Table S1. Representative studies linking hyperferritinemia to MASLD.

Study/year/country	Population (*n*) & setting	MASLD definition/diagnostic modality	Major findings	Refs
Multicentre cohort study/2024/Italy, UK, Spain, Germany, Sweden, and Australia	*n* = 1,342; MASLD cohort with available baseline ferritin values and at least 6 months of follow-up, aged 18 years or above; median follow-up time: 96 months	Biopsy-confirmed MASLD	Baseline HF is associated with a 50% risk of LRE and 27% of all-cause mortality, with a stepwise increase from values of 215.5 μg/L and 272 μg/L, respectively. The inclusion of ferritin improves the performance of FIB-4 and NFS for the prediction of LRE and all-cause mortality.	[1]
Cross-sectional analysis of a prospective cohort/2016–2023/USA	*n* = 523; adults aged 50–80 with T2D and no diagnosis of hemochromatosis	MRI-PDFF ≥ 5%; MRE ≥ 3.0 kPa	Approximately 80% of people with HF and T2D have MASLD, and more than a third have significant hepatic fibrosis. HF may be a useful biomarker for MASLD and significant fibrosis in people with T2D.	[2]
Two-step Mendelian randomization study/2024/China	Genome-wide association studies of T2D (*n* = 933,970), glycemic traits (*n* = 209,605), iron	MRI-PDFF	Genetically elevated ferritin, serum iron, and liver iron were associated with a higher risk of liver steatosis. Ferritin possibly mediates the association of insulin resistance in liver steatosis.	[3]

	biomarkers (n = 246,139), MASLD (n = 972,707), and related biomarkers (ALT and PDFF)			
Population-based study/NHANES (2017–2020)/China	n = 4,466; analysis of 2017–2020 NHANES data to assess the relationship between serum iron status and the prevalence of MASLD and liver fibrosis	Hepatic steatosis in the absence of significant alcohol consumption or viral hepatitis; hepatic steatosis VCTE (CAP ≥ 238 dB/m); liver fibrosis (LSM ≥ 7 kPa)	Elevated serum ferritin, TIBC, and UIBC showed a distinct positive correlation with CAP, while only serum ferritin was positively correlated with LSM.	[4]
Population-based study/NHANES (2017−2018)/USA	n = 1,648; comparison of intake of macro- and micro-nutrient intake in a cohort of individuals with MASLD versus matched controls	CAP (> 280 dB/m); advanced fibrosis: transient elastography (> 10 kPa)	MASLD cases were more likely to be of Mexican American or Hispanic ethnicity (P = 0.002), have a higher BMI, and have a higher prevalence of diabetes, hyperlipidemia, and hypertension (P < 0.001 for all). MASLD cases had higher hs-CRP (P = 0.02) and ferritin (P = 0.02).	[5]
Five-year post-trial monitoring	n = 61; evaluation of the long-term effects of	Various MASLD parameters (hepatic steatosis, liver-to-spleen attenuation ratio	Serum ferritin baseline levels sustained a significant reduction in the 5-year post-trial	[6]

study/2015–2021/Japan	ipragliflozin and pioglitazone on MASLD in patients with T2D	on computed tomography, reductions in serum aminotransferase levels, glycemic parameters)	monitoring period (Pioglitazone: –58.4 ± 81.7 ng/mL; Ipragliflozin: –83.3 ± 79.2 ng/mL).	
Population-based study NHANES (2017–2020)/China	*n* = 5,927 (average age of 46.78 years); analysis of epidemiological and transcriptome data in MASLD and hepatic fibrosis	CAP (>248 dB/m); LSM (≥ 8.2 kPa)	High serum ferritin concentrations were associated with CAP and LSM. Serum ferritin and LSM had linear covariates in people under 40 years old and in female participants, as evidenced by the likelihood ratio test (LR) with a $P > 0.05$.	[7]
Historical longitudinal cohort study/2001–2016/South Korea	SLD (*n* = 17,560); categorized as MASLD (*n* = 15,744), MetALD (*n* = 1,103), cryptogenic without liver-related events at baseline (*n* = 713); aged 20 years and above	SLD was diagnosed based on the presence of hepatic steatosis on ultrasonography.	All SLD subtypes showed an increased risk of LRE with high serum ferritin levels (≥ 300 μg/L for males, ≥ 200 μg/L for females) compared to those with normal to low serum ferritin levels (< 300 μg/L for males, < 200 μg/L for females). Baseline ferritin level is a significant factor for LRE incident.	[8]
Prospective, observational	*n* = 3,393 (aged 20–74 years)	Ultrasound	Individuals with serum iron and transferrin saturation in the third or fourth quartile intervals	[9]

