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Correlation between metabolic dysfunction-associated steatotic liver disease and subclinical coronary atherosclerosis in eastern China

Guanghui Ma[1†], Guohou Xu[1†] and Haixia Huang[1*]

Abstract

Background Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterized by the presence of at least one cardiovascular disease (CVD) risk factor, underscoring its potential to elevate CVD risk in affected individuals. However, evidence linking MASLD to subclinical coronary atherosclerosis remains scarce, and further investigations are necessary to elucidate the independent role of varying MASLD severities as a CVD risk factor.

Methods This study analyzed 7,507 participants aged ≥ 40 who underwent comprehensive health evaluations at the Shanghai Health and Medical Center. Logistic regression analysis was utilized to explore the relationship between MASLD severity and the presence of coronary artery calcification (CAC). Correlation analysis was performed to assess the association between MASLD severity and CAC staging.

Results After adjusting for established CVD risk factors, MASLD showed a significant association with CAC, which intensified with increasing MASLD severity. Among individuals with hypertension, MASLD was markedly correlated with CAC. In contrast, in non-hypertensive participants, only moderate and severe MASLD were significantly associated with CAC, while mild MASLD demonstrated no notable link, even after adjustment for CVD risk factors. Moreover, correlation analysis revealed a positive association between MASLD severity and CAC staging, indicating that higher MASLD severity aligned with more advanced CAC stages.

Conclusion This study highlighted that MASLD severity was independently associated with subclinical atherosclerosis, irrespective of traditional CVD risk factors, in an urban eastern Chinese population without a prior history of coronary atherosclerosis. The strongest associations were observed in individuals with severe MASLD, emphasizing the importance of assessing MASLD severity in CVD risk stratification.

Keywords Non-alcoholic fatty liver disease, Coronary artery calcification, Cardiovascular disease, Coronary artery calcification score, Steatohepatitis, Framingham risk score, Fatty liver disease, Hypertension, Cardiac metabolic criteria, Hepatic lipid deposition

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is defined as steatotic liver disease occurring in conjunction with one or more cardiometabolic risk factors, excluding the influence of harmful alcohol consumption. Previously termed non-alcoholic fatty liver disease (NAFLD) [1], MASLD is primarily characterized

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by the abnormal accumulation of lipids within hepatocytes, detectable via imaging techniques. Globally, MASLD has emerged as the leading cause of chronic liver disease, affecting approximately 30% of adults [2, 3]. This prevalence continues to rise and exhibits notable regional differences. Recent meta-analyses have identified MASLD as an independent risk factor for cardiovascular disease (CVD) [4]. This recognition highlights the significant interplay between metabolic dysfunction and cardiovascular health, warranting heightened clinical attention to MASLD as a contributor to CVD risk. CVD represents the leading cause of mortality among patients with MASLD, accounting for approximately one-third of deaths, predominantly due to coronary artery disease (CAD). Coronary artery calcification (CAC), a non-invasive marker of subclinical coronary atherosclerosis, serves as a critical independent predictor of CAD. Evidence from the Multi-Ethnic Study of Atherosclerosis has highlighted that the coronary artery calcification score (CACS) outperforms other conventional tests in predicting major adverse cardiovascular events, offering substantial prognostic value [5, 6]. Additionally, CACS has proven to be a reliable negative risk indicator for identifying individuals with a low likelihood of coronary atherosclerosis [7, 8]. The U.S. Preventive Services Task Force has recommended that individuals undergoing annual chest computed tomography (CT) scans for lung cancer screening may also be at moderate risk for coronary heart disease [9]. When employing low-dose computed tomography (LDCT) for lung cancer screening, stratifying patients by CACS can effectively guide the prevention and management of subclinical coronary atherosclerosis. The semi-quantitative sequential CACS, derived from routine non-gated chest CT scans, has demonstrated strong concordance with the Agatston score and significant correlation with CAD outcomes [10, 11]. This straightforward and accessible approach enhances the utility of CAC assessment in clinical settings, particularly during lung cancer screening protocols. The simplicity and accessibility of this approach make it an invaluable tool for assessing CAC during lung cancer screenings. With the 2023 introduction of MASLD as the updated terminology for steatohepatitis, the focus has shifted toward the role of metabolic dysfunction. This redefinition highlights an increased CVD risk among MASLD patients [12]. The terminological update underscores the need for a deeper understanding of the interplay between MASLD severity and cardiovascular health. To address this gap, the present study aimed to explore the relationship between MASLD severity and subclinical coronary atherosclerosis in an Asian population through a cross-sectional analysis.

