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Vascular and neural mechanisms linking sexual dysfunction and peripheral artery disease in patients with diabetes

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Abstract

Diabetes mellitus is one of the leading global health concerns, with an increasing burden of cardiovascular morbidity and mortality. Sexual dysfunction and peripheral artery disease are two frequent and interrelated complications in diabetic populations, both serving as potential indicators of systemic vascular and neural damage. The interplay of endothelial dysfunction, atherosclerosis, and diabetic neuropathy provides a mechanistic basis linking these complications with heightened cardiovascular risk. While sexual dysfunction is often underrecognized, it may represent an early marker of vascular impairment. Peripheral artery disease, on the other hand, is a well-established predictor of major cardiovascular events. Patient-centered education and comprehensive management approaches are essential to address these issues and improve outcomes. This narrative review synthesizes current evidence on vascular and neural mechanisms underlying sexual dysfunction and peripheral artery disease in diabetes, highlighting their clinical relevance and implications for cardiovascular risk stratification.

Keywords

diabetes mellitus, sexual dysfunction, peripheral artery disease, cardiovascular risk, endothelial dysfunction

Introduction

Diabetes mellitus (DM) affects over 500 million people worldwide, with projections indicating a continued rise in prevalence in the coming decades [1]. Cardiovascular disease (CVD) remains the principal cause of morbidity and mortality in this population, accounting for more than half of diabetes-related deaths [2]. Among the various complications of DM, sexual dysfunction (SD) and peripheral artery disease (PAD) are highly prevalent yet often underappreciated contributors to the overall cardiovascular risk burden.

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SD in diabetes includes erectile dysfunction (ED) in men and female SD (FSD), with reported prevalence rates of 35–75% in men and 20–45% in women, respectively [3, 4]. Both conditions are closely linked to endothelial dysfunction, impaired nitric oxide (NO) bioavailability, and diabetic neuropathy, all of which contribute to systemic vascular disease. Importantly, ED has been identified as an independent predictor of future cardiovascular events, sometimes preceding overt coronary or peripheral vascular disease [5].

PAD is another major macrovascular complication of DM, characterized by atherosclerotic obstruction of lower extremity arteries. Its prevalence is estimated at 20–30% among diabetic patients, significantly higher than in the general population [6]. PAD not only leads to functional impairment and risk of limb ischemia but also strongly predicts major adverse cardiovascular events (MACE), including myocardial infarction and stroke [7].

Although SD and PAD have been studied extensively as separate complications, there is a growing recognition of their interrelationship through shared vascular and neural mechanisms. Both are considered manifestations of systemic endothelial dysfunction and advanced atherosclerosis, and both may serve as early warning signs of increased cardiovascular risk in diabetic patients. Despite this, the mechanistic links between SD and PAD in diabetes have not been comprehensively summarized.

The purpose of this review is to synthesize current knowledge on the vascular and neural mechanisms linking SD and PAD in patients with diabetes, and to discuss their implications for cardiovascular risk prediction, screening, and management.

This review differs from prior publications by providing an integrated discussion of both vascular and neural mechanisms that jointly underlie SD and PAD in diabetes. Unlike earlier reviews that have examined these complications separately, our aim is to synthesize them within a unified pathophysiological and clinical framework relevant to cardiovascular risk assessment.

SD in diabetes

SD is among the most common complications of diabetes, significantly affecting quality of life and often serving as an early marker of systemic vascular disease. In men, ED is the predominant manifestation, while women with diabetes frequently experience FSD, encompassing decreased libido, arousal difficulties, lubrication problems, and orgasmic disorders.

ED prevalence in men with diabetes is reported to be two to three times higher than in non-diabetic men, with onset occurring approximately 10–15 years earlier [8]. The prevalence increases with age, poor glycemic control, and longer diabetes duration. In women, meta-analyses indicate that diabetic women have a 1.5- to 2-fold higher risk of developing SD compared to non-diabetic women [9]. Recent meta-analyses and cohort studies have confirmed these prevalence patterns and further emphasized the multifactorial nature of SD in diabetes, integrating vascular, neural, and hormonal determinants [10–13].

