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Higher relative fat mass was associated with a higher prevalence of gallstones in US adults

Shangfen Xie[1†], Shanni Ma[2†], Xiaofeng Chen[1], Libiao Fang[1] and Dongen Li[1*]

Abstract

Aims Our study aimed to investigate the association between the relative fat mass (RFM) and gallstones in adults.

Methods Information obtained from the National Health and Nutrition Examination Survey (NHANES) 2017–2023 was utilized to examine the correlation between RFM and gallstones based on weighted multivariable regression analysis, smoothing curve fitting, and threshold effect analyses. Using subgroup analysis and interaction tests, we investigated whether this association remained consistent across different populations. We evaluated the effectiveness of RFM and Body Mass Index (BMI) in detecting gallstones through receiver operating characteristic (ROC) analysis and by calculating the area under the curve (AUC).

Results The study involved 7618 participants in total. RFM mean was 30.74 ± 5.68. Based on the fully adjusted model, gallstone prevalence was positively associated with RFM (OR = 1.09; 95% CI: 1.07–1.11; $p < 0.001$), with a 9% increase for each unit increase in RFM. This correlation was particularly evident among individuals under the age of 40 and among females. Smoothing curve fitting revealed a nonlinear association between RFM and the occurrence of gallstones, with an inflection point identified at 19.8. Additionally, ROC analysis showed that RFM (AUC = 0.674) outperformed BMI (AUC = 0.634) as a predictor of gallstone formation.

Conclusions Higher RFM was associated with higher gallstone prevalence. RFM may be a more useful tool for gallstone prediction than BMI in the general population. Gallstones may be alleviated or improved by RFM management at an early age.

Clinical trial number Not applicable.

Keywords Relative fat mass, Gallstone disease, NHANES, Body fat

Introduction

Gallstone disease (GSD) ranks among the prevalent digestive system diseases, accounting for significant health care utilization and expenses. It significantly affects quality of life and places a significant strain on the healthcare system [1]. GSD affects up to 15–20% of the American and European population [2, 3]. There is a risk of developing gallstone-related symptoms in 10–25% of patients. Some of these symptoms may include acute cholecystitis, pancreatitis, obstruction of the biliary system, and gallbladder cancer [4–6], leading to significant suffering and posing life-threatening risks to the

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patients. Currently, invasive surgical treatment remains the dominant approach for symptomatic gallstones. Due to discontent with clinical outcomes, the etiology and prevention of gallstones have been investigated in greater detail. Therefore, recognizing the risk factors associated with gallstones is especially critical for preventing their development.

Multiple risk factors associated with gallstones include female sex [7], pregnancy [8], metabolic syndrome, obesity [9], insulin resistance and diabetes [10], non-alcoholic fatty liver disease [11], dietary factors [12, 13], long-term fasting [14], gastrectomy, and medication use (ceftriaxone, octreotide, thiazide diuretics) [14, 15]. Furthermore, mutations in the ABCG8 protein pose a significant genetic risk factor, contributing to approximately 25% of the overall risk in this disease [16]. Ultimately, these factors may deteriorate the gallbladder's bile, cholesterol, and phospholipid homeostasis, causing gallstones [17]. Despite previous studies identifying some gallstone risk factors, there are no reliable clinical indicators to predict further.

Metabolic obesity is notably a key risk factor associated with gallstones [18]. And fat accumulation is a red flag for obesity, predisposing individuals to metabolic disorders that may increase susceptibility to cardiovascular disease, diabetes, gallstones, and fatty liver disease [19, 20]. While BMI was commonly employed as a measure of obesity, it failed to consider differences in body frame or to distinguish between fat, bone, and muscle mass [21, 22]. Recently, researchers have proposed a straightforward algorithm, known as relative fat mass, to estimate whole-body fat percentage in adults more effectively [23]. RFM calculates body fat percentage by measuring height and waist circumference, offering a non-invasive and equipment-free method to assess an individual's body fat status [24]. It provides a more precise measure of body fat distribution, particularly in individuals with lean body mass, surpassing traditional indicators like BMI [25, 26]. In recent research, the use of RFM as an indicator of obesity has gained attention. Studies have shown that RFM is a more reliable predictor of advanced liver disease and mortality when compared to BMI [27, 28]. Additionally, RFM has proven to be the most reliable predictor of heart failure risk within the general population [29]. Its growing role in identifying obesity-related health risks has contributed to a deeper understanding of public health trends across diverse populations [30].

However, the connection between RFM and gallstones remains unclear. Thus, a cross-sectional investigation was conducted to examine the relationship between RFM and gallstones by utilizing information from the 2017–2023 NHANES.

Methods

Study population

The NHANES survey, a nationally representative study managed by the Centers for Disease Control and Prevention, has been approved by the Research Ethics Review Board of the National Center for Health Statistics (NCHS) for implementation. Upon recruitment, all participants furnished written consent. Baseline clinical variables were determined using NHANES data from 2017 to 2023. Among the participants, we collected information regarding participants who provided explicit information about the presence of gallstones. Participants in the survey numbered 27,493. Figure 1 shows the following exclusion criteria: (1) age < 20 years or pregnancy; (2) Lack of RFM index; (3) The gallstone questionnaire was incomplete; (4) Lack of covariate information. Finally, this study included 7618 cases, 845 of which had self-reported gallbladder stones.

