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ORIGINAL ARTICLE

Association of Atherogenic Lipid Indices with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): A Cross-Sectional Analysis of NHANES

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ABSTRACT

Metabolic dysfunction-associated steatotic liver disease (MASLD) is closely coupled to an atherogenic lipid profile, but the relative strength of association of lipid-derived indices has not been established in a nationally representative U.S. population under the 2023 nomenclature. We compared nine lipid measures — triglycerides (TG), HDL-C, LDL-C, total cholesterol, non-HDL-C, TG/HDL-C, LDL-C/HDL-C, TC/HDL-C and the atherogenic index of plasma (AIP) — in the fasting subsample of NHANES 2021–2023. A controlled attenuation parameter ≥ 248 dB/m defined steatosis, and MASLD required steatosis plus at least one cardiometabolic criterion. Analyses used survey-weighted logistic regression, weighted ROC analysis with a design-based bootstrap, calibration assessment and eleven sensitivity analyses. Of 2,453 adults, 1,428 (58.2%) met MASLD criteria. After full adjustment the derived ratios showed the largest effects (AIP OR = 6.64, 95% CI 3.38–13.04). On a per-SD scale, TG/HDL-C (1.71), TG (1.71) and AIP (1.70) were formally indistinguishable (p = 0.87). TG/HDL-C and AIP gave the highest discrimination (AUC = 0.724), exceeding TG alone by a small margin (ΔAUC = 0.013, p = 0.001). Associations persisted after excluding participants on lipid-lowering therapy, cases reclassifiable as MetALD or alcohol-related liver disease, and active viral hepatitis. TG/HDL-C is a low-cost, routinely available marker warranting prospective, externally validated evaluation; the design is cross-sectional and no threshold is recommended clinically.

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1- INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), now the leading chronic liver disorder globally, affects approximately 30% of the adult population [1]. In 2023, a multi-society Delphi initiative retired the term non-alcoholic fatty liver disease (NAFLD) in favour of MASLD. The condition was recast as hepatic steatosis together with at least one of five cardiometabolic risk factors, and exclusionary, potentially stigmatising wording was removed [2]. By anchoring the diagnosis in cardiometabolic health, this definition places disturbed lipids elevated triglycerides and reduced high-density lipoprotein cholesterol (HDL-C) among its defining features [3]. MASLD is important well beyond hepatology. A fatty liver is increasingly regarded as an independent contributor to atherosclerotic cardiovascular disease, and multidisciplinary consensus statements emphasis the excess cardiovascular risk carried by these patients [4]. Consistent with this, the MASLD phenotype is associated with

subclinical vascular disease carotid plaque [5] and coronary artery calcification [6] with a greater burden of major adverse cardiac events in chronic coronary syndrome [7], and with increased cardiovascular morbidity and mortality in both lean and non-lean forms [8]. Its consequences are systemic, extending to sarcopenia [9] and heart failure with preserved ejection fraction [10], and its burden is high across world regions [11]. Adiposity and insulin resistance intensify the atherogenic dyslipidaemia that accompanies the disease [12]. These observations, together with the search for low-burden, non-invasive markers that avoid the expense and sampling variability of biopsy [13], have drawn attention to simple lipid-based indices as potential indicators of the shared atherogenic–metabolic basis of MASLD. Given the rapidly evolving therapeutics for MASLD [14] and continuing efforts to refine its case definitions and risk scores [15, 16, 17], identifying which routine lipid marker best signals the disease has practical value. Derived from the routine lipid panel, atherogenic lipid indices are ratios or transformations intended to capture the balance between atherogenic and protective lipoproteins more sensitively than any single value. The most widely studied is the atherogenic index of plasma (AIP), defined as the base-10 logarithm of the molar triglyceride-to-HDL-C ratio, originally proposed as a surrogate for lipoprotein particle size and the fractional esterification rate of cholesterol [18]. Related indices include the triglyceride-to-HDL-C ratio (TG/HDL-C), the LDL-C-to-HDL-C ratio, the total-cholesterol-to-HDL-C ratio (TC/HDL-C), and non-HDL-C. Higher values of these measures have been associated with a range of adverse metabolic and vascular outcomes, including incident type 2 diabetes [19], the extent and occurrence of coronary artery disease [20], carotid atherosclerosis and plaque [21, 22], obesity and inflammatory states [23], and both all-cause and cardiovascular mortality in people with hypertension [24, 25]. Evidence linking these indices specifically to fatty liver is accumulating but remains fragmented. A single-centre study reported that AIP increased with steatosis severity and identified a cut-off for discriminating severe disease [26], and a related inflammation–lipid measure, hs-CRP/HDL-C, showed a positive, non-linear association with MASLD in a U.S. survey [27]. Three recurring limitations, however, constrain the existing literature for present purposes: single indices are usually examined in isolation rather than compared directly; the data often derive from individual centres or selected clinical cohorts rather than nationally representative samples; and the 2023 MASLD definition is seldom combined with the complex-survey methods required for valid national estimates.

1.1 Research gap, aim and questions

A properly weighted, head-to-head comparison of several atherogenic lipid indices with MASLD in a nationally representative U.S. sample, framed by the current 2023 nomenclature, and based on an objective, imaging-based steatosis criterion is therefore lacking. To address this gap, we analysed the 2021–2023 NHANES cycle, in which the controlled attenuation parameter (CAP) from vibration-controlled transient elastography assessed hepatic steatosis [28]. This study had two aims: (i) to quantify and compare the associations of individual lipids (TG, HDL-C, LDL-C, total cholesterol) and derived indices (non-HDL-C, TG/HDL-C, LDL-C/HDL-C, TC/HDL-C, AIP) with MASLD; and (ii) to identify the index with the closest and most reproducible association. Two research questions were posed: whether derived ratios are more strongly associated with MASLD than their component lipids, and which single index shows the largest standardised association and the highest discrimination. Given the cross-sectional design, all results are framed as associations rather than as causal or predictive effects. The intended contribution is a rigorously weighted national benchmark that identifies the routinely available lipid marker most closely associated with MASLD and therefore most deserving of prospective study.

2- MATERIALS AND METHODS

2.1 Research design

This was an observational, cross-sectional study of nationally representative data. NHANES, conducted continuously by the U.S. National Center for Health Statistics, samples the non-institutionalised civilian population through a complex, multistage probability design. Because triglycerides and LDL-C are measured only in the morning fasting subsample, all analyses were restricted to that subsample and its dedicated survey weights. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidance for cross-sectional studies.

2.2 Data source and study population

Data were drawn from the NHANES 2021–2023 cycle (cycle L). Eligible participants were adults aged 18 years or older who met four requirements. First, a completed FibroScan examination (examination status code 1) with a reliable CAP reading, defined as a CAP interquartile range divided by the CAP median of less than 30%. Secondly, a complete fasting lipid panel comprising triglycerides, HDL-C, LDL-C and total cholesterol, and third, a valid body mass index (BMI). Fourth, sufficient data to assess cardiometabolic status, namely blood pressure

together with fasting glucose and/or glycated haemoglobin (HbA1c). FibroScan probe selection (M or XL) followed the standardised, automated NHANES protocol; in the analytic sample the M probe was used in 1,896 participants (77.3%) and the XL probe in 557 (22.7%). Of 11,933 participants with demographic records, 2,463 met every criterion. After excluding 10 participants who had steatosis but no cardiometabolic risk factor (indeterminate or cryptogenic steatotic liver disease), the final analytic sample was 2,453. All 10 excluded participants had complete data on all five cardiometabolic criteria, so their classification as cryptogenic reflects a genuine absence of cardiometabolic risk rather than missing data; their CAP values ranged from 248 to 330 dB/m and their BMI from 20.7 to 24.9 kg/m². The full selection pathway, including the number and weighted proportion retained at each step, is shown in Table 1. Because the analytic sample represents only 20.6% of the initial participants, included and excluded adults were compared directly (Table 2). Alcohol intake (NHANES file ALQ_L) and hepatitis C virus (HCV) and hepatitis B virus (HBV) status (files HEPC_L and HEPBD_L) were linked to the analytic sample for the sensitivity analyses described in Section 2.6; neither was used to define the analytic sample itself.

