challenges. In the USA, musculoskeletal diseases affect over 121 million people and account for the highest rate of disability among all disease groups, underscoring the need for targeted strategies. Although promising solutions encompassing advanced pharmacological therapies, regenerative medicine, and digital health technologies (including artificial intelligence) are available, they remain underutilised in existing care models. This Personal View discusses the need for personalised, multidisciplinary approaches to address these issues, advocating for collaboration among the orthopaedic, geriatric, and health-care sectors in the USA. We propose that prevention of musculoskeletal diseases is key to its effective management in ageing populations, alongside a holistic, scalable approach that integrates diagnostics, therapy, and telemedicine. Early intervention, interdisciplinary collaboration, and personalised care are essential to improving patient outcomes and addressing the growing musculoskeletal disease burden in the USA.
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PT J
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TI Comparative study of individualized 3D-printing navigation technology and free-hand isthmus method in lumbar CBT screw implantation
SO FRONTIERS IN SURGERY
LA English

DT Article
DE cortical bone trajectory screw; 3D-printing navigation molds; free-hand isthmus method; lumbar internal fixation surgery; retrospective study
ID pedicle screw; biomechanical evaluation; part i; insertion; fixation; strength; spine; template; fusion; osteoarthritis
AB Objectives: Traditional cortical bone trajectory (CBT) screws in the lumbar spine offer greater holding strength and are well-suited for patients with osteoporosis. However, the screw implantation procedure is challenging and associated with significant risk. This study aimed to assess whether individualized 3D-printing navigation technology provides higher accuracy and better clinical outcomes compared to the free-hand isthmus method for lumbar CBT screw implantation. Methods: From September 2020 to August 2023, a total of 41 patients who underwent CBT screw surgery were retrospectively collected. Among them, 23 patients underwent the free-hand isthmus method (Group A), while 18 patients underwent the individualized 3D-printing navigation technique (Group B). All imaging and clinical data for these patients were collected in a blinded manner. Results: During the surgery, 185 CBT screws were implanted into the lumbar spines of 41 patients-78 in Group A and 107 in Group B. After the surgery, the majority of implanted screws (86.5%) were classified as grade 0, indicating satisfactory implantation. Compared to Group A, Group B had fewer screws classified as grade 1 or grade 2 ($p = 0.045$), indicating higher accuracy in screw implantation. Additionally, Group B also had a shorter operation duration ($p = 0.02$), fewer fluoroscopy exposures ($p < 0.01$), and less blood loss ($p = 0.03$). In addition, compared to Group A, individuals in Group B showed significant improvement in back pain symptoms at both 3 and 6 months ($p = 0.01$ and <0.01), as well as in physical activity at 3 months ($p = 0.02$) postoperatively. No significant difference in postoperative complications was observed between the two groups. Conclusion: Compared to the free-hand isthmus method, lumbar CBT screw implantation with individualized 3D-printing navigation technology shows higher accuracy, shorter operative time, reduced intraoperative fluoroscopy and blood loss, and better clinical outcomes at three months post-surgery.
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TI Is physical activity in polluted environments beneficial or detrimental to osteoporosis and osteoarthritis? A prospective cohort study
SO INTERNATIONAL JOURNAL OF SURGERY
LA English
DT Article
DE environmental pollutants; osteoarthritis; osteoporosis; physical activity
ID air-pollution; health; exercise; europe
AB Background:Although physical activity and environmental pollutants may influence the risk of osteoporosis and osteoarthritis, their combined effects remain poorly understood. Therefore, we aimed to evaluate the independent associations of environmental pollutants and physical activity with these risks and to explore their interaction.Methods:We conducted a prospective cohort study of 400949 UK Biobank participants. Environmental pollutants comprised particulate matter (PM2.5, PM10, and PM2.5-10), nitrogen oxides (NOx, NO2, and NO), air pollutant score, and 24-hour noise. Physical activity was classified by intensity (low, moderate, and high) and by type [walking for pleasure, strenuous sports, light DIY (do it yourself) heavy DIY and other sports]. We used multivariable Cox models to estimate the independent associations of each exposure with disease risk. Interaction analyses between pollutants and physical activity were then performed on both the additive scale (relative excess risk due to interaction) and the multiplicative scale (interaction term P value).Results:During follow-up, 9667 and 46 782 participants developed osteoporosis and osteoarthritis, respectively. Air

pollutants were generally associated with an increased risk of osteoporosis and osteoarthritis. Physical activity (regardless of intensity and type) reduced osteoporosis risk, while a high level of physical activity increased osteoarthritis risk. Additionally, strenuous sports increased osteoarthritis risk, while walking for pleasure decreased it. Under most conditions, we observed neither additive nor multiplicative interaction between pollutants and physical activity.Conclusions:Caution is warranted for the increased osteoarthritis risk with high intensity of physical activity. However, effects of physical activity (whether beneficial or harmful) on osteoporosis and osteoarthritis are not markedly altered by pollutants.
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NR 59
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PU LIPPINCOTT WILLIAMS & WILKINS
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SC Surgery
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PT J
AU Guha, A
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AF Guha, Adrita
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TI Complement C3 deficiency inhibits osteoclast differentiation and prevents ovariectomy-induced osteoporosis
SO JOURNAL OF IMMUNOLOGY
LA English
DT Article
DE osteoclasts; complement proteins; osteoimmunology; bone biology; osteoblasts
ID 3rd component; bone; cells; proteins
AB The pathomechanistic role of the complement system is well recognized in various pathological conditions affecting bone tissues and the bone microenvironment, including rheumatoid arthritis, osteoarthritis, bone fractures, and periodontitis. The homeostasis of the bone is maintained by continuous remodeling, in which bone-resorbing or demineralizing osteoclast cells remove bone calcification, and osteoblast cells deposit new bone matrix. Major complement protein C3 is reported to control endochondral ossification, cartilage-to-bone transition, and longitudinal bone growth. The role of the

complement protein C3 in differentiating multinucleated osteoclast cells (bone-resorbing cells) from osteoclast precursor cells (OCPs) and its contribution to long bone microarchitecture and strength are unclear. We demonstrated that C3 promotes the differentiation of osteoclasts and the formation of multinucleated osteoclasts from bone marrow-derived OCPs. C3-/- mice OCPs had reduced osteoclast-associated gene expression of TRAP (tartrate-resistant acid phosphatase), cathepsin K, calcitonin receptor, and RANK (receptor activator of nuclear factor kappa B) molecules compared with osteoclasts derived from wild-type (WT) OCPs. C3-/- mice had significantly increased bone mineral density and other bone parameters of the femur compared with WT mice. Furthermore, compared with WT mice, C3-/- mice were protected from ovariectomy-induced osteoporosis, characterized by significantly increased Foxp3+CD4+ T cells in the spleen and interleukin-10-producing B cells in both the spleen and the bone marrow. Intriguingly, C3 knockout mice exhibit reduced differentiation of functional osteoclast cells, which promotes a strong bone microarchitecture, suggesting that complement pathways may be explored as a therapeutic target in bone inflammatory diseases.
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NR 50
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PU OXFORD UNIV PRESS
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AU Gao, KH
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TI Natural Products in the Prevention of Degenerative Bone and Joint Diseases: Mechanisms Based on the Regulation of Ferroptosis
SO PHYTOTHERAPY RESEARCH
LA English
DT Review
DE degenerative bone and joint diseases; ferroptosis; intervertebral disc degeneration; natural products; osteoarthritis; osteoporosis
ID intervertebral disc degeneration; mesenchymal stem-cells; lipid-peroxidation; oxidative stress; nucleus pulposus; osteoarthritis; differentiation; expression; ferritinophagy; inhibition
AB Degenerative bone and joint diseases (DBJDs), characterized by osteoporosis, osteoarthritis, and chronic inflammation of surrounding soft tissues, are systemic conditions primarily affecting the skeletal system. Ferroptosis, a programmed cell death pathway distinct from apoptosis, autophagy, and necroptosis. Accumulating evidence suggests that ferroptosis is intricately linked to the pathogenesis of DBJDs, and targeting its regulation could be beneficial in managing these conditions. Natural products, known for their anti-inflammatory and antioxidant properties, have shown unique advantages in preventing DBJDs, potentially through modulating ferroptosis. This article provides an overview of the latest research on ferroptosis, with a focus on its role in the pathogenesis of DBJDs and the therapeutic potential of natural products targeting this cell death pathway, offering novel insights for the prevention and treatment of DBJDs.
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AU Scattergood, SD
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AF Scattergood, Sean D.
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TI Influence of pre-operative co-morbidities on pain and function outcomes at 1 year after primary total knee arthroplasty
SO KNEE
LA English
DT Article
DE Total knee replacement; Arthroplasty; Western Ontario and McMaster Universities; Osteoarthritis Index (WOMAC); Patient-reported outcome measures; (PROMS); Co-morbidities; Multi-morbidity
ID patient-reported outcm; replacement surgery; comorbidity index; hip; predictors; satisfaction
AB Introduction: Multimorbidity has been found to be associated with more pain and poorer function following total knee arthroplasty (TKA). We describe the relationship between both the total number of pre-operative co-morbidities, and individual co-morbidities, with the Western Ontario and McMaster Universities

Osteoarthritis Index (WOMAC) score at 12 months after TKR. Methods: We performed a secondary analysis on 290 participants from the Arthroplasty Pain Experience (APEX) trial, with seventeen imputations by Chained Equations. Using multivariable adjusted linear regression models, we analysed the relationship between total number of pre-operative co-morbidities, followed by individual co-morbidities, with WOMAC score at 12 months after randomisation. Results: Patients with >= 5 co-morbidities have worse outcomes compared to patients with 3 co-morbidities, scoring -9.6 points for function (95% CI -15.3 to -3.8), and -9.8 points for pain (95%CI -15.9 to -3.8). Patients reported worse pain with osteoporosis (-7.8 95% CI -14.1 to -1.6), peripheral vascular disease (-17.8 95%CI -34 to -1.8), depression (-9.8 95%CI -18.1 to -1.4), anxiety (-9.7 95%CI -18 to -1.4) or degenerative disc disease (-7.5 95%CI -13.3 to -1.7). Worse function was associated with osteoporosis (-7.1 95%CI -12.9 to -1.4), diabetes mellitus (-9.1 95%CI -15.6 to -2.6), anxiety (-8.1 95%CI -16 to -0.2) and degenerative disc disease (-8.6 95%CI -14.1 to -3.2). Conclusion: Pre-operative multimorbidity is associated with worse outcomes after TKA. Patients with pre-operative osteoporosis, anxiety and degenerative disc disease had worse pain and function at 12-months. Surgeons may use these results during discussion with patients about their potential outcome after TKA. (c) 2025 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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Li, Daowei
Sun, Hongchen
TI Autophagy: regulating the seesaw of bone-fat balance
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
LA English
DT Review
DE autophagy; metabolism; lipid metabolism; bone metabolism; bone diseases
ID mesenchymal stem-cells; marrow adipose-tissue; diet-induced obesity; alpha-lipoic acid; factor c/ebp-beta; ppar-gamma; oxidative stress; osteogenic differentiation; osteoclast differentiation; transcription factor
AB The interrelationship between bone and fat can be described as a seesaw in bone homeostasis, in which both osteogenesis and adipogenesis occur in a delicate balance. Osteoblasts and adipocytes share a common origin and play key roles in osteogenesis and adipogenesis. Bone-fat balance indicates osteogenesis and adipogenesis keeps a balance for concordant distribution of trabecular bone and bone marrow adipose tissue in bone, thereby leading to the balance between bone metabolism and lipid metabolism. Bone-fat balance is crucial for metabolic health. When disrupted by various factors, this balance can lead to several bone-related metabolic diseases and systemic disorders, such as obesity, osteoporosis, and osteoarthritis. Recent research highlights the role of autophagy dysfunction in these metabolic conditions. Restoring autophagic function can help restore metabolic homeostasis and re-establish the bone-fat balance. The current review explores the factors that regulate bone-fat balance, the consequences of imbalance under pathological conditions, and the potential of autophagy modulation as a therapeutic approach. Overall, it can be concluded that targeting autophagy presents a promising strategy for treating metabolic disorders and restoring bone-fat balance.
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TI Therapeutic Potential of Bioactive Peptides Derived from Natural Products of Tortoiseshell and Antler in Alleviating Osteoporosis and Osteoarthritis
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DE traditional Chinese medicines; tortoiseshell; antler; bioactive peptides; osteoporosis; osteoarthritis; natural products
AB Tortoiseshell and antler, the main components of Guilu Erxian Jiao, are natural products that can be used as traditional Chinese medicine (TCM) to alleviate osteoporosis and osteoarthritis. However, research on the active ingredients in tortoiseshell and antler for alleviating osteoporosis and osteoarthritis remains insufficient. This study primarily compares the antioxidant capacity of tortoiseshell gelatin and antler gelatin and their bioactive peptides, as well as their effects on the cell viability of MC3T3-E1 osteoblasts and HIG-82 chondrocytes. Our results indicate that when tortoiseshell and antler are combined with their respective bioactive peptides, the antioxidant capacity and cell viability of osteoblasts and chondrocytes are superior to the effects of either used alone. Comparing the antioxidant capacity and cell viability of osteoblasts and chondrocytes of tortoiseshell and antler and their respective bioactive peptides when used alone, we found that tortoiseshell and its bioactive peptides have better cell viability and calcium deposition for osteoblasts compared to the antler and its bioactive peptides. Conversely, antler and its bioactive peptides exhibit stronger antioxidant

capacity and better cell viability for chondrocytes than tortoiseshell and its bioactive peptides. These results suggest that the alleviation of osteoporosis may mainly be attributed to tortoiseshell and its bioactive peptides, while the alleviation of osteoarthritis may mainly be attributed to antler and its bioactive peptides. When tortoiseshell and antler are used together, they can provide the best therapeutic effects for both osteoporosis and osteoarthritis.
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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PT J
AU Cooper, DJ
Sim, J
AF Cooper, Dale J.
Sim, Julius
TI Health among Retired Great Britain's Olympic Athletes: A cross-sectional Study of Disease and Multimorbidity
SO SPORTS MEDICINE-OPEN
LA English
DT Article
DE Prevalence; Olympic Athletes; Multimorbidity; Chronic Diseases; Melanoma
ID physical-activity; osteoarthritis; prevalence; cohort; risk; knee; hip
AB Background: Currently, there is a paucity of long-term health data for retired athletes. This study describes the prevalence of common morbidities and multimorbidity among retired Great Britain's (GB) Olympic athletes, compared to a general population comparator group. Methods: A cross-sectional study of retired athletes was undertaken. The English Longitudinal Study of Ageing (ELSA) served as the reference population. Age- and sex-standardized morbidity ratios (SMRs) and

odd ratios (ORs) determined where morbidity and multimorbidity prevalence amongst retired athletes exceeded or were inferior to those of the reference population. Results: Retired athletes (n = 493) were less likely (SMR < 1) than controls (n = 8024) to report diabetes (0.43, 99% CI 0.22, 0.74), stroke (0.39, 99% CI 0.12, 0.90), obesity (0.35, 99% CI 0.23, 0.50), asthma (0.29, 99% CI 0.12, 0.59), lung disease (0.29, 99% CI 0.06, 0.81), angina (0.18, 99% CI 0.05, 0.46), and eye disorders (0.06, 99% CI 0.01, 0.18). In addition, abnormal heart rhythm (0.45, 99% CI 0.40, 0.54) and osteoporosis (0.46, 99% CI 0.42, 0.51) were lower in female athletes. Retired athletes were more likely (SMR > 1) than controls to report melanoma or other skin cancer (5.64, 99% CI 2.80, 10.06) and osteoarthritis (1.44, 99% CI 1.18, 1.75). There were no differences detected in cancers of the breast, prostate, colon, bowel or bladder. Multimorbidity was less prevalent among retired athletes (OR 0.50, 99% CI 0.38, 0.67). Conclusions: Retired athletes had superior cardiovascular health and a lower risk of multimorbidity, but were more at risk of melanoma or other skin cancer and osteoarthritis.
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TI A Systematic Review of the Potential of Acmella Genus Plants for the Treatment of Musculoskeletal Disorders
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE <italic>Acmella</italic> genus plant; musculoskeletal disorders; osteoporosis; muscle strains; tendonitis; osteoarthritis
ID spilanthes-acmella; postmenopausal women; global burden; osteoporosis; osteoarthritis; epidemiology; pain; mass; hip
AB The genus Acmella has received growing attention for its pharmacological properties, including its potential applications in musculoskeletal disorders (MSDs).

Plants in this genus, such as Spilanthes acmella, Blainvillea acmella, Acmella uliginosa, and Acmella oleracea contain various bioactive compounds which have demonstrated anti-inflammatory, analgesic, and anti-arthritic properties. This systematic review evaluates the clinical and preclinical evidence supporting the use of plants from Acmella genus for the treatment of MSD, such as arthritis, osteoporosis, muscle injuries, joint inflammation, and other related pathologies. The methodology used in this study involved a systematic literature review, following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, along with synthesis analysis and quality appraisal. The articles were retrieved from Scopus, Google Scholar, and PubMed databases. Eleven articles were further analyzed to determine the therapeutic potential of Acmella genus plants for musculoskeletal disorders. The plants included were Spilanthes acmella, Blainvillea acmella, Acmella uliginosa, and Acmella olerecia. The musculoskeletal disorders investigated were osteoporosis, osteoarthritis, and myopathies. The extracts from these plants were shown to decrease inflammation, enhance joint health, relieve pain, and stimulate osteogenic activity. These effects may be attributed to several active compounds found in these plants. The available evidence suggests that Spilanthes acmella and Blainvillea acmella have the potential to treat osteoporosis. Acmella oleracea and Acmella uliginosa have the potential to be used for the treatment of osteoarthritis, while Spilanthes acmella is used to treat myopathies. Further research is needed to establish the efficacy, optimal dosing, and safety of these plants.
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NR 56
TC 0
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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TI Current progress of plant-derived exosome-like nanovesicles on the regulation of osteoporosis and osteoarthritis
SO ANNALS OF MEDICINE
LA English
DT Review
DE Plant deprivative; exosome-like nanovesicles; osteoporosis; osteoarthritis; bone
ID mesenchymal stem-cells; rankl
AB Osteoporosis (OP) and osteoarthritis (OA) are clinically common chronic orthopedic diseases. With the aging of the global population, OP and OA pose a serious threat to human health. Exosomes are nanoscale vesicles secreted by cells and can mediate inter-cell communication. Recent research has shown that plant-derived exosomes-like nanovesicles (PELNs) can affect the proliferation and differentiation of osteoclasts, osteoblasts, bone marrow mesenchymal stem cells (BMSCs) and chondrocytes, regulate the immune system and inhibit inflammatory responses, and have potential value in treating OP and OA. This article summarizes the basic concepts, formation and components, separation and characterization methods of PELNs, and focuses on discussing the impact of PELNs on OP and OA, aiming to provide new ideas for the research of OP and OA.
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TI Cellular senescence in age-related musculoskeletal diseases
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DT Review
DE cellular senescence; aging; musculoskeletal disease; degenerative diseases; senotherapy
ID marrow stromal cells; secretory phenotype; bone-marrow; stem-cells; intervertebral-disk; protein-kinase; osteoarthritis; mitochondrial; homeostasis; mechanisms
AB Aging is typically associated with decreased musculoskeletal function, leading to reduced mobility and increased frailty. As a hallmark of aging, cellular senescence plays a crucial role in various age-related musculoskeletal diseases, including osteoporosis, osteoarthritis, intervertebral disc degeneration, and sarcopenia. The detrimental effects of senescence are primarily due to impaired regenerative capacity of stem cells and the pro-inflammatory environment created by accumulated senescent cells. The secreted senescence-associated secretory phenotype (SASP) can induce senescence in neighboring cells, further amplifying senescent signals. Although the removal of senescent cells and the suppression of SASP factors have shown promise in alleviating disease progression and restoring musculoskeletal health in mouse models, clinical trials have yet to demonstrate significant efficacy. This review summarizes the mechanisms of cellular senescence

in age-related musculoskeletal diseases and discusses potential therapeutic strategies targeting cellular senescence.
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NR 187
TC 3
Z9 3
U1 6
U2 16
PU SPRINGER
PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
SN 2095-0217
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J9 FRONT MED-PRC
JI Front. Med.
PD JUN 15
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BP 409
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WC Oncology; Medicine, Research & Experimental
SC Oncology; Research & Experimental Medicine
GA 3SD8P
UT WOS:001480139500001
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PT J
AU Yemeshev, Y
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AF Yemeshev, Yerlan
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TI Clinical implications of teleradiology in rheumatic and musculoskeletal diseases: improving rheumatic care

SO RHEUMATOLOGY INTERNATIONAL
LA English
DT Review
DE Telemedicine; Teleradiology; Osteoarthritis; Osteoporosis; Rheumatoid arthritis; Spondyloarthritis; Rheumatic diseases; Surveys and questionnaires
ID challenges
AB Teleradiology, the transmission of radiologic images for remote assessment and consultation, has transformed modern medical care by mitigating geographical inequities and improving diagnostic accuracy. This technology employs telecommunications, digital imaging, and data-sharing systems developments to deliver swift and precise image analysis across various healthcare environments. Teleradiology has been essential in identifying and controlling diseases, including osteoarthritis, osteoporosis, rheumatoid arthritis, and spondyloarthritis, especially in musculoskeletal radiology and rheumatology. The combination of teleradiology and telemedicine has transformed multidisciplinary cooperation, enhancing communication among radiologists, rheumatologists, and other healthcare practitioners to provide patient-centered treatment. It has markedly enhanced access to highly specialized knowledge, especially in rural and disadvantaged areas, facilitating prompt consultations and alleviating patient travel constraints. However, despite its benefits, teleradiology encounters several challenges, including standardization issues, ethical dilemmas, and infrastructure constraints. The absence of uniform standards and inequalities in access to high-speed Internet and digital health records impede extensive implementation. Addressing these constraints is crucial to fully utilizing teleradiology's potential in musculoskeletal and rheumatic care. This article highlights the transformational potential of teleradiology and its incorporation into telemedicine for musculoskeletal and rheumatological treatment. Teleradiology is set to enhance global healthcare delivery by addressing disparities in healthcare access, fostering multidisciplinary cooperation, and utilizing advanced technologies. It underscores the necessity for ongoing innovation and investment in infrastructure, education, and standards to optimize the advantages of this crucial technology and guarantee equitable, efficient, and high-quality care for all patients.
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NR 51
TC 1
Z9 1
U1 1
U2 1
PU SPRINGER HEIDELBERG
PI HEIDELBERG
PA TIERGARTENSTRASSE 17, D-69121 HEIDELBERG, GERMANY
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WC Rheumatology
SC Rheumatology
GA X2S4E
UT WOS:001423909100001
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PT J
AU Wang, XY
Jiang, WJ
Zheng, ZC
AF Wang, Xiaoyu
Jiang, Wenjun
Zheng, Zuncheng
TI A novel hypothesis on the pathogenesis of knee osteoarthritis: the muscle weakness-joint instability and stress overload - uneven bone settlement cascade
SO MEDICAL HYPOTHESES
LA English
DT Article
DE Knee osteoarthritis; Muscle weakness; Uneven bone settlement; Stress overload
ID biomechanics; kinematics; complaints; density; disease; women; gait
AB The pathogenesis of knee osteoarthritis (KOA) remains incompletely elucidated. Traditional perspectives emphasize the roles of articular cartilage degeneration and soft tissue laxity. This article synthesizes recent research to propose an integrated musculoskeletal biomechanical hypothesis: weakness of muscles is the initiating factor in KOA development, leading to diminished dynamic joint stability, this instability triggers abnormal distribution of contact stresses and excessive loading within the joint. Coupled with the unique anatomical features of the tibia and fibula (such as fibular support and the abundance of trabecular bone in the medial tibia) and underlying osteoporosis, this process ultimately results in "uneven bone settlement" of tibial plateau changes. This settlement further exacerbates varus deformity, joint space narrowing, soft tissue imbalance, and pain, establishing a

vicious cycle of KOA progression. The clinical efficacy of the currently employed Proximal Fibular Osteotomy (PFO) and the researches related of knee Joint periarticular muscle strength training provides support for this theory. This hypothesis emphasizes the central importance of muscle strengthening to restore joint stability and early intervention in bone metabolism for the prevention and management of KOA.
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NR 35
TC 0
Z9 0
U1 3
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PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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WC Medicine, Research & Experimental
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PT J
AU Zhou, Y
Li, C
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Teng, HL
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Wang, J
AF Zhou, Yang
Li, Chi
Dai, WangYing
Teng, HongLin
Wang, Yu
Zhu, MingYu
Wang, Jing
TI Association between bone mineral density and lower back pain in the general United States population using the NHANES of 1999-2004
SO FRONTIERS IN SURGERY
LA English
DT Article
DE lower back pain; bone mineral density; osteoporosis; economic impact; U-shaped relationship
ID modic changes; risk; osteoporosis; osteoarthritis; disorders; fracture
AB Objectives Lower back pain (LBP) is a prevalent health issue that has substantial effects on individuals and society. However, the association between bone mineral density (BMD) and LBP remains controversial. In this study we aimed to ascertain whether a relationship exists between BMD and LBP in the United States population. Methods Data from the National Health and Nutrition Examination Survey (NHANES) spanning 1999-2004 were analyzed using a cross-sectional approach. BMD and LBP were assessed using multivariate logistic regression, smoothing curves, and generalized additive models. Subgroup analyses were also performed to ensure data stability and mitigate confounding factors. Results In this population-based study, the data of 107,570 adults were analyzed (mean age: 47.13 +/- 18.38 years) and 36.74% of them had LBP. After controlling for all covariates, a positive correlation was established between BMD and LBP [odds ratio (OR) = 1.87, 95% confidence interval (CI) = (1.00, 3.50)]. The two-segment linear

regression model revealed a U-shaped relationship between BMD and LBP with a 1.14 g/cm2 inflection point. BMD values <1.14 g/cm2 were linked to a lower likelihood of experiencing LBP [OR = 0.55, 95% CI = (0.45, 0.68)]. However, a BMD >1.14 g/cm2 increased the risk of LBP [OR = 6.15, 95% CI = (4.51, 8.39)]. Conclusions BMP was significantly and positively correlated with LBP. A U-shaped relationship was observed between BMD and LBP, indicating that both insufficient and excessive BMD may increase the risk of LBP.
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TC 0
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TI Is bone mineral density a risk factor for femoral stem subsidence in primary cementless total hip arthroplasty: a prospective study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Subsidence; Total hip arthroplasty; Bone density; Osseointegration; Dorr classification; Prospective study
ID osteoporosis; replacement; stability; women
AB Background The success of primary total hip arthroplasty (THA) in patiens with primary osteoarthritis (OA) of the hip is significantly influenced by stem osseointegration, migration and implantation. Additionally, the bone mineral density (BMD) of the proximal femur, the femoral morphology and stem design play important roles in these outcomes. This study aimed to evaluate the effect of BMD on subsidence who underwent primary cementless THA with a fit-and-fill stem design for primary OA of the hip, assuming that subsidence is not influenced by BMD. Methods This prospective study included 72 hips from 67 patients who underwent primary cementless THA for OA between May 2019 and March 2022. Two patients were excluded due to intraoperative complications, and the final analysis was conducted on 70 hips. Patients were grouped according to preoperative BMD and proximal femur anatomy based on Dorr classification. Harris Hip Score (HHS), radiological subsidence and Engh score values were used for postoperative clinical evaluation. Results The mean age was 65.99 +/- 8.10 years (range 52 to 83 years). The mean follow-up was 24.6 +/- 5.8 months (range, 12 to 34 months). Amongst 70 OA of the hip cases, 22 (31.43%) were Dorr type A, 44 (62.86%) type B, and 4 (5.71%) type C. Forty-three patients (61.43%) had normal BMD, while 27 patients (38.57%) were osteopenic or osteoporotic. The mean axial migration at the latest follow-up was 1.04 +/- 0.69 mm (range 0 to 3.1 mm). Total Engh score was 22.89 +/- 3.28 (range 14 to 27), and in terms of stabilization bone ingrowth was seen in all of the femoral stems. There was no statistically significant effect of femoral T-score levels ($p = 0.853$) or femoral morphologies ($p = 0.763$) on femoral stem subsidence. Conclusions No statistically significant differences were observed in clinical or radiological outcomes between patients with normal and low BMD. These findings suggest that early stem migration and osseointegration are more closely related to initial mechanical stability than to BMD. Cementless femoral stems can therefore be considered reliable across different bone qualities, offering an innovative perspective that challenges the conventional emphasis on bone density in implant selection.
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NR 34
TC 0
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TI Molecular mechanisms and targeted therapy of progranulin in metabolic diseases
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE PGRN; metabolic diseases; inflammation; cartilage repair; bone homeostasis; targeted therapy
ID tnf-alpha; serum progranulin; osteoarthritis; bone; periodontitis; inflammation; suppresses; apoptosis; roles; pgrn
AB Progranulin (PGRN) is a secreted glycoprotein with cytokine-like properties, exerting tripartite mechanisms of inflammation suppression, tissue repair promotion, and metabolic regulation. This multifaceted functionality positions PGRN as a potential "multi-effect therapeutic strategy" for metabolic disorders characterised by cartilage degradation and imbalanced bone remodelling, potentially establishing it as a novel therapeutic target for such conditions. Osteoarthritis, rheumatoid arthritis, intervertebral disc degeneration, osteoporosis, periodontitis, and diabetes-related complications-representing the most prevalent metabolic diseases-currently lack effective treatments due to incomplete understanding of their precise pathogenic mechanisms. Recent studies have revealed that PGRN expression levels are closely associated with the onset and progression of these metabolic disorders. However, the exact regulatory role of

PGRN in these diseases remains elusive, partly owing to its tissue-specific actions and context-dependent dual roles (anti-inflammatory vs. pro-inflammatory). In this review, we summarise the structure and functions of PGRN, explore its involvement in neurological disorders, immune-inflammatory diseases, and metabolic conditions, and specifically focus on its molecular mechanisms in metabolic diseases. Furthermore, we consolidate advances in targeting PGRN and the application of its engineered derivative, Atsttrin, in metabolic bone disorders. We also discuss potential unexplored mechanisms through which PGRN may exert influence within this field or other therapeutic domains. Collectively, this work aims to provide a new framework for elucidating PGRN's role in disease pathogenesis and advancing strategies for the prevention and treatment of metabolic disorders.
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TI Factors contributing to clinical misdiagnosis of fetal head position: an ultrasound based cohort study from Tanzania
SO JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
LA English
DT Article
DE Ultrasound; labor; fetal position; misdiagnosis; cesarean section
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AB Objectives: Accurate determination of fetal head position is essential for managing labor, particularly in cases of slow progress or before operative vaginal interventions. Several studies have shown that ultrasound examinations are more accurate than clinical examinations, but few ultrasound studies are done in sub-Saharan Africa. Clinical vaginal assessment of fetal position remains the standard in most African settings, but its accuracy is limited by examiner skills and labor conditions. This study aimed to compare clinical and ultrasound assessments of fetal position during active labor, to identify factors contributing to clinical misdiagnosis, and to evaluate the impact of misdiagnosis on delivery mode. Methodology: An observational cohort study was conducted at Kilimanjaro Christian Medical Centre in Moshi, Tanzania, from 19(th) November 2023 to 13(th) April 2024. Fetal position was categorized as a clock; 10 to 2 o'clock as occiput anterior (OA) position, 3 o'clock as left occiput transverse (LOT) position, 4 to 8 o'clock as occiput posterior (OP) position, and 9 o'clock as right occiput transverse (ROT) position. Three trained doctors conducted ultrasound examinations, while midwives performed clinical assessments recording position, station, cervical dilatation, caput succedaneum, and molding. Fetal station ranged from -5 to +5. Caput succedaneum was first graded as 0, +1, +2, or +3 and recategorized as none (0), slight (grade +1), and huge (grade +2 and +3). Molding was categorized as absent or present. Clinical misdiagnosis of position was defined as any discrepancy between clinical and ultrasound assessments using ultrasound examinations as the gold standard. Misdiagnosis included cases where the fetal head position could not be determined clinically, as well as those that were incorrectly assessed through vaginal examination. Blinded comparisons evaluated agreement and clinical misdiagnosis. Factors contributing to clinical misdiagnosis were assessed using logistic regression and potential confounders included maternal age, gestational age, body mass index (BMI), station during the second stage, caput succedaneum, and molding. Results: The final study population comprised 215 women, 204 were examined in the active first labor stage and 210 in the second stage. Fetal position could not be determined clinically in 40/204 (19.6%) women in the active first

stage, but ultrasound successfully determined position in all cases. The overall agreement rate in the active first stage was 101/164 (61.6%), with 60/76 (78.9%) agreement in OA position and 41/88 (46.6%) agreement in non-OA positions. Agreement in classifying position into four categories (OA, LOT, OP, and ROT) was moderate (Cohen's kappa, k = 0.41, 95% CI 0.31-0.52). In the second stage, clinical assessment failed in 11/210 (5.2%) cases, while ultrasound failed in 5/210 (2.4%). The overall agreement rate was 155/194 (79.9%), with 133/152 (87.5%) agreement in OA position and 22/42 (52.4%) agreement in non-OA positions. Cohen's kappa in classifying position into four categories showed moderate agreement (k = 0.46, 95% CI 0.32-0.59). Presence of molding showed a strong association with clinical misdiagnosis, adjusted OR 5.81 (95% CI 1.95-17.30). Slight caput succedaneum was not associated; however, a huge caput succedaneum was significantly associated with clinical misdiagnosis, adjusted OR 5.95 (95% CI 1.85-19.13). Fetal station showed a significant inverse association in unadjusted analysis, where a lower fetal station reduced the likelihood of clinical misdiagnosis, unadjusted OR 0.63 (95% CI 0.41-0.96), but this association was not significant in the adjusted analysis, OR 0.64 (95% CI 0.39-1.06). Maternal age, gestational age, and BMI were not associated with clinical misdiagnosis in either model. The cesarean section (CS) rate among parturients with misdiagnosed positions was 19/50 (38.0%), compared to 14/155 (9.0%) in women with correctly assessed positions ($p < .001$). Conclusions: Clinical and ultrasound assessments showed moderate agreement. Caput succedaneum and molding influenced clinical misdiagnosis, and misdiagnosed positions were associated with higher CS rates.

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TI The Role of PGE2 in Age-related Diseases
SO CURRENT DRUG TARGETS
LA English
DT Review
DE Prostaglandin E2; aging; inflammation; prostaglandin E receptors
ID prostaglandin e-2 receptor; alzheimers-disease; mouse model; alveolar macrophages; dopaminergic-neurons; parkinsons-disease; e synthase-1; fatty-acids; bone loss; expression
AB In the past several years, human life expectancy has increased dramatically, and the global aging process is accelerating at an unprecedented rate. Impaired organ functions and systemic inflammation increase the risk of aging-related diseases. It seriously affects the quality of life in older adults and places a heavy burden on the global economy and public health. Inflammation is the cornerstone of many age-related diseases, and among various inflammatory mediators, Prostaglandin E2 (PGE2) has emerged as a key player. For example, PGE2 could participate in the progression of Alzheimer's disease (AD) by modulating neuroinflammation. Plasma PGE2 is regarded as a potential and specific diagnostic biomarker, and higher initial PGE2 levels are positively correlated with longer survival in AD. PGE2 also mediates bone and muscle metabolism to affect age-related musculoskeletal diseases, including sarcopenia, osteoporosis, and osteoarthritis. It activates the EP4 receptor on sensory nerves to inhibit sympathetic nerve activity and modulate bone formation. Moreover, the PGE2/EP4 axis positively regulates muscle mass and strength. In diabetes, increased Cox-2 and m-PGES2 promote PGE2 production. The activated PGE2/EP3 axis exacerbates the progression of type 2 diabetes (T2D) by impairing glucose metabolism and accelerating beta-cell senescence. Therefore, the role of PGE2 in age-related diseases deserves greater attention. Its involvement is driven by the dysregulation of its biosynthesis, metabolism, and receptor-mediated signaling. Regulating the concentration of PGE2 or modulating receptor activity represents a promising therapeutic strategy for managing

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TI Higher frequency of public hospital utilisation for rheumatological conditions by First Nations people in Western Sydney
SO INTERNAL MEDICINE JOURNAL
LA English
DT Article
DE aboriginal Australian; arthritis; first nations; osteoporosis; Rheumatology
ID systemic-lupus-erythematosus; body-composition; australians; aborigines; sle
AB Objectives There is limited research on the burden of rheumatologic disease affecting First Nations people in Australia. We sought to characterise public

hospital utilisation by First Nations people for a 6-year period (2014-2019) for gout, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), osteoarthritis (OA) and osteoporosis (OP) in Western Sydney, New South Wales. Design A cross-sectional medical records review. Setting All patients who presented to the emergency departments (EDs) of, or who were admitted to, any of the four Western Sydney Local Health District hospitals with a primary diagnosis of gout, SLE, RA, OA or OP between 1 January 2014 and 31 December 2019.Main outcome measures Description of ED presentations and hospital admissions for the five conditions among First Nations and non-First Nations people. The hospital utilization rate was calculated for both First Nations and non-First Nations people. Results There was a higher likelihood of First Nations people accessing public hospital healthcare for gout compared to the non-First Nations population (73.3% vs 62.4%, P < 0.030). The public hospital utilisation rate for First Nations people with rheumatological conditions was almost three times that of the non-First Nations population for those aged >= 45 years (13.1 per 1000 people vs 5.0 per 1000 people respectively). Conclusions This study suggests First Nations people living in Western Sydney access public hospital care for rheumatological conditions at a higher rate than the general population.
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TI Molecular insights and emerging therapeutic perspectives of the lncRNA GAS5/miR-21 axis in cancer, fibrosis, cardiovascular, and immune disorders
SO MUTATION RESEARCH-REVIEWS IN MUTATION RESEARCH
LA English
DT Article
DE LncRNA GAS5; MiR-21; Cancer progression; Fibrosis; Cardiovascular disease; Immune disorders
ID long noncoding rna; systemic-lupus-erythematosus; signaling pathway; gas5; mir-21; osteoporosis; cell; radiosensitivity; mechanisms; expression
AB Non-coding RNAs (ncRNAs) have redefined the complexity of gene regulation, with the long non-coding (lncRNA) GAS5/miR-21 axis emerging as a critical determinant of cell fate across diverse pathological contexts. This review examines the molecular mechanisms by which GAS5 regulates miR-21 activity, thereby restoring tumor suppressor networks and controlling key pathways, including the PI3K/AKT, MAPK/ERK, and Wnt/beta-catenin pathways. We detail how dysregulation of this axis fuels cancer progression, metastasis, therapy resistance, fibrosis, cardiovascular diseases, osteoporosis, osteoarthritis, and autoimmune conditions like systemic lupus erythematosus. Beyond its role as a master regulator of apoptosis, proliferation, and EMT, the GAS5/ miR-21 interaction holds immense promise as a therapeutic target and a liquid biopsy biomarker. However, clinical translation demands solutions to major challenges, including RNA delivery barriers, context-dependent effects, and adaptive resistance. Leveraging multi-omics integration, gene-editing technologies, and personalized RNA therapeutics will be pivotal to overcoming these obstacles. By critically integrating current knowledge and outlining future directions, this review positions the GAS5/miR-21 axis at the forefront of next-generation ncRNA therapeutics. Harnessing its full potential could not only revolutionize treatment paradigms but also transform our understanding of RNA-driven disease networks.
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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TI Cadmium exposure and its role in joint disease: A brief review of experimental and population-based evidence
SO JOURNAL OF TRACE ELEMENTS IN MEDICINE AND BIOLOGY
LA English
DT Review
DE Cadmium; oxidative stress; inflammation; osteoporosis; osteoarthritis; rheumatic and metabolic diseases
ID rheumatoid-arthritis; induction; toxicity; risk
AB Cadmium is a toxic metal released into the environment mainly by mining and industrial activities, posing health risks through inhalation and ingestion. Smoking is a major source of exposure, followed by consuming contaminated foods such as vegetables and offal. Due to its long half-life, Cadmium accumulates in the body and contributes to chronic diseases, including rheumatic and metabolic disorders such as osteoporosis, osteoarthritis, rheumatoid arthritis, systemic lupus erythematosus, gout, and hyperuricemia. The impact of Cadmium on bone health was first documented in Japan in 1955 when contaminated rice consumption caused significant bone mineral loss and severe pain. Recent studies suggest that Cadmium concentrations above 1 mu g/L have osteotoxic effects, likely due to impaired Calcio absorption or its replacement in bone tissue. Cadmium accumulation also disrupts joint homeostasis, promoting cartilage degradation, osteophyte formation, and synovitis. This may result from its interference with essential metals such as Zinc, Iron, Manganese, and Chromium, which are critical for the extracellular matrix. Cadmium has also been linked to rheumatoid arthritis by disrupting immune function, promoting oxidative stress, and increasing inflammatory mediators like TNF-alpha, IL-6, and COX-2. It may contribute to systemic lupus erythematosus by increasing antinuclear antibodies and altering cytokine profiles. Additionally, Cadmium exposure raises the risk of hyperuricemia and gout by interfering with urate metabolism, renal transport, and inducing oxidative stress. This article highlights Cadmium's toxic effects and underscores the need for public health strategies to monitor and reduce exposure, ultimately preventing musculoskeletal, rheumatic, and metabolic diseases while improving quality of life.
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NR 84
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AF Li, Guimiao
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Zhang, Yingze
TI Prediction of joint deformity after MIPPO with double reverse traction repositor based on Hounsfield units derived from CT scans
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Tibial plateau fracture; Post-traumatic osteoarthritis; Hounsfield units; BMD; Alignment
ID bone-mineral density; tibial plateau fractures; knee osteoarthritis; osteoporosis; femur; women
AB Background Tibial plateau fractures (TPFs) account for approximately 1% of all fractures and notably 8% of fractures among the elderly. While both surgical and non-surgical interventions can yield promising short-term results, the long-term

implications, particularly the risk of post-traumatic osteoarthritis (PTOA), necessitate further investigation. Although osteoarthritis (OA) and osteoporosis (OP) share common risk factors, including age and gender, yet the interaction between PTOA and OP remains unclear, thereby warranting in-depth exploration. Methods This study involved a cohort of 103 patients with TPFs who underwent minimally invasive percutaneous plate osteosynthesis (MIPPO) combined with double reverse traction reposition (DRTR) from December 2015 to July 2018. We analyzed the relationship between Bone Mineral Density(BMD), knee alignment, PTOA grading, and joint function. Differences in BMD and knee alignment were compared between patients with HKA < 177 degrees (varus group) and those with HKA >= 177 degrees (non-varus group). BMD was evaluated using computed tomography-derived Hounsfield Units (HUs). Alignment and joint deformation were quantified via hip-knee-ankle angle (HKA), medial proximal tibial angle (MPTA), lateral distal femoral angle (LDFA), joint line convergence angle (JLCA), and posterior tibial slope (PTS), while OA stages were assessed via Kellgren-Lawrence (K-L) classification. The functional outcome was assessed via SF-36 and HSS score. Results There were 30 cases (29.1.0% %) in the varus group and 73 cases (70.9%) in the non-varus group. The K-L classification showed a positive correlation with PTS(r = 0.339, p < 0.001). The SF-36 score was negatively correlated with tibial BMD(medial tibia: r = - 0.235, P = 0.050; lateral tibia: r = - 0.260, P = 0.036; mean tibial BMD: r = - 0.285, P = 0.021). The HSS score was negatively correlated with femoral BMD (medial femur: r = - 0.320, P = 0.017; lateral femur: r = - 0.236, P = 0.050; mean femoral BMD: r = - 0.300, P = 0.018). Among patients with high BMI, the K-L classification was positively correlated with femoral BMD, with stronger associations observed Additionally, HKA demonstrated a negative correlation with the BMD of the medial femur and the mean femoral BMD. Significant differences were observed in medial femoral BMD and MPTA between the varus and non-varus groups. Conclusion BMD in the distal femur and proximal tibia is significantly associated with knee function and quality of life, particularly in patients with elevated BMI. Increased BMD correlates with poorer joint function, reduced quality of life, and greater varus deformity, contributing to the progression of PTOA. Notably, patients with knee varus exhibit increased medial femoral BMD and aggravated tibial varus. These findings suggest that postoperative assessment and management of periarticular BMD may help optimize joint alignment, reduce abnormal stress distribution, and delay PTOA progression, thereby improving clinical outcomes.
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NR 34
TC 0
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PU BMC
PI LONDON
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J9 J ORTHOP SURG RES
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AU Li, L
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AF Li, Li
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Fan, Pei
TI Prevalence of osteoporosis in patients with knee osteoarthritis awaiting total knee arthroplasty is similar to that in the general population
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Bone mineral density; Prevalence of osteoporosis; Osteoarthritis of knee; Arthroplasty
ID bone-mineral density; health; hip
AB Background Osteoporosis is common in patients with knee osteoarthritis (KOA) awaiting total knee arthroplasty (TKA) and varies in different regional and ethnic. However, it is unclear whether the prevalence of osteoporosis and osteopenia in these patients is different from that in the general population. This study aims to investigate the prevalence of osteoporosis and osteopenia in both populations to help exploring the relationship between the osteoporosis and osteoarthritis, and to explore whether knee function and radiological assessments of KOA are associated with osteoporosis. Methods In total, 249 patients diagnosed with KOA awaiting TKA were investigated in this cross-sectional study. The mean age was 70.9 +/- 6.4 years. Bone mineral density (BMD) and T scores at the hip and lumbar spine were used to assess bone status using dual X-ray absorptiometry. A matched cohort

from 2448 individuals in the Health Examination Center of our hospital was set as controls by matching sex, age (+/- 3.0 years) and BMI (+/- 1.0). The Kellgren-Lawrence grades (K-L grades), mechanical femorotibial angle (mFTA), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and range of motion (ROM) of the knee were measured to evaluate radiological assessments and knee function in patients awaiting TKA and used to explore the association between KOA and BMD or T score. Prevalence of osteoporosis and osteopenia were investigated in the two cohorts, and inferential statistical analyses were undertaken. The chi-squared test or Fisher's exact test was used for categorical variables while comparisons of scores were examined by ANOVA with/without Bonferroni correction or the Kruskal-Wallis test. Results The prevalence of osteoporosis and osteopenia in patients awaiting TKA was 30.5% (76/249) and 44.2% (110/249), respectively. In the matched cohort, 72/249 (28.9%) had osteoporosis, while 98/249 (39.4%) had osteopenia. There was no significant difference in the prevalence of osteoporosis or osteopenia between the two groups (chi 2 = 2.603, P = 0.272). mFTA was significantly correlated with BMD and T score (P < 0.05), while no correlation was found between K-L grade, ROM or WOMAC and BMD or T score (P > 0.05). Conclusions The prevalence of osteoporosis in patients awaiting TKA was similar to that in the general population. BMD and T score were not correlated with WOMAC score or K-L grade but were correlated with mFTA.

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JI BMC Musculoskelet. Disord.

