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Association between sarcopenia and the prevalence of gallstone in US adults: a cross-sectional analysis of NHANES

Bo Wang¹, Qianxi Huang², Yongqiang Xiong¹, Na Huang³, Jun Li^{3*} and Shu Zhang^{1,4*}

Abstract

Background Gallstones are a common disease that imposes a significant burden on public health resources. Sarcopenia is an age-related condition characterized by a decline in muscle mass, strength, and function. However, its relationship with gallstones remains unclear.

Methods This cross-sectional study included 2,167 US adults from the National Health and Nutrition Examination Survey. We used the multivariable logistic regression models and restricted cubic spline regression to assess the relationship between sarcopenia and gallstones. Additionally, subgroup analyses and propensity score matching (PSM) were conducted to account for potential confounding factors.

Results We found a significant negative association between the sarcopenia index and the prevalence of gallstones (OR: 0.253, 95% CI: 0.132–0.471, $P < 0.001$). In Model 4, which integrated all covariates, sarcopenia was associated with approximately a 100% increased prevalence of gallstones compared to non-sarcopenia patients (OR: 1.995, 95% CI: 1.340–2.948, $P < 0.001$). The results of PSM also confirmed the association between sarcopenia and gallstones (OR: 1.982, 95% CI: 1.217–3.285, $P = 0.007$). Notably, this association was more pronounced in subgroups including females, non-Hispanic whites, married individuals, and higher education level.

Conclusion In summary, our findings suggest a positive association between sarcopenia and the prevalence of gallstones in US adults. This suggests that we should increase the emphasis on gallstone disease screening in sarcopenia patients. However, this finding needs to be validated through further large-scale prospective studies.

Keywords Sarcopenia, Gallstone, National health and nutrition examination survey

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Introduction

Gallstones, a common digestive disorder, affect approximately 10–15% of the global adult population [1]. In 2015, 1.5 million people in the United States sought medical attention for gallstone-related conditions, with a national expenditure totaling \$10 billion [2, 3]. Gallstones are often asymptomatic in the early stages, but if not promptly screened, they can progress to symptomatic clinical stages and may even lead to complications such as gallbladder cancer, liver cancer, and pancreatic cancer [4]. This progression significantly impacts public health and places a substantial burden on healthcare resources and the economy. The formation of gallstones has been linked to various genetic and environmental factors, including ethnicity, gender, age, family history, obesity, diet, lifestyle, medication use and so on [1, 5].

Sarcopenia is an age-related condition characterized by a decrease in skeletal muscle mass, along with a decline in muscle strength and physical function [6, 7]. In 2019, the European Working Group on Sarcopenia in Older People redefined sarcopenia, proposing that individuals with low muscle strength, low muscle mass, and poor physical performance be diagnosed with sarcopenia [8]. The prevalence of sarcopenia is reported to be 5.5% in men and 13.3% in women [9]. Furthermore, studies have shown that sarcopenia is closely associated with various diseases, including diabetes [10], kidney stones [11], osteoarthritis [12], cirrhosis [13], and other liver diseases [14]. However, to date, few studies have addressed the relationship between sarcopenia and gallstones. Only one Mendelian randomization study explored the association between sarcopenia-related markers including (skeletal muscle index, hand grip strength, and walking pace) and cholelithiasis in the European population [15]. Therefore, it is necessary to further explore the relationship between sarcopenia and gallstones.

This study will fill the gap by further exploring the relationship between sarcopenia and gallstone prevalence using data from the National Health and Nutrition Examination Survey (NHANES) among US adults. At the same time, these findings will also provide valuable insights into future disease screening and clinical practice.

Methods

Data source

The NHANES is an ongoing, nationally representative survey designed to assess the health and nutritional status of the US population. Each year, approximately 5,000 individuals are surveyed, with data collection encompassing dietary information, questionnaire interviews, and laboratory tests. The protocol was approved by the Ethics Review Board of the National Center for Health Statistics, and written informed consent was obtained from all participants.