2.3 Definition of hepatic steatosis and MASLD

Hepatic steatosis was defined as CAP ≥ 248 dB/m, the threshold for detecting any grade of steatosis (≥ S1) in the individual-patient-data meta-analysis of Karlas *et al.* [28]; only reliable examinations (CAP interquartile range/median < 30%) were retained. Among the 2,463 eligible adults, steatosis was present in 1,438 (58.4% unweighted; 57.4% weighted, SE 1.7). In the analytic sample the median CAP was 261 dB/m (interquartile range 222–306 dB/m) and the median CAP interquartile range/median ratio was 12.0%. Because the 248 dB/m threshold lies within a zone in which CAP performance varies by aetiology and prevalence [28], we report that 296 participants (12.1%) had CAP values in the indeterminate band of 248–267 dB/m, and we repeated the primary analysis at two stricter thresholds (Section 2.6). Following the 2023 multi-society nomenclature [2], MASLD required steatosis plus at least one of five cardiometabolic criteria: (1) adiposity (BMI ≥ 25 kg/m² or elevated waist circumference [> 94 cm in men or > 80 cm in women]); (2) dysglycaemia (fasting glucose ≥ 100 mg/dL, HbA1c ≥ 5.7%, or physician-diagnosed diabetes [NHANES item DIQ010]); (3) elevated blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg, calculated as the mean of the available standardised oscillometric readings obtained under the NHANES BPXO protocol, or antihypertensive treatment); (4) elevated triglycerides (≥ 150 mg/dL or lipid-lowering treatment); or (5) low HDL-C (≤ 40 mg/dL in men or ≤ 50 mg/dL in women, or lipid-lowering treatment). The diabetes component was based on self-reported physician diagnosis (n = 312); only 3 participants met the dysglycaemia criterion by diagnosis alone without also meeting the fasting glucose or HbA1c threshold. The number of participants meeting each criterion individually is reported in Table 3.

2.3.1 Alcohol intake and competing aetiologies

The 2023 nomenclature does not exclude alcohol consumption from MASLD, but it does place participants above defined intake thresholds in the separate categories of MetALD (30–60 g/day in men, 20–50 g/day in women) and alcohol-related liver disease (above those levels) [2]. We therefore estimated average daily alcohol intake from the past-12-month drinking frequency (ALQ121) and the average number of drinks per drinking day (ALQ130), converting drinking frequency to days per year and assuming 14 g of ethanol per U.S. standard drink. Participants reporting never drinking, or no drinking in the past 12 months, were assigned 0 g/day. Alcohol data were available for 1,859 participants (75.8%); the questionnaire is administered to a subsample, so the remainder are missing by design. Among the 1,068 MASLD cases with alcohol data, 970 (90.8% unweighted; 90.9% weighted) fell within the MASLD range, 77 (7.2%; 6.6%) within the MetALD range and 21 (2.0%; 2.4%) within the alcohol-related range, so approximately 9% of cases would be reclassified under a strict reading of the 2023 categories. Active viral hepatitis was defined serologically as a positive hepatitis C RNA result (LBXHCR, file HEPC_L) or a positive hepatitis B surface antigen (LBDHBG, file HEPBD_L). Of the 2,440 participants with both results, 12 were HCV RNA-positive and 12 were HBsAg-positive, giving 24 participants (1.02% weighted) with active viral hepatitis, of whom 9 met MASLD criteria; 157 participants were hepatitis B core-antibody positive, indicating past exposure rather than active infection, and no participant was hepatitis D antibody positive. Because these variables are incomplete, they were not applied to the primary case definition but were used in four sensitivity analyses (SA8–SA11).

2.4 Variables and atherogenic indices

The lipid exposures included triglycerides, HDL-C, LDL-C, total cholesterol, and four derived indices. LDL-C was estimated primarily by the Martin–Hopkins method, whose adjustable triglyceride-to-VLDL-C factor is more accurate than the fixed-factor Friedewald equation, particularly at extreme triglyceride levels [29]; the Friedewald estimate was retained for a sensitivity analysis. The derived measures were computed as non-HDL-C = total cholesterol − HDL-C; TG/HDL-C, LDL-C/HDL-C and TC/HDL-C as direct ratios (mg/dL); and AIP = $\log_{10}$

(TG [mmol/L] / HDL-C [mmol/L]) after unit conversion [18]. Covariates were age (years), sex, race/ethnicity and BMI (kg/m²). Race/ethnicity was entered as indicator variables for the six NHANES RIDRETH3 categories, with non-Hispanic White as the reference; it is not a continuous quantity and was not modelled as one. Triglycerides, HDL-C, diabetes and hypertension were deliberately excluded from the covariate set to avoid conditioning on variables that form part of the MASLD definition. BMI was retained because it is a strong, established determinant of both lipid metabolism and steatosis and is conventionally adjusted for in this literature; however, BMI also contributes to the adiposity criterion of MASLD, so its inclusion is a partial adjustment for an outcome-defining domain and may attenuate the estimated associations. Rather than leave this inconsistency unresolved, we quantified it in two pre-specified sensitivity analyses: one removing BMI from the covariate set (SA6) and one removing the adiposity criterion from the outcome definition while retaining BMI as a covariate (SA7).

2.5 Analytical methods

All inferential analyses accounted for the complex survey design, combining the fasting-subsample weight (WTSAF2YR) with the masked variance stratum and primary sampling unit through Taylor-series linearisation; the design comprised 15 strata and 30 primary sampling units, giving 15 degrees of freedom, and no stratum contained a single primary sampling unit. Weighted means (± standard error) and weighted proportions were compared between groups using design-based linearised tests. To avoid severe collinearity among indices sharing components, each index was fitted in a separate survey-weighted logistic model across three nested specifications (Model 1, unadjusted; Model 2, age and sex; Model 3, age, sex, race/ethnicity and BMI). Standardised odds ratios, expressed per 1 weighted standard deviation (SD) increase, were derived from the fully adjusted model to allow comparison on a common scale; the weighted SD used for each index is reported in Table 7. Because AIP is a logarithmic transformation of TG/HDL-C, a 1-SD change on the AIP scale is not the same contrast as a 1-SD change on the ratio scale, which is why the two indices share an identical rank ordering and AUC yet yield slightly different standardised odds ratios.