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AU Wang, P
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AF Wang, Ping
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Liu, Gang
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TI Associations of osteoarthritis with risk of future fracture events: prospective study in UK Biobank
SO INTERNATIONAL JOURNAL OF SURGERY
LA English
DT Article
DE fall; fracture; osteoarthritis
ID bone loss; rheumatoid-arthritis; knee osteoarthritis; trabecular bone; femoral-neck; falls; pain; hip; acetaminophen; osteoporosis
AB Background: Researchers have long been interested in the potential relationship

between osteoarthritis (OA), falls, and fractures; however, the evidence supporting this relationship has been conflicting. This study aimed to investigate the association between osteoarthritis and future fracture events. Materials and methods: This study was designed as a prospective cohort study. We recruited a total of 440 476 individuals from the UK Biobank to investigate the impact of OA on the incidence of fracture. Among the total population, there were 54 581 participants diagnosed with OA. Cox proportional hazard models were used to calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs). Results: A total of 26 083 fracture events were documented over a median follow-up period of 13.5 years. After multivariable adjustment, participants with osteoarthritis had an HR (95% CI) of 1.11 (1.08, 1.15) for future fracture events compared to participants without osteoarthritis ($P < 0.0001$). Falls explained 16.34% of the association between osteoarthritis and fracture events and 14.15% of the association between knee osteoarthritis and fracture events. The association was not substantially altered across the series of sensitivity analyses. Conclusion: Osteoarthritis was associated with a greater risk of future fracture events. This finding highlights the importance of preventing future fracture events in people with osteoarthritis.
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JI Int. J. Surg.
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TI Clinical Progress in Mesenchymal Stem Cell Therapy: A Focus on Rheumatic Diseases
SO IMMUNITY INFLAMMATION AND DISEASE
LA English
DT Review
DE mesenchymal stem cells; osteoarthritis; rheumatic diseases; rheumatoid arthritis; systemic lupus erythematosus; systemic sclerosis
ID ankylosing-spondylitis patients; systemic-lupus-erythematosus; regulatory t-cells; bone-marrow; stromal cells; crohns-disease; osteogenic differentiation; classification criteria; extracellular vesicles; regenerative medicine
AB BackgroundRheumatic diseases are chronic immune-mediated disorders affecting multiple organ systems and significantly impairing patients' quality of life. Current treatments primarily provide symptomatic relief without offering a cure. Mesenchymal stem cells (MSCs) have emerged as a promising therapeutic option due to their ability to differentiate into various cell types and their immunomodulatory, anti-inflammatory, and regenerative properties. This review aims to summarize the clinical progress of MSC therapy in rheumatic diseases, highlight key findings from preclinical and clinical studies, and discuss challenges and future directions.MethodologyA comprehensive review of preclinical and clinical studies on MSC therapy in rheumatic diseases, including systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, osteoporosis, Sj ögren's syndrome, Crohn's disease, fibromyalgia, systemic sclerosis, dermatomyositis, and polymyositis, was conducted. Emerging strategies to enhance MSC efficacy and overcome current limitations were also analyzed.Results and DiscussionEvidence from preclinical and clinical studies suggests that MSC therapy can reduce inflammation, modulate immune responses, and promote tissue repair in various rheumatic diseases. Clinical trials have demonstrated potential benefits, including symptom relief and disease progression delay. However, challenges such as variability in treatment response, optimal cell source and dosing, long-term safety concerns, and regulatory hurdles remain significant barriers to clinical translation. Standardized protocols and further research are required to optimize MSC application.ConclusionMSC therapy holds promise for managing rheumatic diseases, offering potential disease-modifying effects beyond conventional treatments. However, large-scale, well-controlled clinical trials are essential to establish efficacy, safety, and long-term therapeutic

potential. Addressing current limitations through optimized treatment protocols and regulatory frameworks will be key to its successful integration into clinical practice.
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TI Postoperative Physical Therapy Utilization for Anterior Cervical Discectomy and Fusion An Analysis of Practice Patterns in the United States
SO SPINE
LA English
DT Article
DE rehabilitation; cervical spine; spine surgery; radiculopathy; myelopathy; timing; usage; patterns; fusion; visits
ID predictive factors; spine surgery; decompression; management; trends
AB Study Design/Setting. Retrospective Cohort study. Objective. To describe postoperative physical therapy (PostopPT) utilization patterns and evaluate predictors of utilization after anterior cervical discectomy and fusion (ACDF). Background Context. ACDF is the most common cervical spine procedure. PostopPT may improve outcomes, but current usage and program characteristics are unknown. Materials and Methods. PearlDiver Database identified patients who underwent ACDF between 2010 and April 2023. PostopPT utilization was assessed 7 to 365 days postoperatively. Demographics, comorbidities, and procedural characteristics were analyzed. Univariate and multivariate logistic regression identified predictors of PostopPT utilization. Results. Of 309,230 ACDF patients, 17.16% utilized PostopPT within one year. Among users, the average number of visits was 7.4, with mean initiation at 88 days (median: 61 d). PostopPT users were younger, had higher comorbidity burden, higher income, were more often female, and more likely to present with combined radiculopathy and myelopathy (P<0.001).Demographic predictors included commercial insurance (OR: 1.37), residence in the Northeast (OR: 1.35) or Midwest (OR: 1.31), income >$75,000 (OR: 1.17), female gender (OR: 1.14), and age below 50 (OR: 1.10) (all P<0.001). Comorbidity predictors included fibromyalgia (OR: 1.37), osteoarthritis (OR: 1.30), obesity (OR: 1.29), depression (OR: 1.26), osteoporosis (OR: 1.19), ECI >= 4 (OR: 1.13), diabetes (OR: 1.08), and tobacco use (OR: 1.07) (all P<0.001). Procedural predictors included mixed myelopathy/radiculopathy (OR: 1.29), fusion >= 3 levels (OR: 1.22), orthopedic surgeon as provider (OR: 1.10), inpatient surgery (OR: 1.09), and two-level fusion (OR: 1.08) (all P<0.001).Patients with myelopathy alone were more likely to receive gait training, aquatic therapy, and group training, but less

likely to receive manual therapy, electrical stimulation, hot/cold therapy, or ultrasound (all P<0.001). Conclusions. PostopPT usage following ACDF is limited. Distinct demographic, comorbidity, and procedural factors predicted usage. PostopPT programs varied in timing, frequency, and intervention type.
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TI Implication of bone marrow adipose tissue in bone homeostasis during osteoarthritis
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Osteoarthritis; Bone marrow adipose tissue; Subchondral bone; Mineralization; Epiphysis
ID infrapatellar fat pad; osteoporosis; differentiation; proliferation; model; pain
AB Objective: To explore the role of bone marrow adipocytes (BMAds) in osteoarthritis (OA). Methods: Male and female C57BL/6 mice (n=4/group) underwent meniscectomy (MNX) or SHAM surgery. OA was determined using Osteoarthritis Research Society International (OARSI) score, and the number of perilipin+ adipocytes was quantified. Mesenchymal Stromal Cells (MSCs) from MNX and SHAM mice were differentiated into osteoblasts and adipocytes. Human adipocytes and MSCs (n=8) were enzymatically isolated from epiphyseal and metaphyseal marrow, and from subcutaneous adipose tissue (SCAT) of hip OA patients. Human OA MSCs were differentiated into osteoblasts and adipocytes

(OA-Diff-hAdipo). Gene expression patterns of epiphyseal and metaphyseal BMAds, SCAT adipocytes and OA-Diff-hAdipo were evaluated by RNAseq (n=4). The effect conditioned media from OA epiphyseal bone (n=5) on the alkaline phosphatase (ALP) activity and mineralization kinetics was assessed in vitro. Results: Increase in BMAd density was positively correlated with cartilage degradation in MNX mice. OA modified the differentiation capacity of MSCs, accelerating adipocyte differentiation and failing to produce osteoblasts in both human and mice. Human epiphyseal, metaphyseal and SCAT adipocytes from the same OA patients each displayed a specific transcriptome, suggesting different functions. Enrichment analysis defined metaphyseal OA-BMAds as cells implicated in hematopoietic stem cell differentiation. On the other hand, epiphyseal OA-BMAds were considered as osteogenic cells showing an up-regulation of genes related to bone mineralization and remodeling. Specifically, OA epiphysis-secreted molecules decreased ALP activity and altered in vitro the mineralization process. Conclusion: All these results support the emergence of BMAds as new cell partners in OA, opening new venues for therapeutic approaches. (c) 2025 The Authors. Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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NR 74
TC 3
Z9 3
U1 3
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PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 1063-4584
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
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PT J
AU Thuan, MD
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Thanh, TN
AF Thuan, Mai Duc
Viet, Mai Dac
Thanh, Tran Ngoc
TI Clinical, imaging, and histopathological characteristics of Vietnamese patients with late-stage avascular necrosis of the femoral head
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Avascular necrosis of the femoral head (AVNFH); AVNFH stages; Femoral head collapse; Hip joint movement; Histopathology of AVNFH
ID total hip-arthroplasty; nontraumatic osteonecrosis; proximal femur; bone; classification; reliability
AB Introduction Avascular necrosis of the femoral head (AVNFH) causes femoral head (FH) collapse and hip osteoarthritis due to various factors. Objective The purpose of this study is to report on clinical features, MRI imaging, and histopathology of AVNFH in Vietnamese patients. Methods One hundred fifty patients diagnosed with AVNFH (stage IV,V, orVI according to Steinberg's classification) were evaluated for clinical symptoms, blood tests, X-rays, and hip MRI. Histopathological was performed on cancellous bone samples from the neck, greater trochanter, and lesser trochanter of the femur. Results Patients revealed rapid, persistent onset of pain in all three stages, with 100% exhibiting quadriceps atrophy, gluteal atrophy, and shortened limbs. Risk factors for AVNFH include alcohol/smoking (> 70%). Imaging injuries include bone defects/osteoporosis, femoral neck collapse, and joint space constriction (100%). Synovial edema, congestion, and cartilage separation were prevalent in phases V and VI (76.7-100%). Stage IV showed a wrinkled FH cartilage surface (80%) and partial FH collapse (100%), while stages V and VI revealed a jagged cartilage surface and total FH collapse (80-100%). Bone marrow necrosis, marrow edema, subchondral fractures, dead bone trabeculae, and thickening bone trabeculae occurred in all AVNFH patients. Furthermore, articular cartilage had fewer elastic fibers (stages IV and V), but complete articular cartilage degradation occurs only in stage VI. Conclusions Bone defects/osteophytes, FH collapse, and joint space narrowing are common markers for AVNFH in Vietnamese patients. Hip joint effusion, bone

marrow necrosis, edema, subchondral fracture, dead bone trabeculae, and thickening bone trabeculae are common.
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NR 52
TC 0
Z9 0
U1 0
U2 0
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
SN
EI 1471-2474
J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
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IS 1
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DI 10.1186/s12891-025-09327-y
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SC Orthopedics; Rheumatology
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UT WOS:001663026100005
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PT J
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TI Associations between bone mineral density and WOMAC scores in healthy individuals: Insights from the Qatar Biobank

SO JOURNAL OF CLINICAL DENSITOMETRY
LA English
DT Article
DE Bone mineral density; WOMAC scores; Healthy Individuals; Pain and stiffness; Physical function
ID mcmaster universities osteoarthritis; body-mass index; western ontario; smoking; osteoporosis; progression; burden; bmd
AB Background: Bone mineral density (BMD) is an indicator of bone health that predicts future bone fractures. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is used to assess the severity of symptoms related to pain, stiffness, and function in diseased hip and knee joints. Here we assessed whether BMD measured at specific sites predicts WOMAC scores in healthy individuals whilst controlling for sociodemographic variables. Methodology: BMD, sociodemographic, and WOMAC data were collected from 1764 healthy adult individuals attending the Qatar Biobank (QBB). Multiple linear regression was used to examine associations between sociodemographic factors, total body BMD and BMD related to specific skeletal sites (including femoral (femoral neck and trochanter), trunk, pelvis and total spine), and the three WOMAC subscales (pain, stiffness, and physical function). Results: After controlling for sociodemographic variables, total body and specific BMD measures did not predict pain. However, BMD measures significantly contributed to predicting stiffness after controlling for sociodemographic variables ($R^2 = 0.065$, $\Delta F(7, 1724) = 3.34$, $p = 0.002$), with a higher total body BMD associated with increased stiffness and a higher trunk BMD associated with decreased stiffness. Total body BMD measures also significantly contributed to predicting compromised physical function ($R^2 = 0.091$, $\Delta F(7, 1724) = 3.762$, $p < 0.001$) after controlling for sociodemographic variables, with a higher total body BMD associated with an increase in compromised physical function. Conclusion: Total body BMD seems to be a more important predictor of stiffness and physical function than specific skeletal sites BMD measures. Monitoring BMD may have important implications for osteoarthritis patients.
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NR 40
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PI NEW YORK
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SC Endocrinology & Metabolism
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TI Osteo-F, a Newly Developed Herbal Formula, Ameliorates Osteoarthritis Through the NF-κB/IκB/JNK Pathway Based on Network Pharmacology
SO FOOD SCIENCE & NUTRITION
LA English
DT Article
DE functional foods; inflammation; network pharmacology; NF-kappa B/I kappa B/JNK pathway; osteoarthritis
ID osteoporosis; inflammation
AB Osteoarthritis (OA) is a painful joint condition primarily caused by cartilage degradation, leading to pain and reduced mobility. Given the side effects of current treatments, this study investigates Osteo-F, a novel herbal-based functional ingredient formulated with Schizandra chinensis, Lycium chinense, and Eucommia ulmoides, traditionally valued for their bioactive and health-promoting properties. Network pharmacology analysis identified significant interactions involving Osteo-F within the TNF signaling pathway, highlighting its role in modulating key inflammatory processes in OA. In vivo experiments using a monosodium iodoacetate-induced OA rat model demonstrated significant improvements in arthritis scores, bone mineral content, and bone mineral density, alongside preservation of cartilage integrity, as confirmed by histological analyses. In vitro studies further revealed that this formulation reduced the activation of JNK and NF-kappa B pathways, decreasing inflammatory cytokines and matrix metalloproteinases critical in cartilage breakdown. These findings underscore the potential of Osteo-F as a functional food candidate to reduce inflammation and support cartilage preservation in OA. Future clinical trials are required to validate these findings and explore its dietary integration in OA management.
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Z9 0
U1 6
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 FOOD SCI NUTR
JI Food Sci. Nutr.
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WC Food Science & Technology
SC Food Science & Technology
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AU Houel, V
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TI Patients with periprosthetic femoral fractures are older adults who are commonly diagnosed with osteoporosis
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Bone mineral density; Fracture liaison service; Osteoporosis; Periprosthetic femoral fractures; Periprosthetic fractures
ID density; femur
AB This study focused on individuals aged >= 50 years with periprosthetic femoral fractures (PFF). When compared to those with native hip fractures, patients with PFF were older, had a higher BMI, and demonstrated a greater number of comorbidities. Given the high frequency of osteoporosis risk factors and the BMD results, PFF should be classified as osteoporotic fractures. Introduction To compare patients presenting with periprosthetic femoral fractures (PFF) to patients with native hip fractures with a special focus on bone mineral density (BMD) measurements, in order to reinforce the hypothesis that PFF are osteoporotic fractures. Methods A retrospective, single-centre, observational study of all patients aged >= 50 years with low-energy PFF identified at the Lille University Hospital from January 1, 2016, to December 31, 2022, was conducted. The PFF group was compared to a group of patients with native hip fractures hospitalized during the same period. To compare the T-score data, we used a linear mixed model that considered a predefined adjustment for age, sex, and BMI. Adjusted means +/- standard error of the mean (SEM) are derived from the mixed model. Results Among 71 patients with PFF (78.9% female, median (IQR) age 81 (72-88) years), osteoarthritis (57.8%) was the primary indication for hip surgery. Compared with the native hip fracture group (n = 117), patients in the PFF group were significantly older (p = 0.002), had a significantly greater BMI (p = 0.043), and had a higher history of multiple falls (54.3% vs. 26.1%, p < 0.001). A greater frequency of previous low-energy fractures (69.0% vs. 44.0%, p < 0.001) and an increased prescription of anti-osteoporosis medications (26.8% vs. 11.1%, p = 0.006) in patients with PFF were found. Adjusted T-scores differed between the two groups at the lumbar spine (mean adjusted +/- SEM, - 0.5 +/- 0.2 (PFF group) vs. - 1.2 +/- 0.2 (comparator group), p = 0.008) but not at the femoral neck or at the total hip. Conclusion Low-energy PFF should be considered as an osteoporotic fracture and treated accordingly.
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TC 2
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SC Endocrinology & Metabolism

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AU Johari, S
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TI A Scoping Review of Interventions Aimed at Reducing Fear of Falling in Older Adults With Orthopedic Conditions
SO JOURNAL OF GERIATRIC PHYSICAL THERAPY
LA English
DT Review
DE fear of falling; orthopedic conditions; interventions; older adults
ID knee osteoarthritis; exercise programs; physical function; self-efficacy; elderly-women; balance; community; people; gait; osteoporosis
AB Background and Purpose:Fear of falling (FoF) is a persistent anxiety regarding the risk of falling, which can even impact individuals without a history of falls. Fear of falling has been associated with decreased physical functioning and increased risk of falls. Most interventions have focused on reducing FoF in healthy older adults. This study aimed to review the literature's scope, nature, and content related to FoF interventions in older adults with orthopedic conditions.Methods:A scoping literature review was conducted. The method steps included identifying the research question, identifying relevant studies, selecting the studies, charting the data, and synthesizing, summarizing, and reporting the results. Cochrane Library, Medline, PsycINFO, Embase, ProQuest, and Google Scholar were searched. The search strategy used a set of key concepts, including "Fear of Falling," "Orthopedic conditions," "Interventions," and "Older adults."Results and Discussion:Out of the 33 articles that fulfilled the inclusion criteria, 21 were randomized control trials (RCTs), 5 were RCT protocols, 3 were quasi-experimental studies, 2 employed pre-post designs, 1 was a prospective cohort study, and 1 was an experimental study. The review revealed 7 distinct categories of interventions: exercise training, cognitive behavioral therapy, enhanced occupational or physical therapy (OT or PT), motivational interviews, interdisciplinary interventions, education, and mind-body intervention. The Falls Efficacy Scale (FES) was the most frequently used outcome measure for assessing FoF. Other measures were the Fear of Falling Questionnaire (FoFQ), the International Physical Activity Questionnaire

(IPAQ), and the Perceived Ability to Manage Fall (PAMF). The studies varied in their reasoning, content, and how they reported findings, posing challenges for healthcare professionals in choosing and applying FoF intervention programs specific to various orthopedic conditions.Conclusion:This review highlighted the need for adopting more comprehensive approaches for assessing and addressing FoF in older adults with orthopedic conditions.
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NR 51
TC 0
Z9 0
U1 4
U2 7
PU LIPPINCOTT WILLIAMS & WILKINS
PI PHILADELPHIA
PA TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA, PA 19103 USA
SN 1539-8412
EI 2152-0895
J9 J GERIATR PHYS THER
JI J. Geriatr. Phys. Ther.
PD JAN-MAR 15
PY 2025
VL 48
IS 1
BP 42
EP 51
DI 10.1519/JPT.0000000000000426
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WC Geriatrics & Gerontology; Rehabilitation
SC Geriatrics & Gerontology; Rehabilitation
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PT J
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TI Crosstalk Between H-Type Vascular Endothelial Cells and Macrophages: A Potential Regulator of Bone Homeostasis
SO JOURNAL OF INFLAMMATION RESEARCH
LA English
DT Article
DE H-type vascular; endothelial cells; macrophages; molecular crosstalk; angiogenic-osteogenic coupling; bone homeostasis; interventions
ID induced osteonecrosis; vessel formation; stem-cells; angiogenesis; osteogenesis; exosm; microenvironment; polarization; modulation; expression
AB The crosstalk between H-type endothelial cells (ECs) and macrophages is critical for maintaining angiogenesis and osteogenesis in bone homeostasis. As core components of type H vessels, ECs respond to various pro-angiogenic signals, forming specialized vascular structures characterized by high expression of platelet-endothelial cell adhesion molecule-1 (CD31) and endothelial mucin (EMCN), thereby facilitating angiogenesis-osteogenesis coupling during bone formation. Macrophages, as key immune cells in the perivascular region, are primarily classified into the classically activated pro-inflammatory M1 phenotype and the selectively activated anti-inflammatory M2 phenotype, thereby performing dual functions in regulating local tissue homeostasis and innate immunity. In recent years, the complex crosstalk between type H vessel ECs and macrophages has garnered significant interest in the context of bone-related diseases. Orderly regulation of angiogenesis and bone immunity provides a new direction for preventing bone metabolic disorders such as osteoporosis and osteoarthritis. However, their interactions in bone homeostasis remain insufficiently understood, with limited clinical data available. This review comprehensively examines the intricate interactions between type H vessel ECs and macrophages with diverse phenotypes, and Insights into the signaling pathways that regulate their crosstalk, focusing on their roles in angiogenesis and osteogenesis. Furthermore, the review discusses recent interventions targeting this crosstalk and the challenges that remain. These insights may offer new perspectives on bone homeostasis and provide a theoretical foundation for developing novel therapeutic strategies.
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TI Spontaneous facet fusion following lateral lumbar interbody fusion supplemented with percutaneous pedicle screw fixation in degenerative lumbar disease
SO EUROPEAN SPINE JOURNAL
LA English
DT Article
DE Minimally invasive surgery; Lateral lumbar interbody fusion; Spontaneous facet fusion; Facet osteoarthritis
ID mechanical-behavior; spine; instrumentation; osteoarthritis; flexibility; disc
AB PurposeTo identify factors contributing to spontaneous facet fusion (SFF) after lateral lumbar interbody fusion (LLIF) with percutaneous pedicle screw fixation and evaluate its clinical significance.MethodsWe analyzed 43 patients (150 facet joints) who underwent LLIF with percutaneous pedicle screw fixation without posterior decompression and had at least one year of follow-up. Factors associated with SFF included patient-related factors (age, BMI, diabetes, smoking, osteoporosis), lumbar spinal factors (preoperative diagnosis, number of fused segments), and radiologic factors (facet osteoarthritis, interbody fusion status, cage position, and subsidence). Clinical outcomes were assessed using VAS for lower back pain (LBP) and radiating pain (RP) and the Oswestry Disability Index (ODI). Patients were categorized into three groups based on facet and interbody fusion status.ResultsSFF was observed in 65.3% (98/150) of facet joints, and in 52.0% of cases, SFF preceded interbody fusion. Preoperative facet osteoarthritis (p = 0.009, OR = 9.951) and solid interbody fusion (p = 0.048, OR = 9.837) were significant predictors of SFF. Clinical analysis showed significantly lower VAS for LBP in fused segments (p = 0.023), though no difference between facet fusion-only and interbody fusion groups.ConclusionsSFF frequently occurs after LLIF with percutaneous pedicle screw fixation, often before interbody fusion. It was more common in preoperative facet joint osteoarthritis and was frequently seen with solid interbody fusion. SFF correlates with improved LBP outcomes.
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TI Postoperative rehabilitation training adherence and influencing factors in adults with traumatic fractures in China: a cross-sectional study
SO BMJ OPEN

LA English
DT Article
DE Pain management; Cross-Sectional Studies; Fractures, Bone; REHABILITATION MEDICINE
ID exercise adherence; prescribed exercise; home exercise; health-care; patient; people; osteoarthritis; reconstruction; intervention; osteoporosis
AB Objective To explore rehabilitation training adherence as well as its related influencing factors among adult patients with traumatic limb fractures to provide a basis for clinical intervention strategies. Design Cross-sectional study. Setting Department of Rehabilitation Medicine. Participants Adults within 1 year postoperative for traumatic limb fractures and who underwent rehabilitation training were included in this study. Interventions Not applicable. Main outcome measures Patient information was collected using a self-designed general information form. Rehabilitation training adherence was evaluated using the Exercise Adherence Rating Scale (0/64, higher values=higher adherence). Barriers to and facilitators of rehabilitation were assessed using sociodemographic data, ability to perform daily life (ADL), General Self-Efficacy Scale (GSES) and Visual Analogue Scale. Pearson's (r) and determination (R-2) correlation coefficients were calculated to determine the strength of associations between variables. Potential correlates were explored using multiple linear regression analysis. Results Between December 2022 and December 2023, 180 subjects were recruited. The age of the participants ranged from 18 to 93 years, with a mean age of 41.5 years (SD 15.6). The mean Exercise Adherence score was 30.31 (SD 5.8). Adherence to postoperative rehabilitation training tended to be lower in participants of older age (-1.30; 95% CI -2.14 to -0.46; p=0.003), and those who had higher pain scores on the movement (moderate pain (-3.25; 95% CI -4.56 to -1.95; p<0.001) to severe pain (-5.42; 95% CI -7.31 to -3.54; p<0.001)), less education (-2.90; 95% CI -4.17 to -1.64; p<0.001), fewer family income (-1.82; 95% CI -2.77 to -0.87; p<0.001), treated at home (-1.90; 95% CI -3.35 to -0.45; p=0.011) and with lower GSES scores (0.25; 95% CI 0.16 to 0.34; p<0.001). Conclusions Patients with limb fractures require rehabilitation but often struggle with adherence to interventions. Strategies that focus on targeted education programmes, pain management and self-efficacy improvement may be considered to guide future research and programmatic approaches to enhance adherence to rehabilitation training.
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AU Sawai, M
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AF Sawai, Mizuho
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TI Maternal and neonatal outcomes of occiput posterior vaginal delivery
SO JOURNAL OF OBSTETRICS AND GYNAECOLOGY RESEARCH
LA English
DT Article
DE delivery; malpresentation; occiput posterior position
ID fetal head position; anal-sphincter injury; impact; risk
AB AimThe occiput posterior (OP) position is the most common fetal malposition associated with poorer maternal outcomes compared to the occiput anterior (OA) position. However, there are no equivalent reports for women in Japan. This study aimed to investigate the maternal and neonatal outcomes of OP delivery in Japan.MethodsThis retrospective study was conducted at a tertiary hospital in Japan. Singleton pregnant women who delivered vaginally at and after 37 weeks of gestation between January 2000 and May 2023 were included. Participants were divided into OA and OP groups and pregnancy outcomes were compared. Multivariable analysis was performed to adjust for background.ResultsIn total, 13 852 eligible participants were divided into OA (13 633, 98.4%) and OP (218, 1.6%) groups. Maternal weights were significantly higher in the OP group than in the OA group, but there were no significant differences in maternal age, height, BMI, and parity. The incidence of assisted vaginal delivery (6.0% vs. 25.2%, adjusted odds ratios [aOR] 6.97), third- or fourth-degree perineal laceration (0.9% vs. 2.8%, aOR 3.52), postpartum hemorrhage (4.3% vs. 8.7%, aOR 2.17), and prolonged second stage of labor (11.3% vs. 29.4%, aOR 4.75) were significantly higher in the OP group. On the other hand, there were no significant differences in neonatal outcomes.ConclusionThe present study showed that OP vaginal deliveries require more time, and the increased number of assisted vaginal deliveries resulted in more maternal lacerations and hemorrhage. Maternal complications should be noted in the management of OP deliveries.
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TI The role of lactylation modifications in musculoskeletal diseases: From mechanism to clinical application
SO PHARMACOLOGICAL RESEARCH
LA English
DT Article
DE Lactylation; Musculoskeletal diseases; Post-translational modification;

Epigenetic regulation; Therapeutic approaches
ID lactate; metabolism; cell
AB Lactylation, a recently discovered histone and non-histone modification driven by lactate, has redefined the understanding of how metabolic by-products regulate gene expression. Beyond its conventional role as an energy substrate, lactate emerges as a pivotal signaling mediator that couples cellular metabolism with epigenetic regulation. In musculoskeletal disorders, aberrant lactylation has been implicated in the disruption of osteogenic-osteoclastic balance, extracellular matrix homeostasis, and regenerative capacity, thereby linking cellular metabolic stress to pathological tissue remodeling. These findings position lactylation as a unifying mechanism across osteoporosis, osteoarthritis, intervertebral disc degeneration, and sarcopenia. Yet, the field remains in its infancy: the enzymatic machinery of lactylation is incompletely characterized, context-specific functions are poorly defined, and translation to human pathology is scarce. Conceptualizing lactylation as a metabolic-epigenetic nexus not only reframes our understanding of musculoskeletal biology but also highlights new opportunities for biomarker discovery and targeted epigenetic therapies. Addressing these challenges will be essential to harness the clinical potential of this emerging regulatory paradigm.
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TI Study on Bone Mineral Density Around the Knee in Postmenopausal Women with Osteoarthritis and Osteoporosis
SO INTERNATIONAL JOURNAL OF WOMENS HEALTH
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DT Article
DE bone mineral density; osteoarthritis; osteoporosis; dual-energy computed tomography; subchondral bone
ID subchondral bone; proximal tibia; fracture; individuals; injury
AB Background: Osteoporosis (OP) and knee osteoarthritis (KOA) are common comorbidities in postmenopausal women, yet the relationship between OP and localized bone mineral density (BMD) around the knee remains unclear. This study investigated the effect of concomitant OP on periarticular BMD and its associations

with the Western Ontario and McMaster University Osteoarthritis Index (WOMAC), radiographic severity, and hip-knee-ankle (HKA) angle in postmenopausal women with KOA.
 Methods: In this cross-sectional study, 117 postmenopausal women were classified into a KOA combined with OP group (n=59) and a KOA-only group (n=58) based on dual-energy X-ray absorptiometry (DXA) T-scores. All participants underwent dual-energy computed tomography (DECT) to quantify BMD around the distal femur, proximal tibia, and patella; weight-bearing radiographs to assess Kellgren-Lawrence (K&L) grade and HKA angle; and the WOMAC questionnaire to evaluate pain and joint function.
 Results: Patients with KOA combined with OP demonstrated significantly lower knee BMD than those with KOA alone ($P < 0.001$). This reduction in BMD was more pronounced with increasing OP severity. Notably, even after adjusting for pain levels, BMD remained significantly lower in the KOA combined with OP group ($P < 0.05$). Furthermore, medial knee BMD in the KOA combined with OP group exhibited an inverted U-shaped relationship with K&L grade, peaking at grade III before declining. In contrast, BMD increased progressively with K&L grade in the KOA group. A significant inverse correlation was also observed between the HKA angle and medial knee BMD in the KOA combined with OP group, suggesting greater bone loss with increasing valgus deformity.
 Conclusion: Postmenopausal women with KOA combined with OP have markedly lower periarticular BMD, associated with more severe pain, distinctive radiographic changes, and poorer alignment. These findings highlight the need for active bone preservation and OP management in KOA patients to alleviate symptoms and potentially slow disease progression.
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TI Effects of E2F Family on Musculoskeletal System Development and Related Diseases
SO PROGRESS IN BIOCHEMISTRY AND BIOPHYSICS
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DT Article
DE E2F family; bone; muscle; osteosarcoma; osteoarthritis
ID blocks terminal differentiation; duchenne muscular-dystrophy; cell-cycle progression; transcription factor; stem-cells; bone-formation; dna-repair; muscle; proliferation; expression
AB The E2F family consists of transcription factors that mediate the induction of the E2 gene by adenovirus E1a and play a vital role in regulating cell cycle progression, cell proliferation, and cell apoptosis. Given its primary functions in cell proliferation and differentiation, early studies on the E2F family focused on its relationship with cancer. However, as research has expanded, the E2F family has been found to play an independent role in the development of the musculoskeletal system and the mechanisms of related diseases. The E2F family can influence the progression of musculoskeletal diseases by regulating the cell cycle and proliferation of stem cells, osteoblasts, osteoclasts, chondrocytes, and myoblasts, acting as a target gene for various downstream pathways and microRNAs. This review is divided into two parts: the first elaborates on the physiological roles of the E2F family in bone

metabolism, skeletal muscle, and cartilage development, while the second summarizes its roles in the pathological processes of osteosarcoma, rheumatoid arthritis, osteoporosis, and muscle-related diseases. During musculoskeletal system development, the E2F family affects bone metabolism by regulating stem cell differentiation, promoting osteoclast differentiation and metabolism, and increasing osteoblast activity or inhibiting osteoblast differentiation. It also regulates mitosis in cartilage, influencing chondrocyte proliferation and differentiation. Additionally, the E2F family is essential for skeletal muscle development, controlling muscle differentiation and myogenesis. In the pathological mechanisms of musculoskeletal diseases, most E2F family members act as downstream targets of various microRNAs, regulating osteosarcoma progression. Some members function independently through their ability to control cell proliferation. The E2F family also contributes to osteoporosis progression by promoting pathological increases in osteoclast activity and affecting osteoblast function. In rheumatoid arthritis and osteoarthritis, E2F family members aggravate inflammation by increasing inflammatory factors through multiple pathways. Moreover, the E2F family plays a crucial role in muscle-related diseases, influencing skeletal muscle regeneration after injury and affecting symptoms of muscular dystrophies. This review provides a comprehensive overview of the physiological roles of the E2F family in the musculoskeletal system and its mechanisms of action in related diseases. By offering a systematic summary and analysis, this article aims to provide a foundation for future research as well as insights for disease diagnosis and treatment.
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TI Unlocking the therapeutic potential of WISP-1: A comprehensive exploration of

its role in age-related musculoskeletal disorders
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DE WISP-1; Musculoskeletal disorders; Sarcopenia; Osteoporosis; Osteoarthritis
ID nf-kappa-b; ccn family proteins; signaling pathway; skeletal-muscle; chondrocyte apoptosis; wnt; expression; osteoarthritis; proliferation; cartilage
AB As the global population ages, the incidence of age-related musculoskeletal diseases continues to increase, driven by numerous complex and poorly understood factors. WNT-1 inducible secreted protein 1 (WISP-1), a secreted matrix protein, plays a critical role in the growth and development of the musculoskeletal system, including chondrogenesis, osteogenesis, and myogenesis. Numerous in vivo and in vitro studies have demonstrated that WISP-1 is significantly upregulated in age-related musculoskeletal conditions, such as osteoarthritis, osteoporosis, and sarcopenia, suggesting its involvement in the pathogenesis of these diseases. Regulating WISP-1 expression holds promise as a therapeutic strategy for improving musculoskeletal function, potentially offering new avenues for treating age-related musculoskeletal diseases in clinical practice. This review highlights the signaling pathways associated with WISP-1, its physiological roles within the musculoskeletal system, and its therapeutic potential in treating age-related musculoskeletal disorders.
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SO ARCHIVES OF OSTEOPOROSIS
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women; hip fracture
AB The National Osteoporosis Guideline Group (NOGG) has updated the revised UK guideline for the assessment and management of osteoporosis and the prevention of fragility fractures in postmenopausal women, and men age 50 years and older. This guideline is relevant for all healthcare professionals involved in osteoporosis management.IntroductionThe UK National Osteoporosis Guideline Group (NOGG) first produced a guideline on the prevention and treatment of osteoporosis in 2008, with updates in 2013, 2017 and 2021. This paper presents a minor update of the 2021 guideline, the scope of which is to review the assessment and management of osteoporosis and the prevention of fragility fractures in postmenopausal women and men aged 50 years and older.MethodsWhere available, systematic reviews, meta-analyses and randomised controlled trials have been used to provide the evidence base. Conclusions and recommendations have been systematically graded according to the strength of the available evidence.ResultsReview of the evidence and recommendations are provided for the diagnosis of osteoporosis, fracture-risk assessment and intervention thresholds, management of vertebral fractures, non-pharmacological and pharmacological treatments, including duration and monitoring of anti-resorptive therapy, glucocorticoid-induced osteoporosis, as well as models of care for fracture prevention. Recommendations are made for training, service leads and commissioners of healthcare, and for review criteria for audit and quality improvement. Specific 2024 updates include guidance on fracture risk assessment by ethnicity, Parkinson's disease, Down's syndrome and lower-limb amputation; furthermore, the definition of very high fracture risk has been clarified. Hormone replacement therapy (HRT) is now recommended as a first-line treatment option in younger postmenopausal women with high fracture risk and low baseline risk for adverse events; recommendations regarding abaloparatide are included; additional training resources have been added.ConclusionThe guideline provides a comprehensive overview of the assessment and management of osteoporosis for all healthcare professionals involved in its management. This position paper has been endorsed by the International Osteoporosis Foundation and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO).
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TI The application of epigenetic clocks in degenerative musculoskeletal diseases: A systematic review
SO OSTEOARTHRITIS AND CARTILAGE
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DT Review
DE Aging; Epigenetic clocks; Degenerative musculoskeletal diseases; DNA methylation; Epigenetic age acceleration
ID dna methylation; age; osteoarthritis; pain; biomarker
AB Objective: Epigenetic clocks have emerged as powerful tools for quantifying biological aging. Degenerative musculoskeletal disorders (e.g., osteoarthritis [OA], osteoporosis) represent a group of age-related conditions characterized by progressive tissue deterioration. While their epidemiological association with aging is well-established, the precise relationship with epigenetic aging markers remains to be systematically elucidated. This review synthesizes current evidence on the application of epigenetic clocks as biomarkers and their clinical potential in managing these conditions. Methods: We systematically searched four major biomedical databases (PubMed, PMC, Web of Science, ScienceDirect) from inception through December 2024 for observational studies examining the association between the epigenetic clock and degenerative musculoskeletal diseases using controlled vocabulary (e.g., DNA methylation age) combined with disease-specific terms. The protocol was registered with PROSPERO (CRD42024623554). Results: After screening, 14 studies (case-control, cross-sectional, cohort) were included. We identified eight epigenetic clocks (based on cartilage, bone, and blood biomarkers) for assessing degenerative musculoskeletal diseases. DunedinPACE showed significant associations with chronic low back pain severity (r = 0.39-0.45) and functional impairment, while Horvath's clock revealed tissue-specific epigenetic aging in OA cartilage (Delta Age = 3.7 years). GrimAge exhibited the strongest correlations with chronic pain (rho = 0.47) and mediated socioeconomic influences (beta = 0.81). Conclusions: This systematic review of 14 clinical studies establishes epigenetic clocks as promising biomarkers for degenerative musculoskeletal diseases. The differential associations observed across epigenetic metrics highlight the need for disease-specific algorithm development. Future research should prioritize longitudinal validation and mechanistic investigations into socioeconomic influences on epigenetic aging.
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NR 55
TC 1
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U2 7

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PI London
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J9 OSTEOARTHR CARTILAGE
JI Osteoarthritis Cartilage
PD SEP 15
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BP 1052
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
GA 6HC3R
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PT J
AU Marques, EA
Caliskan, O
Brooke-Wavell, K
Folland, J
AF Marques, Elisa A.
Caliskan, Ogulcan
Brooke-Wavell, Katherine
Folland, Jonathan
TI Feasibility of ballistic vs conventional resistance training in healthy postmenopausal women: A three-arm parallel randomised controlled trial
SO MATURITAS
LA English
DT Article
DE Adverse events; Satisfaction; Osteoarthritis; Osteoporosis; Strength training
ID older-adults; strength; osteoporosis
AB Objectives: Power training has gained attention as a method for enhancing functional performance and mitigating fall risk in older adults, yet its long-term feasibility and safety, particularly in ballistic resistance training, remain underexplored in postmenopausal women. We evaluated the feasibility of 8-month

ballistic resistance training compared with conventional resistance training in postmenopausal women. Study design: The Resistance Exercise Programme on Risk of Osteoporosis and Osteoarthritis in Females (REPROOF) study was a three-arm parallel group randomised controlled trial at a university lab in the UK. Healthy postmenopausal women (n = 109) were randomised to 30 weeks (2 sessions/week) of lower-body ballistic resistance training, conventional resistance training, or a non-exercising control group. Main outcome measures: The primary outcomes, collected by questionnaire, were process feasibility, acceptability, perceived exercise efficacy, and adverse events. Results: Eighty-two participants completed the trial (75.2 % retention). Both ballistic resistance training and conventional resistance training were well accepted, with most participants rating the intervention positively. No differences in the perceived improvements in physical function and psychological well-being were found between the resistance training groups. Similarly, there was no significant difference in the rate of muscle-related adverse events between the resistance training groups (ballistic, 2.7 per 100 person-weeks; conventional, 2.3 cases per 100 person-weeks), but the rate was significantly lower in the control group (0.9 cases per 100 personweeks). No serious adverse events occurred during or within 24 h of exercise sessions. Conclusions: The absence of serious adverse events and the observed positive outcomes confirm the safety, satisfaction, and perceived effectiveness of ballistic resistance training, suggesting its potential for broader application in healthy postmenopausal women. ClinicalTrials.gov registry ID NCT05889598
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NR 31
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PU ELSEVIER IRELAND LTD
PI CLARE
PA ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND
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PT J
AU Huang, X
Han, F
Chen, YF
Sun, Q
Guo, JW
Ye, Z
Qi, W
Zhang, DW
AF Huang, Xiao
Han, Fei
Chen, Yong-Feng

Sun, Qiang
Guo, Jian-Wei
Ye, Zi
Qi, Wei
Zhang, Da-Wei
TI Bibliometric analysis of the application of artificial intelligence in orthopedic imaging
SO QUANTITATIVE IMAGING IN MEDICINE AND SURGERY
LA English
DT Article
DE Bibliometric analysis; artificial intelligence (AI); orthopedic; image
ID convolutional neural-networks; classification; segmentation; bone; impact; tissue; joint; hip
AB Background: With the development of artificial intelligence (AI) and the increasing significance of imaging in orthopedics, the application of AI in the field of orthopedic imaging is becoming increasingly extensive. Previous studies show that the application of AI-based orthopedic imaging may break the traditional model of the field. As a result, relevant research has received attention, and numerous articles have been published. Through bibliometric analysis, this study summarized the knowledge structure of AI-based orthopedic imaging and explored its potential research trends and focal points. Methods: In this study, literature on AI in the field of orthopedic imaging available in the Web of Science Core Collection (WoSCC) database from 1 January 2007 to 31 December 2024 was analyzed. In order to identify the main research topics and generate visual charts of countries, institutions, authors, and keyword networks, the search results were imported into VOSviewer and CiteSpace. Results: A total of 3,147 publications were analyzed, revealing a rapid increase in AI research in orthopedic imaging since 2007, with over 90% of studies published after 2017. The United States (US) and China dominate this field, with the US leading in citations and academic influence, and China demonstrating significant growth in productivity. Institutional analysis highlighted Harvard University and Stanford University as key contributors, reflecting their strong academic influence. Keyword analysis identified three main convolutional neural networks (CNNs); (II) applications in orthopedic disease imaging, including osteoarthritis, osteoporosis, and total knee arthroplasty; and (III) innovations in multimodal fusion and three-dimensional (3D) imaging techniques. Emerging trends emphasize integrating imaging data with clinical biomarkers to improve diagnostic accuracy and therapeutic decision-making. These findings provide a comprehensive overview of AI's role in orthopedic imaging, emphasizing areas of high impact and potential future directions for research. Conclusions: The research on the application of AI in orthopedic imaging is a hot topic and indicates broad research prospects in the future. However, this study suggests that research teams should strengthen collaboration, especially international cooperation. Based on comprehensive analysis, the development of DL algorithms (especially CNNs), the use of AI in processing image data related to orthopedic diseases

(segmentation, classification, and feature map extraction), and the expansion of AI imaging applications in different diseases are expected to become hotspots in future research on the application of AI in orthopedic imaging.
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WC Radiology, Nuclear Medicine & Medical Imaging
SC Radiology, Nuclear Medicine & Medical Imaging
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PT J
AU Chen, FJ
Seymour, H
Zheng, NQ
AF Chen, Fangjian
Seymour, Hannah
Zheng, Naiquan (Nigel)
TI Comparative Analysis of Knee Biomechanics in Total Knee Arthroplasty Patients Across Daily Activities
SO BIOENGINEERING-BASEL
LA English
DT Article
DE knee biomechanics index; motion analysis; stair ambulation; gait analysis
AB Total knee arthroplasty (TKA) is a commonly conducted surgery to relieve pain and enhance mobility in patients with end-stage knee osteoarthritis. Patient-reported outcome measures are often used whereas biomechanical variables are too complicated for clinicians and patients to assess functional improvement. There is a need for a simplified integrated knee biomechanics index (KBI) to compare improvements in TKA patients across various daily activities and examine the relationships between clinical functional tests and daily activities. Age-, gender-, and BMI-matched three groups (20 each in posterior stabilized TKA, bi-cruciate stabilized TKA, and healthy controls) were recruited and tested pre-op and 6-month post-op to perform walking on level, slope, and stairs, and two clinical tests (timed-up-go, 10-time sit-to-stand). Knee joint kinematics and kinetics variables were calculated from motion data and ground reactions captured at 120 Hz and 1200 Hz, respectively. KBI was developed based on these variables relative to healthy controls. The longitude comparison of KBI and the differences of KBI across various daily activities were identified using repeated-measure ANOVA. Pearson correlation analysis was used to compare clinical tests and KBI of daily

activities. KBIs of five daily activities were significantly increased following TKA follow-up. KBI improvement during level walking was significantly higher than those during stair ascending and descending. Significant correlations were found between timed-up-go test time and KBIs for stair ascending and descending.
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JI Bioengineering-Basel
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AU Yin, Q
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Gu, Jun
TI The role of the infrapatellar fat pad in osteoporotic knee osteoarthritis: bone-fat crosstalk: cross-sectional studies
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Knee osteoarthritis; Osteoporosis; Obesity; Infrapatellar fat pad; Triglycerides
ID whole joint assessment; body-mass index; articular-cartilage; obesity; mri; association; progression; risk; inflammation; effusion
AB Backgrounds Osteoporosis (OP) and osteoarthritis (OA) of the knee are common and serious human health problems. However, the relationship between

knee OP and the progression of OA, and the potential association between knee OP and adipose tissue within the knee, is not well understood. This study aims to characterize differences in IPFP morphology and lipid metabolism markers, bone metabolism profiles between patients with isolated knee OA and those with concurrent OA and OP, to explore potential mechanisms linking adipose tissue dysfunction to OA-OP comorbidity. Methods This study enrolled 402 participants (89 healthy volunteers, 100 knee OA patients, 108 OP patients, and 105 OA + OP patients) from September 2011 to January 2023. Synovial inflammation markers (effusion grading: 0-3; IPFP abnormalities: 0-3; synovial proliferation: 0-2) and structural knee abnormalities (Whole-Organ Magnetic Resonance Imaging Score [WORMS]: cartilage, bone marrow edema, meniscus sub-scores) were assessed via MRI. Pathological analysis of IPFP tissue (fibrosis: 0-3; vascularization: 0-2) was performed by two blinded pathologists in OA patients undergoing arthroplasty. Clinical outcomes (WOMAC, Oxford Knee Score, Anterior Knee Pain Score) were evaluated preoperatively and at 1-year follow-up. Risk factors (triglycerides, hip BMD, IPFP abnormalities) were analyzed using LASSO regression with 10-fold cross-validation. Results The OA + OP group exhibited higher grades of synovial effusion (mean +/- SD: 2.1 +/- 0.7 vs. 1.3 +/- 0.5, $p < 0.01$), IPFP abnormalities (2.4 +/- 0.6 vs. 1.8 +/- 0.4), and synovial proliferation scores (1.9 +/- 0.5 vs. 1.2 +/- 0.3) compared to the OA group. Total WORMS scores were significantly elevated in OA + OP (32.5 +/- 8.2 vs. 24.1 +/- 6.5, $p < 0.001$), driven by higher cartilage degradation, increase of bone marrow edema, and meniscus damage sub-scores. Pathological analysis confirmed increased fibrosis (2.7 +/- 0.4 vs. 1.9 +/- 0.3) and vascularization (1.8 +/- 0.5 vs. 1.1 +/- 0.2) in OA + OP. At 1-year follow-up, OA + OP patients had worse WOMAC (45.2 +/- 10.1 vs. 33.5 +/- 8.7) and OKS (22.1 +/- 5.3 vs. 28.4 +/- 4.9). LASSO regression identified TG, total hip BMD, and IPFP abnormalities as key risk factors. Conclusion Our results identify a pathophysiological triad of (1) IPFP fibrosis/hypervascularization, (2) systemic hypertriglyceridemia, and (3) low BMD that collectively accelerates structural degeneration and symptom progression in knee OA. While genetic and biomechanical factors initiate OA pathogenesis, these acquired metabolic-inflammatory mechanisms represent tractable therapeutic targets for modifying disease evolution in established OA, particularly with OP comorbidity.
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JI J. Orthop. Surg. Res.
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AF Masante, Beatrice
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TI Insights into bone and cartilage responses to pulsed electromagnetic field stimulation: a review with quantitative comparisons
SO FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY
LA English
DT Review
DE pulsed electromagnetic field (PEMF); bone; cartilage; bone fractures; osteoporosis; osteoarthritis; fracture healing; quantitative comparison
ID mesenchymal stem-cells; subchondral trabecular bone; osteoblast-like cells; osteogenic differentiation; knee osteoarthritis; double-blind; mechanical-property; extracellular-matrix; engineered bone; magnetic-fields
AB Bone fractures and cartilage pathologies represent a heavy socioeconomic burden for the national healthcare systems worldwide. Pulsed electromagnetic field (PEMF) stimulation has become a widely recognized treatment for enhancing bone fracture healing and reducing tissue inflammation, thereby supporting bone tissue regeneration. More recently, its effectiveness in treating cartilage degeneration and osteoarthritis has also been demonstrated. However, the effects of PEMF, particularly the underlying mechanisms related to the activation of specific signaling pathways, are not yet fully known neither correlated with the specific PEMF parameters applied. As a result, standardized protocols for PEMF treatment are lacking in clinical practice, leading to empirical application of PEMF stimulation and heterogeneity in treatment protocols. For these reasons, over the past three decades, the biological effects of PEMF on bone and cartilage tissues have been extensively investigated through both in vitro and in vivo experiments. The aim of this review is to provide a detailed overview of the performed studies, focusing on the applied PEMF stimulation parameters and the induced effects on bone and cartilage tissues. Furthermore, to enable comparisons across various published protocols and to aid in understanding the correlation between applied PEMF parameters and their resulting biological effects, we propose, for the first time, a quantitative descriptor for PEMF stimulation, termed PEMF dose, which accounts for magnetic field intensity, stimulation waveform, and exposure duration. The use of this comprehensive descriptor enabled the identification of common features across different studies and, in the future, it could serve as a valuable tool for refining PEMF stimulation protocols and establishing standardized guidelines to support bone and cartilage repair.
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PT J
AU Yuen, KCJ
AF Yuen, Kevin C. J.
TI Growth Hormone and Bone: Preclinical and Clinical Perspectives
SO ENDOCRINE PRACTICE
LA English
DT Review
DE growth hormone; bone; insulin-like growth factor; growth hormone deficiency; growth hormone excess; acromegaly
ID radiological spinal deformity; morphometric vertebral fractures; term biochemical control; gh-deficient patients; factor-i; mineral density; adult patients; igf-i; replacement therapy; postmenopausal osteoporosis
AB Objective: Growth hormone (GH) is essential for growth and bone metabolism. This article reviews preclinical data that has shaped our understanding of the mechanisms underpinning the effects of GH on bone beyond the downstream activation of insulin-like growth factor-I (IGF-I) generation and summarizes the clinical data of GH deficiency (GHD) and acromegaly on bone health parameters and fracture risk. Methods: A literature search was conducted on PubMed using the following key words: GH, IGF-I, bone, GHD, and acromegaly. The discussion of therapy in GHD and patients with acromegaly, and their fracture risk assessment was based on evidence derived from previously published preclinical and clinical studies. Results: Preclinical and clinical data have demonstrated important pleiotropic effects of GH and IGFI on bone formation and resorption. GH exerts direct and IGF-dependent and independent effects on bone, while IGF-I acts in an endocrine and autocrine/paracrine manner. In GHD, decreased bone turnover, delayed statural growth, low bone mass, and increased fracture risk are observed, whereas acromegaly is associated with increased bone turnover but decreased lumbar bone mineral density and increased vertebral fracture and osteoarthritis risk. Treatment aimed at normalizing the GH/IGF-I axis decreases the fracture risk in GHD, but not acromegaly. Conclusion: Preclinical and clinical studies have improved our understanding of the role of GH in bone in healthy individuals and in disease states. More research is needed to identify the effects of GH on bone and to determine how best to treat patients with GHD and acromegaly, so that their bone health is optimized. (c) 2025 AACE. Published by Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar

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WC Endocrinology & Metabolism
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AU Udagikar, MP
Vaibhav, SL
Changade, J
AF Udagikar, Manasi P.
Vaibhav, S. Ladke
Changade, Jayshree, V
TI Evaluation of osteogenic activity of Plaksha (Ficus lacor Buch. Ham.) stem bark on human dental pulp derived mesenchymal stem cells
SO INDIAN JOURNAL OF BIOCHEMISTRY & BIOPHYSICS
LA English
DT Article
DE Alkaline phosphatase; Ficus lacor; Human dental pulp stem cells; Mesenchymal stem cells; Osteogenesis; Osteonectin; Plaksha
AB The adverse effects and lower efficacy of synthetic drugs have increased scientists' interest in traditional medicine for managing chronic diseases like osteoporosis and osteoarthritis, which raise the risk of bone fractures. Herbal

medications are increasingly used for joint disorders due to their potential benefits in reducing pain, inflammation, and stiffness, as well as their safety when used correctly. Plaksha (Ficus lacor Buch. Ham) possess a great potential in treating bone disorders. The purpose of the study is to determine the osteogenic effect of stem bark extract of Plaksha on mesenchymal stem cells. Aqueous extract of Plaksha obtained via Soxhlet Apparatus. Mesenchymal stem cells were obtained from human dental pulp; Characterized using Cell Surface Antigen Expression Analysis via FluorescenceActivated Cell Sorting (FACS). Cytotoxicity assessed with MTT. Osteogenic potential evaluated through trilineage differentiation and gene expression analysis (RT-PCR) for Alkaline Phosphatase (ALP) and Osteonectin (OSN). Viability assay revealed that the 10 mu g/mL concentration helps for trilineage differentiation of cells. Upregulation of ALP and OSN genes via RT-PCR in treated group showed the osteogenic differentiation of cells. This demonstrates the aq. Extract of FL promotes the osteogenic differentiation of MSCs and facilitate the osteogenesis. Hence the drug can be used in various bone disorders.
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PU NATL INST SCIENCE COMMUNICATION-NISCAIR
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PA DR K S KRISHNAN MARG, PUSA CAMPUS, NEW DELHI 110 012, INDIA
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AU Ueki, S
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AF Ueki, Shinichi
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TI High prevalence and underdiagnosis of osteoporosis in total hip arthroplasty candidates: a comprehensive assessment using bone mineral density, trabecular bone score, and bone turnover markers
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
LA English
DT Article
DE Total hip arthroplasty; Osteoporosis; Bone mineral density; Trabecular bone score; Bone turnover markers; Patient-reported outcome measures
ID vitamin-d deficiency; postmenopausal women; fracture risk; osteoarthritis; metaanalysis; replacement; prediction; diagnosis; therapy; bmd
AB Background Total hip arthroplasty (THA) effectively alleviates symptoms in individuals with hip osteoarthritis. However, some candidates may have undiagnosed osteoporosis, and bone mineral density (BMD) alone may not sufficiently reflect bone fragility. The trabecular bone score (TBS) and bone turnover markers (BTMs) provide additional information on bone quality and metabolism. This study aimed to comprehensively evaluate osteoporosis prevalence using BMD, TBS, and BTMs, and to assess whether preoperative osteoporosis affects postoperative pain and patient-reported outcome measures (PROMs). Methods This retrospective study included 357 patients who underwent primary THA. Comprehensive evaluation involved dual-energy X-ray absorptiometry to assess BMD and lumbar TBS, along with serum levels of tartrate-resistant acid phosphatase 5b (TRACP-5b), and 25-hydroxyvitamin D (25(OH)D). The subsequent analysis excluded patients receiving preoperative osteoporosis treatment (n = 33) to avoid treatment-related confounding. Patients (n = 324) were initially stratified by sex, and then classified as normal, osteopenia, or osteoporosis group based on total hip BMD. Postoperative outcomes were assessed using the Numerical Rating Scale for pain and the Hip Disability and Osteoarthritis Outcome Score for Joint Replacement for PROMs at preoperatively and 12 months postoperatively. Results Osteoporosis and osteopenia were identified in 23.8% and 37.5% of all patients, respectively. TBS revealed

compromised bone microarchitecture (Low TBS) in 25.7% of patients. Elevated TRACP-5b and vitamin D deficiency were observed in 15.6% and 72.3% of patients, respectively. Only 9.2% received osteoporosis pharmacologic treatment. No complications were observed within 12 months postoperatively. In only female patients, the osteopenia and osteoporosis groups, compared with the normal group, showed significantly lower TBS and 25(OH)D levels, and significantly higher TRACP-5b levels ($p < 0.05$); however, no significant differences were observed between the osteopenia and osteoporosis groups for these parameters. Furthermore, the improvement in HOOS JR scores from baseline to 12 months was significantly lower in the osteoporosis group compared with the normal and osteopenia groups ($p = 0.02$). Conclusion This comprehensive assessment, which included BMD, TBS and BTMs, revealed that female patients exhibited abnormalities in bone microarchitecture and bone turnover starting from the osteopenia stage. Furthermore, the osteoporosis group showed a significantly lower improvement in PROMs 12 months postoperatively.
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Xiao PL, 2022, ARCH OSTEOPOROS, V17, P0, DOI 10.1007/s11657-021-01055-9
NR 54
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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Liao, Shijie
TI Targeting type H vessels with bioactive metabolites from traditional Chinese botanical drugs: a therapeutic strategy for skeletal disorders
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE bioactive metabolites; type H vessels; osteoporosis; osteoarthritis; bone defects; fracture; osteonecrosis of the femoral head
ID endothelial-cells; attenuates osteoarthritis; femoral-head; bone; angiogenesis; osteogenesis; mechanisms; differentiation; subtype
AB Type H vessels are a specialized subtype of bone capillaries, first identified in 2014, characterized by high co-expression of CD31 and Endomucin. These vessels play a key regulatory role in bone development, repair, and remodeling through angiogenesis-osteogenesis coupling, which is essential for maintaining skeletal homeostasis. Type H vessels are abundant in the bones of young individuals but gradually decline with age, and their dysregulation is closely associated with skeletal disorders, including osteoporosis, osteoarthritis, bone defects, fractures, and osteonecrosis of the femoral head. Previous studies have identified the molecular mechanisms underlying the regulation of type H vessels, and recent investigations have examined pharmacological strategies to modulate these pathways. Among these, bioactive metabolites derived from traditional Chinese botanical drugs have attracted attention for their ability to regulate type H vessel formation and improve skeletal health. This review summarizes the molecular mechanisms by which these bioactive metabolites target type H vessels, highlighting their therapeutic potential in skeletal disorders and suggesting that modulation of type H vessel formation represents a promising strategy for intervention. Future studies are needed to further clarify the mechanisms of action of these metabolites and to assess their safety and clinical efficacy for translation into human therapy.
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TI Synthetic Nanopillars for Stimulating Osteoblast Activity and Osteointegration in Bone-Related Disorders
SO INTERNATIONAL JOURNAL OF NANOMEDICINE
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DT Review
DE synthetic polymers; nanopillars; bone repair; osteoblast activity;

osteointegration
ID surface; arrays; nanotopography; nanoparticles; particles; therapy; scaffolds; adhesion; disease; cells
AB Osteoporosis, osteoarthritis, and fractures are bone-related disorders that have a huge impact on the quality of life and healthcare systems worldwide. Traditional treatments, including bone grafts, have their limitations, with bone grafts often being rejected by the immune system and infected, making new treatments necessary. Nanopillars based on synthetic polymers have been demonstrated to be promising tools for bone regeneration and repair, showing to emulate the extracellular matrix composition, stimulate osteoblast activity and induce osteointegration. In this review, nanopillars fabrication techniques, such as electrospinning, nanoimprint lithography and self-assembly, also the state of the art of nanopillars technology are presented. Their role in modulating cellular responses via both physical and biochemical means, to enhance mineralization and to stabilize implants is also discussed. Additionally, their applications in treating bone-related disorders, eg promotion of fracture healing, augmentation of dental or orthopedic implants, and improvement of bone tissue engineering are discussed in the review. Using these focuses, each section examines opportunities and challenges (eg optimizing fabrication processes, improving biocompatibility, and investigating the integration of nanopillars with upcoming therapies like gene and stem cell therapy) for the potential of nanopillar technology. Finally, this review points out the requirement of scalable fabrication techniques, long term biocompatibility studies and multifunctional therapeutic strategies to fully employ the therapeutic applications of nanopillars in clinical scenarios. This review seeks to consolidate current knowledge of synthetic polymer based nanopillars and identify future directions for their use in bone related disorders through a comprehensive synthetic polymer nanopillar review.
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TI Comparative analysis of statistical and machine learning approaches for predicting fish length from otoliths
SO FRONTIERS IN MARINE SCIENCE
LA English
DT Article
DE data-limited fisheries; demersal and pelagic fish; generalized additive models (GAMs); K-nearest neighbors; otolith morphometry; random forest

ID size; shape; growth; body; identification; north; stock; width; coast; city
AB Accurate estimation of fish length from otoliths is essential for stock assessment, bycatch monitoring, and automated length reconstruction workflows. However, the strength and consistency of otolith-somatic scaling can vary across species and environments. This study examined the predictive performance of otolith morphometric variables for estimating fish length across six pelagic and demersal species from major Philippine fishing grounds. We evaluated 11 otolith morphometric and shape metrics using linear and nonlinear regressions, generalized additive models (GAMs), and machine learning (ML) algorithms. Model performance was compared across species to identify both the most informative predictors and ecological factors influencing otolith-length relationships. Otolith length (OL) and otolith area (OA) consistently produced the highest predictive power, whereas otolith perimeter (OP) showed the weakest performance. Demersal species and the midwater schooling Decapterus kurroides exhibited highly predictable otolith-length relationships (R-2 > 0.95), reflecting relatively stable habitats and uniform growth dynamics. In contrast, Selar crumenophthalmus and Thunnus albacares displayed lower predictability (R-2 <= 0.70), likely due to exposure to dynamic thermal regimes, variable prey fields, and ontogenetic shifts that increase plasticity in otolith accretion. ML models, particularly Random Forest, outperformed classical approaches for species with heterogeneous growth patterns by capturing nonlinearities and interactions among morphometric variables. Our findings demonstrate that OL and OA are robust and broadly transferable predictors of fish length in tropical multispecies fisheries, while species inhabiting variable pelagic environments benefit from more flexible ML frameworks. Integrating ecological context with advanced modeling tools can significantly improve otolith-based size estimation. The study highlights the value of expanding sampling coverage and refining ML approaches to enhance future applications in fisheries monitoring and assessment.
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TI Identifying key components from Melastoma dodecandrum in TNF-α-induced osteoblast injury model through a combination of cell membrane chromatography and mass spectrometry
SO JOURNAL OF ETHNOPHARMACOLOGY
LA English
DT Article
DE Melastoma dodecandrum; Isovitexin; TNF-alpha; Cell membrane chromatography; Key component
ID bone; activation
AB Ethnopharmacological relevance: Melastoma dodecandrum (MD), a traditional ethnomedicine, has been widely used for the treatment of fractures, osteoarthritis, and osteoporosis due to its remarkable anti-inflammatory activity. However, the specific active components responsible for its therapeutic effects on orthopedic conditions remain unidentified. Aim of the study: This study aimed to screen and identify key active components in MD using a combination of cell membrane chromatography and mass spectrometry, followed by cellular validation. Materials

and methods: A TNF-alpha-induced osteoblast injury model and an osteoblast membrane chromatography screening system were established to select and identify chemical components of MD that directly act on osteoblasts. The protective effects of MD on osteoblasts were assessed by evaluating cell viability, alkaline phosphatase (ALP) activity, cell mineralization and the expression of osteogenesis-related proteins OCN, RUNX2, and the TNF-alpha receptor protein TNFR1. Validation of the activity of individual components was also conducted. Results: MD significantly improved the viability of osteoblasts under TNF-alpha-induced injury, enhanced ALP activity, stimulated the expression of OCN and RUNX2 proteins, and decreased the expression of TNFR1. Cell membrane chromatography screening identified 32 chemical components, including 21 flavonoids, 6 organic acids, 2 phenylpropanoids, 2 terpenes, and 1 nucleotide. Molecular docking revealed that isovitexin could bind to the specific receptor TNFR1 on the cell membrane. Furthermore, cellular validation demonstrated that isovitexin significantly protected osteoblasts. Conclusions: MD and its pharmacologically active component, isovitexin, exhibit protective effects against TNF alpha-induced inflammatory injury in osteoblasts, laying a solid foundation for future drug development.
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TC 0
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J9 J ETHNOPHARMACOL
JI J. Ethnopharmacol.
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WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
SC Plant Sciences; Pharmacology & Pharmacy; Integrative & Complementary Medicine
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AU Zhou, J
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Yuan, Fang
Liu, Lu
Li, Bin
TI Influencing factors of flexion contracture among patients with knee

osteoarthritis: a multi-center retrospective cross-sectional study
SO SCIENTIFIC REPORTS
LA English
DT Article
DE Knee osteoarthritis; Flexion contracture; Risk factors; Protective factors
ID articular-cartilage; arthroplasty; joint
AB Knee osteoarthritis (KOA) is a chronic disease with a high prevalence and disability rate. Alterations in lower limb alignment and reduction in lower limb muscle strength are important factors in the progression of KOA. Although pain is the main reason for KOA patients to seek medical treatment, the presence or absence of joint deformity is one of the crucial factors influencing the prognosis and recurrence of the disease. Approximately half of KOA patients may become disabled due to the development of joint deformity. To investigate the prevalence, characteristics, and influencing factors of knee flexion contracture in patients with KOA, providing a basis for preventing and delaying the occurrence of knee joint deformities in such patients. From January 2022 to June 2022, a survey was conducted on 870 patients with KOA visiting 7 community hospitals. Patients whose knees could fully extend to 0 degrees were categorized as the none flexion contracture (NFC) Group, while those whose knees could not fully extend to 0 degrees were categorized as the flexion contracture (FC) Group. Data were collected on patients' demographic characteristics, work and lifestyle habits, dietary preferences, and clinical evaluations. Compare the results of the two groups, and perform a Logistic regression analysis on the influencing factors that show differences to identify the risk factors and protective factors for joint deformity. A total of 853 patients with KOA were included in the study, with a questionnaire recovery rate of 98.05%. Among them, 308 patients were in the FC Group, with a prevalence of knee flexion contracture at 36.11%, and 545 patients were in the NFC Group. The risk factors (OR > 1) included being female, older age, higher Body Mass Index (BMI), history of knee trauma, history of osteoporosis, physically demanding occupations, living in high-rise buildings without elevators, squatting posture during defecation, disease duration, and Kellgren-Lawrence (KL) III-IV grade. Protective factors (OR < 1) included commuting by cycling or driving, regular knee exercises, and calcium supplementation. Standing occupational posture, mountain climbing or hiking activities, and KL II grade were not associated with the occurrence of joint deformity (P > 0.05). Among patients with KOA, KL III-IV grade, living in high-rise buildings without elevators, history of knee injury, and squatting posture during defecation were identified as risk factors for knee joint deformity, which should be prevented early to delay joint deformity.
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NR 39
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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AU Zhou, LY
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Feng, Jianying
TI Role and mechanism of Actein on condylar bone metabolism in APOE deletion-induced osteoporotic mice
SO BONE
LA English
DT Article
DE Actein; APOE; Osteochondral; Condylar; Bone lipid metabolism
ID mineral density; progression; growth
AB Aims: To investigate the effects of Actein from Cimicifugae Rhizoma on condylar bone and cartilage in APOE deletion-induced osteoporotic mice, and to preliminarily explore the underlying mechanism. Methods: Sixty 8-week-old female mice were used, which underwent APOE-/- and ovariectomy procedures, followed by oral administration of Actein (15 mg/kg) and Atorvastatin Calcium (AC, 3 mg/kg) for eight weeks. Body weight, uterine weight, and systemic indexes related to bone metabolism and lipid metabolism were assessed in each group. Changes in condylar bone histomorphometric parameters were evaluated using Micro- CT. Morphological changes in the condyle were observed with Hematoxylin-Eosin (H&E), Safranin O/Fast Green, and Alcian Blue Hematoxylin/Orange G (ABH/OG)

staining, with OARSI pathology scoring performed. Sirius red staining and immunofluorescence were used to determine the expression levels of Collagen I (Col I) and Collagen III (Col III) in bone matrix, and Col II in cartilage matrix. Immunohistochemistry assessed the relative expression levels of ALP and proteins associated with the Wnt/(3-catenin/RUNX2 signaling pathway. Results: APOE- /- exacerbates ovariectomy-induced osteoporosis (OP) in condylar of mice. Actein and AC significantly reversed OP, improved bone mineral density (BMD), increased bone microarchitecture, and restored abnormal calcium and phosphorus metabolism in the blood and urine. Morphologically, APOE- /- and ovariectomy reduced condylar cartilage thickness, disrupted chondrocyte arrangement, chondrocyte cleavage, and clustered aggregation, resembling osteoarthritis (OA)-like changes. Actein and AC partially restored the disrupted chondrocyte arrangement, smoothed chondrocyte cleavage, and up-regulated the levels of chondrocyte matrix (Col II, aggrecan) and bone matrix (Col III, ALP). Actein reversed the OA process, potentially through the Wnt/(3-catenin/RUNX2 signaling pathway. Conclusion: APOE- /- and ovariectomy induced OP, leading to OA-like lesions in condylar of mice. Actein promoted cartilage repair and trabecular bone recovery by increasing extracellular matrix synthesis (Col II, Col III, aggrecan), reversing the OA process, possibly through the Wnt/(3-catenin/RUNX2 signaling pathway.
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PU ELSEVIER SCIENCE INC
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J9 BONE
JI Bone
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WC Endocrinology & Metabolism
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TI The Roles of Forkhead Box O3a (FOXO3a) in Bone and Cartilage Diseases - A Narrative Review
SO DRUG DESIGN DEVELOPMENT AND THERAPY
LA English
DT Review
DE FOXO3a; osteoporosis; osteoarthritis; rheumatoid arthritis; ankylosing spondylitis; intervertebral disc degeneration
ID mesenchymal stem-cells; nf-kappa-b; transcription factor foxo3a; oxidative stress; rheumatoid-arthritis; promotes tumorigenesis; articular-cartilage; survival signals; inhibition; proliferation
AB Bone and cartilage diseases are significantly associated with musculoskeletal disability. However, no effective drugs are available to cure them. FOXO3a, a member of the FOXO family, has been implicated in cell proliferation, ROS detoxification, autophagy, and apoptosis. The biological functions of FOXO3a can be modulated by post-translational modifications (PTMs), such as phosphorylation and acetylation. Several signaling pathways, such as MAPK, NF-kappa B, PI3K/AKT, and AMPK/Sirt1 pathways, have been implicated in the development of bone and cartilage diseases by mediating the expression of FOXO3a. In particular, FOXO3a acts as a transcriptional factor in mediating the expression of various genes, such as MnSOD, CAT, BIM, BBC3, and CDK6. FOXO3a plays a critical role in the metabolism of bone and cartilage. In this article, we mainly discussed the biological

functions of FOXO3a in bone and cartilage diseases, such as osteoporosis (OP), osteoarthritis (OA), rheumatoid arthritis (RA), ankylosing spondylitis (AS), and intervertebral disc degeneration (IDD). FOXO3a can promote osteogenic differentiation, induce osteoblast proliferation, inhibit osteoclast activity, suppress chondrocyte apoptosis, and reduce inflammatory responses. Collectively, up-regulation of FOXO3a expression shows beneficial effects, and FOXO3a has become a potential target for bone and cartilage diseases.
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TI Risk Factors for Subchondral Insufficiency Fracture of the Knee in the Setting of Medial Meniscus Posterior Root Tear
SO AMERICAN JOURNAL OF SPORTS MEDICINE
LA English
DT Article
DE SIFK; SONK; spontaneous osteonecrosis; subchondral insufficiency; joint space; meniscus root; meniscal tear; osteoarthritis; risk factors
ID spontaneous osteonecrosis; tibial slope; radiological assessment; femoral condyle; osteoarthritis; injury; osteoporosis; reliability; conversion; extrusion
AB Background: Subchondral insufficiency fracture of the knee (SIFK) is commonly associated with medial meniscus posterior root tears (MMPRTs). However, there is limited research investigating risk factors for SIFK in patients with MMPRTs. Purpose/Hypothesis: The purpose of this investigation was to identify the risk factors for SIFK in patients with MMPRTs. It was hypothesized that age, body mass index, and extent of meniscal extrusion would emerge as significant risk factors for SIFK. Study Design: Case series; Level of evidence, 4. Methods: Patients with a primary isolated MMPRT confirmed via magnetic resonance imaging were included. Data on patient demographics, medical and surgical history, and imaging parameters were assessed for associations with SIFK. Imaging parameters included mechanical axis, medial tibial slope, tibiofemoral joint space, and meniscal extrusion. Patients were identified and divided into 2 groups based on the presence or absence of findings of SIFK on magnetic resonance imaging. Continuous variable distribution normality was assessed using the Shapiro-Wilk test. Demographic comparisons were made by t tests and chi-square tests. Multivariable logistic regression was used to identify SIFK risk factors. The threshold of joint space for predicting SIFK was determined through receiver operating characteristic analysis. The optimal threshold was determined with the Youden index. Results: A total of 153 patients were included (mean +/- SD age, 56.2 +/- 9.1 years): 90 patients (26 male, 64 female) in the non-SIFK group and 63 patients (16 male, 47 female) in the SIFK group. There were no differences in patient demographics between the cohorts. Patients with SIFK had a greater incidence of previous knee injections (P = .047), a significantly smaller tibiofemoral joint space (P < .001), and a significantly greater degree of meniscal extrusion (P = .041). Multivariable logistic regression analysis identified diminished joint space as

the only independent predictor of SIFK (odds ratio, 0.41; P = .017). Receiver operating characteristic analysis determined a predictive threshold for joint space <3.93 mm, yielding an acceptable area under the curve of 0.766. Conclusion: The development of SIFK is likely multifactorial; however, decreased tibiofemoral joint space is a significant independent risk factor for SIFK in patients with MMPRTs, with a greater risk in patients with a tibiofemoral joint space <3.93 mm.
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AU Wang, CX
Ye, SW
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AF Wang, Chengxin
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Chen, Shengao
TI Identification of Schizothorax species in Yarkand River, (Xinjiang, China) based on otolith morphology
SO JOURNAL OF OCEANOLOGY AND LIMNOLOGY
LA English
DT Article
DE <italic>Schizothorax</italic>; otolith morphological analysis; elliptic Fourier transform; species discrimination
ID sagittal otolith; somatic growth; shape-analysis; mackerel; atlantic; marmara; stocks; tool
AB This study explored the morphological characteristics and differences of the otoliths in three native species, Schizothorax biddulphi, S. eurystomus and S. curvifrons, in the Yarkand River of the Tarim River, Xinjiang, China. A total of 93 specimens (27 S. biddulphi, 39 S. eurystomus, and 27 S. curvifrons) were analyzed using six basic otolith morphological parameters (OA, Rmax, Rmin, OP, OL, OW) to derive six factors (F1, F2, F3, F4, F5, F6) and seven indices (RO, FF, CI, RE, EL, RR, AR) for morphological assessment. A discriminant analysis incorporating 77 Fourier coefficients of the otoliths revealed distinct morphological differences among the species. A significant power function relationship between otolith morphology and standard length was observed across the species, with R2 values ranging from 0.409 to 0.749. Principal component analysis (PCA) of 7 traditional otolith morphological indicators explained 81.243% of the variance, yielding an overall

species discrimination rate of 81.65%. Further PCA of 77 Fourier harmonic values enhanced the discrimination accuracy, with the first 3 components accounting for 77.49% of the total variation and an improved discrimination rate of 100.00%. Cluster analysis resulted in the grouping of S. biddulphi and S. curvifrons together and revealed their association with S. eurystomus, indicating notable morphological distinctions. Both otolith shape indices and elliptical Fourier analysis have been useful in distinguishing the phenotypic units of different fish species. In this study, otolith morphology was applied for the first time to identify Schizothorax species, providing an in-depth description of species distribution and evolutionary history. This study provides a reference for the identification and systematic classification of Schizothorax species and a scientific basis for formulating effective species protection measures, for promoting the sustainable management of species and important habitats.
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AU Wu, ZP
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Shi, Jiejun
TI Emerging roles of the metabolite succinate in bone-related diseases
SO JOURNAL OF ZHEJIANG UNIVERSITY-SCIENCE B
LA English
DT Review
DE Succinate; Osteoarthritis; Rheumatoid arthritis; Osteoporosis; Fracture; Periodontitis
ID receptor gpr91; sdh mutations; reperfusion; cancer; fumarate; hypoxia; dicarboxylate; transporters; metabolomics; macrophages
AB Bone-related diseases, including osteoporosis (OP), osteoarthritis (OA), rheumatoid arthritis (RA), fracture, and periodontitis, significantly impact human health. Succinate, primarily known as a metabolic intermediate in the tricarboxylic acid (TCA) cycle, has emerged as a regulator of cellular functions beyond its metabolic role. Under stress, succinate accumulates in mitochondria and acts as a signaling molecule, modulating cellular processes. Notably, succinate activates angiogenesis and inflammation by stabilizing hypoxia-inducible factor-1 alpha (HIF-1 alpha). Moreover, it influences various pathophysiological processes by interacting with the succinate receptor 1 (SUCNR1), thereby impacting immune response, inflammation, cancer metastasis, and bone homeostasis. The multifaceted roles of succinate as a signaling molecule vary depending on its cellular location and concentration. Recent metabolomic analyses have revealed elevated succinate levels in bone-related diseases, indicating its potential association with these conditions. The objective of this review is to elucidate the impacts of succinate on different bone-related diseases and to discuss potential therapeutic targets and drug molecules based on its mechanisms of action.
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TI Current status of nano-embedded growth factors and stem cells delivery to bone for targeted repair and regeneration
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Review
DE Bone regeneration; Growth factors; Osteoporosis; Stem cells; Targeted delivery
ID platelet-rich plasma; bmp-2-induced osteogenic differentiation; drug-delivery; tissue regeneration; endothelial-cells; fracture; scaffolds; nanoparticles; expression; cartilage
AB Bone-related diseases like osteoarthritis and osteoporosis impact millions globally, affecting quality of life. Osteoporosis considerably enhances the probability of bone fractures of the wrist, hip, and spine. Enhancement and acceleration of functional bone development can be achieved through the sustained delivery of growth factors (GFs) and cells in biomaterial carriers. The delivery of bioactive compounds in a targeted, spatiotemporal way that most closely resembles the natural defect repair process can be achieved by designing the carrier system with established release kinetics. Furthermore, the carrier can serve as a substrate that mimics the extracellular matrix, facilitating osteoprogenitor cell infiltration and growth for integrative tissue healing. In this report, we explore the significance of GFs within the realm of bone and cartilage tissue engineering, encompassing their encapsulation and delivery methodologies, the kinetics of release, and their amalgamation with biomaterials and stem cells (SCs) to facilitate the mending of bone fractures. Moreover, the significance of GFs in evaluating the microenvironment of bone tissue through reciprocal signaling with cells and biomaterial scaffolds is emphasized which will serve as the foundation for prospective advances in bone and cartilage tissue engineering as well as therapeutic equipment. Nanoparticles are being used in regenerative medicine to promote bone regeneration and repair by delivering osteoinductive

growth factors like BMP-2, VEGF, TGF-(3. These nanocarriers allow controlled release, minimizing adverse effects and ensuring growth factors are concentrated at the injury site. They are also mixed with mesenchymal stem cells (MSCs) to improve their engraftment, differentiation, and survival. This approach is a key step in developing multi-model systems that more efficiently facilitate bone regeneration. Researchers are exploring smart nanoparticles with immunomodulatory qualities to improve bonre regeneration and reduce inflammation in injury site. Despite promising preclinical results, challenges include cost manage- ment, regulatory approval, and long term safety. However, incorporating stem cell transport and growth factors in nanoparticles could revolutionize bone regeneration and offer more personalized therapies for complex bone disorders and accidents. The translational potential of this article: Stem cell transport and growth factors encapsulated in nanoparticles are becoming revolutionary methods for bone regeneration and repair. By encouraging stem cells to develop into osteoblasts, osteoinductive GFs like BMP-2, VEGF, and TGF-(3 can be delivered under control due to nano- materials like nanoparticles, nanofibers, and nanotubes. By ensuring sustained release, these nanocarriers lessen adverse effects and enhance therapeutic results. In order to prove their survival and development, MCSs, which are essential for bone regeneration, are mixed with nanoparticles, frequently using scaffolds that resemble the ECM of bone. Furthermore, by adjusting to the injured environment and lowering inflammation, immunomodulatory nanostructures and stimuli-responsive nanomaterials can further maximize. While there are still shotcomings to overcome, including managing expenses, negotiating regulatory processes, and guaranteeing long-term safety, this method promises to outperform traditional bone grafting by providing quicker, more individualized, and more efficient treatments. Nano-embedded growth factors and stem cell technologies have the potential to revolutionize orthopedic therapy and significantly enhance patient outcomes with further research.

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PT J
AU Yang, JJ
He, SQ
Huang, B
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Liu, J
AF Yang, Jun-Jie
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Xu, Feng
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TI A bibliometric and visualized analysis of extracellular vesicles in degenerative musculoskeletal diseases (from 2006 to 2024)
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Article
DE degenerative musculoskeletal diseases; bibliometric analysis; extracellular vesicles; senescence; cell-free therapy
ID exosm; osteoarthritis; osteoporosis; delivery; therapy; diagnosis; knowledge
AB Background With the rapid development of extracellular vesicles (EVs) in regenerative medicine research, they have become a promising new direction in the mechanistic, diagnosis and treatment studies of degenerative musculoskeletal diseases (DMDs), and has attracted increasing attention. However, there is currently a lack of comprehensive and objective summary analysis to help researchers quickly and conveniently understand the development trajectory and future trends of this field.Method This study collected articles and reviews published from 2006 to 2024 on EVs in DMDs from the Web of Science database. Bibliometric and visual analysis was conducted using several tools, including Microsoft Excel Office, VOSviewer, CiteSpace, Pajek, and R packages.Results 1,182 publications were included in the analysis from 2006 to 2024. Notably, there was a rapid increase in the number of publications starting in 2016, suggesting that this field remains in a developmental stage. Co-authorship analysis revealed that China ranked first in terms of publications, whereas the United States led in citations. The journal with the highest number of publications was International Journal of Molecular Sciences (INT J MOL SCI). The most prolific authors were Ragni, E with 23 publications, while the most cited author was Toh, WS. Additionally, nine of the top 10 institutions were from China, with Shanghai Jiao Tong University leading in the number of publications. The most cited article was "MSC exosomes mediate cartilage repair by enhancing proliferation, attenuating apoptosis and modulating immune reactivity", authored by Zhang, S, and published in BIOMATERIALS in 2018.Conclusion This study, through bibliometric and visual analysis, clearly illustrates the collaborative relationships among countries, authors, institutions, and journals, providing valuable insights for researchers seeking academic collaboration opportunities. Moreover, the analysis of keywords and citations allows researchers to better understand key research hotspots and frontiers in this field, and points toward

promising directions for future research. The growing interest in EV research in DMDs over recent years indicates increasing attention and a dynamic progression in this field.
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NR 95
TC 0
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PI LAUSANNE
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WC Pharmacology & Pharmacy
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AU Welch, JM
Klifto, CS
Klifto, KM
Lunn, KN

Adu-Kwarteng, K
Hammert, WC
Pean, CA
Pidgeon, TS
AF Welch, Jessica M.
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Klifto, Kevin M.
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Adu-Kwarteng, Kwabena
Hammert, Warren C.
Pean, Christian A.
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TI Prevalence and predictors of bone mineral density testing after distal radius fracture in menopausal women
SO INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
LA English
DT Article
DE Bone mineral density; Distal radius fracture; DEXA scan; Fragility; Osteoporosis
ID osteoporosis; health
AB Background: Osteoporosis screening guidelines recommend bone mineral density (BMD) testing following fragility fractures. Nevertheless, previous studies have demonstrated low rates of osteoporosis screening. Diagnosis and treatment of osteoporosis is essential for prevention of future fractures, however not much is known about the factors associated with receiving BMD testing in this patient population. The purpose of this study was to evaluate the prevalence, timing, and predictors of BMD testing following distal radius fractures (DRF) in menopausal women. Methods: We queried a national insurance database to identify menopausal women aged 45-64 years with a DRF between years 2013 and 2020. The rate of BMD testing within 1 year of injury was calculated. Multivariable logistic regression analysis was used to evaluate the effect of patient- and injury-related variables on the likelihood of undergoing BMD testing following DRF. Results: Among 31,728 patients meeting inclusion criteria (mean +/- SD age: 57.5 +/- 4.3), 3,886 (12.2 %) received a BMD test within 1 year following DRF. The rate of BMD tests decreased with the highest rate of 14.5 % in 2015 and the lowest rate of 10.5 % in 2020. Mean time from DRF to BMD testing was 143 +/- 102 days. Patients aged 60-64 had the highest adjusted odds of receiving BMD testing (OR 2.85 [95 % CI: 2.26 to 3.64]). Factors associated with increased likelihood of BMD testing included surgical intervention (OR 1.38 [1.28-1.48]), rheumatoid arthritis (OR 1.22 [1.06-1.40]), osteoarthritis (OR 1.28 [1.19-1.37]), breast cancer (OR 1.35 [1.16-1.56]), and vitamin D deficiency (OR 1.29 [1.17-1.43]). Factors associated with decreased likelihood of testing included tobacco use (OR 0.90 [0.84-0.97]), patients with Medicaid (OR 0.73 [0.61-0.86]) or Medicare (OR 0.76 [0.65-0.88]) insurance, and living in Southern (OR 0.67 [0.62-0.73]) or Western (OR 0.69 [0.62-0.77]) regions of the United States. Obesity, diabetes, renal disease, and early menopause were not

associated with BMD testing. Conclusions: Despite guidelines recommending BMD testing after low-energy fractures, rates of BMD testing were low and decreased among menopausal women with DRF. Mean time to BMD testing was 4.7 months, indicating substantial delays in workup. Known risk factors for osteoporosis did not reliably predict likelihood of BMD testing. Level of Evidence: Level III, prognostic
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NR 30
TC 1
Z9 1
U1 0
U2 1
PU ELSEVIER SCI LTD
PI London
PA 125 London Wall, London, ENGLAND
SN 0020-1383
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J9 INJURY
JI Injury-Int. J. Care Inj.
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WC Critical Care Medicine; Emergency Medicine; Orthopedics; Surgery
SC General & Internal Medicine; Emergency Medicine; Orthopedics; Surgery
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ER

PT J
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TI Stress Analysis in Conversion Total Hip Arthroplasty: A Finite Element Analysis on Stem Length and Distal Screw Hole
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE osteoporosis; femoral trochanteric fracture; conversion total hip arthroplasty; periprosthetic fracture; stress distribution
ID failed internal-fixation; periprosthetic fractures; intertrochanteric fracture; surgical-treatment; cortical defects; femoral-neck; salvage; complications; management; femur
AB Background/Objectives: Proximal femoral fractures are particularly common in older adults, and cases requiring conversion to total hip arthroplasty may arise because of treatment failure or osteoarthritis. Fractures around the distal screw removal holes can be problematic. This study aimed to analyze the relationship between stem length and femoral stress distribution to determine the optimal stem length. Methods: A finite element analysis simulation was conducted using pre-existing femoral computed tomography data, an intramedullary nail, and three types of stems of varying lengths. Loads simulating normal walking and stair climbing were applied, and the average and maximum equivalent stresses were measured on both the medial and lateral sides of the distal screw removal hole for each stem length. Statistical analysis was then performed to evaluate the stress distributions. Results: The average stress around the distal screw removal hole tended to decrease as stem length increased. The maximum stress was significantly lower with the 160-mm stem, which provides a 40-mm bridging length, compared to the 120-mm and 130-mm stems, where the stem tip aligned with or only slightly extended past the distal screw removal hole (bridging lengths of 0 mm and 10 mm, respectively). Conclusions: In conversion hip total arthroplasty following proximal

femoral fractures, using a sufficiently long stem can help avoid stress concentration around the distal screw removal hole, thereby potentially reducing the risk of periprosthetic fractures.
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SO TURKISH JOURNAL OF BIOCHEMISTRY-TURK BIYOKIMYA DERGISI
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DT Review
DE oxidative stress; iron overload; ferroptosis; bone-degenerative conditions; homeostasis
ID mesenchymal stem-cells; plasma-membrane; differentiation; expression; transport; metabolism; osteoclastogenesis; transferrin; mechanisms; inhibitor
AB Introduction Bone-degenerative conditions, including osteoporosis, rheumatoid arthritis, and osteoarthritis, are major public health concerns worldwide, associated with oxidative stress and iron overload that disrupts bone homeostasis. Ferroptosis, an iron-mediated form of cell death, has emerged as a critical factor in bone degeneration, necessitating a comprehensive review of its role in these conditions.Content This review comprehensively examined the latest research on oxidative stress, iron metabolism, and ferroptosis related to bone biology and degeneration, focusing on their interconnections and potential therapeutic implications. The review revealed that oxidative stress affects various bone cell types, including osteoclasts, osteoblasts, and chondrocytes, contributing to bone loss and cartilage degradation. Iron homeostasis was found to be crucial for bone cell function, with both iron overload and deficiency potentially leading to pathological conditions. Ferroptosis regulation involves a complex interplay between iron metabolism, lipid peroxidation, and antioxidant systems, including the SLC7A11-GSH-GPX4 network and the FSP1-CoQ10H2 pathway. Different bone cell lineages, including mesenchymal stem cells, osteoblasts, osteoclasts, and chondrocytes, exhibit varied responses to ferroptosis induction and regulation.Summary Understanding the molecular mechanisms underlying ferroptosis regulation in bone cells offers promising avenues for developing targeted therapies for bone-degenerative conditions.Outlook Future research should focus on elucidating the specific roles of ferroptosis in different bone disorders and exploring potential therapeutic interventions targeting oxidative stress, iron overload, and ferroptosis pathways to improve the management of these debilitating conditions.

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TI Recent Advances on the Analysis and Biological Functions of Cinnamaldehyde and Its Derivatives
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ID trans-cinnamaldehyde; in-vitro; oxidative stress; diabetic mice; brain-injury; cinnamon; cells; model; nanoparticles; inflammation
AB Natural antioxidants isolated from fruits, vegetables, herbs and spices have drawn great attention owing to their numerous health-promoting effects. Cinnamaldehyde (CA), an abundant antioxidant in cinnamon spice, has been explored more intensely over the last decade as it has been demonstrated to be effective and safe in the treatment of various diseases. Structurally, a substituted aldehyde group with an unsaturated carbon-carbon double bond with two electrophilic sites for reaction with receptors and enzymes can exert diverse biological effects. Although cinnamon has been traditionally used as a spice and herbal remedy, many studies investigating the most dominant functional compound, CA, and its biological activities have been reported in recent years. This review article intends to present an overview of recent advances in analytical methods and the application of cinnamon extract/oil, CA and its derivatives, CA-polymer/biomolecule conjugates and CA micro/nanosystems in alleviating various chronic diseases including cancer, diabetes, obesity, cardiovascular disease,

neurological disorders, osteoarthritis and osteoporosis. Both in vitro and in vivo studies have demonstrated the improved pharmacological efficiency of CA and its derivatives as well as their polymer/drug/biomolecule conjugates and micro/nanoencapsulated forms, suggesting a possible alternative natural therapy and adjuvant therapy with conventional drugs via a synergistic process.
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NR 179
TC 3
Z9 3
U1 9
U2 9
PU MDPI
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J9 ANTIOXIDANTS-BASEL
JI Antioxidants
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BP
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DI 10.3390/antiox14070765
PG 67
WC Biochemistry & Molecular Biology; Chemistry, Medicinal; Food Science & Technology
SC Biochemistry & Molecular Biology; Pharmacology & Pharmacy; Food Science & Technology
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PT J
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TI Vitamin D Alleviates Osteoarthritis Progression by Targeting Cartilage and

Subchondral Bone via Myd88-TAK1-ERK Axis Suppression
SO DRUG DESIGN DEVELOPMENT AND THERAPY
LA English
DT Article
DE vitamin D; bone; cartilage; osteoarthritis; rat
ID nf-kappa-b; d supplementation; inflammatory response; knee osteoarthritis; deficiency; volume; drug; pain
AB Background: Osteoarthritis (OA) causes irreversible joint damage, but current treatments fail to fully address its complex pathology. Emerging evidence suggests subchondral bone metabolic dysfunction may initiate OA. While vitamin D (VitD) is well-established for bone metabolism regulation in osteoporosis, its therapeutic potential in OA remains unclear despite observational studies suggesting protective effects. Our integrated in vivo/in vitro study demonstrates VitD's dual chondroprotective and osteogenic actions in OA. Methods: Sprague-Dawley rats (n=24) were divided into three groups: sham operation (Sham), OA model (OA), and OA+VitD treatment, with 8 rats in each group. Oral cholecalciferol (2.34 mu g/kg/day) was administered for 6 weeks post-Monosodium iodoacetate (MIA) induction. The therapeutic potential of vitamin D was evaluated through a series of in vivo experiments. Human chondrocyte C28 cells were pretreated with TNF alpha (1ng/mL) to model inflammatory injury, followed by 1,25(OH)2 D3 (10-2 mu M) exposure for 72 hours to assess the VitD's effects of chondrogenesis and further investigate its underlying mechanism. Results: In OA rats, VitD suppressed femoral cartilage degradation (evidenced by 567.76% increased cartilage area, and 39.13% decreased Osteoarthritis Cartilage Histopathology (OACH) score and enhanced subchondral bone mass (61.81% higher BV/TV). At the molecular level, VitD downregulated the expression of cartilage matrix metalloproteinase 13 (MMP13), with a reduction of 74.72% compared to OA group. Additionally, VitD inhibit inflammatory signaling pathways, particularly through the MyD88-TAK1ERK axis in chondrocytes, and decrease serum IL-6 level. Mechanistic validation of these findings was demonstrated by protein expression reduction of Myd88 (31.22%), phospho-ERK1/2 (66.11%), AP-1 (61.43%) and NF kappa B (34.36%) compared to OA group. In vitro, VitD also rescued ethanol-induced C28 cell viability loss while significantly upregulating cartilage anabolic markers. Conclusion: These findings establish VitD as a multimodal OA therapeutic agent targeting both cartilage catabolism and subchondral bone remodeling through Myd88-TAK1-ERK axis.
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NR 67
TC 0
Z9 0
U1 2
U2 3
PU DOVE MEDICAL PRESS LTD
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SN 1177-8881
EI
J9 DRUG DES DEV THER
JI Drug Des. Dev. Ther.
PD JUN 15
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IS
BP 5855
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DI 10.2147/DDDT.S526064
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WC Chemistry, Medicinal; Pharmacology & Pharmacy
SC Pharmacology & Pharmacy
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PT J
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TI Effects of nonstationary system blur on radiomic texture features of trabecular bone in normal and ultra-high resolution CT
SO MEDICAL PHYSICS
LA English
DT Article
DE CT spatial resolution; reproducibility; texture analysis
ID image noise uniformity; subchondral bone; position; number
AB Background CT image texture features (TFs) of trabecular bone are being investigated as predictive markers in osteoporosis (OP) and osteoarthritis (OA). To support the development of such radiomic approaches, the reproducibility of bone TFs to CT system factors needs to be characterized. We hypothesize that, in addition to the well-established inter- and intra-scanner effects (e.g., changes in reconstruction algorithm), the non-stationarity of CT spatial resolution may introduce inconsistencies in TFs of morphologically similar bone regions placed in different locations within the scanner field-of-view (FOV).Purpose To characterize the impact of spatially-variant CT blur on the reproducibility of trabecular bone TFs to radial shift within the FOV for a conventional normal resolution (NR) protocol with similar to 0.5 mm slice thickness, and an ultra-high resolution (UHR) protocol representative of the new generation of high-resolution CT (0.25 mm slice thickness).Methods Canon Aquilion Precision CT (Canon Medical Systems, Japan) was used to scan four human femora placed at 0, 9, and 18 cm radial shifts from the isocenter. NR (similar to 0.26 mm in-plane voxel size) and UHR (similar to 0.13 mm in-plane voxel) images were obtained at 1.5 s rotation. At each CT resolution, a total of 377 spherical regions of interest (ROIs) of 2.5 mm radius were seeded within the trabecular bone of the femora at 0 cm shift and transported via rigid registration to the images at 9 cm and 18 cm shift. TFs of the Gray Level Co-Occurrence and Run Length matrices (GLCM and GLRLM) were obtained for all ROIs. Reproducibility across radial shifts was evaluated (separately in NR and UHR) in terms of the concordance correlation coefficient (CCC) between the registered ROIs. Support vector machine (SVM) classifiers were applied to evaluate whether the radial shift of an ROI can be predicted from its TFs.Results In NR, the median CCCs for 0 cm vs. 9 cm radial shifts were similar to 0.9 for both GLCM and GLRLM