study/NHANES III (1988–1994)/China			had a 20–40% reduction in long-term mortality. High ferritin concentration was significantly associated with elevated all-cause mortality in patients with MASLD. However, this association disappeared in models adjusted for age, sex, and other covariates.	
Prospective cohort study (Dalian health management cohort)/2015–2022/China	*n* = 492; participants who attended health examinations at least three times and developed MASLD	Ultrasound with at least one of the following five cardiometabolic risk factors: (1) BMI ≥ 23 kg/m^2 or waist circumference ≥ 90/80 cm in men and women; (2) FPG ≥ 5.6 mmol/L, or HbA1c ≥ 5.7%, or T2D or treatment for T2D; (3) blood pressure ≥ 130/85 mmHg or specific drug treatment; (4) TG ≥ 1.70 mmol/L or lipid-lowering treatment; (5) HDL-C < 1.0 mmol/L for men and < 1.3 mmol/L for women or lipid-lowering treatment	Multivariate Cox proportional regression showed that higher baseline ferritin levels are an independent risk factor for MASLD.	[10]
Multi-center, cross-sectional study/2025/UK, Italy, Spain, France, and	*n* = 1,709 (with a median age of 53 years); the Study included consecutive patients with CHB in 19	Ultrasound, CAP score (≥ 275 dB/m), or histology; fibrosis: LSM ≥ 8 kPa in the CHB-MASLD population and ≥ 9 kPa in the CHB sub-group	High ferritin levels were significantly associated with MASLD incidence. Patients with CHB with MASLD have almost 3 times higher risk for advanced fibrosis compared with patients with	[11]

Greece	centers from five European countries		CHB without MASLD.	
Prospective randomized controlled trial/2019–2021/Japan	*n* = 24; patients with MASLD and comorbid T2D; *n* = 13 received dapagliflozin; *n* = 11 controls received Vitamin E	Ultrasound	Dapagliflozin treatment for 24 weeks showed a beneficial effect on MASLD parameters and a significant reduction in serum ferritin.	[12]
Two-sample bidirectional MR, multivariable MR, and mediation/NA/China	8,434 NAFLD and 770,180 controls (dataset 1 [13]), 4,761 NAFLD and 373,227 controls [14]); ferritin: *n* = 23,986 genome-wide association study (GWAS) meta-analysis iron homeostasis dataset 1 [15]; *n* = 246,139 [16]; Analyses to investigate the causal associations among obesity-related traits,	Histological, electronic health records, or radiological	Increased ferritin was associated with an increased risk of MASLD by multivariable Mendelian randomization. By two-step MR analysis, we found that genetic liability to ferritin mediated 3.34% (95% CI: 0.17–8.08%) of the waist circumference effects on MASLD risk and 18.84% (95% CI: 3.01–40.51%) of its effects on PLC risk.	[17]

