BMC Public Health

RESEARCH

Open Access

Positive association between cardiometabolic index and gallstones, with greater impact on women and those younger than 50 years: the NHANES 2017–2020 cross-sectional study

Jing Zheng[1†], Huqiang Dong[2†], Hongli Wan[3], Qingye Yang[1], Shujuan Xu[4], Tingting Hu[1], Chang Fu[5*] and Keyun Cheng[1*]

Abstract

Background Gallstones are a common hepatobiliary disorder. It is unclear whether cardiometabolic index (CMI) is associated with gallstones. The purpose of this study was to examine the association between CMI levels and gallstone prevalence among US adults.

Methods We investigated data from 3711 participants aged 20 years or older in the 2017–2020 National Health and Nutrition Examination Survey (NHANES). Confounder adjustment, multivariate logistic regression modeling, and restricted cubic spline (RCS) analyses were used to assess the association between CMI and gallstone prevalence, and threshold effect analyses were performed. We conducted subgroup analyses to evaluate the impact of confounding variables, including age and gender. A sensitivity analysis was also performed to increase the robustness of the results.

Results The weighted prevalence of gallstones in this study was 11.04%. The risk of gallstones increased significantly with higher CMI quartiles. Logistic regression analysis showed that there was a significant positive correlation between CMI and the risk of gallstones, with a 5% increase in the risk of gallstones for each one-unit increase in CMI (OR = 1.05). In the adjusted model, the positive correlation between CMI and the risk of gallstones remained significant. RCS analysis showed a nonlinear relationship between CMI and gallstones, with an inflection point of 0.69. Subgroup analyses showed that elevated CMI was significantly associated with the risk of gallstones in females and in the 20–50 year old population.

Conclusion As the first study to show a significant association between CMI and the occurrence of gallstones in an adult population in the United States. However, further longitudinal studies are needed to verify this association.

†Jing Zheng and Huqiang Dong contributed equally to this work and share first authorship.

*Correspondence:
Chang Fu
fuchang23@mails.jlu.edu.cn
Keyun Cheng
cky802299@126.com

Full list of author information is available at the end of the article

Keywords Gallstones, Cardiometabolic index, NHANES, Cross-sectional study, HDL-C

Background

Gallstones are one of the most common hepatobiliary disorder worldwide, formed by the accumulation of deposits, such as minerals, in the gallbladder or common bile duct, and can cause symptoms such as nausea, vomiting, and abdominal discomfort [1]. Epidemiologic studies have shown that approximately one in ten people worldwide have gallstones [2, 3], with prevalence varying by region and placing a heavy burden on the healthcare system [4]. The formation of gallstones is influenced by a number of factors, including gender, age, environment, and genetics [5–8]. In recent years, the increase in high-fat and high-salt diets and the rise in obesity rates have led to a continuous rise in the incidence of gallstones [9–11]. At the same time, obesity-induced metabolic disorders, such as increased cholesterol synthesis and abnormal bile secretion, significantly increase the risk of gallstones [12, 13]. Therefore, abnormal lipid metabolism, visceral fat accumulation, and insulin resistance are considered important causative factors for gallstones [14, 15].

The cardiometabolic index (CMI) is a new body fat index that combines obesity and lipid metabolism metrics to assess the distribution and functional abnormalities of visceral fat [16]. Compared with traditional obesity indicators, CMI provides a more comprehensive picture of an individual's metabolic health through waist-to-height ratio (WHTR) and triglyceride/high-density lipoprotein cholesterol ratio (TG/HDL-C) [17]. Studies have shown that CMI is superior to BMI and single lipid indices in predicting diseases such as metabolic syndrome, kidney stones, insulin resistance and atherosclerosis [18–20]. Moreover, it has higher clinical value in the prediction of depression, chronic obstructive pulmonary disease (COPD), diabetes mellitus, osteoporosis and depression [21–24]. Therefore, CMI may be more suitable for assessing the risk of gallstones than traditional indicators of obesity or lipids [25, 26].

There are still few studies on the association between CMI and gallstones. Exploring the relationship between CMI and gallstones is important to clarify its influence on gallstone occurrence. Therefore, this study focused on the correlation between CMI and gallstones using NHANES data to reveal the potential role of lipid metabolism in gallstone formation.

Materials and methods

Study population

Data from the National Health and Nutrition Examination Survey (NHANES) served as the foundation for this investigation, which included 3,711 participants between 2017 and 2020. NHANES is a national study designed to assess the health and nutritional status of adults and children in the U.S. Using a complex multi-stage stratified probability design to ensure representativeness, the survey has been conducted biennially since 1999 and examines associations between environmental factors, lifestyle, nutrition, and health. The National Center for Health Statistics' Ethical Review Committee authorized the study methodology (#2018-01), and each participant completed an informed consent form. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies.

This study focused on data from patients with gallstones from the NHANES survey during 2017–2020. Of the initial 15,560 participants, individuals under 20 years of age, individuals with missing gallstone data, individuals with missing CMI data, and individuals with missing covariates were excluded, and a total of 3,711 participants ultimately met the study criteria. In addition, participants who had undergone gallbladder surgery were not excluded from our analyses because we were unable to obtain a clear understanding of the chronology between the occurrence of gallbladder surgery and the diagnosis of gallstones. (Fig. 1)

Definition of CMI

The cardiometabolic index (CMI) is calculated based on waist circumference (WC), height, high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG). Height and waist circumference are both expressed in cm, whereas TG and HDL-C are expressed in mg/dL [16, 17]. The calculation formula is as follows.

$$WHtR = \frac{WC}{height}$$
$$CMI = \frac{TG}{HDL-C} \times WHtR$$

Definition of gallstones

The "MCQ" section of the NHANES questionnaire: "Has your doctor ever told you that you have gallstones?" was used as the basis for the diagnosis of gallstones. If respondents answered "yes," they were considered to have gallstones [27, 28].

