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Associations of metabolic syndrome and its components with sarcopenia, and the mediating role of insulin resistance: Findings from NHANES database

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Abstract

Background To investigate the association between metabolic syndrome (MetS) and its components with sarcopenia, and to explore the extent to which insulin resistance (IR) mediates this association, using data from the National Health and Nutrition Examination Survey (NHANES).

Methods We analyzed cross-sectional data from 15,779 adults in the NHANES from 1999 to 2006 and 2011–2018. Multivariable logistic regression models were used to determine the odds ratios (ORs) between MetS, its components, the number of MetS components, and sarcopenia. Mediation analysis was performed to explore the role of the homeostatic model assessment of insulin resistance (HOMA-IR) in MetS and its components-induced sarcopenia.

Result In the fully adjusted model, MetS increased the prevalence of sarcopenia by 1.96-fold (95% CI: 1.73–2.22). Among the individual components, central obesity, hypertension, and hyperglycemia were associated with an increased prevalence of sarcopenia. Sarcopenia prevalence also increased linearly with the number of MetS components, with the highest prevalence observed in the presence of all five components (OR: 3.80, 95% CI: 2.79–5.16). Sex-stratified analysis showed that the prevalence of MetS for sarcopenia was higher in males than females. The mediating effects of HOMA-IR on the association between MetS and its components (central obesity, hypertension, and hyperglycemia) with sarcopenia were significant, with mediation effects of 51.7%, 30.7%, 33.2%, and 79.1%, respectively. There was no significant direct association between hyperglycemia and sarcopenia beyond the HOMA-IR pathway.

Conclusion MetS and its individual components, excluding hypertriglyceridemia and low high density lipoprotein cholesterol, were associated with a higher prevalence of sarcopenia, especially in males. This association was partially or fully mediated by IR.

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Keywords Metabolic syndrome, Metabolic syndrome components, Insulin resistance, Sarcopenia

Introduction

Sarcopenia, characterized by a progressive decline in muscle mass, strength, and function, is associated with physical and functional disabilities, as well as an increased risk of mortality [1]. The global prevalence of sarcopenia was estimated to be over 50 million adults in 2000 and is expected to rise to over 200 million by 2040 [2], emphasizing the urgent need to accurately identify its risk factors. Obesity, hypertension, and diabetes are considered modifiable risk factors for the onset and progression of sarcopenia, and these conditions are core components of metabolic syndrome (MetS) [3, 4].

MetS is a cluster of metabolic dysregulations, including abdominal obesity, hypertension, hyperglycemia, and dyslipidemia, which are recognized as significant risk factors for cardiovascular diseases [5]. MetS has become a significant public health concern, with a prevalence rate of 20–25% among adults worldwide [6]. Increasing evidence suggests a bidirectional relationship between MetS and sarcopenia. The potential pathophysiological mechanisms mainly involve a series of adverse effects induced by insulin resistance (IR). IR not only leads to glucose intolerance but also exacerbates lipid metabolism disorders (atherogenic dyslipidemia), raising the risk of MetS [7, 8]. IR can also contribute to muscle mass atrophy through insulin signaling pathways and anabolic stimulators, such as phosphatidylinositol 3-kinase, 3-phosphoinositide-dependent protein kinase-1, Akt, mammalian target of rapamycin, and p70S6 kinase [9–11]. Despite this recognition, the association between MetS and sarcopenia varies across epidemiological studies. A systematic review and meta-analysis of 13 cross-sectional studies involving 35,581 middle-aged and older non-obese adults found a positive correlation between MetS and sarcopenia [12]. In a cross-sectional analysis of community-dwelling elderly individuals, MetS was positively associated with sarcopenia in men aged 65 to 74 years, but not in older men or women [13]. Another cross-sectional study of 81 community-dwelling, overweight, and obese older adults found that MetS was associated with greater lean body mass and increased forearm muscle size but poorer muscle quality [14]. Although numerous studies have investigated the relationship between MetS and sarcopenia, there is a significant gap in the literature concerning the independent associations between MetS, its individual components, and sarcopenia, as well as the mediating role of IR in this context. Further elucidation of the interplay between MetS and sarcopenia, especially the role of IR, could offer valuable insights into preventive strategies and therapeutic targets for vulnerable populations.

The objectives of this study were to investigate the association between MetS, its components, and the number of MetS components with sarcopenia in American adults, and to examine the potential mediating role of IR in these associations, using data from the National Health and Nutrition Survey (NHANES) database.

Methods

Survey designs and study populations

This cross-sectional study utilized NHANES data from 1999 to 2006 and 2011–2018, during which dual-energy X-ray absorptiometry (DXA) measurements of muscle mass were available. Details of the design, methods, and participants of NHANES have been previously described at https://www.cdc.gov/nchs/products/databriefs.htmprogram=nhanes. Briefly, NHANES is a continuous, stratified, multistage sampling study conducted by the U.S. Centers for Disease Control and Prevention (CDC) to assess the health and nutritional status of adults and children in the United States. NHANES is approved by the research ethics review board of the CDC, and all participants provided informed consent.