Exposure variable

RFM provides a simple, non-invasive method to estimate body fat percentage without requiring specialized equipment, making it suitable for large-scale studies. The development and validation of RFM are described in detail in the original publication [23]. It is determined through a formula that incorporates waist circumference (WC), height, and gender. In this calculation, individuals are assigned a gender value of 1 for females and 0 for males. The measurements for both height and WC were precisely taken by healthcare professionals at the Mobile Examination Center.

$$RFM = 64 - \left(20 \times \frac{height\,(cm)}{WC\,(cm)}\right) + (12 \times\ gender)$$

Outcome Definitions

Gallbladder stone was assessed via questionnaires by "Ever been told you have gallstones?". Participants were considered to have cholelithiasis if they indicated that they had ever had a gallstone. Gallbladder stones were intended to be an outcome variable.

Covariables

Covariates included gender, age, ethnicity, education level, poverty income ratio (PIR), marital status, alcohol intake, smoking status, hypertension, diabetes, asthma, cancer, cholesterol, and dietary factors, including total energy, fat, sugar, and water. Each participant was required to recall their diet for 24 h during 2017 and 2023. In this analysis, we will employ the mean consumption rate for both recalls. A comprehensive account of the measurement processes was revealed on www.cdc.gov/nchs/nhanes.

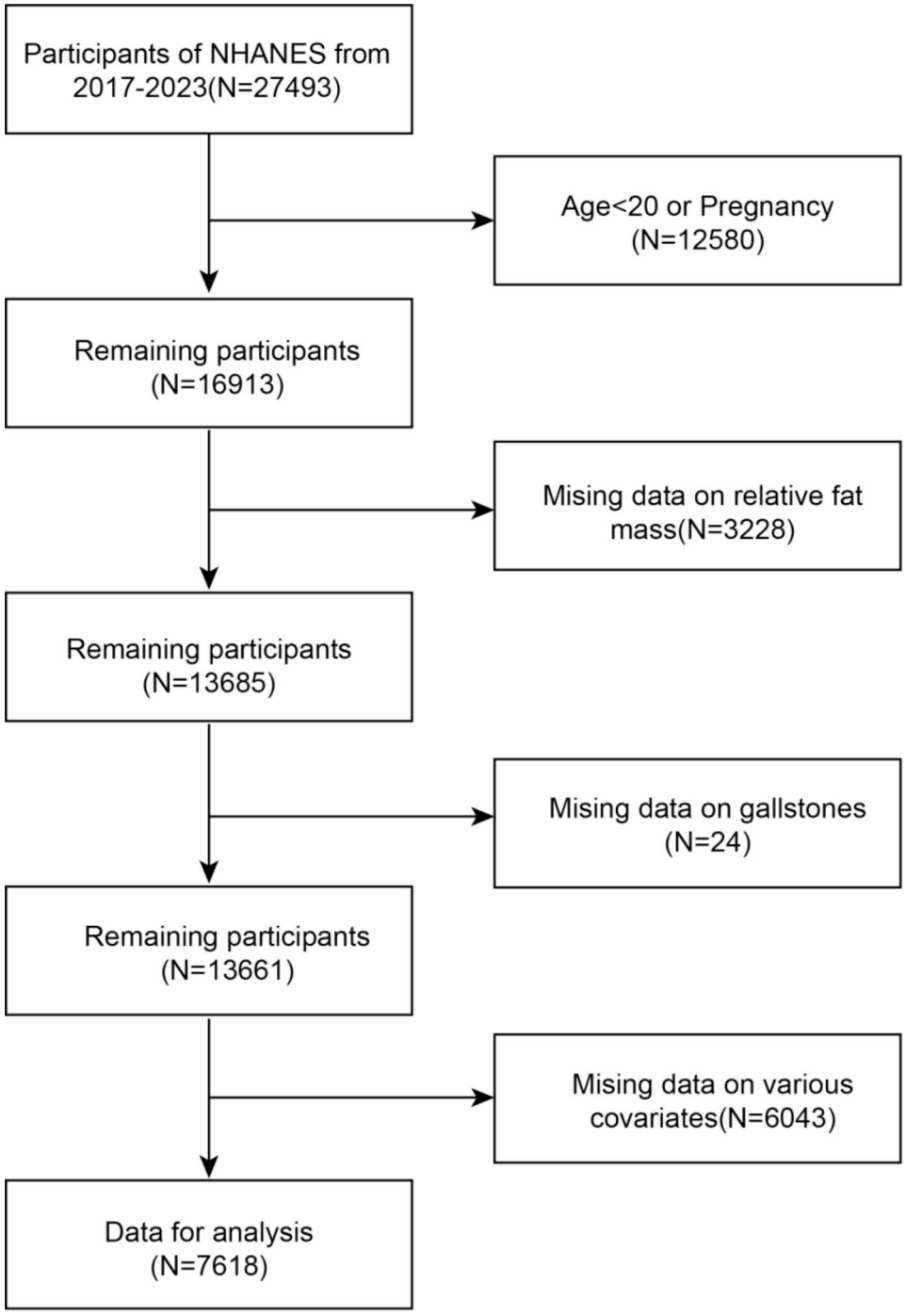

Fig. 1 Flowchart of participants selection. NHANES, National Health and Nutrition Examination Survey