Covariates

Covariate selection was based on previous studies and the Directed acyclic graph (DAG) (Figure S1), adjusting for variables that were potentially confounding for exposure-outcome. Age, gender, race, education level, marital status, PIR, smoking status, alcohol, diabetes, hypertension,

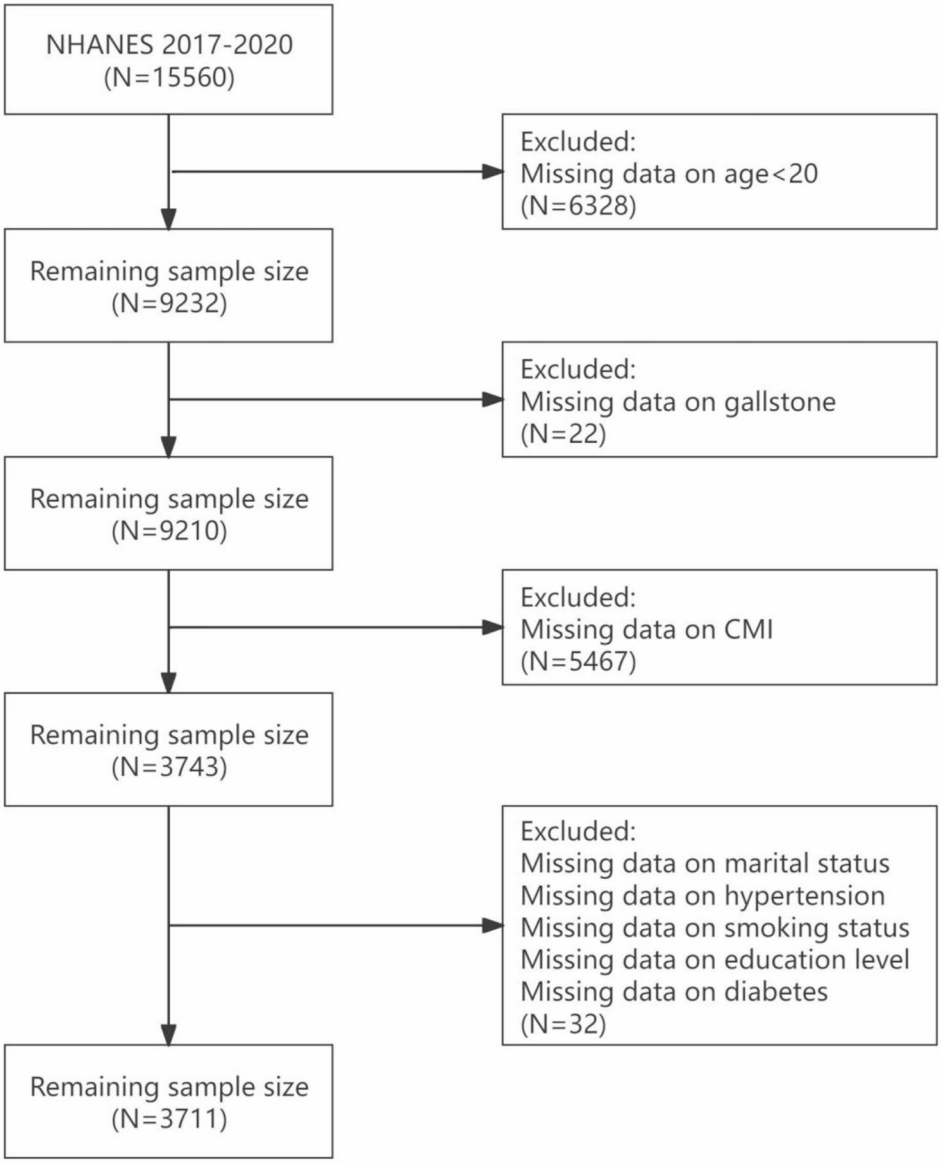

Fig. 1 NHANES 2017–2020 participant selection flowchart

HEI-2020, and physical activity were used as influential factors in this study. Diabetes mellitus was defined based on any of the following criteria: (1) fasting blood glucose (FBG) ≥ 126 mg/dL, (2) a previous physician diagnosis of diabetes, (3) current use of insulin or other antidiabetic medications. Hypertension was defined as a previous diagnosis, current use of antihypertensive medications, or a blood pressure reading ≥ for 140/90 mm Hg. Participants were categorized into three classes, based on standardized scores from the International Physical Activity Questionnaire (IPAQ). low (< 600MET min/week), moderate (300–3000 MET min/week), High (≥ 3000 MET min/week) [29]. The HEI-2020 (Healthy Eating Index-2020), developed by the U.S. Department of Agriculture (USDA), is a scoring system used to assess dietary quality and measure how well an individual's dietary patterns conform to the 2020–2025 U.S. Dietary Guidelines. The index consists of 13 components, of which 9 sufficiency components (e.g., fruits, vegetables, whole grains, protein, etc.) are encouraged to be consumed at higher levels, while 4 moderation components (e.g., refined grains, sodium, added sugars, saturated fats) should be reduced in moderation. Data collection was done by trained interviewers who recorded the food and beverage intake of the respondents and calculated the total HEI-2020 score and its component scores. This indicator has been widely used in nutritional epidemiologic studies to quantify overall dietary quality [30]. We consulted earlier research for comprehensive details on these factors in order to make our technique more transparent [27].

Measurements of all study variables can be accessed on the NHANES website. (www.cdc.gov/nchs/nhanes/).

Statistical analyses

In this study, all statistical analyses were conducted according to CDC guidelines. We used sample weights in our analyses to account for the complex multi-stage probabilistic sampling design of NHANES to improve the representativeness and statistical efficacy of the estimates. The study used Mean ± SD for continuous variables and percentages for categorical factors to investigate the association between CMI and gallstone prevalence in the U.S. population. To examine the connection between gallstone prevalence and CMI, we employed three regression models. Of the three logistic regression models we used, one was unadjusted Model 1. Model 2 was adjusted for race, gender, and age. Age, gender, race, education level, marital status, PIR, smoking status, alcohol, diabetes, hypertension, HEI-2020, and physical activity were taken into account when adjusting for model 3. Logistic regression analyses were performed using CMI as a continuous and categorical variable to analyze the relationship between CMI and gallstone, and trends were estimated by including continuous variables, quartiles. To further minimize the impact of possible anomalously high values on the model, we attempted to re-model the CMI after Ln transformation to enhance the stability of the study results (Table S2). BMI was adjusted on Model 3 in the sensitivity analysis to enhance the robustness of the conclusions (Table S3).