Of these, 23,228 participants from the 1999–2006 survey cycle were excluded due to missing data required for diagnosing metabolic syndrome, defining sarcopenia, and calculating biomarkers of insulin resistance (i.e., height, weight, waist circumference [WC], blood pressure, high density lipoprotein cholesterol [HDL], triglycerides [TG], DXA, fasting plasma glucose [FPG], and fasting insulin [FINS]). In the 2011–2018 survey period, 32,623 participants were excluded using the same exclusion criteria as described above. Thus, the remaining 15,779 participants were included in the final analysis, of whom 1,729 were diagnosed with sarcopenia (Fig. 1).

Assessment of MetS and IR

MetS is defined according to the criteria established in a 2009 joint statement by the American Heart Association, the National Heart, Lung, and Blood Institute, and the International Diabetes Federation [15]. The diagnosis requires the presence of at least three of the following criteria: (1) Central obesity: WC≥102 cm for men and ≥88 cm for women. (2) Hyperglycemia: FPG≥5.6 mmol/L (100 mg/dL) or receiving drug treatment for elevated glucose. (3) Hypertriglyceridemia: TG≥1.7 mmol/L (150 mg/dL) or receiving drug treatment for elevated TG. (4) Hypertension: systolic blood pressure≥130 mmHg and/or diastolic blood pressure≥85 mmHg, or receiving antihypertensive drug treatment. (5) Dyslipidemia: HDL<1.0 mmol/L (40 mg/dL) in men, < 1.3 mmol/L

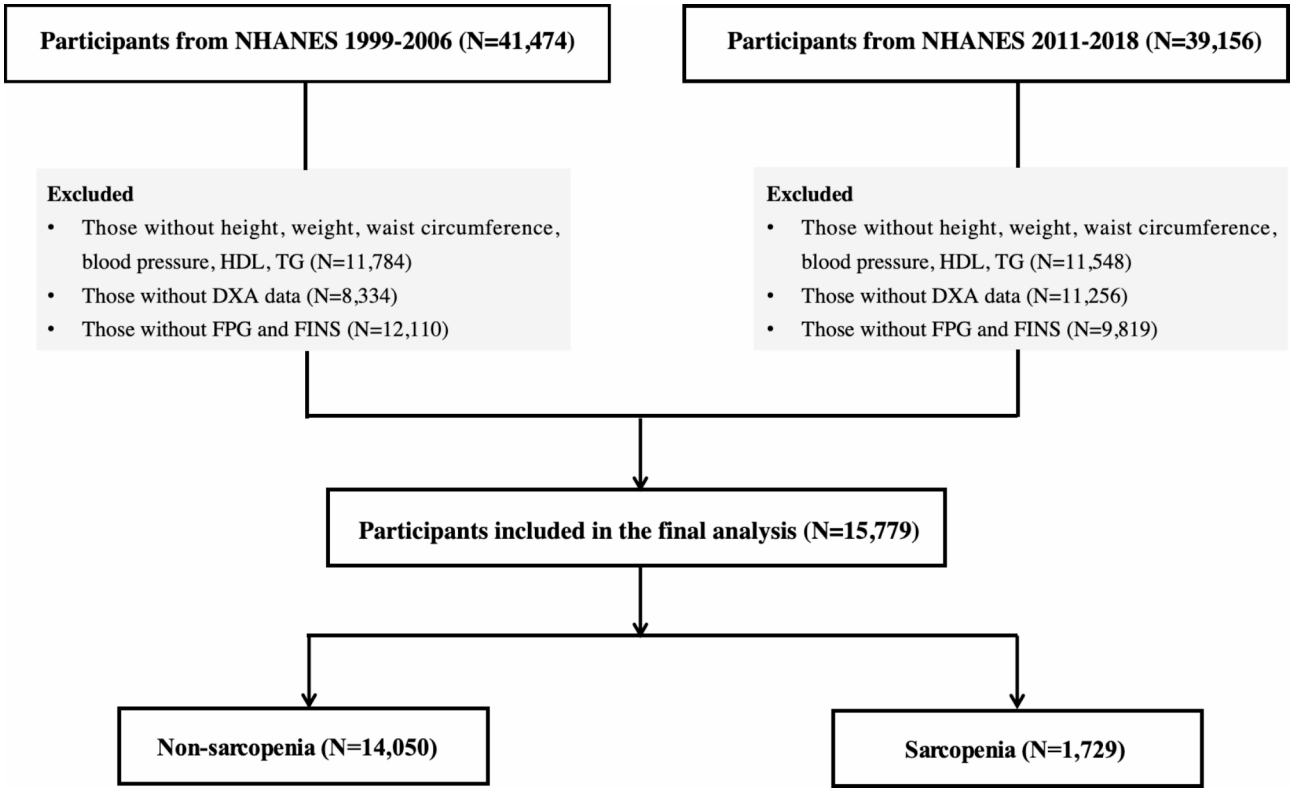

Fig. 1 Flowchart of participants included in this study. NHANES, National Health and Nutrition Examination Survey; HDL, high density lipoprotein cholesterol; TG, triglycerides; DXA, dual-energy X-ray absorptiometry; FPG, fasting plasma glucose; FINS, fasting insulin

(50 mg/dL) in women, or receiving drug treatment for reduced HDL.

