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Relative fat mass and risk of metabolic dysfunction associated steatotic liver disease and severe hepatic steatosis in U.S. adults: analysis of NHANES 2017–2020 data

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Abstract

Background Relative fat mass (RFM) is a novel, easily calculated, and cost-effective index of fat content and distribution in the body, associated with the odds of developing various obesity-related diseases. However, its association with metabolic dysfunction associated steatotic liver disease (MASLD) and severe hepatic steatosis (SHS) is underexplored. This study aims to examine the relationship between RFM and the odds of having MASLD or SHS in the general adult population.

Methods This was a population-based cross-sectional study using data from the National Health and Nutrition Examination Survey (2017.01–2020.03). The aim of the statistical analysis was to examine the association between RFM and the prevalence of MASLD and SHS. Logistic regression was applied to explore this relationship. Nonlinear associations between RFM levels and MASLD or SHS prevalence were assessed using smoothed curve fitting and threshold effect models. Subgroup analyses were conducted to evaluate the consistency of this association across different population groups.

Results A total of 6699 participants were included in this study, of whom 2825 had MASLD and 1834 had SHS. After adjusting for confounders, significant positive associations were observed between RFM and the prevalence of MASLD and SHS (odds ratio [OR]: 1.22, 95% confidence interval [CI:] 1.18–1.26 and OR: 1.26, 95% CI: 1.21–1.30). Smoothed curve fitting and threshold effect analysis showed a nonlinear relationship between RFM and the

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prevalence of MASLD and SHS, with thresholds of 41.96 for MASLD prevalence and 40.42 for SHS prevalence. When the subgroups were analyzed according to sex, age, race, education level, smoking status, household income, body mass index, hypertension, and diabetes, no significant interactions were found between RFM and most subgroups.

Conclusions Our results demonstrated a positive nonlinear relationship between RFM and the prevalence of MASLD and SHS, with a threshold effect. Lower RFM levels are associated with lower odds of MASLD and SHS. These findings suggest that RFM may serve as a simple, cost-effective tool for identifying individuals at increased odds of NAFLD and SHS in the general population.

Keywords Nonalcoholic fatty liver disease, Severe hepatic steatosis, Relative fat mass, Metabolic syndrome, Obesity, Cross-sectional study

Background

Nonalcoholic fatty liver disease (NAFLD) is a prevalent liver condition, affecting approximately one-third of adults globally [1, 2]. It encompasses a spectrum of liver diseases, ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), which can progress to cirrhosis and hepatocellular carcinoma [3]. NAFLD is also closely linked to several extrahepatic conditions, including type 2 diabetes mellitus, cardiovascular disease, chronic kidney disease, and neuropsychiatric disorders [4]. Despite extensive research, the U.S. Food and Drug Administration has not yet approved a specific treatment for NAFLD [5], making its management particularly challenging. Identifying reliable prognostic indicators remains critical for improving clinical outcomes. In addition, in 2023, the Multi-Society Delphi Consensus Statement on a new nomenclature for fatty liver introduced the term metabolic dysfunction associated steatotic liver disease (MASLD) and effectively abolished the term NAFLD.

The increasing prevalence of MASLD, which affects a large number of people, may be related to the increased prevalence of obesity [6, 7]. In recent years, the transformation of dietary habits and lifestyle choices has resulted in obesity emerging as a significant global health issue, affecting over 2 billion individuals worldwide [8]. Body Mass Index (BMI) is a conventional metric for evaluating obesity, extensively utilized in cross-sectional research; however, it has inherent limitations. The calculation of BMI is based only on weight and height and does not consider the content and distribution of adipose tissue in the body or the differences in adipose tissue between men and women, which are essential for evaluating metabolic risk.

Relative fat mass (RFM) is an innovative anthropometric index that offers several advantages over traditional BMI. It provides a refined approach to estimating body fat content and distribution by integrating height and waist circumference. Additionally, RFM adjusts for sex, making it more applicable and accurate across genders. RFM is simple, easily calculated, and cost-effective, making it a valuable tool for assessing obesity-related diseases. A study including 365 anthropometric indices found that RFM was the most accurate and user-friendly measure of whole-body fat content [9]. Previous studies have shown that RFM is closely related to the odds of many obesity-related diseases, such as diabetes, periodontitis, and cardiovascular disease [10–13].

However, there are relatively few studies on RFM and the odds of developing MASLD, and existing studies are highly controversial. Studies like those by Shen et al. [14] have examined the nonlinear relationship between RFM and MASLD in specific populations. But these studies have focused on ethnically homogeneous cohorts. Conversely, another study found that there was no significant relationship between RFM levels and the odds of having MASLD [15]. Notably, these studies were conducted over a shorter period with small sample sizes. Additionally, the relationship between RFM levels and the odds of developing severe hepatic steatosis (SHS) has not been reported. This study is among the first population-based studies to explore nonlinear associations and threshold effects of RFM on SHS in the general adult population. Therefore, we aimed to elucidate the association between RFM levels and the odds of developing MASLD and SHS in the general adult population using the National Health and Nutrition Examination Survey (NHANES), which is designed to assess the health and nutritional status of adults and children in the United States. The survey is distinctive in that it incorporates both physical examinations and interviews. It covers a wide range of topics, including demographics, health insurance status, dietary habits, acute and chronic diseases, mental health, and medication use, as well as various physical examinations and laboratory assessments. NHANES data are nationally representative and have significant value for clinical and public health research.

Methods

Study methodology

This study used a retrospective, population-based, cross-sectional approach to analyze secondary data.

Data source

Data were obtained from the NHANES 2017–2018 and 2019–March 2020 cycles. NHANES was administered by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention to assess the health and nutritional status of the United States population and employing a stratified multistage probability sampling design (consisting of stratification, primary sampling units, secondary sampling units, household sampling, oversampling, etc.) to ensure that samples drawn are nationally representative of the United States' non-institutionalized civilian population. The NHANES comprises four major components: demographics, physical examination, laboratory examination, and questionnaire data. The program is a valuable resource for understanding and tracking health trends and needs in the United States. The NHANES plays a very important role in identifying health priorities, developing disease prevention strategies and public health policies, preventing chronic disease, improving nutrition, and promoting healthy lifestyles.

Participants

The NHANES is updated every two years and covers a population of approximately 10,000. The program was suspended in March 2020 due to the COVID-19 epidemic. For this study, adult participants aged 18 years and older who had undergone vibration-controlled transient elastography (VCTE) were included. Beginning in 2017, NHANES participants were allowed to voluntarily choose whether they had a VCTE examination; therefore, we selected participants from this period (2017-2020.03) for the study.

During this period, a total of 15,560 participants were enrolled. The inclusion and exclusion criteria were as follows:

Inclusion criteria:

- Adult participants aged 18 years and older who had undergone VCTE.