The underlying mechanisms are multifactorial, involving both vascular and neural pathways. Endothelial dysfunction and reduced NO bioavailability impair penile smooth muscle relaxation, leading to compromised erectile function [14]. Similarly, in women, impaired clitoral and vaginal blood flow caused by microvascular damage contributes to decreased arousal and lubrication. Autonomic neuropathy further disrupts neurogenic vasodilation and genital sensory function [15]. Hormonal dysregulation, including reduced testosterone in men and altered estrogen levels in women, can exacerbate sexual difficulties. Psychological factors such as depression and anxiety also play a reinforcing role.

ED has been recognized as an independent predictor of cardiovascular events in men with diabetes. Large cohort studies demonstrate that ED precedes coronary artery disease by several years, making it a sentinel marker for subclinical vascular disease [16]. Similarly, FSD, though less studied, has been associated with poor metabolic control and higher cardiovascular risk, though longitudinal evidence remains limited [17]. More recent studies have strengthened this association, demonstrating that ED serves as an early clinical marker of systemic vascular impairment even in asymptomatic diabetic patients [18–20].

Validated questionnaires such as the International Index of Erectile Function (IIEF) and the Female Sexual Function Index (FSFI) are widely used to assess sexual health in clinical and research settings. Penile Doppler ultrasound and nocturnal penile tumescence testing may provide additional objective evaluation in men, whereas vascular and hormonal assessments can be considered in women with persistent dysfunction.

The presence of SD in diabetic patients often indicates broader endothelial impairment and correlates with increased risk for PAD and cardiovascular events. As such, SD should not be considered merely a quality-of-life issue but also a potential early signal of systemic vascular pathology (Table 1). These updated findings reinforce the clinical importance of routinely assessing sexual function in diabetic populations as part of comprehensive cardiovascular risk evaluation. Updated international guidelines also support the integration of vascular and sexual health assessment into comprehensive diabetes management [21, 22].

Table 1. Prevalence of sexual dysfunction and PAD in diabetes.

Condition	Reported prevalence of diabetes	Key predictors	References
Erectile dysfunction (men)	35–75%	Age, duration of diabetes, poor glycemic control, hypertension, dyslipidemia	[3, 8, 12]
Female sexual dysfunction	20–45%	Poor glycemic control, depression, menopausal status, and vascular risk factors	[4, 9, 13]
PAD	20–30%	Diabetes duration, smoking, hypertension, dyslipidemia	[6, 14–16]

PAD: peripheral artery disease.

PAD in diabetes

PAD is more common in diabetes and presents earlier. U.S. population data show higher PAD prevalence in adults with diabetes versus those without after adjustment for age and risk factors [23]. Ankle-brachial index (ABI)-based cohorts and meta-analyses confirm increased incidence of cardiovascular events and mortality when PAD is present [24]. TransAtlantic Inter-Society Consensus (TASC II) also highlights diabetes as a major PAD accelerator across vascular beds [25].

Presentation ranges from asymptomatic disease to claudication and chronic limb-threatening ischemia. ABI ≤ 0.90 supports diagnosis; however, medial arterial calcification in diabetes can elevate ABI and mask disease [25, 26]. In suspected noncompressible arteries (ABI > 1.40) or when ABI is borderline, the toe-brachial index (TBI) and toe pressures improve detection [27]. Duplex ultrasound defines anatomy and flow; computed tomography/magnetic resonance (CT/MR) angiography is used for mapping when revascularization is considered [25, 28].

Hyperglycemia, dyslipidemia, hypertension, and inflammation drive accelerated atherosclerosis and impaired endothelial function in diabetes, producing diffuse, distal disease with poor collateralization [25]. Mechanisms include oxidative stress, advanced glycation end products (AGEs), smooth muscle dysfunction, and impaired vascular repair [25]. These processes overlap with those implicated in SD, reflecting shared systemic vasculopathy.