Discrimination was assessed by weighted ROC analysis using Hand's weighted Mann–Whitney statistic. Confidence intervals and all formal comparisons were obtained from 1,000 replications of a Rao–Wu rescaled bootstrap that resampled primary sampling units within strata, thereby respecting the complex design (random seed 20260912). The conventional DeLong test was not used because it does not accommodate stratification and clustering. In place of an informal comparison of overlapping intervals, competing indices were compared formally using the paired bootstrap distribution of the difference in AUC and of the difference in standardised odds ratio, with percentile confidence intervals and two-sided bootstrap *p*-values. Calibration of the fully adjusted model was assessed by the weighted calibration slope and intercept and by the F-adjusted mean residual goodness-of-fit test of Archer and Lemeshow, using ten groups of predicted risk, together with a weighted calibration plot (Figure 3). Log-transformed liver stiffness was examined as a secondary outcome using survey-weighted linear regression. A complete-case approach was used; missingness in triglycerides and LDL-C is attributable to the fasting-subsample design rather than to non-random dropout, and the fasting weights are intended to account for selection into that subsample, an assumption examined empirically in Table 2. Statistical significance was set at a two-sided α of 0.05. Analyses were carried out in Python 3.11 using a purpose-written implementation of design-based linearised variance estimation; the analysis code is available from the author on request.

2.6 Reliability, validity and sensitivity analyses

Several procedures supported validity: steatosis was assessed by a standardised imaging method rather than by self-report; only reliable CAP examinations were included; and all reported figures were recomputed directly from the public NHANES data files. Robustness was evaluated through eleven sensitivity analyses, seven pre-specified and four added during revision: (SA1) redefining cardiometabolic risk using non-lipid criteria only (adiposity, dysglycaemia, hypertension) to examine partial circularity between the case definition and the lipid exposures; (SA2) a stricter steatosis threshold of CAP ≥ 268 dB/m; (SA3) a further threshold of CAP ≥ 288 dB/m; (SA4) substitution of Friedewald for Martin–Hopkins LDL-C; (SA5) exclusion of all participants receiving lipid-lowering therapy, which removes the treatment-based components of the triglyceride and HDL-C criteria; (SA6) removal of BMI from the covariate set; (SA7) removal of the adiposity criterion from the outcome definition; (SA8) exclusion of all participants whose estimated alcohol intake exceeded the MASLD threshold, so that every remaining case is an alcohol-verified MASLD case rather than MetALD or alcohol-related liver disease; (SA9) adjustment for estimated alcohol intake in grams per day among all participants with alcohol data; (SA10) exclusion of participants with active viral hepatitis (hepatitis C RNA-positive or hepatitis B surface antigen-positive); and (SA11) the restrictions of SA8 and SA10 applied together. For SA2 and SA3 the cryptogenic-steatosis exclusion was re-applied at the new threshold, so the analytic sample differs slightly from the primary analysis.

3- RESULTS AND DISCUSSION

3.1 Study population and participant characteristics

After the stepwise exclusions, 2,453 of the 11,933 NHANES 2021–2023 participants were eligible (Table 1); of these, 1,428 (58.2% unweighted) met MASLD criteria and 1,025 (41.8%) did not. The weighted MASLD prevalence was 57.1% (SE 1.7). The final sample represented 20.6% of the initial participants, principally because triglyceride and LDL-C measurements are confined to the fasting subsample. Included adults were closely similar to the 2,612 adults who had a reliable CAP examination but were excluded at a later step (Table 2): weighted BMI, waist circumference, HbA1c and sex distribution did not differ, while included adults were 1.7 years older on average (48.6 vs. 46.9 years, $p = 0.049$) and had marginally lower mean CAP (264.4 vs. 269.1 dB/m, $p = 0.050$). These differences are small relative to the between-group contrasts of interest, but they indicate that selection into the fasting subsample is not entirely at random, and residual selection bias cannot be excluded. Compared with participants without MASLD, those with MASLD were older (weighted mean 50.1 vs. 44.4 years) and had higher BMI (32.4 vs. 25.6 kg/m²), waist circumference (107.6 vs. 89.4 cm), HbA1c, fasting glucose, and both systolic and diastolic blood pressure (all $p < 0.0001$; Table 3). The individual cardiometabolic criteria were met as follows (unweighted; weighted percentages in Table 3): adiposity 2,038 (83.1%), dysglycaemia 1,574 (64.2%), elevated blood pressure 1,159 (47.2%), elevated triglycerides 1,024 (41.7%) and low HDL-C 1,149 (46.8%). A total of 684 participants (27.9% unweighted; 21.1% weighted) were receiving lipid-lowering therapy, and participants met a mean of 2.83 of the five criteria.

3.2 Lipid profile by MASLD status

All lipid parameters and derived indices differed between the two groups (all $p < 0.0001$; Table 4). Participants with MASLD had higher triglycerides, LDL-C, total cholesterol, non-HDL-C, TG/HDL-C, LDL-C/HDL-C, TC/HDL-C and AIP, and lower HDL-C. Notably, mean AIP was positive in the MASLD group (0.006) and negative in the group without MASLD (−0.206).

3.3 Association of lipid indices with MASLD

Across all three survey-weighted logistic models, each index was independently associated with MASLD (Table 5). Under full adjustment (Model 3), the derived ratios produced the largest odds ratios AIP (OR = 6.64, 95% CI 3.38–13.04), LDL-C/HDL-C (OR = 1.70, 95% CI 1.40–2.05), TC/HDL-C (OR = 1.62, 95% CI 1.35–1.94) and TG/HDL-C (OR = 1.38, 95% CI 1.17–1.63) — while HDL-C was inversely associated with MASLD (OR = 0.980 per mg/dL, 95% CI 0.968–0.992). The single lipids (TG, LDL-C, total cholesterol, non-HDL-C) were statistically significant but had odds ratios close to 1, reflecting their per-mg/dL scaling; the unit for each index is given in Table 5, and strength across indices should be compared using the standardised estimates in Table 7.

Expressed in absolute terms, weighted MASLD prevalence rose monotonically across quartiles of TG/HDL-C (and, identically, of AIP), from 31.9% (SE 2.7) in the lowest quartile to 48.8%, 66.8% and 80.9% (SE 1.8) in the highest; the corresponding gradients for triglycerides, LDL-C/HDL-C and TC/HDL-C are given in Table 8. The prevalence difference between the extreme quartiles of TG/HDL-C was therefore 49.0 percentage points.

3.4 Standardised associations

Because the indices are measured on different scales, standardised odds ratios (per 1 weighted SD) were compared (Table 7; Figure 1). On this common scale, TG/HDL-C showed the highest standardised association (OR per 1 SD = 1.71, 95% CI 1.30–2.26), followed by triglycerides alone (1.71), AIP (1.70), TC/HDL-C (1.69) and LDL-C/HDL-C (1.61). These differences were formally tested using the paired design-based bootstrap and were not statistically distinguishable: TG/HDL-C versus TG, $\Delta = +0.004$ (95% CI −0.101 to +0.168, $p = 0.87$); versus AIP, $\Delta = +0.014$ ($p = 0.86$); versus TC/HDL-C, $\Delta = +0.025$ ($p = 0.78$); versus LDL-C/HDL-C, $\Delta = +0.099$ ($p = 0.43$). The ranking of the leading indices should therefore not be over-interpreted. HDL-C was inversely associated (OR per 1 SD = 0.75, 95% CI 0.63–0.89), and the single cholesterol measures were weakest (LDL-C 1.41; total cholesterol 1.35).