Statistical analysis

In accordance with CDC guidelines, statistical analyses in this study were performed incorporating relevant NHANES sampling weights. The mean and standard deviation (SD) for continuous variables were reported, and the percentage for categorical variables. We employed a weighted t-test or a weighted chi-square test to assess differences among groups based on RFM (quartiles). Multivariate logistic regression analyses were utilized to investigate the relationship between RFM and gallstones across three distinct models. Model 1 did not account for covariates, while Model 2 was adjusted for race, gender, and age. Model 3 accounted for gender, age, ethnicity, education level, PIR, marital status, alcohol intake, cholesterol, smoking status, hypertension, diabetes, asthma, cancer, and dietary components. The

nonlinear association of RFM and gallstones was further examined using smooth curve fitting. A segmented regression model was used if nonlinear correlations were observed. An analysis of subgroups stratified based on sex, age, ethnicity, smoking status, drinking status, hypertension, and diabetes was also assessed using stratified multivariate regression. Furthermore, a log likelihood ratio test model was used to evaluate subgroup heterogeneity. To further investigate, we examined the performance of RFM and BMI in detecting gallstones through ROC analysis and the calculation of AUC values. The comparison of AUC values for RFM and BMI was conducted using the Delong test. Statistical significance was set at $P < 0.05$. R version (www.Rproject.org) and Empower software (www.empowerstats.com) were conducted for all analysis.

Results

Baseline characteristics

As shown in Table 1, detailed demographic data about the participants was provided. In the study, 7618 individuals were included, the mean (SD) age was 52.50 ± 16.89 years, with 48.16% were male and 51.84% were female. The mean RFM was 30.74 ± 5.68. Participants were categorized into four groups based on the quartiles of RFM levels: Q1 group (RFM < 27.12, $n = 1905$), Q2 group (27.12 ≤ RFM < 31.12, $n = 1904$), Q3 group (31.12 ≤ RFM < 34.82, $n = 1904$), Q4 group (RFM ≥ 34.82, $n = 1905$). As shown in Table 1, significant differences were found in age, sex, race, education level, marital status, PIR, alcohol use, cholesterol, hypertension, diabetes, asthma, cancers, GBD, smoking status, and dietary factors among the four groups ($P < 0.01$).

Higher RFM was associated with higher prevalence of gallstones

The findings revealed a significant positive connection between RFM and the prevalence of gallstones(Table 2). Fully adjusted (Model 3) showed a stable positive association (OR = 1.09; 95% CI: 1.07–1.11; $p < 0.001$). RFM was further categorized into quartiles for analysis. Compared to the first RFM quartile (Q1), higher RFM quartiles were associated with higher stone prevalence. (Q2 (OR = 1.97, 95% CI:1.47, 2.64); Q3(OR = 2.51, 95% CI:1.89, 3.33); Q4(OR = 3.63, 95% CI:2.75, 4.79)) (Table 2).

The likelihood ratio test indicated a significant overall trend ($P < 0.001$) and a nonlinear relationship ($P = 0.04$) between RFM and the prevalence of gallstones (Fig. 2). Additionally, threshold effect analysis revealed an inflection point for RFM at 19.8. A two-segment linear regression model further demonstrated that when RFM < 19.8, there is no significant association between RFM and gallstone incidence. When RFM ≥ 19.8, the prevalence of gallstones is positively correlated with RFM (OR = 1.08, 95% CI = 1.07–1.10, $P < 0.0001$) (Table 3).

Subgroup analyses

Subgroup analyses and interaction tests were performed stratified by age, gender, race, smoking habits, drinking status, hypertension and diabetes, to determine whether the association between RFM and gallstones is stable and what variations may exist across different populations (Fig. 3). According to our results, the association between RFM and gallstones differed significantly by age and gender subgroups (P for interaction < 0.01).

Comparison between RFM and BMI

The ROC curve analysis results are presented in Table 4. As illustrated in Fig. 4, the ROC curve showed that RFM (AUC = 0.674) outperformed BMI (AUC = 0.634) in predicting the presence of gallstones. Delong's test further confirmed a statistically significant difference in AUC values between RFM and BMI ($P < 0.001$), supporting the conclusion that RFM provides a more reliable prediction of gallstones compared to BMI.

Discussion

To our understanding, the research represents the first thorough examination of the correlation between RFM and gallstones. The characteristic of RFM is that it combines height and waist circumference, which can better reflect the whole-body fat distribution. Over the span of two cycles from 2017 to 2023, a population-based investigation was assessed using the NHANES database. RFM was found to be positively correlated with gallstone prevalence, as each unit increase in RFM is associated with a 9% increase in gallstone prevalence after full model adjustment (OR = 1.09, 95% CI: 1.07, 1.11). It was also found that this association was more significant among younger adults and females. The results strongly prominent RFM as a significant predictor of gallstone development. To further assess RFM's predictive capacity for gallstones, we conducted a ROC analysis and compared its performance with that of BMI. The results revealed that RFM outperformed BMI in predicting gallstone risk, with the difference being statistically significant.