To estimate IR, we used the homeostatic model assessment of insulin resistance (HOMA-IR) [16]. HOMA-IR is calculated by multiplying FINS by FPG, then dividing by the constant 22.5: HOMA-IR = (FINS × FPG)/22.5 [17].

Sarcopenia

Appendicular skeletal muscle mass adjusted by body mass index (ASMBMI) is recommended by the Foundation for the National Institutes of Health as a size-normalized muscle mass value for the diagnosis of sarcopenia. Males and females were classified as sarcopenic if their ASMBMI was less than 0.789 or 0.512, respectively [18, 19]. DXA was used to assess muscle mass in the arms and legs, enabling the calculation of appendicular skeletal muscle mass [20]. For safety reasons and due to DXA table limitations, individuals who were pregnant, weighed more than 136 kg, or were taller than 196 cm were excluded from DXA measurements.

Covariates

Covariates were selected based on previous literature and a change of more than 10% in effect estimates [13, 14, 21, 22]. Information on age, sex, ethnicity, education level, smoking status, alcohol intake, and physical activity was collected through standardized interview questionnaires. Ethnicity was classified as Mexican American, non-Hispanic white, non-Hispanic black, other Hispanic, or other races. Marital status was classified into never married, married and others (including divorced, widowed, or living with partner). Educational level was stratified as less than high school, high school or above. Smoking status was classified as never, former, and current smokers based on their responses to questions about smoking at least 100 cigarettes in their lifetime and whether they were currently smoking. Alcohol consumption was categorized as never (<12 drinks throughout lifetime), former (≥12 drinks in any one year of life and not drinking now), and current (≥12 drinks in any one year of life and drinking now) drinking. Consistent with previously self-reported physical activity categories, physical activity was classified into four groups according to metabolic equivalents (MET)-min/week: sedentary (<100 MET-min/week), low (100 to <500 MET-min/week), moderate (500 to <1200 MET-min/week), and high (≥1200 MET-min/week) [23]. The family poverty income ratio (PIR) was calculated as the ratio of annual earnings to the poverty threshold, adjusted for family size. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared [24].

Statistical analysis

Data analyses were performed with Empower Stats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA) and R Software (version 4.2.0), with $P<0.05$ considered statistically significant. Continuous variables are reported as mean ± standard deviation (SD) or median (interquartile range [IQR]), whereas categorical variables are expressed as percentages. Differences between participants with or without sarcopenia were assessed using Kruskal Wallis test (for continuous variables) or χ square test (for categorical variables). Due to the skewed distribution of HOMA-IR values, a normalizing logarithmic transformation was performed. Multivariate logistic regression analyses were used to investigate the associations between MetS, MetS components, and the number of MetS components with the prevalence of sarcopenia. In the crude model, no covariates were adjusted. In Model 1, adjustments were made for age, sex, ethnicity, marital status, education, and PIR. In Model 2, further adjustments were made for smoking status, drinking status, physical activity, and when evaluating individual MetS components, all components except the exposure factors were adjusted. Additionally, considering the differences in sarcopenia prevalence among sex groups, we stratified the analyses by gender and investigated the interaction of sex-specific MetS, its components (central obesity, hypertension, hyperglycemia), and the quantity of MetS components with sarcopenia.

Mediation analysis was performed to examine the effects of HOMA-IR on the associations between MetS and its components (central obesity, hypertension, hyperglycemia) with sarcopenia. The total effect of MetS and its components on sarcopenia odds can be divided into direct effects (not through mediators) and indirect/mediation effects (via mediators). The proportion of HOMA-IR's mediation effect relative to the total effect was estimated. This estimation was performed by constructing an outcome model and a mediator model, with standard errors generated by bootstrapping with 1,000 simulations.

For sensitivity analysis, multiple imputation was used to handle missing variables, and subgroup analyses were performed for two periods (1999–2006 and 2011–2018). The random forest method was used to impute five complete datasets. Multivariate logistic regression models were employed to explore the association between MetS and sarcopenia. Sensitivity analyses were adjusted for sex, age, race, education, PIR, smoking status, alcohol consumption, and physical activity. When analyzing individual MetS components, all other components except the exposure variables were also adjusted. The results of the sensitivity analyses are provided in the supplementary files (Supplementary Table S2 and Figure S1).

Results

Population characteristics

Among the 15,779 participants included in this study (52.2% male), the mean age was 35.7 years. Of these, 4,084 (25.9%) had MetS, and 1,729 (10.9%) were diagnosed with sarcopenia. Participants with sarcopenia had higher rates of MetS, central obesity, hypertension, hyperglycemia, hypertriglyceridemia, and low HDL. They were mostly older married men with higher BMI, lower education levels, lower PIR, and less physical activity (Table 1). Males with MetS were younger, had a lower BMI, were primarily Non-Hispanic White, had higher PIR and HOMA-IR, smoked, drink alcohol, had higher rates of dyslipidemia and sarcopenia, and had lower rates of central obesity than females (Supplementary Table S1).