PAD in diabetes signals high systemic risk. Low ABI associates with approximately twofold higher risk of major cardiovascular events and all-cause mortality in pooled analyses [24, 28]. Limb outcomes are worse in diabetes due to neuropathy, infection risk, and impaired wound healing, raising ulceration and amputation rates [29].

Guidelines advise ABI screening in diabetic patients with exertional leg symptoms, nonhealing wounds, age ≥ 50 with additional risk factors, or age ≥ 65 regardless of symptoms; the TBI is recommended when ABI is noncompressible [21, 22]. Identifying PAD should trigger intensive risk modification: smoking cessation, statins, blood pressure control, antiplatelet therapy when indicated, glycemic optimization, exercise therapy, and timely referral for revascularization in limb-threatening ischemia [21, 22] (Table 1).

Vascular mechanisms linking SD and PAD in diabetes

Endothelial dysfunction

Endothelial dysfunction is a hallmark of both SD and PAD in diabetes. Hyperglycemia, oxidative stress, and reduced NO availability impair vasodilation and vascular homeostasis. In the penile vasculature, impaired endothelial NO synthase (eNOS) activity results in inadequate smooth muscle relaxation, contributing to ED [14]. Similarly, in peripheral arteries, endothelial dysfunction accelerates atherosclerosis and diminishes blood flow, which underpins PAD progression [30]. Flow-mediated dilation studies consistently demonstrate reduced endothelial responsiveness in diabetic patients with either ED or PAD [31]. Recent studies continue to confirm the central role of endothelial dysfunction in diabetic vasculopathy and its close link with ED and PAD progression [32].

Atherosclerosis and arterial stiffness

Diabetes accelerates atherosclerosis through dyslipidemia, chronic inflammation, and AGEs. Atherosclerotic plaque formation in penile and peripheral arteries restricts perfusion and increases arterial stiffness [33]. Arterial stiffness, measured by pulse wave velocity, is associated with ED severity and PAD extent, linking macrovascular pathology across vascular beds [34].

Microvascular disease

In addition to macrovascular atherosclerosis, diabetes-induced microangiopathy contributes to impaired tissue perfusion. Structural changes such as capillary basement membrane thickening and pericyte loss impair penile and lower-limb microcirculation [35]. These microvascular alterations play a central role in FSD as well, where impaired clitoral and vaginal blood flow leads to reduced arousal and lubrication [4, 17].

Inflammation and oxidative stress

Both ED and PAD are characterized by heightened oxidative stress and chronic low-grade inflammation. Biomarkers such as C-reactive protein, interleukin-6, tumor necrosis factor-α, and adhesion molecules are elevated in diabetic patients with vascular complications [36]. Oxidative stress reduces NO bioavailability, while inflammatory cytokines accelerate endothelial injury and plaque instability [37].

Circulating biomarkers and progenitor cells

Reduced levels of circulating endothelial progenitor cells (EPCs) and impaired angiogenic function have been observed in diabetic men with ED and in patients with PAD [38]. This highlights defective vascular repair mechanisms as a shared pathway. EPC dysfunction correlates with disease severity, reinforcing its potential as a marker of systemic vascular health.

Integration of mechanisms

The convergence of endothelial dysfunction, atherosclerosis, microangiopathy, inflammation, and impaired vascular repair creates a continuum of vascular injury that explains the coexistence of SD and PAD in diabetes. Recognizing these shared mechanisms underscores the importance of viewing SD not only as a quality-of-life condition but as a systemic vascular warning sign (Table 2). These interrelated vascular and neural mechanisms are summarized schematically in Figure 1, which illustrates how chronic hyperglycemia and endothelial dysfunction converge to produce both SD and PAD in diabetes.

Table 2. Vascular mechanisms shared by SD and PAD in diabetes.