Consistent with previous studies, our findings support the use of RFM as a predictor for gallstone assessment. Moreover, RFM demonstrated superior predictive accuracy compared to the conventional BMI. As a relatively recent obesity index, RFM shows considerable promise in predicting the likelihood of gallstone formation. Nevertheless, additional large-scale prospective cohort research is required to validate these findings. According to smooth curve fitting and threshold analysis, the inflection point of RFM is 19.8. When RFM values exceed 19.8, the risk of gallstones increases significantly, and we

Table 1 Baseline characteristics of participants according to quartiles of relative fat mass

Variables	Quartile 1 (< 27.12)	Quartile 2 (27.12–31.12)	Quartile 3 (31.12–34.82)	Quartile 4 (> 34.82)	*P*
N	1905	1904	1904	1905	
Age (year)	45.34 ± 17.14	53.73 ± 16.39	55.89 ± 16.04	55.06 ± 15.80	< 0.001
PIR	3.04 ± 1.70	3.10 ± 1.65	2.83 ± 1.59	2.60 ± 1.58	< 0.001
Cholesterol (mg/dL)	183.99 ± 38.76	192.14 ± 43.27	188.89 ± 42.54	184.22 ± 40.97	< 0.001
Gender, n (%)					< 0.001
Male	1040 (54.59%)	1096 (57.56%)	968 (50.84%)	565 (29.66%)	
Female	865 (45.41%)	808 (42.44%)	936 (49.16%)	1340 (70.34%)	
Cancers, n (%)					< 0.001
No	1725 (90.55%)	1658 (87.08%)	1596 (83.82%)	1631 (85.62%)	
Yes	180 (9.45%)	246 (12.92%)	308 (16.18%)	274 (14.38%)	
Race, n (%)					< 0.001
Mexican American	106 (5.56%)	180 (9.45%)	230 (12.08%)	177 (9.29%)	
White	1059 (55.59%)	1139 (59.82%)	1142 (59.98%)	1142 (59.95%)	
Black	400 (21.00%)	338 (17.75%)	346 (18.17%)	449 (23.57%)	
Other Races	340 (17.85%)	247 (12.97%)	186 (9.77%)	137 (7.19%)	
Education level, n (%)					< 0.001
Less than high school	28 (1.47%)	71 (3.73%)	104 (5.46%)	65 (3.41%)	
High school	493 (25.88%)	525 (27.57%)	589 (30.93%)	672 (35.28%)	
Above high school	1384 (72.65%)	1308 (68.70%)	1211 (63.60%)	1168 (61.31%)	
Asthma, n (%)					< 0.001
Yes	307 (16.12%)	266 (13.97%)	306 (16.07%)	419 (21.99%)	
No	1598 (83.88%)	1638 (86.03%)	1598 (83.93%)	1486 (78.01%)	
Smoking status, n (%)					< 0.001
Never	1160 (60.89%)	1080 (56.72%)	987 (51.84%)	1013 (53.18%)	
Current	745 (39.11%)	824 (43.28%)	917 (48.16%)	892 (46.82%)	
Diabetes, n (%)					< 0.001
No	1820 (95.54%)	1710 (89.81%)	1587 (83.35%)	1427 (74.91%)	
Yes	85 (4.46%)	194 (10.19%)	317 (16.65%)	478 (25.09%)	
Hypertension, n (%)					< 0.001
No	1555 (81.63%)	1233 (64.76%)	1030 (54.10%)	860 (45.14%)	
Yes	350 (18.37%)	671 (35.24%)	874 (45.90%)	1045 (54.86%)	
Total energy (kcal)	2202.76 ± 883.13	2086.85 ± 814.96	2001.67 ± 775.88	1926.18 ± 749.01	< 0.001
Total fat (g)	90.00 ± 41.72	86.08 ± 38.92	83.21 ± 37.92	82.69 ± 38.15	< 0.001
Total sugars (g)	103.85 ± 66.31	100.80 ± 62.98	98.58 ± 59.07	96.40 ± 59.01	0.009
Total water (g)	2981.09 ± 1500.13	2870.82 ± 1191.50	2839.02 ± 1234.13	2766.61 ± 1241.90	< 0.001
Alcohol, n (%)					< 0.001
No	1122 (58.90%)	1149 (60.35%)	1286 (67.54%)	1497 (78.58%)	
Yes	783 (41.10%)	755 (39.65%)	618 (32.46%)	408 (21.42%)	
Marital Status, n (%)					< 0.001
Cohabitation	1052 (55.22%)	1185 (62.24%)	1146 (60.19%)	1010 (53.02%)	
Solitude	853 (44.78%)	719 (37.76%)	758 (39.81%)	895 (46.98%)	
GBD, n (%)					< 0.001
No	1833 (96.22%)	1744 (91.60%)	1670 (87.71%)	1526 (80.10%)	
Yes	72 (3.78%)	160 (8.40%)	234 (12.29%)	379 (19.90%)	

PIR: Poverty income ratio

Data of continuous variables are shown as mean (95% CI); P-value was calculated by linear regression

Data of categorical variables are shown as percentage (95% CI), P-value was calculated by Chi-square test

recommend that patients undergo further abdominal ultrasound for a definitive diagnosis. In clinical practice, this may contribute to the preliminary screening of gallstones in the general population and improve the early diagnosis of gallstones, thereby reducing the pain of patients, avoiding complications, and benefiting the health and quality of life of patients. Obesity remains a significant risk factor for gallstone development, with numerous epidemiological studies highlighting its strong association with the condition [31, 32]. Research has