Materials and methods

Study population

The study protocol was reviewed and approved by the Ethics Committee of Shanghai Health and Medical Center (Approval No. LLSC2024027). Given the retrospective nature of this analysis, the Ethics Committee waived the requirement for obtaining informed consent from participants. Data were retrospectively collected from comprehensive health examinations conducted at Shanghai Health and Medical Center between January 1 and December 31, 2020. Inclusion criteria encompassed the following: chest LDCT, abdominal ultrasound, and other imaging examinations; complete physical assessments, including measurements of waist circumference, hip circumference, height, weight, and blood pressure; and detailed blood biochemical tests for glucose and lipid profiles. All participants were asymptomatic at the time of evaluation. Exclusion criteria were applied as follows: 2,899 individuals aged under 40 years, 127 participants with a history of CVD, 267 individuals with excessive alcohol consumption, and 48 HBsAg-positive participants. After these exclusions, a total of 7,507 individuals with complete clinical and imaging data were included in the final analysis (Fig. 1).

Clinical history records and laboratory data

Demographic details, cardiovascular risk factors, and anthropometric data were extracted from the database of Shanghai Health and Medical Center. These data included age, gender, hypertension status, systolic and diastolic blood pressure (SBP and DBP, respectively), diabetes, hyperlipidemia, hyperuricemia, history of cardiovascular and liver diseases, smoking and alcohol consumption habits, as well as height, weight, body mass index (BMI), waist circumference, and hip circumference. Height and weight were measured using an ultrasonic height and weight device (SK-L06B) to calculate BMI. Blood pressure was recorded using an Omron electronic blood pressure monitor, with particular attention to SBP and DBP. Participants fasted for at least 12 h overnight prior to the collection of venous blood samples for laboratory analysis. The samples were processed using ROCHE C702 automated biochemical analyzers and Roche original reagents to measure fasting blood glucose, glycated hemoglobin (HbA1c), uric acid, creatinine, blood urea nitrogen, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Hypertension and diabetes were diagnosed based on medical history, medication use, blood pressure readings, or HbA1c levels. Hyperlipidemia was identified either from a prior diagnosis or by meeting one or more of the following

criteria: LDL-C ≥ 3.4 mmol/L, HDL-C < 1.0 mmol/L, TG ≥ 1.70 mmol/L, or TC ≥ 5.2 mmol/L. Central obesity was defined as a waist-to-hip ratio (WHR) > 0.9 in males and > 0.85 in females. Hyperuricemia was diagnosed when fasting serum uric acid levels exceeded 420 μmol/L in males or 360 μmol/L in females, based on two separate measurements under normal dietary conditions. The Framingham risk score (FRS) was calculated using age, gender, TC, HDL-C, SBP, and smoking status to estimate the 10-year risk of coronary heart disease. Participants were classified as either "low risk" (< 10% 10-year risk) or "intermediate to high risk" (≥ 10% 10-year risk) based on their FRS results.

Measurement of CAC by LDCT

CAC was assessed using a 256-slice CT scanner (GE Healthcare Revolution CT Scanner) following a standardized protocol. The assessment adhered to the guidelines set by the International Cardiovascular CT Association, which categorize the presence of CAC in the left main artery (LM), left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA) as absent, mild, moderate, or severe, corresponding to scores of 0, 1, 2, or 3, respectively. Mild CAC was defined as calcification occupying less than one-third of the artery length (CACS = 1), moderate as calcification involving one-third to two-thirds (CACS = 2), and severe as calcification extending over more than two-thirds of the artery length (CACS = 3). The total CAC score was calculated by summing the individual scores of all four arteries, resulting in a range from 0 to 12. Scores were categorized into three severity levels: 0 indicating absence, 1–3 representing mild CAC, and 4–12 corresponding to moderate or severe CAC [10, 13]. Subclinical coronary atherosclerosis was defined as a CAC score (CACS) of ≥ 1 in asymptomatic individuals. The evaluation process adhered to a consensus-based approach, requiring agreement between the two attending physicians, who were blinded to clinical data derived from CT images. This rigorous methodology ensured objective and consistent CAC assessment.

MASLD assessment

MASLD was identified in individuals with hepatic steatosis who met at least one of the following cardiometabolic criteria: BMI: ≥ 25 kg/m^2 or waist circumference > 94 cm in men and > 80 cm in women; Glucose metabolism: fasting serum glucose ≥ 5.6 mmol/L, postprandial 2-h blood glucose ≥ 7.8 mmol/L, HbA1c ≥ 5.7%, or a diagnosis of type 2 diabetes (T2D) or current treatment for T2D; blood pressure: ≥ 130/85 mmHg or receiving antihypertensive medication; lipid profile: plasma TG ≥ 1.70 mmol/L or on lipid-lowering therapy; plasma HDL-C ≤ 1.0 mmol/L for men and ≤ 1.3 mmol/L for women, or receiving lipid-lowering therapy [1]. Hepatic echogenicity, indicative of fatty liver, was evaluated using the Siemens EPIQ 7 real-time color Doppler ultrasound system. This high-resolution device, equipped with a probe frequency range of 1.0–5.0 MHz, was operated by experienced sonographers. Fatty liver disease was diagnosed based on standardized ultrasonic grading criteria: mild fatty liver: liver parenchyma echo slightly stronger than that of the kidney/spleen, with clear visualization of intrahepatic venous structures and the diaphragm; moderate fatty liver: moderately increased liver parenchyma echo compared to the kidney/spleen, with reduced clarity of intrahepatic venous structures and weaker diaphragm echo; severe fatty liver: significantly elevated liver parenchyma echo relative to the kidney/spleen, with blurred or undetectable intrahepatic venous structures and diaphragm echoes [14, 15]. MASLD severity was classified into three categories, mild, moderate, and severe, based on the ultrasonic grading of fatty liver disease. This standardized approach provided a robust framework for evaluating MASLD and its severity.