Following covariate adjustment in Model 3, the dose-response association between gallstones and CMI number was shown using restricted cubic spline (RCS). When a nonlinear link was found, a threshold effect was calculated, and a log-likelihood ratio test was used to compare the two-stage linear regression model with a single linear model. We then used subgroup analyses and interaction tests to assess possible confounders mentioned in the baseline table. Data were analyzed with the use of the statistical packages R (The R Foundation; http://www.r-project.org; version 4.4.2) and EmpowerStats (www.empowerstats.net, X&Y Solutions, Inc., Boston, Massachusetts). The significance threshold was $P < 0.05$.

Results

Baseline characteristics of the study population

Table 1 shows the weighted baseline characteristics of the 3,711 participants in this study. The weighted mean age of the participants was 47.89 years, with 49.29% males and 50.71% females. Participants in the highest CMI quartile (Q4) group had a higher proportion of males, were older, had a higher proportion of obesity, and had larger waist circumferences compared to the lowest CMI quartile (Q1). In addition, the high CMI group had a higher prevalence of hypertension and diabetes and lower levels of education. In addition, the highest CMI quartile group had a higher proportion of low physical activity levels compared to the lowest CMI group, and there were some differences in smoking and drinking behaviors. Notably, CMI levels were positively associated with gallstone prevalence, with the highest prevalence of gallstones in the highest CMI quartile group ($P < 0.001$). (Table 1)

Association between cardiometabolic index and gallstones

Multiple logistic regression analysis showed that CMI was significantly and positively associated with the prevalence of gallstones (Table 2). In the unadjusted model, the risk of gallstones prevalence increased by 5% per unit increase in CMI (OR = 1.05, 95% CI: 1.01, 1.09). In Models 2 and 3, which adjusted for potential confounders, this correlation remained significant, with a 6% (OR = 1.06, 95% CI: 1.02, 1.11) and 5% (OR = 1.05, 95% CI: 1.01, 1.09) increase in the risk of gallstone prevalence for each unit increase in CMI, respectively. In the CMI quartile groupings, the risk of gallstones was significantly increased in the highest quartile group (Q4) compared with the lowest quartile group (Q1). Moreover, the *p*-value of the test for trend showed statistical significance in all models (p for trend < 0.0001), suggesting a progressive increase in the risk of gallstones with increasing CMI levels.

Nonlinear analysis of CMI and gallstones

Because Model 3 adjusts for all covariates in multiple regression models, it is able to provide estimates that are relatively more stable and closer to the true effect. Therefore, we used RCS analysis based on this model to explore whether there was a nonlinear relationship between CMI and gallstones. The findings, which are displayed in Fig. 2, demonstrate that there is a nonlinear relationship between CMI and gallstones. The *P* value for nonlinearity was $P < 0.001$. After multivariate adjustment, the inflection point of the association between CMI and gallstones was found to be 0.69. (Table 3)

Subgroup analysis

To assess the robustness of the correlation between CMI and gallstone prevalence, subgroup analysis was performed. The results showed that in the age subgroup, elevated CMI was associated with a higher prevalence of gallstones in people aged 20–50 years, and in the gender subgroup, elevated CMI was associated with a higher prevalence of gallstones in women. (Fig. 3)

Sensitivity analysis

Given that BMI may serve as a factor in gallstone risk, we adjusted for BMI as a covariate in our multiple logistic regression model and found that the association of CMI as a continuous variable was weakened, but its

Table 1 Baseline characteristics of the study population based on CMI quartiles

Characteristics	Total ($n=3711$)	CMI quartile				*P* value
		Q1 (0.06–0.58) $n=928$	Q2 (0.58–1.06) $n=927$	Q3 (1.06–1.86) $n=928$	Q4 (1.86–56.08) $n=928$	
Age (years)	47.89 ± 17.09	43.37 ± 17.75	48.87 ± 17.26	49.97 ± 16.72	49.76 ± 15.66	< 0.001
Gender (%)						< 0.001
Male	49.29	41.76	46.56	47.67	61.01	
Female	50.71	58.24	53.44	52.33	38.99	
Race (%)						< 0.001
Mexican American	8.94	5.73	8.29	10.27	11.70	
Other Hispanic	6.78	4.91	7.00	8.64	6.87	
Non-Hispanic White	63.25	64.85	63.37	56.90	67.02	
Non-Hispanic Black	10.76	14.70	12.59	11.31	4.52	
Other Race	10.26	9.82	8.75	12.88	9.89	
Education level (%)						< 0.001
Less than high school	10.92	6.71	9.42	13.68	14.27	
High school	26.19	23.83	26.11	25.56	29.22	
More than high school	62.89	69.45	64.47	60.76	56.51	
Marital status (%)						< 0.001
Never married	19.15	27.02	17.29	15.95	15.67	
Married/Living with partner	61.94	56.49	60.22	65.48	66.09	
Widowed/divorced/Separated	18.91	16.49	22.49	18.58	18.24	
PIR (%)						< 0.001
<1.3	19.36	15.90	18.53	21.24	22.05	
1.3–3.5	35.33	31.94	36.06	35.92	37.59	
≥3.5	45.31	52.17	45.40	42.85	40.36	
BMI (%)						< 0.001
<25	27.11	58.80	26.76	13.26	7.06	
25–30	32.68	29.14	38.82	35.76	27.75	
≥30	40.22	12.06	34.42	50.99	65.19	
Ever had a drink (%)						0.123
Yes	93.72	95.05	92.52	94.06	93.22	
No	6.28	4.95	7.48	5.94	6.78	
Hypertension (%)						< 0.001
Yes	31.81	18.38	28.86	39.56	41.63	
No	68.19	81.62	71.14	60.44	58.37	
Diabetes (%)						< 0.001
Yes	11.58	2.81	7.36	13.62	22.82	
No	88.42	97.19	92.64	86.38	77.18	
Smoke at least 100 cigarettes per year (%)						< 0.001
Yes	43.71	40.55	40.31	42.67	51.09	
No	56.29	59.45	59.69	57.33	48.91	
Physical activity (MET min/week) (%)						< 0.001
Low	30.48	20.45	30.31	37.79	34.54	
Moderate	31.43	32.44	32.31	28.74	31.87	
High	38.10	47.11	37.37	33.47	33.59	
Gallstones (%)						< 0.001
Yes	11.04	6.58	11.29	11.75	14.75	
No	88.96	93.42	88.71	88.25	85.25	
Height (cm)	168.34 ± 9.90	167.71 ± 9.74	168.84 ± 10.06	167.36 ± 9.72	169.38 ± 9.92	< 0.001
Waist circumference (cm)	100.30 ± 16.96	87.08 ± 11.91	98.75 ± 14.32	104.47 ± 14.77	111.68 ± 15.82	< 0.001
TG (mg/dL)	111.09 ± 91.47	50.13 ± 14.98	78.71 ± 18.81	111.82 ± 26.03	203.73 ± 132.83	< 0.001
HDL-C (mg/dL)	54.05 ± 15.90	50.13 ± 14.98	78.71 ± 18.81	111.82 ± 26.03	203.73 ± 132.83	< 0.001
WHTR	0.60 ± 0.10	0.52 ± 0.07	0.59 ± 0.09	0.63 ± 0.09	0.66 ± 0.10	< 0.001