	iron homeostasis biomarkers, MASLD, and liver cancer			
Retrospective study/2023/USA	*n* = 7,333 adult patients with MASLD; analysis of the association between HF and adverse clinical outcomes and identification of common genetic variants related to iron metabolism and liver fibrosis	Hepatic steatosis on imaging, biopsy, or vibration-controlled transient elastography, plus metabolic/genetic risk factors in the absence of chronic liver diseases other than hemochromatosis, such as *PNPLA3* and *TM6SF2* allelic variants	Of 7,333 patients with MASLD, 1,468 (20%) had elevated ferritin. In multivariate analysis, MHF was associated with increased mortality and incident liver-related events. MHF was associated with cirrhosis-promoting alleles, including *PNPLA3*-rs738409-G allele and *TM6SF2*-rs58542926-T allele, but not with common iron overload-promoting *HFE* mutations.	[18]
Single-center cross-sectional study (SAKKOPI)/2023/Austria and Switzerland	4,286 asymptomatic adults aged 45–80 participating in opportunistic screening for colorectal cancer. Of these, 1,903 were diagnosed with hepatic steatosis; the study	Hepatic steatosis: ultrasound; MASLD: steatosis accompanied by one of the following criteria of metabolic dysfunction: (1) overweight (BMI ≥ 25 kg/m²) or waist circumference ≥ 94/80 cm in Caucasian men and women, (2) blood pressure ≥ 130/85 mmHg or specific drug treatment, (3) triglycerides ≥ 150 mg/dL or	While the mean ferritin level was 118 ng/mL in the overall cohort (*n* = 4,286), it was 153 ng/mL in the hepatic steatosis cohort (*n* = 1,903) and 95 ng/mL in the no hepatic steatosis cohort (*n* = 2,383).	[19]

	analysed the relevance of metabolic dysfunction according to MAFLD, MASLD, and metabolic syndrome criteria (i.e., the population of interest regarding SLD) and steatosis for cardiovascular health	specific drug treatment, (4) plasma HDL-cholesterol < 40 mg/dL for men and <50 mg/dL for women or specific drug treatment, (5) T2D or prediabetes (i.e., fasting blood glucose 100 mg/dL to 125 mg/dL, or 2 h post-load glucose levels 140 mg/dL to 199 mg/dL or HbA1c 5.7–6.4%)		
Population-based observational cohort study/2013–2020/Austria and Italy	10,044 participants randomized and selected from the local population surrounding the region of Salzburg, Austria, aged 40–77 years	Not provided	Of all subjects with MASLD (*n* = 2,669) in our cohort, 24% (*n* = 636) had HF, supporting estimates of increased HF prevalence in MASLD. HF and, in particular, MHF are associated with metabolic alterations. In addition, a higher prevalence of MASLD of 57% in subjects with HF and a further increase in MASLD prevalence along with the severity of HF was observed.	[20]
Cohort study/2022–2023/Romania	*n* = 271 T2D patients with MASLD with a mean age of 65.0 ± 8.4 years and a mean	Hepatic steatosis/steatohepatitis in the absence of other secondary causes of liver disease and patient history	Male patients with T2D and MASLD had lower platelet count and PTC and larger PDW. Higher insulin resistance was associated with lower platelet count and PTC and higher PDW.	[21]

	duration of diabetes of 9.7 ± 5.0 years		Moreover, patients with a higher HOMA-IR had higher platelet counts and increased concentrations of ferritin.	
Cross-sectional study/NHANES (2017–2018)/China	*n* = 2,145; investigation of the association between serum ferritin and MAFLD	Ultrasound and several non-invasive markers	Elevated serum ferritin levels are associated with a higher prevalence of MAFLD and advanced liver fibrosis. Elevated serum ferritin levels combined with diabetes are important risk factors for liver fibrosis.	[22]

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; CAP: controlled attenuation parameter; CHB: chronic hepatitis B; FIB-4: fibrosis-4 score; HbA1c: glycated haemoglobin; HCC: hepatocellular carcinoma; HF: hyperferritinemia; HOMA-IR: homeostatic model assessment for insulin resistance; LRE: liver-related event; LSM: liver stiffness measurement; MAFLD: metabolic-associated fatty liver disease; MASLD: metabolic dysfunction-associated steatotic liver disease; MetALD: metabolic dysfunction and alcohol-related liver disease; ASLD with moderate-to-high alcohol intake; MHF: metabolic hyperferritinemia; MR: Mendelian randomization; MRI: magnetic resonance imaging; NFS: non-alcoholic fatty liver disease fibrosis score; NHANES: National Health and Nutrition Examination Survey; PDFF: proton density fat fraction; PDW: platelet distribution width; PLC: primary liver cancer; PTC: plateletcrit; SLD: steatotic liver disease; T2D: type 2 diabetes; TIBC: total iron-binding capacity; UIBC: unsaturated iron-binding capacity.

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