Statistical analysis

Histograms and QQ plots were employed to evaluate data normality. Continuous variables with a non-normal distribution were expressed as medians with interquartile ranges (Q1–Q3), while categorical variables were presented as frequencies and percentages. Comparisons of continuous variables among MASLD severity groups were performed using the Kruskal–Wallis test, followed by post-hoc Bonferroni adjustments for pairwise comparisons. Categorical variables were analyzed using the χ^2 test. Binary logistic regression analysis was conducted to explore the association between MASLD severity and subclinical coronary atherosclerosis, with adjustments for potential confounding factors. Covariates included in the multivariable model were selected based on clinical relevance, encompassing age, gender, diabetes, BMI, smoking status, hypertension, central obesity, hyperlipidemia, hyperuricemia, and FRS. To further examine the relationship between CAC staging and MASLD severity, the Goodman–Kruskal γ correlation was utilized. Statistical significance was set at $P < 0.05$. Data analysis was performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA), and GraphPad Prism, version 9.5 (GraphPad Software, San Diego, CA, USA).

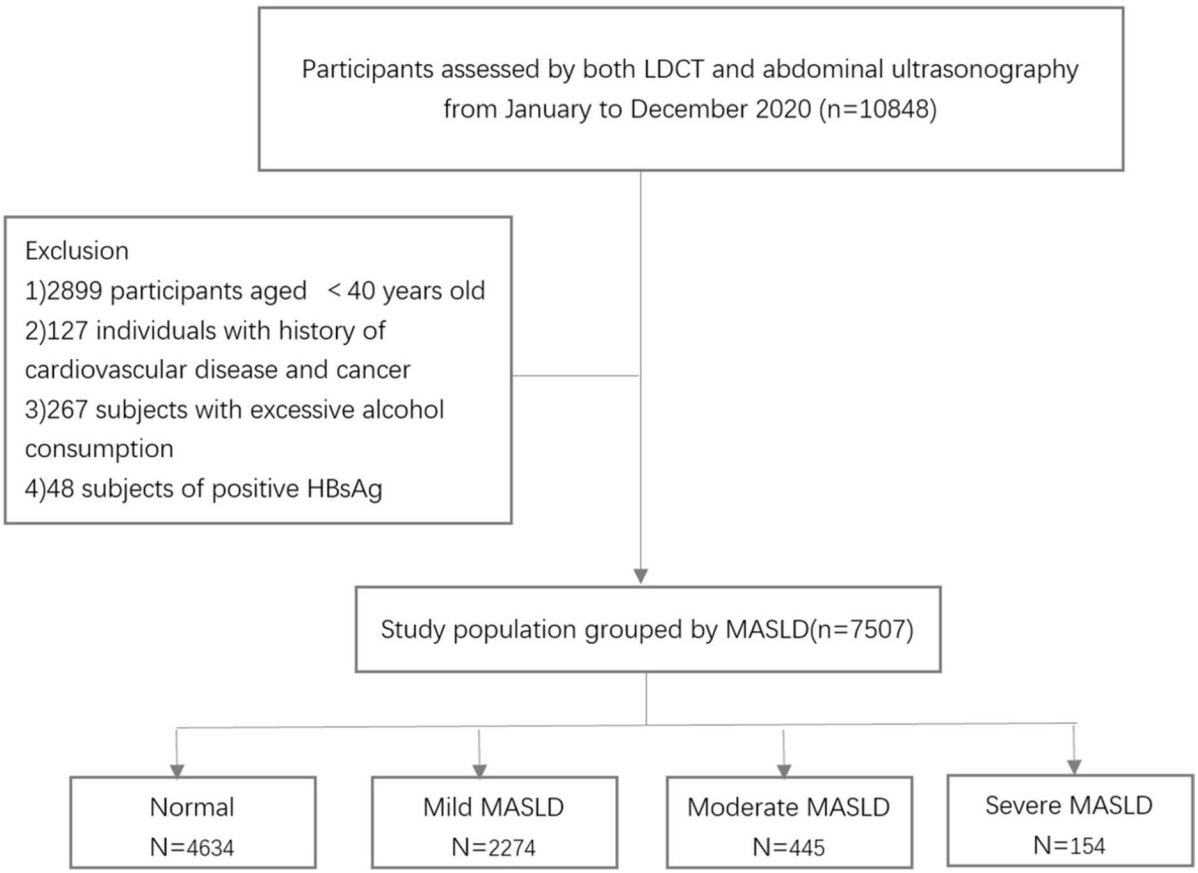

Fig. 1 Participant selection flowchart

Results

Baseline features

This study included 7,507 participants with a median age of 52 years and a median BMI of 24.34 kg/m^2. The cohort comprised 60.84% males (n = 4,567) and 39.16% females (n = 2,940), with 38.27% (n = 2,873) meeting the diagnostic criteria for MASLD. Based on MASLD severity, participants were categorized into four groups: non-MASLD (n = 4,634), mild MASLD (n = 2,274), moderate MASLD (n = 445), and severe MASLD (n = 154). Across all MASLD groups, the prevalence of MASLD was significantly higher in males compared to females. Participants with MASLD exhibited distinct baseline characteristics compared to those without MASLD. Individuals in the MASLD group were older, had higher BMI values, and displayed a greater prevalence of central obesity, current smoking habits, hypertension, diabetes, hyperlipidemia, and metabolic syndrome. Furthermore, MASLD participants demonstrated significantly elevated levels of SBP and DBP, fasting blood glucose, glycated hemoglobin, TC, TG, LDL-C, blood urea nitrogen, uric acid, and creatinine, while showing lower HDL-C levels. All these differences were statistically significant ($P < 0.05$).

In the study cohort, 17.26% (n = 1296) of participants had CAC. The prevalence of CAC was 24.63% in the mild MASLD group, 31.69% in the moderate MASLD group, and 39.61% in the severe MASLD group. Mild CAC (CACS 1–3) was observed in 12.20% (n = 916) of participants, while moderate to severe CAC (CACS 4–12) accounted for 5.06% (n = 380). The LAD artery was the most frequently affected among coronary arteries, with calcium proportions in the LM, LAD, RCA, and LCX increasing progressively with MASLD severity (Table 1).