Table 1 (continued)

Characteristics	Total ($n=3711$)	CMI quartile				*P* value
		Q1 (0.06–0.58) $n=928$	Q2 (0.58–1.06) $n=927$	Q3 (1.06–1.86) $n=928$	Q4 (1.86–56.08) $n=928$	
HEI-2020	50.07 ± 12.21	51.71 ± 12.41	50.13 ± 12.16	48.69 ± 12.06	49.55 ± 12.00	< 0.001
CMI	1.52 ± 1.93	0.39 ± 0.12	0.82 ± 0.14	1.41 ± 0.22	3.44 ± 2.97	< 0.001

Mean ± SD for continuous variables: the *P* value was calculated by the weighted linear regression model. (%) for categorical variables: the *P* value was calculated by the chi-square test. Abbreviations: PIR, the ratio of income to poverty; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; CMI, cardiometabolic index; WHTR, waist-to-height ratio; HEI-2020, Healthy Eating Index 2020

Table 2 Multiple logistic regression analysis of the association between CMI and gallstones

Characteristic	Model 1		Model 2		Model 3	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
CMI	1.05 (1.01, 1.09)	0.0071	1.06 (1.02, 1.11)	0.0020	1.05 (1.01, 1.09)	0.0316
CMI quartile						
Q1	reference		reference		reference	
Q2	2.14 (1.50, 3.07)	< 0.0001	2.02 (1.40, 2.92)	0.0002	1.91 (1.32, 2.77)	0.0006
Q3	2.52 (1.77, 3.58)	< 0.0001	2.29 (1.60, 3.28)	< 0.0001	2.01 (1.39, 2.91)	0.0002
Q4	3.15 (2.23, 4.44)	< 0.0001	3.05 (2.13, 4.36)	< 0.0001	2.55 (1.76, 3.69)	< 0.0001
P for trend		< 0.0001		< 0.0001		< 0.0001

Model 1: No covariates were adjusted

Model 2: Age, gender and race were adjusted

Model 3: Age, gender, race, education level, marital status, PIR, smoking status, alcohol, diabetes, hypertension, HEI-2020, and physical activity were adjusted

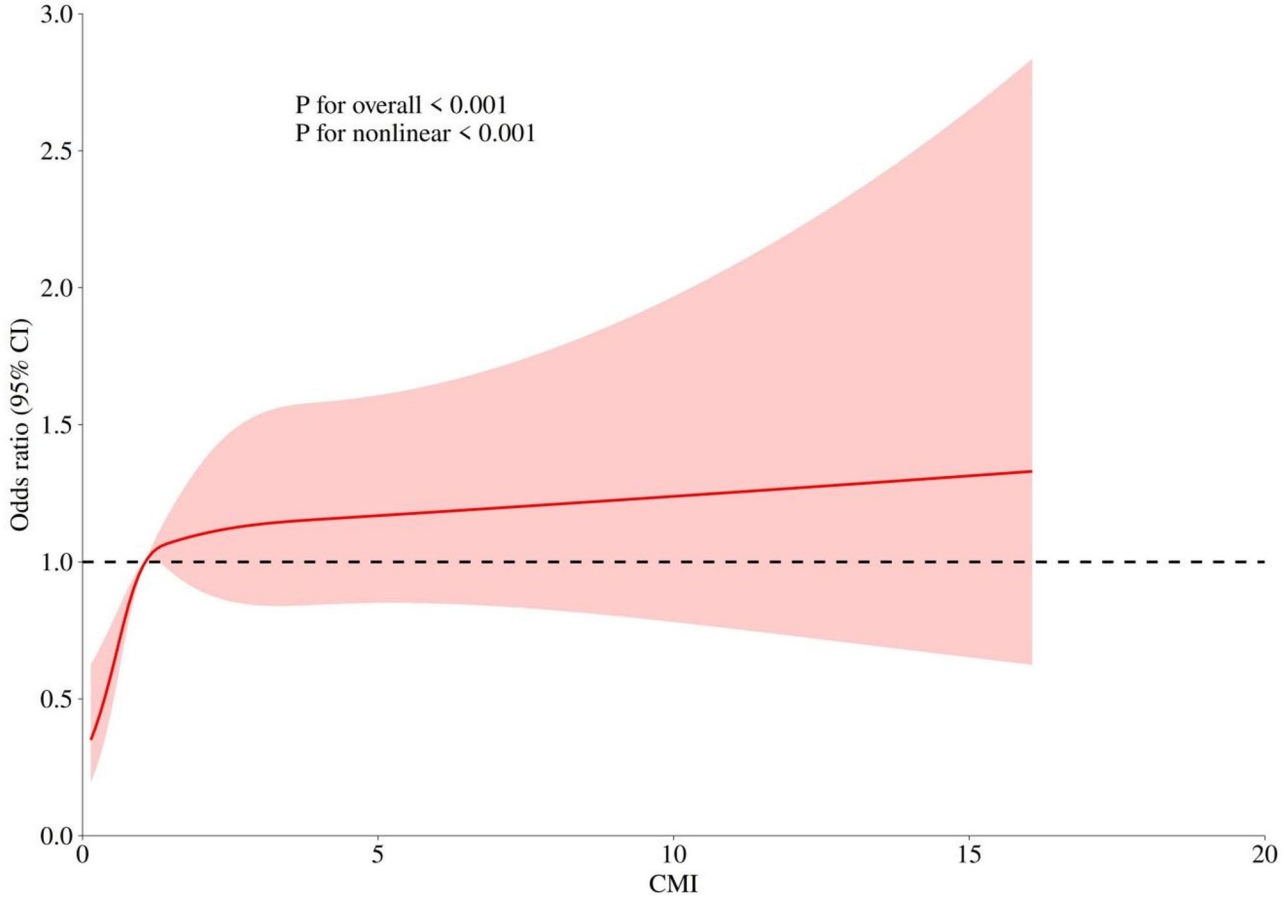

Fig. 2 The RCS curve shows how each research participant's CMI and odds ratio for gallstones relate to one another. RCS, restricted cubic spline; CMI, cardiometabolic index. 95% CI, 95% confidence interval