Table 2 Association between relative fat mass and GBD prevalence

GBD	Model 1		Model 2		Model 3	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Relative fat mass	1.13 (1.11, 1.14)	< 0.0001	1.11 (1.09, 1.12)	< 0.0001	1.09 (1.07, 1.11)	< 0.0001
Categories						
Q1	1		1		1	
Q2	2.34 (1.76, 3.11)	< 0.0001	2.01 (1.50, 2.68)	< 0.0001	1.97 (1.47, 2.64)	< 0.0001
Q3	3.57 (2.72, 4.68)	< 0.0001	2.80 (2.12, 3.71)	< 0.0001	2.51 (1.89, 3.33)	< 0.0001
Q4	6.32 (4.87, 8.21)	< 0.0001	4.50 (3.44, 5.89)	< 0.0001	3.63 (2.75, 4.79)	< 0.0001
P for trend	< 0.0001		< 0.0001		< 0.0001	

The relative fat mass was converted from a continuous variable into a categorical variable (quartiles)

Model 1 = no covariate was adjusted

Model 2 = Model 1 + age, gender, and race were adjusted

Model 3 = Model 2 + education level, PIR, marital status, alcohol consumption, smoking status, hypertension, diabetes, asthma, cancer, cholesterol, total energy, total fat, total sugar, and total water

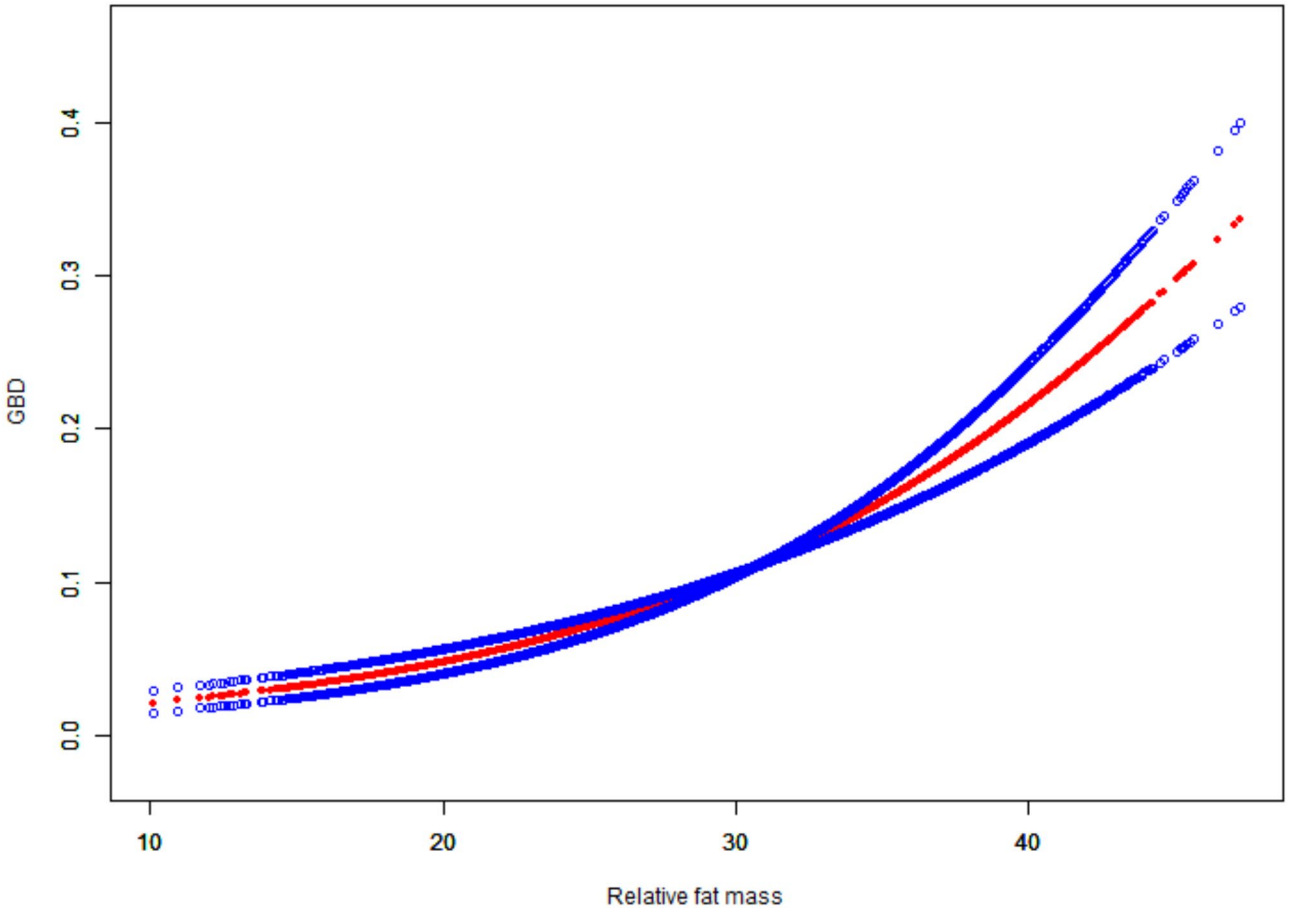

Fig. 2 Smoothing curve fitting between relative fat mass and GBD prevalence. Adjusted for all covariates include gender, age, ethnicity, education status, poverty income ratio (PIR), marital status, alcohol intake, smoking status, hypertension, diabetes, asthma, cancer, cholesterol, total energy, total fat, total sugar, and total water

explored the relationship between gallstones and various obesity indicators. It has been established that BMI significantly increases the risk of gallstone formation, with the likelihood being twice as high in individuals classified as overweight or obese [33, 34]. A Mendelian randomization analysis conducted by Zhu further supported the results, showing that larger waist circumference is linked to an elevated risk of gallstone formation [35]. Additionally, the waist-to-height ratio, a dependable indicator of central obesity, has been identified in studies from Taiwan and Iran as the primary risk factor for gallstones in women [36, 37].