Exclusion criteria:

- Participants younger than 18 years of age ($n = 5,867$).
- Participants without VCTE results ($n = 433$) or RFM information ($n = 1,258$).
- Patients with viral hepatitis ($n = 225$), autoimmune hepatitis ($n = 5$), or heavy drinkers (alcohol intake > 30 g/day for men and > 20 g/day for women) ($n = 883$).
- Participants with liver stiffness measurement (LSM) values exhibiting an IQR/median ≥ 30% ($n = 190$), in accordance with established quality criteria for transient elastography. This threshold reflects reduced measurement reliability and is widely adopted in VCTE-based studies to ensure data validity.

Ultimately, 6,699 individuals were included in the study (Fig. 1).

Ethical statement

The NHANES is publicly accessible, and all participants have signed an informed consent form. The NHANES dataset provided by the NCHS maintains de-identification and anonymity, thus exempting investigators from obtaining duplicate ethical clearance or informed consent. Documents approved by the NCHS Research Ethics Review Board are available on the official NHANES website (https://www.cdc.gov/nchs/nhanes/irba98.htm).

Diagnosis of MASLD

The gold standard for diagnosing liver disease is liver biopsy; however, given the high global prevalence of MASLD, it is impractical for assessing hepatic steatosis in large populations. VCTE is a widespread, non-invasive, and user-friendly method for identifying hepatic steatosis, liver fibrosis, and cirrhosis using controlled attenuation parameters (CAP) and LSM. VCTE was performed using ultrasound (FibroScan® 502 V2 Touch instrument). According to previous studies, MASLD is defined as CAP is ≥ 274 dB/m, and SHS is present when CAP is ≥ 302 dB/m [16, 17]. Liver fibrosis was assessed based on the latest guidelines of the European Association for the Study of the Liver [18]. Liver fibrosis was categorized into classes F2, F3, and F4, corresponding to thresholds of 8.2, 9.7, and 13.6 kPa, respectively [19].

Calculation of RFM

RFM was calculated using the following formula: 64–(20×height/waist circumference) + (12×sex), where sex = 0 for men and 1 for women [9].

Covariates

The covariates included for this study were demographic variables (e.g., age, sex, ethnicity), comorbidities (e.g., diabetes mellitus, hypertension), dietary intake factors (e.g., energy, sugar, water intake), and laboratory test results. Additional details are provided in Supplemental Table 1.

Statistical analysis

All statistical analyses accounted for the complex, multistage, probability sampling design of NHANES by incorporating appropriate sample weights, stratification, and clustering variables, in accordance with the NHANES analytic guidelines. Weighted analyses were conducted using the MEC examination weights for the 2017–2020

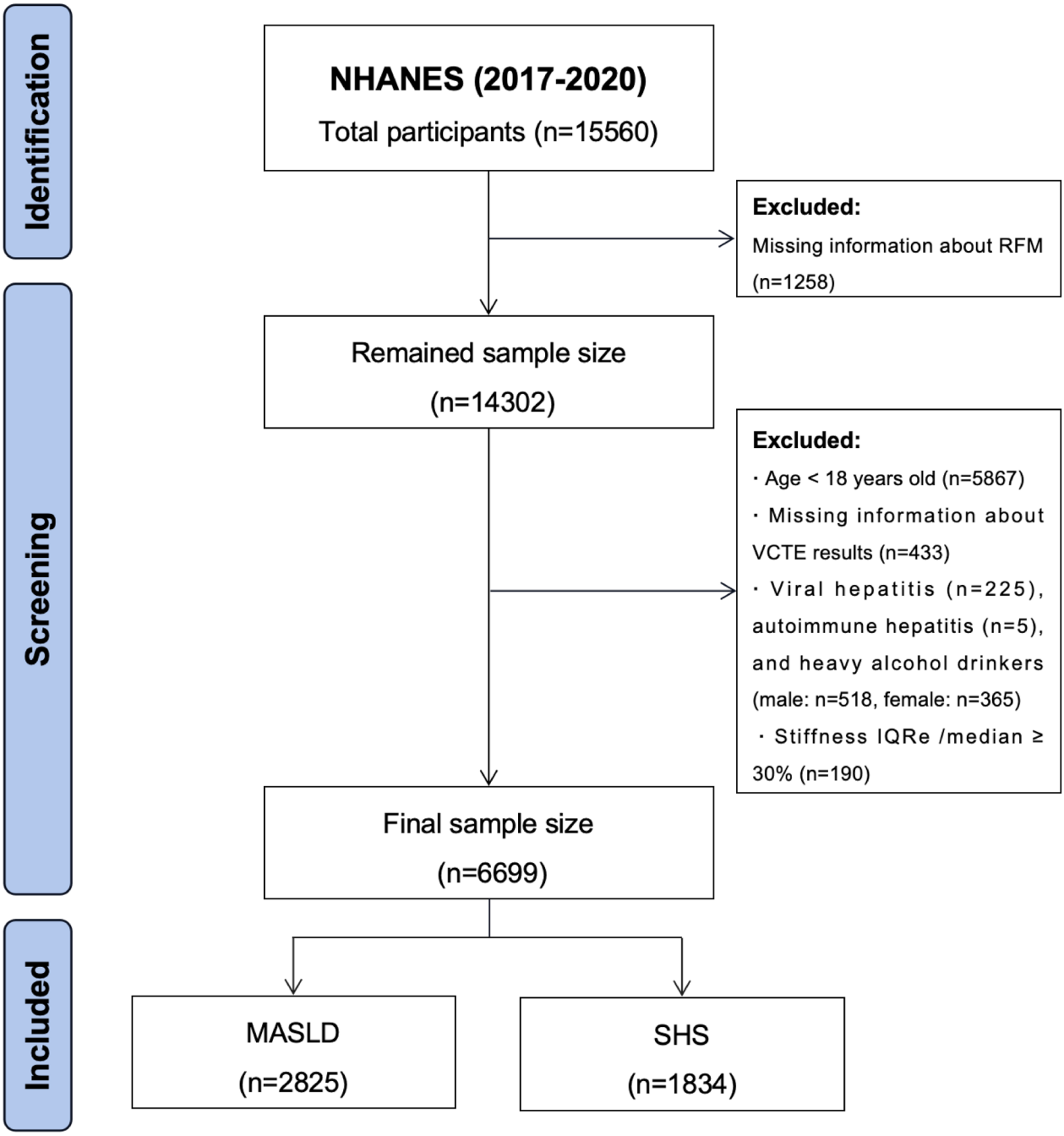

Fig. 1 Flowchart for participants from NHANES (2017–2020). NHANES, National Health and Nutrition Examination Survey; RFM, relative fat mass; VCTE, vibration-controlled transient elastography; MASLD, metabolic dysfunction associated steatotic liver disease; SHS, severe hepatic steatosis

cycles to ensure national representativeness of the estimates.