Mechanisms	Pathophysiology	Impact on SD	Impact on PAD	References
Endothelial dysfunction	↓ NO bioavailability, oxidative stress	Impaired penile/clitoral vasodilation	Reduced arterial compliance, atherosclerosis	[10, 23, 24]
Atherosclerosis	Plaque formation, arterial stiffness	Arterial inflow restriction causing ED	Limb ischemia, claudication	[25, 26]
Microangiopathy	Basement membrane thickening, pericyte loss	Reduced genital perfusion	Poor distal limb perfusion	[27]

Table 2. Vascular mechanisms shared by SD and PAD in diabetes. (*continued*)

Mechanisms	Pathophysiology	Impact on SD	Impact on PAD	References
Inflammation and oxidative stress	↑ CRP, IL-6, TNF-α	Vascular injury, impaired erection	Plaque instability, PAD progression	[28, 29]
Impaired vascular repair	↓ EPCs	Reduced penile vascular recovery	Impaired collateral formation	[30]

NO: nitric oxide; CRP: C-reactive protein; IL-6: interleukin-6; TNF-α: tumor necrosis factor-alpha; EPCs: endothelial progenitor cells; SD: sexual dysfunction; PAD: peripheral artery disease; ED: erectile dysfunction; ↓ indicates decreased/reduced; ↑ indicates increased/elevated.