Definitions of key variables

The exposure variable in this study is sarcopenia. Sarcopenia is defined according to the guidelines established by the Foundation for the National Institutes of Health, characterized by a sarcopenia index of <0.512 for women and <0.789 for men [16, 17]. Appendicular lean mass (ALM) was measured using dual-energy X-ray absorptiometry (DEXA). The sarcopenia index was calculated as follows: Sarcopenia Index = Total Appendicular Skeletal Muscle Mass (kg) / BMI (kg/m^2). Participants weighing over 136.4 kg or taller than 192.5 cm were excluded from the study, as they could not be accurately measured using DEXA [7, 17].

The outcome variable of this study is gallstones. Since 2017, NHANES has included gallstone-related information in its questionnaire. Gallstones were defined based on participants' responses to the question, "Has a doctor ever told you that you have gallstones?" Participants who answered "yes" were identified as having a history of gallstones. Unfortunately, there is no information on the type of gallstones.

Meanwhile, we included several covariates from the available data that are associated with gallstones and sarcopenia. Specifically, age, sex, smoking status, and body mass index (BMI) are closely linked to gallstones [1, 5], while conditions such as diabetes [18], cancer [19, 20], and liver-related diseases [14, 21, 22] are commonly comorbid with sarcopenia. Additionally, certain sociological factors, including age and marital status, also appear to be associated with sarcopenia [23]. Most of the disease-related information within these covariates was obtained through questionnaires, in which participants self-reported the presence or absence of specific conditions by responding with "yes" or "no." Detailed information on these covariates can be found in Supplementary Table 1.

Study population

In this study, we utilized all participants from the 2017–2018 NHANES survey cycle ($n=9254$), and only data within this cycle reported information related to sarcopenia and gallstone. At the same time, we used the following exclusion criteria: (1) individuals with missing gallstone questionnaire data ($n=3,700$); (2) individuals with missing sarcopenia-related data ($n=3,346$); (3) individuals with missing covariate data ($n=41$). Ultimately, a total of 2,167 eligible participants were included in our analysis. The data inclusion and exclusion criteria are illustrated in Fig. 1.

Statistical analysis

The student's *t*-test (continuous variables) or chi-square test (categorical variables) were employed to compare differences in baseline characteristics between the