TFs, dropping to similar to 0.6 for 0 cm vs. 18 cm shifts. In UHR CT, the median CCCs of GLCM TFs were 0.92 for 0 cm vs. 9 cm and 0.52 for 0 cm vs. 18 cm; for GLRLM, the median CCCs were 0.88 for 0 cm vs. 9 cm and 0.53 for 0 cm vs. 18 cm. In a separate analysis on only high contrast ROIs (upper quartiles of voxel value variance at 0 cm), we found an additional 20% (for 0 cm vs. 9 cm) to 40% (for 0 cm vs. 18 cm) reduction in CCC in both UHR and NR. The somewhat worse reproducibility in UHR CT is attributed to more pronounced effects of gantry motion blur. The classification models were able to discriminate ROIs at 0 cm from the other radial shifts with median accuracy of 0.54 (0.67 in high contrast ROIs) in NR and 0.46 (0.67 in high contrast ROIs) in UHR. The ROIs at 9 cm were identified with 0.31 (0.5) accuracy in NR and 0.46 (0.58) accuracy in UHR; the ROIs at 18 cm were identified with 0.60 (0.83) accuracy in NR and 0.77 (0.83) accuracy in UHR.Conclusions Nonstationary CT spatial resolution leads to a loss of reproducibility of trabecular bone TFs between different regions of the scan FOV, potentially confounding radiomic predictors in clinical data where the lateral shift of the skeletal site of interest changes with patient size.
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NR 37
TC 1
Z9 1
U1 1
U2 1
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JI Med. Phys.
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WC Radiology, Nuclear Medicine & Medical Imaging
SC Radiology, Nuclear Medicine & Medical Imaging
GA 6TZ4W
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TI Epigenetic roles of chromatin remodeling complexes in bone biology and the pathogenesis of bone-related disease (Review)
SO INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE
LA English
DT Review
DE chromatin remodeling complexes; epigenetic regulation; bone biology; bone development; bone-related diseases
ID mesenchymal stem-cells; self-renewal; osteoblast differentiation; swi/snf complex; gene-expression; brg1; transcription; pluripotency; protein; chd7

AB Chromatin remodeling complexes are essential regulators of chromatin architecture, facilitating critical processes such as nucleosome sliding, eviction, histone exchange and post-translational modifications. By providing an additional layer of epigenetic regulation beyond the canonical genetic code, these complexes significantly influence bone biology and health. Epigenetic regulation through chromatin remodeling complexes is crucial in modulating gene expression and cellular behavior in bone cells. However, alterations in the activity of chromatin remodeling complexes can also contribute to the progression of various bone diseases. Emerging evidence suggests that specific chromatin remodeling factors may serve as potential biomarkers for diagnosing bone-related conditions and as therapeutic targets for intervention. The present review aims to elucidate the intricate relationship between chromatin remodeling complexes and bone-related diseases, including osteoporosis, osteoarthritis and osteosarcoma. The present review discusses the diverse subunits of these complexes and their multifaceted roles in regulating key cellular processes such as stemness, differentiation, proliferation, senescence and apoptosis in bone cells. Notably, the present review provides a comprehensive overview of the roles of various chromatin remodeling subunits, such as BRG1, BAF47 and chromodomain-helicase-DNA binding 7 (CHD7), in bone metabolism, highlighting their disease-specific mechanisms, including bromodomain-containing protein (BRD)9-mediated pyroptosis in intervertebral disc degeneration and CHD7-driven bone-fat imbalance. Furthermore, the present review highlights the therapeutic potential of targeting dysfunctional subunits (such as BRD7 in osteosarcoma and SS18 in synovial sarcoma) and propose AI-driven structural biology approaches to design chemical modulators. The understudied impact of aging on chromatin remodeling activity in bone homeostasis is also underscored, advocating for longitudinal studies to address this gap. Finally, the distinct functions of each chromatin remodeling complex and its specific subunits in the context of bone-related diseases were also explored, providing a comprehensive understanding of their contributions to both normal bone physiology and pathological conditions.
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TI Anthocyanins and musculoskeletal diseases: mechanisms and therapeutic potential
SO FRONTIERS IN NUTRITION
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DE anthocyanins; osteoporosis; rheumatoid arthritis; osteoarthritis; osteosarcoma; inflammatory; oxidative stress

ID nf-kappa-b; rheumatoid-arthritis; gene-expression; bone loss; cartilage degradation; osteosarcoma cells; signaling pathway; clinical scores; global burden; rankl
AB Background Musculoskeletal diseases (MSDs) are a common group of conditions involving bones, muscles, cartilage, ligaments, and nerves, which significantly impact patients' quality of life and ability to participate in society. Anthocyanins (ACNs), as phytochemicals, possess various pharmacological and biological activities, including anti-apoptotic, antioxidant, anti-inflammatory, and immunosuppressive properties. In recent years, ACNs have shown remarkable potential in improving MSDs. This review article aims to recapitulate the therapeutic potential of ACNs and its mechanism of action in treating MSDs.Methods Extensive literature was searched and reviewed through online electronic databases (PubMed, Embase, and Web of Science), focusing on analysing the specific roles and molecular mechanisms of ACNs in in vivo and in vitro studies.Results ACNs exert protective effects on MSDs by targeting multiple key signaling pathways, including mitogen-activated protein kinase (MAPK), nuclear factor-kappaB (NF-kappa B), Wingless-related integration site (Wnt)/beta-catenin, phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt), adenosyl monophosphate-dependent protein kinase (AMPK), receptor activator of nuclear factor-kappa Beta/receptor activator of nuclear factor-kappaB ligand/osteoprotegerin (RANK/RANKL/OPG) and oxidative stress signaling. In addition, ACNs exhibited anti-inflammatory, anti-apoptotic, and immunosuppressive properties. This article reviews the mechanisms and potential therapeutic applications of ACNs in the prevention and alleviation of MSDs, providing valuable reference points for further research and development of ACNs.Conclusion ACNs improve the prevention of MSDs through multiple actions such as antioxidant, anti-inflammatory, immunomodulatory and bone metabolism homeostasis regulation. However, results from in vitro and in vivo studies still need to be further validated by human clinical trials.
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TI Anti-Osteoporosis Treatment Alleviates Osteoarthritis Symptoms and Partially Reverses Disease Progression
SO ORTHOPAEDIC SURGERY
LA English
DT Article
DE alendronate; bone remodeling; cartilage; osteoarthritis; osteoporosis
ID subchondral bone; knee osteoarthritis; articular-cartilage; risedronate; markers
AB ObjectiveOsteoarthritis (OA) and osteoporosis (OP) are highly prevalent in postmenopausal women; however, their relationship remains complex and controversial. This study aimed to investigate whether anti-OP treatment alleviates osteoarthritis symptoms and reverses disease progression.MethodsThis prospective clinical study enrolled 30 postmenopausal women diagnosed with OP and concomitant knee OA who visited our outpatient clinic between January and June 2023. Patients received anti-osteoporotic treatment comprising calcium carbonate, vitamin D3, and alendronate (ALN). BMD, WOMAC, and VAS scores were assessed at 6 and 12 months. In animal studies, OP was induced in rats by ovariectomy, followed by OA induction via anterior cruciate ligament sectioning and meniscectomy. ALN treatment was administered for 8 weeks, and evaluations of behavior, macroscopic appearance, pathology, and subchondral bone microstructure were performed 8 weeks after OA induction. One-way ANOVA was used for multiple group comparisons, and Spearman's rank correlation was used to assess associations.ResultsClinical outcomes demonstrated that one-year anti-OP therapy achieved dual therapeutic benefits: a 9.3% increase in bone mineral density (BMD) was accompanied by a 36.54% reduction in knee OA symptoms. Statistical analysis revealed a strong positive correlation between BMD improvement and symptomatic relief ($r = 0.76$, $p < 0.05$). In the animal model, OP markedly accelerated OA progression, leading to more severe cartilage damage, as confirmed by symptoms, macroscopic cartilage appearance, and histological

evaluations. Micro-CT analysis revealed abnormal subchondral bone microarchitecture in OP animals. Notably, ALN treatment partially reversed OA progression, as evidenced by reduced cartilage degeneration, improved subchondral bone microstructure, and enhanced bone remodeling.ConclusionAnti-OP treatment alleviates knee OA symptoms in OP patients. Postmenopausal OP accelerates OA progression, while anti-OP therapy can partially reverse this effect. These findings highlights the importance of anti-OP treatment in managing both conditions.
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J9 ORTHOP SURG
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PT J
AU Ripic, Z
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TI Knee joint mechanics during gait after anterior cruciate ligament reconstruction using a partial or full thickness quadriceps tendon autograft at 2 years after surgery
SO PM&R
LA English
DT Article
ID osteoarthritis; walking; strength; predictors; criteria; sports; injury; return
AB BackgroundDespite quadriceps weakness in individuals after quadriceps tendon anterior cruciate ligament reconstruction (QT-ACLR), and its association with knee joint mechanics, no studies have addressed gait mechanics in both partial-thickness

(PT-Q) and full-thickness (FT-Q) options for QT-ACLR.ObjectiveTo assess gait mechanics across a QT-ACLR cohort. We hypothesized that QT-ACLR would show changes in knee joint mechanics compared to control participants (CON) and nonoperated limbs. Additionally, we hypothesized that FT-Q operated limbs would show greater changes compared to PT-Q and CON.DesignRetrospective cohort study.SettingUniversity-affiliated sports medicine institute.ParticipantsSixteen patients who underwent QT-ACLR (7 FT-Q: Age (years) = 28.6 +/- 7.3, post-op (months) = 23.5 +/- 10.7, 9 PT-Q: Age = 25.2 +/- 4.3, post-op = 24.4 +/- 11.7) were recruited and compared to 11 CON (age = 23.4 +/- 4.8).InterventionParticipants underwent gait testing with force plate integrated motion capture.Main Outcome MeasuresMixed repeated-measures analyses of covariance, adjusted for gait speed, were used to determine significant main effects or interactions in peak knee flexion angle, sagittal knee range of motion, peak internal knee extension moment (KEM), and peak internal knee flexion moment.ResultsWhen measured an average of 2 years after surgery, no main effect for limb or limb by depth interaction were detected. A significant effect by group was observed for peak KEM (p = .03, eta 2 = .27) and peak knee flexion angle (p = .04, eta 2 = .24) in the loading response phase. FT-Q (p = .02) and PT-Q (p = .03) showed lower KEM compared to the CON group in both limbs. The FT-Q group showed lower peak knee flexion angle compared to the CON group (p = .01).ConclusionsKnee joint symmetry may be recovered 2 years following QT-ACLR, but lower KEM compared to CON for both graft options and lower peak knee flexion angle than CON for the FT-Q group may indicate a need for further investigation in QT-ACLR.
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Z9 3
U1 0
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WC Rehabilitation; Sport Sciences
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TI Diurnal aging of biomass burning emissions: impacts on secondary organic aerosol formation and oxidative potential
SO ATMOSPHERIC CHEMISTRY AND PHYSICS
LA English
DT Article
ID residential wood combustion; oxygen species ros; particulate-matter; mass-spectrometry; nighttime chemistry; wide variety; urban areas; fuels; particles; photooxidation
AB Residential biomass burning is an important wintertime source of aerosols. These particles are subjected to complex diurnal aging processes in the atmosphere, contributing to urban and regional air pollution. The cumulative impact of these aging cycles on aerosol composition and oxidative potential, a key toxicity metric, remains unclear. This study examined the oxidation cycles of biomass burning emissions during day-to-night and night-to-day transitions in the FORTH (Foundation for Research and Technology - Hellas) atmospheric simulation chamber, focusing on emissions from burning of olive wood. The final high-resolution AMS spectra of biomass burning organic aerosol (bbOA) after either oxidation cycle were almost identical (R-2 > 0.99, theta= 3 degrees). This indicates transformation into similar biomass burning secondary organic aerosol (bbSOA) regardless of the initial step of the diurnal cycle. A 56 % average increase in the bbOA oxygen-to-carbon (O:C) ratio was observed during both cycle cases (from 0.38 +/- 0.06 for the fresh to 0.59 +/- 0.07 after aging). Additional OA mass was produced after the two cycles, varying from 35 % to 90 % of the initial OA. The aging of the emissions led to a final water-soluble oxidative potential (WS-OP) increase of 60 % to 68 +/- 18 pmol min(-1) mu g(-1) for both cycles, but with notably different transient values that depend on the order of the oxidation regimes. The effect of each oxidation regime on the WS-OP of the bbOA depends on the airmass history. The evolution of the WS-OP was not well correlated with that of the O:C.
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NR 91
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U1 9
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PU COPERNICUS GESELLSCHAFT MBH
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J9 ATMOS CHEM PHYS
JI Atmos. Chem. Phys.
PD NOV 18
PY 2025
VL 25
IS 22
BP 15835
EP 15855
DI 10.5194/acp-25-15835-2025
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WC Environmental Sciences; Meteorology & Atmospheric Sciences
SC Environmental Sciences & Ecology; Meteorology & Atmospheric Sciences
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AF Zhang, Jing
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Xu, Gang
TI The impact of uric acid on musculoskeletal diseases: clinical associations and underlying mechanisms
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE uric acid; musculoskeletal diseases; sarcopenia; osteoarthritis; intervertebral disc degeneration; gout; osteoporosis
ID skeletal-muscle; knee osteoarthritis; oxidative stress; mitochondrial dysfunction; xanthine-oxidase; blood-pressure; gout; hyperuricemia; risk; insulin
AB Serum urate (SU) levels are significantly elevated in conditions such as gout, type 2 diabetes (T2D), obesity, and other metabolic syndromes. Recently, due to the high prevalence of hyperuricemia (HUA), numerous clinical connections between SU and musculoskeletal disorders like sarcopenia, osteoarthritis (OA), rheumatoid arthritis (RA), intervertebral disc degeneration (IDD), and osteoporosis (OP) have been identified. This review discusses the mechanisms linking SU to musculoskeletal disorders, as well as the clinical associations of SU with conditions such as sarcopenia, T2D with sarcopenia, McArdle disease, heart failure, gout, OA, IDD, OP and exercise-induced acute kidney injury (EIAKI), offering valuable insights for improved prevention and treatment strategies. Mechanisms linking SU to musculoskeletal disorders include oxidative stress, MSU (monosodium urate) crystal deposition, inflammation, and other factors. In adults, both age and SU levels should be considered for preventing sarcopenia, while gender and SU may directly impact muscle mass in children and adolescents. HUA and gout may be risk factors for OA progression, although some reports suggest otherwise. A U-shaped relationship between SU and IDD has been reported, particularly in Chinese men, indicating lower or higher SU level may be risk factors for IDD. Maintaining SU levels within a certain range may help prevent OP and fractures. Future research, including epidemiological studies and new pathogenesis findings, will further clarify the relationship between musculoskeletal diseases and SU.
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TI Current Applications and Development of Radiomics in Osteoporosis: A Narrative Review

SO APPLIED SCIENCES-BASEL
LA English
DT Review
DE osteoporosis; radiomics; bone strength assessment; diagnosis; fracture risk prediction
ID machine learning analysis; texture analysis; trabecular bone; computed-tomography; plain radiograph; proximal femur; fracture load; prediction; diagnosis; strength
AB Osteoporosis is a prevalent disease among the elderly, with fractures being one of the most serious consequences. Early diagnosis and accurate assessment of fracture risk could help prevent fractures. Radiomics employs advanced image analysis techniques for the development of diagnostic tools, thereby improving the accuracy of disease diagnosis and treatment strategies. Specifically, in the application of bone diseases, radiomics has proven effective in the diagnosis and prognostic evaluation of osteoporosis, osteoarthritis, and bone tumors. Radiomics allowed for quantitative characterization of bone geometry, material distribution, and microstructure, making it applicable to osteoporosis as well. In this review, an overview was provided regarding the current progress of radiomics based on clinical bone imaging in osteoporosis, including bone strength assessment, osteoporosis diagnosis, and fracture risk prediction. Additionally, the potential and challenges for their clinical application were summarized.
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TI A ZnCl2-based pH-responsive low-melting mixture solvent for extracting psoralen from Ficus carica L. leaves: Insights from experimental and mechanism investigation
SO CHEMICAL ENGINEERING RESEARCH & DESIGN
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DT Article
DE Low-melting mixture solvent; Metal salt; Sustainability; Extraction mechanism; Psoralen
ID purification; biomass; bond
AB Ficus carica L. is one of the most ancient fruit crops which is being cultivated in sub-tropical regions worldwide. Ficus carica L. leaves, which are considered

agricultural by-products, are frequently discarded, leading to the wastage of biological resources. However, Ficus carica L. leaves are valuable source of psoralen (PSO) that displays multiple bioactive properties beneficial for the treatment of osteoporosis, viruses, bacteria, and inflammation. Therefore, enhancing the efficient isolation of PSO from Ficus carica L. leaves using sustainable solvents has been a focus. In this study, a switchable ZnCl2-based pH-responsive low-melting mixture solvent (LoMMSZnCl2) for sustainable extraction of PSO from Ficus carica L. leaves was developed. The LoMMS-ZnCl2 system, consisting of ZnCl2, DL-menthol, and octanoic acid (OA), demonstrates exceptional performance with an extraction yield of 30.68 mg & sdot;g- 1 for PSO. After removing ZnCl2 from the LoMMS-ZnCl2 system using reverse extraction, the polarity of LoMMS was changed rapidly by pH stimulus, resulting in in-situ separation and enrichment of PSO. The extraction mechanism was further investigated by DFT simulation and nuclear magnetic resonance analysis, revealing that hydrogen bonding, halogen bonding, coordination bonding, and Van der Waals forces are the primary intermolecular interactions between LoMMS-ZnCl2 and PSO. This strategy highlights the potential of LoMMS-ZnCl2 for efficient and sustainable extraction of PSO from Ficus carica L. leaves. Furthermore, it also offers a valuable reference for utilizing LoMMS-ZnCl2 in the extraction of natural bioactive compounds from various plant materials.
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TI Urinary 4-pyridoxic acid as a non-invasive biomarker for evaluating osteoarthritis severity: findings from the ROAD study
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Article
DE 4-pyridoxic acid; Knee osteoarthritis; Lumbar spondylosis; Population-based cohort ROAD; Predictive biomarker
ID plasma; vitamin-b-6; pyridoxal
AB Background The early detection of osteoarthritis (OA) requires reliable biomarkers; however, reports identifying such biomarkers remain limited. Aims This study aimed to evaluate the potential of urinary 4-pyridoxic acid (4PA) as a biomarker for the severity of knee osteoarthritis (KOA) and lumbar spondylosis (LS) in Japanese adults, using data from the population-based cohort study. Methods Data were analysed from 1566 participants (510 men and 1,056 women) aged >= 40 years, who were enrolled in the Research on Osteoarthritis/Osteoporosis against Disability (ROAD) cohort, a population-based study initiated in 2005. Participants underwent radiographic assessments of the knees and lumbar spine, and urinary

4PA levels were measured using high-performance liquid chromatography. Logistic regression analyses were performed to evaluate the association between urinary 4PA levels and the Kellgren-Lawrence (KL) grade of KOA and LS, adjusting for age, sex, body mass index (BMI), and lifestyle factors. Results Urinary 4PA levels were significantly higher in participants with KL grade 4 KOA compared to those with lower KL grades ($p < 0.001$). This association remained significant after adjusting for confounding factors. In contrast, no significant differences in 4PA levels were observed across the KL grades for LS, although a slight increase in 4PA levels was noted in KL grade 4 cases. Discussion and conclusions These findings suggest that urinary 4PA could serve as a biomarker for assessing KOA severity, particularly in advanced stages. While the detection of early OA using 4PA remains challenging, the significant increase in KL grade 4 cases highlights its potential role in guiding treatment decisions, such as surgical intervention.
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NR 23
TC 0
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AF Chen, Tian-Xin
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TI High prevalence and multifactorial risks of sarcopenia in knee osteoarthritis: a systematic review and meta-analysis
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
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DT Review
DE Knee osteoarthritis; Sarcopenia; Prevalence; Risk factors; Meta-analysis
ID smoking; obesity; classification; hip
AB ObjectiveThis study aimed to evaluate the prevalence and risk factors of sarcopenia in patients with knee osteoarthritis (KOA) through a systematic review and meta-analysis.MethodsA comprehensive search was conducted in PubMed, Web of Science, Cochrane Library, Scopus, China National Knowledge Infrastructure, and WanFang databases for studies published between January 2000 and June 2025. Eligible studies were screened according to predefined inclusion and exclusion criteria. Data were extracted, study quality was assessed, and meta-analyses were performed using Stata 17.0.ResultsA total of 35 studies involving 13,528 KOA patients were included, of whom 3597 were diagnosed with sarcopenia. The pooled prevalence of sarcopenia and sarcopenic obesity was 25.07% (95% CI 18.85-31.29%) and 12.06% (95% CI 8.24-15.87%), respectively. Subgroup analyses revealed that sarcopenia prevalence increased with disease severity, reaching 26.01% (95% CI 16.27-35.75%) in patients with Kellgren-Lawrence grade 4 KOA. Prevalence was 25.65% (95% CI 20.30-31.00%) among female and 25.85% (95% CI 18.64-33.06%) among Asian populations. Among patients with osteoporosis and diabetes mellitus, prevalence rates were 21.68% (95% CI 8.84-34.53%) and 28.36% (95% CI 17.43-39.29%), respectively. Additionally, sarcopenia was more common among alcohol consumers (30.72%, 95% CI 15.58-45.86%) and smokers (29.82%, 95% CI 18.87-40.77%), with the prevalence being notably higher at 35.20% (95% CI 28.09-42.31%) among patients with irregular physical activity.ConclusionSarcopenia and sarcopenic obesity are highly prevalent in patients with KOA and are significantly associated with disease severity, gender, geographic region, comorbidities, and lifestyle factors. These findings highlight the clinical importance of assessing sarcopenia in KOA management. Early screening and timely interventions may improve patient outcomes and quality of life.
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NR 93
TC 0
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JI J. Orthop. Surg. Res.
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PT J
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Arora, Rohit
Pallua, Johannes Dominikus
TI Advancements in High-Resolution Computed Tomography: Revolutionising Bone Health Micro-Research

SO BIOENGINEERING-BASEL
LA English
DT Article
DE bone health; micro-computed tomography; high-resolution peripheral quantitative computed tomography; finite element analysis; machine learning
AB Bone disorders such as osteoporosis, osteopenia, and osteoarthritis affect millions worldwide, creating an urgent need for earlier and more accurate assessment of bone health. High-resolution imaging has transformed this field: micro-computed tomography remains the research gold standard for ex vivo and preclinical studies, while high-resolution peripheral quantitative computed tomography enables in vivo clinical assessment of trabecular and cortical bone microarchitecture. Combined with finite element analysis and machine learning, these modalities enable biomechanical modelling, predictive risk stratification, and progress toward personalised treatment. Remaining challenges include cost, limited availability, motion artefacts, and lack of standardisation. This review summarises current advances in imaging and computational methods, highlights their respective strengths and limitations, and outlines future directions required to translate these technologies into routine clinical practice.
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TI ZBTB16 exerts anti-angiogenic effects in rheumatoid arthritis by regulating HIF-1 α pathway
SO ALLERGOLOGIA ET IMMUNOPATHOLOGIA
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DT Article
DE GRK2/HIF-1 alpha pathway; rheumatoid arthritis; ZBTB16
ID differentiation
AB Background: Rheumatoid arthritis (RA) is one complex chronic autoimmune disease, resulting body pain and badly affect the health of RA patients. Zinc finger and BTB domain containing 16 (ZBTB16) has been reported to participate into many diseases including osteoarthritis and osteoporosis. Objective: To verify the regulatory functions of ZBTB16 in RA progression keep dimness. Methods: The mRNA expressions were tested through RT-qPCR. The protein expressions were evaluated through western blot. The pathological changes of synovial tissues were determined through HE staining. The erosion and destruction of bone tissues were examined through safranin-O/fast green staining. The levels of TNF-alpha, IL-1 beta, IL-6 and MMP-3 were testified through ELISA. The fluorescence intensity of proteins was assessed through IF assay. Results: Firstly, it was uncovered that ZBTB16 expression was markedly reduced in the synovium tissues of RA patients through analyzing GSE55235 expression profile by GEO2R online tool. Next, ZBTB16 expression was down-regulated in synovial tissues of RA patients. Moreover, ZBTB16 can alleviate the degree of paw swelling in CIA mice. ZBTB16 improved the pathological changes of synovial tissues in CIA mice. The levels of inflammatory factors and matrix metalloproteinase were increased in CIA mice, but these impacts were reversed after ZBTB16 amplification. ZBTB16 can relieve pannus in CIA mice. Besides, the triggered GRK2/ HIF-1 alpha pathway in CIA mice can be retarded after ZBTB16 overexpression. Conclusion: ZBTB16 exerted anti-angiogenic effects in RA by blocking GRK2/HIF-1 alpha pathway. This work hinted that ZBTB16 may be one useful target for RA treatment. (c) 2025 Codon Publications. Published by Codon Publications.

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TI The Association Between Serum Ergothioneine Concentration and Japanese Dietary Habits: The Third Survey of the ROAD Study
SO NUTRIENTS
LA English
DT Article
DE ergothioneine; ROAD study; dietary habit; fish
ID 3-year follow-up; lower back-pain; knee osteoarthritis; risk-factors; lumbar spondylosis; men; women; biosynthesis; accumulation; history
AB Background/Objectives: As a result of aging societies, the increasing number of older adults requiring nursing care has become a serious issue and the extension of healthy life expectancy has become an urgent priority. Ergothioneine (EGT) is a sulfur-containing amino acid found in foods such as mushrooms. Low EGT blood concentrations have been reported to be associated with the risk of onset and progression of various diseases. However, the distribution of EGT blood concentrations and their association with dietary habits in the Japanese general population remains unclear. Methods: This cross-sectional study was conducted using data from the third survey of the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study, which analyzed 1457 participants (474 men and 983 women) aged >= 40 years. Serum EGT concentrations and their association with dietary habits were analyzed. Results: Serum EGT concentrations (1) peaked in the 70s in men and the 60s in women, (2) were higher in women than in men, and (3) showed a significant positive correlation with fish intake and nutrients

commonly found in fish. Conclusions: In the present study, we report for the first time an age- and sex-specific serum EGT distribution in a Japanese population and its association with dietary habits, particularly fish intake. These findings help define normal and abnormal EGT levels and suggest new potential sources of EGT.
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AF Barylak, Martin
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Queen, Robin M.
TI Gait stability improves following unilateral total ankle arthroplasty
SO JOURNAL OF ORTHOPAEDIC RESEARCH
LA English
DT Article

DE gait; gait stability; margin of stability (MoS); total ankle arthroplasty
ID clinical-outcm; dynamic stability; walking; falls; osteoarthritis; arthrodesis; balance; margin; performance; arthritis
AB End-stage ankle arthritis is often treated surgically by total ankle arthroplasty (TAA) due to its potential to improve gait through increased joint range of motion and reduce pain. However, TAA's effect on gait stability is not well understood. This study explores the impact of TAA on gait stability, measured by Margin of Stability (MoS), in 148 patients with end-stage ankle arthritis. Kinematic data were collected pre-operatively, at 1-year post-op, and at 2-years post-op and the MoS was determined at heel strike and midstance for the anteroposterior (MoSAP) and mediolateral (MoSML) directions. A linear mixed effects model including gait speed as a factor was used to assess the effects of limb, session, and their interaction on outcome measures. A significant interaction ($p < 0.002$) between limb (surgical, nonsurgical) and session (pre-op, 1-year post-op, 2-years post-op) was identified for each MoS variable of interest. Cumulatively, our results suggest that the nonsurgical limb, MoSAP at heel strike and MoSML at midstance improved (increased) as time from surgery increased. These results suggest patients developed a compensatory movement pattern to navigate surgical limb single support. TAA reduces this compensation improving side-to-side symmetry, while not fully restoring symmetry by 2-years post-op. These results indicate that TAA could improve gait stability in patients with end-stage ankle arthritis, but further work is needed to understand the impact of TAA on altering fall risk.
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TC 2
Z9 2
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TI DNA-Based Hydrogels for Musculoskeletal Reconstruction: Harnessing Dynamic Programmability and Multimodal Therapeutic Integration
SO ADVANCED SCIENCE
LA English
DT Review
DE DNA-based hydrogel; dynamic crosslinking; musculoskeletal regeneration; therapeutic delivery; tissue engineering
ID mesenchymal stem-cells; articular-cartilage; plasmid dna; osteogenic differentiation; induced osteoporosis; muscle injury; nucleic-acids; bone; tissue; delivery
AB Musculoskeletal disorders, including bone fractures, osteoarthritis, and muscle injuries, represent a leading cause of global disability, revealing the urgency for advanced therapeutic solutions. However, current therapies face limitations including donor-site morbidity, immune rejection, and inadequate mimicry of dynamic tissue repair processes. DNA-based hydrogels emerge as transformative platforms for musculoskeletal reconstruction, with their sequence programmability, dynamic adaptability, and biocompatibility to balance structural support and biological functions. These hydrogels are classified into two categories: 1) DNA hydrogels, where DNA serves as the structural backbone; 2) DNA component-loaded hydrogels, integrating functional DNA elements like aptamers and therapeutic genes into non-DNA matrices. Through dynamic crosslinking strategies, primarily Watson-Crick base pairing, DNA networks achieve shear-thinning injectability and self-healing behaviors while providing binding sites for bioactive DNA components. Hybrid systems further enhance functionality by incorporating diverse materials to improve mechanical strength, drug delivery, and cellular guidance. This review systematically examines molecular design principles, classification frameworks, and preclinical applications of DNA-based hydrogels, aiming to bridge gaps between material innovation and clinical translation. Finally, current challenges are highlighted, and future directions to advance these intelligent biomaterials toward next-generation musculoskeletal therapies are proposed.
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TI Research progress of circRNAs in bone-related diseases
SO FRONTIERS IN ONCOLOGY
LA English
DT Review
DE circRNAs; non-coding RNAs; orthopedic diseases; therapeutic target; biomarker
ID circular rna; stem-cells; osteogenic differentiation; osteoclast differentiation; doxorubicin resistance; osteosarcoma cells; expression; osteoporosis; contributes; promotes
AB Circular RNAs (circRNAs) are non-coding RNAs that exist naturally in various eukaryotic organisms. The majority of circRNAs are produced through the splicing of exons, although there are a limited number that are generated through the circularization of introns. Studies have shown that circRNAs play an irreplaceable role in the pathogenesis, disease progression, diagnosis, and targeted therapy of motor system tumors (osteosarcoma), metabolic diseases (osteoporosis), and degenerative diseases (osteonecrosis of the femoral head, osteoarthritis,

intervertebral disc degeneration). This review summarizes the advancements in circRNA detection techniques and the research progress of circRNAs in orthopedic diseases.
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TI Development and validation of the BPDKC model for predicting sarcopenic knee osteoarthritis in community-dwelling older adults: a cross-sectional study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
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ID guidelines; management
AB Background Sarcopenia and knee osteoarthritis frequently coexist as sarcopenic knee osteoarthritis (SPKOA), a clinically significant and burdensome condition among older adults. Despite its high prevalence and functional impact, no validated, practical tool exists for early identification of SPKOA in community settings. This study aimed to develop and internally validate a parsimonious, clinically applicable prediction model for SPKOA risk stratification in community-dwelling older adults. Methods We conducted a cross-sectional

analysis of 640 community-dwelling adults aged 65-85 years, recruited between March and October 2024 from the Yuyuan Community Health Service Center in Shanghai, China (median age: 71 years; 57% female). SPKOA was diagnosed using established criteria for both sarcopenia and knee osteoarthritis. Participants were randomly split (7:3) into training (n = 448) and internal test (n = 192) sets. In the training set, we employed a hybrid variable selection strategy: age, gender, BMI, physical activity (PA), diabetes mellitus (DM), Knee Visual Analog Scale(KVAS), and calf circumference (CC) were prespecified based on clinical relevance; remaining candidate variables underwent univariate screening ($P < 0.05$), followed by forward stepwise logistic regression (entry: $P < 0.05$; removal: $P > 0.10$). Three candidate models were derived and compared: Model 1 (7 predictors: CC, KVAS, BMI, DM, PA, osteoporosis, age); Model 2 - the BPDKC model (5 predictors: BMI, PA, DM, KVAS, CC); and Model 3 (5 predictors: DM, PA, KVAS, CC, age). Model performance was evaluated using discrimination (AUC with 95% CI), calibration (Brier score, calibration plots), clinical utility (decision curve analysis). The optimal model was translated into a nomogram and an interactive web-based calculator. Results Among 640 participants, 12.5% (n = 80) met SPKOA criteria, with balanced prevalence across training (12.5%, n = 56) and test sets (12.5%, n = 24). In the training set, all models showed strong discrimination (Model 1 AUC = 0.953; Model 2 AUC = 0.951; Model 3 AUC = 0.934) and excellent calibration (Brier scores: 0.053-0.062). However, in the internal test set, Model 2 (BPDKC) demonstrated the best generalizability and balance of performance: AUC = 0.861 (95% CI: 0.795-0.926), specificity = 94.6% (95% CI: 90.1-97.5%), precision = 50.0% (95% CI: 26.0-74.0%), F1-score = 0.429 (95% CI: 0.243-0.618), and Brier score = 0.1038 (95% CI: 0.068-0.139). Although sensitivity remained modest (37.5%, 95% CI: 18.8-59.4%), calibration curves and decision curve analysis confirmed robust risk estimation and superior net clinical benefit across clinically relevant risk thresholds (10-40%). Model 2 also achieved the best trade-off between performance and parsimony (AIC = 178.41 vs. Model 3 AIC = 194.79). A user-friendly web calculator implementing the BPDKC model is freely accessible at (https://lgmyyyy.shinyapps.io/bpdkc_spkoa_app/) . Conclusion The BPDKC model is a simple, internally validated, and clinically practical tool for SPKOA risk prediction in community-dwelling older adults. Its high specificity and calibration support its utility in ruling out low-risk individuals, while its web-based implementation facilitates integration into primary care workflows. Although sensitivity remains limited-reflecting the challenge of case-finding in low-prevalence settings-the model offers meaningful clinical value for targeted screening and early intervention. External validation in diverse populations is recommended prior to broader implementation.

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TI Weaker subchondral bone and thinner articular cartilage of the knee are associated with elevated baseline fracture risk independently of osteoarthritis risk factors
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Fracture risk; FRAX; Knee osteoarthritis; MRI; Bone marrow lesion; Cartilage morphometry; Subchondral bone structure; BMD
ID mineral density; osteoporosis; prediction; frax; prevalence; parameters; falls; pain
AB Objectives To examine how well fracture risk predicts subchondral bone and cartilage morphometry independently of osteoarthritis (OA) clinical risk factors. Methods Male and female participants in the Osteoarthritis Initiative (OAI) at visit 5 (36 months) were evaluated for fracture risk using FRAX and categorized into low-, moderate-, or high-risk groups. These groups were compared for bone marrow lesion (BML) size, number and effusion, subchondral bone structure, density, and cartilage morphometry in the most affected knee at either same time point, 1 or 2 years later, using general linear models. Sex interactions were examined in each

case and probed if significant. Results Among 1240 participants (58.8% female, age: 63.7 +/- 8.8 years, and BMI: 30.1 +/- 4.9 kg/m(2)), 20.32% had moderate or high FRAX and showed lower subchondral bone density (- 0.12 to - 0.25 g/cm(2)), less intact trabeculae, and thinner cartilage (- 0.14 to - 0.47 mm) compared to low FRAX ($p < 0.05$). Males showed larger positive FRAX correlations with bone density, and females had protective effects of FRAX against BML numbers, although the effects were small (sex interaction, $p < 0.05$). All FRAX models adjusting for OA risk factors yielded better model fit than OA risk factors alone. Having moderate/high versus low FRAX at baseline predicted a 1.36 (1.00, 1.86)-fold higher odds of reaching a Kellgren-Lawrence score of 3 or 4 within a year. Conclusions High FRAX predicts thinner cartilage and weaker subchondral bone within a year. Complementing standard OA clinical risk factors with FRAX calculation could help identify individuals likely to develop worse knee OA radiologic outcomes.
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TI The Role of the Immune Microenvironment on Osteoblast Differentiation
SO IMMUNOLOGICAL INVESTIGATIONS
LA English
DT Review
DE Immune microenvironment; osteoblast differentiation; cytokine; immune cell; osteoimmunology
ID mesenchymal stem-cells; regulatory t-cells; tgf-beta; bone-formation; rheumatoid-arthritis; knee osteoarthritis; in-vitro; growth; osteogenesis; expression
AB Background: Osteoblasts, derived from mesenchymal stem cells (MSCs) in the bone marrow, are responsible for bone formation. Osteoblast differentiation is orchestrated by a spectrum of biological signals, with immune-derived components serving as indispensable regulators in this network. Dysfunctional osteoblast differentiation underlies bone-related pathologies such as osteoarthritis, rheumatoid arthritis, and osteoporosis, where immune dysregulation drives inflammatory cascades that disrupt the osteoblast-osteoclast equilibrium. This bidirectional crosstalk has propelled the emergence of osteoimmunology as a pivotal discipline.Methods: By analyzing immune cells and cytokines in the immune microenvironment, we synthesize evidence on their roles in regulating osteoblast differentiation, with focus on inflammatory bone disorders, particularly in

osteoarthritis.Results: Thus, bone growth, development, and healing are intrinsically coupled with the dynamics of the immune microenvironment, which contributes to subchondral bone sclerosis and disease progression in osteoarthritis. Therefore, targeting immune-osteoblast crosstalk offers therapeutic potential for bone pathologies.Conclusion: This review consolidates recent advances in understanding how the immune microenvironment impacts osteoblast differentiation, aiming to provide novel insights for clinical strategies targeting bone repair and disease mitigation.
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TI Intermuscular adipose tissue and lean muscle mass assessed with MRI in people with chronic back pain in Germany: a retrospective observational study
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ID health; force; time
AB Background Chronic back pain (CBP) affects over 80 million people in Europe, contributing to substantial healthcare costs and disability. Understanding modifiable risk factors, such as muscle composition, may aid in prevention and treatment. This study investigates the association between lean muscle mass (LMM) and intermuscular adipose tissue (InterMAT) with CBP using noninvasive whole-body magnetic resonance imaging (MRI). Methods This cross-sectional analysis used whole-body MRI data from 30,868 participants in the German National Cohort (NAKO), collected between 1 May 2014 and 1 September 2019. CBP was defined as back pain persisting >3 months. LMM and InterMAT were quantified via MRI-based muscle segmentations using a validated deep learning

model. Associations were analyzed using mixed logistic regression, adjusting for age, sex, diabetes, dyslipidemia, osteoporosis, osteoarthritis, physical activity, and study site. Findings Among 27,518 participants (n = 12,193/44.3% female, n = 14,605/55.7% male; median age 49 years IQR 41; 57), 21.8% (n = 6003; n = 2999/50.0% female, n = 3004/50% male; median age 53 years IQR 46; 60) reported CBP, compared to 78.2% (n = 21,515; n = 9194/42.7% female, n = 12,321/57.3% male; median age 48 years IQR 39; 56) who did not. CBP prevalence was highest in those with low (<500 MET min/week) or high (>5000 MET min/week) self-reported physical activity levels (24.6% (n = 10,892) and 22.0% (n = 3800), respectively) compared to moderate (500-5000 MET min/week) levels (19.4% (n = 12,826); p < 0.0001). Adjusted analyses revealed that a higher InterMAT (OR 1.22 per 2-unit Z-score; 95% CI 1.13-1.30; p < 0.0001) was associated with an increased likelihood of chronic back pain (CBP), whereas higher lean muscle mass (LMM) (OR 0.87 per 2-unit Z-score; 95% CI 0.79-0.95; p = 0.003) was associated with a reduced likelihood of CBP. Stratified analyses confirmed these associations persisted in individuals with osteoarthritis (OA-CBP LMM: 22.9 cm3/kg/m; InterMAT: 7.53% vs OA-No CBP LMM: 24.3 cm3/kg/m; InterMAT: 6.96% both p < 0.0001) and osteoporosis (OP-CBP LMM: 20.9 cm3/ kg/m; InterMAT: 8.43% vs OP-No CBP LMM: 21.3 cm3/kg/m; InterMAT: 7.9% p = 0.16 and p = 0.0019). Higher pain intensity (Pain Intensity Numerical Rating Scale >= 4) correlated with lower LMM (2-unit Z-score deviation = OR, 0.63; 95% CI, 0.57-0.70; p < 0.0001) and higher InterMAT (2-unit Z-score deviation = OR, 1.22; 95% CI, 1.13-1.30; p < 0.0001), independent of physical activity, osteoporosis and osteoarthritis. Interpretation This large, population-based study highlights the associations of InterMAT and LMM with CBP. Given the limitations of the cross-sectional design, our findings can be seen as an impetus for further causal investigations within a broader, multidisciplinary framework to guide future research toward improved prevention and treatment.
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NR 52
TC 2
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PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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WC Health Care Sciences & Services; Public, Environmental & Occupational Health
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AU Zhu, XY
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AF Zhu, Xiuyuan
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TI The causal role of homocysteine in multiple diseases: a systematic review of

Mendelian randomization studies
SO NUTRITION & METABOLISM
LA English
DT Review
DE Homocysteine; Mendelian randomization; Nervous system diseases; Cardiovascular diseases; Musculoskeletal system diseases
ID oxidative stress; hyperhomocysteinemia; pathogenesis; risk
AB BackgroundHomocysteine (Hcy) has been implicated in the development of multiple diseases; however, its causal role remains unclear. Mendelian randomization (MR) studies provide a robust approach to assessing causality by minimizing confounding and reverse causation.ObjectiveThis study aimed to evaluate the causal role of Hcy in various diseases by synthesizing evidence from MR studies.MethodsWe performed a comprehensive literature search in PubMed, the Cochrane Library, Embase, and Web of Science for MR studies published up to May 30, 2024. Studies investigating the association between genetic predisposition to Hcy levels and specific diseases were included.ResultsFindings from 33 MR studies (covering 31 distinct primary outcomes) suggest that genetically elevated Hcy levels are associated with an increased risk of several health conditions, including: Five cardiovascular diseases: small vessel stroke, small artery occlusion stroke, stroke, subarachnoid hemorrhage, and ischemic stroke. Six musculoskeletal diseases: soft tissue disorders, osteoporosis with pathological fractures, hospital-diagnosed osteoarthritis (OA), overall OA, knee OA, and hip OA. One musculoskeletal biomarker: waist-to-hip ratio (WHR) adjusted for BMI. Two digestive system diseases: gastric cancer and non-alcoholic fatty liver disease. Three digestive biomarkers: alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). One urogenital system disease: chronic kidney disease. Two mental disorders: schizophrenia and bipolar disorder type I. One metabolic disorder: metabolic syndrome. Conversely, elevated Hcy levels are associated with a reduced risk of: One neurological disorder: multiple sclerosis. Two neurological biomarkers: gray matter volume and total brain volume. Five musculoskeletal biomarkers: heel bone mineral density (BMD), right/left grip strength, walking pace, and appendicular lean mass. One urogenital system biomarker: estimated glomerular filtration rate. Additionally, genetically reduced plasma Hcy levels correlated with higher forearm BMD.ConclusionThese findings provide significant evidence for the role of Hcy in disease causation and may contribute to the development of future preventive measures or therapeutic strategies.
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NR 57
TC 1
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PU BMC
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TI Analysis of Risk Factors for Lumbar Spondylolisthesis: A Logistic Regression Study
SO WORLD NEUROSURGERY
LA English
DT Article
DE Age; Body mass index; Facet joint osteoarthritis; Logistic regression; Lumbar spondylolisthesis
ID natural-history; prevalence
AB <black square> OBJECTIVE: Lumbar spondylolisthesis is the forward displacement of one vertebra over another, commonly occurring at the L4/5 or L5/S1 levels. The condition is influenced by various risk factors, including age, body

mass index (BMI), long-term physical labor, pelvic incidence (PI), and facet joint osteoarthritis. This study aims to identify the significant risk factors associated with lumbar spondylolisthesis through univariate and multivariate logistic regression analyses. <black square> METHODS: A retrospective analysis of 531 patients diagnosed with lumbar spondylolisthesis between September 2019 and September 2024 was conducted. Data were collected on age, BMI, PI, history of lumbar trauma, long-term physical labor, congenital pedicle dysplasia, osteoporosis, intervertebral disc degeneration, and facet joint osteoarthritis. Univariate logistic regression was used to screen for significant variables, followed by multivariate logistic regression to adjust for confounding factors. Receiver operating characteristic curve analysis was performed to assess the sensitivity of significant factors. <black square> RESULTS: Univariate analysis identified age, BMI, longterm physical labor, PI, and facet joint osteoarthritis as significant risk factors. Multivariate analysis confirmed that age (P = 0.035), BMI (P = 0.005), and facet joint osteoarthritis (P = 0.002) remained statistically significant. Interaction effect analysis did not reveal any significant interactions between variables. Receiver operating characteristic curve analysis showed that age, BMI, and facet joint osteoarthritis were key predictors of lumbar spondylolisthesis. CONCLUSIONS: Age, BMI, and facet joint osteoarthritis (Grade III or above) were observed as potential risk factors for lumbar spondylolisthesis, with facet joint osteoarthritis showing the highest odds ratio. These findings indicate that degenerative changes in the spine, particularly those involving the facet joints, may contribute significantly to the development of lumbar instability, although further research is needed to establish causal relationships.
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NR 16
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PI NEW YORK
PA STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA
SN 1878-8750
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J9 WORLD NEUROSURG
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AU Wang, YXJ
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AF Wang, Yi Xiang J.
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Kwok, Timothy C. Y.
TI Lower osteoporotic-like vertebral fractural deformity (OLVF) prevalence and severity among older Thais and Indonesians than among older Chinese
SO QUANTITATIVE IMAGING IN MEDICINE AND SURGERY
LA English
DT Article
DE Osteoporotic vertebral fracture; osteoporosis; Chinese; Thais; Indonesians
ID united-states; risk-factors; end-plate; hong-kong; men; women; osteoarthritis
AB Background: Chinese are known to have a lower vertebral fragility fracture risk than Caucasians. This study evaluates radiographic osteoporotic-like vertebral fractural deformity (OLVF) prevalence and severity among Chinese, Thai, Indonesian women and men. Methods: In an epidemiological study with community subjects, spine radiographs (T4-L5) were sampled for 195 Thai women (mean: 73.6 years), 202 Thai men (mean: 73.7 years), 236 Indonesian women (mean: 70.4 years), and 174 Indonesian men (mean: 70.2 years). Spine radiographs of age-matched subjects were also sampled for Chinese. OLVF classification included no OLVF (grade 0), and OLVFs with <20% (grade 0.5, minimal grade), >= 20-25% (grade 1, mild grade), >= 25%-1/3 (grade 1.5, moderate grade), >= 1/3-40% (grade 2, marked grade), >= 40%-2/3 (grade 2.5, severe grade), and >= 2/3 height loss (grade 3, collapsed grade). OLVF sum score (OLVFss) was calculated with each vertebra assigned a score of 0, -0.5, -1, -1.5, -2, -2.5, and -3 for no OLVF or OLVF grades 0.5-3. Osteoporosis prevalences were estimated based on OLVFss. For a woman, OLVFss <=-1.0 and OLVFss <=-1.5 were the thresholds to classify the case being osteoporotic according to the lowest T-score or femoral neck T-score respectively. For men, these thresholds were OLVFss <=-2.5 and OLVFss <=-3.0. Results: Compared with Southeast Asians, Chinese had overall higher prevalences of all-inclusive OLVF, apparent OLVF, and OLVF among Chinese were more likely to be multiple. A trend was noted that Chinese women were more likely to have severe and collapsed grades OLVFs than Southeast Asian women, while such a trend was not noted for Chinese men vs. Southeast Asian men comparison. For men, the Chinese vs. Southeast Asians difference was that Chinese had a higher prevalence of milder OLVFs. For the Thais vs. Indonesians comparison, OLVFss (mean +/- standard deviation) was -0.62 +/- 1.43 for Thai men, -0.47 +/- 0.98 for Indonesian men, -0.82 +/- 2.39 for Thai women, and -0.76 +/- 2.18 for Indonesian women. The lowest T-score based osteoporosis prevalence and femoral neck

T-score based osteoporosis prevalence was 9.4% and 6.9% respectively for Thai men, and 6.9% and 2.9% for respectively Indonesian men; 19.5% and 14.9% respectively for Thai women, 18.9% and 14.5% respectively for Indonesian women. Conclusions:<bold> </bold>The prevalence and severity of radiographic OLVF show a weak trend of 'Chinese > Thais > Indonesians', both for older women and for older men. The results of the current study support the notion that 'populations from a warmer climate have better spine health'.
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TI The Impact of Total Hip Arthroplasty on the Incidence of Hip Fractures in Romania
SO JOURNAL OF CLINICAL MEDICINE
LA English
DT Article
DE total hip arthroplasty; hip fracture; orthopedics surgery; osteoporosis; public health; epidemiology; implants
ID osteoarthritis; trends
AB Background/Objectives: The increase in life expectancy and the share of the elderly population has the effect of increasing the number of osteoporotic hip fractures. At the same time, the number of total hip arthroplasty (THA) interventions is continuously increasing. The objective of this study is to investigate the incidence rates of hip fractures during the period 2008-2019, in Romania, among people who are at least 40 years old, as well as to determine the extent to which the increase in the prevalence of people who have undergone THA has affected the incidence of hip fractures, given that the operated hip no longer presents a risk of fracture. Methods: We extracted the information, between 2008 and 2019, from nationwide retrospective studies about the incidence and time trend of hip fractures in Romania. Information on primary THA interventions during the period 2001-2019 was obtained from the Romanian Arthroplasty Register (RAR). We obtained the population size, by gender and age groups, from the reports of the National Institute of Statistics. For the period 2008-2019, we calculated the standardized annual hip fracture incidence rates by sex and by age. Given that each person has two hips at risk of fracture, we calculated hip fracture rates in a scenario without THA interventions. For this, we subtracted 0.5 people from the at-risk population for each prevalent hip prosthesis. Thus, we revealed the effects of decreasing fracture rates due to having hip prostheses. Results: From 2008 to 2019, age-standardized incidence rates of hip fractures increased by 10.8% in women, and by 2.8% in men. By excluding hips being replaced with prostheses in the at-risk population, we obtained higher hip fracture incidence rates. These recorded values were considerably higher for the elderly population. The variation in hip fracture rates during the observed period was 10.16% (9.76% in women and 11.68% in men) lower due to the increased prevalence of hip prostheses. Conclusions: Although the incidence of hip fractures has continued to rise, the growing number of people who have undergone THA and are living with hip prostheses has helped to blunt this increase.
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TI IL-34 as a Novel Mediator Linking Vitamin D Deficiency with Osteoporosis and Knee Osteoarthritis
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE body composition; fat mass; inflammation; cytokines; structural equation modeling
ID d supplementation; adipose-tissue; d metabolism; cross-talk; inflammation; association; expression; bone; interleukin-34; mechanism
AB Vitamin D deficiency (VDD) is a widespread human condition closely associated with musculoskeletal disorders, involving alterations in body composition and systemic inflammation. In this cross-sectional study, 1075 adults were classified into a VDD (n = 304) group and a VD sufficient (VDS) group (n = 771). Body composition measurements, including the fat mass-to-weight ratio (FM/WT), were assessed using bioelectrical impedance analysis. Plasma levels of IL-9, IL-34, and MCP-1 were also measured. Data on osteoporosis (OP) and knee osteoarthritis (KOA) were collected. Regression analyses indicated that FM/WT was independently associated with VDD, which in turn was linked to elevated IL-34 levels. Individuals with VDD had a significantly higher prevalence of OP and KOA compared with those with VDS. Structural equation modeling confirmed and quantified these associations, suggesting that FM/WT is a significant predictor of VDD status (beta = 0.305, 95% CI: 0.231-0.367). VDD is directly associated with elevated IL-34 levels (beta = 0.353, 95% CI: 0.308-0.398), while IL-34 levels, in turn, are a possible cause of KOA (beta = 0.573, 95% CI: 0.460-0.687) and OP (beta = 0.433, 95% CI: 0.329-0.536). Our data clearly demonstrate existence of a physiological-pathological continuum: obesity-VDD-IL-34 and both OP and KOA.
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TC 0
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U1 2
U2 2
PU MDPI
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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JI Int. J. Mol. Sci.
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WC Biochemistry & Molecular Biology; Chemistry, Multidisciplinary
SC Biochemistry & Molecular Biology; Chemistry
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TI Independent association between sarcopenic obesity and knee osteoarthritis: A cross-sectional study
SO JOURNAL OF SPORTS SCIENCES
LA English
DT Article
DE Muscle ultrasonography; older adults; osteoarthritis; sarcopenic obesity
ID older-adults; muscle mass; reliability; ultrasound; strength; validity
AB Although obesity is a known risk factor for knee osteoarthritis (OA), the impact of sarcopenic obesity (SO) on OA remains unclear. This study aimed to investigate the association between SO and knee OA in older adults. This cross-sectional study included 101 obese outpatients, of whom 61 (60.3%) had knee OA. SO was diagnosed using ESPEN/EASO criteria. OA presence was determined by two specialists based on bilateral standing knee radiographs and Kellgren-Lawrence (KL) grading (0-4). Joint cartilage was assessed via ultrasonography. Frailty was evaluated using the Clinical Frailty Scale. Osteoporosis (OP) was defined by bone mineral density measurements and confirmed fragility fractures. The study participants comprised 74 (73%) females and 27 (27%) males with a median age of 72.0 [8.0] years. The patients were divided into two groups: patients with OA (60.3%, n = 61) and those without OA (39.7%, n = 40). In regression analysis, the

presence of SO increased the risk of OA independent of age, sex, body mass index (BMI), frailty, and OP (OR = 5.82, 95% CI = 1.55-21.94 and p = 0.009). The study results highlight the independent role of SO in OA development, suggesting that body composition assessment should be integrated into OA risk evaluation.
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NR 65
TC 0
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JI J. Sports Sci.
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TI Prevalence and risk factors of musculoskeletal symptoms among treated coeliac disease patients
SO SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY
LA English
DT Article
DE Coeliac disease; adults; extraintestinal; musculoskeletal; gluten-free diet
ID extraintestinal manifestations; premenopausal women; arthritis; children; pattern; mass
AB Objective: Varying musculoskeletal symptoms, such as joint pain and myalgia, are recognized as possible extraintestinal complaints of coeliac disease (CeD), but little is known about the prevalence and risk factors of these symptoms. In this study the aim was to evaluate the prevalence of and factors associated with self-reported musculoskeletal symptoms among adult CeD patients on a gluten-free diet (GFD). Materials and methods: The presence of current musculoskeletal symptoms was studied in 614 CeD patients on a GFD and 539 of their non-CeD relatives by a systematic interview. The association between musculoskeletal symptoms and various patient-related factors was investigated using logistic regression. Results: CeD patients reported more often current musculoskeletal symptoms than controls (37.8% vs. 22.8%, $p < 0.001$). CeD was an independent risk factor for musculoskeletal symptoms even after adjusting for age, gender and previously diagnosed co-morbidities, including autoimmune thyroid disease, osteoarthritis and osteoporosis/osteopenia (odds ratio 1.95, 95% confidence interval 1.48-2.59). Factors associated with these symptoms were female sex, higher age at present, long duration of any CeD-related symptoms before diagnosis and presence of autoimmune thyroid diseases and osteoarthritis.