3.5 Discriminatory performance

In weighted ROC analysis (Table 6; Figure 2), AIP and TG/HDL-C yielded the highest — and arithmetically identical — area under the curve (AUC = 0.724, 95% CI 0.694–0.750); this identity is expected, because AIP is a monotonic log-transformation of TG/HDL-C and ranks individuals identically. Triglycerides alone reached 0.711, TC/HDL-C 0.701, LDL-C/HDL-C 0.683, HDL-C (inverted) 0.655 and non-HDL-C 0.634. Unlike in the previous version of this analysis, these differences were tested formally using the paired design-based bootstrap.

The advantage of TG/HDL-C over triglycerides alone was small but statistically supported (ΔAUC = +0.013, 95% CI +0.004 to +0.023, p = 0.001), as were its advantages over TC/HDL-C (+0.023, p = 0.028), LDL-C/HDL-C (+0.041, p = 0.001) and non-HDL-C (+0.090, p = 0.001). A difference of 0.013 in AUC is of negligible clinical consequence, however, and the two findings should be read together: TG/HDL-C ranks individuals slightly better than triglycerides alone, but the two convey essentially the same information about the odds of MASLD. Because valid weighted ROC curves require individual-level scored data, the curves themselves are not reproduced; Figure 2 shows the weighted AUC point estimates with their bootstrap confidence intervals. Overall discrimination was moderate, and no index is proposed as a stand-alone diagnostic test for MASLD.

3.6 Calibration

Calibration was assessed for the fully adjusted model. The weighted calibration slope was 1.00 (95% CI 0.79–1.21) with an intercept of 0.00 (95% CI −0.11 to 0.11), indicating no systematic over- or under-estimation overall. The F-adjusted mean residual test nevertheless indicated departure from perfect calibration for the model in which TG/HDL-C entered linearly (F (10,6) = 7.92, p = 0.010): observed prevalence was lower than predicted in the lowest two deciles of predicted risk (8.7% vs. 11.3% and 12.7% vs. 23.3%) and higher than predicted in the middle of the distribution (Figure 3). The same model specified with AIP, that is with the exposure on the logarithmic scale, calibrated adequately (F (10,6) = 2.25, p = 0.17), which indicates that the residual misfit reflects the assumed linear functional form of the untransformed ratio rather than the underlying association. This is a direct argument against proposing any single TG/HDL-C threshold for clinical use on the basis of these data.

3.7 Sensitivity analyses

The seven sensitivity analyses yielded consistent results (Table 9). Restricting cardiometabolic risk to non-lipid criteria (SA1) attenuated but did not remove the associations (AIP OR = 6.40 vs. 6.64; TG/HDL-C OR = 1.37 vs. 1.38). This analysis reduces, but does not eliminate, definitional overlap, because it redefines the outcome rather than the exposures and because the non-lipid criteria are themselves correlated with atherogenic dyslipidaemia; it is therefore best interpreted as a test of a related but distinct hypothesis rather than as proof that the associations are free of circularity. Stricter steatosis thresholds reclassified 301 participants (CAP ≥ 268 dB/m) and 584 participants (CAP ≥ 288 dB/m) from steatosis to no steatosis relative to the primary threshold, yet produced directionally and statistically consistent results (SA2, SA3), as did substitution of Friedewald for Martin–Hopkins LDL-C (SA4).
The analysis specifically requested to address residual circularity, SA5, excluded the 684 participants receiving lipid-lowering therapy, leaving 1,769 participants of whom 959 met MASLD criteria. The associations persisted without attenuation: AIP OR = 7.69 (95% CI 3.32–17.80) and TG/HDL-C OR = 1.42 (95% CI 1.14–1.79), with LDL-C/HDL-C (1.84) and TC/HDL-C (1.73) also strengthened. The treatment-based components of the case definition therefore do not account for the observed associations. The two analyses addressing the adjustment for BMI behaved as anticipated: removing BMI from the covariate set (SA6) markedly increased the estimates (AIP OR = 22.39; TG/HDL-C OR = 1.74), confirming that Model 3 is a conservative specification, while removing the adiposity criterion from the outcome definition but retaining BMI as a covariate (SA7) also increased them (AIP OR = 12.28; TG/HDL-C OR = 1.52). Neither manipulation altered the direction, significance or relative ordering of the indices, so the reported associations are not an artefact of adjusting for a variable that partly defines the outcome. Four further analyses examined whether the associations depend on how competing causes of steatosis are handled. Excluding the 159 participants whose estimated alcohol intake exceeded the MASLD threshold 98 of them cases, properly classified as MetALD or alcohol-related liver disease, and 61 non-cases left 1,700 participants with 970 alcohol-verified MASLD cases, and the associations were essentially unchanged (SA8: AIP OR = 7.53, 95% CI 3.19–17.76; TG/HDL-C OR = 1.41, 95% CI 1.11–1.78; LDL-C/HDL-C 1.72; TC/HDL-C 1.64). Discrimination in this alcohol-verified subsample was also unchanged (weighted AUC for TG/HDL-C 0.721 vs. 0.724 in the primary sample). Adjusting for estimated alcohol intake in grams per day rather than excluding drinkers gave the same result (SA9: AIP OR = 6.28; TG/HDL-C OR = 1.39). Excluding the 24 participants with serological evidence of active viral hepatitis changed the estimates in the second decimal place (SA10: AIP OR = 6.53, 95% CI 3.27–13.02; TG/HDL-C OR = 1.38, 95% CI 1.16–1.63), and applying both restrictions together gave the same picture (SA11, N = 1,686: AIP OR = 7.44; TG/HDL-C OR = 1.40). The associations reported here are therefore not explained by misclassification of MetALD or alcohol-related liver disease as MASLD, nor by undetected hepatitis B or hepatitis C infection.

3.8 Secondary outcome: liver stiffness

Liver stiffness was available for all 2,453 participants in the analytic sample (100%), because NHANES releases stiffness only for examinations meeting the same interquartile-range/median reliability criterion applied to

CAP. The weighted mean was 5.88 kPa (SE 0.14), with a weighted median of 5.0 kPa (interquartile range 4.1–6.3 kPa), an observed range of 1.5–75.0 kPa, and 11.5% of participants at or above 8 kPa. When log-transformed liver stiffness replaced the steatosis-based outcome in fully adjusted survey-weighted linear regression, the associations were weaker and inconsistent in direction (Table 10): TG/HDL-C was positively associated ($\beta = +0.0118$, $p = 0.021$) whereas LDL-C, total cholesterol, non-HDL-C and LDL-C/HDL-C were inversely associated, and AIP, HDL-C and TC/HDL-C were not significant. This divergence is expected, because stiffness indexes fibrosis rather than steatosis, and it does not undermine the primary findings, which concern steatosis-defined MASLD. These exploratory results should not be interpreted as evidence of histologically confirmed fibrosis, and no clinical fibrosis-stage cut-off was applied.

3.9 Interpretation of findings

That ratio-based indices outperform single lipids is biologically plausible. Together, TG/HDL-C and AIP encapsulate the atherogenic-dyslipidaemia triad high triglycerides, low HDL-C, and a predominance of small, dense LDL particles that characterises insulin resistance, the metabolic basis from which MASLD develops [18]. A single lipid captures one dimension of this disturbance, whereas a ratio combines two opposing fractions and therefore reflects the underlying imbalance more sensitively. The large crude odds ratio for AIP and its marked attenuation after adjustment (from 23.6 to 6.6) indicates strong confounding by adiposity and demographic factors; the more modest standardised TG/HDL-C estimate is the more stable and interpretable summary. At the same time, the formal comparisons reported here show that the apparent superiority of TG/HDL-C over triglycerides alone rests on a very small difference in ranking ability and on no detectable difference in the standardised association.