Association between MetS, MetS components and the prevalence of sarcopenia

The associations between sarcopenia, MetS, its components, and the number of MetS components are shown in Table 2. MetS and its components (central obesity, hypertension, hyperglycemia) were significantly associated with sarcopenia in all three models. After adjusting for all confounders in Model 2, MetS as a binary variable increased the odds of sarcopenia by 1.96-fold (95% CI: 1.73–2.22). MetS components increased the prevalence of sarcopenia by 2.42-fold (95% CI: 2.07–2.82) for central obesity, 1.40-fold (95% CI: 1.21–1.63) for hypertension, and 1.36-fold (95% CI: 1.20–1.55) for hyperglycemia. However, the associations of hypertriglyceridemia and dyslipidemia with sarcopenia disappeared after further adjustment for all variables including the other components of MetS in Model 2. When MetS was treated as a continuous variable, the prevalence of sarcopenia increased by 1.32-fold (95% CI: 1.26–1.38) per component increment. Sensitivity analyses showed that the associations of MetS, its components (central obesity, hypertension, hyperglycemia), and the number of MetS components with sarcopenia remained stable (Supplementary Table S2). In addition, there were no significant differences between the 1999–2006 cycles and 2011–2018 cycles (all P for interaction >0.05, Supplementary Figure S1).

Mediation analysis

The mediating effects of HOMA-IR on the associations between MetS, its components (central obesity, hypertension, and hyperglycemia), and sarcopenia are shown in Fig. 2. HOMA-IR played significant mediating roles in the associations between MetS, its individual components (central obesity, hypertension, and hyperglycemia), and sarcopenia, with mediation ratios of 51.7%, 30.7%, 33.2%, and 79.1%, respectively. Notably, there was no significant direct association between hyperglycemia and

Table 1 Characteristics of participants

Variables[a]	Total (*N* = 15,779)	Non-sarcopenia (*N* = 14,050)	Sarcopenia[b] (*N* = 1,729)	*P*-value
Age, (years)	35.7 ± 19.0	34.6 ± 18.1	44.6 ± 23.8	< 0.001
Gender, n (%)				< 0.001
Female	7537 (47.8)	6883 (49.0)	651 (37.7)	
Male	8247 (52.2)	7167 (51.0)	1078 (62.3)	
BMI (kg/m)^2	26.8 ± 6.3	26.4 ± 6.0	29.8 ± 7.2	< 0.001
Ethnic, n (%)				< 0.001
Non-Hispanic White	6072 (38.5)	5459 (38.9)	609 (35.2)	
Non-Hispanic Black	3529 (22.4)	3409 (24.3)	120 (6.9)	
Mexican American	3568 (22.6)	2842 (20.2)	726 (42.0)	
Other Hispanic	1063 (6.7)	912 (6.5)	150 (8.7)	
Other Races	1552 (9.8)	1428 (10.2)	124 (7.2)	
Education, n (%)				< 0.001
< high school	4180 (26.5)	3408 (24.3)	772 (44.8)	
≥ high school	11,592 (73.5)	10,634 (75.7)	953 (55.2)	
Marital status, n (%)				< 0.001
Never married	4398 (33.7)	4185 (35.7)	211 (16.0)	
Married	5777 (44.3)	5016 (42.8)	760 (57.5)	
Others	2863 (22.0)	2511 (21.4)	350 (26.5)	
PIR, n (%)	2.4 ± 1.6	2.5 ± 1.6	2.1 ± 1.5	< 0.001
Drinking status, n (%)				< 0.001
Never	1493 (14.0)	1233 (13.1)	260 (21.6)	
Former	1563 (14.7)	1271 (13.5)	290 (24.1)	
Current	7572 (71.2)	6918 (73.4)	652 (54.2)	
Smoking status, n (%)				< 0.001
Never	6194 (55.3)	5497 (55.4)	696 (54.4)	
Former	2444 (21.8)	2074 (20.9)	368 (28.8)	
Current	2572 (22.9)	2356 (23.7)	215 (16.8)	
Physical activity level[c], (%)				< 0.001
sedentary	1811 (14.8)	1613 (14.6)	198 (17.2)	
low	2961 (24.2)	2641 (23.9)	317 (27.5)	
moderate	2379 (19.5)	2138 (19.3)	241 (20.9)	
high	5078 (41.5)	4679 (42.3)	398 (34.5)	
Metabolic syndrome, n (%)				< 0.001
No	11,700 (74.1)	10,761 (76.6)	936 (54.1)	
Yes	4084 (25.9)	3289 (23.4)	793 (45.9)	
Central obesity, n (%)				< 0.001
No	6935 (44.2)	6471 (46.3)	464 (27.1)	
Yes	8763 (55.8)	7511 (53.7)	1248 (72.9)	
Hypertension, n (%)				< 0.001
No	12,509 (79.5)	11,391 (81.3)	1114 (64.9)	
Yes	3231 (20.5)	2627 (18.7)	603 (35.1)	
Hyperglycemia, n (%)				< 0.001
No	10,622 (67.3)	9767 (69.5)	854 (49.4)	
Yes	5162 (32.7)	4283 (30.5)	875 (50.6)	
Hypertriglyceridemia, n (%)				< 0.001
No	12,475 (79.1)	11,301 (80.5)	1170 (67.7)	
Yes	3306 (20.9)	2746 (19.5)	559 (32.3)	
Dyslipidemia, n (%)				< 0.001
No	11,565 (73.3)	10,396 (74.0)	1165 (67.4)	