Table 3 Threshold effect analysis of CMI on gallstones using the two-piecewise regression model

Outcome: Gallstones	Adjusted OR (95% CI)	*P*-value
Inflection point	0.69	
<0.69	10.76 (3.57, 32.41)	< 0.0001
>0.69	1.02 (0.98, 1.07)	0.2932
Log likelihood ratio test		< 0.001

The results of subgroup analysis were adjusted for all covariates as model 3

CMI, cardiometabolic index; OR, odds ratio, 95% CI, 95% confidence interval

interquartile grouping remained significant (Table S3), and exploratory mediation analyses were performed (Table S4).

Discussion

This study systematically assessed the association between cardiometabolic index (CMI) and gallstone prevalence based on a cross-sectional survey of 3711 US adults. The results indicate a nonlinear relationship between higher gallstone prevalence and increasing CMI, and this association remains robust even in fully adjusted models. In addition, the reliability of the findings was further validated by subgroup analyses and restricted triple spline. Subgroup analyses showed that this association was particularly significant in the 20–50 age group and in women. Interventions that target CMI may help lower the risk of gallstones, according to the study's findings.

CMI, mentioned by Wakabayashi et al., is a novel anthropometric measure commonly used to identify risks associated with metabolic diseases [31]. Research has indicated a strong correlation between CMI and both hyperglycemia and diabetes mellitus, as well as showing promising prediction capabilities across various demographics [24]. CMI has also been shown to be an independent risk factor for proteinuria and renal insufficiency, suggesting its potential in early screening for kidney disease [32]. CMI has significant advantages over traditional indicators in the detection and risk assessment of metabolic diseases. The present study was the first to investigate the relationship between CMI and the prevalence of gallstones, and it demonstrated a significant correlation between a higher CMI and a higher incidence of gallstones.

Previous studies have indicated that both gender and age are significant factors in gallstone formation [33, 34]. Our study similarly found a higher prevalence of gallstones among younger individuals and women, which aligns with the findings of Jiang et al. [35]. The increased risk in women is largely attributed to estrogen, which promotes hepatic cholesterol uptake and biliary secretion, leading to bile supersaturation—a key factor in cholesterol gallstone formation [36, 37]. In addition, high CMI in younger people is more often a reflection of visceral fat accumulation and severe metabolic disturbances, which are strongly associated with gallstone formation [38]. Unlike older adults, young people may not yet have other significant health problems, so the impact of CMI on gallstone formation is more prominent at this stage. High CMI in younger people may also be strongly associated with unhealthy lifestyles such as high-fat diets and physical inactivity [39]. In addition, older adults usually have multiple underlying diseases, such as atherosclerosis [40]. These factors may interact with the effects of CMI, resulting in a dilution of the effects of CMI when analyzed separately.

The particular processes behind the link between metabolic risk and gallstones are not entirely known. First, Chen et al.'s study found a strong correlation between gallstone incidence and alterations in gut microbiota [41]. By altering the mix of bile acids and the release of bile cholesterol, the intestinal microbiota can encourage the development of gallstones, according to a research by Hu et al. [42]. Trimethylamine (TMA), a substance produced by intestinal flora, is oxidized in the liver by flavin monooxygenase 3 to produce N-trimethylamine oxide (TMAO) [43, 44]. TMAO, by regulating lipid metabolism, may contribute to the development of several cardiovascular diseases, including atherosclerosis [45]. TMAO in plasma enhances cholesterol secretion to bile and hepatic cholesterol uptake by upregulating hepatic ABCG5/G8 and SRB1 gene expression [41]. Excess cholesterol secretion leads to oversaturation of cholesterol in bile, which is a prerequisite for gallstone formation [46]. Secondly, hepatic-specific insulin receptor deficiency can lead to increased cholesterol secretion in bile along with reduced bile acid synthesis, resulting in the production of gallstone-prone struvite bile, i.e., bile containing a higher cholesterol concentration, which is prone to the formation of gallstones [47]. Systemic and hepatic insulin resistance not only leads to abnormal bile composition, but also affects gallbladder function, including a decrease in gallbladder contractility [48]. These changes further promote gallstone formation. In addition, inflammation is closely associated with gallstone formation, as well as a higher risk of gallstones linked to elevated levels of circulating inflammatory proteins and cytokines [49]. These factors may induce an inflammatory response in the gallbladder epithelium, leading to epithelial damage and gallbladder wall fibrosis, which in turn reduces gallbladder contractility [35, 50]. At the same time, inflammation-induced dysfunction of gallbladder dynamics may interfere with normal gallbladder contraction and bile drainage, establishing ideal circumstances for cholesterol nucleation and gallstone development [35, 51].

In the present study, exploratory sensitivity informed that BMI mediated the association between CMI and gallstones. The possible mechanism is that since both CMI and BMI can reflect the fat distribution and