Figure 2 illustrates the distribution of CAC percentages across varying degrees of MASLD severity. In the non-MASLD group, the proportion of mild CAC cases was 8.33%, whereas in the MASLD group, the percentages increased with severity, reaching 17.06%, 23.15%, and 25.32% for mild CAC. For moderate to severe CAC, the respective percentages were 2.98%, 8.00%, 8.54%, and 25.32%, showing a notable upward trend with MASLD severity.

The corresponding forest plot highlights the odds ratios (ORs) linking MASLD severity with CAC across all participants. To disentangle the independent

Table 1 Clinical characteristics of participants classified according to MASLD

	Non-MASLD (n = 4634)	Mild MASLD (n = 2274)	Moderate MASLD (n = 445)	Severe MASLD (n = 154)	*p-value*
Sociodemographics					
Male, n(%)	2342(50.54%)	1771(77.88%)a	341(76.63%)a	113(73.38%)a	< 0.001
Age, years	51.00(45.00,57.00)	54.00(48.00,59.00)a	57.00(48.50,61.00)ab	57.00(49.75.59.00)a	< 0.001
BMI(kg/m^2)	23.15(21.47,25.06)	25.98(24.31,27.82)a	27.41(25.31,29.38)ab	26.96(25.16,29.31)ab	< 0.001
Central obesity, n(%)	735(15.86%)	1083(47.63%)a	298(66.97%)ab	96(62.34%)ab	< 0.001
SBP, mmHg	119 (108–130)	129(118–138)a	130(120–140)ab	130(120–143)a	< 0.001
DBP, mmHg	71(64–79)	77(70–84)a	78(72–86)ab	79(73–86)a	< 0.001
Smoking, n(%)	1277(27.56%)	1024(45.03%)a	201(45.17%)a	64(41.56%)a	< 0.001
FRS ≥ 10%, n(%)	1591(34.33%)	1532(67.37%)a	334(75.06%)ab	119(77.27%)ab	< 0.001
Metabolic components					
HTN, n(%)	1034(22.31%)	1164(51.19%)a	247(55.51%)a	88(57.14%)a	< 0.001
Diabetes, n(%)	289(6.24%)	446(19.61%)a	138(31.01%)ab	54(35.06%)ab	< 0.001
Hyperlipidemia, n(%)	2289(49.4%)	1668(73.35%)a	343(77.08%)a	120(77.92%)a	
Biomarkers					
FBG, mmol/L	5.02(4.76,5.34)	5.41(4.78,6.00)a	5.58(5.12,6.50)ab	5.86(5.29,6.91)ab	< 0.001
HbAlc, (%)	5.60(5.40,5.80)	5.80(5.50,6.10)a	5.90(5.6 0,6.30)ab	5.90(5.50,6.50)a	< 0.001
TG, mmol/L	1.03(0.74,1.49)	1.74(1.24,2.49)a	2.02(1.40,3.00)ab	2.07(1.52,3.15)ab	< 0.001
TC, mmol/L	4.87[4.32,5.49]	4.91[4.31,5.58]	4.93[4.36,5.63]	5.10[4.52,5.76]a	0.006
LDL-C, mmol/L	2.85[2.46,3.31]	2.95[2.54,3.42]a	2.96[2.55,3.38]a	3.08[2.68,3.45]a	< 0.001
HDL-C, mmol/L	1.42[1.22,1.65]	1.21[1.06,1.38]a	1.18[1.05,1.36]a	1.16[1.04,1.32]a	< 0.001
BUN, mmol/L	5.26[4.54,6.08]	5.45[4.76,6.29]a	5.49[4.68,6.32]b	5.33[4.70,6.11]	< 0.001
UA, umol/L	290.40[236.70,349.83]	360.70[306.95,413.70]a	370.80[320.55,434.10]ab	373.45[322.70,445.85]a	< 0.001
Cr, umol/L	68.50[58.70,80.20]	75.70[65.90,84.10]a	73.00[62.15,84.15]ab	74.00[62.08,84.43]a	< 0.001
CAC > 0, n(%)	524(11.31%)	560(24.63%)a	141(31.69%)ab	61(39.61%)ab	< 0.001
CACS = 1–3,n(%)	386(8.33%)	388(17.06%)a	103(23.15%)ab	39(25.32%)ab	< 0.001
CACS ≥ 4, n(%)	138(2.98%)	182(8.0%)a	38(8.54%)a	22(14.29%)abc	< 0.001
LM, n(%)	226(4.88%)	265(11.65%)a	66(14.83%)a	25(16.23%)a	< 0.001
LAD, n(%)	485(10.47%)	518(22.78%)a	123(27.64%)ab	53(34.42%)ab	< 0.001
LCX, n(%)	139(3.0%)	191(8.4%)a	49(11.01%)a	23(14.94%)ab	< 0.001
RCA n(%)	203(4.38%)	273(12.01%)a	62(13.93%)a	36(23.38%)abc	< 0.001