Table 1 (continued)

Variables[a]	Total (*N* = 15,779)	Non-sarcopenia (*N* = 14,050)	Sarcopenia[b] (*N* = 1,729)	*P*-value
Yes	4216 (26.7)	3652 (26.0)	563 (32.6)	
HOMA-IR	2.3 (1.5–3.8)	2.2 (1.4–3.6)	3.2 (2.0–5.6)	< 0.001

BMI body mass index; PIR family poverty income ratio; HOMA-IR homeostasis model assessment of insulin resistance

[a] Mean (SD) or N (%) shown in the table. HOMA-IR show median (IQR)

[b] Sarcopenia was defined based on the guidelines established by the Foundation for the National Institutes of Health (FNIH)

[c] The physical activity categories were based on the distribution of MET-minute levels for the present NHANES sample

Table 2 Odd ratios for the associations between MetS, subcomponents of MetS, and the number of MetS components with Sarcopenia

	Crude Model		Model 1		Model 2[a]	
	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Presence of MetS	2.77 (2.50, 3.07)	< 0.001	1.92 (1.70, 2.17)	< 0.001	1.96 (1.73, 2.22)	< 0.001
Central obesity	2.32 (2.07, 2.59)	< 0.001	2.21 (1.92, 2.54)	< 0.001	2.42 (2.07, 2.82)	< 0.001
Hypertension	2.35 (2.11, 2.61)	< 0.001	1.66 (1.44, 1.92)	< 0.001	1.40 (1.21, 1.63)	< 0.001
Hyperglycemia	2.34 (2.11, 2.58)	< 0.001	1.50 (1.33, 1.70)	< 0.001	1.36 (1.20, 1.55)	< 0.001
Hypertriglyceridemia	1.97 (1.76, 2.19)	< 0.001	1.24 (1.09, 1.41)	< 0.001	1.04 (0.91, 1.19)	0.523
Dyslipidemia	1.38 (1.24, 1.53)	< 0.001	1.26 (1.12, 1.43)	< 0.001	1.02 (0.90, 1.16)	0.743
Per component increment	1.44 (1.40, 1.50)	< 0.001	1.28 (1.22, 1.34)	< 0.001	1.32 (1.26, 1.38)	< 0.001
0 (ref)						
1	1.50 (1.27, 1.78)	< 0.001	1.44 (1.19, 1.74)	< 0.001	1.60 (1.32, 1.94)	< 0.001
2	2.24 (1.90, 2.64)	< 0.001	1.84 (1.52, 2.24)	< 0.001	2.21 (1.81, 2.70)	< 0.001
3	3.34 (2.82, 3.95)	< 0.001	2.54 (2.07, 3.11)	< 0.001	3.03 (2.45, 3.75)	< 0.001
4	4.54 (3.76, 5.48)	< 0.001	2.76 (2.19, 3.48)	< 0.001	3.31 (2.60, 4.21)	< 0.001
5	5.64 (4.39, 7.26)	< 0.001	3.35 (2.48, 4.51)	< 0.001	3.80 (2.79, 5.16)	< 0.001

Crude Model: unadjusted

Model 1: adjusted for age, sex, marital status, ethnic, education and PIR

Model 2: adjustment for sex, age, marital status, ethnic, education, PIR, smoke status, drink status, physical activity

[a] In the analysis of each MetS component, the remaining MetS components, excluding the exposure variables, are also adjusted

Abbreviations MetS: Metabolic Syndrome; PIR: family poverty income ratio; OR: odd ratio; CI: confidence interval

sarcopenia beyond the HOMA-IR pathway in the mediation analyses.

Subgroup analysis

Figure 3 shows the sex-stratified associations of MetS, its components (central obesity, hypertension, hyperglycemia), and the number of MetS components with sarcopenia. There was a significant interaction between sex and MetS (*P* for interaction = 0.004), with MetS increasing the prevalence of sarcopenia by 2.24-fold (95% CI: 1.90–2.64) in males and 1.53-fold (95% CI: 1.25–1.87) in females. Each MetS component significantly increased the risk of sarcopenia. Among males, central obesity, hypertension, and hyperglycemia increased the prevalence of sarcopenia by 2.28-fold, 1.63-fold, and 1.38-fold, respectively, while among females, these components increased the prevalence by 3.26-fold, 1.17-fold, and 1.35-fold, respectively. Statistically significant differences were observed in the hypertension subgroup (*P* for interaction = 0.024). Additionally, the association between the number of MetS components and sarcopenia also showed significant differences by sex (*P* for interaction = 0.013). Each additional MetS component was associated with an increased prevalence of sarcopenia in males (OR: 1.38, 95% CI: 1.30–1.47) and females (OR: 1.22, 95% CI: 1.13–1.32) (Fig. 3).