Table 3 Two-piecewise linear regression and logarithmic likelihood ratio test explained the threshold effect analysis of relative fat mass with gallstones prevalence

RFM	ULR Test	PLR Test	LRT test
	OR (95%CI)	OR (95%CI)	P value
< 19.8	1.09 (1.07, 1.11)	2.44 (0.75, 7.92)	0.04
≥ 19.8		1.08 (1.07, 1.10)	

ULR, univariate linear regression; PLR, piecewise linear regression; LRT, logarithmic likelihood ratio test, statistically significant: $p < 0.05$

Table 4 Comparison of ROC curves for RFM and BMI in predicting gallstones

Test	AUC (95% CI)	Cutoff	Sensitivity	Specificity
RFM	0.674(0.656,0.692)	31.79	0.69	0.57
BMI	0.634(0.615,0.653)	27.75	0.75	0.44

While BMI is widely employed to define obesity, it does not provide an accurate representation of body fat percentage. For example, a BMI greater than 30 may fail to identify approximately 50% of females who have a body fat percentage classified as obese [38]. As obesity arises from an accumulation of excess body fat, and fat accumulation plays a key role in the onset of certain diseases [39, 40], it is crucial to use a reliable measure that accurately reflects this condition. Studies have demonstrated that RFM leads to fewer misclassifications of obesity compared to Body Mass Index (BMI). Furthermore, RFM has proven effective in predicting obesity-related disorders, including type 2 diabetes and heart failure [23, 29, 30]. RFM has also proven effective in estimating total body fat percentage, a finding supported by validation through dual-energy X-ray absorptiometry [23, 41]. In a prospective study involving 26,754 participants, Wang observed that higher RFM value related to abnormal metabolic markers, increased cardiovascular risk factors, and a higher incidence of cerebrovascular disease [42]. In a study involving 95,003 participants, Zwartkruis et al. identified a strong association between RFM and conditions such as coronary artery disease, heart failure, and atrial fibrillation [43]. Their team suggested that RFM might function as a simple yet reliable indicator for assessing both obesity and cardiovascular risk within the broader population. Although Li et al. found that cardiometabolic index was also a good predictor of gallstones [44], there was no significant correlation between cardiometabolic index and gallstones in the fully adjusted model, and the quantity of participants was small.

Obesity increases the possibility of developing gallstones through a variety of pathophysiological mechanisms. Several factors may explain how excess body weight contributes to a higher incidence of gallstones.