Continuous variables are expressed as median and interquartile range, and comparisons were performed by a t-test or one-way analysis of variance. Categorical variables are expressed as numbers and percentages (%), and comparisons between groups were performed by Pearson's $\chi 2$ test or Fisher's exact test. Logistic regression models were performed to analyze the association between RFM and the prevalence of MASLD and SHS. The analysis used three models: Model 1 did not adjust for any variables; Model 2 was adjusted for age, sex, ethnicity, and BMI; and Model 3 was further adjusted for smoking status, albumin, hemoglobin A1c, education level, poverty income ratio, diabetes, hypertension, total cholesterol, alanine aminotransferase, C-reactive

protein, ferritin, and total daily sugar intake. Odds ratios (OR) and 95% confidence intervals (CI) were calculated and reported throughout the analysis. For the smoothed curve fitting, we utilized the ggplot2 package with the geom_smooth function to model the relationship between RFM and the prevalence of MASLD and SHS. To assess the nonlinear relationship between RFM and the prevalence of MASLD and SHS, we used smoothed curve fitting and threshold effects analysis. For the threshold effect analysis, we employed the segmented package to perform piecewise regression and used the likelihood ratio test to compare the goodness-of-fit between the linear and piecewise models. Subgroup analyses were performed considering smoking status, education level, household income, age, sex, BMI, race, hypertension, and diabetes. Statistical significance was defined as $P < 0.05$. All analyses were performed using R version 4.3.2 (http://www.R-project.org, The R Foundation).

Handling of missing data

Missing data for covariates were addressed using multiple imputation with the fully conditional specification method, implemented through the mice package in R. Sensitivity analyses were conducted to ensure the robustness of the results. The imputed datasets were combined according to NHANES analytic guidelines, and appropriate sample weights were applied to ensure national representativeness.

Results

Baseline characteristics of participants

Ultimately, 6,699 participants were included in this study, of whom 2,825 were diagnosed with MASLD and 1,834 were diagnosed with SHS. Table 1 demonstrates details of the participants' baseline characteristics. The prevalence of MASLD, SHS, and liver fibrosis increased with increasing RFM levels (all $P < 0.001$). Significant differences were observed across RFM quartiles for the following variables: age, sex, smoking status, BMI, education level, waist circumference, race, household income, high-density lipoprotein cholesterol, hypertension, diabetes, blood transfusion, total cholesterol, triglycerides, total daily energy intake, gamma-glutamyl transferase, albumin, alanine aminotransferase, hemoglobin A1c, aspartate aminotransferase, C-reactive protein, total daily fat intake, ferritin, CAP, LSM, and total daily sugar intake (all $P < 0.001$). No statistically significant differences were found between RFM quartiles for total daily moisture intake ($P = 0.07$).

Relationships between RFM and clinical parameters

Table 2 shows RFM was positively correlated with age, BMI, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, hemoglobin A1c, C-reactive protein, CAP, and LSM ($r = 0.205$, 0.625, 0.104, 0.063, 0.072, 0.020, 0.160, 0.196, 0.319, and 0.087, respectively, all $P < 0.001$), and was negatively correlated with alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase, albumin, and ferritin (r = -0.067, -0.094, -0.010, -0.404, and −0.166, respectively, all $P < 0.001$).

Relationship between RFM and the prevalence of MASLD and SHS

Table 3 shows the relationship between RFM, MASLD and SHS prevalence. In Model 1, not adjusted for any confounders, and a significant positive association was observed between RFM and the odds of MASLD and SHS (OR: 1.07, 95% CI: 1.06–1.07 and OR: 1.06, 95% CI: 1.06–1.07, respectively). In Model 2, adjusting for age, gender, race, and BMI, and the results showed consistent correlations (OR: 1.25, 95% CI: 1.21–1.28 and OR: 1.29, 95% CI: 1.24–1.33, respectively). In Model 3, in addition to the variables considered in Model 2, additional adjustments were made for covariates such as smoking status, diabetes, hypertension, total cholesterol, alanine aminotransferase, albumin, hemoglobin A1c, C-reactive protein, ferritin, and total daily sugar intake, and the results still revealed a positive association between RFM and the prevalence of MASLD and SHS. In addition, our results revealed an association between RFM quartiles and the odds of MASLD and SHS (OR: 1.22, 95% CI: 1.18–1.26 and OR: 1.26, 95% CI: 1.21–1.30, respectively). Using the first quartile of RFM as the reference point, the OR for the second quartile of MASLD and SHS prevalence were 2.49 (95% CI: 2.03–3.04) and 2.55 (95% CI: 2.03–3.21), respectively, the OR of the third quartile was 4.27 (95% CI: 2.93–6.22) and 4.45 (95% CI: 3.06–6.47), and the OR of the fourth quartile was 6.47 (95% CI: 4.02–10.40) and 7.23 (95% CI: 4.36–11.98) (Table 3, Model 3).

Smoothed curve fitting and threshold effect analysis

As shown in Fig. 2, the association between RFM levels and the prevalence of MASLD and SHS was not completely linear. The results of the threshold effect model showed a nonlinear correlation between RFM levels and the odds of MASLD and SHS prevalence (all log-likelihood ratio < 0.001) (Table 4). To determine the RFM threshold, a two-part logistic regression model was applied, with a threshold of 41.96 for MASLD and 40.42 for SHS. RFM levels were positively associated with MASLD prevalence when either RFM < 41.96 or RFM > 41.96 (OR: 1.24, 95% CI: 1.20–1.29 and OR: 1.11, 95% CI: 1.06–1.16, respectively). There was also a positive correlation between RFM levels and SHS prevalence when RFM < 40.42 or RFM > 40.42 (OR: 1.29, 95% CI: 1.24–1.34 and OR: 1.17, 95% CI: 1.12–1.23, respectively).