Discussion

This study is the first to systematically examine the association between MetS and sarcopenia prevalence in adults in a large American community. We found that MetS was significantly increased sarcopenia prevalence, especially among males. The components of MetS including central obesity, hypertension, and hyperglycemia, were significantly and positively associated with sarcopenia. Additionally, IR accounted for 51.7%, 30.7%, 33.2%, and 79.1%, respectively, in the associations between MetS, its components (central obesity, hypertension, hyperglycemia), and sarcopenia. Notably, there was no significant direct association between hyperglycemia and sarcopenia beyond the HOMA-IR pathway.

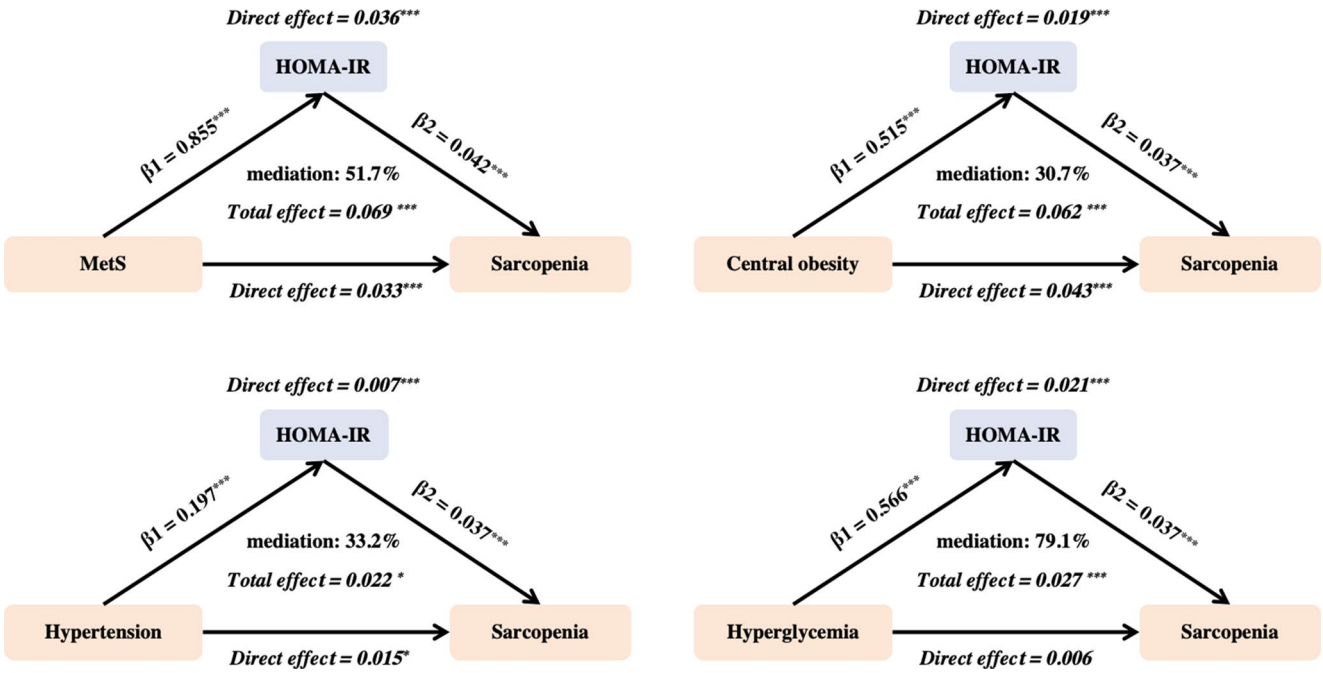

Fig. 2 Mediation analyses of HOMA-IR on the associations between MetS, its components (central obesity, hypertension, and hyperglycemia), and sarcopenia. Adjustment for sex, age, marital status, ethnic, education, PIR, smoke status, drink status, physical activity. In the analysis of each MetS component, the remaining MetS components, excluding the exposure variables, are also adjusted. $^{*}P < 0.05$. $^{**}P < 0.01$. $^{***}P < 0.001$