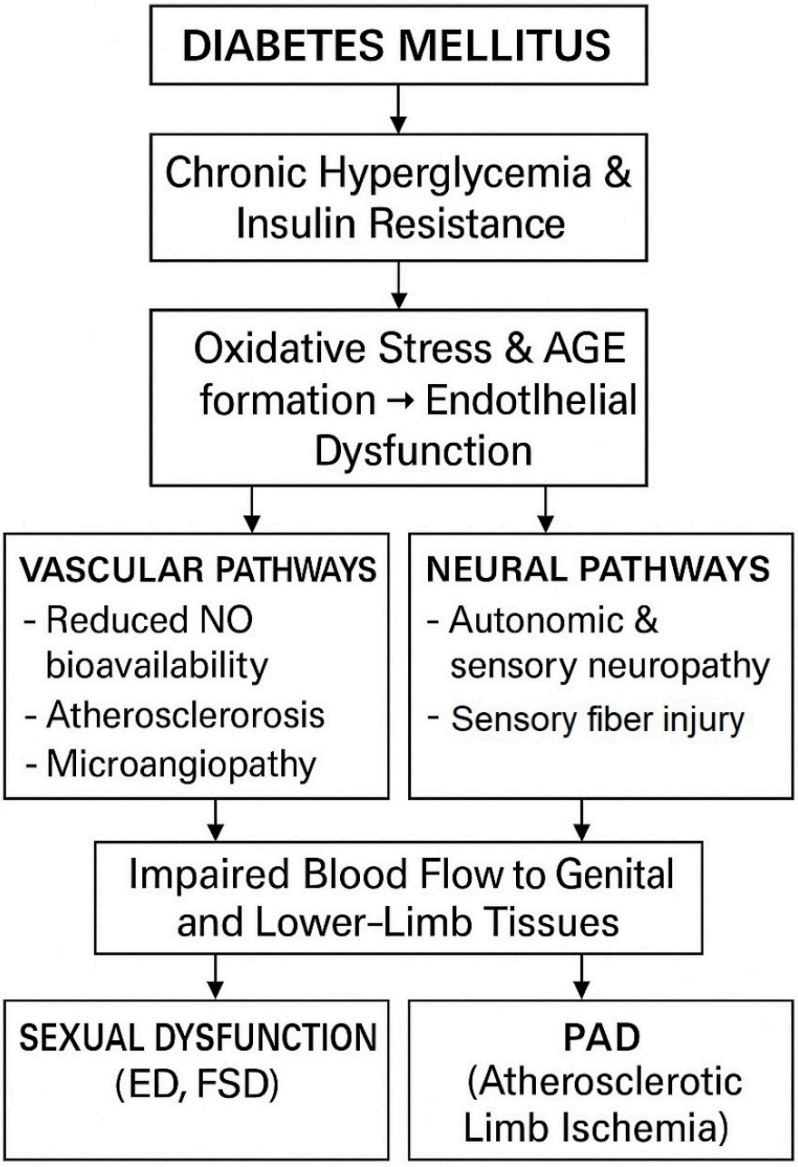

Figure 1. Integrated vascular-neural mechanisms linking sexual dysfunction and peripheral artery disease in diabetes mellitus. This schematic illustrates the shared vascular and neural pathways through which diabetes mellitus contributes to both sexual dysfunction and peripheral artery disease. AGE: advanced glycation end product; ED: erectile dysfunction; FSD: female sexual dysfunction; PAD: peripheral artery disease.

It should be noted that reported associations between endothelial dysfunction and sexual or peripheral vascular impairment vary across studies, largely due to differences in patient populations, diagnostic criteria, and study design. These methodological variations partly explain conflicting findings in the literature.

Neural mechanisms linking SD and PAD in diabetes

Cardiovascular autonomic neuropathy (CAN) and neurogenic vasomotor control

Diabetes-induced CAN shifts the sympathetic–parasympathetic balance toward sympathetic predominance and blunts baroreflexes, producing basal vasoconstriction, impaired flow reserve, and reduced heart rate variability [15, 39, 40]. This autonomic pattern limits end-organ perfusion in the pelvis and lower limbs and augments afterload, reinforcing macro- and microvascular ischemia relevant to both ED/FSD and PAD [15, 39–41].

Nitrergic neurotransmission and neurovascular coupling

Penile erection and clitoral/vaginal engorgement require intact nitrergic signaling from cavernosal autonomic nerves. Diabetic neuropathy reduces neuronal NO synthase (nNOS) activity and axonal integrity, weakening neurogenic NO release and downstream smooth muscle relaxation. Impaired neurovascular coupling thereby amplifies endothelial dysfunction documented in diabetic vasculopathy and contributes to coexisting PAD via reduced activity-dependent vasodilation in distal beds [14, 42, 43].

Somatic small-fiber neuropathy and sensory dysfunction

Small-fiber injury diminishes afferent sexual sensation and reflex pathways and also impairs neurogenic inflammation and antidromic vasodilation mediated by peptidergic fibers, reducing microcirculatory recruitment in genital and distal limb tissues [40, 44, 45]. Clinically, sensory loss delays symptom recognition in lower-extremity ischemia and worsens wound biology, interacting with PAD to increase ulceration risk [45, 46].

Central and hormonal interfaces

Autonomic and sensory neuropathies intersect with hypothalamic–pituitary–gonadal regulation via altered autonomic outflow and inflammatory signaling, which can secondarily affect sex steroid milieu and sexual function. These effects are ancillary compared with peripheral nitrergic and autonomic defects but can modulate phenotype severity [39, 42, 43].

Integrated model

Diabetic neuropathy drives: (I) sympathetic predominance with vasoconstriction and poor flow reserve, (II) loss of parasympathetic/nitrergic input to erectile and vulvovaginal tissues, and (III) small-fiber failure of sensory-mediated microvascular recruitment. These neural defects interact bidirectionally with endothelial dysfunction and atherosclerosis, providing a mechanistic bridge between SD and PAD within a shared neurovascular failure continuum [44–46] (Table 3). Interpretation of neurogenic mechanisms should consider methodological diversity among studies, including heterogeneity in neuropathy assessment and small sample sizes, which limit the generalizability of findings.

Table 3. Neural mechanisms linking SD and PAD in diabetes.