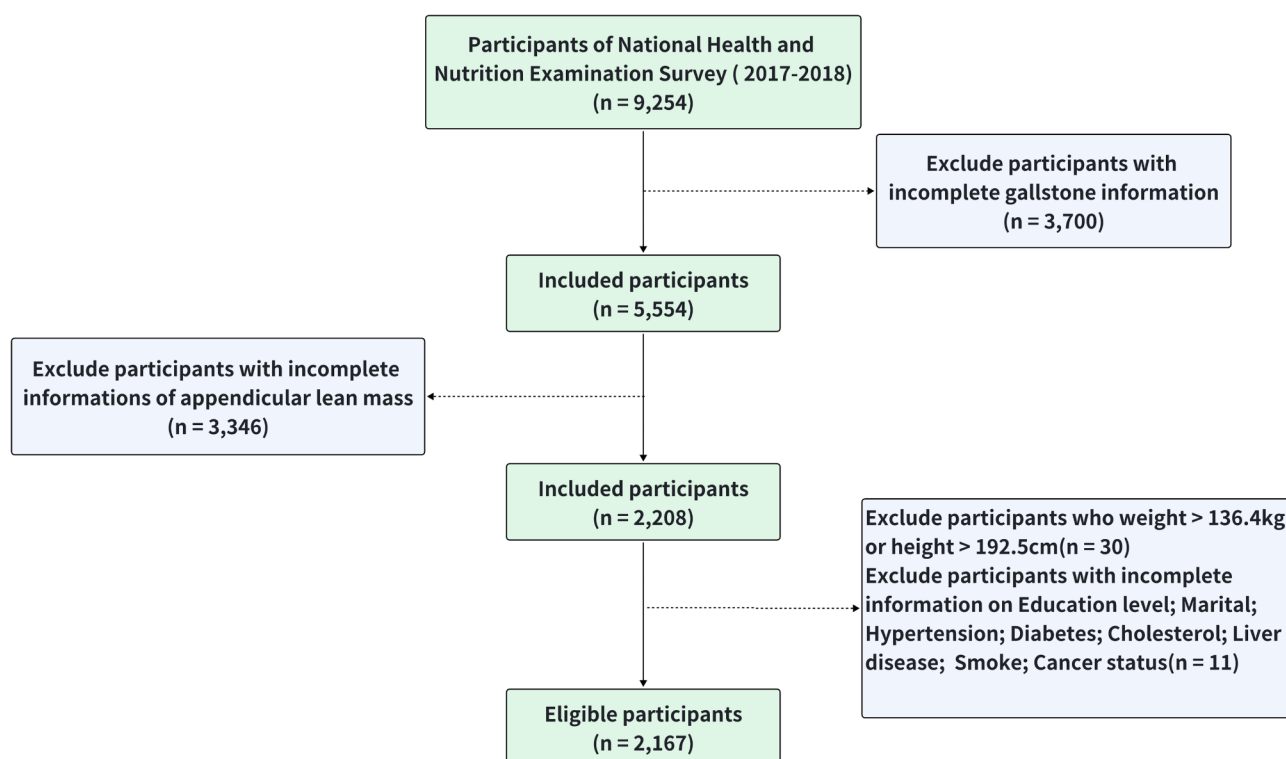


Fig. 1 The flow diagram of eligible participant selection in the national health and nutrition examination survey

sarcopenia and non-sarcopenia groups. Multivariable logistic regression analysis was conducted to assess the relationship between sarcopenia and the prevalence of gallstones, with odds ratio (OR) and corresponding 95% confidence interval (95% CI) used to describe the association. Statistical analyses were performed using R version 4.2.2. *P* value of <0.05 was considered statistically significant.

Results

Baseline characteristics

We included 2,167 eligible participants from the NHANES database, as illustrated in Fig. 1. Table 1 summarizes the baseline characteristics of the participants. They were divided into a sarcopenia group (601, 27.7%) and a non-sarcopenia group (1,566, 72.3%). The sarcopenia indexes for the two groups were 0.56 [0.47; 0.68] and 0.92 [0.77; 1.14], respectively. Compared to the non-sarcopenia group, patients in the sarcopenia group had a higher BMI, a higher proportion of males, and a greater prevalence of hypertension, diabetes, hypercholesterolemia, and smoking. Supplementary Table 2 outlines the baseline characteristics of participants categorized by gallstone status, with approximately 8% of participants having a history of gallstones. Additionally, we observed statistically significant differences between the two groups, except for education level and marital status.

Relationship between sarcopenia and gallstones

We utilized a weighted multivariable logistic regression model to investigate the relationship between sarcopenia and gallstones, with results detailed in Table 2. Model 1, which was unadjusted for any factors, indicated that a higher sarcopenia index was associated with a lower prevalence of gallstones (OR: 0.203, 95% CI: 0.108–0.371, *P*<0.001). However, the relationship between defined sarcopenia and gallstones did not appear to be statistically significant. In Model 2, which adjusted for age, gender, race, marital status, and education level, sarcopenia was associated with a 120% increased prevalence of gallstones compared to non-sarcopenia patients (OR: 2.202, 95% CI: 1.492–3.228, *P*<0.001). Model 3, which adjusted for comorbid conditions such as hypertension, hypercholesterolemia, diabetes, liver disease, smoking, and cancer, showed that although the relationship between sarcopenia and gallstones was not statistically significant (OR: 1.157, 95% CI: 0.810–1.634, *P*=0.415), a negative association between the sarcopenia index and gallstone prevalence persisted (OR: 0.236, 95% CI: 0.124–0.436, *P*<0.001). Model 4, which adjusted for all the above factors, also indicated a positive correlation between sarcopenia and the prevalence of gallstones (OR: 1.995, 95% CI: 1.340–2.948, *P*<0.001). Additionally, the prevalence of gallstones decreased with increasing sarcopenia index (OR: 0.253, 95% CI: 0.132–0.471, *P*<0.001).