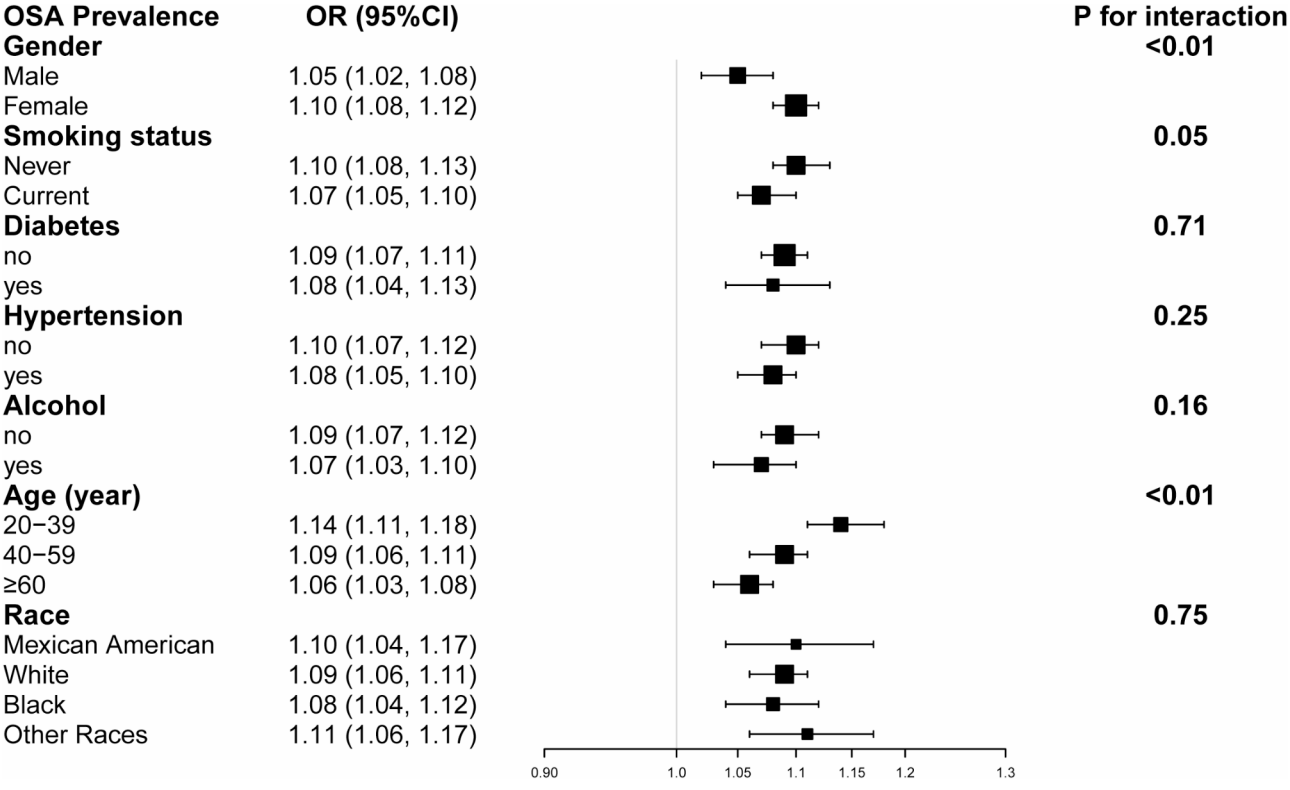

Fig. 3 Subgroup analysis for the association between relative fat mass and OSA. Models were adjusted for age (years), sex, race/ethnicity (Mexican American, White, Black, Other Race), educational level (less than high school, high school, above high school), marital status, smoking status (current or never), drinking status (yes, or no), PIR, diabetes (yes or no), hypertension (yes or no), asthma, cancer, cholesterol, total energy, total fat, total sugar, and total water