Conclusion: CeD is associated with musculoskeletal symptoms even on a strict GFD. Possible susceptibility to current musculoskeletal complaints should be kept in mind, especially among certain risk patients such as those with long diagnostic delay and osteoarthritis.
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NR 38
TC 0
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JI Scand. J. Gastroenterol.
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WC Gastroenterology & Hepatology
SC Gastroenterology & Hepatology
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PT J
AU Sharafi, M
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Mohsenpour, MA
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Keshavarzian, Omid
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Nekouei, Fatemeh
Farjam, Mojtaba
TI Investigating multimorbidity patterns and associated risk factors in the fasa

adults cohort study (FACS): A latent class analysis
SO PLOS ONE
LA English
DT Article
ID physical-activity; sleep duration; health-care; prevalence; mortality
AB Background Multimorbidity, defined as the co-occurrence of multiple health conditions, is a major global public health concern. This study aimed to identify latent classes of multimorbidity and associated risk factors in Iranian adults.Method This cross-sectional study analyzed baseline data from 10,131 adults who participated in the Fasa Adults Cohort Study (FACS) in southern Iran. Multimorbidity was defined as the presence of two or more of 11 chronic diseases, including hypertension, dyslipidemia, stroke, osteoarthritis, depression, type two diabetes mellitus, obesity, osteoporosis, cardiovascular disease, thyroid disease, and respiratory disease. Latent class analysis (LCA) was used for cluster participants, and multinomial logistic regression was conducted to investigate the association between age, sex, education level, socioeconomic status, daily sleep duration, physical activity, and multimorbidity.Result The prevalence of multimorbidity was 40.3%. Three latent classes were identified: healthy (66.8%), dyslipidemia (14.1%), and cardio-metabolic conditions (19.1%). Older age increased the odds of belonging to dyslipidemia (odds ratio (OR) = 1.04 [95% confidence interval (CI): 1.03-1.05]) and cardio-metabolic conditions (OR = 1.10 [95% CI: 1.09-1.11]) classes. Similarly, women were at higher odds than men of being in dyslipidemia (OR = 2.49 [95% CI: 2.05-3.02]) and cardio-metabolic conditions (OR = 3.35, 95% CI: 2.79-4.03]) classes. Employed participants showed decreased odds of having cardio-metabolic conditions (OR = 0.66 [95% CI: 0.55-0.80]). However, very high socioeconomic status was a risk factor for cardio-metabolic conditions (OR = 1.44 [95% CI: 1.16-1.78]) and dyslipidemia (OR = 1.35 [95% CI: 1.10-1.65]). Higher physical activity and sleeping for 8 hours or more were protective factors against cardio-metabolic conditions (OR = 0.74 [95% CI: 0.63-0.87]). Moreover, medium or high dietary intake increased the odds of belonging to the dyslipidemia class (OR = 1.46 [95% CI: 1.09-1.94] and OR = 1.57 [95% CI: 1.16-2.11], respectively).Conclusion Using LCA, we identified distinct subgroups of chronic diseases, showing hidden patterns of multimorbidity associated with several risk factors. This approach offers deeper knowledge of disease clustering, contributes to a more comprehensive understanding of multimorbidity, and shows the importance of regional health challenges in designing targeted public health interventions.
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NR 52
TC 0
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PU PUBLIC LIBRARY SCIENCE
PI SAN FRANCISCO
PA 1160 BATTERY STREET, STE 100, SAN FRANCISCO, CA 94111 USA
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JI PLoS One
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WC Multidisciplinary Sciences
SC Science & Technology - Other Topics
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PT J
AU Ho, ST
Kuo, CY
Chen, MJ
AF Ho, Shang-Tse
Kuo, Ching-Yun
Chen, Ming-Ju
TI Characterizing therapeutic effects of velvet antler using different omics strategies
SO JOURNAL OF TRADITIONAL AND COMPLEMENTARY MEDICINE
LA English
DT Article
DE Velvet antler; Therapeutic effects; Microbiomics; Proteomics; Transcriptomics
ID formosan sambar deer; pilose antler; rna-seq; polypeptides; tip; transcriptome; expression; components; stress
AB Velvet antler (VA) has been widely used in traditional Chinese medicine more than thousand years. Several pharmacological properties of VA have been demonstrated, such as anti-osteoporosis, anti-osteoarthritis, anti-aging, and anti-ischemia-hypoxia effects. Recently, many studies applied different omics in VA studies to illustrate biological pathways or processes, identify bioactive compounds, and discover pharmacological properties. This mini-review article summarizes the application of different omics for investigating therapeutic effects of VA. The limitation and future challenges facing the application of multi-omics in VA is also briefly discussed.
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NR 90
TC 1
Z9 1
U1 2
U2 5
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 2225-4110
EI
J9 J TRADIT COMPL MED
JI J. Tradit. Complement. Med.
PD MAY 15
PY 2025
VL 15
IS 3
BP 229
EP 236
DI 10.1016/j.jtcme.2024.08.002
EA MAY 2025
PG 8
WC Integrative & Complementary Medicine
SC Integrative & Complementary Medicine
GA 3CM6D
UT WOS:001497059100001

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PT J
AU Chen, JC
Liao, XF
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AF Chen, Jincai
Liao, Xiaofei
Wu, Longhuo
TI The Protective Activity of Apigenin Against Bone and Cartilage Diseases
SO CLINICAL INTERVENTIONS IN AGING
LA English
DT Review
DE apigenin; osteogenic differentiation; osteoporosis; rheumatoid arthritis; osteoarthritis; gouty arthritis
ID mesenchymal stem-cells; promotes osteogenic differentiation; rheumatoid-arthritis; inhibiting inflammation; synovial fibroblasts; osteosarcoma cells; global burden; osteoclastogenesis; osteoarthritis; expression
AB Bone and cartilage diseases have become the leading causes of joint disability due to the destruction of bone and cartilage. No effective drugs are available to cure bone and cartilage diseases. Exploring natural compounds as therapeutic alternatives shows promise. Apigenin, a naturally occurring flavonoid, exhibits various pharmacological activities, such as anti-inflammation, antioxidant, and immune modulation. Apigenin acts as a phytoestrogen and mediates the balance of bone remodeling by inducing osteogenic differentiation, promoting osteoblast-associated bone formation, and inhibiting osteoclast-related bone resorption. In addition, apigenin exhibits protective effects against osteoporosis (OP), rheumatoid arthritis (RA), osteoarthritis (OA), gouty arthritis (GA), and intervertebral disc degeneration (IDD). Apigenin can be a promising agent in treating bone and cartilage. However, the application of apigenin is limited due to its low water solubility and bioavailability. More efforts are still needed.
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NR 135
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
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PT J
AU Liu, Z
Chen, XM
Ruan, Z
Wang, C
Yuan, DL
Xiao, WF
Li, YS
Zhao, SS
AF Liu, Zhi
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Wang, Chao
Yuan, Dongliang
Xiao, Wenfeng
Li, Yusheng
Zhao, Shushan
TI Genetic analysis of comorbidities between osteoarthritis, sarcopenia, and osteoporosis
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Article
DE Osteoarthritis; Sarcopenia; Osteoporosis; Genetic correlation; Shared genetic structure; Causal association
ID hand osteoarthritis; common variants; metaanalysis; traits
AB Background: Osteoarthritis (OA), sarcopenia (SCP), and osteoporosis (OP) pose a substantial global morbidity and mortality burden, and previous studies have

observed potential associations among them. This study aims to comprehensively characterize the common genetic structure, biological basis, and underlying causal relationship among OA, SCP, and OP. Methods: We used pooled statistics from the largest European genome-wide association study to investigate the genetic overlap and underlying causal relationships among OA, SCP, and OP. LD Score Regression (LDSC) was first used for estimating global and local genetic associations, cross-trait meta-analysis was then conducted to identify shared loci, and mendelian randomization (MR) analysis was performed to test causal association. Results: In global and local genetic correlation analysis, we found strong positive correlations among OA, SCP, and OP. Cross-trait meta-analysis revealed 9 novel pleiotropic loci for HandOA_SCP trait-pairs, 1 for ThumbOA_SCP (females), and 6 for KneeOA_SCP (males)0.10 novel pleiotropic loci were also identified for HipOA_TBMD, while none for WLM_FinOP. Bidirectional MR analyses indicated significant causal associations between HandOA and SCP(Forward: OR: 1.41, 95 % CI: 1.25-1.60, p < 0.01,Reverse: OR: 1.77, 95 % CI: 1.34-2.35, p < 0.01). Reverse analyses suggested that ThumbOA.female (OR: 1.92, 95 % CI:1.18-3.13, p < 0.01) and KneeOA.male (OR: 1.58, 95 % CI: 1.13-2.12, p < 0.01) were positively correlated with SCP, while TBMD was positively correlated with HipOA (OR: 1.23, 95 % CI: 1.16-1.31, p < 0.01). Conclusions: Our work demonstrates a shared genetic basis, pleiotropic loci, and putative causal relationships among OA, SCP, and OP, highlighting the intrinsic links behind these three complex skeletal diseases.
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NR 47
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U1 5
U2 6
PU PERGAMON-ELSEVIER SCIENCE LTD
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EA MAY 2025
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WC Geriatrics & Gerontology
SC Geriatrics & Gerontology
GA 3ER5G
UT WOS:001498549600002
PM 40389141
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PT J
AU Zhang, CX
Chen, Y
Zhang, J
AF Zhang, Chengxuan
Chen, Yu
Zhang, Jian
TI Non-coding RNAs in osteoarthritis and osteoporosis-related hip fractures: molecular biomarkers for precision diagnosis and prognosis

SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE hip fracture; osteoporosis; osteoarthritis; non-coding RNAs; biomarkers; diagnostics
ID osteoblast differentiation; circular rna; bone loss; promotes; expression; osteogenesis; delivery
AB As individuals age, bone density declines and the likelihood of fractures increases, particularly in women experiencing menopause. Hip fractures, the most severe consequence of osteoporosis, are becoming more common due to the aging global population and a 1-3% annual increase in hip fractures in most regions. The specific epigenetic mechanisms underlying the onset of osteoporosis and its related fractures remain predominantly unexamined. Research indicates that epigenetic modifications can elevate the risk of osteoarthritis, osteoporosis and bone fractures, especially hip fractures, by linking genetic predispositions with environmental factors. Essential regulatory components in these factors encompass microRNAs, lncRNAs, and circular RNAs. This review examines the function of miRNAs, lncRNAs, and circRNAs in the advancement of osteoporosis, with an emphasis on osteoblasts and osteoclasts. The objective is to enhance comprehension of RNA classes in osteoporotic hip fractures, which may facilitate early detection and prognosis, as well as clarify cellular interactions, potentially resulting in innovative diagnostic techniques and targeted therapies.
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TI Multimodal analysis investigating the shared pathogenic mechanisms of osteoporosis and osteoarthritis with an initial exploration of the role of ferroptosis
SO PLOS ONE
LA English
DT Article
AB Background Osteoarthritis (OA) and osteoporosis (OP) are prevalent conditions with overlapping molecular mechanisms. Recent studies have brought attention to ferroptosis, a type of cell death that relies on iron, as a possible connection between these diseases.Methods We performed a comprehensive analysis with datasets obtained from the Gene Expression Omnibus (GEO), focusing on differentially expressed genes (DEGs) in OA and OP. Functional enrichment and integrated analyses identified ferroptosis-related pathways. The role of ferroptosis in OP was further explored through in vivo studies using an ovariectomy-induced OP mouse model.Results The analysis revealed significant overlaps in DEGs related to ferroptosis pathways in both OA and OP. Key genes like TXNIP and SLC2A3 were implicated in the regulation of ferroptosis and associated with disease mechanisms. In vivo results confirmed increased ferroptosis markers in bone marrow stromal cells (BMSCs) from OP mice, supporting the hypothesis that ferroptosis contributes to bone density reduction and structural deterioration.Conclusion Our findings highlight ferroptosis as a critical pathway in the pathogenesis of both OA and OP. Targeting ferroptosis-related genes and pathways could provide new therapeutic opportunities for managing these musculoskeletal diseases.
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TI Relationships between Otolith Morphometrics and Fish Size in an Economically Important Fish, Boops Boops (Linnaeus, 1758) from Aegean and Mediterranean Seas (Türkiye)
SO THALASSAS
LA English
DT Article

DE Otolith morphometrics; Fish size; Linear and non-linear regressions; Boops boops; T & uuml;rkiye
ID shape-analysis; stock discrimination; body-size; growth; bogue; age; sparidae; south
AB The present study was conducted to investigate the comparative biometric relationship between fish size and otolith morphometrics in bogue, Boops boops collected from Aegean and Mediterranean Seas in T & uuml;rkiye. Linear and non-linear regression equations between otolith morphometrics and fish size were established in the fish samples of both the ecosystems. The values of "R2" of regression analysis between TL to otolith morphometrics (OL, OH, OP and OA) showed the positive relationships and all data were well fitted in the regression model where a greater degree of fit was recorded in the stocks of bogue fish in Aegean Sea and Mediterranean Sea. The highest correlations were observed between TL-OL and TL-OA, with both regression coefficients (R-2) reaching 0.765 to 0.900 in Aegean Sea Mediterranea Sea, respectively. In addition, all relationships were found statistically important ($p < 0.001$). The results obtained from this examination were the first to address the relationship between otolith measurements and total length for B.boops collected from Aegean Sea and Mediterranean Sea.
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WC Marine & Freshwater Biology; Oceanography
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AU Xiao, DQ
Zhang, DS
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AF Xiao, Dongqiong
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TI Methyltransferase-Like 3-Mediated N6-Methyladenosine Modification on RNAs: A Novel Perspective for the Pathogenesis and Treatment of Bone Diseases
SO JOURNAL OF CELLULAR AND MOLECULAR MEDICINE
LA English
DT Review
DE diagnosis; methyltransferase-like 3; osteoarthritis; osteoporosis; osteosarcoma; RNA N-6-methyladenosine modification; treatment
ID osteosarcoma; osteoarthritis; osteoporosis
AB Osteoarthritis, osteoporosis, and osteosarcoma are prevalent osseous pathologies associated with the aberrant functionality of chondrocytes, osteoclasts, and osteoblasts, respectively. These conditions frequently exhibit therapeutic resistance and possess a high mortality risk, thus representing substantial health threats. To mitigate these concerns, it is imperative to investigate novel mechanistic insights. Methyltransferase-like 3 (METTL3) is pivotal in these disorders by modulating gene expression via N-6-methyladenosine (m(6)A) modifications on RNA, thereby impacting cellular processes. Although considerable research has elucidated METTL3's involvement in these diseases, a systematic review is essential to summarise these findings and evaluate METTL3's significance. This review endeavours to aggregate and examine contemporary studies to elucidate METTL3's role in bone pathologies and its clinical implications. We propose that METTL3 constitutes a risk gene in these conditions by mediating m(6)A modifications on both mRNAs and non-coding RNAs, suggesting that METTL3 may serve as a critical diagnostic biomarker and therapeutic target. In conclusion, this review provides an extensive analysis of METTL3 and its correlation with osteoarthritis, osteoporosis, and osteosarcoma, offering valuable perspectives on extant research and serving as a valuable reference for researchers engaged in both basic and translational studies.
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NR 71
TC 1
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PU WILEY
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
SN 1582-1838
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J9 J CELL MOL MED
JI J. Cell. Mol. Med.
PD MAR 7
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DI 10.1111/jcmm.70483
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WC Cell Biology; Medicine, Research & Experimental
SC Cell Biology; Research & Experimental Medicine
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PT J
AU Cai, QJ
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Shang, Jingjie
Tang, Yongjin
Ling, Xueying
Li, Yuefeng
Gong, Jian
Guo, Bin
Xu, Hao
TI Age-related bone mass and body composition dynamics in female cynomolgus monkeys: dual-energy X-ray absorptiometry insights for osteoporosis etiology
SO QUANTITATIVE IMAGING IN MEDICINE AND SURGERY
LA English
DT Article
DE Female cynomolgus monkeys; dual-energy X-ray absorptiometry (DXA); bone mineral density (BMD); body composition
ID mineral density; primate model; menopausal; difference; children; cycle; fat; sex
AB Background: Osteoporosis, characterized by reduced bone mass and increased fracture risk, is a major global health burden. Nonhuman primates, particularly female cynomolgus monkeys, are critical preclinical models due to their skeletal and hormonal similarity to humans. Dual-energy X-ray absorptiometry (DXA) is the gold standard for measuring bone mineral density (BMD) and body composition. However, data on age-related changes in these metrics in cynomolgus monkeys are inconsistent, and the relationship between body composition and BMD remains debated and understudied in this model. The objectives of this study were to delineate the age-dependent trends in bone mass and body composition and to evaluate the impact of body composition on bone mass. This study aims to furnish a data reference for experiments involving bone mass and body composition in cynomolgus monkeys as a disease model. Methods: A cohort of 112 healthy female cynomolgus monkeys was stratified into four age-based groups. DXA scans were conducted to ascertain total body bone mass, subcranial bone mass, spine BMD (BMDs), central region-of-interest bone mineral density (BMDCROI), and body

composition metrics. A generalized additive model (GAM) was utilized for non-linear regression analysis of the aging trends in bone mass and body composition parameters. Spearman's rank correlation and multiple linear regression analyses were conducted to investigate the interplay between body composition and bone mass. Results: In female cynomolgus monkeys <= 10 years of age, bone mass parameters showed a significant increase with age. Beyond the age of 10 years, BMDs remained stable with age, while total body BMD (BMDTB) and subcranial BMD exhibited a slight increasing trend in advanced age. A relative decline in BMDCROI was observed in the elderly cohort, with a higher cumulative bone loss rate compared to BMDs (-10.0% vs. 1.8%). BMDTB demonstrated a strong positive correlation with subcranial BMD, with correlation coefficients ranging from 0.947 to 0.990 (P<0.001). Similarly, total body bone mineral content (BMCTB) was highly correlated with subcranial BMC, with correlation coefficients ranging from 0.961 to 0.996 (P<0.001). In the correlation analysis of bone mass and body composition in female cynomolgus monkeys prior to peak age (<= 10 years old), both lean mass (LM) and fat mass (FM) positively influenced BMD, with LM contributing more significantly. Post-peak age (>10 years), FM had a more pronounced effect on total body bone mass. Conclusions: The bone mass and body composition data of female cynomolgus monkeys across different age groups serve as a valuable reference for studies employing female cynomolgus monkeys as animal models. BMDCROI is a sensitive indicator for detecting spinal bone mass loss, minimizing the confounding effects of osteoarthritis (OA). The variable contributions of LM and FM to bone mass in female cynomolgus monkeys at different ages offer significant insights for investigating the etiological factors of osteoporosis.
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SC Radiology, Nuclear Medicine & Medical Imaging
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AU You, YH
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AF You, Yanghao
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TI Interactions between the gut microbiota and immune cell dynamics: novel insights into the gut-bone axis
SO GUT MICROBES
LA English
DT Review
DE Gut microbiota; bone homeostasis; bone-related diseases; gut-immune-bone axis
ID aryl-hydrocarbon receptor; b-cells; dendritic cells; t-cells; arthritis; osteoporosis; osteoarthritis; inflammation; activation; acid
AB Over the past few decades, accumulating evidence has demonstrated that gut microbiota engages in a sustained dialog with the immune system, leading to microbiota-driven immune responses that mediate the regulation of bone-related diseases. Despite the complexity of the dynamic interactions within the gut-immune-bone axis, advancements in high-throughput multi-omics sequencing have significantly facilitated the detailed exploration of this intricate network, thereby providing the potential to develop novel therapeutic strategies for bone-related diseases. In this review, we first summarize the variations in gut microbiota composition observed in patients with bone-related diseases, such as rheumatoid arthritis (RA), osteoarthritis (OA), and osteoporosis (OP), in comparison to healthy controls, along with the factors influencing these changes. The review that follows synthesize evidences highlighting the profound effects of gut microbial dysbiosis on immune homeostasis and bone microenvironment, respectively. We further elaborate that the gut-immune axis and gut-bone axis are not independent but three-dimensional networks, emphasizing gut microbial dysbiosis as a pivotal driver of immune dysregulation and subsequent bone homeostasis imbalance. Therapeutic strategies to manipulate the gut-immune-bone axis based on the use of probiotics as well as prebiotics, fecal microbiota transplantation, dietary modifications, and pharmacological interventions are also discussed. Finally, we discuss the challenges of current research on the gut-immune-bone axis and propose future directions for identifying novel therapeutic targets based on this axis to treat these diseases.
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TI Exploring the Four-Dimensional Impact of Pain-Related and/or Intra-Articular Temporomandibular Disorder Symptoms on Oral Health-Related Quality of Life Among Young Adults
SO JOURNAL OF ORAL REHABILITATION
LA English
DT Article
DE intra-articular; oral health-related quality of life; pain; symptoms; temporomandibular disorders
ID malocclusion; prevalence; severity; tmd
AB Objectives A four-dimensional structure for oral health-related quality of life (OHRQoL) was recently proposed, comprising oral function (OF), orofacial pain (OP), orofacial appearance (OA) and psychosocial impact (PI). This study examined the impact of different temporomandibular disorder (TMD) symptoms on the four OHRQoL dimensions in young adults. It also correlated the four dimensions with the seven Oral Health Impact Profile (OHIP) domains. Methods Young adults were recruited from a large university. The quintessential five TMD symptoms (5Ts) and OHIP-14 were used to assess TMD symptoms and OHRQoL. Participants were categorised into no (NT), pain-related (PT), intra-articular (IT) and combined (CT) TMD groups, and total, dimension and domain OHIP scores were computed. Data were evaluated using the chi-square test and non-parametric analyses (alpha = 0.05). Results Among the 1097 eligible participants (mean age 19.9 years [SD = 1.3]; 69.7% women), 47.2% reported no TMD symptoms, while 20.5%, 14.9% and 17.4% had PT, IT and CT TMD symptoms, respectively. Significant differences in OHIP

scores were noted between individuals with and without TMD symptoms across all dimensions and domains (CT, PT, IT > NT). Additionally, notable distinctions in normalised dimension scores were evident in all participant groups (OP, OA > OF, PI). Moderate to strong correlations were discerned between OHIP dimensions and domain, except for OA with functional limitation (rs = 0.35). Conclusions Adopting the four dimensions as the standard metric for assessing OHRQoL can improve study comparability and enhance understanding of TMD impacts.
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TI Systemic Inflammation in Hip Fracture and Osteoarthritis: Insights into Pathways of Immunoporosis
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Article
DE aging; osteoporosis; hip fracture; inflammaging; osteoimmunology; immunoporosis
ID c-reactive protein; osteoporosis; association
AB Inflammaging has been implicated in age-related bone loss and fragility fractures through immune-mediated effects on bone turnover. We aimed to explore the relationship between systemic inflammatory markers and bone health in older adults, focusing on the differences between patients with osteoporotic fractures and non-fractured controls. We retrospectively analyzed 40 older patients (20 with hip fractures and 20 with osteoarthritis without prior fragility fractures). We compared routine inflammatory markers, including red cell distribution width (RDW), C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and the composite CRP-albumin-lymphocyte index (CALLY), between groups. Bone mineral density (BMD) at the hip, lumbar spine, and wrist, as well as the FRAX score, were assessed. Correlations between inflammatory markers, BMD, and FRAX scores were evaluated using Spearman's coefficient. Patients with fractures exhibited significantly elevated CRP (66.2 +/- 70.3 vs. 3.8 +/- 4.0 mg/L, p = 0.0008) and SII (1399.7 +/- 1143.4 vs. 751.4 +/- 400.8, p = 0.025) compared to controls. RDW, NLR, and CALLY scores did not differ significantly between the groups. Higher CRP levels were associated with lower BMD at all sites (hip: r approximate to -0.63, p = 0.002; spine: r approximate to -0.60, p = 0.005; wrist: r approximate to -0.60, p = 0.005). No significant correlations were observed between the SII and BMD or FRAX values. Elevated systemic inflammation, particularly indicated by CRP and SII, was associated with osteoporotic fracture status and low bone density in our cohort. These findings support the concept that inflammatory pathways may contribute to osteoporosis and fracture risk and suggest that inflammatory markers could serve as adjunctive tools in fracture risk assessment. Further studies are required to clarify the causality and evaluate whether targeting chronic inflammation can improve bone health in older adults.
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TI The Role of mRNA Modifications in Bone Diseases
SO INTERNATIONAL JOURNAL OF BIOLOGICAL SCIENCES
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DT Article
DE messenger RNA; RNA modifications; bone diseases
ID ankylosing-spondylitis; staphylococcus-aureus; nuclear-rna; binding-protein; ribosomal-rna; nat10; n6-methyladenosine; methyltransferase; osteoarthritis; methylome
AB As a type of epigenetic modifications, mRNA modifications regulate the metabolism of mRNAs, thereby influencing gene expression. Previous studies have indicated that dysregulation of mRNA modifications is closely associated with the occurrence and progression of bone diseases (BDs). In this study, we first introduced the dynamic regulatory processes of five major mRNA modifications and their effects on the nucleus export, stability, and translation of mRNAs. We then summarized the mechanisms of mRNA modifications involved in the development of osteoporosis, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, fractures, osteomyelitis, and osteosarcoma. Finally, we reviewed therapeutic strategies for BDs based on the above mechanisms, focusing on regulating osteoblast and osteoclast differentiation, inhibiting cellular senescence and injury, and alleviating inflammation. This review identified mRNA modifications as potential targets for treating BDs and proposes perspectives on the diversity, targetability, and safety of mRNA-modifying therapies.
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TI Quality by design strategy of human mesenchymal stem/stromal cell drug products for the treatment of knee osteoarthritis
SO WORLD JOURNAL OF STEM CELLS
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DT Review
DE Mesenchymal stem/stromal cells; Knee osteoarthritis; Quality by design; Critical quality attributes; Critical material attributes
ID stem-cells; stromal cells; therapy; differentiation; heterogeneity; proliferation; osteoporosis; expression; expansion; criteria
AB Knee osteoarthritis (KOA), characterized by heterogeneous arthritic manifestations and complex peripheral joint disorder, is one of the leading causes of disability worldwide, which has become a high burden due to the multifactorial nature and the deficiency of available disease-modifying treatments. The application of mesenchymal stem/stromal cells (MSCs) as therapeutic drugs has provided novel treatment options for diverse degenerative and chronic diseases including KOA. However, the complexity and specificity of the "live" cells have posed challenges for MSC-based drug development and the concomitant scale-up preparation from laboratory to industrialization. For instance, despite the considerable progress in ex vivo cell culture technology for fulfilling the robust development of drug conversion and clinical trials, yet significant challenges remain in obtaining regulatory approvals. Thus, there's an urgent need for the research and development of MSC drugs for KOA. In this review, we provide alternative solution strategies for the preparation of MSC drugs on the basis of the principle of quality by design, including designing the cell production processes, quality control, and clinical applications. In detail, we mainly focus on the quality by design method for MSC manufacturing in standard cell-culturing factories for the treatment of KOA by using the Quality Target Product Profile as a starting point to determine potential critical quality attributes and to establish relationships between critical material attributes and critical process parameters. Collectively, this

review aims to meet product performance and robust process design, and should help to reduce the gap between compliant products and the production of compliant good manufacturing practice.
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TI Targeting chemokine signaling networks for therapeutics in skeletal disorders
SO FRONTIERS IN ENDOCRINOLOGY
LA English
DT Review
DE chemokine networks; bone remodeling; osteoimmunology; osteoporosis; osteoarthritis; bone regeneration; targeted therapy
ID cancer; axis; osteoclasts; inhibition; activation; expression; migration; cells
AB Chemokine signaling networks have emerged as pivotal regulators of skeletal homeostasis, integrating inflammation, angiogenesis, and immune activation with the processes of bone remodeling and regeneration. Recent evidence demonstrates that dysregulated chemokine-receptor interactions, including CCL2/CCR2, CCL5/CCR5, and CX3CL1/CX3CR1, disrupt the equilibrium between osteogenesis and osteoclastogenesis, thereby contributing to the pathogenesis of osteoporosis, osteoarthritis, multiple myeloma, and bone metastasis. This review synthesizes current insights into how chemokine-mediated signaling cascades intersect with canonical pathways such as JAK/STAT3, NF-kappa B, PI3K/Akt, and Wnt/beta-catenin to coordinate cellular communication within the bone microenvironment. Furthermore, it highlights recent progress in therapeutic

strategies targeting chemokine axes to mitigate inflammatory bone loss and promote tissue regeneration, while addressing translational barriers including receptor redundancy, context-dependent specificity, and limited in vivo validation. By positioning chemokines as dynamic mediators at the interface of the immune and skeletal systems, this review establishes a conceptual foundation for the development of precision therapeutics aimed at restoring bone homeostasis and treating skeletal disorders.
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TI Expressions of insulin-like growth factor-1, interleukin-1β, and matrix metalloproteinase-13 in patients with knee osteoarthritis and their associations with the severity

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DT Article
DE expression; insulin-like growth factor; interleukin; knee osteoarthritis; matrix metalloproteinase
AB Background A key factor in the pathogenesis of osteoarthritis is an imbalance in cytokines, favoring proinflammatory activity. This study aimed to explore the expressions of insulin-like growth factor-1 (IGF-1), interleukin-1 beta (IL-beta) and matrix metalloproteinase-13 (MMP-13) in patients with knee osteoarthritis (KOA), as well as their associations with the severity. Methods Subjects (166 in total) were recruited from KOA patients treated between January 2021 and June 2023. Their clinical data were collected, disease severity was assessed by Kellgren-Lawrence (K-L) grades, and venous blood was drawn to measure the serum levels of IGF-1, MMP-13, and IL-1 beta. Factors affecting the severity of KOA were analyzed by multivariate logistic regression model incorporating the aforementioned information. Results There were more cases of disease course >1 year, body mass index (BMI) >25 kg/m2, heavy physical labor, and osteoporosis in the severe group ($P<0.05$). Multivariate logistic regression analysis revealed that disease course >1 year, BMI >25 kg/m2, heavy physical labor, osteoporosis, lowly expressed MMP-13, and lowly expressed IL-1 beta were risk factors for the severity of KOA [odds ratio (OR) >1, $P<0.05$], while highly expressed IGF-1 was a protective factor ($OR<1$, $P<0.05$). The areas under the receiver operating characteristic (ROC) curves (95% confidence interval) of IGF-1, MMP-13, and IL-1 beta levels and their combination for assessing the severity of KOA were 0.883 (0.823-0.942), 0.880 (0.827-0.934), 0.895 (0.847-0.943), and 0.923 (0.877-0.968), respectively. Conclusions IGF-1 is lowly expressed, whereas MMP-13 and IL-1 beta are highly expressed. The combined application of the three indicators has the highest value for assessing the severity of KOA.
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TI RANKL-mediated osteoclastic subchondral bone loss at a very early stage precedes subsequent cartilage degeneration and uncoupled bone remodeling in a mouse knee osteoarthritis model
SO JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH
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DT Article
DE Subchondral bone loss; Early stage; Knee osteoarthritis; Mouse destabilization of the medial meniscus (DMM) model; Tsukuba hypertensive mice; High-turnover bone metabolism; Osteoporosis
ID mineral density; hypertrophic differentiation; osteoporosis; resorption; progression; inhibition; activation; apoptosis; renin; mice
AB IntroductionUncoupled bone remodeling in the subchondral bone (SB) has recently been considered as an important process in the progression of knee osteoarthritis (KOA). In this study, we aimed to investigate changes in SB and articular cartilage using a mouse model of destabilization of the medial meniscus (DMM) and determine the effects of bone metabolism on KOA progression.MethodsDMM or sham surgery was performed on the left knees of 40-week-old male wild-type (WT) mice and Tsukuba hypertensive mice (THM), which exhibit high-turnover bone metabolism. Bone volume/tissue volume (BV/TV) and bone mineral density (BMD) in the medial tibial SB were measured longitudinally in vivo using mu CT at 0 (immediately after surgery), 1, 2, 4, 8, and 12 weeks postoperatively. Concurrently, histological evaluations of the articular

cartilage in the medial tibial plateau were conducted. Furthermore, the number of endo-periosteal tartrate-resistant acid phosphatase-positive osteoclasts, trabecular RANKL-positive osteocytes, and osteocytes in the trabeculae were measured at 0, 1, 2, and 4 weeks.ResultsIn the WT + DMM group, BV/TV and BMD in the SB significantly decreased with time, whereas cartilage degeneration significantly increased. In the THM + DMM group, these changes in BMD and cartilage degeneration were significantly pronounced. Interestingly, in the THM + DMM group, BV/TV significantly decreased up to 4 weeks but then began to increase, although BMD continued to decrease until the 12-week mark. The number of osteoclasts and the percentage of RANKL-positive osteocytes per total number of osteocytes within the total trabecular bone area (%) in the WT + DMM group significantly increased with time, with a significant difference between the WT + DMM and WT + sham groups at 4 weeks. The number of osteocytes in the WT + DMM group significantly decreased with time, and the difference between the WT + DMM and WT + sham groups was significant at 4 weeks postoperatively. These histological changes were significantly enhanced in the THM + DMM group.ConclusionsThe results indicate that early-stage osteocyte death in the SB and RANKL-mediated osteoclastic SB loss precede histological cartilage degeneration and contribute to uncoupled bone remodeling at the later stage. Acceleration of disease processes in the THM + DMM group suggests that high-turnover bone metabolism is a potential risk factor for KOA. Maintaining SB integrity and avoiding continuous SB overload may be key strategies for mitigating disease progression.

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TI The role of RGS12 in tissue repair and human diseases
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DT Review
DE Cancer; Nervous disorders; Osteoporosis; RGS12; Tissue repair
ID protein signaling 12; goloco motif; regulators; osteoclastogenesis; osteoporosis; cancer; osteoarthritis; periodontitis; inflammation; receptors
AB Regulator of G protein signaling 12 (RGS12) belongs to the superfamily of RGS proteins defined by a conserved RGS domain that canonically binds and deactivates heterotrimeric G-proteins. As the largest family member, RGS12 is widely expressed in many cells and tissues. In the past few decades, it has been found that RGS12 affects the activity of various cells in the human body, participates in many physiological and pathological processes, and plays an important role in the pathogenesis of many diseases. Here, we set out to comprehensively review the role of RGS12 in human diseases and its mechanisms, highlighting the possibility of RGS12 as a therapeutic target for the treatment of human diseases. <feminine ordinal indicator> 2024 The Authors. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co., Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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TI Integrating exercise and medication management in geriatric care: a holistic strategy to enhance health outcomes and reduce polypharmacy
SO LANCET HEALTHY LONGEVITY
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ID older-adults; skeletal-muscle; atrial-fibrillation; stroke prevention; heart-failure; resistance; metformin; people; falls; anticholinergics
AB Integrating exercise prescriptions with medication management represents a novel approach for enhancing health and function, optimising medication effectiveness, and reducing adverse drug reactions and polypharmacy in older adults (ie, those aged >= 60 years). This Personal View highlights the need for a comprehensive assessment of lifestyle, diagnoses, geriatric syndromes, and medications with an emphasis on fully incorporating exercise treatment into geriatric care. Exercise is an alternative to less effective or unsafe medications for many conditions, including depression, anxiety, insomnia, osteoarthritis, and dementia. Exercise is an important adjunct to pharmacotherapy for many common chronic conditions such as coronary artery disease, heart failure, diabetes, osteoporosis, cancer, and chronic obstructive pulmonary disease. Adding exercise to drug management can mitigate adverse drug reactions, enhance medication compliance, and reduce the adverse effects of sedentary behaviour and ageing processes on chronic disease expression. Targeted exercise programmes have also been shown to ameliorate drug-induced sideeffects, including anorexia, falls, sarcopenia, osteoporosis, and orthostatic hypotension, and to overcome constraints such as reduced aerobic fitness, balance impairment, and muscle atrophy due to some medications. Health-care professionals require additional training and support to ensure that exercise assumes a key, central role in older adults with multimorbidity and polypharmacy, as supported by the current literature. This Personal View describes practical approaches to incorporating exercise into clinical practice as a step towards an integrated geriatric care model, with the ultimate aim of increasing health span and minimising disability.
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TI Differential Pattern of Obesity in Total Hip and Knee Arthroplasty Candidates
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DE creatinine; hip and knee; obesity; osteoarthritis; sex
ID body-mass index; osteoarthritis; men; risk; associations; mortality; gender; women; hand; oa