Neural pathway	Defect in diabetes	Clinical consequence	References
Autonomic neuropathy	Sympathetic predominance, reduced vagal activity, impaired baroreflex	Erectile failure, impaired genital engorgement, and abnormal vasomotor tone in limbs	[11, 31–33]
Nitrergic signaling (nNOS)	Reduced nNOS activity, axonal degeneration	Impaired erection and vaginal engorgement, reduced neurogenic vasodilation	[10, 34, 35]
Somatic small-fiber neuropathy	Sensory loss, impaired neurogenic inflammation, defective peptidergic signaling	Decreased arousal, reduced genital sensation, delayed PAD recognition, ulcer risk	[36–38]

SD: sexual dysfunction; PAD: peripheral artery disease; nNOS: neuronal nitric oxide synthase.

Clinical and translational evidence

Prospective cohorts and meta-analyses show ED independently predicts total CVD, coronary heart disease (CHD), stroke, and all-cause mortality beyond traditional risk factors [47, 48]. The artery-size hypothesis

provides a mechanistic clinical framework in which smaller penile arteries manifest atherosclerosis earlier than coronary or peripheral beds, explaining the temporal lead of ED before overt CVD [49].

Population studies indicate ED associates with lower ABI and higher PAD prevalence; ED can uncover previously undiagnosed PAD and may justify ABI screening in at-risk men [50]. Recent NHANES analyses reaffirm an independent association between ED and PAD after multivariable adjustment [51]. These data align with shared vascular mechanisms outlined earlier [33–37].

Penile duplex Doppler parameters, especially reduced cavernosal peak systolic velocity and arterial wall abnormalities, correlate with generalized vascular disease and predict adverse cardiovascular outcomes [52, 53]. Such measures can refine vascular risk assessment in men with ED, complementing ABI/TBI for lower-limb perfusion [26, 27].

FSD is more prevalent in diabetes and is associated with worse metabolic control; evidence connecting FSD to hard cardiovascular outcomes is limited but consistent with microvascular and neurovascular impairment [4, 17].

Inflammatory markers and endothelial dysfunction indices track with both ED and PAD, and lower EPC levels reflect impaired vascular repair capacity across phenotypes [36–38, 54]. These signals support a systemic vasculopathy linking genital and limb vascular beds.

Across epidemiology, imaging, and biomarkers, ED clusters with PAD and global atherosclerosis often precede clinical CVD events [47–49]. Incorporating sexual health assessment and simple vascular tests (ABI/TBI, targeted penile Doppler) may improve early cardiovascular risk identification in diabetes [21, 22, 52].

Clinical implications

Recognition of SD and PAD in diabetes has direct implications for cardiovascular risk stratification and clinical management. SD, particularly ED in men, should be regarded not only as a quality-of-life issue but also as an early vascular warning sign. Its presence warrants a careful reassessment of overall atherosclerotic cardiovascular risk and should prompt formal screening for PAD and other complications. The ABI remains the cornerstone diagnostic tool for PAD, although in patients with noncompressible vessels, the TBI and toe pressures provide superior diagnostic accuracy [21, 26]. In symptomatic or high-risk patients, duplex ultrasonography offers further evaluation, while CT or MR angiography is reserved for those being considered for revascularization [22].

Once SD or PAD is identified, aggressive risk modification becomes essential. Smoking cessation, statin therapy, blood pressure control, antiplatelet therapy where indicated, and optimization of glycemic management are all priorities in accordance with major diabetes and cardiovascular guidelines [21, 22]. Supervised exercise therapy has demonstrated clear benefit for claudication and should be the first-line intervention [55, 56]. Pharmacologic therapy such as cilostazol can be considered for symptom relief in the absence of heart failure [57, 58]. In the context of type 2 diabetes and elevated cardiovascular risk, glucose-lowering therapies with proven cardiovascular benefit, including glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT2) inhibitors, should be integrated into the treatment plan [59, 60].