Table 1 Demographic characteristics of study participants by sarcopenia status

Characteristic	Total n = 2167	Non-Sarcopenia n = 1566	Sarcopenia n = 601	P value
ALM	22.7 [18.1;27.9]	25.3 [20.9;29.5]	17.4 [15.3;20.3]	< 0.001
BMI	27.8 [24.0;32.5]	26.4 [22.8;30.6]	31.7 [28.0;36.8]	< 0.001
Sarcopenia index	0.81 [0.62;1.04]	0.92 [0.77;1.14]	0.56 [0.47;0.68]	< 0.001
Age	40.0 [29.0;50.0]	39.0 [29.0;50.8]	41.0 [30.0;50.0]	0.534
Age category:				0.061
< 40	1071 (49.4%)	794 (50.7%)	277 (46.1%)	
≥ 40	1096 (50.6%)	772 (49.3%)	324 (53.9%)	
Gender:				< 0.001
Male	1015 (46.8%)	564 (36.0%)	451 (75.0%)	
Female	1152 (53.2%)	1002 (64.0%)	150 (25.0%)	
Race				0.123
Non-Hispanic White	641 (29.6%)	473 (30.2%)	168 (28.0%)	
Mexican American	346 (16.0%)	232 (14.8%)	114 (19.0%)	
Other Hispanic	211 (9.74%)	153 (9.77%)	58 (9.65%)	
Non-Hispanic Black	440 (20.3%)	313 (20.0%)	127 (21.1%)	
Other Race	529 (24.4%)	395 (25.2%)	134 (22.3%)	
Education:				0.074
Less than 9th grade	122 (5.63%)	80 (5.11%)	42 (6.99%)	
9-11th grade	232 (10.7%)	173 (11.1%)	59 (9.82%)	
High school graduate	501 (23.1%)	358 (22.9%)	143 (23.8%)	
Some college or AA degree	728 (33.6%)	512 (32.7%)	216 (35.9%)	
College graduate or above	583 (26.9%)	442 (28.2%)	141 (23.5%)	
Marital:				0.105
Married/Living with Partner	1292 (59.6%)	912 (58.2%)	380 (63.2%)	
Never married	566 (26.1%)	424 (27.1%)	142 (23.6%)	
Widowed/Divorced/Separated	309 (14.3%)	230 (14.7%)	79 (13.1%)	
Gallstone				0.203
Yes	164 (7.57%)	111 (7.09%)	53 (8.82%)	
No	2003 (92.4%)	1455 (92.9%)	548 (91.2%)	
Hypertension				0.013
Yes	493 (22.8%)	334 (21.3%)	159 (26.5%)	
No	1674 (77.2%)	1232 (78.7%)	442 (73.5%)	
Diabetes				0.001
Yes	156 (7.20%)	93 (5.94%)	63 (10.5%)	
No	1967 (90.8%)	1441 (92.0%)	526 (87.5%)	
Borderline	44 (2.03%)	32 (2.04%)	12 (2.00%)	
Cholesterol				0.011
Yes	488 (22.5%)	330 (21.1%)	158 (26.3%)	
No	1679 (77.5%)	1236 (78.9%)	443 (73.7%)	
Smoke				0.017
Yes	781 (36.0%)	540 (34.5%)	241 (40.1%)	
No	1386 (64.0%)	1026 (65.5%)	360 (59.9%)	
Liver disease				0.999
Yes	77 (3.55%)	56 (3.58%)	21 (3.49%)	
No	2090 (96.4%)	1510 (96.4%)	580 (96.5%)	
Cancer				0.093
Yes	88 (4.06%)	71 (4.53%)	17 (2.83%)	
No	2079 (95.9%)	1495 (95.5%)	584 (97.2%)	

ALM, Appendicular lean mass; BMI, body mass index

Table 2 Logistic regression analyzed the relationship between sarcopenia and gallstone

Model	Sarcopenia	OR	95% CI		P value
			Lower limit	Upper limit	
Model 1	No	Ref			
	Yes	1.268	0.895	1.775	0.174
	Sarcopenia index	0.203	0.108	0.371	<0.001
Model 2	No	Ref			
	Yes	2.202	1.492	3.228	<0.001
	Sarcopenia index	0.217	0.114	0.399	<0.001
Model 3	No	Ref			
	Yes	1.157	0.810	1.634	0.415
	Sarcopenia index	0.236	0.124	0.436	<0.001
Model 4	No	Ref			
	Yes	1.995	1.340	2.948	<0.001
	Sarcopenia index	0.253	0.132	0.471	<0.001

Model 1 was not adjusted. Model 2 was adjusted for age, gender, race, marital status, and educational level. Model 3 was adjusted for hypertension, cholesterol level, diabetes, smoke, liver disease and cancer status. Model 4 was adjusted for model 2 plus model 3. OR, odds ratio; CI, confidence interval.