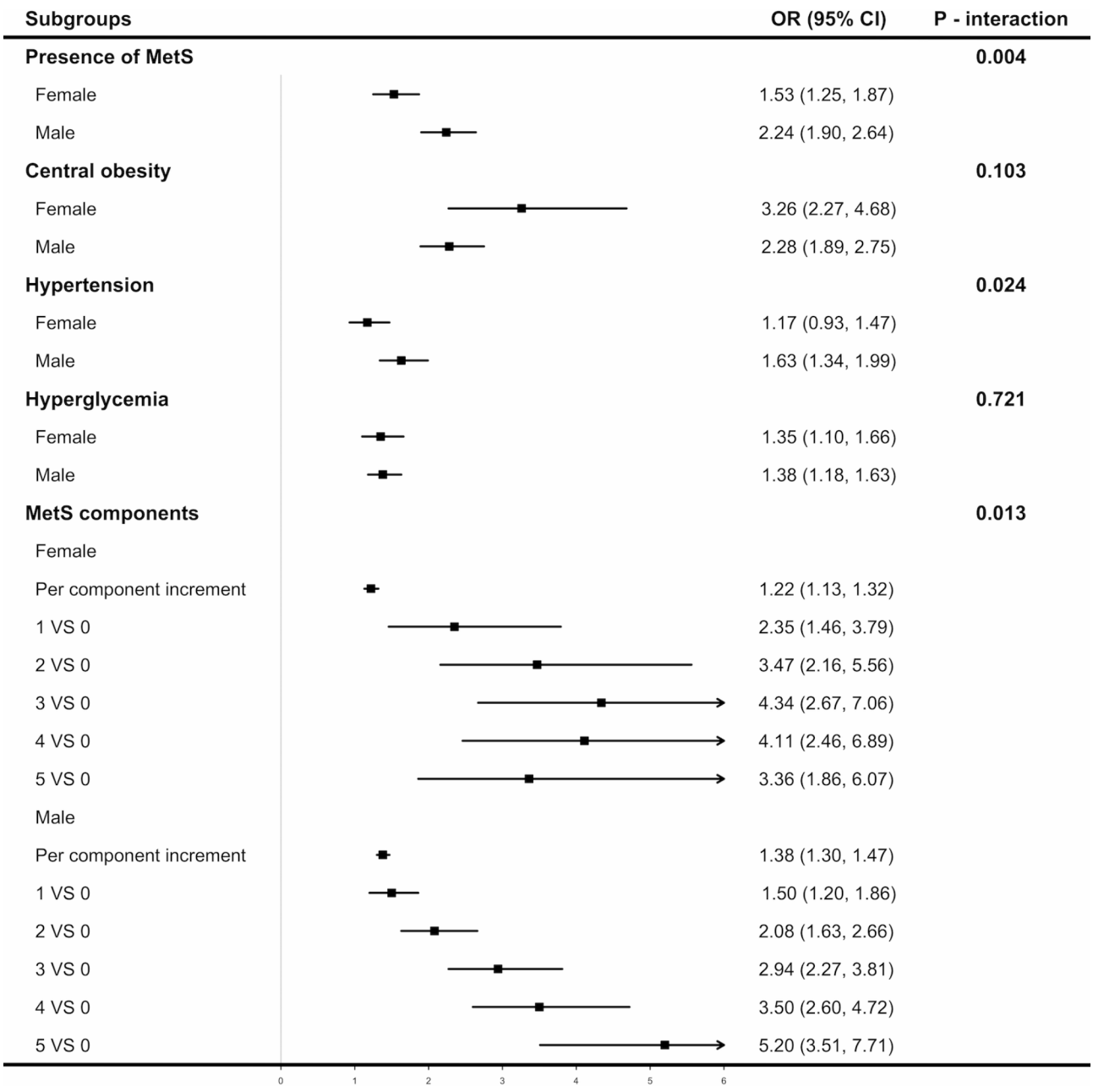

Fig. 3 Sex-specific odd ratios for the association between MetS, MetS components and the number of MetS components and sarcopenia. Adjustment for sex, age, marital status, ethnic, education, PIR, smoke status, drink status, physical activity. In the analysis of each MetS component, the remaining MetS components, excluding the exposure variables, are also adjusted

It is important to note that only a limited number of studies have investigated MetS and its components in association with sarcopenia, and the results have been inconsistent. The Kashiwa study, conducted in a community of 1971 elderly individuals in Japan, found a significant association between MetS and sarcopenia in men aged 65 to 74 years but not in older men or women. Among all MetS components, only abdominal obesity was significantly and positively associated with sarcopenia in men, but not in women [13]. Mesinovic et al. [14] identified positive associations between MetS, waist circumference, low HDL, hypertension, and muscle mass and size in 84 overweight and obese elderly individuals. Similarly, Tong et al. [21] showed that among 251 older community-dwelling Chinese individuals, male participants with increased waist circumference and diastolic blood pressure had higher muscle mass, whereas only waist circumference was significantly associated with muscle mass in women. Contrary to the aforementioned studies, we found that MetS and its components (central

obesity, hypertension, and hyperglycemia) were significantly associated with a higher prevalence of sarcopenia in both males and females compared to individuals without MetS. This discrepancy can be attributed to several factors: (1) Most previous studies were conducted in elderly populations (aged 60 years and older) from East Asia; (2) there is inconsistency in the diagnostic criteria for sarcopenia; and (3) the sample sizes were relatively small, with inadequate adjustments for potential confounding factors. Furthermore, it is notable that certain components of MetS have been reported to be associated with sarcopenia. Murat et al. [24] found that hypertension can lead to at least a twofold increase in the risk of sarcopenia. A meta-analysis of 16 observational studies demonstrated that high hemoglobin A1c levels, prediabetes, diabetes, and diabetic complications were associated with an increased risk of sarcopenia [25]. Although dyslipidemia was considered a risk factor for sarcopenia, the data remain inconsistent. Some studies indicate a positive association between TG/HDL and sarcopenia [26, 27], while others suggest a negative association [28]. Our results show that the associations of hypertriglyceridemia and low HDL with sarcopenia disappeared after further adjusting for other MetS components. These findings suggest that dyslipidemia may not be independently associated with sarcopenia. Further cohort studies are needed to validate these findings.