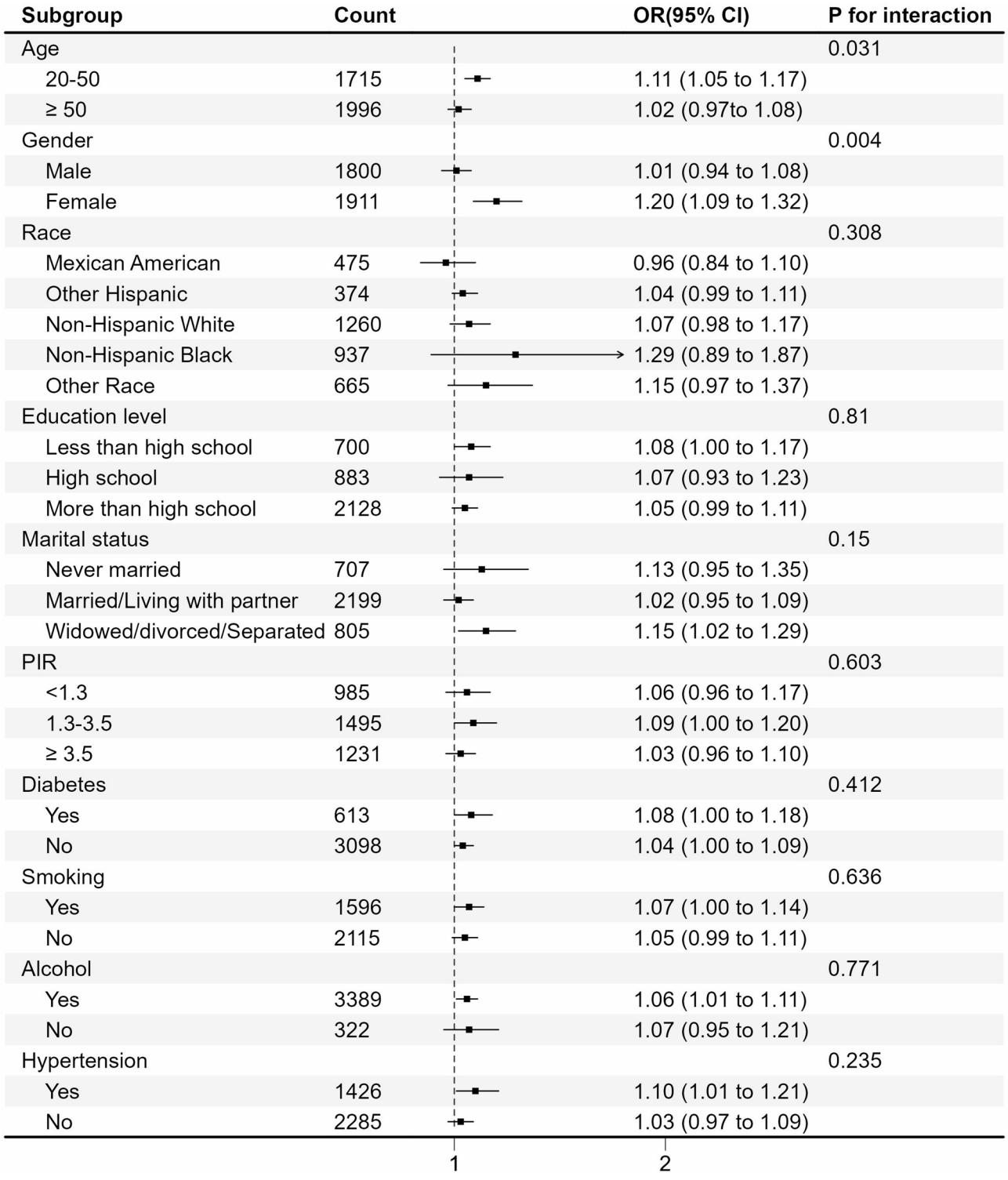

Fig. 3 Subgroup analysis of the association between CMI and gallstones. Note 1: Age, gender, race, education level, marital status, PIR, smoking status, alcohol, diabetes, hypertension, HEI-2020, and physical activity were all taken into account while adjusting the aforementioned model. Note 2: The model does not account for the stratification variable in any of these situations

metabolic status of an individual to a certain extent, they share physiological functional similarities in measuring the risk associated with metabolic syndrome [18, 52]. Increased BMI is an important indicator of visceral fat accumulation, which in turn may promote cholesterol metabolism disorders and thus increase the risk of gallstone formation [53–55]. In addition, obesity in particular leads to processes such as biliary cholesterol supersaturation, diminished gallbladder emptying, and enhanced inflammatory responses, all of which are key mechanisms for gallstone formation [34, 51, 56]. Therefore, BMI may play a partial mediating role in the effect of CMI on gallstone risk.

Strengths and limitations

The following is a summary of this study's strengths. First off, the association between the occurrence of gallstones and the CMI index has never been examined before, which provides a direction for future research. Second, this study is based on the NHANES database, which has a large and nationally representative sample size and provides reliable data support for the results. Third, this study corrected for a variety of potential confounders through extensive questionnaires and multivariate modeling to ensure the accuracy and credibility of the findings. Fourth, the measurement of CMI is simple, cost-effective, and has good clinical applicability, which facilitates the assessment and screening of gallstone-related diseases. This study validates the feasibility of CMI as a metabolic marker in the assessment of gallstone prevalence and lays the foundation for its application as a risk prediction tool in clinical practice.

However, there are several restrictions on the current study. First, the gallstone data used in this study did not distinguish between cholesterol stones and pigment stones, ignoring their different etiologic mechanisms. Diagnosis was mainly based on questionnaires rather than imaging, which might result in the omission of untreated cases and induce recollection bias. Second, the cross-sectional study design limited the ability to establish a causal relationship between CMI and gallstones, revealing only correlations. Third, gallstone judgments in this study were based on self-reported data and may have been affected by recall bias. Fourth, individuals who had undergone gallbladder surgery were not excluded because of the lack of a clear time frame to distinguish the sequence in which gallstone diagnosis and surgery occurred. Patients who have undergone cholecystectomy may no longer report having gallstones, possibly leading to an underestimation of the prevalence of gallstones. Fifth, although we adjusted for a variety of possible confounders in our model, there may still be unadjusted residual confounders that affect the accuracy of the study findings.

Conclusion

This study identified a significant association between higher CMI and increased gallstone prevalence, particularly in individuals younger than 50 years and in women. This finding suggests that CMI may be a valuable marker for assessing gallstone risk. However, as a cross-sectional study, this research does not establish causality, and further longitudinal studies are needed to validate this association.

Abbreviations

BMI	Body mass index
CMI	Cardiometabolic index
DAG	Directed acyclic graph
HDL-C	High-density lipoprotein cholesterol
HEI-2020	Healthy Eating Index 2020
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
PA	Physical activity
PIR	Poverty-to-income ratio
RCS	Restricted cubic spline
TG/HDL-C	Triglyceride to high-density lipoprotein-cholesterol
TG	Triglycerides
TMA	Trimethylamine
TMAO	N-trimethylamine oxide
WC	Circumference
WHTR	Waist-to-height ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-23323-w.