AB Purpose: This study examined the differential pattern of obesity between men and women with severe OA of the knee or hip joint. The relationship between creatinine, a pro-inflammatory parameter and obesity, sex, and site of joint involvement was examined.Design: This study involved a secondary analysis of prospectively collected data of patients who underwent hip or knee arthroplasty.Results: Data of 5,130 patients (1,989 males, 39%, 3,141 females, 62%), mean age: 66 (11) were used for data analysis. Of these patients, 2,038 patients underwent hip and 3,092 patients underwent knee arthroplasty. Prevalence of obesity (grade I and II) was higher in the TKA group as compared with THA group (55% vs. 38%) with the prevalence of morbid obesity (Grade II) being twice as many in the TKA group (27% vs. 14%), $p < 0.001$. There was a statistically significant association between obesity and site of joint involvement ($p < 0.001$) and for the interaction between sex of the patient and site of arthritis ($p < 0.001$). In the TKA group, the sex factor was the only factor that was related to the pre-op creatinine level ($p < 0.001$). In THA group, both sex ($p < 0.001$) and obesity ($p = 0.002$) showed an association with pre-op creatinine.Conclusion: This study provides further evidence that obesity has a multifaceted interaction with osteoarthritis with a differential pattern in hip and knee joints. Creatinine considered as a pro-inflammatory factor appears to have a differential role in hip and knee OA.
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TI Interoceptive regulation of bone homeostasis: The interplay between the nervous and skeletal systems in pathophysiology
SO PHARMACOLOGICAL RESEARCH
LA English
DT Article
DE Skeletal interoception; Nervous system; Neuropeptides; Skeletal tissue homeostasis; Therapeutic strategies for skeletal diseases
ID gene-related peptide; serotonin reuptake inhibitors; nicotinic acetylcholine-receptors; osteoblast-like cells; neuropeptide-y; substance-p; osteoclast differentiation; neurons contribute; leptin regulation; mineral density
AB Studies have demonstrated that the nervous system can perceive and respond to signaling from bone tissue, a process termed interoception, which plays a crucial role in the homeostasis of bone tissue. Sensory nerves extensively innervate bone tissue and transmit interoceptive signals to the central nervous system (CNS). The hypothalamus, located within the CNS, is instrumental in processing these interoceptive signals and regulating bone homeostasis through the autonomic nervous system, the release of neuropeptides, and neuroendocrine mechanisms. Although CNS regulation of bone has been recognized for decades, the specific interoceptive mechanisms governing skeletal homeostasis remain an emerging research focus. This review explores the latest advancements in interoceptive regulation of bone homeostasis, highlighting its role in skeletal diseases such as osteoporosis and osteoarthritis(OA). Furthermore, we discuss potential therapeutic strategies targeting interoceptive pathways, including biomaterials, pharmacological interventions, and non-pharmacological approaches. By elucidating the interplay between the nervous and skeletal systems, this review provides new insights into the regulation of bone health and its implications for future treatments of skeletal disorders.
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TI Total Body PET/CT: A Role in Musculoskeletal Diseases
SO SEMINARS IN NUCLEAR MEDICINE
LA English
DT Review
ID regional bone metabolism; lumbar spine; risedronate; f-18-fdg; pain
AB Recent advancements in PET technology have culminated in the development

of total-body PET (TB-PET) systems, which overcome many limitations of traditional scanners. These TB- PET scanners, while still becoming widely available, represent the forefront of clinical imaging across numerous medical institutions worldwide. Early clinical applications have demonstrated their enhanced image quality, precise lesion quantification, and overall superior performance relative to conventional scanners. The capabilities of TB-PET technology, including extended scan range, ultrahigh sensitivity, exceptional temporal resolution, and dynamic imaging, offer significant potential to tackle unresolved clinical challenges in medical imaging. In this discussion, we aim to explore the emerging applications, opportunities, and future perspectives of TB-PET/CT in musculoskeletal disorders (MSDs). Clinical applications for both oncologic and non-oncologic musculoskeletal diseases are discussed, including inflammatory arthritis, infections, osteoarthritis, osteoporosis, and skeletal muscle disorders. From the ability to visualize small musculoskeletal structures and the entire axial and appendicular skeleton, TB-PET shows significant potential in the diagnosis and management of MSD conditions as it becomes more widely available. Semin Nucl Med 55:86-97 (c) 2024 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.
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TI Overview of biomembrane-derived nanoparticles as emerging drug delivery

systems for treating bone aging diseases
SO INTERNATIONAL JOURNAL OF PHARMACEUTICS
LA English
DT Review
DE Biomembrane; Bone aging diseases; Nanoparticles; Osteoporosis; Osteoarthritis
ID mesenchymal stem-cells; red-blood-cell; responsive nanoparticles; engineered exosome; membrane; cartilage; osteoporosis; therapy; cancer; osteoarthritis
AB Bone aging diseases, including osteoporosis and osteoarthritis, present significant global health challenges, particularly in countries experiencing demographic aging. Conventional treatment strategies such as pharmacotherapy and lifestyle adjustments frequently yield suboptimal therapeutic outcomes and are carry risks of longterm adverse effects. In recent years, biomembrane-derived nanoparticles have emerged as promising candidates for advanced drug delivery systems to overcome these limitations. By encapsulating therapeutic agents within biomembranes (cell membrane, extracellular vesicles), these systems enhance biocompatibility, prolong circulation time, and enable targeted delivery to pathological sites. Moreover, biomembranes can be functionally modified to optimize their therapeutic performance. In this review, we explore the pathophysiology of bone aging diseases, current treatment approaches, and the development of biomembrane-derived nanoparticles, with a focus on their potential applications in osteoporosis and osteoarthritis. These innovative delivery systems offer the potential to improve treatment efficacy and minimize side effects, thereby laying the foundation for clinical translation in the future.
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NR 133
TC 1
Z9 1
U1 10
U2 15
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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J9 INT J PHARMACEUT
JI Int. J. Pharm.
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WC Pharmacology & Pharmacy
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PT J
AU Arita, S
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TI Age-related prevalence of radiographic lumbar spondylolisthesis and its associations with low back pain, walking speed, and muscle index: findings from the second survey of the ROAD study
SO EUROPEAN SPINE JOURNAL
LA English
DT Article
DE Lumbar spondylolisthesis; Low back pain; Prevalence; Walking speed; Appendicular lean mass
ID bioelectrical-impedance analysis; dwelling elderly subjects; degenerative spondylolisthesis; natural course; risk-factors; sarcopenia; cohort; mass; men
AB ObjectivesTo determine the prevalence of lumbar spondylolisthesis (LS) and its association with low back pain, walking speed, grip strength, and muscle mass in the general population.MethodsParticipants included 1551 members of the general population from the 2nd ROAD (Research on Osteoarthritis/osteoporosis Against Disability) study conducted in Wakayama Prefecture, Japan, between 2008 and 2010. Lumbar radiography diagnosed LS when the slip was >= 3 mm in the lateral views. Logistic regression analysis (adjusted for sex, age, area, and BMI) assessed the association between LS and low back pain, walking speed, grip strength, and appendicular lean mass.ResultsComplete data from 1522 participants (510 men, 1012 women, mean age 65.7 +/- 12.2 years) were analyzed. The prevalence of LS increases with age, with an estimated one in five men aged 80 years or older and one in four women aged 70-79 years affected. Logistic regression showed LS was significantly associated with low back pain (OR: 1.36, CI: 1.03-1.80). Walking speed, grip strength, and appendicular lean mass were not significantly associated with LS. The prevalence of LS at any level was 17.4% in the total sample, 13.3% in men, and 19.5% in women (P = 0.005).ConclusionLS was prevalent in 17.4% of the general population, with a higher prevalence in women. Patients with LS had more low back pain than those without LS.
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PI NEW YORK
PA ONE NEW YORK PLAZA, SUITE 4600, NEW YORK, NY, UNITED STATES
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J9 EUR SPINE J
JI Eur. Spine J.
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WC Clinical Neurology; Orthopedics
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AF Hu, Wanyan
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TI A modified minimally invasive subvastus approach shows superior early postoperative clinical outcomes compared to the medial parapatellar approach in total knee arthroplasty for osteoarthritis patients: a comparative study
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Modified minimally invasive subvastus approach; Total knee arthroplasty; Osteoarthritis
ID femoral nerve block; mini-subvastus; surgical approach; analgesia; efficacy; anatomy
AB ObjectiveThis study compared the modified minimally invasive subvastus approach (MMSA) versus the medial parapatellar approach (MPA) in total knee arthroplasty (TKA) for osteoarthritis, focusing on perioperative blood loss, postoperative pain, quadriceps strength, and knee mobility.MethodsIn this retrospective cohort study, we enrolled patients undergoing TKA from June 2020 to June 2022. Inclusion criteria were adults aged 40-80 with end-stage knee osteoarthritis undergoing primary TKA. Exclusion criteria included neuromuscular disorders, active infections, severe osteoporosis, prior knee surgery, and rheumatoid arthritis. We compared the MMSA group (n = 36) with the MPA group (n = 57) for primary outcomes including blood loss, postoperative pain, quadriceps strength, knee range of motion, and clinical scores including Oxford Knee Score (OKS) and Western Ontario and McMaster Universities (WOMAC) score.ResultsThe MMSA group showed reduced blood loss, less pain on day 3, and better quadriceps strength and knee mobility compared to the MPA group. Clinical scores (WOMAC and OKS) were significantly better in the MMSA group in the early postoperative period, indicating improved function and reduced pain. However, the MMSA group had longer operation times. Long-term recovery and prosthesis placement accuracy, including prosthesis angles, were similar in both groups.ConclusionThe MMSA offers superior short-term outcomes post-TKA without compromising long-term recovery, indicating its potential as a preferred approach for patients aiming to minimize postoperative complications and expedite recovery. This study provides evidence for the clinical superiority of MMSA in the early postoperative period.
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TI From neuromodulation to bone homeostasis: therapeutic targets of nerve growth factor in skeletal diseases
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE nerve growth factor; bone homeostasis; bone formation; bone resorption; skeletal diseases
ID mesenchymal stem-cells; mouse model; pain; ngf; expression; kinase; trka; blockade; immunoreactivity; differentiation
AB The skeletal system is an important support structure in the human body, and

its homeostatic state is highly relevant to the development of a wide range of orthopaedic diseases. The search for key regulatory factors associated with skeletal development is essential for exploring potential therapeutic targets for bone diseases. Nerve Growth Factor (NGF), the first neurotrophic factor to be discovered, plays an important role in regulating immune cell function, influencing angiogenesis and participating in the physiological and pathological processes of bone homeostasis. Here, we mainly review the biological functions of NGF in the skeletal system and its molecular mechanisms, analyse the pathophysiological roles of the NGF signaling pathway in skeletal diseases such as osteoporosis, osteoarthritis, and fracture healing, and summarize the progress and challenges of the current clinical research on therapeutic strategies targeting NGF. In addition, we provide an overview of NGF and highlight the role of NGF in the regulation of bone formation and bone resorption. Therefore, by reviewing the literature related to NGF and bone diseases, this paper summarises the specific regulatory mechanisms of NGF in various bone diseases, which provides new perspectives and intervention targets for the treatment of skeletal diseases, especially in the field of diseases in which the effects of traditional treatments are limited. The therapeutic strategies targeting neurotrophic factors show broad prospects for clinical application.
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TI Update on the role of bone turnover markers in the diagnosis and management of osteoporosis: a consensus paper from The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO), International Osteoporosis Foundation (IOF), and International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)
SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE BALP; Bone status indices; Bone turnover markers; PINP; TRACP5b; beta-CTX-I
ID chronic kidney-disease; n-terminal propeptide; growth-factor 23; serum osteoprotegerin levels; age-related-changes; i procollagen pinp; biochemical markers; postmenopausal women; reference intervals; mineral density
AB Purpose The International Osteoporosis Foundation (IOF) and the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) have proposed procollagen type I N propeptide (PINP) and beta isomerized C-terminal telopeptide of type I collagen (beta-CTX-I) as reference bone turnover markers (BTMs) for osteoporosis. This report examines the published literature since the 2011 IOF-IFCC position paper in order to determine the clinical potential of the reference BTMs and newer markers for the prediction of fracture risk and monitoring the treatment of osteoporosis. Methods Evidence for the relationship between BTMs and subsequent fractures was gathered from prospective studies through literature

review of the Medline database from years 2011 to May 2024. The impact of treatment on BTMs was also studied by examining publications in that period. Studies of the accuracy of BTMs in the assessment of bone turnover in the setting of advanced chronic kidney disease were also examined. Results Increased BTM concentrations are associated with higher fracture risk in postmenopausal women. PINP and beta-CTX-I measured in blood are associated with fracture risk but their interaction with other risk factors has not been sufficiently studied limiting their incorporation into fracture risk algorithms. Treatment-induced changes in PINP and beta-CTX-I account for a substantial proportion of fracture risk reduction and are useful for improving adherence; they are recommended for inclusion in studies to examine adherence in individual patients. However, total PINP (tPINP) and beta-CTX-I may be elevated in CKD due to renal retention. Bone alkaline phosphatase (BALP), intact PINP (iPINP), and tartrate resistant acid phosphatase 5b (TRACP5b) show the most promise in discriminating high and low turnover bone diseases in patients with advanced CKD and for predicting fracture risk, monitoring treatment response, and assessing the risk of treatment-related complications. Conclusion We re-affirm the use of serum/plasma tPINP and plasma beta-CTX-I as reference BTMs with appropriate patient preparation and sample handling and measurement by standardized/harmonized assays in clinical studies to accumulate further data, and for monitoring treatment of osteoporosis in the setting of normal renal function in clinical practice. BALP and TRACP5b, measured by standardized assays, are recommended as reference BTMs for CKD-associated osteoporosis and should be included in observational and intervention studies to ascertain their utility for risk-evaluation, treatment initiation, and assessment of treatment response in CKD-associated osteoporosis.

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TI Hospital-Treated Infections and 15-year Incidence of Musculoskeletal Disorders: A Large Population-Based Cohort Study
SO CLINICAL EPIDEMIOLOGY
LA English
DT Article
DE infectious disease; osteoarthritis; rheumatoid arthritis; osteoporosis; gout; low back pain
ID rheumatoid-arthritis; bacterial-infection; risk; disease; periodontitis; osteoporosis; association; databases
AB Background: Basic science evidence reveals interactions between the immune and bone systems. However, population studies linking infectious diseases and musculoskeletal (MSK) disorders are limited and inconsistent. We aimed to examine the risk of six main MSK disorders (osteoarthritis, rheumatoid arthritis, osteoporosis, gout, low back pain, and neck pain) following hospital-treated infections in a large cohort with long follow-up periods. Methods: We analysed data from 502,409 UK Biobank participants. Participants free of specific MSK disorders at baseline were included in each analysis. Hospital-treated infections before baseline were identified using national inpatient data, while incident MSK outcomes were ascertained from inpatient records, primary care, and death registers. Participants with prior infections were propensity score matched (1:5) with those without. Hazard ratios (HRs) and absolute rate differences (ARDs) with 95% confidence intervals (CIs) were calculated using Cox proportional hazards

models. To assess potential reverse causality due to delayed diagnosis of preexisting illness, analyses were repeated excluding MSK disorder cases that occurred within the first 5 and 10 years post-baseline. Results: A hospital-treated infection was associated with increased risks of all six MSK disorders, with particularly strong associations for osteoporosis (HR, 1.55 [1.48-1.63]; ARD, 1.48 [95% CI 1.29-1.68] per 1000 person-years) and rheumatoid arthritis (HR, 1.53 [1.41-1.65]; ARD, 0.58 [0.46-0.71] per 1000 person-years), while other disorders showed HRs of 1.28-1.32. Bacterial and viral infections showed similar associations, with MSK infections (generally stronger risk) and other locations both linked to increased risks. Associations remained significant even for incident cases that occurred more than 10 years postbaseline. Conclusion: Hospital-treated infections are associated with long-term MSK disorder risks, regardless of pathogen type or disorder nature (inflammatory or degenerative). Long-term monitoring and care for MSK health in patients with prior hospital-treated infections are recommended. frequent and severe infections, suggesting a systemic rather than pathogen-specific effect. The risk persists beyond 10 years, highlighting the need for long-term MSK care for individuals with a history of severe infections.
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TI Fetal rotation examined with ultrasound in a sub-Saharan population: A longitudinal cohort study
SO ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA
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DT Article
DE birth; cesarean; maternity care; obstetrics; ultrasound
ID occiput posterior position; head position; intrapartum sonography; labor; 2nd-stage; delivery; association; duration; outcm; 1st
AB Introduction Occiput posterior (OP) position rates at birth are 5%-8% in studies mainly comprising white European women. The anthropoid pelvis is common in black African women. This pelvic shape has a narrow anterior segment and an ample room posteriorly. The fetal head is wider posteriorly, and the OP position may be favorable in women with an anthropoid pelvic shape. We aimed to examine the fetal rotation with ultrasound longitudinally during the active phase of labor in a sub-Saharan population. We also aimed to examine associations between fetal position, delivery mode, and duration of labor. Material and Methods The study was conducted at Kilimanjaro Christian Medical Centre in Moshi, Tanzania from the 19th of November 2023 to 13th of April 2024. Women with a single fetus in cephalic presentation, gestational age >37 weeks, without previous or pre-labor cesarean section were eligible. Fetal position was classified as occiput anterior (OA) from 10 to 2 o'clock, occiput transverse (OT) at 3 or 9 o'clock, and OP position from 4 to 8 o'clock. Results The study participants comprised 215 women. Fetal positions at admission, in the first and second stage of labor and at birth are presented in the graphical figure. In all, 65/215 (30.2%) fetuses were in OP position at admission, 59/204 (28.9%) in the first stage, 38/210 (18.1%) in the second stage and 35/215 (16.3%) were delivered in OP position. The OP rates at birth were 25/92 (27.2%) in nulliparous and 10/123 (8.1%) in parous women. The operative delivery rate was 10/157 (6.4%) in women with ultrasound assessed fetal position as OA in the second stage (six cesarean section and four vacuum extractions), and 28/48 (58.3%) in the non-OA group (27 cesarean section and one vacuum extraction) ($p < 0.01$). The hazard ratio for delivery in the second stage was 0.26 (95% CI 0.13-0.52) for the non-OA versus the OA group in nulliparous women and 0.25 (95% CI 0.12-0.52) in parous women. Conclusions The persistent OP position rate at birth was higher than previously reported, and the operative intervention rate was nine time higher

in women with the fetus in non-OA versus OA position in the second stage.
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TI Research progress on mesenchymal stem cell-derived exosomes in the treatment of osteoporosis induced by knee osteoarthritis (Review)
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DT Review
DE exosomes; mesenchymal stem cells; knee osteoarthritis; osteoporosis
ID bone-mineral density; epigenetic regulation; differentiation; polymorphisms; angiogenesis; mechanisms; arthritis; repair; susceptibility; regeneration
AB Knee osteoarthritis (KOA) and osteoporosis (OP) are closely related, age-related, degenerative orthopedic conditions. Elderly patients with OP frequently develop concurrent KOA, with high co-occurrence rates. Studies indicate that OP significantly increases KOA risk and that these conditions mutually exacerbate each other. Anti-OP therapies show significant efficacy in KOA management, substantially delaying disease progression. Mesenchymal stem cell-derived exosomes (MSC-Exos) have significant therapeutic potential for both KOA and OP. These exosomes enhance chondrocyte proliferation, modulate cartilage matrix synthesis and degradation, and suppress synovial inflammation, suggesting a novel therapeutic approach for KOA. However, their OP mechanisms remain unclear but may involve disrupted bone metabolic signaling, amplified inflammation, and dysregulated intercellular communication in the bone microenvironment. The present review summarizes MSC-Exos research advances in KOA and OP, providing a foundation for future studies and clinical applications.
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AU Kim, HC
AF Kim, Hee-Cheol
TI Risk of dementia in patients with age-related medical conditions: a retrospective cohort study
SO PSYCHOGERIATRICS
LA English
DT Article
DE ageing; comorbidity; dementia; retrospective studies; risk factors
ID mild cognitive impairment; obstructive pulmonary-disease; midlife blood-pressure; alzheimers-disease; heart-disease; follow-up; association; decline
AB ObjectiveThis retrospective cohort study aimed to investigate the impact of age-related medical conditions on the incidence of dementia, considering factors such as hypertension, diabetes mellitus, cerebrovascular disease, cardiovascular disease, chronic kidney disease, osteoarthritis, osteoporosis, chronic obstructive pulmonary disease, and hearing difficulties.MethodsData from 513 640 patients at Keimyung University Dongsan Hospital were analyzed using the Observational Medical Outcomes Partnership Common Data Model. Patients with and without age-related medical conditions were assigned to experimental and control groups, respectively, with propensity score matching. Cox proportional hazards models assessed the association between each condition and dementia

incidence.ResultsHypertension, diabetes mellitus, cerebrovascular disease, cardiovascular disease, chronic kidney disease, osteoarthritis, osteoporosis, and hearing difficulties were associated with increased dementia risk. Chronic obstructive pulmonary disease showed no significant association with increased risk of dementia. Incidence rates ranged from 4.52 to 8.05 per 1000 person-years in the control group and 7.46 to 14.99 per 1000 person-years in the experimental group. Hazard ratios ranged from 1.38 to 2.36.ConclusionsThe study highlights the importance of managing age-related medical conditions to mitigate dementia risk. Understanding these risk factors can inform preventive strategies and improve cognitive health outcomes. Problems with deidentification data analysis and the need for further multicentred studies are among the limitations of this study.
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NR 67
TC 1
Z9 1
U1 0
U2 4
PU WILEY
PI HOBOKEN
PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 PSYCHOGERIATRICS
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WC Geriatrics & Gerontology; Psychiatry
SC Geriatrics & Gerontology; Psychiatry
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UT WOS:001362525000001
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PT J
AU Bergum, JM
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AF Bergum, Jeppe Markussen
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TI Runners with osteoarthritis sustain more injuries than healthy runners: An observational cohort study
SO PHYSICAL THERAPY IN SPORT
LA English
DT Article
DE Running; Risk factors; Comorbidity
ID risk; prevention; distance
AB Objective: Examine whether runners with specific diseases, including osteoarthritis, osteoporosis, rheumatoid arthritis, diabetes, multiple sclerosis (MS), cancer, or multiple diseases, sustain more running-related injuries (RRI) compared with healthy runners in the Garmin-RUNSAFE Running Health Study. Design: 18-month cohort study. Setting/participants: Participants were runners >= 18 years, proficient in English, and using a Garmin watch. Exposure included having one of the following diseases: osteoarthritis, osteoporosis, rheumatoid arthritis, diabetes type 1 or 2, multiple sclerosis (MS), cancer, or multiple diseases. Main outcome measures: Outcome was sustaining an RRI and was reported through weekly questionnaires. Appropriate censoring methods were applied for discontinued participation. Time-to-event analysis assessed after 1000 km running. Results: Of 7038 included runners, 6207 had no disease and 831 had at least one of the specified diseases. After 1000 km, 64.4 % of runners with a disease and 56.7 % of healthy runners sustained an RRI, yielding a cumulative incidence risk difference (cIRD) of 8.0 % (95 %CI: 4.0-12.0 %). Among separate diseases, a significant risk

difference was observed between the osteoarthritis group and the healthy group, with a cIRD of 14.7 % (95 %CI: 9.0-20.4 %). Conclusions: A significantly higher incidence of running-related injuries was observed among adult runners reporting a disease. Runners with osteoarthritis is a particularly vulnerable sub-group.
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NR 35
TC 0
Z9 0
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TI Raloxifene Is Associated with Total Knee Arthroplasty in Postmenopausal Women: A Comparative Cohort Study
SO LIFE-BASEL
LA English
DT Article
DE post-traumatic knee osteoarthritis; raloxifene; total knee replacement; postmenopausal women; anti-osteoporotic medications; bisphosphonates; denosumab
ID osteoporosis; bisphosphonates; denosumab; risk
AB Post-traumatic osteoarthritis (PTOA) is a distinct form of knee osteoarthritis

characterized by accelerated joint degeneration following injury. It poses unique challenges in post-menopausal women due to hormonal changes and altered bone metabolism that create complex pathophysiological environments. This retrospective cohort study compared the effectiveness of different anti-osteoporotic medications in preventing total knee replacement (TKR) in 6155 postmenopausal women with PTOA treated between 2011 and 2021. We compared raloxifene and denosumab with bisphosphonates serving as the reference group. The primary outcome was TKR occurrence. Cox proportional hazards regression and inverse probability of treatment weighting (IPTW) were performed to estimate hazard ratios, with Kaplan-Meier survival analysis for time-to-event assessment. Participants' mean (SD) age was 69.4 (10.0) years. Given the retrospective nature and typical delayed presentation of PTOA symptoms, cohort entry was defined as the concurrent diagnosis of PTOA and osteoporosis requiring anti-resorptive therapy. Over a mean follow-up of 5.47 years, 99 patients (1.6%) underwent TKR. Raloxifene was associated with a significantly reduced TKR risk compared to bisphosphonates (IPTW-HR 0.81, 95% CI 0.67-0.99, p = 0.040), representing a 19% relative risk reduction. Kaplan-Meier analysis demonstrated raloxifene maintained the lowest cumulative TKR incidence compared to bisphosphonates and denosumab over time, particularly beyond 5 years. These findings suggest that raloxifene may offer superior joint protection compared with bisphosphonates and denosumab in postmenopausal women with PTOA, supporting its potential as a disease-modifying therapeutic option for this vulnerable population.
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NR 38
TC 1
Z9 1
U1 0
U2 0
PU MDPI
PI BASEL
PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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VL 15
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SC Life Sciences & Biomedicine - Other Topics; Microbiology
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TI Muscle Atrophy Around the Hip Joint in Patients with Femoral Neck Fracture is Associated with Postoperative Walking Ability
SO GERIATRIC ORTHOPAEDIC SURGERY & REHABILITATION
LA English
DT Article
DE femoral neck fractures; osteoarthritis; muscle weakness; muscle volume; walking ability; computer tomography; rehabilitation
AB Introduction: Patients with femoral neck fractures (FNF) have reduced walking ability owing to muscle weakness. Preoperative muscle volume and quality may have an association with prolonged rehabilitation and can be useful to predict the postoperative walking ability in patients with FNF. This study aimed to compare the muscle volume and computed tomography (CT)-assessed density around the hip joint in patients with FNF with patients having hip osteoarthritis (HOA) and assess the association of these measurement with postoperative walking ability. Materials and Methods: This retrospective observational study included 15 patients with FNF and 15 with unilateral HOA who were matched for age, sex, and osteoporosis medication. Muscle volume and CT-assessed density of the gluteus maximus, gluteus medius, gluteus minimus, iliacus, psoas major, rectus femoris, and rectus abdominis on the unaffected side were measured three-dimensionally using 3D Slicer software with preoperative CT data. The associations of muscle measurement with patient background, load to FNF (measured using the finite element method), and pre- or postoperative walking ability were assessed. Results: Muscle volume of gluteus maximus, CT-assessed density of all muscles, and femoral strength were significantly lower in the FNF group than in the OA group ($P < .01$, $P < .01$, and $P = .04$, respectively). Muscle volume showed a moderate-to-strong correlation with body mass index ($r = 0.66$-0.81) and FNF load ($r = 0.51$-0.70), and CT-assessed density showed a moderate correlation with serum nutritional markers ($r = 0.33$-0.60). Postoperative walking ability was significantly correlated with the muscle volumes of iliacus and gluteus maximus ($r = 0.40$ and 0.49) and CT-assessed density of all muscles ($r = 0.47$-0.64). Conclusion: Muscle volume and CT-assessed density significantly correlated with femoral bone strength, serum total protein levels, and pre- and postoperative walking ability. These findings suggest that muscle CT analysis around the hip joint may serve as a valuable tool for assessing musculoskeletal status in patients with FNF.
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WC Geriatrics & Gerontology; Orthopedics; Rehabilitation; Surgery
SC Geriatrics & Gerontology; Orthopedics; Rehabilitation; Surgery
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Kamli, Hossam
Islam, Muhammad Torequl
TI Therapeutic Promises of Bioactive Linarin, a Glycosylated Flavonoid: A Comprehensive Review With Mechanistic Insight

SO JOURNAL OF TROPICAL MEDICINE
LA English
DT Review
DE flavonoid glycoside; linarin; molecular mechanism; pharmacological effects
ID cytochrome-c release; expression in-vitro; natural-products; drug discovery; cytokine production; daflon 500mg; risk-factors; apoptosis; disease; pharmacokinetics
AB Linarin, a flavonoid glycoside found in the Asteraceae, Lamiaceae, and Scrophulariaceae families, shows diverse therapeutic benefits in laboratory studies. This study aims to evaluate the pharmacological effects of linarin through clinical and preclinical experiments, investigating its mechanisms against different diseases. To achieve this, data collection and search operations were carried out (current as of April 09, 2024) in several reliable online databases, such as PubMed/Medline, Scopus, Springer Link, ScienceDirect, Wiley Online, Web of Science, and Google Scholar, as part of this research. Studies revealed that linarin provides benefits against inflammation and various diseases, including osteoporosis, osteoarthritis, liver injuries, diabetes, hypertension, and neurodegenerative conditions, such as Alzheimer's, ischemia-reperfusion, convulsions, and depression. Our results further reveal that linarin displays remarkable anticancer potentials through multiple molecular pathways, including apoptotic cell death, oxidative stress induction, cytotoxic effect, antiproliferative effect, genotoxic effect, and mitigation of cancer cell migration and invasion and migration against a range of malignancies, including lung, brain, prostate, and glioma cell cancers. Database reports and the current literature-based study suggest that linarin might be a prospective lead chemical for treating a range of illnesses and ailments. For linarin to be proven as a medicine, further clinical and preclinical trials are required.
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TI Nanotechnology in Orthopedic Care: Advances in Drug Delivery, Implants, and Biocompatibility Considerations
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DT Review
DE orthopedics; nanomaterials; toxicity of nanomaterials; biocompatibility; orthopedic implants; drug delivery; diagnostics; rheumatoid arthritis; osteoporosis; osteoarthritis
ID in-vivo; targeted delivery; oxide nanoparticles; bone; arthritis; cartilage; cells; osteoporosis; titanium; release
AB Nanotechnology has profoundly transformed medical science, with orthopedics experiencing significant advancements diagnostic techniques, drug delivery systems, and tissue regeneration. The complex nature of orthopedic tissues presents substantial challenges for conventional therapeutic interventions, but the development of nanomaterials with specialized chemical, physical, biological properties has facilitated the creation of novel treatment modalities. Nanotechnology has significantly advanced orthopedic care by enabling targeted drug delivery, enhanced implant performance, and improved diagnostic tools. This review uniquely integrates recent breakthroughs in biocompatible nanomaterials, focusing on their clinical translation and regulatory challenges. highlights the complexity of orthopedic tissues and the limitations of conventional therapies, emphasizing how nanomaterials address these through controlled drug release, and improved tissue regeneration. Key sections address advancements in drug delivery systems, innovative implant technologies, toxicity issues, and biocompatibility considerations. It also explores the existing regulatory landscape, challenges in clinical approval, and future directions for the successful translation of nanotechnologies in orthopedic care.
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TI Effects of regional variations and occupation on hand osteoarthritis: Insights from the research on osteoarthritis/osteoporosis against disability study
SO MODERN RHEUMATOLOGY
LA English
DT Article
DE Hand osteoarthritis; occupational workload; population-based; prevalence; regional variation
ID knee osteoarthritis; elderly-patients; japanese women; grip strength; united-states; finger joints; prevalence; association; population; determinants
AB Objectives This study aimed to investigate the prevalence of radiographic hand osteoarthritis (HOA) in older Japanese individuals in three distinct regions with unique geographic and occupational characteristics and explore the regional variations and factors, including occupational workload, that affect HOA.Methods We analysed the radiographic images and data of 1642 participants aged >= 60 years (mean, 75.6 years). After grading the radiographs of both hands using the modified Kellgren-Lawrence (KL) classification, HOA was defined as at least one joint with a KL grade >= 2, and severe HOA was defined as at least one joint with a KL grade >= 3.Results The overall prevalence rates of HOA and severe HOA were 95.9% and 54.2%, respectively. Regional differences were observed: residence in the mountainous region was associated with HOA and severe HOA, whereas residence in the coastal region was associated with only HOA. Occupational workload was associated with severe HOA in a dose-dependent manner, and heavy work was associated with a higher number of osteoarthritis-affected joints.Conclusion The present study revealed a high prevalence of HOA in older Japanese individuals and highlighted regional variations in HOA prevalence. A higher occupational workload was associated with a higher risk of severe HOA.
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PA GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
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WC Rheumatology
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PT J
AU Liu, Y

Chen, HL
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Gong, Yan
Liu, Lingjuan
Jiang, Yixuan
Ren, Hui
Jiang, Xiaobing
Shen, Gengyang
TI Plumbagin alleviates muscle atrophy in female mice through inhibiting the DANCR/NF-κB axis
SO PHYTOMEDICINE
LA English
DT Article
DE Plumbagin; DANCR; NF-kappa B pathway; myogenic differentiation; muscle atrophy
ID protein; pathway
AB Background: Muscle atrophy is a condition of the skeletal muscular system

closely related to inflammation and significantly affects a person's quality of life and physical activity. It is characterized primarily by the progressive loss of muscle mass, strength, and function. Plumbagin (PB), the main bioactive component of the traditional Chinese medicine Plumbago zeylanica L., has bFeen shown to treat various inflammatory diseases, such as osteoporosis, osteoarthritis, and sepsis. Furthermore, many biological processes, including inflammation, involve differentiation antagonistic nonprotein-coding RNA (DANCR). However, their role and clinical importance in myogenesis and amyotrophy are not well understood. Purpose: This study aimed to explore the role of DANCR and the inflammatory response in the anti-muscle atrophy effects of PB. Methods: The expression of DANCR in muscle atrophic mice and during myogenic differentiation was examined using quantitative reverse transcription PCR (RT-qPCR). The mechanism of DANCR in muscle atrophy was confirmed through gene knockdown, RNA sequencing (RNA-seq), RNA pull-down, RNA immunoprecipitation (RIP), immunofluorescence (IF), and luciferase reporter gene assays. Bioinformatics was utilized to investigate the mechanism by which PB treatment affects muscle atrophy. The relationship between PB and DANCR was verified by surface plasmon resonance (SPR) and RT-qPCR. Additionally, the role of PB in muscle atrophy was explored through its control of DANCR-mediated regulation of the NF-kappa B pathway. Finally, the effect of PB on the myogenic differentiation of human skeletal muscle cells (HsKMCs) was investigated. Results: DANCR expression was upregulated in the muscle tissues of mice with muscle atrophy and downregulated during myogenic differentiation. Knockout of DANCR promoted myogenic differentiation and significantly alleviated the loss of muscle mass, strength, and function in mice with muscle atrophy. The primary mechanism involved DANCR directly binding to the p65 protein to regulate NF-kappa B pathway activity. Experiments revealed that PB could target the degradation of DANCR, reduce the nuclear entry of p65, and inhibit the activation of the NF-kappa B pathway. Consequently, PB significantly inhibited myotube atrophy and the inflammatory response in HsKMCs and promoted their myogenic differentiation by regulating the NF-kappa B pathway. Conclusions: Our results suggest that PB regulates myogenesis and prevents amyotrophy by targeting the degradation of DANCR and inhibiting the activation of the NF-kappa B pathway. This study reveals the crucial role of DANCR in maintaining muscle physiology during muscle atrophy and identifies PB as an effective drug that can target DANCR degradation to alleviate muscle atrophy.
C1 [Liu, Yu; Chen, Honglin; Zhang, You; Shang, Qi; Qin, Weicheng; Lin, Feng; Liu, Huiwen; Chen, Xingda; Gong, Yan; Liu, Lingjuan; Jiang, Yixuan] Guangzhou Univ Chinese Med, Guangzhou 510405, Peoples R China.

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NR 49
TC 2
Z9 2
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U2 11
PU ELSEVIER GMBH
PI MUNICH
PA HACKERBRUCKE 6, 80335 MUNICH, GERMANY
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EA NOV 2024
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WC Plant Sciences; Chemistry, Medicinal; Integrative & Complementary Medicine; Pharmacology & Pharmacy
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AU Wei, GH
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Ao, J
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AF Wei, Guihuo
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Qin, Jianpu
Ao, Jun
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TI O-GlcNAcylation: Sagacious Orchestrator of Bone-, Joint-, and Spine-Related Diseases
SO JOURNAL OF PROTEOME RESEARCH
LA English
DT Review
DE O-GlcNAcylation; intervertebral disc degeneration; osteoarthritis; osteoporosis; osteosarcoma
ID n-acetylglucosamine modification; mesenchymal stem-cells; kinase-c isozymes; glcnac transferase; in-vitro; posttranslational modifications; transcription factor;

protein modification; chondrogenesis; differentiation
AB O-linked beta-N-acetylglucosamine glycosylation (O-GlcNAcylation), a post-translational modification of proteins, occurs in multiple physiological and pathological processes. Despite comprehensive study of protein modifications, such as phosphorylation, acetylation, and ubiquitination in musculoskeletal diseases, the role of O-GlcNAcylation in this field has been largely overlooked. However, in recent years, several studies have initially elucidated the biological mechanisms through which O-GlcNAcylation regulates the development and progress of musculoskeletal diseases, including osteoarthritis, osteoporosis, osteosarcoma, and intervertebral disc degeneration. This review aims to systematically and comprehensively summarize the existing evidence, sketching the contours of the underlying mechanisms and related signaling pathways, discussing the limitations and controversies, and providing guidance for future studies on the role of O-GlcNAcylation modifications in musculoskeletal diseases.
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TI Radiofrequency Echographic Multi Spectrometry-A Novel Tool in the Diagnosis of Osteoporosis and Prediction of Fragility Fractures: A Systematic Review
SO DIAGNOSTICS
LA English
DT Review
DE REMS; DXA; comparison; accuracy; fracture risk; osteoporosis
ID x-ray absorptiometry; bone-mineral density; osteoarthritis; spine; score
AB Background/Objectives: Given the significant economic and social burden of osteoporosis, there is growing interest in developing an efficient alternative to the traditional dual-energy X-ray absorptiometry (DXA). Radiofrequency Echographic Multi Spectrometry (REMS) is an innovative, non-ionizing imaging technique that recently emerged as a viable tool to diagnose osteoporosis and estimate the fragility fracture risk. Nevertheless, its clinical use is still limited due to its novelty and continuing uncertainty of long-term performance. Methods: In order to evaluate the accuracy of the REMS, a systematic review of the English-language literature was conducted. Three databases were searched for relevant publications from 1 January 2015 until 1 December 2024 using the keyword combinations "(radiofrequency echographic multi spectrometry OR REMS) AND (dual-energy X-ray absorptiometry OR DXA)". The initial search yielded 602 candidate articles. After screening the titles and abstracts following the eligibility criteria, 17

publications remained for full-text evaluation. Results: The reviewed studies demonstrated strong diagnostic agreement between REMS and DXA. Additionally, REMS showed enhanced diagnostic capabilities in cases where lumbar bone mineral density measurements by DXA were impaired by artifacts such as vertebral fractures, deformities, osteoarthritis, or vascular calcifications. REMS exhibited excellent intra-operator repeatability and precision, comparable to or exceeding the reported performance of DXA. The fragility score (FS), a parameter reflecting bone quality and structural integrity, effectively discriminated between fractured and non-fractured patients. Moreover, REMS proved to be a radiation-free option for bone health monitoring in radiation-sensitive populations or patients requiring frequent imaging to assess fracture risk. Conclusions: This current study underscores the robustness of REMS as a reliable method for diagnosing and monitoring osteoporosis and evaluating bone fragility via the FS. It also identifies critical knowledge gaps and emphasizes the need for further prospective studies to validate and expand the clinical applications of REMS across diverse patient populations.
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NR 72
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TI Which Approach to Choose to Counteract Musculoskeletal Aging? A Comprehensive Review on the Multiple Effects of Exercise
SO INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES
LA English
DT Review
DE aging; musculoskeletal system; physiology; senescence; senotherapeutic; physical exercise; prevention
ID mesenchymal stem-cells; skeletal-muscle; osteoblast differentiation; senescent cells; resveratrol; sirt1; bone; quercetin; expression; bioavailability
AB Aging is a complex physiological process that profoundly affects the functionality of the musculoskeletal system, contributing to an increase in the incidence of diseases such as osteoporosis, osteoarthritis, and sarcopenia. Cellular senescence plays a crucial role in these degenerative processes, promoting chronic inflammation and tissue dysfunction through the senescence-associated secretory phenotype (SASP). Recently, senotherapeutics have shown promising results in improving musculoskeletal health. Natural compounds such as resveratrol, rapamycin, quercetin, curcumin, vitamin E, genistein, fisetin, and epicatechin act on key signaling pathways, offering protective effects against musculoskeletal decline. On the other hand, molecules such as dasatinib, navitoclax, UBX0101, panobinostat, and metformin have been shown to be effective in eliminating or modulating senescent cells. However, understanding the mechanisms of action, long-term safety, and bioavailability remain areas for further investigation. In this context, physical exercise emerges as an effective non-pharmacological countermeasure, capable of directly modulating cellular senescence and promoting tissue regeneration, representing an integrated strategy to combat age-related diseases. Therefore, we have provided an overview of the main anti-aging compounds and examined the potential of physical exercise as a strategy in the management of age-related musculoskeletal disorders. Further studies should focus on identifying synergistic combinations of pharmacological and non-pharmacological interventions to optimize the effectiveness of anti-aging strategies and promoting healthier musculoskeletal aging.
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TI Musculoskeletal diseases, infections and vaccines: state of the art, research perspectives and educational needs
SO AGING CLINICAL AND EXPERIMENTAL RESEARCH
LA English
DT Review
DE Musculoskeletal disease; Infection; Vaccination; Older adults
ID rheumatoid-arthritis; influenza; frailty; risk
AB Musculoskeletal disorders are a significant public health burden concern, projected to increase in the coming decades, and will substantially contribute to the rising prevalence of functional impairment, frailty and disability in a growing global population. Since persons with musculoskeletal disorders tend to have immune dysfunction, inflammation or be taking immunosuppressive medication, prevention of vaccine-preventable diseases (VPDs) in this group is particularly important. The European Interdisciplinary Council for Aging (EICA) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) jointly convened a 2-day in-person and virtual meeting on 26-27 September 2023, to review the state of the evidence on the link between musculoskeletal diseases, infections and vaccines. We present here the Executive Summary of the proceedings of this meeting. We review the importance of physical activity in preventing or mitigating both musculoskeletal diseases and risk of infection. We summarize current knowledge of the impact of common VPDs on the development and progression of musculoskeletal diseases, and the role of selected vaccines in preventing onset and worsening of frailty and disability in these individuals. This report summarizes the evidence presented at the two-day meeting, highlighting the need to raise awareness among scientists, healthcare professionals, decision-makers, civil society and the general public about the long-term sequelae of VPDs, with focus on the health status of older patients with musculoskeletal diseases.
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TI Nucleic acid aptamers in orthopedic diseases: promising therapeutic agents for bone disorders
SO BONE RESEARCH
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DT Review
ID necrosis-factor-alpha; mesenchymal stem-cells; factor-kappa-b; macrophage inflammatory protein-1-alpha; human osteoarthritic chondrocytes; osteoclast-associated receptor; human articular chondrocytes; parathyroid-hormone 1-34; nitric-oxide production; affinity dna aptamers
AB Precision medicine has become a cornerstone in modern therapeutic strategies, with nucleic acid aptamers emerging as pivotal tools due to their unique properties. These oligonucleotide fragments, selected through the Systematic Evolution of Ligands by Exponential Enrichment process, exhibit high affinity and specificity toward their targets, such as DNA, RNA, proteins, and other biomolecules. Nucleic acid aptamers offer significant advantages over traditional therapeutic agents, including superior biological stability, minimal immunogenicity, and the capacity for universal chemical modifications that enhance their in vivo performance and targeting precision. In the realm of osseous tissue repair and regeneration, a complex physiological process essential for maintaining skeletal integrity, aptamers have shown remarkable potential in influencing molecular pathways crucial for bone regeneration, promoting osteogenic differentiation and supporting osteoblast survival. By engineering aptamers to regulate inflammatory responses and facilitate the proliferation and differentiation of fibroblasts, these oligonucleotides can be integrated into advanced drug delivery systems,

significantly improving bone repair efficacy while minimizing adverse effects. Aptamer-mediated strategies, including the use of siRNA and miRNA mimics or inhibitors, have shown efficacy in enhancing bone mass and microstructure. These approaches hold transformative potential for treating a range of orthopedic conditions like osteoporosis, osteosarcoma, and osteoarthritis. This review synthesizes the molecular mechanisms and biological roles of aptamers in orthopedic diseases, emphasizing their potential to drive innovative and effective therapeutic interventions.
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PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON, N1 9XW, ENGLAND
SN 2095-4700
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J9 BONE RES
JI Bone Res.
PD JUL 24
PY 2025
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IS 1
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DI 10.1038/s41413-025-00447-8
PG 29
WC Cell & Tissue Engineering
SC Cell Biology
GA 5IC5F
UT WOS:001536221300001
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AU Yoshimura, N
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TI Trends in the prevalence of hypovitaminosis D over a 10-year period in Japan: the research on osteoarthritis/osteoporosis against disability study 2005-2015
SO ARCHIVES OF OSTEOPOROSIS
LA English
DT Article
DE Vitamin D deficiency; Vitamin D insufficiency; Prevalence; Secular trend; Population-based cohort ROAD study
ID vitamin-d deficiency; bone; osteoporosis; association; criteria
AB The Summary We examined the trends in vitamin D insufficiency and deficiency over a 10-year period in the general population. The prevalence of deficiency significantly decreased (29.5% vs. 21.6%), whereas mean serum levels increased (23.3 ng/mL vs. 25.1 ng/mL). These trends may reduce the incidence of osteoporosis and osteoporotic fractures. Purpose: We aimed to clarify the trends in the prevalence of vitamin D insufficiency and deficiency in the general population using population-based cohort data from a baseline survey and a follow-up survey conducted 10 years later. Methods: A baseline survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study was conducted from 2005 to 2007. Blood samples were collected to measure serum 25-hydroxyvitamin D (25D) and intact parathyroid hormone levels from 1,683 participants (595 men, 1,088 women). Participants also completed an interviewer-administered questionnaire, and underwent bone mineral density measurements and radiographic examinations. The fourth survey was conducted from 2015 to 2016 with 1,906 individuals (637 men, 1,269 women), including both follow-up participants from the baseline survey and newly recruited individuals to increase the sample size for future longitudinal analyses. All participants completed assessments identical to those in the baseline survey. Vitamin D deficiency and insufficiency were defined as serum 25D levels of < 20 ng/mL and >= 20 ng/mL but < 30 ng/mL, respectively. Results: The mean serum vitamin D levels were 23.3 ng/mL at baseline and 25.1 ng/mL at the fourth survey, indicating a significant increase ($p < 0.001$). The prevalences of vitamin D insufficiency and deficiency were 52.9% and 29.5%, respectively, at baseline, and 54.8% and 21.6%, respectively, in the fourth survey, indicating a significant decrease in vitamin D deficiency ($p <$

0.001). Conclusions: In this population-based survey with a 10-year interval, the prevalence of hypovitaminosis D significantly decreased. This favourable trend may contribute to future reductions in the incidence of osteoporosis and osteoporotic fractures.
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SN 1862-3522
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J9 ARCH OSTEOPOROS
JI Arch. Osteoporos.
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WC Endocrinology & Metabolism; Orthopedics
SC Endocrinology & Metabolism; Orthopedics
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PT J
AU Li, K
Hu, SH
Chen, H
AF Li, Ke
Hu, Sihan
Chen, Hao
TI Cellular senescence and other age-related mechanisms in skeletal diseases
SO BONE RESEARCH
LA English

DT Review
ID vertebral end-plate; bone-marrow; intervertebral disc; beta-galactosidase; stem-cell; rheumatoid-arthritis; senile osteoporosis; articular-cartilage; oxidative stress; nucleus pulposus
AB Cellular senescence and its senescence-associated secretory phenotype (SASP) represent a pivotal role in the development of skeletal diseases. Targeted elimination or rejuvenation of senescent cells has shown potential as a therapeutic strategy to reverse age-related skeletal senescence and promote bone regeneration. Meanwhile, other age-related mechanisms, involving altered cellular functions, impaired intercellular crosstalk, disturbed tissue microenvironment, and decreased regenerative capacity, synergistically contribute to the pathogenesis. In this review, we outline the cellular senescence and other age-related mechanisms in developing skeletal diseases, including osteoporosis, intervertebral disc degeneration, osteoarthritis, rheumatoid arthritis, bone tumors and ankylosing spondylitis, with the aim of comprehensively understanding their detrimental effects on the aged skeleton and screening the potential targets for anti-aging therapy within the skeletal system.
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TI The functional roles and mechanisms of polyamines in age-related bone diseases
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DT Review
DE Polyamine; Bone disease; Osteoporosis; Osteoarthritis; Sarcopenia; Bone metabolism; Spermine; Spermidine
ID spermidine; autophagy; metabolism; risk; eflornithine; inhibition; muscle; cells
AB Age-related bone diseases such as osteoporosis, osteoarthritis, and sarcopenia present complex pathogenesis. These conditions are associated with high morbidity, disability, and mortality rates, underscoring the urgent need for effective prevention and treatment strategies. Polyamines, a group of small-molecule compounds, regulate critical biological processes, including cell proliferation, differentiation, and apoptosis, and show potential bone-protective effects. Following the elucidation of polyamines' therapeutic effects in cancer and neurodegenerative diseases, growing research attention has been directed toward their role in age-related bone disorders. This review synthesizes the current understanding of polyamines' mechanisms in age-related bone diseases, analyzing their biological functions and bone-protective effects to explore the therapeutic potential for these conditions, thereby offering valuable perspectives to guide future investigations and clinical applications in this emerging field.
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AU Park, SH
AF Park, See-Hyoung
TI Recent Research on the Role of Phytochemicals from Ginseng in Management of Osteosarcoma, Osteoporosis, and Osteoarthritis
SO NUTRIENTS
LA English
DT Review
DE ginseng; ginsenoside; polysaccharide; extract; osteosarcoma; osteoporosis; osteoarthritis
ID inhibits osteoclast differentiation; glucocorticoid-induced osteoporosis; panax-quinquefolius l.; korean red ginseng; cell-cycle arrest; inflammatory mediators; mg-63 cells; dna-damage; compound k; ginsenosides
AB Ginseng phytochemicals have attracted considerable attention for their potential therapeutic applications in bone-related diseases including osteosarcoma, osteoporosis, and osteoarthritis. Recent research has highlighted the promising effects of ginsenosides and polysaccharides from ginseng by studying multi-target effects and combination therapies in osteosarcoma progression. Beyond osteosarcoma, ginseng phytochemicals have been explored for their effects on osteoporosis. Various ginsenosides and ginseng extract were shown to regulate signaling pathways involved in activating osteoblast and inhibiting osteoclast in vitro and in vivo models. Ginseng ginsenosides have also demonstrated potential anti-osteoarthritic properties. Recent studies discussed how ginsenoside reduced inflammation and cartilage degradation as a therapeutic candidate for osteoarthritis management. In this review, we examine the anti-osteosarcoma, anti-osteoporotic, and anti-osteoarthritic activities of ginseng-derived phytochemicals reported in studies published between 2014 and 2024. This review also provides a comprehensive overview of the working mechanisms of these compounds in various model systems. Furthermore, we address the limitations of current research approaches and outline future directions to maximize the therapeutic application of ginseng phytochemicals in the management of bone-related diseases.
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TI Exploring the Role of Exercise and the Lysosomal Cathepsin Family in the Regulation of Vascular-Musculoskeletal Degenerative Diseases
SO FASEB JOURNAL
LA English
DT Review
DE exercise; lysosomal cathepsin family; musculoskeletal degenerative diseases; vascular aging
ID skeletal-muscle; older-adults; endochondral ossification; knee osteoarthritis; bone loss; cells; women; expression; gene; osteoporosis
AB Musculoskeletal degenerative diseases significantly compromise patient quality of life through muscle loss, bone fragility, and cartilage degeneration. Given the established link between vascular aging and musculoskeletal disorders, the vascular-skeletomuscular axis represents a complex network wherein conditions interact via mechanisms including impaired blood flow, inflammation, oxidative stress, and hormonal imbalances. As pharmacological interventions targeting lysosomal cathepsins face developmental and application challenges, exploring non-pharmacological alternatives becomes imperative. This review investigates the regulatory roles of the lysosomal cathepsin family, especially cathepsins B, K, and L, in musculoskeletal degenerative diseases and evaluates how exercise interventions modulate their activities. It proposes exercise as a viable non-pharmacological strategy to selectively influence lysosomal cathepsin functions, thereby offering therapeutic potential in managing vascular-musculoskeletal degenerative diseases.