3.10 Comparison with previous studies

Our results align with and extend earlier work. De Matteis *et al.* [26] reported that AIP increased with steatosis severity and discriminated severe disease in a single-centre cohort; the present study reproduces the AIP–steatosis association in a nationally representative sample and shows that AIP and TG/HDL-C are, by construction, identical for discrimination. Liang *et al.* [27] linked a related inflammation–lipid measure (hs-CRP/HDL-C) to MASLD in NHANES 2017–2018, consistent with the central role of the HDL-C axis observed here. Fotros *et al.* [12] reported that atherogenic indices including AIP and the triglyceride-glucose index increased with adiposity and insulin resistance within a MASLD population; the present findings extend that MASLD-only analysis by contrasting MASLD with a non-MASLD comparison group drawn from the general population. More broadly, the association between TG/HDL-C and MASLD is consistent with evidence that these indices track adverse cardiometabolic outcomes incident diabetes [19], coronary artery disease burden [20]–[22] and cardiovascular mortality [24] and with the consensus view of fatty liver as a cardiovascular risk amplifier [4], [5]. Consistent with the wider non-invasive-marker literature, however, no single index including TG/HDL-C yet replaces imaging or biopsy [13].

3.11 Theoretical and practical implications

Conceptually, the findings reinforce a unifying model in which MASLD and atherogenic dyslipidaemia are parallel manifestations of systemic insulin resistance rather than independent conditions. That a simple ratio of two routine lipid measurements captures the association as well as a logarithmic index, and better than any single lipid, supports the view that the informative quantity is the balance between triglyceride-rich and HDL particles rather than the absolute concentration of any single lipoprotein. This is consistent with the cardiometabolic basis of the 2023 MASLD definition [2]. In practice, the TG/HDL-C ratio is attractive because it adds no cost, is derived directly from a routine lipid panel, and — unlike AIP — requires neither logarithmic nor unit transformation, making it easy to calculate and interpret at the point of care [3]. In this sample the Youden-optimal weighted cut-off was 1.85, with a sensitivity of 0.65 and a specificity of 0.70 (Youden J = 0.34; Table 6), corresponding to a balanced error rate of 32.8%: roughly one individual in three is misclassified at that threshold. Taken with the evidence of imperfect calibration reported in Section 3.6 and with the absence of external validation, this means that no threshold derived here can be recommended for clinical use. At most, the ratio may serve as a low-cost triage signal that complements and does not replace imaging-based assessment such as CAP or ultrasonography, particularly because MASLD frequently coexists with obesity and other simple anthropometric predictors of fatty liver [30].

3.12 Strengths and limitations

The strengths of this study include a large, nationally representative sample analysed with appropriate complex-survey weighting; an objective, imaging-based steatosis definition rather than self-report; head-to-head modelling of nine lipid measures on a common standardised scale; formal design-based bootstrap comparison of

competing indices rather than informal inspection of overlapping intervals; explicit calibration assessment; and robustness across eleven sensitivity analyses, among them an analysis restricted to participants not receiving lipid-lowering therapy, an analysis restricted to alcohol-verified MASLD cases, a non-lipid MASLD definition, and two stricter steatosis thresholds. Several limitations warrant emphasis. First, the cross-sectional design precludes any causal or temporal inference; the associations reported here describe co-occurrence, not prediction. Second, partial circularity between the MASLD definition and the triglyceride- and HDL-based indices is intrinsic to testing lipid markers against a lipid-inclusive definition. SA1 and SA5 address the two principal channels the lipid thresholds themselves and the treatment-based components and neither accounts for the associations, but the primary analysis cannot fully disentangle definitional overlap, and the conclusions are framed accordingly. Third, the medication proxy for lipid-lowering therapy was inferred from the questionnaire item BPQ101D rather than verified against prescription records, risking misclassification. Fourth, BMI contributes to the adiposity criterion; SA6 and SA7 show that this adjustment makes the primary estimates conservative rather than inflated, but the fully adjusted model remains a partial adjustment for an outcome-defining domain. Fifth, the fasting-subsample requirement reduced the eligible pool substantially and the final sample represented 20.6% of the initial participants; the comparison in Table 2 shows only small differences between included and excluded adults, yet residual selection bias cannot be excluded. Sixth, alcohol intake was estimated from self-reported questionnaire responses and was available for 75.8% of the analytic sample, so although SA8–SA11 show the findings to be robust to the exclusion of MetALD and alcohol-related cases and to adjustment for intake, residual misclassification of these categories cannot be excluded; participants with missing alcohol data were older (57.4 vs. 51.8 years) than those with data.

Hepatitis B and C infection were excluded serologically in SA10 and SA11, but autoimmune, drug-induced and monogenic causes of steatosis were not identified, so a small number of participants with a competing aetiology may remain. Seventh, whether FibroScan operators were blinded to participants' laboratory results is not documented in the public NHANES material and could not be verified, and the 248 dB/m threshold was adopted from a meta-analysis of mixed aetiologies; 12.1% of participants fell within 20 dB/m of that threshold, although the stricter thresholds examined in SA2 and SA3 produced consistent results. Eighth, discrimination was only moderate and calibration was imperfect for the linear TG/HDL-C specification. Ninth, the weighted AUC with a design-based bootstrap is a reasonable approximation rather than a fully validated survey-adjusted ROC method, and no closed-form survey analogue of the DeLong test is available. Finally, a single survey cycle (2021–2023) limits temporal generalisability, and the sample represents the U.S. non-institutionalised population and may not generalise to other settings. External validation in independent samples is essential before any clinical application.

3.13 Future research directions

Prospective cohorts are needed to determine whether an elevated TG/HDL-C ratio precedes and predicts incident MASLD, moving beyond association. Head-to-head studies that incorporate insulin-resistance indices (such as the triglyceride-glucose index) and inflammation–lipid composites [27] could clarify whether combinations improve discrimination materially, given that the differences between the leading single indices reported here are negligible. External validation in other populations and ethnic groups, evaluation across the full spectrum from simple steatosis through steatohepatitis to fibrosis, the development of a closed-form survey-adjusted test for comparing AUCs, and replication in a sample with complete alcohol histories and full exclusion of competing aetiologies would strengthen the evidence base. Finally, given the close association between MASLD and cardiovascular risk [4], studies linking lipid-index trajectories to hard cardiovascular endpoints in people with MASLD are a priority.

Table (1): Participant selection and exclusion flow

Stage	Remaining *N*	Excluded *N*	% retained	Reason for exclusion
Total DEMO_L participants	11,933	—	100.0	—
Age ≥ 18 years	8,153	3,780	68.3	Paediatric/adolescent
Complete FibroScan with valid CAP	5,525	2,628	46.3	Exam not completed / no CAP
Reliable CAP (IQR/median < 30%)	5,065	460	42.4	Unreliable CAP
Valid triglycerides	2,562	2,503	21.5	Not in fasting subsample
Valid HDL-C	2,562	0	21.5	—
Valid LDL-C (Martin–Hopkins)	2,528	34	21.2	Missing LDL-C
Valid total cholesterol	2,528	0	21.2	—

Valid BMI	2,516	12	21.1	Missing anthropometry
Sufficient cardiometabolic data	2,463	53	20.6	Missing BP and/or glucose/HbA1c
Exclude cryptogenic SLD	2,453	10	20.6	Indeterminate MASLD status

Note: Final analytic sample: *N* = 2,453 (MASLD 1,428 [58.2%]; no MASLD 1,025 [41.8%]; unweighted). Weighted MASLD prevalence 57.1% (SE 1.7). "% retained" is relative to the initial 11,933 participants (unweighted). CAP, controlled attenuation parameter; SLD, steatotic liver disease.