Additionally, we conducted a restricted cubic spline regression to visualize the relationship between the sarcopenia index and gallstone, as shown in Fig. 2. Based on the model 4, we observed a linear trend where the OR for gallstones decreased with increasing sarcopenia index (Fig. 2A, P for overall < 0.008, P for nonlinear > 0.05). Further analysis revealed that this linear relationship remained significant in the female subgroup

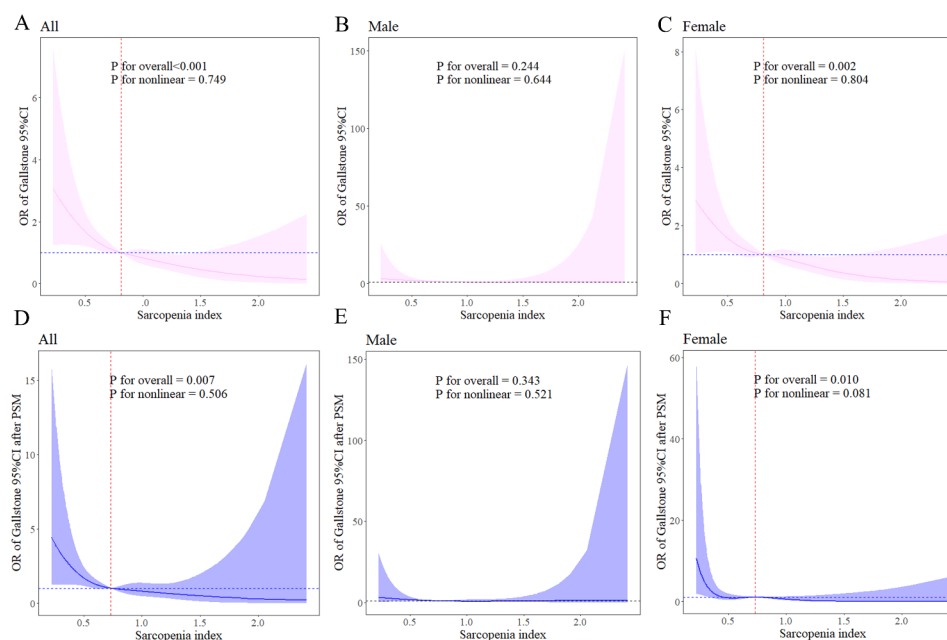
(Fig. 2C, P for overall = 0.002, P for nonlinear > 0.05), but was not significant in the male subgroup (Fig. 2B, P for overall = 0.244).

Subgroup analysis

We also performed a subgroup analysis to assess the relationship between sarcopenia and gallstones across different populations, as illustrated in Fig. 3. After controlling for confounding factors, we found that in the female population, sarcopenia was associated with a significantly increased prevalence of gallstones (OR: 1.915, 95% CI: 1.161–3.085, P = 0.009), whereas this association was not significant in males (OR: 1.861, 95% CI: 0.949–3.751, P = 0.074). Similarly, the relationship between sarcopenia and gallstones was more pronounced among non-Hispanic whites (OR: 2.861, 95% CI: 1.468–5.534, P = 0.002), married individuals (OR: 2.407, 95% CI: 1.465–3.940, P < 0.001), and those with college education or higher (OR: 2.468, 95% CI: 1.508–4.021, P < 0.001). The stratified analysis by comorbid conditions revealed that sarcopenia was associated with a higher prevalence of gallstones in subgroups without diabetes, liver disease, or cancer (Fig. 3, P < 0.05).

Propensity score matching analysis

Given the baseline differences between the sarcopenia and non-sarcopenia groups that might impact the results, we performed propensity score matching (PSM) on the participants. The baseline characteristics after PSM were detailed in Supplementary Tables 3, and the results of PSM were illustrated in Fig. 4. Based on the data after

**Fig. 2** Restricted cubic spline for OR(95%CI) of gallstone on sarcopenia index

(A) all, (B) male, (C) female subgroup before propensity score matching and (D) all, (E) male, (F) female subgroup after propensity score matching