The review elucidates several key concepts: the intricate interaction between vascular aging and musculoskeletal degenerative pathologies; the pivotal roles of lysosomal cathepsins in disease progression through metabolic regulation, inflammatory modulation, macrophage polarization, and autophagy dysfunction; and the multifaceted mechanisms by which exercise influences cathepsin activity, including calcium homeostasis, cellular energy metabolism enhancement, inflammatory response reduction, autophagy stimulation, myokine secretion, and vascular function improvement. This comprehensive analysis provides novel insights into exercise as a selective modulator of lysosomal cathepsin activity, highlighting its significant potential for advancing diagnostic and clinical therapeutic approaches.
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TI The Multifaceted Role of p53 in Musculoskeletal Diseases: A Comprehensive Review
SO INTERNATIONAL JOURNAL OF RHEUMATIC DISEASES
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DE gout; lower back pain; musculoskeletal diseases; osteoarthritis; osteoporosis; p53; rheumatoid arthritis; scoliosis
ID nucleus pulposus cells; chondrocyte apoptosis; oxidative stress; rheumatoid-arthritis; cellular senescence; bone; osteoarthritis; gene; degeneration; pathogenesis
AB Background While extensively studied for its central role in tumor suppression (regulating cell cycle, DNA repair, and apoptosis), the p53 gene is now recognized for its significant involvement in musculoskeletal diseases. Aberrant p53 expression and function are key factors in the pathogenesis and progression, although the specific mechanisms and clinical change potential remain incompletely defined.Objective This review systematically summarizes the multifaceted roles of p53 in major musculoskeletal diseases, analyzes the molecular mechanisms driving disease progression, and evaluates its potential as a therapeutic target.Methods A comprehensive literature search was conducted in PubMed January 2008 to March 2025 using keywords including P53, osteoporosis, osteoarthritis, rheumatoid arthritis, gout, low back pain, and scoliosis. Original research, reviews, and clinical trials focusing on p53 mechanisms were included. 90 relevant articles were selected for analysis.Results & Conclusion p53 critically influences the development and progression of musculoskeletal diseases (osteoporosis, osteoarthritis, rheumatoid arthritis, low back pain, gout, and scoliosis) through diverse mechanisms: Disrupting bone formation/resorption balance (via the p53-Nedd4-Runx2 axis in osteoporosis). Promoting chondrocyte apoptosis (via the miR-34a-SIRT1-p53 pathway in osteoarthritis). Modulating inflammatory mediators (TNF-alpha, IL-6 in rheumatoid arthritis). Regulating oxidative stress responses (p53-SLC2A9 axis in gout). p53 exhibits dual roles (pro-apoptotic vs. anti-inflammatory), necessitating precise targeting strategies. Promising therapeutic interventions include p53-focused gene editing (CRISPR/Cas9), small-molecule inhibitors (PFT-alpha), and natural products (naringin). However, further clinical validation is essential. Future research requires multidisciplinary approaches to deepen understanding of p53 mechanisms and advance clinical applications in musculoskeletal disorders.
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TI Advances in copper-containing biomaterials for managing bone-related diseases
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ID calcium-phosphate cement; mesenchymal stem-cells; in-vitro; cartilage repair; bioactive glass; antibacterial activity; antimicrobial activity; cu; alloy; osteonecrosis
AB Bone-related diseases pose a major challenge in contemporary society, with significant implications for both health and economy. Copper, a vital trace metal in the human body, facilitates a wide range of physiological processes by being crucial for the function of proteins and enzymes. Numerous studies have validated copper's role in bone regeneration and protection, particularly in the development and expansion of bone collagen. Owing to copper's numerous biological advantages, an increasing number of scientists are endeavoring to fabricate novel, multifunctional copper-containing biomaterials as an effective treatment strategy for bone disorders. This review integrates the current understanding regarding the biological functions of copper from the molecular and cellular levels, highlighting its potential for bone regeneration and protection. It also reviews the novel fabrication techniques for developing copper-containing biomaterials, including copper-modified metals, calcium phosphate bioceramics, bioactive glasses, bone cements, hydrogels and biocomposites. The fabrication strategies and various applications of these biomaterials in addressing conditions such as fractures, bone tumors, osteomyelitis, osteoporosis, osteoarthritis and osteonecrosis are carefully elaborated. Moreover, the long-term safety and toxicity assessments of these biomaterials are also presented. Finally, the review addresses current challenges and future prospects, in particular the regulatory challenges and safety issues faced in clinical implementation, with the aim of guiding the strategic design of multifunctional copper-based biomaterials to effectively manage bone-related diseases.
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AF Hua, Yu
Jaiswal, Suman
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Wang, Xinwei
TI Direct observation of the strong thermal non-equilibrium between optical and acoustic phonons in monolayered 2D materials
SO APPLIED PHYSICS LETTERS
LA English
DT Article
ID hot-carrier diffusion; transport; graphene; raman
AB Quantifying thermal non-equilibrium between different phonon branches in supported monolayered two-dimensional materials remains a significant challenge due to complex substrate interactions and optical interference in Raman measurements. Here, we report on the direct quantification of optical-acoustic phonon thermal non-equilibrium in supported monolayered WS2 materials by leveraging the distinct thermal response of optical phonons (OPs) and acoustic phonons (APs) under modulated laser excitation of different frequencies. The temperature response of different phonon branches is separated based on the measured Raman shift power coefficient (psi) with high precision. The reduction of the laser spot radius from similar to 1.7 to similar to 0.4 mu m increases the psi(OA)/psi(AP) ratio by over 2.5 times, revealing a pronounced enhancement of optical-acoustic phonon thermal non-equilibrium. Comparisons between transferred monolayered WS2 and hetero-bilayered WS2/WSe2 show that the heterogeneous interface strongly strengthens optical to acoustic phonon scattering. In addition, smaller laser spots intensify the hot carrier diffusion effect, reducing the associated OP-AP temperature difference by over 60%. Our method establishes a powerful experimental platform for probing phonon transport in nanoscale materials.
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Yam, Michael Gui Jie

Chew, Justin Linghui
Tan, Alvin Wai Kit
Sidarta, Ananda
Yee, Emily
Chua, Karen Sui Geok
TI Targeting osteosarcopenia and multimorbidity for frailty prevention through identification and deep phenotyping methods in healthy ageing and high-burden disease cohorts (OPTIMA-C): a longitudinal observational cohort study protocol for neuromusculoskeletal muscle health
SO BMJ OPEN
LA English
DT Article
DE Frailty; Stroke; Brain Injuries; Knee; Breast tumours; Physical Fitness
ID older-adults; sarcopenia; ultrasound; osteoporosis; validity; architecture; reliability; consensus; people; stroke
AB Introduction Sarcopenia and frailty have been identified as negative predictors of health outcomes. Patients with stroke, traumatic brain injury (TBI), knee osteoarthritis (OA) and breast cancer commonly experience low physical activity levels in the chronic phase of recovery. This prospective study aims to explore the feasibility of multimodal screening and longitudinal tracking of various biomarkers from the acute to chronic phase of disease to determine the relationship with frailty outcomes.Methods and analysis A prospective longitudinal observational cohort study involving Asian populations is planned over 3 years. Enrolled participants with index conditions of acute stroke, TBI, knee OA and breast cancer will be recruited from rehabilitation hospitals and clinics and followed longitudinally. Reference thresholds from the Asian Working Group on Sarcopenia will be used. Variables include self-reported questionnaires, disease and comorbidity characteristics, anthropometric measurements, appetite questionnaires, muscle ultrasound (MUS), muscle/bone mass, blood biomarkers and markerless gait motion systems. In particular, physical performance (short physical performance battery and hand grip strength), sarcopenia (SARC-F questionnaire) and frailty assessment (FRAIL score, clinical frailty scale), four-region MUS, body composition analysis, dual X-ray absorptiometry, bone mineral densitometry, physical activity levels (International Physical Activity Questionnaire for the elderly [IPAQ-E], fitness trackers) and health-related quality of life assessment (EuroQoL-5D questionnaire five level [EQ5D-5L]) will be used. Blood biomarkers measuring metabolic health (eg, glycated haemoglobin, cholesterol, fasting glucose and 25-OH vitamin D) and inflammation (eg, Tumor Necrosis Factor-alpha [TNF-alpha] and Monocyte Chemoattractant Protein-1 [MCP-1]) will be measured at baseline. Data collection will take place at postrecruitment baseline (hospital admission), 1, 6 months, 12 months and 2 years postrecruitment (inpatient) and at postrecruitment baseline, 6 months, 12 months and 2 years postrecruitment (outpatient).Ethics and dissemination Ethical approval has been obtained from the National Healthcare Group Domain Specific Review Board

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TI Deciphering the toxicological mechanisms of per-and polyfluoroalkyl substances (PFAS) in musculoskeletal disorders via integrated network toxicology and molecular docking
SO ENVIRONMENT INTERNATIONAL
LA English
DT Article
DE PFAS; Musculoskeletal disorders; Network toxicology; Molecular docking
ID perfluoroalkyl substances; growth-factor; association; osteoarthritis; proteins
AB Per-and polyfluoroalkyl substances (PFAS) have been extensively used in everyday products; however, their effects on human health remain largely unknown. This study aimed to investigate the potential mechanisms by which PFAS may contribute to functional disorders in the human musculoskeletal system. Four representative musculoskeletal disorders were selected, which included intervertebral disc degeneration, myositis, osteoarthritis, and osteoporosis. Advanced network toxicology approaches integrating data from the Comparative Toxicogenomics Database (CTD) and GeneCards identified potential PFAS-associated targets for each disorder. Molecular docking simulations were employed to assess interactions between PFAS and target proteins. Molecular docking of a series of PFAS molecules against multiple protein targets revealed strong binding affinities. Prioritization based on average binding energies highlighted the targets with the greatest PFAS-binding potential. A subsequent comprehensive analysis further discussed these findings by integrating the functional roles of the targets and the classification of the various PFAS compounds. Evidence synthesis confirmed that these core targets are critically involved in key pathological processes common to musculoskeletal diseases, including chronic inflammation, oxidative stress, apoptosis, extracellular matrix degradation, and impaired bone remodeling. This study provides innovative insights into the mechanisms by which environmental pollutants contribute to human diseases, thereby establishing a theoretical foundation for disease prevention and therapeutic strategies.
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TI Calcium pyrophosphate deposition disease is associated with increased risk of fractures: A retrospective cohort study using electronic health record data
SO OSTEOARTHRITIS AND CARTILAGE
LA English
DT Article
DE Calcium pyrophosphate deposition; Pseudogout; Osteoarthritis; Fracture; Osteoporosis; Bone mineral density
ID chondrocalcinosis
AB Objective: To evaluate the risk of fractures in older adults with calcium pyrophosphate deposition (CPPD) disease and osteoarthritis (OA) compared to those with OA alone, and to assess site-and gender-specific fracture risk. Methods: Using predominantly North American electronic health record data from 2005-2025, we defined CPPD as patients aged >= 60 years with >= 2 administrative codes for CPPD plus OA, excluding other inflammatory arthritides. Comparators were defined analogously with >= 2 OA codes but without CPPD. The primary outcome was any fracture of spine, upper limb, lower limb. We used Cox proportional hazards models 1:1 propensity score-matched for demographics, comorbidities, and medications. Subgroup analyses assessed gender-specific outcomes and site-specific fractures. Sensitivity analyses excluded individuals with prior exposure to glucocorticoids or anti-osteoporosis medications or prior fracture history. Results: Among 20,176 matched pairs (mean age 73 years, 59% female) with 4015 and 3349 fracture events over 81,291 and 85,802 patient-years, CPPD was associated with 29% increased hazard of any fracture (HR 1.29, 95%CI 1.23, 1.35) which was consistent in males (HR 1.36, 95%CI 1.23, 1.49) and females (HR 1.30, 95%CI 1.23, 1.38). Site-specific analyses similarly showed elevated fracture risks at the upper limb (HR 1.37; 1.28, 1.46), lower limb (HR 1.31; 1.23, 1.39), and spine (HR 1.18; 1.11, 1.26). Results were similar across all sensitivity analyses. Conclusion: CPPD disease is associated with increased fracture risk across gender and fracture sites. Clinicians should consider screening for bone health in these patients. Future research should clarify underlying mechanisms and refine targeted interventions. (c) 2025 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies.
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TI Biomedical Applications of Functionalized Composites Based on Metal-Organic Frameworks in Bone Diseases
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ID drug-delivery-system; osteogenic differentiation; therapy; nanoparticles; osteosarcoma; scaffolds; membrane; release; mofs; ag
AB Every year, millions of people worldwide suffer from bone tissue damage caused by bone trauma and surgical operations, as well as diseases such as osteoporosis, osteoarthritis, osteomyelitis, and periodontitis. Bone defect repair is one of the major challenges in the field of regenerative medicine. Although bone grafts are the gold standard for treating bone defects, factors such as donor

sources and immune responses limit their application. Functionalized nanomaterials have become an effective means of treating bone diseases due to their good biocompatibility and osteoinductivity, anti-inflammatory, and antibacterial properties. Metal-organic frameworks (MOFs) are porous coordination polymers composed of metal ions and organic ligands, featuring unique physical properties, including a high surface area-volume ratio and porosity. In regenerative medicine, MOFs function as the functions of drug carriers, metal ion donors, nanozymes, and photosensitizers. When combined with other functional materials, they regulate cellular reactive oxygen species, macrophage phenotypic transformation, bone resorption, osteogenesis, and mineralization, providing a new paradigm for bone tissue engineering. This study reviews the classification of functionalized MOF composites in biomedicine and the application of their synthesis techniques in bone diseases. The unique in vivo and in vitro applications of MOFs in bone diseases, including osteoarthritis, osteoporosis, bone tumors, osteomyelitis, and periodontitis, are explored. Their properties include excellent drug loading and sustained release abilities, high antibacterial activity, and bone induction abilities. This review enables readers to better understand the cutting-edge progress of MOFs in bone regeneration applications, which is crucial for the design of and functional research on MOF-related nanomaterials.
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TI Research Progress on Icariin Promoting Bone Injury Repair and Regeneration
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DE icariin; bone regeneration; signaling pathways; anti-inflammatory; angiogenesis; multi-organ protection; pharmacokinetics; multi-target effects
ID osteogenic differentiation; rat model; network pharmacology; osteoporosis; cells; epimedium; apoptosis; osteoarthritis; cytotoxicity; metabolism
AB Icariin (ICA) is a bioactive flavonoid compound extracted from Epimedium plants. In recent years, it has attracted significant research interest in the field of bone tissue repair due to its pharmacological effects via multiple targets and pathways. Studies have shown that ICA promotes the osteogenic differentiation of mesenchymal stem cells (MSCs) and enhances bone matrix formation by regulating signaling pathways such as Akt and Wnt/beta-catenin. It concurrently inhibits osteoclast activity to maintain the balance of bone remodeling, thereby simultaneously stimulating new bone regeneration and suppressing bone resorption. At the same time, ICA exerts potent anti-inflammatory and antioxidant effects and promotes angiogenesis, improving the local microenvironment of bone injury and significantly facilitating the regeneration of bone and cartilage tissues. Additionally, ICA exhibits notable protective effects in multiple organ systems including the cardiovascular, hepatic, renal, and nervous systems. Specifically, ICA reduces cardiomyocyte apoptosis and fibrosis to preserve cardiac function, improves hepatic metabolic function and alleviates oxidative stress, attenuates renal inflammation and fibrosis, and-through neuroprotective actions-reduces neuroinflammation and promotes neuronal survival. These multi-organ effects help optimize the systemic environment for bone healing. However, ICA faces significant pharmacokinetic challenges. It has low oral bioavailability (due to poor absorption and extensive first-pass metabolism) as well as a short half-life. Consequently, maintaining effective drug concentrations in vivo is difficult, which limits its therapeutic efficacy and impedes clinical translation. To fully realize its regenerative potential, advanced drug delivery strategies (e.g., nanocarrier-based delivery systems) are being explored to enhance ICA's bioavailability and prolong its duration of action. Overall, ICA's multi-modal actions on bone cells, the immune microenvironment, and systemic factors make it a promising multi-target agent for bone regeneration. Addressing its pharmacokinetic limitations through optimized delivery and conducting further clinical studies will be crucial to realize its full therapeutic potential. This review provides a comprehensive overview of recent advances and challenges in translating ICA's benefits into orthopedic therapy.
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TI The Role of Oral and Gut Microbiota in Bone Health: Insights from Bacterial Extracellular Vesicles
SO MICROORGANISMS
LA English
DT Review
DE bacterial extracellular vesicles; microbiota; dysbiosis; osteoporosis; osteoarthritis; neuroinflammation
ID outer-membrane vesicles; porphyromonas-gingivalis; osteoclast differentiation; periodontal-disease; tgf-beta; biogenesis; infection; system; mass; pathogenesis
AB Bone health is critically influenced by the oral and gut microbiota, which are

among the largest microbial reservoirs in the human body. These microbiota play essential roles in maintaining bone mass through immune modulation, metabolite production, and nutrient resorption. Recent observations have underscored that extracellular vesicles (EVs) derived from oral and gut microbiota may circulate to the brain and bone marrow, suggesting their integral roles in the gut-brain-bone axis and oral-brain-bone axis. This review outlines the current research status of bacterial extracellular vesicles (BEVs), including their biogenesis, classification, structural features, and cargo composition, with emphasis on factors influencing cargo heterogeneity and the consequences of cellular uptake and presentation. Oral-microbiota-derived BEVs and their cargo associated with bone health are highlighted, along with recent evidence linking BEVs to systemic dis-eases and the potential integration into the oral-gut-bone axis. Preclinical animal studies on BEV dosage, routes of administration, and disease models are summarized, together with the limitations of current approaches and strategies for engineering BEVs. Finally, an overview of translational applications and future therapeutic prospects is provided, aiming to advance the understanding of BEVs as innovative tools for the treatment and prevention of bone-related diseases.
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TI Recent advances in targeting the cGAS-STING pathway for immunotherapy in orthopedic diseases
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Review
DE cGAS-STING pathway; orthopedic diseases; innate immunity; bone remodeling; immunotherapy
ID cyclic gmp-amp; innate immune-response; cytosolic dna; 2nd-messenger; inflammation; combination; mechanism
AB With increasing evidence highlighting the role of immune dysregulation in orthopedic diseases such as osteoarthritis, osteoporosis, intervertebral disc degeneration, delayed fracture healing, and bone tumors, the cyclic GMP-AMP synthase-stimulator of interferon genes (cGAS-STING) pathway has emerged as a central mediator of innate immune sensing and sterile inflammation. This review summarizes the core mechanisms of cGAS-STING activation and its involvement in regulating inflammatory responses, bone remodeling, cell death, and immune cell polarization in musculoskeletal tissues. In particular, we discuss recent findings on how aberrant cGAS-STING signaling contributes not only to chronic inflammatory bone loss but also to the tumor immune microenvironment in primary bone cancers and bone metastases. Furthermore, we highlight the therapeutic prospects of targeting this pathway using agonists or inhibitors, which show promise for novel immunomodulatory approaches in the treatment of orthopedic diseases, including skeletal malignancies.
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TI Weight-Adjusted Waist Index (WWI)-A Promising Anthropometric Indicator of Depressive Symptoms in Hospitalized Older Patients
SO NUTRIENTS
LA English
DT Article
DE WWI; BMI; depressive symptoms; older adults
ID body-mass index; instrumental activity; obesity; association; risk; people; dyslipidemia; hypertension; osteoporosis
AB Objectives: The aim of this study was to evaluate which anthropometric index, either body mass index (BMI) or weight-adjusted waist index (WWI), is more accurately associated with the prevalence of the most common chronic diseases and components of geriatric assessment in hospitalized older adults. Methods: The study included a total of 2945 hospitalized older adults (median age 82 years). The associations between the presence of chronic diseases and Comprehensive Geriatric Assessment (CGA) results were compared with WWI and BMI values. Results: The WWI was significantly higher in both sex groups suffering from hypertension, diabetes, osteoarthritis, and depression. In women, the parameter was increased among individuals with previous myocardial infarction, who presented heart failure symptoms or had chronic kidney disease diagnosed, whereas in men, among those with pulmonary diseases and osteoporosis, WWI was related to many CGA parameters oftentimes where BMI proved to fail. There was a positive correlation of WWI with the presence of depressive symptoms assessed with the geriatric depression scale (GDS) but no significant correlation with BMI. In multiple logistic regression models, WWI was a stronger predictor of depression as compared to waist circumference or the waist-to-height ratio. Conclusions: There is an association between a higher WWI and depression diagnosis as well as the presence of depressive symptoms according to the GDS in hospitalized older adults, both women and men. There is no such correlation between depression and BMI. Both high BMI and high WWI values seem to identify older patients with cardiometabolic diseases such as hypertension and diabetes. According to this study, WWI seems to be a promising indicator of depression risk and, similarly to BMI, a useful parameter for the assessment of cardiometabolic risk in older hospitalized adults.

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Lee, Yong Seuk
TI Osteoarthritis progression pattern based on patient specific characteristics using machine learning
SO NPJ DIGITAL MEDICINE
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DT Article
ID individual radiographic features; bone-mineral density; knee osteoarthritis; disease; risk; mass; phenotypes; incident; atlas; hip
AB This study aimed to identify key factors associated with different progression patterns of early osteoarthritis (OA) by developing a predictive model using patient-specific characteristics. From 2003 to 2017, data from 833 knees were analyzed. Demographic factors included age, body mass index, bone mineral density (BMD), metabolic diseases, and other comorbidities. Radiographic factors included joint space narrowing (JSN) and osteophyte formation grades. Three classification models were developed using logistic regression and a light gradient boosting machine: unicompartmental/tricompartmental OA, tricompartmental JSN-dominant OA, and tricompartmental osteophyte-dominant OA. Feature importance was evaluated using SHapley Additive exPlanations feature explanations. Patients with osteoporosis were likely to progress to tricompartmental OA with JSN, while those with a high BMD were likely to progress to unicompartmental OA. Metabolic disease-related OA was associated with tricompartmental OA involving large osteophytes. Identifying OA progression patterns and patient information may enable more effective personalized treatment and prevention strategies in the future.
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DI 10.1038/s41746-025-01878-7
PG 11
WC Health Care Sciences & Services; Medical Informatics
SC Health Care Sciences & Services; Medical Informatics
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PT J
AU Hou, ZX
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Gao, YZ
AF Hou, Zhenxing
Wang, Haoran
He, Bing
Wang, Qichao
Gao, Yanzheng
TI The association between glycemic indicators and bone mineral density and osteoporosis: a cross-sectional study
SO SCIENTIFIC REPORTS
LA English
DT Article
DE HbA1c; Bone mineral density; Osteoarthritis; Fasting plasma glucose; Cross-sectional study
ID fracture risk; older white; complications; pentosidine; glucose; adults; dxa; qus
AB To investigate the relationship between glycemic indicators (HbA1c and FPG) and bone mineral density (BMD) as well as osteoporosis in adults. A total of 1445 participants from the "The longitudinal investigation of osteoarthritis and cardiovascular health status" cohort were recruited and classified into normal BMD, osteopenia, and osteoporosis groups based on BMD. Data on sociodemographic factors, anthropometric measurements, medical history, and FPG samples were collected. BMD was measured by tibial ultrasound. Logistic regression analysis was performed to calculate the Odds Ratio (OR) and 95% confidence interval (CI), with adjustments for confounding factors. Participants in the osteopenia and osteoporosis groups were older, had higher triglycerides and body mass index, and fewer smokers and alcohol consumers compared to the normal BMD group. HbA1c levels were significantly lower in the osteopenia and osteoporosis groups than in the normal BMD group, while FPG showed no significant differences. Logistic regression indicated a significant negative correlation between HbA1c and the risk of osteoporosis (OR (95% CI) 0.914 (0.838, 0.997)) and osteopenia (OR (95% CI) 0.904 (0.826, 0.989)). After adjusting for confounding factors, a significant positive correlation exists between HbA1c and BMD, and higher HbA1c levels are associated with a relatively lower risk of osteoporosis. These findings highlight the importance of considering long-term blood glucose control in clinical practice for bone health management.
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PA HEIDELBERGER PLATZ 3, BERLIN, 14197, GERMANY
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SC Science & Technology - Other Topics
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AU Chen, MY
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Lei, L
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AF Chen, Minyou
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TI Role of SOST in Response to Mechanical Stimulation in Bone and Extraosseous Organs
SO BIOMOLECULES
LA English
DT Review
DE SOST; extra-skeletal organs; osteoporosis; exercise; mechanical stimulation
ID serum sclerostin increases; articular-cartilage; disease; expression; decreases; men
AB Sclerostin (SOST) is a specific osteocyte protein. During the differentiation and proliferation of osteoblasts and osteoclasts, the high expression of SOST can inhibit bone formation and contribute to osteoporosis and the bone metastasis of malignant tumors. Most of the research on SOST has focused on bone cells, but studies have found that SOST is not a specific product of bone cells but that it is also expressed by articular chondrocytes. SOST can regulate the progression of osteoarthritis in bone and cartilage, promote subchondral bone sclerosis, and inhibit cartilage degeneration. A review of the literature found that SOST can not only regulate bone metabolism, but it is also expressed in cardiovascular, kidney, liver, and other tissues, influencing the occurrence and development of diseases in these organs and tissues. Studies have found that diseases of extra-bone organs, such as atherosclerosis, aneurysm, chronic kidney disease, and cirrhosis, may be related to the expression of SOST. Simultaneously, long-term exercise can reduce SOST levels, especially in areas of high bone strain. Prolonged exercise induces bone adaptation to mechanical stress, resulting in diminished responsiveness of bone cells to exercise and a reduction in serum SOST levels. Short-term acute exercise can elevate serum SOST levels, but these results are often limited by age, gender, and energy status. In general, serum SOST rises immediately after

short-term acute exercise, returning to baseline or even decreasing after exercise.
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PA MDPI AG, Grosspeteranlage 5, CH-4052 BASEL, SWITZERLAND
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JI Biomolecules
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WC Biochemistry & Molecular Biology
SC Biochemistry & Molecular Biology
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Thakar, Ranee
TI Does the fetal head station and position affect the pelvic floor muscles in labour? A prospective study using 3 dimensional transperineal ultrasound
SO EUROPEAN JOURNAL OF OBSTETRICS & GYNECOLOGY AND REPRODUCTIVE BIOLOGY
LA English
DT Article
DE Levator ani muscle avulsion; Fetal head position; Fetal head station; Transperineal ultrasound

ID levator ani muscle; reliability; 2nd-stage; diagnosis; avulsion; delivery; stretch; hiatus; impact
AB Aims: The passage of the fetus through the birth canal, stretches the soft tissues of the pelvic floor, in particular the levator ani muscle. Excessive distension of the levator ani muscle (LAM) hiatus and LAM avulsions are associated with pelvic organ prolapse. Our aim was to evaluate the impact of the fetal head position and station on the LAM. Methods: A prospective cross-sectional observational study of women undergoing their first vaginal birth. Women were examined vaginally by a doctor or midwife to assess the fetal head station in relation to the ischial spines. Three dimensional transperineal ultrasound (3D TPUS) was performed on these women in the second stage of labour when they had a vaginal examination. The 3D TPUS was done to identify LAM avulsion and measure the anteroposterior (AP) diameter and the hiatal area. In addition, transabdominal ultrasound (TAUS) was used to determine the fetal head position. A Kruskal-Wallis test was performed to compare non-parametric variables. Results: 274 women were invited and 264 (95 %) agreed to participate. 52 women had a TPUS performed during the second stage of labour. The fetal head position was occiput anterior (OA) 32 (62 %), occiput posterior (OP) 9 (17 %), and occiput transverse (OT) 11 (21 %). There was a significant increase in the AP diameter and hiatal area as the fetal head descended from-1 to +2. (AP diameter: 6.1 vs 8.1 cm, p = 0.002; hiatal area: 16.3 vs 30.3 cm2, p = 0.01). The fetal head position did not affect the AP diameter or hiatal area measurements. No LAM avulsions were diagnosed in the second stage of labour before birth. No LAM avulsions were found following caesarean section (n = 7). Women who gave birth vaginally were invited to have a repeat scan after three months, and 35/45 (78 %) came for follow-up. LAM avulsions were diagnosed three months postpartum in 10/35 (29 %) women following their vaginal birth. Conclusions: This is the first study to evaluate how the fetal head station and position affect the LAM after active second stage of labour. There is a 25 % increase in AP diameter and a doubling of the hiatal area as the head descends from station-1 to +2. LAM avulsions are known to occur following a vaginal birth, and this study demonstrates that LAM avulsions do not occur until the birth of the head. It also highlights that despite pushing in the active second stage of labour, an unsuccessful vaginal delivery followed by CS is not associated with a LAM avulsion. This information will be useful to counsel women regarding mode of delivery.
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PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
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TI Targeting mitochondria in bone and cartilage diseases: A narrative review
SO REDOX BIOLOGY
LA English
DT Review
DE Mitochondria; Bone; Cartilage; Mitochondrial dynamics; Osteoarthritis; Osteoporosis; Osteomyelitis
ID transplantation; metabolism; chondrocytes; apoptosis; differentiation; osteoclast; activation; mechanisms; phosphate; autophagy
AB Mitochondria are essential regulators of bone health, controlling cell differentiation, cellular energy production, immune function, osteogenesis, and osteoclast activity. Their dysfunction is linked to orthopedic disorders such as osteoporosis, osteoarthritis, and osteomyelitis, contributing to impaired bone homeostasis and increased fracture risk. While mitochondrial research has been more advanced in fields such as cardiology and neurology, emerging therapeutic strategies from these areas are beginning to show potential for translation into orthopedics. These include mitochondrial biogenesis stimulation, mitochondrial fission inhibition, antioxidant therapies, mitochondrial transplantation, and photobiomodulation, which have demonstrated success in enhancing tissue repair, reducing oxidative stress, and improving overall cellular function in non-orthopedic applications. The novel inhibitor of mitochondrial fission and accumulation of reactive oxygen species Mdivi-1 offers potential to improve clinical outcomes of bone diseases by alleviating cellular dysfunction and preventing bone loss. While these treatments are still in the developmental phase, they present innovative approaches to address mitochondrial dysfunction in orthopedic conditions, potentially transforming bone disease management and enhancing patient outcomes. This report explores research regarding the involvement of mitochondrial health in bone and joint function and discusses possible future

treatment strategies targeting mitochondria in orthopedic conditions.
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AU Li, HM
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TI Pyroptosis: candidate key targets for mesenchymal stem cell-derived exosomes for the treatment of bone-related diseases
SO STEM CELL RESEARCH & THERAPY
LA English
DT Review
DE Pyroptosis; Mesenchymal stem cells; Exosomes; Osteoarthritis; Spinal cord injury; Disc herniation; Osteoporosis
ID inflammasome activation; extracellular vesicles; rheumatoid-arthritis; nlrp3 inflammasome; spinal-cord; injury; osteoarthritis; communication; osteoporosis; diagnosis
AB Bone-related diseases impact a large portion of the global population and, due to their high disability rates and limited treatment options, pose significant medical and economic challenges. Mesenchymal stem cells (MSCs) can differentiate into multiple cell types and offer strong regenerative potential, making them promising for treating various diseases. However, issues with the immune response and cell survival limit the effectiveness of cell transplantation. This has led to increased interest in cell-free stem cell therapy, particularly the use of exosomes, which is the most studied form of this approach. Exosomes are extracellular vesicles that contain proteins, lipids, and nucleic acids and play a key role in cell communication and material exchange. Pyroptosis, a form of cell death involved in innate immunity, is also associated with many diseases. Studies have shown that MSC-derived exosomes have therapeutic potential for treating a range of conditions by regulating inflammation and pyroptosis. This study explored the role of MSC-derived exosomes in modulating pyroptosis to improve the treatment of bone-related diseases.
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DT Article
DE Total knee arthroplasty; Tourniquet; Cement penetration; Bone mineral density; Randomized controlled trial
ID soft-tissue damage; blood-loss; society; mantle; pain; hip
AB Background The use of tourniquets in total knee arthroplasty (TKA) remains controversial, with growing interest in tourniquet-less techniques to improve patient outcomes. However, concerns persist regarding the adequacy of cement penetration and long-term implant stability. This study evaluated whether tourniquet-less TKA compromises cement penetration compared to conventional tourniquet-assisted procedures. Methods A double-blind randomized controlled trial included 120 patients with end-stage osteoarthritis undergoing cemented TKA. Patients were randomized into two groups: tourniquet (n = 60) and tourniquet-less (n = 60). All patients received standardized protocols including tranexamic acid, spinal anaesthesia with controlled hypotension, and identical cementing techniques. The primary outcome was cement penetration depth measured on standardized radiographs at 60 days. Secondary analysis assessed the impact of bone mineral density on cement penetration. Results Both groups achieved optimal cement penetration (2-3 mm) across the measured zones, with no clinically significant differences in average penetration depth. Bone mineral density did not affect penetration in either group, with 28.9% of patients having osteoporosis. Statistically significant differences in select zones (0.06-0.5 mm) were not clinically meaningful. Conclusions Tourniquet-less TKA achieves equivalent cement

penetration to tourniquet-assisted procedures when performed with modern standardized techniques. These findings support surgical decision-making for tourniquet-less approaches without compromising implant fixation quality, potentially enabling improved patient-centered outcomes.
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U1 0
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AF Hwang, Ji Sup
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TI Effect of Antiresorptive Therapy on Development of Posttraumatic Osteoarthritis after Intra-articular Distal Radius Fracture in Female Patients
SO CLINICS IN ORTHOPEDIC SURGERY
LA English
DT Article
DE Radius fractures; Osteoarthritis; Bisphosphonates; Denosumab; Osteoporosis
ID bisphosphonate use; bone; alendronate; cartilage; damage; model
AB Background: Subchondral bone is a potential target for osteoarthritis (OA) prevention. Antiresorptive therapy has been demonstrated to be chondroprotective in surgically induced OA animal models, but results were mixed in clinical studies. We aimed to determine whether patients with traumatic joint injury could benefit from antiresorptive therapy and whether the osteoporosis status might affect the chondroprotective effect, if any, of the therapy. Methods: We retrospectively reviewed 299 women (mean age, 64.7 +/- 8.6 years) who underwent surgery for an intra-articular distal radius fracture (DRF). We evaluated radiographic and symptomatic OA development at 1 year postoperatively. The odds ratio (OR) for the OA development was analyzed using logistic regression for factors including age, lowest T score, bone mineral density, presence of osteoporosis, residual intra-articular step-off, and antiresorptive therapy. To delineate the effect of the

osteoporosis status, subgroup analyses were performed. Results: Development of radiographic OA was identified in 80 patients (27%), and the mean pain score on a visual analog scale was 2.2 +/- 1.1. In the regression analysis, radiographic OA was associated with the presence of osteoporosis (OR, 3.97; 95% CI, 1.89-8.32), residual intra-articular step-off (OR, 3.68; 95% CI, 1.45-9.39), and not starting antiresorptive therapy (OR, 0.29; 95% CI, 0.14-0.61). In subgroup analysis, radiographic OA was associated with not starting antiresorptive therapy (OR, 0.24; 95% CI, 0.07-0.93) for patients without osteoporosis. However, for patients with osteoporosis, no association was found between radiographic OA and the evaluated factors. Conclusions: Initiation of antiresorptive therapy was associated with a lower incidence of radiographic OA after an intra-articular DRF, especially in those without osteoporosis. This study suggests that attempts to decrease bone remodeling might be effective for OA prevention in a joint at risk.
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NR 30
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TI The therapeutic potential of icariin in the intervention of bone and joint diseases through multiple pathways: a narrative review
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE icariin; natural flavonoids; Osteometabolic balance; inflammation; oxidativestress; mechanisms
ID intervertebral disc degeneration; osteogenic differentiation; stem-cells; udp-glucuronosyltransferases; ankylosing-spondylitis; articular-cartilage; controlled-release; signaling pathway; oxidative stress; herbal fufang
AB The prevalence of bone and joint diseases is projected to increase owing to rapidly aging populations, sedentary lifestyles, and unhealthy diets. This poses a significant challenge for the global healthcare system. In recent years, natural herbal medicines have been used to treat various types of orthopedic diseases, opening new frontiers in new drug research. Epimedium is a traditional Chinese herb with a long history of medicinal use. It is commonly used to treat osteoporosis, joint disorders, cardiovascular diseases, sexual dysfunction and aging.

The primary active component of Epimedium is icariin (ICA), an isoprenylated flavonoid. Recent studies have demonstrated its significant positive effects on bone metabolism and remodeling, including promoting osteoblast proliferation and mineralization, reducing osteoclast activity, and inhibiting inflammation and oxidative stress. Thus, ICA represents a potential compound for treating bone and joint diseases. However, the specific mechanisms underlying these effects have not yet been fully elucidated. This paper focuses on the latest advances in the use of ICA for the treatment of skeletal and joint diseases, covering a range of conditions including osteoporosis, osteoarthritis, rheumatoid arthritis, intervertebral disc degeneration and fractures. Building on this, we have systematically integrated its multi-target pharmacological mechanism network for the first time, elucidating its multi-pathway synergistic effects mediated by regulating the balance of the bone microenvironment. In summary, as a multi-target natural compound, ICA demonstrates significant translational medicine potential in the comprehensive treatment of bone and joint diseases, providing a critical theoretical foundation for the development of novel therapeutic strategies.
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Wang, Yuxuan
Cui, Zifan
Qiao, Zihong
Wu, Hongzhuo
Shi, Chenxia
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TI Exploring new therapeutic drugs for osteoarthritis and osteoporosis: Glucagon-like peptide-1 receptor agonists: A review
SO MEDICINE
LA English
DT Article
DE bone; cartilage; glucagon-like peptide-1 receptor agonist; osteoarthritis; osteoclasis; osteogenesis; osteoporosis
ID bone-mineral density; extracellular-matrix; glp-1 receptor; liraglutide; exendin-4; degradation; fracture; cells; risk; differentiation
AB As the 2 most common diseases of bone and joint, osteoarthritis (OA) and osteoporosis (OP) have a high incidence. The two diseases are often accompanied in clinical practice, affecting the health and quality of life of patients, but the relationship is complex. So far, there are no very effective drugs for the treatment of both diseases, so it is very meaningful to search for drugs that are suitable for OA and OP. Glucagon-like peptide-1 (GLP-1), as a type of enterotropic insulin, has hypoglycemic and weight loss effects. Recently, the effects of GLP-1 receptor agonists (GLP-1RA) on OA and OP have attracted more and more attention. This review aims to summarize the mechanism of GLP-1RA affecting bone metabolism in OA and OP, such as anti-inflammatory, affecting chondrocyte matrix metabolism, analgesia, promoting bone formation, inhibiting bone resorption, and reducing fracture incidence, to provide new methods for drug treatment of OA and OP.
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TI Recent Advances in pH-Responsive Coatings for Orthopedic and Dental Implants: Tackling Infection and Inflammation and Enhancing Bone Regeneration
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LA English
DT Review
DE pH-sensitive materials; bone implants; coating; antibiotic resistance; bone healing
ID mesoporous silica nanoparticles; controlled drug-release; delivery-system; osteogenic differentiation; surface-roughness; titania nanotubes; ti implants; antibacterial; polymers; chitosan
AB Bone is a structurally complex and dynamic tissue that plays a crucial role in mobility and skeletal stability. However, conditions such as osteoporosis, osteoarthritis, trauma-induced fractures, infections, and malignancies often necessitate the use of orthopedic and dental implants. Despite significant progress in implant biomaterials, challenges such as bacterial infection, inflammation, and loosening continue to compromise implant longevity, frequently leading to revision surgeries and extended recovery times. Smart coatings have emerged as a next-generation solution to these problems by providing on-demand, localized therapeutic responses to microenvironmental changes around implants and promoting bone regeneration. Such coatings can minimize antibiotic resistance by enabling controlled, stimulus-triggered drug release. Although the idea of using pH-sensitivity as a tool to make smart coatings is not a new thought, there are no options currently good enough to enter clinical studies. This review provides a comprehensive overview of recent advances in pH-sensitive polymers, hybrid composites, porous architectures, and bioactive linkers designed to dynamically respond to pathological pH variations at implant sites. By investigating the mechanisms of action, antibacterial and anti-inflammatory effects, and roles in bone regeneration, it is shown that the ability to provide time-dependent drug release for both short-term and long-term infections, as well as keeping the environment welcoming to the bone cell growth and replacement, is not an easy goal to reach, even with a fully biocompatable, non-toxic, and semi-biodegradable (one that releases the drug, but does not fade away) coating material compound. Reviewing all available options, including their functions and failures, finally,

emerging trends, translational barriers, and future opportunities for clinical implementation are highlighted, underscoring the transformative potential of bioresponsive coatings in orthopedic and dental implant technologies.
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TI The potential role of GLP-1 receptor agonists in the management of psoriatic disease: a scoping review
SO INFLAMMATION RESEARCH
LA English
DT Review
DE Psoriatic disease; Psoriasis; Glucagon-like peptide-1 receptor agonists; Obesity; Type 2 diabetes mellitus; Cardiovascular disease
ID peptide-1 analog therapy; bone-mineral density; once-weekly semaglutide; adipose-tissue; body-weight; collagen vi; cardiovascular events; extracellular-matrix; human macrophages; controlled-trial
AB BackgroundPsoriatic disease (PsD) is a chronic systemic inflammatory condition associated with significant cardiometabolic comorbidities, including obesity, type 2 diabetes mellitus (T2DM), and cardiovascular (CV) disease. These comorbidities are interlinked via shared immunopathogenic mechanisms, notably chronic low-grade inflammation driven by Th1/Th17 cytokines such as TNF, IL-6, and IL-17. Obesity, in particular, exacerbates PsD severity and treatment resistance, underscoring the need for integrated therapeutic strategies. This scoping review investigates the biological rationale and evidence for the use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in PsD.FindingsOriginally developed for T2DM, GLP-1RAs have demonstrated efficacy in reducing weight and improving glycemic control and CV outcomes. Evidence also suggests immunomodulatory properties through modulation of key inflammatory pathways and immune cell activity. We examined studies addressing: (1) the impact of obesity, T2DM, and CV disease on PsD; (2) outcomes of GLP-1RAs in these comorbidities; and (3) their potential in related rheumatologic and dermatologic diseases. GLP-1RAs show promise in reducing PsD burden by improving metabolic parameters and reducing systemic inflammation. Early clinical and preclinical data suggest benefits also in rheumatoid

arthritis, osteoarthritis, osteoporosis, psoriasis, and hidradenitis suppurativa.ImplicationsGLP-1RAs represent a novel, multifaceted therapeutic option in PsD, targeting both metabolic and inflammatory components. Further clinical trials are warranted to define their role in comprehensive PsD management and validate their disease-modifying potential.
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TI Depressive Symptoms and Osteoporosis in Middle-Aged and Older Adults: A Cross-Sectional Analysis of NHANES and HRS Data
SO GERIATRIC ORTHOPAEDIC SURGERY & REHABILITATION
LA English
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DE osteoporosis; depressive symptoms; NHANES; HRS; subgroup analysis
ID bone-mineral density; fracture risk; epidemiology; system; osteoarthritis; receptors; cytokines; diagnosis; cortisol; insulin
AB Background & Aims: Depression and osteoporosis are common among middle-aged and older adults, both impacting morbidity and quality of life. Their shared risk factors suggest a potential link, but this relationship remains underexplored. This study aimed to assess the association between depressive symptoms and osteoporosis in two large cohorts: the National Health and Nutrition Examination Survey (NHANES, 2005-2010) and Health and Retirement Study (HRS, 2012). Methods: We analyzed data from adults aged >= 50 years in NHANES (n = 3612) and HRS (n = 4307). Depressive symptoms were measured using PHQ-9 in NHANES and CES-D 8 in HRS, while osteoporosis was defined by self-reported diagnosis and medication use. Generalized linear models were used to evaluate the association, adjusting for demographic, lifestyle, and comorbidity factors. Subgroup analyses and sensitivity tests were conducted to explore effect modifiers and result robustness. Results: Depressive symptoms were positively associated with osteoporosis in both cohorts (NHANES: adjusted OR = 1.061, 95% CI: 1.034-1.088; HRS: adjusted OR = 1.063, 95% CI: 1.014-1.115). Significant associations were observed across subgroups, with stronger effects in individuals with diabetes and arthritis. Sex differences showed higher odds ratios for men in HRS. The relationship exhibited a linear trend, with increasing risk as depressive severity intensified. Conclusion: Depressive symptoms (PHQ-9/CES-D8) significantly associate with higher osteoporosis risk in older adults, with consistent cross-sectional findings across populations. While causality remains unclear, results

support clinical bone density monitoring in depression care and depression screening in osteoporosis management. Future longitudinal studies should clarify mechanisms, while public health strategies should integrate mental-bone health prevention approaches.
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TI The role of the brain-bone axis in skeletal degenerative diseases and psychiatric disorders, A genome-wide pleiotropic analysis
SO PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY
LA English
DT Article
DE Skeletal degenerative diseases; Psychiatric disorders; Immune dysfunction; Inflammation; Genome-wide association study; Mendelian randomization
ID nervous-system; health; set
AB Introduction: Skeletal degenerative diseases and psychiatric disorders often coexist clinically. However, the genetic correlations and underlying biological mechanisms between these two types of diseases remain unclear. Objectives: To investigate the genetic correlations between skeletal degenerative diseases and psychiatric disorders and to identify shared genomic loci, genes, and pathways. Methods: This comprehensive genome-wide pleiotropic association study utilized summary statistics from publicly available genome-wide association data. Various statistical genetic correlation methods were employed, including LDSC, HDL, PLACO, Coloc, Hyprcoloc, and Mendelian randomization (MR) analysis, along with immune cell colocalization analysis. The study aimed to identify potential shared genetic factors among three skeletal degenerative diseases (osteoarthritis, intervertebral disc degeneration, and osteoporosis) and three psychiatric disorders (schizophrenia, anxiety disorder, and major depressive disorder). Results: Analyses using LDSC, HDL, and Bonferroni corrections revealed significant genetic correlations between intervertebral disc degeneration (IVDD) and anxiety disorder (ANX); fractures, IVDD, and arthritis with major depressive disorder (MDD); and arthritis with schizophrenia (SCZ). Significant genetic correlations were also observed between VDD and ANX, fractures, IVDD, hip osteoarthritis (HipOA), knee osteoarthritis (KneeOA) and MDD, and KneeOA and SCZ. Pleiotropy analysis using PLACO, MAGMA, and multitrait colocalization Hyprcoloc identified 65 pleiotropic loci, 27 shared causal loci, and 9 shared risk loci involving immune cells related to both psychiatric and bone-related diseases. Additionally, tissue-specific enrichment analysis showed that genes mapped to these loci were enriched in brain,

cardiovascular, pancreatic, and other tissues. The IVW method demonstrated that MDD increased the risk of IVDD and KneeOA, while IVDD increased the risk of ANX and MDD. Conversely, SCZ was associated with a reduced risk of KneeOA. Multiple sensitivity analyses further supported a positive causal effect of IVDD on MDD. Conclusion: These findings suggest significant genetic correlations between skeletal degenerative diseases and psychiatric disorders, highlighting multiple shared comorbid genes and key immune cell types. Importantly, the study supports the role of the brain-bone axis in the regulation of skeletal degenerative diseases and psychiatric disorders, which could provide valuable insights for potential therapeutic targets and interventions for these conditions.
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NR 55
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TI Association between vertebral fractures and brain volume: insights from a community cohort study