a indicates a comparison with the standard group, $P < 0.05$; b indicates a comparison with mild MASLD, $P < 0.05$; c indicates a comparison with moderate MASLD, $P < 0.05$; d indicates a comparison with severe MASLD, $P < 0.05$; all pair-wise comparisons have undergone multiple adjustments

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FRS, Framingham risk score; HTN, Hypertension; FBG, Fasting blood glucose; TG, Triglycerides; TC, Total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; BUN, Blood Urea Nitrogen; UA, Uric Acid; Cr, serum Creatinine; CACS, coronary artery calcification score; LM, Left main artery; LAD, Left anterior descending; LCX, Left Circumflex; RCA, right coronary artery; MASLD, metabolic dysfunction-associated steatotic liver disease

associations, we applied multiple adjustment models. Model 2 controlled for age and sex; model 3 included additional adjustments for diabetes, BMI, central obesity, smoking, hypertension, hyperlipidemia, and hyperuricemia; and model 4 further accounted for the FRS. In the unadjusted model, significant associations were evident between mild, moderate, and severe MASLD and CAC. After adjusting for confounding factors, these associations persisted across models 2, 3, and 4. Further stratification by hypertension status revealed distinctive patterns. Among hypertensive participants, a significant correlation between mild, moderate, and severe MASLD and CAC was consistently observed across all four models. In contrast, for non-hypertensive participants, models 1 and 2 demonstrated significant associations for mild, moderate, and severe MASLD with CAC. However, in models 3 and 4, the association remained significant only for moderate and severe MASLD, while mild MASLD did not exhibit a statistically significant link to CAC (Fig. 3).

A study investigating the relationship between MASLD severity and CAC staging revealed a significant positive correlation ($\gamma = 0.436$, $P < 0.001$). As the severity of MASLD-associated fatty liver degeneration increased, the proportion of individuals with subclinical coronary artery atherosclerosis, characterized by a