Table 1 Characteristics of the participants

Variable	Total (*n* = 6699)	Q1 (*n* = 1674)	Q2 (*n* = 1675)	Q3 (*n* = 1675)	Q4 (*n* = 1675)	*P* value
RFM	35.42 (29.34–43.52)	25.62 (22.07–27.7)	32.26 (30.86–33.69)	39.63 (37.42–41.67)	47.03 (45.35–49.29)	< 0.001
Age, years	50 (33–64)	41 (26–60)	51 (33–65)	50 (35–63)	55 (40–66)	< 0.001
Male, n (%)	3226 (48.16)	1592 (95.10)	1291 (77.07)	343 (20.48)	0 (0.00)	< 0.001
BMI, kg/m^2	28.5 (24.6–33.5)	24.4 (22-26.6)	29.6 (25.5–32.6)	27.2 (24.5–31.6)	34.7 (31.1–39.6)	< 0.001
Waist circumference, cm	98.4 (87.5-110.4)	89 (80.9–95)	105 (94.9-111.9)	92 (86-99.6)	110.3 (102.9–120)	< 0.001
Ethnicity, n (%)						< 0.001
Non-Hispanic White	2228 (33.26)	498 (29.75)	622 (37.13)	554 (33.07)	554 (33.07)	
Non-Hispanic Black	1739 (25.96)	484 (28.91)	337 (20.12)	397 (23.70)	521 (31.10)	
Mexican American	1533 (22.88)	303 (18.10)	418 (24.96)	396 (23.64)	416 (24.84)	
Other Race	1199 (17.9)	389 (23.24)	298 (17.79)	328 (19.58)	184 (10.99)	
Education level, n (%)						< 0.001
Less than high school	1549 (23.12)	448 (26.76)	404 (24.12)	325 (19.40)	372 (22.21)	
High school	1553 (23.18)	360 (21.51)	379 (22.63)	404 (24.12)	410 (24.48)	
More than high school	3597 (53.69)	866 (51.73)	892 (53.25)	946 (56.48)	893 (53.31)	
Household income, n (%)						< 0.001
PIR < 1	1662 (24.81)	409 (24.43)	370 (22.09)	401 (23.94)	482 (28.78)	
PIR 1 to < 3	2289 (34.17)	531 (31.72)	570 (34.03)	569 (33.97)	619 (36.96)	
PIR ≥ 3	1820 (27.17)	479 (28.61)	517 (30.87)	463 (27.64)	361 (21.55)	
Unclear	928 (13.85)	255 (15.23)	218 (13.01)	242 (14.45)	213 (12.72)	
Smoking status, n (%)						< 0.001
Never smoker	4192 (62.58)	982 (58.66)	936 (55.88)	1157 (69.07)	1117 (66.69)	
Current smoker	1046 (15.61)	363 (21.68)	253 (15.10)	210 (12.54)	220 (13.13)	
Former smoker	1461 (21.81)	329 (19.65)	486 (29.01)	308 (18.39)	338 (20.18)	
Diabetes, n (%)	959 (14.32)	127 (7.59)	269 (16.06)	230 (13.73)	333 (19.88)	< 0.001
Hypertension, n (%)	2339 (34.92)	363 (21.68)	609 (36.36)	576 (34.39)	791 (47.22)	< 0.001
Blood transfusion, n (%)	669 (9.99)	115 (6.87)	140 (8.36)	171 (10.21)	243 (14.51)	< 0.001
TC, mg/dL	4.71 (4.03–5.41)	4.5 (3.87–5.24)	4.66 (4.03–5.38)	4.78 (4.14–5.51)	4.78 (4.14–5.43)	< 0.001
TG, mg/dL	112 (78–164)	95 (67-143.5)	120 (80–179)	107 (76–155)	125 (91–171)	< 0.001
HDL-C, mg/dL	1.29 (1.09–1.55)	1.29 (1.09–1.55)	1.19 (1.01–1.5)	1.4 (1.11–1.71)	1.29 (1.11–1.53)	< 0.001
LDL-C, mg/dL	2.77 (2.22–3.41)	2.66 (2.15–3.34)	2.77 (2.21–3.44)	2.79 (2.25–3.44)	2.85 (2.33–3.44)	0.01
ALT, U/L	17 (13–25)	18 (14–25)	20 (14–30)	15 (12–22)	16 (12–22)	< 0.001
AST, U/L	19 (16–23)	20 (17–24)	20 (17–24)	18 (15–22)	17 (15–21)	< 0.001
GGT, U/L	20 (14–30)	20 (14–29)	24 (16–37)	18 (12–27)	20 (15–29)	< 0.001
Alb, g/dL	41 (39–43)	43 (40–45)	41 (40–43)	40 (39–42)	39 (37–41)	< 0.001
HbA1c, %	5.6 (5.3-6)	5.5 (5.2–5.7)	5.6 (5.3-6)	5.5 (5.3–5.9)	5.8 (5.4–6.3)	< 0.001
CRP, mg/L	1.88 (0.81–4.35)	0.93 (0.49–2.06)	1.68 (0.79–3.7)	1.82 (0.87–4.08)	4.06 (2.05–7.66)	< 0.001
Ferritin, ng/mL	104 (48.9–192)	133 (81.1–223)	131 (63.6–239)	75.9 (36.3–157)	73.5 (35.1–138)	< 0.001
Total daily energy intake, kcal/day	1892 (1382–2538)	2170 (1582–2906)	2043 (1518–2735)	1752 (1287–2314)	1677 (1248–2212)	< 0.001
Total daily fat intake, g/day	76.93 (52.33–109.9)	86.91 (57.35-124.92)	83.87 (55.57-117.38)	72.09 (49.63-100.25)	68.74 (47.85–97.8)	< 0.001
Total daily moisture intake, mL/day	1920 (720–3480)	1763.85 (600–3402)	1920 (630–3600)	2001(900–3480)	1920 (720–3480)	0.07
Total daily sugar intake, g/day	90.39 (55.26-137.41)	99.47 (61.26-149.51)	96.4 (58.05-143.89)	85.28 (51.93-130.97)	81.13 (51.05-120.91)	< 0.001
CAP, dB/m	260 (216–307)	227 (199–265)	277 (219–320)	250 (214–299)	287 (251–326)	< 0.001
LSM, kPa	5 (4.1–6.1)	4.8 (4.1–5.8)	5.1 (4.2–6.2)	4.6 (3.8–5.9)	5.3 (4.3–6.7)	< 0.001
Hepatic fibrosis, n (%)						< 0.001
No	6091 (90.92)	1604 (95.82)	1525 (91.04)	1518 (90.63)	1444 (86.21)	
F2	244 (3.64)	45 (2.69)	51 (3.04)	60 (3.58)	88 (5.25)	
F3	211 (3.15)	14 (0.84)	60 (3.58)	56 (3.34)	81 (4.84)	
F4	153 (2.28)	11 (0.66)	39 (2.33)	41 (2.45)	62 (3.70)	

Table 1 (continued)

Variable	Total ($n=6699$)	Q1 ($n=1674$)	Q2 ($n=1675$)	Q3 ($n=1675$)	Q4 ($n=1675$)	*P* value
SHS, n (%)	1834 (27.38)	168 (10.04)	410 (24.48)	592 (35.34)	664 (39.64)	< 0.001
MASLD, n (%)	2825 (42.17)	337 (20.13)	618 (36.90)	865 (51.64)	1005 (60.00)	< 0.001