Addressing sexual health requires coordination between specialties. Cardiology, endocrinology, urology, and vascular medicine must work in concert to optimize patient outcomes. Risk stratification of sexual activity should follow established cardiovascular guidelines, ensuring that patients with unstable or severe disease are stabilized before resuming sexual activity [61]. The Princeton consensus offers a structured approach to evaluating ED in the context of CVD, including risk categories based on exercise tolerance and medication use [62]. Phosphodiesterase type-5 inhibitors remain the mainstay of pharmacologic management for ED and can be safely used in most patients not receiving nitrates [41, 61, 62]. For women, systematic assessment of sexual function is often neglected, but FSD is common in diabetes and deserves structured evaluation and management. Interventions should include attention to glycemic control, management of depression, hormonal status, and comorbid pelvic floor disorders [4, 17, 21].

Patient education plays a pivotal role in the management of both SD and PAD. Structured diabetes education programs, such as Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND), have demonstrated efficacy in improving lifestyle factors, adherence, and cost-effectiveness in long-term care [63, 64]. Education should include information on foot checks, recognition of PAD symptoms, open discussion of sexual health, and reinforcement of lifestyle modifications, including exercise and diet. By integrating education into routine care, clinicians can empower patients to recognize early signs of vascular complications and engage more actively in risk reduction.

In practical terms, a clinical algorithm begins with systematically asking about sexual function and leg symptoms during diabetes visits. When dysfunction is reported, this should trigger reassessment of cardiovascular risk, targeted vascular testing, and appropriate therapeutic adjustments. Confirmed PAD requires initiation of guideline-directed medical therapy and, if necessary, referral for revascularization in cases of limb-threatening ischemia. Coordinated, multidisciplinary care supported by structured patient education offers the best chance of reducing both cardiovascular events and quality-of-life impairments associated with these complications (Table 4).

Table 4. Clinical implications and management strategies.

Domain	Recommendations	Outcomes	References
Screening	Ask about sexual function; ABI/TBI for PAD in at-risk patients	Improves early detection	[17, 21, 22, 42, 43]
Risk modification	Smoking cessation, statins, BP control, antiplatelet therapy, optimal glycemia	Reduces ASCVD events	[21, 22]
Symptom management	PDE5 inhibitors for ED (avoid nitrates); cilostazol for claudication	Symptom relief, improved function	[47, 48, 51, 52]
Lifestyle and education	Structured diabetes education (DESMOND); exercise therapy for PAD	Cost-effective, improves outcomes	[49, 50, 53, 54]
Novel therapies	GLP-1 RA, SGLT2 inhibitors in T2D with high CV risk	Proven CV benefit, potential vascular protection	[55–58]

PAD: peripheral artery disease; ABI: ankle-brachial index; TBI: toe-brachial index; BP: blood pressure; PDE5: phosphodiesterase type-5; ED: erectile dysfunction; DESMOND: Diabetes Education and Self-Management for Ongoing and Newly Diagnosed; GLP-1 RA: glucagon-like peptide-1 receptor agonist; SGLT2: sodium-glucose cotransporter-2; ASCVD: atherosclerotic cardiovascular disease; CV: cardiovascular.

Research gaps and future directions

This review offers a unique synthesis by combining vascular and neural mechanisms into a single conceptual model linking SD and PAD in diabetes. This integrated perspective aims to highlight overlapping pathophysiological pathways and their translational relevance, which have not been comprehensively summarized in previous literature.

Despite growing evidence that SD and PAD share vascular and neural mechanisms in diabetes, several gaps remain in both research and clinical practice. First, much of the available data concerns ED in men, whereas FSD is underexplored. Although small observational studies suggest that women with diabetes have impaired genital blood flow and worse sexual function, longitudinal studies linking these findings to cardiovascular outcomes are lacking [4, 17]. Addressing this gap requires prospective cohorts and mechanistic imaging studies specifically designed for women. Future research should aim to resolve current inconsistencies by standardizing diagnostic definitions and employing longitudinal designs to better clarify causal pathways.