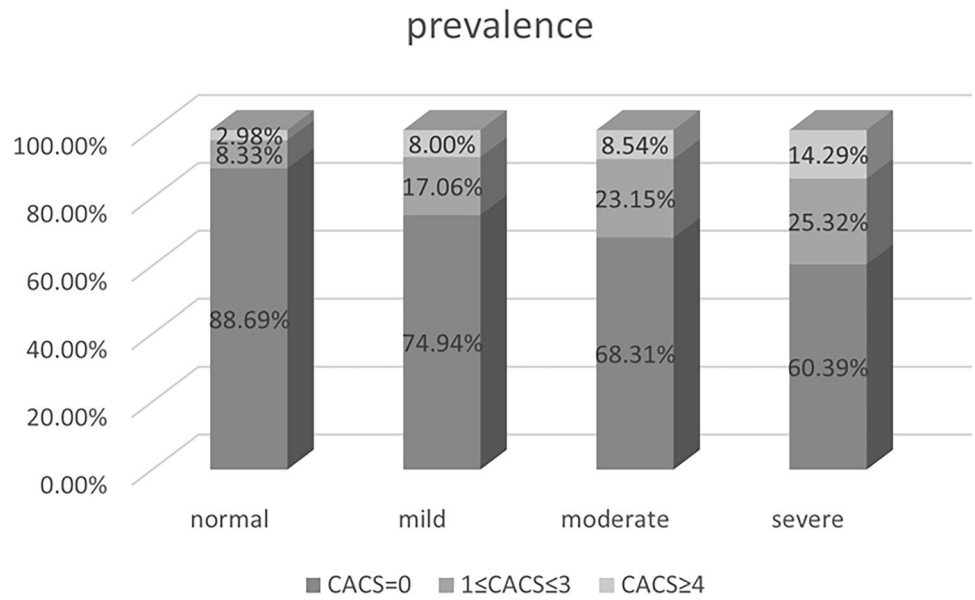

Fig. 2 The distribution of CAC percentages across various severity levels of MASLD

CACS ≥ 4, rose markedly. This finding underscored the progressive cardiovascular risk associated with advancing MASLD severity.

Discussion

This study aimed to elucidate the relationship between the severity of MASLD and subclinical coronary artery atherosclerosis in individuals undergoing health screenings with no prior history of CVD. After adjusting for established cardiovascular risk factors, a significant association was identified between varying degrees of MASLD and subclinical coronary artery atherosclerosis, with the strength of this connection intensifying as MASLD severity increased. The hypertensive subgroup exhibited a particularly strong correlation between MASLD severity and subclinical coronary artery atherosclerosis, underscoring the compounding effect of hypertension on this relationship. In contrast, within the non-hypertensive cohort, moderate and severe MASLD showed a clear and significant association with subclinical coronary artery atherosclerosis after adjustment for cardiovascular risk factors. However, no significant correlation was observed for mild MASLD, highlighting potential differences in cardiovascular risk profiles based on MASLD severity and hypertensive status.

Previous studies have consistently demonstrated a robust association between NAFLD and subclinical coronary atherosclerosis, as well as an elevated risk of adverse cardiovascular events in the global adult population [16–19]. Recent evidence from a 4.4-year longitudinal cohort study further corroborates this link, reporting a significant relationship between adverse outcomes in coronary computed tomography angiography (CCTA) and MASLD ($P=0.007$). Moreover, MASLD is strongly associated with adverse cardiac events, with a hazard ratio of 1.82 (95% CI 1.18–2.83, $P=0.007$) [20]. In addition, The global prevalence of MASLD has risen dramatically, increasing from 25% in 2016 to over 30% in recent years, with a steadily growing annual incidence rate, underscoring its emergence as a critical public health concern [21, 22]. In our cohort of 7,507 patients, the prevalence of MASLD was approximately 38.27%, slightly lower than the 47.2% reported in a Korean cohort but closely aligning with the findings of a recent meta-analysis that has estimated a prevalence of 38.77% (95% CI, 32.94–44.95%) [23, 24]. These observations highlight the urgent need for large-scale, population-based cohort studies to further explore MASLD, with particular attention to racial and gender differences.

In our study, we accounted for potential confounders, including age, gender, diabetes, BMI, central obesity, smoking, hypertension, hyperlipidemia, hyperuricemia, and the FRS, among participants with CVD. The OR for subclinical coronary atherosclerosis was 1.488 (95% CI, 1.258–1.760; $P<0.001$) in patients with mild MASLD, 1.720 (95% CI, 1.317–2.272; $P<0.001$) in those with moderate MASLD, and increased significantly to 3.256 (95% CI, 2.182–4.858; $P<0.001$) in severe MASLD patients. A correlation analysis further confirmed a positive association between MASLD severity and CAC staging, as evidenced by a direct correlation coefficient ($\gamma=0.436$, $P<0.001$). These results highlighted a strong and