RFM, relative fat mass; BMI, body mass index; PIR, poverty income ratio; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; Alb, albumin; HbA1c, hemoglobin A1c; CRP, C-reactive protein; CAP, controlled attenuation parameter; LSM, liver stiffness measurement; SHS, severe hepatic steatosis; MASLD, metabolic dysfunction associated steatotic liver disease. *P*-values represent overall differences across RFM quartiles for continuous variables

Table 2 Relationships between RFM and clinical parameters

Variable	*r*	*P* value
Age	0.205	< 0.001
BMI	0.625	< 0.001
TC	0.104	< 0.001
TG	0.063	< 0.001
LDL-C	0.072	< 0.001
HDL-C	0.020	< 0.001
ALT	-0.067	< 0.001
AST	-0.094	< 0.001
GGT	-0.010	< 0.001
Alb	-0.404	< 0.001
HbA1c	0.160	< 0.001
CRP	0.196	< 0.001
Ferritin	-0.166	< 0.001
CAP	0.319	< 0.001
LSM	0.087	< 0.001

BMI, body mass index; TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; Alb, albumin; HbA1c, hemoglobin A1c; CRP, C-reactive protein; CAP, controlled attenuation parameter; LSM, liver stiffness measurement

Furthermore, we also performed threshold effect modeling separately for men and women. The detailed results are shown in Supplementary Fig. 1 and Supplementary Table 2.

Subgroup analysis

Subgroup analyses were conducted to explore whether the relationship between RFM levels and the odds of MASLD and SHS prevalence was robust across different populations. In this part, we focused on age, gender, smoking status, BMI, race, household income, education level, hypertension, and diabetes. The results suggested that RFM interacted with gender and BMI in the subgroup analysis regarding MASLD (all *P* for interaction < 0.05). In contrast, RFM only interacted with gender in the subgroup analysis regarding SHS (*P* for interaction < 0.001). The detailed results are shown in Fig. 3.

Discussion

In this study, we found that elevated RFM was significantly associated with an increased odds of both MASLD and SHS after adjusting for potential confounders.

Table 3 Association between RFM and prevalence of MASLD and SHS

	Model 1, OR (95% CI)	Model 2, OR (95% CI)	Model 3, OR (95% CI)
MASLD			
Continuous	1.07 (1.06–1.07)	1.25 (1.21–1.28)	1.22 (1.18–1.26)
Quintiles			
Q1	Reference	Reference	Reference
Q2	4.24 (3.64–4.94)	2.65 (2.18–3.22)	2.49 (2.03–3.04)
Q3	2.32 (1.99–2.71)	4.79 (3.32–6.93)	4.27 (2.93–6.22)
Q4	5.95 (5.10–6.94)	7.60 (4.79–12.04)	6.47 (4.02–10.40)
P for trend	< 0.001	< 0.001	< 0.001
SHS			
Continuous	1.06 (1.06–1.07)	1.29 (1.24–1.33)	1.26 (1.21–1.30)
Quintiles			
Q1	Reference	Reference	Reference
Q2	4.90 (4.06–5.92)	2.82 (2.27–3.52)	2.55 (2.03–3.21)
Q3	2.90 (2.39–3.53)	5.00 (3.49–7.17)	4.45 (3.06–6.47)
Q4	5.89 (4.88–7.10)	9.04 (5.57–14.68)	7.23 (4.36–11.98)
P for trend	< 0.001	< 0.001	< 0.001

Model 1: unadjusted model

Model 2: adjusted for age, sex, ethnicity and body mass index

Model 3: Model 2 + additionally adjusted for education level, poverty income ratio, smoking status, diabetes, hypertension, total cholesterol, alanine aminotransferase, albumin, hemoglobin A1c, C-reactive protein, ferritin, and total daily sugar intake

MASLD, metabolic dysfunction associated steatotic liver disease; SHS, severe hepatic steatosis

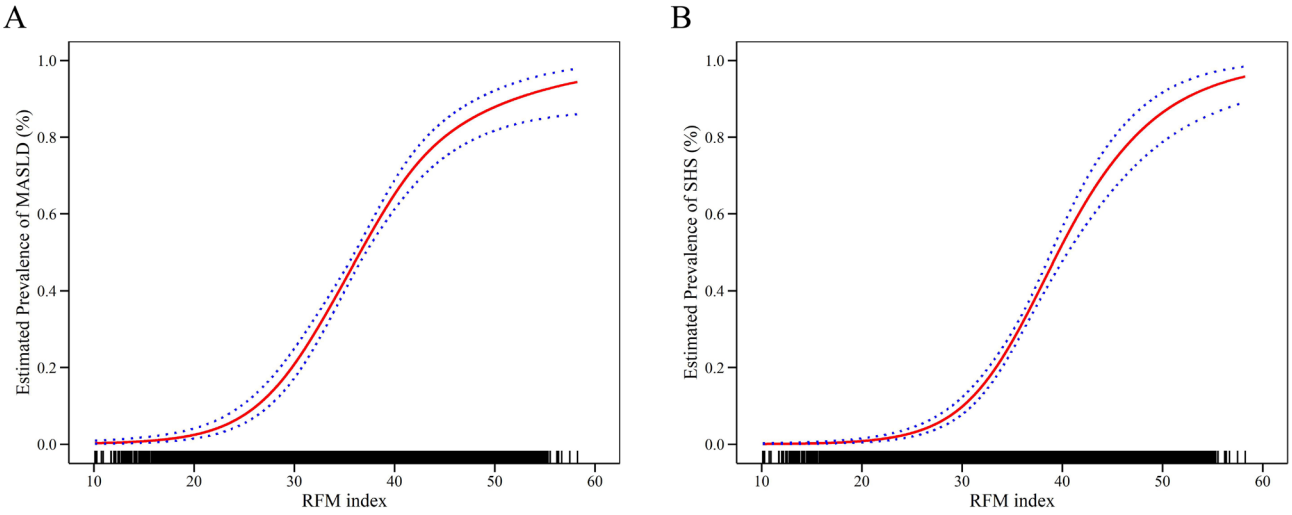

Fig. 2 Smoothed curve fitting and threshold effect analysis of the relationship between RFM and the prevalence of MASLD and SHS. Panel **A** shows the prevalence of MASLD, while Panel **B** shows the prevalence of SHS across different RFM levels. The red solid line represents the fitted smoothed curve, and the blue dotted lines indicate the 95% confidence intervals for each curve. RFM, relative fat mass; MASLD, metabolic dysfunction associated steatotic liver disease; SHS, severe hepatic steatosis