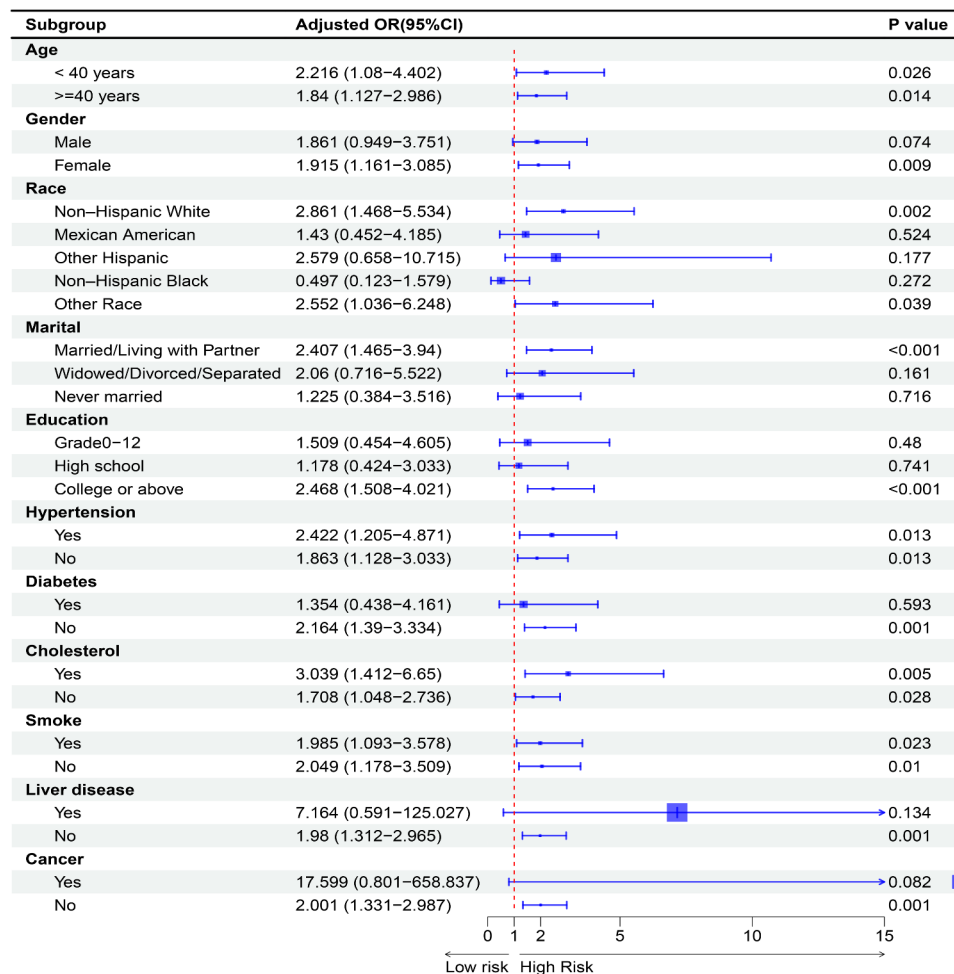


Fig. 3 OR(95%CI) of gallstone disease on sarcopenia stratified by selected factors

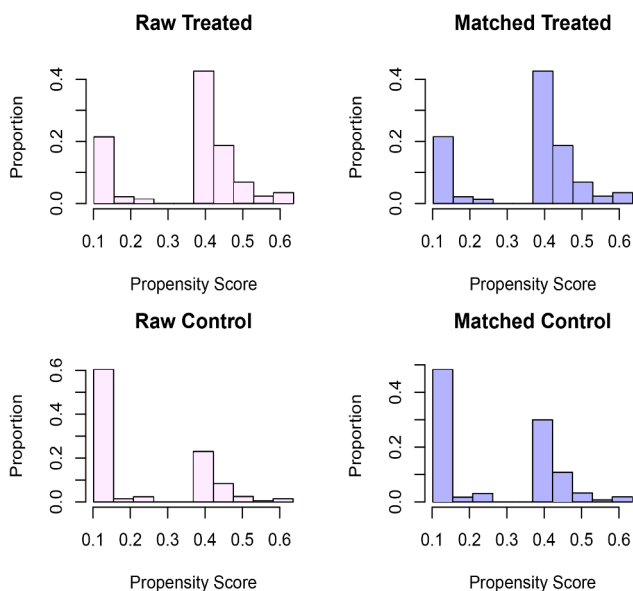


Fig. 4 Distribution of propensity score before and after matching

Table 3 Logistic regression analyzed the relationship between sarcopenia and gallstone after propensity score matching,