Table (2): Comparison of included and excluded adults with a reliable CAP examination (selection-bias check)

Characteristic	Included (*n* = 2,453)	Excluded (*n* = 2,612)	*p*
Age, years	48.56 ± 0.77	46.87 ± 0.77	0.049
Female sex, proportion	0.509 ± 0.012	0.492 ± 0.010	0.291
BMI, kg/m²	29.45 ± 0.31	29.63 ± 0.25	0.507
Waist circumference, cm	99.79 ± 0.73	100.33 ± 0.66	0.454
HbA1c, %	5.70 ± 0.04	5.69 ± 0.03	0.876
CAP, dB/m	264.37 ± 2.19	269.11 ± 2.04	0.050

Note: Weighted mean ± standard error, using the examination weight (WTMEC2YR) so that the two groups are placed on a common basis; *p*-values are design-based. Excluded adults are those who passed the reliable-CAP step but were removed at a later stage, chiefly because they were not part of the morning fasting subsample.

Table (3): Weighted characteristics by MASLD status, and cardiometabolic criteria met

Characteristic	MASLD (*n* = 1,428)	No MASLD (*n* = 1,025)	*p*
Age, years	50.10 ± 0.75	44.40 ± 1.03	<0.0001
Male sex, %	54.2 ± 1.3	45.4 ± 2.1	0.0005
BMI, kg/m²	32.35 ± 0.30	25.60 ± 0.30	<0.0001
Waist circumference, cm	107.56 ± 0.56	89.37 ± 0.94	<0.0001
HbA1c, %	5.93 ± 0.05	5.37 ± 0.03	<0.0001
Fasting glucose, mg/dL	114.52 ± 1.47	99.08 ± 0.96	<0.0001
Systolic BP, mmHg	121.95 ± 0.65	117.58 ± 0.59	<0.0001
Diastolic BP, mmHg	76.01 ± 0.42	71.70 ± 0.53	<0.0001
Cardiometabolic criteria met, *n* (%) / weighted %			
Adiposity	2,038 (83.1)	80.3%	—
Dysglycaemia	1,574 (64.2)	58.9%	—
Elevated blood pressure	1,159 (47.2)	38.6%	—
Elevated triglycerides	1,024 (41.7)	35.9%	—
Low HDL-C	1,149 (46.8)	42.0%	—
Lipid-lowering therapy	684 (27.9)	21.1%	—

Note: Weighted mean ± standard error unless indicated; *p*-values are design-based. For the cardiometabolic criteria the second column gives the unweighted count and percentage in the whole analytic sample and the third the weighted percentage; these criteria are components of the case definition and are therefore not tested between groups. BP, blood pressure.

Table (4): Weighted lipid profile by MASLD status

Lipid index	MASLD (*n* = 1,428)	No MASLD (*n* = 1,025)	*p*
TG, mg/dL	128.19 ± 1.47	89.39 ± 2.30	<0.0001
HDL-C, mg/dL	50.95 ± 0.45	58.23 ± 0.64	<0.0001
LDL-C (Martin–Hopkins), mg/dL	117.08 ± 1.15	104.16 ± 1.39	<0.0001
Total cholesterol, mg/dL	191.59 ± 1.39	180.83 ± 1.81	<0.0001
Non-HDL-C, mg/dL	140.63 ± 1.27	122.60 ± 1.57	<0.0001
TG/HDL-C	2.79 ± 0.05	1.71 ± 0.07	<0.0001
LDL-C/HDL-C	2.42 ± 0.03	1.89 ± 0.03	<0.0001
TC/HDL-C	3.92 ± 0.04	3.24 ± 0.04	<0.0001
AIP	0.006 ± 0.006	−0.206 ± 0.012	<0.0001

Note: Weighted mean ± standard error; *p*-values are design-based. AIP, atherogenic index of plasma.

Table (5): Survey-weighted logistic regression of each lipid index with MASLD

Index	Unit	Model 1, OR (95% CI)	Model 2, OR (95% CI)	Model 3, OR (95% CI)
TG, mg/dL	per mg/dL	1.015 (1.011–1.019)	1.014 (1.010–1.018)	1.009 (1.006–1.013)
HDL-C, mg/dL	per mg/dL	0.963 (0.955–0.971)	0.958 (0.948–0.968)	0.980 (0.968–0.992)
LDL-C (Martin–Hopkins), mg/dL	per mg/dL	1.011 (1.008–1.014)	1.011 (1.008–1.014)	1.010 (1.006–1.013)
Total cholesterol, mg/dL	per mg/dL	1.007 (1.003–1.010)	1.007 (1.003–1.010)	1.007 (1.004–1.011)
Non-HDL-C, mg/dL	per mg/dL	1.013 (1.009–1.016)	1.013 (1.010–1.016)	1.010 (1.007–1.014)
TG/HDL-C	per unit	1.771 (1.454–2.157)	1.730 (1.430–2.093)	1.381 (1.168–1.634)
LDL-C/HDL-C	per unit	2.147 (1.790–2.576)	2.224 (1.863–2.655)	1.695 (1.399–2.053)
TC/HDL-C	per unit	2.050 (1.727–2.432)	2.095 (1.770–2.480)	1.622 (1.354–1.943)
AIP	per unit	23.592 (12.414–44.836)	21.163 (11.375–39.373)	6.643 (3.384–13.038)

Note: Model 1, unadjusted; Model 2, age and sex; Model 3, age, sex, race/ethnicity (six indicator categories) and BMI. Each index was modelled separately. All $p < 0.001$ except HDL-C in Model 3 ($p = 0.003$). Odds ratios are expressed per the unit shown, so their magnitudes are not comparable across indices; use the standardised estimates in Table 7 for comparison. For AIP the unit is one $\log_{10}$ unit of the molar TG/HDL-C ratio, a very large contrast, which is why its per-unit odds ratio is numerically extreme.

Table (6): Weighted ROC analysis for discrimination of MASLD

Index	Weighted AUC	95% CI	Sensitivity	Specificity	Youden *J*	Cut-off
TG/HDL-C	0.724	0.694–0.750	0.649	0.695	0.344	1.854
AIP	0.724	0.694–0.750	0.649	0.695	0.344	−0.092
TG, mg/dL	0.711	0.678–0.740	0.642	0.680	0.322	96
TC/HDL-C	0.701	0.677–0.723	0.665	0.645	0.310	3.379
LDL-C/HDL-C	0.683	0.659–0.706	0.662	0.619	0.281	1.976
HDL-C, mg/dL (inverted)	0.655	0.632–0.680	0.618	0.623	0.241	52
Non-HDL-C, mg/dL	0.634	0.604–0.660	0.502	0.701	0.203	139
LDL-C (Martin–Hopkins), mg/dL	0.607	0.579–0.633	0.494	0.670	0.164	117
Total cholesterol, mg/dL	0.580	0.549–0.609	0.589	0.548	0.137	183

Note: Weighted Mann–Whitney (Hand's) formulation. Confidence intervals from 1,000 replications of a Rao–Wu rescaled bootstrap resampling primary sampling units within strata (seed 20260912). Sensitivity, specificity and the cut-off are those maximising the Youden index *J* = sensitivity + specificity − 1. HDL-C was inverted so that higher values indicate higher risk. Formal paired bootstrap comparisons: TG/HDL-C vs. TG, ΔAUC = +0.013 (95% CI +0.004 to +0.023, *p* = 0.001); vs. TC/HDL-C, +0.023 (*p* = 0.028); vs. LDL-C/HDL-C, +0.041 (*p* = 0.001); vs. non-HDL-C, +0.090 (*p* = 0.001). AIP and TG/HDL-C are monotonic transformations of one another and therefore have an identical AUC by construction. Discrimination is moderate throughout and no index is proposed as a diagnostic test.