Previous studies have shown that the prevalence of sarcopenia differs between sexes, likely because men are more prone to adverse lifestyle factors (such as smoking and alcohol consumption) and have a higher incidence of chronic conditions (such as hypertension and diabetes) associated with sarcopenia [29]. Consistent with previous studies, we also found a significantly higher prevalence of sarcopenia among males with MetS compared to females (21.6% vs. 17.1%) (Supplementary Table S1). In addition, our study found that MetS, hypertension as an individual MetS components, and increases in the numbers of MetS components were more strongly associated with sarcopenia in male participants than in female participants (Fig. 3). These findings suggest that greater attention should be given to sarcopenia in males with MetS and consider targeted measures for early intervention. Furthermore, maintaining normal blood pressure levels in men with MetS may be effective in reducing the risk of sarcopenia.

Our findings also indicate a strong link between IR and sarcopenia, consistent with the findings of another study [30]. Several review articles have suggested that IR may contribute to the development of sarcopenia [31, 32]. Our mediation analysis revealed that HOMA-IR mediated 51.7%, 30.7%, 33.2%, and 79.1% of the associations between MetS and its components (central obesity, hypertension, hyperglycemia) and sarcopenia, respectively. IR plays a dual role as both a trigger and a consequence of MetS and sarcopenia. IR contributes to the development of MetS by inducing hyperglycemia, increasing apolipoprotein B (apoB) production, and enhancing cholesterol secretion in bile, all of which collectively exacerbate the condition [7, 33]. In skeletal muscle, IR leads to increased protein catabolism, reduced protein synthesis, and heightened expression of the FoxO family of transcription factors, which directly or indirectly weaken muscle tissue and induce autophagy, ultimately resulting in sarcopenia [32]. MetS is characterized by central obesity, hypertension, dyslipidemia, and hyperglycemia, with IR serving as the core pathological mechanism [34]. The accumulation of fatty acids and triglycerides in muscle cells due to IR triggers local inflammation and lipotoxicity, impairing insulin signaling and promoting muscle protein degradation. This process is further exacerbated by systemic inflammation, characterized by elevated levels of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which inhibit muscle protein synthesis. Additionally, mitochondrial dysfunction caused by oxidative stress leads to increased production of reactive oxygen species (ROS), which activates nuclear factor-kappa B (NF-κB) and accelerates muscle atrophy. Given that skeletal muscle is crucial for maintaining glucose homeostasis, muscle atrophy is often linked to a chronic low-grade inflammatory state. Elevated pro-inflammatory cytokines, abnormal lipid infiltration, lipotoxicity, increased amino acid catabolism, and a lower proportion of type I muscle fibers all contribute to disrupted insulin signaling and enhanced insulin resistance [32, 35].

To the best of our knowledge, this is the first study to investigate the association between MetS, its components, and sarcopenia using a large sample size. With nearly 15,000 participants, our study included a substantial number of MetS and sarcopenia cases, providing sufficient statistical power for analysis. Moreover, this study systematically explored the mediating role of IR in the association between MetS, its components, and sarcopenia using mediation analysis. Finally, a significant association between MetS and sarcopenia was identified in men. This research introduces novelty and importance to the field, and ongoing scientific exploration is critical to refining our understanding of these mechanisms and their impact on public health. Future longitudinal studies are needed to further confirm the association of MetS and its components with sarcopenia, using more accurate muscle mass measurements or combining muscle strength and low physical performance diagnostic criteria to define sarcopenia.

However, this study had several limitations. First, we used a cross-sectional study design to investigate these associations, making it difficult to determine causality.

Future longitudinal studies are needed to elucidate the causal relationships between MetS and sarcopenia. Second, although DXA is widely used to measure muscle mass for sarcopenia diagnosis, low muscle strength and physical performance, which are also required, were not measured. Third, there may be recall bias due to the fact that the sociodemographic characteristics of the research sample were obtained through questionnaires. Finally, insufficient information on MetS components may have led to an underestimation of their overall prevalence. Nonetheless, this random exclusion is unlikely to have significantly affected the overall results.

Conclusions

In summary, our results indicate that MetS, its components (central obesity, hypertension, and hyperglycemia), and an increased number of these components are positively associated with the sarcopenia prevalence. Additionally, the associations of MetS, hypertension, and the number of MetS components with sarcopenia prevalence were stronger in males than in females. Moreover, IR partially or fully mediates the relationship between MetS, its components (central obesity, hypertension, hyperglycemia), and sarcopenia prevalence. Future prospective studies are needed to confirm the relationship between MetS and the risk of sarcopenia.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

X.L. and Y.W. contributed to the conception and design of the study; M.L. and R.J. contributed to manuscript drafting; M.L. and R.J. contributed to the statistics analysis; M.L. and R.J. contributed to the acquisition of data; M.L., R.J., X.L., and Y.W. contributed to critical revisions of the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets generated and analyzed in the current study are available at NHANES website: https://www.cdc.gov/nchs/nhanes/index.htm

Declarations

Ethics approval and consent to participate

The NHANES study protocol was approved by the U.S. National Center for Health Statistics Research Ethics Review Board, and written informed consent was provided by all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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