Second, most epidemiological studies are cross-sectional, which limits the ability to infer temporal relationships and causality between SD, PAD, and cardiovascular events. Long-term prospective cohorts are needed to determine whether combined screening for SD and PAD improves the prediction of cardiovascular outcomes beyond traditional risk factors [47–51].

Third, while endothelial dysfunction, inflammation, and neuropathy have been identified as overlapping mechanisms, the translation of mechanistic biomarkers into clinical risk stratification tools is still incomplete. Circulating EPCs, arterial stiffness indices, and inflammatory markers show promise but

lack validation in large diabetic populations with integrated sexual health and PAD outcomes [36–38, 53]. More translational research is required to bridge this mechanistic–clinical gap.

Fourth, education and behavioral interventions are established components of diabetes care, but their specific impact on SD and PAD has not been systematically studied. Existing trials, such as DESMOND, demonstrate benefits for weight and smoking cessation [63, 64], but they rarely include sexual health or PAD endpoints. Designing education programs that explicitly incorporate vascular complication awareness, sexual health counseling, and self-care practices could address an important unmet need.

Finally, current management algorithms for ED and PAD are still siloed across disciplines. Multidisciplinary strategies that integrate endocrinology, cardiology, urology, gynecology, and vascular medicine remain underutilized. Implementation research is needed to test whether coordinated care models improve both vascular outcomes and quality of life. Large-scale trials incorporating novel antidiabetic agents with proven cardiovascular benefit, such as GLP-1 receptor agonists and SGLT2 inhibitors, could also explore their influence on SD and PAD endpoints [65, 66].

In summary, the future direction of research should include prospective, sex-specific studies, validation of vascular biomarkers, integration of education and behavioral interventions, and multidisciplinary trials targeting both SD and PAD. Such efforts will strengthen the evidence base and support a more comprehensive approach to cardiovascular risk reduction in diabetes.

Conclusions

SD and PAD are common complications of diabetes that reflect the same systemic vascular and neural injury underlying CVD. Both arise from overlapping mechanisms, including endothelial dysfunction, atherosclerosis, microvascular damage, and autonomic neuropathy, and together indicate heightened cardiovascular risk. ED and, to a growing extent, FSD often precede overt CVD and should be regarded as early clinical warning signs rather than isolated quality-of-life concerns. Likewise, the presence of PAD in diabetes identifies patients at particularly high systemic risk.

Integrating sexual health assessment and PAD screening into routine diabetes care can enable earlier identification of at-risk individuals and support timely preventive interventions. Multidisciplinary management, combining optimal medical therapy, patient education, and use of antidiabetic agents with proven cardiovascular benefit, may improve both prognosis and quality of life. Further research should clarify sex-specific aspects, validate mechanistic biomarkers, and evaluate coordinated care models. Recognizing the shared neurovascular basis of SD and PAD offers a pathway toward more precise and preventive cardiovascular risk management in diabetes.

Abbreviations

ABI: ankle-brachial index

AGEs: advanced glycation end products

CAN: cardiovascular autonomic neuropathy

CT: computed tomography

CVD: cardiovascular disease

DESMOND: Diabetes Education and Self-Management for Ongoing and Newly Diagnosed

DM: diabetes mellitus

ED: erectile dysfunction

EPC: endothelial progenitor cell

FSD: female sexual dysfunction

GLP-1: glucagon-like peptide-1

MR: magnetic resonance

NO: nitric oxide

PAD: peripheral artery disease

SD: sexual dysfunction

SGLT2: sodium-glucose cotransporter-2

TBI: toe-brachial index

Declarations

Author contributions

AB: Conceptualization, Investigation, Writing—original draft. MCÇ: Conceptualization, Investigation, Writing—original draft. MK: Conceptualization, Writing—review & editing. MY: Writing—review & editing. LB: Supervision, Validation. YK: Supervision, Validation. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Consent to participate

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Consent to publication

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Availability of data and materials

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