Table (7): Standardised odds ratios (per 1 weighted SD increase), fully adjusted model

Index	Weighted SD	OR per 1 SD	95% CI
TG/HDL-C	1.663	1.712	1.295–2.262
TG, mg/dL	58.6	1.708	1.381–2.111
AIP	0.279	1.697	1.406–2.049
TC/HDL-C	1.080	1.686	1.387–2.050
LDL-C/HDL-C	0.906	1.613	1.355–1.919
Non-HDL-C, mg/dL	39.2	1.502	1.322–1.705
LDL-C (Martin–Hopkins), mg/dL	35.2	1.406	1.249–1.584
Total cholesterol, mg/dL	41.0	1.345	1.178–1.535
HDL-C, mg/dL	14.3	0.750	0.630–0.892

Note: Standardised OR = (OR per unit) raised to the power of the weighted standard deviation. Paired design-based bootstrap comparisons of the leading indices were not statistically significant: TG/HDL-C vs. TG, Δ = +0.004 (*p* = 0.87); vs. AIP, +0.014 (*p* = 0.86); vs. TC/HDL-C, +0.025 (*p* = 0.78); vs. LDL-C/HDL-C, +0.099 (*p* = 0.43). The ordering of the leading indices should therefore not be over-interpreted.

Table (8): Weighted MASLD prevalence (%) by quartile of each lipid index

Index	Quartile cut-points	Q1	Q2	Q3	Q4
TG/HDL-C	1.17 / 1.85 / 2.92	31.9 (2.7)	48.8 (3.0)	66.8 (2.2)	80.9 (1.8)
AIP	−0.290 / −0.092 / 0.106	31.9 (2.7)	48.8 (3.0)	66.8 (2.2)	80.9 (1.8)
TG, mg/dL	69 / 96 / 139	33.2 (3.4)	49.1 (2.2)	66.5 (1.9)	78.7 (1.7)
LDL-C/HDL-C	1.54 / 2.07 / 2.67	35.4 (3.0)	52.4 (2.7)	64.2 (2.4)	76.5 (1.9)
TC/HDL-C	2.83 / 3.45 / 4.18	32.8 (2.9)	51.6 (3.0)	66.3 (1.9)	77.8 (1.9)

Note: Weighted prevalence (standard error). Quartiles were defined on the weighted distribution of each index. TG/HDL-C and AIP give identical quartiles because one is a monotonic transformation of the other.

Table (9): Sensitivity analyses (fully adjusted model)

Scenario	Index	*N*	Events	OR (95% CI)
SA1: non-lipid cardiometabolic criteria only	AIP	2,446	1,421	6.402 (3.348–12.239)
SA1: non-lipid cardiometabolic criteria only	TG/HDL-C	2,446	1,421	1.373 (1.167–1.614)
SA2: CAP ≥ 268 dB/m	AIP	2,458	1,132	7.784 (4.766–12.712)
SA2: CAP ≥ 268 dB/m	TG/HDL-C	2,458	1,132	1.383 (1.239–1.543)
SA3: CAP ≥ 288 dB/m	AIP	2,460	851	8.433 (5.419–13.123)
SA3: CAP ≥ 288 dB/m	TG/HDL-C	2,460	851	1.348 (1.232–1.475)
SA4: Friedewald LDL-C	LDL-C	2,453	1,428	1.008 (1.005–1.011)
SA4: Friedewald LDL-C	LDL-C/HDL-C	2,453	1,428	1.619 (1.344–1.950)
SA5: excluding lipid-lowering therapy	AIP	1,769	959	7.689 (3.322–17.797)
SA5: excluding lipid-lowering therapy	TG/HDL-C	1,769	959	1.424 (1.136–1.785)
SA5: excluding lipid-lowering therapy	TG	1,769	959	1.009 (1.005–1.014)
SA5: excluding lipid-lowering therapy	LDL-C/HDL-C	1,769	959	1.842 (1.563–2.170)
SA5: excluding lipid-lowering therapy	TC/HDL-C	1,769	959	1.727 (1.459–2.043)

SA6: Model 3 without BMI	AIP	2,453	1,428	22.39 (11.77–42.59)
SA6: Model 3 without BMI	TG/HDL-C	2,453	1,428	1.740 (1.433–2.112)
SA7: MASLD without adiposity criterion	AIP	2,322	1,297	12.28 (5.92–25.45)
SA7: MASLD without adiposity criterion	TG/HDL-C	2,322	1,297	1.517 (1.254–1.835)
SA8: MetALD/ALD excluded (alcohol-verified MASLD)	AIP	1,700	970	7.531 (3.194–17.758)
SA8: MetALD/ALD excluded (alcohol-verified MASLD)	TG/HDL-C	1,700	970	1.409 (1.114–1.783)
SA8: MetALD/ALD excluded (alcohol-verified MASLD)	TG	1,700	970	1.009 (1.005–1.014)
SA8: MetALD/ALD excluded (alcohol-verified MASLD)	LDL-C/HDL-C	1,700	970	1.716 (1.351–2.180)
SA8: MetALD/ALD excluded (alcohol-verified MASLD)	TC/HDL-C	1,700	970	1.644 (1.307–2.068)
SA9: adjusted for alcohol intake (g/day)	AIP	1,859	1,068	6.282 (2.683–14.707)
SA9: adjusted for alcohol intake (g/day)	TG/HDL-C	1,859	1,068	1.386 (1.096–1.753)
SA10: excluding active viral hepatitis (HBV/HCV)	AIP	2,429	1,419	6.528 (3.272–13.024)
SA10: excluding active viral hepatitis (HBV/HCV)	TG/HDL-C	2,429	1,419	1.377 (1.163–1.629)
SA11: alcohol-verified MASLD, no viral hepatitis	AIP	1,686	965	7.439 (3.127–17.699)
SA11: alcohol-verified MASLD, no viral hepatitis	TG/HDL-C	1,686	965	1.404 (1.110–1.777)

Note: Primary comparison (Model 3, *N* = 2,453, 1,428 events): AIP OR = 6.643; TG/HDL-C OR = 1.381. In SA2 and SA3 the cryptogenic-steatosis exclusion was re-applied at the new threshold, so *N* differs slightly from the primary analysis; 301 and 584 participants respectively were reclassified from steatosis to no steatosis relative to the 248 dB/m threshold. SA5 excluded the 684 participants receiving lipid-lowering therapy. SA8 excluded the 159 participants whose estimated alcohol intake exceeded the MASLD threshold, of whom 98 were cases reclassifiable as MetALD or alcohol-related liver disease; SA9 retained all participants with alcohol data and adjusted for intake in grams per day; SA10 excluded the 24 participants with a positive hepatitis C RNA result or a positive hepatitis B surface antigen. All $p < 0.01$.