Table 4 Threshold effect analysis of RFM with prevalence of MASLD and SHS

Outcomes	MASLD	SHS
Model 1, OR (95% CI)		
Linear effect model	1.22 (1.18–1.26)	1.26 (1.21–1.30)
Model 2, OR (95% CI)		
Inflection point (K)	41.96	40.42
< K	1.24 (1.20–1.29)	1.29 (1.24–1.34)
> K	1.11 (1.06–1.16)	1.17 (1.12–1.23)
Log-likelihood ratio	< 0.001	< 0.001

Threshold effect analysis was detected after adjusting for age, sex ethnicity, body mass index, education level, poverty income ratio, smoking status, diabetes, hypertension, total cholesterol, alanine aminotransferase, albumin, hemoglobin A1c, C-reactive protein, ferritin, and total daily sugar intake

MASLD, metabolic dysfunction associated steatotic liver disease; SHS, severe hepatic steatosis

Moreover, there was a nonlinear relationship between RFM and the prevalence of MASLD and SHS, with a threshold of 41.96 for MASLD risk and 40.42 for SHS risk. In addition, subgroup analyses suggested that the relationship between RFM levels and the odds of MASLD and SHS prevalence did not significantly interact in most subgroups.

MASLD is one of the most prevalent liver diseases globally and has become a major cause of liver transplantation in developed countries, placing a substantial economic burden on healthcare systems [20]. MASLD is initially caused by the accumulation of fat in the liver. If left untreated, it may progress to NASH and even lead to serious complications such as liver fibrosis, cirrhosis and hepatocellular carcinoma [1]. In addition, MASLD is often associated with other extrahepatic diseases, including metabolic disorders, diabetes, hypertension, and cardiovascular disease, which also increase the all-cause mortality risk of the patients [21]. Therefore, an in-depth understanding and exploration of the pathophysiological mechanisms and adverse effects of MASLD are important for early diagnosis, effective intervention, and prevention of complications.

Obesity is a major risk factor for MASLD and involves multiple physiological and metabolic mechanisms [22, 23]. Obesity, particularly visceral fat accumulation, leads to insulin resistance, which is a central mechanism in the pathogenesis of MASLD [24]. When insulin resistance occurs, insulin is unable to properly regulate blood glucose and fat metabolism, leading to excessive fat accumulation in the liver, mainly manifested as triglyceride accumulation in the hepatocytes, which becomes the basis of MASLD [24, 25]. Adipose tissue in obese patients tends to show functional abnormalities [26, 27]. Adipocytes release large amounts of free fatty acids, which enter the blood circulation and are eventually absorbed by the liver, which leads to an over-accumulation of fat in the liver [26, 27]. Obesity can also lead to the secretion of abnormal pro-inflammatory factors from adipose tissue, such as interleukin-6 and tumor necrosis factor-alpha, which further aggravate the inflammatory response and liver injury, driving the progression of MASLD from simple fatty liver to NASH [28, 29]. Third, leptin and lipocalin are two hormones secreted by adipose tissue that are important in regulating energy balance and lipid metabolism [30, 31]. Obesity leads to elevated leptin levels and decreased lipocalin levels [30, 31]. Elevated leptin is associated with insulin resistance, whereas decreased lipocalin diminishes its protective effect on the liver, making the liver more prone to fat accumulation and inflammation, driving the onset and progression of

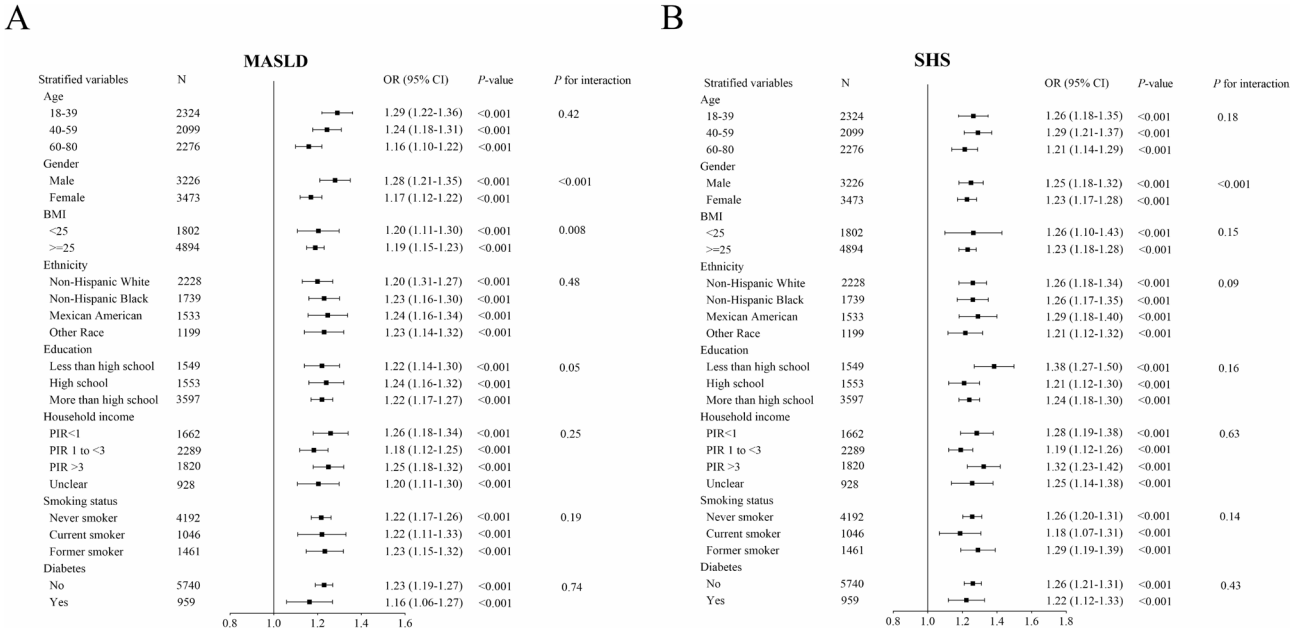

Fig. 3 Subgroup analysis of the association between RFM and the prevalence of MASLD and SHS. Panel **A** presents the odds ratios (OR) and 95% confidence intervals (CIs) for MASLD, stratified by age, gender, BMI, ethnicity, education level, household income, smoking status, and diabetes. Panel **B** presents similar subgroup analyses for SHS. The forest plots show the ORs and corresponding 95% CIs for each subgroup, with the size of the squares representing the weight of each subgroup and the horizontal lines representing the 95% CIs. RFM, relative fat mass; MASLD, metabolic dysfunction associated steatotic liver disease; SHS, severe hepatic steatosis

MASLD [30, 31]. In addition, obesity is closely associated with changes in the intestinal flora [32]. It has been found that the imbalance of intestinal flora in obese individuals may lead to increased production of endotoxins, which enter the liver through the intestinal barrier and activate the hepatic inflammatory response, thus contributing to the development of MASLD [32, 33]. Furthermore, an altered intestinal flora may exacerbate hepatic fat accumulation by affecting short-chain fatty acid and bile acid metabolism [32, 33]. In addition, the increased oxidative metabolism of free fatty acids in the liver in the obese state generates large amounts of reactive oxygen species, which can lead to oxidative stress, damage hepatocytes, exacerbate the inflammatory response, and promote the development of MASLD [29]. Thus, obesity affects the liver through multiple mechanisms, including insulin resistance, abnormal adipose tissue function, intestinal flora imbalance, imbalanced leptin and lipocalin levels, and oxidative stress. These complex metabolic and inflammatory changes work together to cause fat accumulation in the liver and hepatocyte damage; thus, obesity plays a pivotal role in the onset and progression of MASLD.