SO OSTEOPOROSIS INTERNATIONAL
LA English
DT Article
DE Brain volume; Gray matter volume; Magnetic resonance imaging; Vertebral fracture; Voxel-based morphometry
ID mini-mental-state; parahippocampal cortex; osteoarthritis/osteoporosis; hippocampus; memory
AB Investigating vertebral fractures and brain structure, we found significant gray matter volume reductions in the right hippocampus, amygdala, and parahippocampal gyrus, especially in males. These findings emphasize the importance of integrating skeletal and neural health in osteoporosis management. Purpose Vertebral fractures (VF) due to osteoporosis impact morbidity and quality of life in the elderly. The relationship between VF and changes in brain structure remains underexplored. This study aimed to investigate the association between VF and gray matter volume (GMV) reductions in specific brain regions and to explore potential sex differences.MethodsData from 1,751 participants (571 males, 1,180 females; mean age 64.9, range 18-97) in the fourth survey of the population-based Research on Osteoarthritis/Osteoporosis Against Disability study (2015-2016) were used. Participants were classified into those with and without VF (VF + and VF - groups) based on Genant's semiquantitative method, assessed by spine radiographs. Voxel-based morphometry was applied to MRI images to measure GMV, and a general linear model analysis was performed to compare GMV between groups, adjusting for age, sex, total brain volume, and Mini-Mental State Examination scores as covariates. Additionally, a two-way analysis of variance was conducted on the significant GMV cluster, with sex and VF presence as independent variables, to explore interaction effects. Results The VF+ group consisted of 113 participants, while the VF- group included 1,638 participants. The analysis identified a significant cluster with reduced GMV in the VF + group compared to the VF - group. This cluster included the right hippocampus, right amygdala, and right parahippocampal gyrus. Further analysis revealed that males in the VF + group exhibited more pronounced GMV reductions in the significant cluster compared to females. Conclusion These findings suggest that VF is associated with significant reductions in brain regions critical for memory, emotional processing, and visuospatial memory, with more severe effects observed in males.
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10.1177/21514593231153106
NR 37
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TI Insights into the bone morphogenetic protein signaling in musculoskeletal disorders: Mechanisms and crosstalk
SO JOURNAL OF ORTHOPAEDIC TRANSLATION
LA English
DT Review
DE BMP signaling; Musculoskeletal disorders; Osteoporosis; Osteoarthritis; Rheumatoid arthritis; Sarcopenia
ID mesenchymal stem-cells; human articular chondrocytes; necrosis-factor-alpha; platelet-rich plasma; growth-factor; rheumatoid-arthritis; gene-expression; rat model; osteoblast differentiation; osteogenic differentiation
AB Musculoskeletal disorders are age-related illnesses that substantially impact the locomotor system. These problems can lead to serious complications, such as fractures, which can severely compromise the quality of life of patients. With the aging of the global population, the incidence and prevalence of musculoskeletal disorders are gradually increasing. Proliferation, differentiation, and cellular fate are extensively regulated by the BMP signaling pathway, which is expressed in approximately all organ systems. Musculoskeletal diseases are generally influenced by BMP signaling, which impedes the degeneration of musculoskeletal diseases. In this review, the pathophysiological functions of BMP signaling in four main musculoskeletal disorders (osteoporosis, osteoarthritis, rheumatoid arthritis, and sarcopenia) are summarized, and the role of cross talk between BMP signaling and other signaling pathways in the development of musculoskeletal disorders is reviewed. Finally, a conclusion regarding research on the role of BMP signaling in musculoskeletal disorders is formulated. Targeting the BMP signaling pathway is a promising therapeutic approach, and related studies have offered insights into the

pathophysiological mechanism of musculoskeletal disorders. The Translational Potential of This Article: The identification of the BMP signaling pathway involved in the development of musculoskeletal disorders and the investigation of their signaling cross talk can pave the way for effective treatments and management strategies for patients with musculoskeletal disorders
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TI Helicobacter pylori-Related Chronic Gastritis as a Risk Factor for Lower Bone Mineral Density
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DE Population-based study; Pepsinogen; Atrophic gastritis; <italic>Helicobacter pylori</italic>; Bone mineral density
ID postmenopausal osteoporosis; combination; gastrectomy; pepsinogen; infection; diagnosis; arthritis; estrogen; cohort
AB We evaluated the role of Helicobacter pylori (H. pylori)-related chronic gastritis in the development of osteoporosis in a population-based study. A total of 1690 subjects in the cohort of the Research on Osteoarthritis/ osteoporosis Against Disability (ROAD) were investigated, and the association between gastritis and osteoporosis was evaluated by the presence of serologically assessed H. pylori-related chronic gastritis and its stage, based on H. pylori antibody titer and pepsinogen. The presence of the gastritis was associated with significantly lower bone mineral density (BMD) assessed by dual-energy x-ray absorptiometry and a significant risk of lower BMD was observed in femoral neck (adjusted odds ratio [OR]: 0.78, 95% confidence interval [CI]: 061-0.99). The progression of the gastritis appeared to further increase the risk. In the stage of non-atrophic gastritis, the risk of lower BMD was significantly high, especially in a subgroup with higher gastritis activity in the femoral neck (adjusted OR: 0.61, 95% CI: 0.42-0.89). Meanwhile, in the stage of atrophic gastritis, the highest and significant risk of lower BMD was observed in a subgroup with the most extensive and severe atrophy in femoral neck (adjusted OR: 0.62, 95% CI: 0.42-0.91). These results suggest that H. pylori-related chronic gastritis is involved in the risk of osteoporosis, with higher activity of gastritis and more extensive atrophy leading to further increased risk. The serologically assessed stage of the gastritis could be used to identify a high-risk group for osteoporosis in H. pylori-infected subjects from general population.
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TI Research Progress of Senolytic Drugs in the Treatment of Orthopedic Diseases
SO GERONTOLOGY
LA English
DT Review
DE Senolytic drugs; Orthopedic diseases
ID oxidative stress; senescent cells; heat-shock; osteoarthritis; apoptosis; activation; mechanisms; cartilage; agent
AB Background: Orthopedic diseases, including osteoarthritis, osteoporosis, and age-related musculoskeletal disorders, significantly impact quality of life and are becoming increasingly prevalent with aging populations. A growing body of evidence highlights the role of cellular senescence in the pathogenesis of these conditions. Senescent cells(SCs), characterized by irreversible cell cycle arrest, accumulate in tissues over time, contributing to inflammation, tissue degeneration, and impaired regeneration. The emerging field of senolytics, which aims to selectively eliminate these SCs, has garnered attention as a novel therapeutic strategy in orthopedics. Summary: Senolyticdrugs, including small molecules, peptides, and natural compounds, have shown promise in preclinical models and

early clinical trials for the treatment of various age-related diseases. In orthopedics, senolytics have been investigated for their potential to ameliorate cartilage degradation, bone fragility, and other degenerative changes associated with aging. Recent studies have demonstrated that targeting SCsin musculoskeletal tissues can improve tissue function, re-duce inflammation, and promote regeneration. Although the majority of research is still in the preclinical phase, the positive outcomes from animal studies and early clinical trials suggest that senolytic drugs may offer new therapeutic avenues for orthopedic diseases.
 Key Messages: Senolytic therapies hold significant potential for treating orthopedic diseases by targeting the underlying cellular senescence that contributes to tissue degeneration and inflammation. Preclinical and clinical studies indicate that senolytic drugs may enhance tissue repair, alleviate symptoms, and slow disease progression in musculoskeletal disorders. Further research is needed to optimize drug efficacy, ensure safety, and identify patient populations that may benefit the most from these treatments. The development of senolytic drugs could revolutionize the management of aging-related orthopedic diseases, providing a more targeted and effectiveapproach than current treatments
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TI Autoimmune thyroid disease and human health: a systematic review of Mendelian randomization studies
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Article
DE autoimmune thyroid disease; human health; systematic review; Mendelian randomization; Grave's disease
ID graves-disease; risk; association; depression; prevalence; disorder
AB We systematically summarized current Mendelian randomization (MR) evidence on the causal relationships between autoimmune thyroid disease (AITD) and a wide range of human health outcomes. Original MR studies related to AITD published up to March 1, 2025, were retrieved from PubMed and Embase. For studies investigating the same exposure-outcome associations, meta-analyses were performed to synthesize the evidence after excluding overlapping samples where applicable. The methodological quality of the included studies was assessed using the STROBE-MR checklist. A total of 123 MR publications met the inclusion criteria. MR analyses indicated that AITD significantly increased the risk of coronary atherosclerosis, deep venous thrombosis, chronic obstructive pulmonary disease, major depression, diabetic neuropathy, carpal tunnel syndrome, neuromyelitis

optica spectrum disorder, diabetic retinopathy, childhood absence epilepsy, rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, inflammatory bowel disease, crohn's disease, vitiligo, myasthenia gravis, alopecia areata, type 1 and type 2 diabetes, sarcoidosis, frozen shoulder, drug eruptions, cataract, early age-related macular degeneration, pernicious anemia, Helicobacter pylori infection, temporomandibular disorders, migraine, frailty, primary biliary cholangitis, knee osteoarthritis, gout, and osteoporosis, while decreasing the risk of lung cancer, polyneuropathies, allergic rhinitis, telomere length, and serum vitamin A levels. The included MR studies were of high methodological quality and provided robust evidence supporting the bidirectional relationships between AITD and various health outcomes. These findings emphasize the importance and necessity of preventing and managing AITD while offering new perspectives and directions for future research on its prevention and treatment.Systematic review registration https://www.crd.york.ac.uk/prospero/, identifier CRD42023469038.
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TI Cuproptosis and its potential role in musculoskeletal disease
SO FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY
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DT Review
DE cuproptosis; osteoporosis; osteoarthritis; osteosarcoma; intervertebral disc degeneration; spinal cord injury; osteomyelitis
ID copper homeostasis; oxidative stress; multidisciplinary approach; extracellular vesicles; rheumatoid-arthritis; cell-death; osteosarcoma; toxicity; tumor; zinc
AB Cuproptosis, a recently identified form of copper-dependent cell death, arises from intracellular copper dyshomeostasis. As an essential trace element, copper plays a critical role in bioenergetic metabolism, redox regulation, and synaptic transmission. However, excessive copper exerts cytotoxic effects through multiple pathways, including increased reactive oxygen species (ROS) production, apoptotic cascade activation, necrotic membrane rupture, inflammatory responses, and mitochondrial dysfunction. Distinct from other cell death mechanisms, cuproptosis is characterized by copper ion binding to acetylated mitochondrial respiratory chain proteins, leading to pathogenic protein aggregation, iron-sulfur cluster depletion, and cellular collapse. Emerging evidence underscores aberrant copper accumulation and resultant proteotoxic stress as pivotal contributors to the pathogenesis of multiple musculoskeletal pathologies, including osteoporosis, osteoarthritis, sarcopenia, osteosarcoma, intervertebral disc degeneration, spinal cord injury, and biofilm-associated orthopedic infections. Understanding the spatiotemporal regulation of cuproptosis may provide novel opportunities for advancing diagnostic and therapeutic approaches in orthopedic medicine. This review synthesizes current insights into the molecular mechanisms of cuproptosis, its pathogenic role in musculoskeletal diseases, and the potential for biomarker-driven therapeutic interventions.
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TI The short isoform of Tango1 is dispensable for zebrafish survival but is required for skeletal patterning and integrity
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DE TANGO1; Extracellular matrix; Zebrafish; Collagen secretion; Matrix secretion
ID unfolded protein response; gtp-binding protein; er-exit sites; endoplasmic-reticulum; extracellular-matrix; articular-cartilage; collagen secretion; vesicle formation; copii; osteogenesis
AB Collagen is the most abundant protein in the human body, providing structural stability to connective tissues. It organises and interacts with other proteins to form a complex extracellular matrix (ECM), with loss of collagen in the ECM seen in diseases such as osteoarthritis and osteoporosis. As collagen, and other ECM components, are atypically large proteins, they require specific endoplasmic reticulum (ER) export machinery. A key player in the export of procollagen from the ER is the MIA3 gene product, TANGO1. We introduced mutations to both tango1 isoforms in zebrafish independently to understand the importance of the previously unexplored short isoform in zebrafish development and tissue homeostasis. We show that the long isoform of tango1 (tango1L) is mostly able to compensate for loss of the short isoform (tango1S) in larvae. However, non-collagenous components of the ECM (such as proteoglycans) were disrupted during development, leading to abnormal matrix patterning, visible by electron microscopy. Adult tango1S zebrafish show altered spinal morphology and changes to intervertebral discs, suggesting that tango1S plays a role in skeletal patterning and homeostasis that is independent of the long isoform.
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TI Notch signaling pathway in osteogenesis, bone development, metabolism, and diseases
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DT Review
DE bone formation; <italic>Notch</italic> signal pathway; osteoarthritis; osteoblast differentiation; osteoporosis
ID mesenchymal stem-cells; causes spondylocostal dysostosis; nf-kappa-b; osteoblast differentiation; alagille-syndrome; morphogenetic protein-2; missense mutations; wnt/beta-catenin; sonic hedgehog; beta-catenin
AB The skeletal system provides vital importance to support organ development and functions. The Notch signaling pathway possesses well-established functions in organ development and cellular homeostasis. The Notch signaling pathway comprises five typical ligands (JAG1, JAG2, DLL1, DLL3, and DLL4), four receptors (Notch1-4), and four intracellular domains (NICD1-4). Each component of the Notch signaling pathway has been demonstrated to be fundamental in osteoblast differentiation and bone formation. The dysregulation in the Notch signaling

pathway is highly linked with skeletal disorders or diseases at the developmental and postnatal stages. Recent studies have highlighted the importance of the elements of the Notch signaling pathway in the skeletal system, as well as its interaction with signaling, such as Wnt/beta-catenin, BMP, TGF-beta, FGF, autophagy, and hedgehog (Hh) to construct a potential gene regulatory network to orchestrate osteogenesis and ossification. Our review has provided a comprehensive summary of the Notch signaling pathway in the skeletal system, as well as the insights targeting Notch signaling for innovative potential drug discovery targets or therapeutic interventions to treat bone disorders, such as osteoporosis and osteoarthritis. An in-depth molecular mechanistic strategy to modulate the Notch signaling pathway and its associated signaling pathway will be encouraged for consideration to trigger enhanced therapeutic approaches for bone disorders by defining Notch-regulating drugs for clinical use.
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NR 189
TC 7
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U2 19
PU WILEY
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PA 111 RIVER ST, HOBOKEN 07030-5774, NJ USA
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J9 FASEB J
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WC Biochemistry & Molecular Biology; Biology; Cell Biology
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Zhou, Y
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TI The YAP1/GPX4 axis alleviates osteoporosis by affecting ferroptosis in osteoblasts
SO MOLECULAR MEDICINE
LA English
DT Article
DE GPX4; YAP1; Ferroptosis; Osteoblasts; Osteoporosis
AB BackgroundOsteoporosis (OP) is a disease in which weak bones increase the risk of fracture. It has been reported that the occurrence of ferroptosis accelerated the progression of OP. However, the underlying mechanism of ferroptosis in OP remains unclear.MethodsClinical samples from OP patients were collected and ovariectomized (OVX)-induced mouse models with GPX4 knockout was established. The expression of genes and proteins was determined by RT-qPCR, western blot, IHC and IF. Bone mineral density (BMD) of the lumbar vertebrae was evaluated using DXA. Pearson correlation analysis was used to analyze the relationship between GPX4 expression and BMD. The femoral morphology was detected by HE staining. Images and relevant parameters of the femur were acquired using micro-CT. Ultrastructural changes in mitochondria were observed using TEM. MDA and GSH levels in mice and cells were examined using commercial kits. Lipid peroxidation was detected using Bodipy-C11 fluorescent probe. ALP activity was measured using ALP staining and calcified nodules were examined using ARS staining. The interaction between YAP1 and GPX4 promoter was validated using ChIP and dual-luciferase reporter gene assay.ResultsGPX4 expression was downregulated in clinical samples of OP and positively correlated with BMD. GPX4 knockout exacerbated bone loss and promoted ferroptosis in OVX-induced mice. Besides, GPX4 overexpression inhibited ferroptosis and enhanced osteogenic potential of osteoblasts. Moreover, YAP1 positively regulated GPX4 expression in

osteoblasts through activating transcriptional activity of GPX4 promoter and YAP1 overexpression suppressed ferroptosis and enhanced osteogenic potential of osteoblasts via enhancing GPX4 expression.ConclusionGPX4 was positively regulated by YAP1, which in turn inhibited ferroptosis and enhanced osteogenic potential of osteoblasts, thereby alleviating OA progression.
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NR 43
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SC Biochemistry & Molecular Biology; Cell Biology; Research & Experimental Medicine
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AU Wang, JX
Xin, YJ
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AF Wang, Jianxu
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Yang, Guang
TI The interplay between the immune microenvironment and bone aging: From molecular mechanisms to therapeutic interventions
SO EXPERIMENTAL GERONTOLOGY
LA English
DT Review
DE Bone aging; Bone cells; Immune cells; Immune microenvironment; Therapy
ID stem-cells; osteoblastic differentiation; cellular senescence; dendritic cells; t-cells; macrophages; ferroptosis; diseases; osteoclastogenesis; osteoarthritis
AB The core mechanism of skeletal aging lies in the comprehensive disruption of microenvironmental homeostasis, involving a multidimensional interactive network comprising immune cells, mesenchymal stem cells, and their differentiated lineages. Although osteoporosis (OP) and osteoarthritis (OA) have traditionally

been viewed as distinct degenerative disorders, recent breakthroughs in osteoimmunology reveal their shared immune-aging mechanism: immune cell dysfunction within the bone marrow microenvironment triggers inflammaging, subsequently driving a vicious cycle of bone formation and resorption through the senescence-associated secretory phenotype (SASP). This review not only integrates the molecular landscape of osteoclast-osteoblast-immune triangular crosstalk but also highlights emerging mechanisms such as mitochondrial dysfunction, exosomal communication, and cell death mechanisms, systematically establishing the pivotal role of the immune microenvironment in bone aging and providing a theoretical framework for developing next-generation targeted therapies against skeletal aging.
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TI Essential role of the metabolite α-ketoglutarate in bone tissue and bone-related diseases
SO ACTA BIOCHIMICA ET BIOPHYSICA SINICA
LA English
DT Review
DE alpha-ketoglutarate; bone metabolism; osteoporosis; osteoarthritis; rheumatoid arthritis; periodontitis
ID 2-oxoglutaric acid; growth-plate; amino-acids; sodium-salt; differentiation; absorption; cartilage; glutamine; supplementation; dehydrogenase
AB Bone metabolism in bone tissue is constantly maintained in a state of dynamic equilibrium. The mass of bone and joint tissues is determined by both bone formation and bone resorption. It is hypothesized that disrupted metabolic balance leads to osteoporosis, osteoarthritis, rheumatoid arthritis, and bone tumors. Such disruptions often manifest as either a reduction or abnormality in bone mass and are frequently accompanied by pathological changes such as inflammation, fractures, and pain. alpha-Ketoglutarate (alpha-KG) serves as a pivotal intermediate in various metabolic pathways in mammals, significantly contributing to cellular energy metabolism, amino acid metabolism, and other physiological processes. alpha-KG may be a therapeutic target for a variety of bone-related diseases, such as osteoporosis, osteoarthritis, and rheumatoid arthritis, because of its role in maintaining the metabolic balance of bone. After the application of alpha-KG, bone loss and inflammation in bone tissue are alleviated. This review focuses on the regulatory effects of alpha-KG on various cells in bone and joint tissues. Owing to the regulatory effect of alpha-KG on the balance of bone metabolism, the application of alpha-KG in the treatment of osteoporosis, osteoarthritis, rheumatoid arthritis, bone tumors, and other bone tissue diseases has been clarified.
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TI Research Progress of Bone Grafting A Comprehensive Review

SO INTERNATIONAL JOURNAL OF NANOMEDICINE
LA English
DT Review
DE bone graft; true bone ceramics; decalcified bone matrix; freeze-dried bone; bone regeneration
ID ridge preservation; tooth extraction; morphogenetic protein-2; extracellular-matrix; progenitor cells; calcium-sulfate; bioactive glass; fiber membrane; bovine bone; scaffold
AB Bone tissue, the second most transplanted tissue after blood, is utilized in over 2.2 million bone grafts annually to address various bone-related conditions including fractures, tumors, bone infections, scoliosis, congenital defects, osteoporosis, osteoarthritis, and osteogenesis imperfecta. According to incomplete statistics, $4.3 billion was spent on bone graft materials in 2015 alone, with projections suggesting this figure may reach $66 billion by 2026. The limited availability of autogenous bone graft considered the gold standard due to their three critical biological properties: osteoconduction, osteoinduction, and osteogenesis-alongside the increasing global aging population, may be contributing to this rising expenditure. Furthermore, advancements in biomaterials and engineering technologies have created opportunities for the exploration of new bone graft substitutes. In this review, we will examine the fundamental structure of natural bone and the characteristics of ideal bone graft, highlighting common bone graft materials currently available, such as true bone ceramics, decalcified bone matrix, freeze-dried bone and demineralized freeze-dried bone, bioactive glasses, bone marrow aspirate concentrate, polymer nanocomposites, which have different characteristics in osteogenic, osteoconductivity, osteoinductivity, biocompatibility, mechanical properties, and resorption. How to utilize its advantages to maximize the osteogenic effect will be the focus of this review, and some of the current challenges in the field of bone grafting will be identified, outlining potential directions for future development. In conclusion, the choice of bone graft is critical to bone repair and regeneration, and a comprehensive understanding of the advantages and disadvantages of bone graft materials can improve the effectiveness of related surgical interventions.
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TI A Comparison Between Two Bearing Surfaces for Total Hip Arthroplasty-Ceramic-on-Ceramic and Metal-Polycarbonate-Urethane-A Pseudo-Randomized Study
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DT Article
DE polycarbonate-urethane; ceramic-on-ceramic; total hip arthroplasty; bearing surface; Harris Hip Score; WOMAC; implant survival; patient satisfaction; complications; squeaking

ID polyethylene; uhmwpe; motion; range
AB Background: Polycarbonate-urethane (PCU) is a recently developed bearing surface used in prosthetic hip surgery. It offers several theoretical advantages, including an elasticity modulus similar to that of natural cartilage, good lubrication properties, low wear, and the possibility of using large heads. However, comparative clinical experience is limited. The purpose of this study was to analyze the results of the PCU bearing surface and compare them with those of ceramic-on-ceramic (CoC) bearings using the same femoral stem model. (2) Methods: Following a propensity score matching analysis of a prospectively collected database, patients with a primary total hip arthroplasty aged between 18 and 60 years were included. Subjects were divided into two groups (PCU and CoC). Demographic, patient satisfaction, and implant survival data were recorded. Clinical results were evaluated using the Harris Hip Score (HHS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). (3) Results: A total of 105 patients were included in each group. All patients exhibited a positive evolution on both the HHS and the WOMAC subscales between pre-op and one year post-op, no statistically significant differences being found between the groups with respect to improvement on the HHS ($p = 0.172$) or the pain ($p = 0.523$), stiffness ($p = 0.448$), and physical function ($p = 0.255$) subscales of the WOMAC. Head sizes in the PCU group were found to be larger, but this was not seen to have any effect on the patients' clinical status or the prostheses' dislocation rate. Although the complication rate was similar across the groups ($p = 0.828$), the incidence of squeaking was higher in the PCU group ($p = 0.010$). No differences were observed when comparing the implant survival rate ($p = 0.427$). nor in mean patient satisfaction ($p = 0.138$). (4) Conclusions: No differences were found in terms of clinical results, complications, implant survival, or patient satisfaction between the bearing surfaces under analysis, indicating that all of them are valid alternatives in total hip replacement, although the higher proportion of squeaking observed makes it advisable to exercise some caution.
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NR 37
TC 0
Z9 0
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U2 1
PU MDPI
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EI 2079-4983
J9 J FUNCT BIOMATER
JI J. Func. Biomater.
PD OCT 1
PY 2025
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IS 10
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WC Engineering, Biomedical; Materials Science, Biomaterials
SC Engineering; Materials Science
GA 9AM2Y
UT WOS:001601706100001
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TI Reduction of subchondral bone marrow lesions concurrent with early recovery of trabecular bone mineral density in knee osteoarthritis following RANKL inhibitor administration for the treatment of osteoporosis: Implying human osteoporotic osteoarthritis?
SO SEMINARS IN ARTHRITIS AND RHEUMATISM
LA English
DT Article
DE Knee osteoarthritis; Osteoporosis; Subchondral bone marrow lesions; Hounsfield unit; Bone mineral density
ID postmenopausal women; cartilage damage; pain; progression; replacement; spine
AB Objective: To illustrate the correlation between the reduction of subchondral bone marrow lesions (BMLs) and the early recovery of trabecular bone mineral density (TBMD) in symptomatic knee osteoarthritis (KOA) patients. Methods: A RANKL inhibitor was applied to osteoporosis (OP) patients who also had symptomatic KOA and BMLs and whose knee symptoms were refractory to NSAID therapy. Clinical symptoms, HRQoL, BMLs, knee TBMD, systemic BMD, and bone turnover markers were evaluated within a 6-month follow-up. The correlation between early TBMD recovery and BML reduction was explored. Results: Following a RANKL inhibitor application: (1) At the first-week follow-up, clinical symptoms were relieved and persisted until the final follow-up; HRQoL showed improvement. (2) BMLs and TBMD progressively improved at 4-week and 3-month follow-ups; the bone turnover markers significantly decreased. (3) Systemic BMD improved at the 6-month follow-up. (4) At the 3-month follow-up, the reduction in subchondral BML areas positively correlated with the increase in CT-HU values (r = 0.329; BML areas reduction: 173.09 +/- 45.23 mm2; CT-HU values increase: 23.72 +/- 3.77). Conclusion: In this clinical study, after the application of a RANKL inhibitor for OP treatment, BMLs and knee pain were effectively reduced in OP patients with symptomatic KOA and BMLs. In addition, the correlation between early recovery of TBMD and reduction in BML area was also demonstrated. This study supports the concept of osteoporotic osteoarthritis (OPOA) and highlights the potential of subchondral bone as a target for KOA treatment.
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NR 61
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J9 SEMIN ARTHRITIS RHEU
JI Semin. Arthritis Rheum.
PD DEC 15
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WC Rheumatology
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AF Wagner, Moritz
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TI Changes of spino-pelvic characteristics post-THA are independent of surgical approach: a prospective study
SO ARCHIVES OF ORTHOPAEDIC AND TRAUMA SURGERY
LA English
DT Article
DE Pelvic tilt; Outcomes; Approach; Change; Spinopelvic
ID total hip-arthroplasty; acetabular component; orientation; risk
AB Aims Spinopelvic characteristics change after THA. Whether this change varies between approaches, is of interest for pre-op cup orientation planning. The aims of this study were to (1) Characterize changes in standing PT amongst patients with hip osteoarthritis treated with THA; (2) Test whether certain patient-related factors may predict PT change; and (3) Assess the association between surgical approach and PT change. Methods This was a prospective, two-center, radiographic outcome study including 424 hips, consisting of anterior approach for 171 (40.3%) hips, lateral approach for 181 hips (42.7%) and posterior approach for 72 hips (17.0%). Spinopelvic characteristics were determined from lateral radiographs (before and one year after THA). Parameters of interest included: Pelvic tilt (PT), lumbar lordosis, sacral slope, pelvic incidence. PT change of more than 7 degrees was considered clinically relevant. Results Pelvic tilt increased by 2 degrees from 15.1 degrees (+/- 8.9) to 17.1 degrees (+/- 9.7) after THA ($p < 0.001$). 19 hips (4.5%) experienced a relevant PT decrease, 337 (79.5%) had no clinically significant change in pelvic tilt, and 68 (16.0%) showed a moderate increase. Age, female sex and preoperative spinopelvic parameters including PT, SS and PI were predictive of PT change more than 7 degrees. PT increased most with lateral approach (2.9 +/- 6.2) and least with anterior approach (1.1 +/- 6.2, $p = 0.024$). Conclusion Preoperative PT is the best predictor for PT change. PT is generally normalizing after THA and patients with

low PT due to hip flexion contractures tend to increase PT after THA, few patients with high PT will decrease after THA. Anterior approach with capsulectomy was associated with the least change in PT post-THA. However, the approach-specific changes, although statistically significant, were too small to be considered during clinical practice, therefore no approach-specific prediction of PT change needs to be considered during preoperative planning for primary THA.
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NR 28
TC 0
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U1 0
U2 2
PU SPRINGER
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SN 0936-8051
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J9 ARCH ORTHOP TRAUM SU
JI Arch. Orthop. Trauma Surg.
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SC Orthopedics; Surgery
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UT WOS:001424393300001
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TI Angelica gigas Nakai (Korean Dang-gui) Root Alcoholic Extracts in Health Promotion and Disease Therapy - active Phytochemicals and In Vivo Molecular Targets
SO PHARMACEUTICAL RESEARCH
LA English
DT Article
DE decursin; decursinol; decursinol angelate; nodakenin; ROCK1/2
ID decursinol angelate; compound; pharmacokinetics; identification; mice; pyranocoumarins; decarboxylase; antiandrogen; inhibition; metabolism
AB Angelica gigas Nakai (AGN) root is a medicinal herbal widely used in traditional medicine in Korea. AGN root ethanolic extracts have been marketed as dietary supplements in the United States for memory health and pain management. We have recently reviewed the pharmacokinetics (PK) and first-pass hepatic metabolism of ingested AGN supplements in humans for the signature pyranocoumarins decursin (D, C-max 1x), decursinol angelate (DA, C-max similar to 10x) and their common botanical precursor and hepatic metabolite decursinol (DOH, C-max similar to 1000x). Here we update in vivo medicinal activities of AGN and/or its pyranocoumarins and furanocoumarin nodakenin in cancer, pain, memory loss, cerebral ischemia reperfusion stroke, metabolic syndrome and vascular endothelial dysfunctions, anxiety, sleep disorder, epilepsy, inflammatory bowel disease, osteoporosis and osteoarthritis. Given their polypharmacology nature, the pertinent mechanisms of action are likely misrepresented by many cell culture studies that did not consider the drug metabolism knowledge. We report here Rho-associated protein kinases (ROCK1/2) as novel targets for DA and DOH. Combining with published inhibitory activity of DOH on acetylcholinesterase,

agonist activity of DOH and antagonist/degrader activity of DA/D on androgen and estrogen receptors, D/DA promoting activity for glutamic acid decarboxylase (GAD)- gamma-aminobutyric acid (GABA) inhibitory axis and inhibition of glutamate dehydrogenase (GDH), monoamine oxidase-A (MAO-A) and transient receptor potential vanilloid 1 (TRPV1), we postulate their contributions to neuro-cognitive, metabolic, oncologic, vascular and other beneficial bioactivities of AGN extracts. A clinical trial is being planned for an AGN extract to manage side effects of androgen deprivation therapy in prostate cancer patients.
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TI Thiram-induced ER stress promotes mitochondrial calcium signaling and NLRP3 inflammasome activation in a tissue specific manner
SO ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY
LA English
DT Article
DE Thiram; Endoplasmic reticulum; Calcium signaling; NLRP3; Inflammasome; Liver-bone axis
ID bone
AB Thiram, a broadly used dithiocarbamate fungicide, exaggerates endoplasmic reticulum (ER) stress and interferes with mitochondrial function, thus disrupting cellular homeostasis. Here, we intend to identify the molecular actions of thiram at the mitochondrial-associated ER membranes (MAMs) that lead to the induction of ER stress and mitochondrial calcium overload in both liver and bone tissues. Taken together, we show that thiram-induced remodelling of MAMs leads to huge ER stress and calcium dysregulation. Histological and immunohistochemical examinations revealed that thiram-induced hyperactivation of IP3R1 mediated the release of endoplasmic reticulum calcium, but mitochondrial calcium uptake was

mediated by voltage-dependent anion channels VDAC1. This stress response was characterized by increased glucose regulated protein 78 (GRP78) expression in the liver and tibial growth plates (GP). In this respect, a new liver-bone axis was delineated for thiram-induced ER stress. More interestingly, the activation of NLRP3 inflammasome was very striking in tibial growth plates but not in liver tissues. Hence, the results highlight the systemic effects of thiram by identifying a critical metabolic junction that might play a role in metabolic disorders such as tibial dyschondroplasia and related bone disorders, e.g., osteoarthritis and osteoporosis.
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TI Eucommia ulmoides Oliv. and its bioactive compounds: therapeutic potential in bone diseases
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DT Review
DE <italic>Eucommia ulmoides</italic> Oliv.; bioactive compounds; aging-related bone diseases; bone formation; bone resorption; pharmacological mechanisms
ID induced osteoporosis; inhibits osteoarthritis; water extract; in-vitro; cortex; differentiation; phytochemistry; proliferation; inflammation; apoptosis
AB Background Aging-related bone diseases encompass a range of conditions that emerge or worsen with advancing age, including osteoporosis and osteoarthritis, and they are placing an increasing burden on society. Although these diseases differ in clinical manifestations and pathological features, they often share common

age-associated mechanisms such as impaired bone remodeling, chronic low-grade inflammation, cellular senescence, oxidative stress, and hormonal changes. Current therapies often face limitations in efficacy or long-term safety, highlighting the need for alternative strategies. Phytochemicals derived from Chinese medicine herb have emerged as promising candidates due to their multi-target effects on bone homeostasis. Eucommia ulmoides Oliv. (EU) and its bioactive compounds (e.g., quercetin, aucubin, geniposide, geniposidic acid). may regulate key pathways to restore bone balance, offering potential for treating osteoporosis and other aging-related bone diseasesObjectives This study aims to assess the therapeutic potential of EU in the treatment of aging-related bone diseases.Methods A literature search was conducted on the PubMed database up to November 2024 using the search term: "Eucommia AND (bone OR cartilage OR joint)."Results The review indicates that EU formulas, extracts, and bioactive components promote osteogenesis, suppress bone resorption, and exert anti-inflammatory and antioxidant properties. These effects contribute positively to the treatment of aging-related bone diseases.Conclusion The therapeutic benefits of EU support its development as a promising tool for preventing and treating aging-related bone diseases. These findings provide new research directions to address related health challenges associated with population aging.
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TI Ultra-Processed Food and Its Impact on Bone Health and Joint Diseases: A Scoping Review

SO NUTRIENTS
LA English
DT Review
DE ultra-processed; food; osteoporosis; bone; osteoarthritis; rheumatoid arthritis; gout
ID mineral density; dietary pattern; consumption; risk; guidance; milk
AB Background/Objectives: This scoping review explores the relationship between ultra-processed food (UPF), bone health, and joint diseases, focusing on its potential impact on bone mineral density (BMD), osteoporosis, osteoarthritis, and inflammatory arthritis, including rheumatoid arthritis (RA), gout, and spondyloarthritis. Methods: A search strategy was developed using key terms such as "ultra-processed food" and related terms like "fast food," alongside various definitions of bone health impairment, chronic degenerative joint diseases, and inflammatory arthritis. Results: A total of 19 studies were included: 12 on bone health, 3 on osteoarthritis, and 4 on inflammatory arthritis. Preclinical studies showed that UPF consumption negatively affects bone structure and strength. In studies on children and adults, four investigations (2013-2017) found no association between fast food intake and BMD. However, more recent large-scale cross-sectional studies linked higher UPF consumption to lower BMD, increased osteoporosis risk, and greater prevalence of osteopenia, particularly in postmenopausal women. UPF intake was associated with knee osteoarthritis risk, with evidence suggesting an interaction with cartilage thickness, though no association was found for hip osteoarthritis. In inflammatory arthritis, UK Biobank data indicated a higher risk of RA and gout in UPF consumers, while a Brazilian study reported worse metabolic profiles in RA patients. No significant differences in UPF intake were found in spondyloarthritis. Conclusions: This review highlights relevant considerations about the deleterious role of UPF on bone health and joint diseases, providing additional evidence to suggest healthier dietary patterns to patients and to the general population.
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TI Genomic structural equation modeling uncovers novel risk loci for bone metabolic disorders: cross-tissue genetic mechanisms and bone-brain axis regulation
SO BMC MUSCULOSKELETAL DISORDERS
LA English
DT Article
DE Bone metabolic disorders; Genomic structural equation modeling; Risk loci; Bone-brain axis; Transcriptome-wide association study
ID markers; cells
AB Objective The genetic architecture underlying bone metabolic disorders

(BMetDs) remains poorly characterized. Utilizing genomic structural equation modeling (Genomic-SEM) and multiple post-GWAS approaches, we estimated causal single nucleotide polymorphisms (SNPs) associated with BMetDs-independent metabolic variations, identifying 26 novel risk loci (including 14 genome-wide significant loci). Multi-omics analyses-including tissue-specific, cellular-level, and genomic element annotations-were applied to prioritize susceptibility loci and regulatory elements. Additionally, polygenic risk scores (PRS) derived from summary statistics were used to evaluate chromosomal contributions to BMetDs risk. For the first time, we present a comprehensive genetic landscape of BMetDs through a GWAS targeting an unmeasured latent phenotype. Methods We conducted a multivariate GWAS of BMetDs using genomic structural equation modeling (Genomic-SEM) on six BMetDs-related traits: osteoporosis, type 2 diabetes (T2D), body mass index (BMI), osteoarthritis (OA), ankylosing spondylitis (AS), and rheumatoid arthritis (RA) (total sample size: N = 462,933-461,194 Europeans). Genetic covariance matrices were constructed via LD score regression, followed by latent factor modeling to dissect shared genetic architecture. Novel loci were prioritized using FUMA-based functional annotation, fine-mapping (SuSIE/FINEMAP), transcriptome-wide association studies (TWAS/FUSION), and cell-type enrichment analyses. Results Genomic-SEM identified 37 novel risk loci ($P < 5 \times 10(-)(8)$), including 14 genome-wide significant loci ($P < 5 \times 10(-)(1)(6)$). Fine-mapping revealed causal variants (posterior probability > 0.95) on chromosome 1 (rs1415145), chromosome 2 (rs35802221), and chromosome 7 (rs2367906). TWAS implicated FERMT3 (beta = +1.85, $P = 2.3 \times 10(-)(6)$), CCDC88B (beta = +2.01, $P = 1.7 \times 10(-)(5)$), and USP53 (beta = -1.72, $P = 4.1 \times 10(-)(4)$) in BMetDs through cerebellar-hypothalamic gene expression. Cell-type enrichment highlighted pancreatic B cells (FDR = 0.03) and brain non-myeloid neurons (FDR = 0.04) as key mediators. Partitioned heritability analysis demonstrated significant enrichment in enhancer (H3K27ac, $P = 1.1 \times 10(-)(7)$) and chromatin boundary (CTCF, $P = 3.4 \times 10(-)(5)$) regions, supporting epigenetic dysregulation in BMetDs pathogenesis. Conclusion This study uncovers novel genetic loci and cross-tissue regulatory mechanisms driving BMetDs, emphasizing the pivotal roles of the bone-brain axis and non-coding regulatory elements. Our findings bridge genomic insights with translational applications, offering actionable targets for precision interventions in metabolic bone diseases.

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NR 73
TC 0
Z9 0
U1 3
U2 3
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 BMC MUSCULOSKEL DIS
JI BMC Musculoskelet. Disord.
PD NOV 17
PY 2025
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WC Orthopedics; Rheumatology
SC Orthopedics; Rheumatology
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UT WOS:001617175400001
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PT J
AU Hou, JY
Li, YB
Zhang, Y
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Chen, B
Ma, GY
Zhu, NQ
AF Hou, Jingyi

Li, Yubo
Zhang, Yu
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TI Integrated network pharmacology reveals the mechanism of action of Xianlinggubao prescription for inflammation in osteoarthritis
SO BMC COMPLEMENTARY MEDICINE AND THERAPIES
LA English
DT Article
DE Bioinformatics analysis; Hub gene; Network pharmacology; NF-kappa B; Osteoarthritis; Xianlinggubao prescription
ID progression; severity; luteolin; access; il-17
AB BackgroundOsteoarthritis (OA), a leading cause of disability worldwide, is characterized by complex interactions between cartilage degradation and synovial inflammation. While NSAIDs are the primary treatment, their prolonged use exacerbates gastrointestinal risks and does not alter disease progression. Xianlinggubao (XLGB), an approved Chinese herbal remedy for osteoporosis, has demonstrated promising anti-osteoarthritic effects in preliminary studies. However, its multi-component mechanisms targeting OA-related inflammation require further clarification. This study integrates network pharmacology with experimental validation to investigate XLGB's anti-inflammatory mechanisms in OA.MethodsBioactive compounds of XLGB and their respective targets were sourced from the TCMSP, ETCM, SymMap, and ChEMBL databases. Targets linked to OA-related inflammation were identified through differential expression analysis and by querying OMIM, GeneCards, and PubMed Gene databases. Network pharmacology and bioinformatics approaches were employed to construct compound-target and protein-protein interaction (PPI) networks, enabling the identification of pivotal therapeutic targets. Functional enrichment of these targets was performed using the ClusterProfiler package in R. The binding affinity of compounds to anti-inflammatory OA targets was assessed through molecular docking, dynamics simulations, RT-PCR, and immunofluorescence assays.ResultsFifty-five bioactive compounds corresponding to 475 XLGB targets and 125 genes involved in OA-related inflammation were identified. PPI network analysis revealed that XLGB may alleviate OA inflammation by modulating key genes, including COX-2, IL-1 beta, TNF, IL-6, and MMP-9. Molecular simulations indicated strong binding affinities between bioactive compounds in XLGB and these critical targets. Functional enrichment analysis suggested that XLGB's anti-inflammatory action in OA may involve regulation of pathways such as IL-17, TNF, and NF-kappa B. In vitro experiments further confirmed that XLGB mitigates OA inflammation by modulating these genes, proteins, and signaling pathways.ConclusionsThrough network pharmacology, this study elucidated the mechanisms of XLGB in OA inflammation, highlighting its modulation of IL-6, IL-1

beta, TNF-alpha, PTGS2, MMP-9, and the NF-kappa B pathway. These findings provide strong support for the clinical application of XLGB in managing OA-related inflammation.
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NR 63
TC 0
Z9 0
U1 6
U2 11
PU BMC
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PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
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J9 BMC COMPLEMENT MED
JI BMC Complement. Med. Ther.
PD MAY 27
PY 2025
VL 25
IS 1
BP
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DI 10.1186/s12906-025-04928-5
PG 22
WC Integrative & Complementary Medicine
SC Integrative & Complementary Medicine
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PT J
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TI Side-to-side differences in hip bone mineral density in patients with unilateral hip osteoarthritis
SO BONE
LA English
DT Article
DE Artificial intelligence; Discordance; Divergence; Deep learning; DXA; Quantitative computed tomography
ID diagnosis; osteoporosis; association; prevalence; validation; dysplasia; femur; women; knee
AB Background: Accurately evaluating bone mineral density (BMD) in patients with unilateral hip osteoarthritis (OA) is crucial for diagnosing osteoporosis and selecting implants for hip arthroplasty. Our goal was to measure the BMD differences between sides, examine contributing factors, and identify the optimal side for BMD assessment in these patients. Methods: We analyzed 108 women with unilateral hip OA. Bilateral hip BMD was assessed automatically through quantitative CT (QCT) utilizing a validated, deep-learning-based approach. We evaluated BMD variations between the OA and healthy hips across total, neck, and distal regions. To determine their contributions, we analyzed factors, including patient demographics, Crowe classification, Bombelli classification, knee OA status, hip functional score, and gluteal muscle volume and density. Furthermore, we examined how side-to-side BMD differences influenced osteoporosis diagnosis using T-scores based on QCT. Results: The average BMD on the OA side was 6.9 % lower in the total region, 14.5 % higher in the neck region, and 9.4 % lower in the distal region than on the healthy side. Contributing factors to the reduced BMD in the OA hip included younger age, Bombelli classification (atrophic type), and significant gluteal muscle atrophy. Diagnoses from the OA side revealed lower sensitivity (61 %) than those from the healthy side (88 %). Conclusions: Analysis on one side alone yields a more precise osteoporosis diagnosis from the healthy side. Nonetheless, bilateral BMD assessment remains crucial, particularly in younger individuals and those with atrophic OA types. Although based on QCT, our findings support bilateral analysis by dual-energy X-ray absorptiometry for these patients.

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Zhu K, 2022, J CLIN DENSITOM, V25, P577, DOI 10.1016/j.jocd.2022.04.003
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WC Endocrinology & Metabolism
SC Endocrinology & Metabolism
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PT J
AU Liu, MD
Liu, YQ
Yu, JY
Gong, JQ
Zhao, CG
Liu, Z
AF Liu, Mingdong
Liu, Yaqi
Yu, Jiayao
Gong, Jiaqi
Zhao, Chunguang
Liu, Zheng
TI Molecular mechanisms and therapeutic implications of the sympathetic nervous system in bone-related disorders: a brain-bone axis perspective
SO BONE RESEARCH
LA English
DT Review
ID vasoactive-intestinal-peptide; neuropeptide-y; leptin receptor; rheumatoid-arthritis; synovial tissue; innervation; expression; osteoporosis; antagonist; inhibition
AB The global aging crisis has increased the prevalence of skeletal disorders, necessitating innovative therapeutic strategies. This review employs the brain-bone axis (BBA) framework to examine the role of the sympathetic nervous system (SNS) in bone metabolism. The research systematically elucidates the molecular mechanisms by which the SNS mediates signaling pathways through neurofibers and neurotransmitters, such as norepinephrine, dopamine, neuropeptide Y, and leptin, regulating interactions between bone-related cells to maintain skeletal homeostasis. It also identifies the pathological associations between the dysregulation of these pathways and the progression of bone-related conditions, such as osteoporosis, osteoarthritis, and intervertebral disc degeneration. By integrating current evidence, we identify novel therapeutic targets within the BBA and propose neuro-centric intervention strategies to mitigate skeletal diseases. This review deepens the understanding of neuro-skeletal interactions and lays a foundation for innovative treatments for bone-related pathologies.

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TI Treatment of Osteoporosis and Osteoarthritis in the Oldest Old
SO DRUGS
LA English
DT Review
ID nonsteroidal antiinflammatory drugs; bone-mineral density; dietary-protein intake; proton-pump inhibitors; women aged 80; postmenopausal women; fracture risk; hip fracture; knee osteoarthritis; zoledronic acid
AB Osteoporosis and osteoarthritis are key diseases of musculoskeletal ageing and are increasing in prevalence and burden with the progressively ageing population worldwide. These conditions are thus particularly common in 'the oldest old', and there are complexities of managing them within the context of extensive multimorbidity, physical and mental disability, and polypharmacy, the rates for all of which are high in this population. In this narrative review, we explore the epidemiology of osteoporosis and osteoarthritis in the oldest old before examining trials and real-world data relating to the pharmacological treatment of these diseases in older adults, including anti-resorptives and bone-forming agents in osteoporosis and symptomatic slow-acting drugs for osteoarthritis, paracetamol, and non-steroidal anti-inflammatory drugs in osteoarthritis, recognising that the oldest old are usually excluded from clinical trials. We then review the potential benefits of nutritional interventions and exercise therapy before highlighting the health economic benefits of interventions for osteoporosis and osteoarthritis. The high prevalence of risk factors for both disease and adverse events associated with treatment in the oldest old mean that careful attention must be paid to the potential benefits of intervention (including fracture risk reduction and improvements in osteoarthritis pain and function) versus the potential harms and adverse effects. Further direct evidence relating to such interventions is urgently needed from future research.
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TI Bone mineral density assessment using radiofrequency echographic multispectrometry (REMS) in patients before and after total hip replacement
SO OSTEOPOROSIS INTERNATIONAL
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DT Article
DE Bone mineral density; Osteoporosis; Radiofrequency echographic multispectrometry
ID calcaneus in-vivo; methodology
AB REMS-BMD by radiofrequency echographic multispectrometry is primarily determined by a patient's BMI, age, and sex. Only about 2.8% of the changes in

femoral neck REMS-BMD can be attributed to replacement of the total hip with metal implants. Purpose This study aimed to evaluate how total hip replacement affects femoral neck REMS-BMD and to examine the contributions of a patient's sex, age, and BMI to the REMS-BMD assessment. Methods REMS-BMD was measured at the proximal femur using EchoStation (Echolight Spa, Lecce, Italy) in 27 women and 23 men with advanced hip osteoarthritis before surgery and again on the third day following total hip joint arthroplasty. For seven men, REMS-BMD was measured at both the proximal femur and lumbar spine, taking into account their actual as well as varying age, height, and weight. Results The patients' ages ranged from 49 to 84 years, with the REMS-BMD T-score values for the femoral neck varying from + 1.8 to - 3.2. There was a significant correlation between the femoral neck REMS-BMD values measured before and after total hip arthroplasty. Post-surgery, the femoral neck REMS-BMD values showed a consistent decrease of - 0.021 g/cm(2) (approximately 2.8%, $p < 0.05$) compared to pre-operative measurements. A model incorporating age, sex, and BMI accurately predicted femoral neck REMS-BMD in both pre- and postoperative settings, with no evidence of systematic bias. Variations in REMS-BMD were observed in both the femoral neck and lumbar spine when measurements were taken in the same patients under different conditions of age, height, and weight. Conclusion Approximately 90% of the variability in REMS-BMD of the femoral neck can be attributed to the patient's age, sex, and BMI. Further research is needed to determine the extent to which REMS-BMD reflects areal or volumetric BMD, and how backscattered radiofrequency ultrasound signals influence the REMS-BMD.
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