Supplementary Material 1

Acknowledgements

We would like to thank all participants in this study.

Author contributions

ZJ and DH designed the research. WH, YQ and XS collected and analyzed the data, and drafted the manuscript. FC and CK revised the manuscript. All authors contributed to the article and approved the submitted version.

Funding

This work did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

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

Ethics 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 National Center for Health Statistics (NCHS) Ethics Review Board (#2018-01). 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.

Author details
[1]Department of Cardiology, The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital, Quzhou 324000, Zhejiang, China
[2]School of Public Health, Ningxia Medical University, Yinchuan 750004, Ningxia, China
[3]Department of central laboratory, The First Affiliated Hospital of Northwest University, Xi'an No.1 Hospital, Xi'an 710002, Shaanxi, China
[4]Graduate School, China Academy of Chinese Medical Sciences, Beijing 100700, China
[5]Department of Hepatobiliary and Pancreatic Surgery, General Surgery Center, The First Hospital of Jilin University, Changchun 130021, Jilin, China

Received: 4 January 2025 / Accepted: 23 May 2025
Published online: 07 June 2025

References

1. Lammert F, Gurusamy K, Ko CW, et al. Gallstones[J]. Nat Reviews Disease Primers. 2016;2(1):1–17.
2. Zhang J, Liang D, Xu L et al. Associations between novel anthropometric indices and the prevalence of gallstones among 6,848 adults: a cross-sectional study[J]. Front Nutr. 2024;11.
3. Shaffer EA. Epidemiology of gallbladder stone disease[J]. Best Pract Res Clin Gastroenterol. 2006;20(6):981–96.
4. Li H, Zhang C. Association between triglyceride-glucose index and gallstones: a cross-sectional study[J]. Sci Rep. 2024;14(1):17778.
5. Cheng Q, Wang Z, Zhong H, et al. Association of non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) and gallstones among US adults aged ≤ 50 years: a cross-sectional study from NHANES 2017–2020[J]. Lipids Health Dis. 2024;23(1):265.
6. Everhart JE, Khare M, Hill M, et al. Prevalence and ethnic differences in gallbladder disease in the United States[J]. Gastroenterology. 1999;117(3):632–9.
7. Rebholz C, Krawczyk M, Lammert F. Genetics of gallstone disease[J]. Eur J Clin Invest. 2018;48(7):e12935.
8. Stokes CS, Krawczyk M, Lammert F. Gallstones: environment, lifestyle and genes[J]. Dig Dis (Basel Switzerland). 2011;29(2):191–201.
9. Zhang H, Xu C, Zhu X, et al. Associations between temporal eating patterns and energy distribution patterns with gallstones: a cross-sectional study based on NHANES 2017–2018[J]. BMC Public Health. 2024;24(1):2994.
10. Fu C, Li X, Wang Y, et al. Association between triglyceride glucose index-related indices with gallstone disease among US adults[J]. Lipids Health Dis. 2024;23(1):203.
11. Li H, Jiang G, Yu W, et al. Association between triglyceride-glucose index and risk of gallstone disease: a prospective cohort study of 395 391 individuals[J]. J Gastroenterol Hepatol. 2025;40(2):404–12.
12. Patel H, Jepsen J, Gallstone, Disease. Common questions and answers[J]. Am Family Phys. 2024;109(6):518–24.
13. Simonsen MH, Erichsen R, Frøslev T, et al. Postmenopausal estrogen therapy and risk of gallstone disease: a population-based case-control study[J]. Drug Saf. 2013;36(12):1189–97.
14. Parra-Landazury NM, Cordova-Gallardo J, Méndez-Sánchez N. Obesity and gallstones[J]. Visc Med. 2021;37(5):394–402.
15. Portincasa P, Di Ciaula A, Bonfrate L, et al. Metabolic dysfunction-associated gallstone disease: expecting more from critical care manifestations[J]. Intern Emerg Med. 2023;18(7):1897–918.
16. Sun M, Bao S. Association between cardiometabolic index and biological aging in the US population: evidence from NHANES 2015–2020[J]. Front Aging Neurosci. 2024;16.
17. Wei Y, Yu J. Association between cardiometabolic index and frailty among patients with diabetes mellitus: a cross-sectional study[J]. Front Nutr. 2024;11.
18. Lazzer S, D'Alleva M, Isola M, et al. Cardiometabolic index (CMI) and visceral adiposity index (VAI) highlight a higher risk of metabolic syndrome in women with severe obesity[J]. J Clin Med. 2023;12(9):3055.
19. Liu H, Guo M, Zhou Y, et al. Association between cardiometabolic index and kidney stones in US diabetic patients: NHANES 2007–2018[J]. World J Urol. 2024;42(1):653.
20. Tamini S, Bondesan A, Caroli D, et al. The lipid accumulation product index (LAP) and the cardiometabolic index (CMI) are useful for predicting the presence and severity of metabolic syndrome in adult patients with obesity[J]. J Clin Med. 2024;13(10):2843.
21. Cheng L, Wu Q, Wang S. Cardiometabolic index is associated with increased depression: a population-based study[J]. J Affect Disord. 2024;348:259–64.
22. Wang L, Liu X, Du Z, et al. Cardiometabolic index and chronic obstructive pulmonary disease: a population-based cross-sectional study[J]. Heart Lung: J Crit Care. 2024;68:342–9.
23. Wu X, Jin X, Xu W, et al. Cardiometabolic index is associated with increased bone mineral density: a population-based cross-sectional study[J]. Front Public Health. 2024;12:1403450.
24. Xu B, Wu Q, Yin G, et al. Associations of cardiometabolic index with diabetic statuses and insulin resistance: the mediating role of inflammation-related indicators[J]. BMC Public Health. 2024;24(1):2736.
25. Li H, Zhang Y, Luo H, et al. The lipid accumulation product is a powerful tool to diagnose metabolic dysfunction-associated fatty liver disease in the United States adults[J]. Front Endocrinol. 2022;13:977625.
26. Chen X, Zhao Y, Sun J, et al. Identification of metabolic syndrome using lipid accumulation product and cardiometabolic index based on NHANES data from 2005 to 2018[J]. Nutr Metab. 2024;21(1):96.
27. Gong L, Fan S, Peng Z, et al. The association between triglyceride-glucose index and gallstones: NHANES 2017–2020[J]. Front Endocrinol. 2024;15:1437711.
28. Wang J, Shen Z, Liang Y, et al. Association of neutrophil percentage to albumin ratio with gallstones: a cross-sectional study from the United States NHANES[J]. BMC Public Health. 2024;24(1):3503.
29. Wu J, Wang Y, Qiu P, et al. Associations of exercise snacks with cognitive function among older adults in NHANES 2011–2014[J]. Gen Hosp Psychiatry. 2025;94:167–73.
30. Wu W, Pei Y, Wang J, et al. Association of dietary quality indicators with gallstones in the US: NHANES 2017–2020[J]. BMC Public Health. 2025;25(1):976.
31. Wakabayashi I, Daimon T. The cardiometabolic index as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus[J]. Clinica Chimica Acta; International Journal of Clinical Chemistry. 2015;438:274–278.
32. Miao M, Deng X, Wang Z, et al. Cardiometabolic index is associated with urinary albumin excretion and renal function in aged person over 60: data from NHANES 2011–2018[J]. Int J Cardiol. 2023;384:76–81.
33. Rodriguez Gatta D, Huidobro L, Petermann-Rocha F, et al. Sex disparities in gallstone disease: insights from the MAUCO prospective population-based cohort study[J]. BMJ Open Gastroenterol. 2024;11(1):e001457.
34. Sun H, Warren J, Yip J, et al. Factors influencing gallstone formation: a review of the literature[J]. Biomolecules. 2022;12(4):550.
35. Jiang Z, Jiang H, Zhu X et al. The relationship between high-sensitivity C-reactive protein and gallstones: a cross-sectional analysis[J]. Front Med. 2024;11.
36. Wang HH, de Bari O, Arnatt CK et al. Activation of estrogen receptor G protein-coupled receptor 30 enhances cholesterol cholelithogenesis in female mice[J]. Hepatology (Baltimore, Md.). 2020;72(6):2077–89.
37. Rudling M, Laskar A, Straniero S. Gallbladder bile supersaturated with cholesterol in gallstone patients preferentially develops from shortage of bile acids[J]. J Lipid Res. 2019;60(3):498–505.
38. Su PY, Hsu YC, Cheng YF, et al. Strong association between metabolically-abnormal obesity and gallstone disease in adults under 50 years[J]. BMC Gastroenterol. 2019;19(1):117.
39. Yuan S, Gill D, Giovannucci EL, Obesity, et al. Type 2 diabetes, lifestyle factors, and risk of gallstone disease: a Mendelian randomization investigation[J]. Clin Gastroenterol Hepatol. 2022;20(3):e529–37.
40. Shimizu Y, Yamanashi H, Honda Y, et al. Low-density lipoprotein cholesterol, structural atherosclerosis, and functional atherosclerosis in older Japanese[J]. Nutrients. 2022;15(1):183.
41. Chen Y, Weng Z, Liu Q et al. FMO3 and its metabolite TMAO contribute to the formation of gallstones[J]. Biochimica et biophysica acta (BBA) - Molecular basis of disease. 2019;1865(10):2576–85.
42. Hu H, Shao W, Liu Q, et al. Gut microbiota promotes cholesterol gallstone formation by modulating bile acid composition and biliary cholesterol secretion[J]. Nat Commun. 2022;13(1):252.
43. Janeiro MH, Ramírez MJ, Milagro FI, et al. Implication of trimethylamine N-oxide (TMAO) in disease: potential biomarker or new therapeutic target[J]. Nutrients. 2018;10(10):1398.
44. Ufnal M, Zadlo A, Ostaszewski R. TMAO: a small molecule of great expectations[J]. Nutrition. 2015;31(11):1317–23.