BMI, which is the most commonly used index to assess obesity, is however calculated based on weight and height only and does not take into account the distribution of body fat. Therefore, BMI only roughly reflects whether an individual is overweight [34]. Recently, RFM has emerged as a new index for estimating obesity, showing high accuracy when predicting percent body fat [9]. RFM reflects the body fat content more directly by calculating the height-to-waist circumference ratio [11, 35]. Additionally, BMI does not distinguish gender differences in fat content and distribution and thus may have some inherent limitations in assessing obesity across sexes, whereas sex adjustment of the RFM allows for greater applicability and accuracy in sex-specific populations [11, 35]. Furthermore, the superiority of RFM over BMI in predicting liver fat accumulation is supported by its ability to more accurately reflect abdominal fat, particularly visceral fat. Unlike BMI, which cannot distinguish between fat and lean body mass or the distribution of fat, RFM is based on the waist-to-height ratio, which is more sensitive to visceral fat accumulation. Existing evidence indicates that visceral fat is closely associated with the development of MASLD, mediating liver fat deposition through mechanisms such as inflammation, insulin resistance, and lipotoxicity [1, 5]. Therefore, RFM may more sensitively capture fat distribution patterns related to liver fat accumulation, making it a more reliable predictor of liver fat content compared to BMI.

Although high RFM levels are associated with an increased odds of developing many obesity-related diseases, including diabetes, periodontitis, and cardiovascular disease [10–13], the relationship between RFM and the odds of MASLD prevalence remains controversial. In addition, the relationship between RFM and the prevalence of SHS has not been elucidated. Shen et

al. [14] discovered that after adjustment for confounding variables, RFM was significantly associated with the prevalence of MASLD. In men, the odds of prevalence of MASLD increased more than threefold for every 1 standard deviation increase in RFM (OR: 4.33, 95% CI: 3.79–4.93), and in women, each 1 standard deviation increase in RFM was associated with an approximately fourfold increase in the odds of developing MASLD (OR: 5.16, 95% CI: 4.62–5.77) [14]. However, Lee et al. [15] reported that there was no significant association between elevated RFM levels and the odds of MASLD (OR: 1.54, 95% CI: 0.89–2.69). The controversy in existing studies may be related to differences in the gender distribution of study cohorts, demographic characteristics, and variations in covariates adjusted for in statistical analyses. We used data from a nationally representative general adult population in NHANES to enhance existing research. We found that increased RFM levels were not only associated with an increased odds of MASLD, but also with an increased odds of SHS. The NHANES stratified multistage probability sampling design ensures that the sample drawn is nationally representative of the United States civilian non-institutionalized population. Therefore, Thus, these findings reflect the prevalence in the general adult U.S. population.

Moreover, RFM demonstrated a threshold effect on the odds of developing both MASLD and SHS, with a curvilinear relationship between RFM and liver fat accumulation. A better understanding of this relationship, particularly the inflection points, can enhance clinical decision-making and inform more effective prevention strategies for these conditions. Previous studies suggest that as adiposity increases, hepatic fat deposition and insulin resistance rise in a nonlinear manner [14]. Once a certain "fat threshold" is surpassed, hepatic lipid metabolism becomes overwhelmed, leading to oxidative stress, lipotoxicity, and inflammation, which contribute to the progression of MASLD and SHS. Considering established sex-related differences in fat distribution, we further explored sex-specific RFM thresholds in supplementary analyses. The findings revealed differential threshold patterns between men and women, suggesting that sex-specific cutoffs may better capture the risk of MASLD and SHS. This highlights the importance of incorporating sex-specific considerations in future risk assessments and clinical interventions. However, it is important to note that these precise threshold values are intended to illustrate the nonlinear relationship between RFM and MASLD and SHS and should not be directly interpreted as clinical diagnostic or prognostic cutoffs. Instead, they can serve as a basis for hypothesis generation in future mechanistic studies, which are needed to confirm and further explore these transitions.

In this study, we observed a negative correlation between RFM and liver enzymes. Several factors could explain this negative correlation. First, the NHANES data represents a broad, heterogeneous U.S. adult population, which may include individuals not diagnosed with MASLD or with lower liver enzyme levels, potentially confounding the relationship between RFM and liver enzymes. Additionally, RFM is specifically an indicator of abdominal fat, particularly visceral fat, while liver enzymes can be influenced by a range of factors beyond fat accumulation, such as liver injury or metabolic dysfunction. Visceral fat may not always correlate directly with elevated liver enzymes, particularly in the early stages of MASLD or certain subtypes of the disease. Moreover, liver enzyme levels can also be affected by various other factors, such as acute or chronic liver damage, medications, and comorbid conditions, all of which could influence the relationship with body fat. These factors highlight the need for cautious interpretation of the negative correlation observed and suggest that further research is needed to better understand the dynamics between abdominal fat, liver enzymes, and MASLD progression.

This study presents several strengths. First, our study extends previous research by utilizing a nationally representative U.S. adult population from NHANES, improving the generalizability and relevance of our findings across diverse racial, socioeconomic, and demographic groups. In contrast to earlier studies, we include SHS in our analysis, providing a more comprehensive view of the adiposity–liver disease relationship. Additionally, through advanced analytical techniques like smoothed curve fitting and threshold effect models, we uncover significant nonlinear associations between RFM and both MASLD and SHS, offering more precise insights into these relationships. We also identify population-specific RFM thresholds, highlighting the potential for demographic variation in RFM's clinical application. These contributions provide a more robust understanding of adiposity-related risks and underscore the utility of RFM as a biomarker for liver disease across diverse populations. In summary, we believe that maintaining low RFM levels may help to reduce the odds of MASLD and SHS, and thus RFM can be used as a simple screening tool for early intervention in high-risk populations, especially in resource-limited settings.