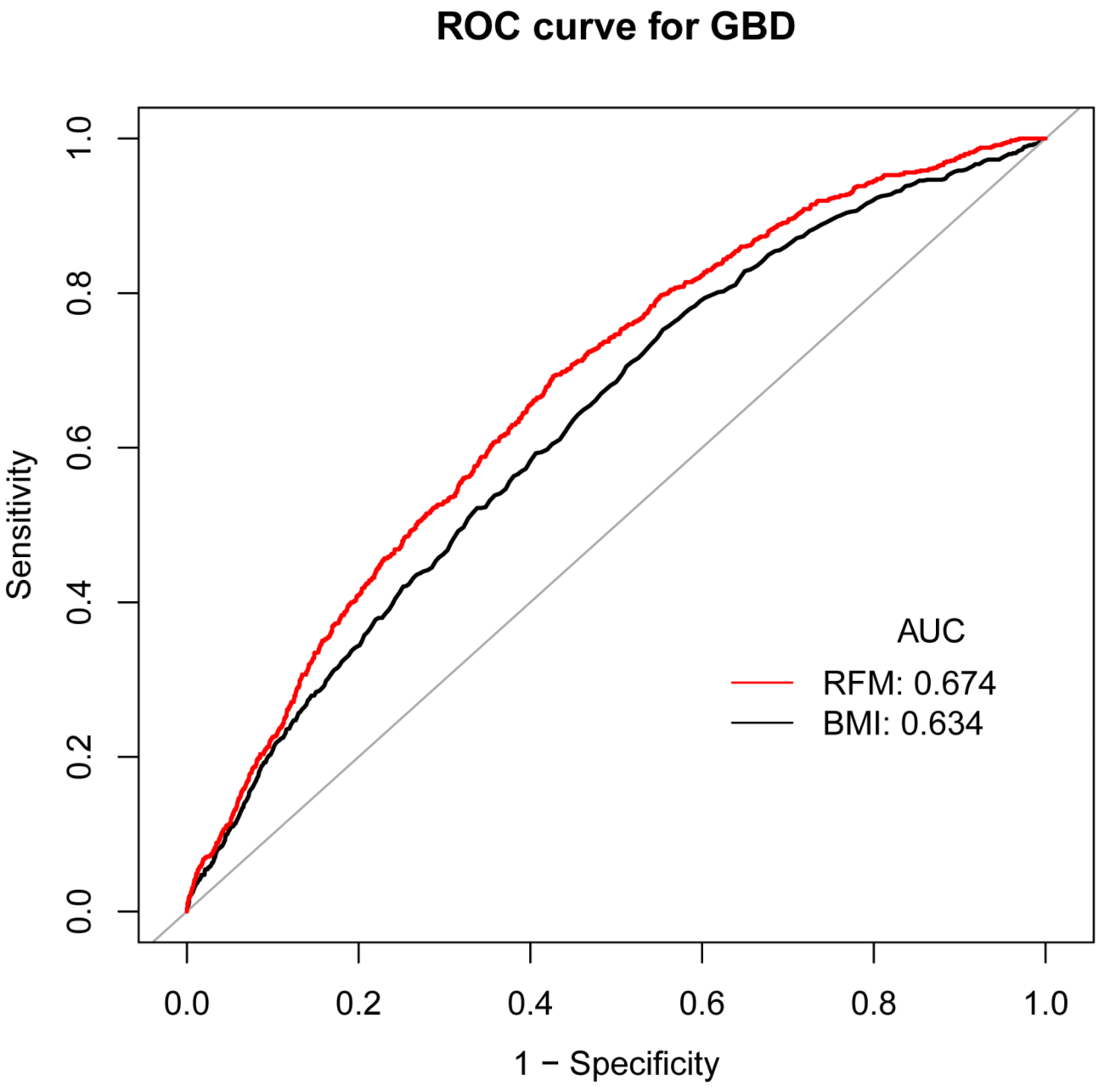

Fig. 4 ROC curves for RFM and BMI prediction of gallstones

First, a key mechanism is that obesity exacerbates insulin resistance, which in turn triggers metabolic disturbances that increase the risk of gallstone development [45]. Research conducted within a high-risk Hispanic population revealed that insulin resistance disrupts gallbladder function by stimulating the production of cholesterol-rich bile, thereby facilitating gallstone formation [46]. This mechanism may be linked to an elevated expression of biliary cholesterol transporters, a process potentially driven by the disinhibition of the forkhead transcription factor FoxO1 [47]. Another potential mechanism involves hepatic insulin resistance, which reduces the expression of enzymes responsible for bile acid synthesis, leading to the production of a bile salt profile that is more prone to forming gallstones [48]. Second, in individuals with obesity, due to the increased activity of 3-hydroxy-3-methylglutaryl-CoA reductase, it catalyzes the conversion of HMG-CoA into mevalonate, promoting cholesterol generation and forming crystallization, which further promotes the development of cholesterol gallstones [49]. Third, leptin, a hormone critical to obesity development, has been associated with cholelithiasis formation through its impact on bile acid metabolism [50]. This hormone plays a role in modulating obesity and also

regulates genes within the gallbladder that are associated with the pathogenesis of cholesterol gallstones [51]. Moreover, the rapid weight loss that often follows metabolic bariatric surgery, which has become more common in recent years, can contribute to the long-term development of gallstones. This occurs as a result of cholesterol supersaturation and decreased gallbladder motility [52]. Other studies have shown that changes in the composition of the gut microbiota may also affect lipid metabolism, inflammation, and bile acid production, all of which can contribute to gallstone formation [53–55].

In line with previous research, it has been shown that the effects of obesity and metabolic syndrome on gallstone development are more significant in younger populations [56]. This age group tends to have dietary patterns that are high in calories, cholesterol, and fat, while often lacking sufficient dietary fiber. Additionally, the increasing prevalence of obesity in this population is associated with disruptions in lipid metabolism, further elevating gallstone development [56–58]. According to our findings, the relationship between RFM and gallstones was also more significant in women. This may be attributed to the fact that men generally have lower body fat compared to women, and male RFM has a stronger influence on lipid metabolism [26]. And the increased susceptibility in women may also be related to hormonal differences. Elevated estrogen levels in women, especially during certain life stages, such as pregnancy or after menopause, can cause changes in lipid metabolism. These hormone fluctuations often lead to increased cholesterol saturation in the bile, which is a key precursor to the formation of gallstones. Therefore, this physiological process driven by estrogen may influence the increased incidence of gallstones in women [59]. In clinical practice, we recommend further ultrasonography or other gallstone screening in high-risk groups with RFM greater than 19.8, especially young people and women. We can integrate RFM thresholds into existing health risk assessment tools to automatically calculate RFM and prompt physicians to focus on high-risk individuals. For high-risk individuals, clinicians can recommend lifestyle interventions such as reducing belly fat, improving diet, and increasing exercise to reduce gallstone risk.

The research conducted offers several strengths. Initially, the NHANES study cohort comprised a representative selection of individuals from America who adhered rigorously to a meticulously designed research protocol, incorporating robust quality assurance and quality control measures to ensure the dependability of the findings. Additionally, adjustments were made for potential confounding variables, and subgroup analyses were conducted to enhance the credibility of the outcomes and their generalizability to a wider population. Nonetheless, the study is not without its limitations. Notably, its design was cross-sectional, excluding a causal relationship between RFM and gallstones. Furthermore, the diagnosis of gallstones relied on self-reported information; recall bias may result. Owing to constraints within the database, not all covariates could be included, such as drug use, family history of gallstones and other genetic factors. Despite these constraints, the study investigates the first exploration of the relationship between RFM and gallstones, offering preliminary evidence supporting RFM as a potential predictor of gallstone development. In resource-limited Settings, RFM can be used as an auxiliary tool to help physicians more accurately identify high-risk individuals.

Conclusion

In conclusion, we discovered that higher RFM was associated with an increased gallstones prevalence, and this connection was more significant among younger adults and females. Furthermore, RFM demonstrates superior predictive accuracy for gallstones when compared to BMI. However, additional studies are required to shed light on the causality of this connection.

Abbreviations

RFM	Relative fat mass
NHANES	National Health and Nutrition Examination Survey
SD	Standard deviations
CDC	Centers for Disease Control and Prevention
ROC	Receiver operating curve
WC	Waist circumference
PIR	Poverty income ratio
AUC	Area under the curve
BMI	Body mass index
GSD	Gallstone disease
NCHS	National Center for Health Statistics

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Author contributions

Xie S and Li D designed the research. Xie S, Li d, Fang L, and Chen X collected, analyzed the data, and drafted the manuscript. Xie S, Ma S, and Li D revised the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability

The survey data are publicly available on the internet for data users and researchers throughout the world (www.cdc.gov/nchs/nhanes/).

Declarations

Ethical approval and consent to participate

The portions of this study involving human participants, human materials, or human data were conducted in accordance with the Declaration of Helsinki and were approved by the NCHS Ethics Review Board. The patients/participants provided their written informed consent to participate in this study.

Consent for publication

Not applicable.

Competing interests
The authors declare no competing interests.

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