Model	Sarcopenia	OR	95% CI		P value
			Lower limit	Upper limit	
Model 1	No	Ref			
	Yes	1.778	1.132	2.840	0.014
	Sarcopenia index	0.096	0.035	0.241	<0.001
Model 2	No	Ref			
	Yes	1.969	1.220	3.233	0.006
	Sarcopenia index	0.183	0.066	0.465	0.001
Model 3	No	Ref			
	Yes	1.775	1.120	2.858	0.016
	Sarcopenia index	0.110	0.040	0.281	<0.001
Model 4	No	Ref			
	Yes	1.982	1.217	3.285	0.007
	Sarcopenia index	0.207	0.073	0.534	0.002

PSM, we conducted a reanalysis using multivariable logistic regression models, with results shown in Table 3. We found that the results from all four models consistently indicated a positive association between sarcopenia and gallstone prevalence (Table 3, $P < 0.05$). Similarly,

the results also suggested that an increase in the sarcopenia index was associated with a reduced prevalence of gallstones (Table 3; Fig. 2D-F).

Model 1 was not adjusted. Model 2 was adjusted for age, gender, race, marital status, and educational level. Model 3 was adjusted for hypertension, cholesterol level, diabetes, smoke, liver disease and cancer status. Model 4 was adjusted for model 2 plus model 3. OR, odds ratio; CI, confidence interval.

Discussion

In this study, we conducted a cross-sectional analysis using data from NHANES to investigate the relationship between sarcopenia and gallstones. We found that the prevalence of gallstones decreased with increasing sarcopenia index, suggesting that sarcopenia may be a risk factor for gallstones. To mitigate the effects of confounding factors, we performed propensity score matching. The results from the propensity score-matched analysis also confirmed the positive relationship between sarcopenia and gallstones. Notably, this association was more pronounced among females, non-Hispanic whites, married individuals, those with college education or higher, and in subgroups without diabetes, liver disease.

Gallstone formation is influenced by a variety of risk factors, including non-modifiable factors such as age, race, and gender, as well as modifiable factors such as diet, obesity, metabolic syndrome, surgery, and medication [1, 5]. Specifically, behaviors associated with higher BMI, diabetes, increased intake of high-sugar, high-fat, low-fiber foods, and reduced physical activity can contribute to the increased incidence and prevalence of gallstones [24, 25]. Sarcopenia is an age-related systemic skeletal muscle disease characterized by a loss of muscle mass and accelerated functional decline, which is associated with numerous adverse outcomes such as frailty, functional decline, and mortality [6]. The mechanisms related to sarcopenia include inflammation, immune senescence, and increased oxidative stress [7, 26].

We observed that sarcopenia and gallstones share several similar pathophysiological mechanisms, such as obesity, insulin resistance, physical inactivity, and chronic inflammation [11]. Sarcopenia often involves a sedentary lifestyle with prolonged bed rest and physical inactivity, which are known risk factors for gallstones. Skeletal muscle is the main organ of insulin-induced glucose metabolism. Some previous studies have shown that sarcopenia is closely associated with insulin resistance and metabolic syndrome [27]. An animal study found that insulin-resistant mice (LIRKO mice) were more likely to develop cholesterol gallstones, which may be related to decreased bile acid synthesis and increased bile cholesterol secretion [28, 29]. Additionally, the interplay between muscle and adipose tissue is significant in sarcopenia [30].

Microstructural changes in sarcopenia include reductions in muscle fiber size and number, particularly affecting type II fibers. With aging, type II fibers can transition to type I fibers, and there can be infiltration of fat into muscle tissue [6, 31]. Furthermore, ectopic fat deposition in the liver and skeletal muscle can induce inflammatory responses and insulin resistance, thereby promoting gallstone formation. Additionally, some studies have found that sarcopenia patients exhibit elevated levels of inflammatory cytokines and markers, which may contribute to the development of gallstones [32, 33].