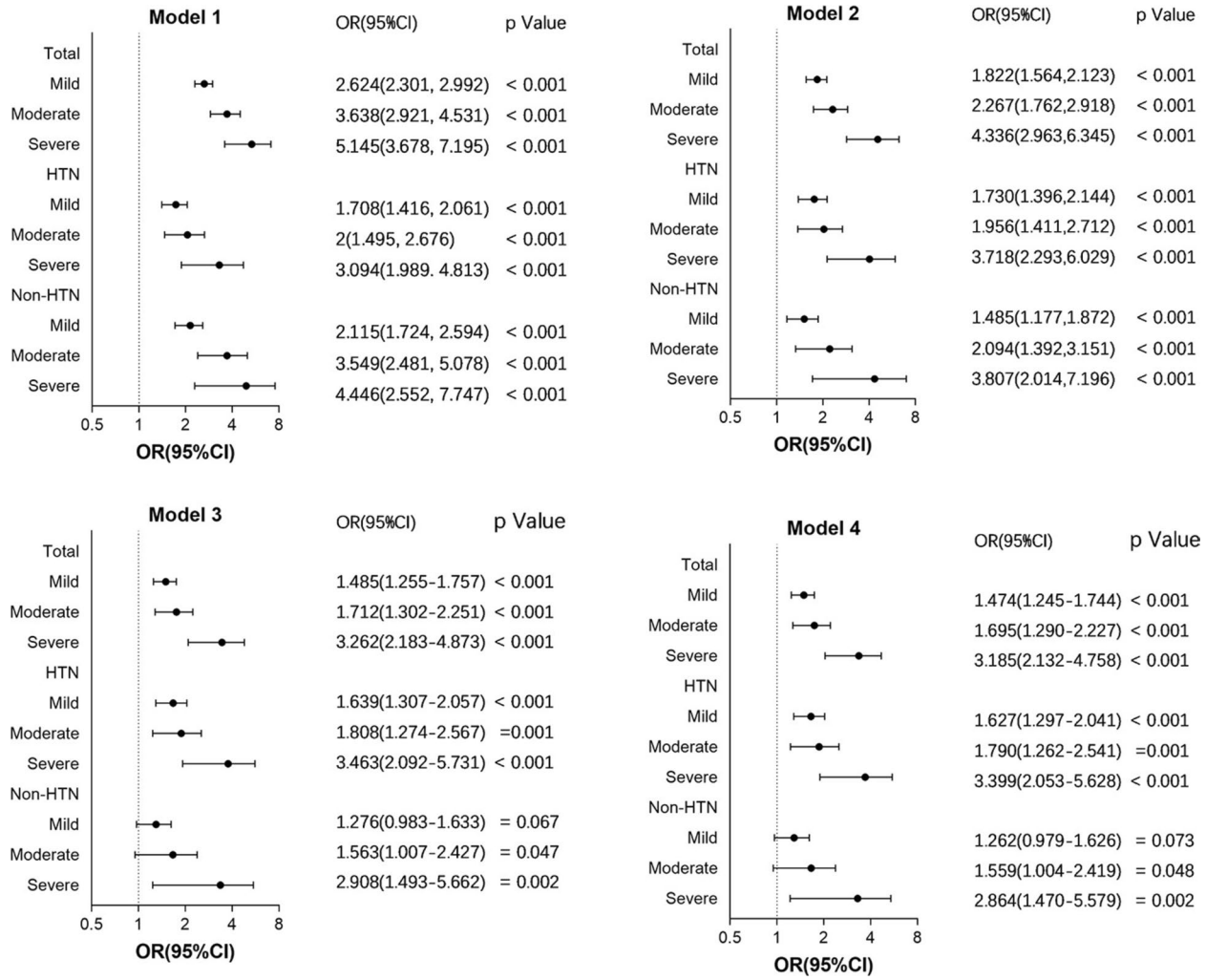

Fig. 3 Forest plot of risk estimates for MASLD and CAC stratified by fatty liver and hypertension status. Plots illustrate the ORs for identifying the association between CAC and MASLD stratified by fatty liver and hypertension status after adjustment for multiple confounders

progressive relationship between MASLD severity and subclinical atherosclerosis.

Notably, a meta-analysis has revealed that approximately 60% of NAFLD patients have hypertension [25], closely aligning with the 52.18% prevalence of hypertension observed in MASLD patients in this study. This finding points to a potential role of hypertension in influencing hepatic lipid deposition. Supporting this, data from the Framingham Heart Study, which has analyzed 1,051 participants, show that individuals with elevated liver fat are at greater risk of developing hypertension (OR 1.42; 95% CI, 1.15–1.76; $P=0.001$). Additionally, a 6-year follow-up study in middle-aged and elderly participants has underscored a bidirectional relationship between liver fat accumulation and cardiovascular risk factors [26]. Interestingly, a recent cross-sectional study has linked severe NAFLD to a heightened risk of subclinical coronary atherosclerosis, independent of FRS or body fat percentage, whereas mild and moderate NAFLD do not exhibit a significant association with subclinical atherosclerosis [27]. This nuanced distinction emphasizes the importance of stratifying NAFLD and MASLD by severity to better understand their respective impacts on cardiovascular health.

When stratifying participants by hypertension status, our study revealed a significant association between MASLD and subclinical coronary atherosclerosis among hypertensive individuals. In the non-hypertensive subgroup, a notable correlation was observed between moderate and severe MASLD and subclinical coronary atherosclerosis after adjusting for cardiovascular risk factors. However, this association was not significant for mild MASLD, potentially influenced by differences in study population characteristics. A recent meta-analysis

encompassing 19 studies has reported a pooled OR of 1.27 (95% CI, 1.13–1.41; $I^2=76.68\%$) for subclinical atherosclerosis in patients with mild steatosis, with the risk escalating to 1.68 (95% CI, 1.41–2.00; $I^2=89.02\%$) in those with moderate to severe steatosis [28]. Furthermore, a prior longitudinal cohort study has demonstrated a dose-dependent relationship between the severity of ultrasound-diagnosed NAFLD steatosis and CAC development in individuals with baseline CACS = 0, independent of traditional risk factors [29]. These findings underscore the potential utility of liver fat quantification in refining cardiovascular risk assessments for MASLD patients.