Table (10): Association of lipid indices with liver stiffness (secondary outcome; log-transformed median stiffness, survey-weighted linear regression)

Index	β (log kPa)	95% CI	*p*
TG, mg/dL	+0.00025	−0.00001 to +0.00051	0.057
HDL-C, mg/dL	−0.00077	−0.00229 to +0.00075	0.299
LDL-C (Martin–Hopkins), mg/dL	−0.00117	−0.00196 to −0.00037	0.007
Total cholesterol, mg/dL	−0.00093	−0.00156 to −0.00029	0.007
Non-HDL-C, mg/dL	−0.00094	−0.00162 to −0.00025	0.011
TG/HDL-C	+0.01178	+0.00206 to +0.02151	0.021
LDL-C/HDL-C	−0.03035	−0.05891 to −0.00179	0.039
TC/HDL-C	−0.01924	−0.04168 to +0.00320	0.088
AIP	+0.04790	−0.01617 to +0.11197	0.132

Note: Adjusted for age, sex, race/ethnicity and BMI. Liver stiffness was available for all 2,453 participants (weighted mean 5.88 kPa, SE 0.14; weighted median 5.0 kPa, interquartile range 4.1–6.3 kPa; range 1.5–75.0 kPa). Median stiffness does not equate to histologically confirmed fibrosis; these results are exploratory, small in magnitude and mixed in direction.

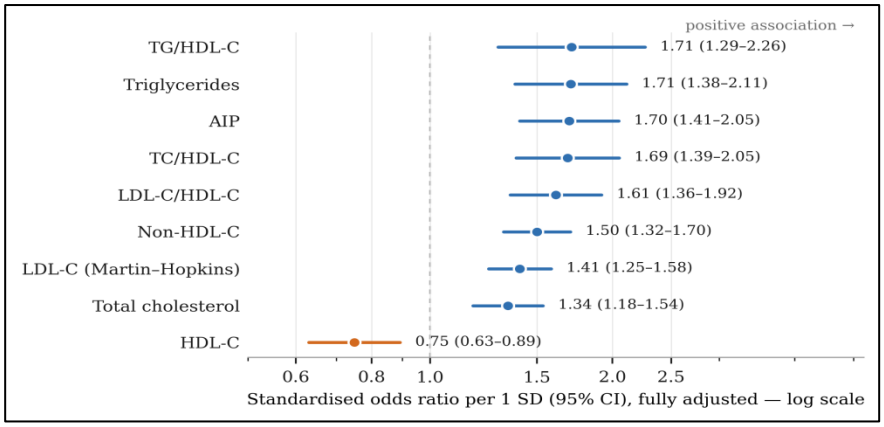

Fig (1): Standardised odds ratios (per 1 weighted SD, 95% CI) for the association of each lipid index with MASLD, fully adjusted model. The x-axis is on a logarithmic scale; the dashed vertical line marks the null value OR = 1. Values to the right of that line indicate higher odds of MASLD; HDL-C (orange) is inversely associated

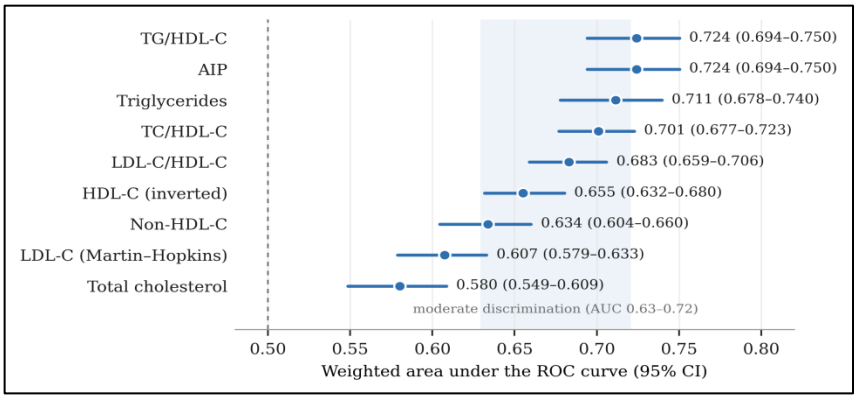

Fig (2): Weighted area under the ROC curve (95% CI) for discrimination of MASLD by lipid index. The dashed line marks chance (AUC = 0.5). The shaded band marks the range of moderate discrimination observed here (AUC 0.63–0.72). Confidence intervals are percentile intervals from 1,000 Rao–Wu bootstrap replications respecting strata and primary sampling units. AIP and TG/HDL-C are mathematically equivalent and share an identical AUC

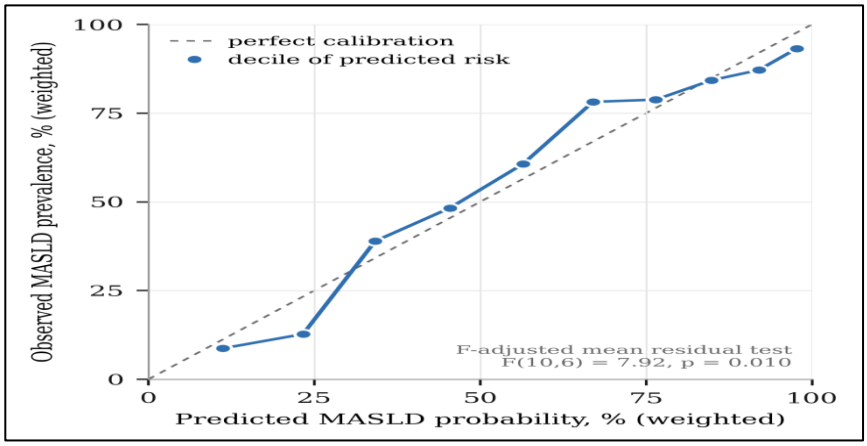

Fig (3): Weighted calibration plot for the fully adjusted model with TG/HDL-C as the exposure. Points show observed versus predicted weighted MASLD prevalence within deciles of predicted risk; the dashed line is perfect calibration

4- CONCLUSION

In a nationally representative sample of U.S. adults classified by the 2023 MASLD nomenclature, lipid ratios were more strongly associated with MASLD than single lipid measures. TG/HDL-C and its log-transformed equivalent, the atherogenic index of plasma showed the strongest standardised association and the best discrimination, and remained robust across eleven sensitivity analyses, including analyses restricted to participants not receiving lipid-lowering therapy and to alcohol-verified MASLD cases. Formal design-based comparison nevertheless showed that its advantage over triglycerides alone was negligible in magnitude, statistically undetectable on the standardised odds-ratio scale, and only marginally significant in discrimination. Because the design is cross-sectional, because definitional overlap between the lipid indices and the MASLD criteria cannot be entirely excluded, and because the fitted model was imperfectly calibrated at the extremes of predicted risk, these findings describe association rather than causation or diagnostic accuracy, and no cut-off derived here is recommended for clinical use. As an inexpensive, panel-derived and easily computed marker, TG/HDL-C remains a reasonable candidate for identifying individuals with MASLD, but it requires prospective, externally validated evaluation before any clinical application.

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