Additionally, some findings from the subgroup analysis were particularly intriguing. We observed a significant positive association between sarcopenia and gallstones in women, whereas this relationship was not significant in men. Several factors may contribute to this sex-specific difference. First, previous epidemiological studies have suggested that the prevalence of sarcopenia varies by sex and may be influenced by the diagnostic criteria used. In the United States, the prevalence of sarcopenia is higher in women than in men [34]. Second, intrinsic physiological differences between sexes may play a role. Women generally have lower muscle mass and higher body fat levels compared to men [35, 36], which predisposes them to insulin resistance—an important factor that can contribute to gallstone formation. Additionally, hormonal influences may be involved, as estrogen has been shown to affect gallbladder motility and cholesterol metabolism, both of which are crucial in gallstone formation [37]. Lastly, female itself is an independent risk factor for gallstones, and this intrinsic factor, combined with other metabolic and hormonal differences, might explain the stronger association observed between sarcopenia and gallstones in women compared to men.

At the same time, we also observed differences across racial/ethnic subgroups. Specifically, the positive association between sarcopenia and gallstones was primarily observed in non-Hispanic White individuals, whereas in non-Hispanic Black individuals, the association appeared to be negative, although not statistically significant. Previous studies have demonstrated racial differences in muscle mass. A nationwide epidemiological survey found that Black women have significantly higher lean mass compared to White women, whereas no such difference was observed among men [9, 38]. Meanwhile, another study reported that the incidence of gallstones is lower in non-Hispanic Black individuals compared to White individuals [39]. Therefore, we speculate that these contrasting epidemiological characteristics may contribute to the observed racial differences in the relationship between sarcopenia and gallstones. The reason this relationship is more pronounced among people with higher education levels may be related to their sedentary lifestyle. Subgroup analysis of complications also showed that these

diseases did not affect the positive relationship between sarcopenia and gallstone. Similarly, our propensity score matching analysis confirmed that sarcopenia remained the positive association with gallstone after confounding factors were eliminated.

To the best of our knowledge, this is the first study to assess the relationship between sarcopenia and gallstones using a nationally representative US population. Our study demonstrates an association between sarcopenia and the risk of gallstones, while also controlling for potential variables through propensity score matching. These findings have important clinical implications, suggesting that sarcopenia may serve as an additional risk factor for gallstone disease. Given this association, routine assessment of sarcopenia, particularly among older adults or those with metabolic disorders, could be integrated into gallstone screening strategies. Additionally, interventions aimed at improving muscle mass and function, such as resistance training and nutritional optimization, may help reduce gallstone risk, though further research is needed to confirm this potential preventive strategy.

However, there are still limitations in our study. First, being a cross-sectional analysis, it does not establish causality between sarcopenia and gallstones. Second, due to data limitations, only the NHANES 2017–2018 cycle provided simultaneous information about sarcopenia and gallstones, which makes our data volume small and may cause bias. Furthermore, since most gallstones are clinically silent, the use of questionnaires rather than a clinical diagnosis is also a limitation, along with a lack of information on the type of gallstones. Therefore, further large randomized controlled trials are needed to confirm our findings.

Conclusion

In summary, our findings suggest a positive association between sarcopenia and the prevalence of gallstones in US adults. Healthcare providers should consider incorporating routine sarcopenia assessments in high-risk populations as part of gallstone disease screening. Early interventions focused on muscle mass preservation, including resistance exercises and nutritional optimization, may also help reduce the risk of gallstones. These findings warrant further validation through large-scale prospective studies to confirm their clinical relevance.

Abbreviations

NHANES	National Health and Nutrition Examination Survey
ALM	Appendicular lean mass
DEXA	Dual-energy X-ray absorptiometry
BMI	Body mass index
OR	Odds ratio
CI	Confidence interval
PSM	Propensity score matching

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12876-025-03808-z>.

Supplementary Material 1

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Author contributions

Bo Wang, Qianxi Huang, Jun Li, and Shu Zhang conceived and designed the study. Bo Wang and Qianxi Huang drafted the initial manuscript. Yongqiang Xiong and Na Huang, along with Jun Li and Shu Zhang, analyzed the results and critically revised the manuscript. All authors have reviewed and approved the final manuscript.

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Data availability

The data during the current study are available at National Health and Nutrition Examination Survey (<https://www.cdc.gov/Nchs/Nhanes/>). Further inquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by The National Center for Health Statistics Research Ethics Review Board. The participants provided their written informed consent to participate in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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