Although the precise mechanisms linking MASLD to increased cardiovascular risk remain unclear, prevailing theories implicate abnormal insulin resistance, ectopic fat deposition, chronic inflammation, oxidative stress, and endothelial dysfunction as critical contributors to the pathogenesis of atherosclerosis. These processes collectively drive systemic inflammation and a prethrombotic state. As MASLD severity progresses, these pathological conditions are likely to intensify and synergize, exacerbating adverse cardiovascular outcomes [30]. Further research is essential to delineate the specific pathways through which MASLD amplifies CVD risk, paving the way for targeted therapeutic interventions. Research demonstrates that dietary and physical activity interventions can significantly improve the histological features of MASLD, particularly by reducing inflammation and fibrosis [31]. One study reported that lifestyle modifications could mitigate steatosis in up to 97% of affected patients [32]. Additionally, passive exercise using whole-body periodic acceleration has been shown to enhance coronary microcirculation and glucose tolerance in patients with T2D, potentially contributing to better prognoses [33].

Current clinical guidelines advise against routine imaging for screening asymptomatic patients [34, 35]. However, CACS is recognized as a reliable and cost-effective method for detecting CAD and serves as a valuable marker of subclinical atherosclerosis. While there is insufficient evidence to warrant specific CAD screening in patients with MASLD, our findings, supported by existing literature, indicated that MASLD could be a risk-enhancing factor for atherosclerotic CVD. In clinical scenarios where CAD is suspected, MASLD may serve as an additional risk-enhancing factor, supporting the decision to perform pre-screening for obstructive CAD [36]. This approach underscores the importance of tailored cardiovascular risk assessments in patients with MASLD to optimize prevention and management strategies.

Strengths and limitations

Our research is distinguished by several strengths, including a substantial sample size and the integration of a broad spectrum of metabolic variables, enabling a comprehensive and contemporary evaluation of the relationship between MASLD and CVD. Nonetheless, certain limitations warrant consideration. First, the study's cross-sectional retrospective design precluded the establishment of causal relationships between subclinical coronary atherosclerosis and MASLD. Furthermore, while accumulating evidence links MASLD to various CVD manifestations, such as cardiac arrhythmias, valvular heart disease, and heart failure with or without preserved ejection fraction [37, 38], further longitudinal investigations are essential to delineate these associations. Second, CAC was evaluated using a visual assessment of LDCT images without confirmation via coronary angiography, limiting the ability to comprehensively verify the relationship between MASLD and CAC. Additionally, non-calcified plaques, composed predominantly of lipids, cholesterol, cellular debris, and inflammatory cells, are inherently more unstable than their calcified counterparts [39]. This fragility renders them highly prone to rupture, significantly elevating the risk of severe cardiovascular events, such as myocardial infarction, stroke, or the necessity for coronary revascularization. Accurate evaluation of noncalcified plaque burden through coronary angiography is critical for outcome prediction, underscoring the need for further research to address this crucial dimension. Third, the degree of fatty liver degeneration was assessed using ultrasound, a diagnostic approach that is inherently subjective and dependent on the expertise and experience of the interpreting clinician. Fourth, the study was confined to a single center, utilized a relatively modest sample size, and lacked comprehensive inclusion of metabolic diseases and cardiovascular risk factors, potentially introducing selection bias. Lastly, the study cohort predominantly consisted of individuals from Shanghai and its surrounding regions, characterized by higher income and educational attainment, which may limit the broader applicability of the findings to more diverse populations.

Conclusion

In conclusion, our findings underscored a strong association between MASLD severity and subclinical atherosclerosis in healthy population screenings, independent of traditional CVD risk factors. This reinforced the connection between MASLD and subclinical atherosclerosis, particularly within Asian populations. Looking ahead, future research will focus on expanding the sample size and longitudinally monitoring the incidence of

cardiovascular events to deepen our understanding of the interplay between MASLD and CVD, thereby providing more precise insights into its impact on Asian populations.

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Author contributions
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Availability of data and materials
All relevant data from this research are available by contacting the corresponding author.

Declarations

Ethics approval and consent to participate
This study protocol was approved by the Ethics Committee of Shanghai Health and Medical Center in Wuxi, China (Approval No. LLSC2024027) and conducted in accordance with the ethical standards outlined in the Helsinki Declaration of 1975, as revised in 1983. Given the retrospective nature of this study involving clinical data analysis, the Ethics Committee waived the requirement for obtaining informed consent from participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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