However, this study had several limitations. First, due to the cross-sectional study design, we were unable to elucidate the causal relationship between RFM and the prevalence of MASLD and SHS. Longitudinal and interventional studies can contribute to overcoming these limitations. Second, this study included adults 18 years of age or older; therefore, the applicability of these findings to those under 18 years of age needs to be further explored.

In addition, unmeasured or uncontrolled covariates may affect our results, although we adjusted for potential many confounders. Another limitation is the wide confidence intervals observed for the odds ratios in the highest RFM quartile. While the association was strongest in this group, the broad intervals suggest potential uncertainty in the risk estimation, which may be influenced by factors such as sample size, covariate adjustment, and population heterogeneity. Finally, although VCTE provides valuable clinical data, the voluntary nature of participation could introduce selection bias, as individuals with better health status or no symptoms of liver disease may be more likely to participate. This could affect the generalizability of the results, especially in underrepresented populations. Moreover, we acknowledge a potential limitation in our regression modeling. In the fully adjusted Model 3, we included variables such as hemoglobin A1c, C-reactive protein, and ferritin, which may lie on the causal pathway between RFM and the prevalence of MASLD and SHS. This could introduce overadjustment bias, as these variables may act as mediators in the causal pathway. While the adjustment was made to control for potential confounders, we recognize the possibility that it could impact the interpretability of our results.

Additionally, a potential misclassification of NAFLD/SHS could occur due to the use of VCTE with CAP thresholds instead of liver biopsy, which is considered the gold standard for diagnosis. While VCTE is a non-invasive and widely used tool, its diagnostic accuracy can be influenced by factors such as the patient's body type and liver anatomy, potentially leading to misclassification, particularly in cases of mild steatosis. Although we acknowledged this limitation, a more detailed discussion of this potential misclassification bias has been added.

In addition, this study used data from NHANES and has not been validated in an independent cohort. Therefore, the derived threshold values of RFM require external validation. Future research should focus on validating these findings in separate cohorts to confirm their applicability across different populations. Furthermore, in this study, we utilized CAP cutoffs of ≥ 274 dB/m for diagnosing MASLD and ≥ 302 dB/m for SHS, based on established validation from high-quality studies [16, 17]. These thresholds have demonstrated adequate diagnostic performance in both prospective and cross-sectional settings. However, as noted by Karlas et al. [36], CAP cutoffs can vary depending on the population and underlying liver disease etiology. In their analysis, they recommended lower CAP cutoffs of 248 dB/m, 268 dB/m, and 280 dB/m for mild, moderate, and severe steatosis, respectively. While our use of higher cutoffs may increase specificity, it could also lead to an underestimation of disease prevalence. Thus, while VCTE/CAP remains a valuable tool for large-scale epidemiological studies, caution is necessary when generalizing results across different populations or etiologies, and further research is needed to refine these diagnostic thresholds. Finally, although RFM is a simple and effective tool, it is not as precise as other imaging methods (such as liver biopsy) in assessing visceral fat. Therefore, RFM may have limitations as an alternative tool in some cases.

Moreover, while we included variables such as total daily energy intake and total daily sugar intake, broader dietary patterns and physical activity levels were not considered. These lifestyle factors could confound the relationship between RFM and liver disease. Future studies incorporating more detailed dietary and physical activity data could help better elucidate the role of RFM in liver disease.

Conclusion

In this study, we found that increased RFM levels were positively (nonlinearly) associated with the odds of MASLD and SHS prevalence, with a threshold effect. Lower RFM levels are associated with lower odds of MASLD and SHS. RFM may serve as a valuable, non-invasive screening tool for assessing the odds of MASLD and SHS in diverse adult populations.

Abbreviations

BMI	Body mass index
CAP	Controlled attenuation parameter
CI	Confidence interval
LSM	Liver stiffness measurement
NAFLD	Nonalcoholic fatty liver disease
MASLD	Metabolic dysfunction associated steatotic liver disease
NASH	Nonalcoholic steatohepatitis
OR	Odds ratio
RFM	Relative fat mass
SD	Standard deviation
SHS	Severe hepatic steatosis
VCTE	Vibration-controlled transient elastography

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-04006-7.

Supplementary Material 1

Supplementary Material 2: Fig. 1. Smoothed curve fitting and threshold effect analysis of the relationship between RFM and the prevalence of MASLD and SHS in male and female. Panel A shows the prevalence of MASLD in male, while Panel B shows the prevalence of SHS in male with different RFM levels. Panel C shows the prevalence of MASLD in female, while Panel D shows the prevalence of SHS in female with different RFM levels. The red solid line represents the fitted smoothed curve, and the blue dotted lines indicate the 95% confidence intervals for each curve. RFM, relative fat mass; MASLD, metabolic dysfunction associated steatotic liver disease; SHS, severe hepatic steatosis.

Supplementary Material 3

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Author contributions
Conceptualization: Jianjun Wang, Wei He, Xianfu Cai, Zhaohui Hu, Yonghai Peng; Methodology: Jianjun Wang, Wei He, Xianfu Cai; Software: Jianjun Wang, Wei He, Xianfu Cai, Zhaohui Hu, Yonghai Peng, Xi Chen; Validation: Zhaohui Hu, Yonghai Peng, Xi Chen, Pei Yang, Xintao Zeng, Sirui Chen, Decai Wang; Formal analysis: Xintao Zeng, Sirui Chen, Decai Wang; Investigation: Jianjun Wang, Wei He, Xianfu Cai; Resources: Zhaohui Hu, Yonghai Peng, Xi Chen, Pei Yang, Xintao Zeng, Sirui Chen, Decai Wang; Data curation: Jianjun Wang, Wei He, Xianfu Cai, Xintao Zeng, Sirui Chen, Decai Wang; Writing—original draft preparation: All authors; Writing—review and editing: All authors; Visualization: Zhaohui Hu, Yonghai Peng, Xi Chen, Pei Yang, Xintao Zeng, Sirui Chen, Decai Wang; Supervision: Xintao Zeng, Sirui Chen, Decai Wang; Project administration: Xintao Zeng, Sirui Chen, Decai Wangg; Funding acquisition: Zhaohui Hu, Xintao Zeng, Jianjun Wang, Decai Wang. Jianjun Wang, Wei He, and Xianfu Cai contributed equally to this work and share first authorship. Xintao Zeng, Sirui Chen and Decai Wang contribute equally to this work and share corresponding authorship. All authors have read and agreed to the published version of the manuscript.

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Data availability
Raw data supporting the conclusions of this paper will be made available by the authors without reservation and may be requested from the corresponding author.

Declarations

Ethics approval and consent to participate
The NHANES is publicly accessible, and all participants signed an informed consent form. The NHANES dataset provided by the NCHS maintains de-identification and anonymity, thus exempting investigators from obtaining duplicate ethical clearance or informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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