45. Schiattarella GG, Sannino A, Toscano E, et al. Gut microbe-generated metabolite trimethylamine-N-oxide as cardiovascular risk biomarker: a systematic review and dose-response meta-analysis[J]. Eur Heart J. 2017;38(39):2948–56.
46. Wang Q, Jiao L, He C, et al. Alteration of gut microbiota in association with cholesterol gallstone formation in mice[J]. BMC Gastroenterol. 2017;17(1):74.
47. Biddinger SB, Haas JT, Yu BB, et al. Hepatic insulin resistance directly promotes formation of cholesterol gallstones[J]. Nat Med. 2008;14(7):778–82.
48. Nakeeb A, Comuzzie AG, Al-Azzawi H et al. Insulin resistance causes human gallbladder dysmotility[J]. Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract. 2006;10(7):940–948; discussion 948–949.
49. Meng C, Liu K. Higher levels of systemic immune-inflammatory index are associated with the prevalence of gallstones in people under 50 years of age in the United States: a cross-sectional analysis based on NHANES[J]. Front Med. 2024;10.
50. Liu Z, Kemp TJ, Gao YT, et al. Association of circulating inflammation proteins and gallstone disease[J]. J Gastroenterol Hepatol. 2018;33(11):1920–4.
51. Wang HH, Portincasa P, Wang DQH. Update on the molecular mechanisms underlying the effect of cholecystokinin and cholecystokinin-1 receptor on the formation of cholesterol Gallstones[J]. Curr Med Chem. 2019;26(19):3407–23.
52. Hb B, C G. K H. Metabolic phenotyping of BMI to characterize cardiometabolic risk: evidence from large population-based cohorts[J]. Nat Commun. 2023;14(1).
53. Song X, Wu et al. Equations for predicting DXA-measured visceral adipose tissue mass based on BMI or weight in adults[J]. Lipids Health Dis. 2022;21(1).
54. Jabłonowska-Lietz B, Wrzosek M, Włodarczyk M, et al. New indexes of body fat distribution, visceral adiposity index, body adiposity index, waist-to-height ratio, and metabolic disturbances in the obese.[J]. Kardiologia Polska. 2017;75(11):1185–91.
55. Shi A, Xiao S, Wang Y, et al. Metabolic abnormalities, liver enzymes increased risk of gallstones: a cross-sectional study and multivariate Mendelian randomization analysis[J]. Intern Emerg Med. 2024;20(2):501–8.
56. ADC, Dq W, P P. An update on the pathogenesis of cholesterol gallstone disease[J]. Curr Opin Gastroenterol. 2018;34(2).

Publisher's note