

Relationship between skeletal muscle mass with metabolic syndrome in Chinese elders

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Abstract

Background: The association between regional skeletal muscle mass and metabolic syndrome (MetS) remains unclear. Therefore, the present study aimed to investigate these associations with MetS risk among Chinese elders.

Methods: On the basis of health check-up program, a case-control study was performed among participants over 65 years of age, 250 MetS participants were identified and 750 healthy subjects were randomly selected as controls. Skeletal muscle mass was estimated via bioelectric impedance analysis. Muscle mass of each region was standardized by weight to obtain its muscle mass index. Conditional logistic regression models and restricted cubic spline models were implemented to evaluate the associations between MetS and the muscle mass in different regions.

Results: As compared the highest category with the lowest category, leg muscle mass index (LMI) (OR = 0.12; 95%CI: 0.05, 0.32; P for trend < 0.001), trunk muscle mass index (TMI) (OR = 0.11; 95%CI: 0.04, 0.29; P for trend < 0.001) and skeletal muscle mass index (SMI) (OR = 0.11; 95%CI: 0.04, 0.29; P for trend < 0.001) were inversely associated with MetS risk after adjusting for age, gender, duration of education, exercise, smoking status, alcohol drinking status, total energy intake, proteins, fats, carbohydrates, serum fasting glucose and lipid profiles. Dose-response analysis showed that per standard deviation increment of LMI (OR = 0.45; 95%CI: 0.34, 0.58; P for trend < 0.001), TMI (OR = 0.39; 95%CI: 0.28, 0.53; P for trend < 0.001) and SMI (OR = 0.29; 95%CI: 0.19, 0.43; P for trend < 0.001) were inversely associated with MetS risk, respectively.

Conclusion: The present results showed that higher LMI, TMI and SMI were associated with the low risk of MetS in Chinese elders.

Introduction

Metabolic syndrome (MetS) is a complex metabolic disorders with central obesity as the core, combined with increased blood glucose, blood pressure, triglyceride concentration or decreased high density lipoprotein concentration [1]. Obesity, insulin resistance, hypertension and glucose and lipid metabolism disorders are the main manifestations of this chronic disease. Nowadays, the prevalence of MetS has shown an increasing trend in recent years with the changes of lifestyles and dietary pattern, especially for older people. It has been estimated that more than 1 billion adults are diagnosed as MetS, affecting a quarter of the world's population [2]. In United States, the overall prevalence of MetS increased from 32.5% in 2011–2012 to 36.9% in 2015–2016, with 48.6% among people over 60 years old [3]. According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria and International Diabetes Federation (IDF) definition, the estimated prevalence of MetS among Chinese adults aged over 40 years in 2014–2015 was 18.4% and 26.9%, respectively [4]. Additionally, MetS is associated with increased risk of cardiovascular disease, atherosclerosis and cancer [5–7]. As an emerging public health problem, MetS has brought serious threats to people's health.

Skeletal muscle is the major tissue of insulin-mediated glucose uptake and utilization, and the loss of skeletal muscle mass may lead to metabolic impairments [8]. In addition, skeletal muscle is considered to be an endocrine organ, and its release of myokines can not only mediate crosstalk between muscle, adipose tissue, liver, brain and other organs, but also prevent insulin resistance [9, 10]. There is mounting evidence that the reduction of skeletal muscle mass is closely related to MetS. In elderly Japanese women, greater muscle mass was related to lower MetS risk after controlling for visceral fat mass [11]. Similarly, a cohort study also found that an increase in relative skeletal muscle mass had a potential preventive effect on developing metabolic syndrome after adjustment for baseline relative skeletal muscle mass and glycol-metabolic parameters [12]. The body composition of older people changes as they lose muscle gradually. Therefore, it is significant and necessary to investigate the correlation between muscle mass and MetS in the elderly. Different regional of adipose tissue have various biological functions, and the upper and lower body adipose tissue might exert different roles in metabolic processes [13]. Therefore, we speculate that different regional of skeletal muscle might have different physiological functions. To date, studies that assessing regional muscle distribution and its relationship with MetS risk among Chinese elders are still lacking. Therefore, a case-control study is implemented to investigate the relationship between regional muscle mass and MetS.

Methods

Study design and population

Community-dwelling of local Qingdao residents aged 65 and over were received annual physical check-up in community service center. Of these, 1336 senior citizens in 2 neighborhoods (Fushan and Ningxia Community) were participated in health examination between Mar. and Nov. 2020. After excluding missing data of skeletal muscle ($n = 196$) and the participants with unreliable 24-hour recall data ($n = 17$), 1123 participants were available for data analyses, including 494 males and 629 females. A total of 250 MetS patients were selected as the cases, excluding those with severe heart failure, liver and kidney disease, malignancy, or cognitive impairment. Meanwhile, the residents without MetS who underwent physical examination in the same period at the community hospital were selected as the control group. Controls were individually matched to cases by age (± 3 y), gender, with a 1:3 case-to-control ratio. Written informed consent was obtained from all participants, and this research was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University.

According to Diabetes Society of the Chinese Medical Association (CDS), MetS was defined as three or more of the following indexes: (1) overweight or obesity ($\text{BMI} \geq 25.0 \text{ kg/m}^2$); (2) hyperglycemia ($\text{FPG} \geq 6.1 \text{ mmol/L}$ or 2 h post-meal glucose $\geq 7.8 \text{ mmol/L}$, or diagnosed before); (3) hypertension ($\text{SBP} \geq 140 \text{ mmHg}$, $\text{DBP} \geq 90 \text{ mmHg}$ or diagnosed before); and (4) dyslipidemia ($\text{TG} \geq 1.7 \text{ mmol/L}$, or $\text{HDL} < 1.0 \text{ mmol/L}$ in female, or $\text{HDL} < 0.9 \text{ mmol/L}$ in male) [14].

Questionnaire Interview

A face-to-face questionnaire interview was conducted by well-trained investigators to collect the information on the socio-demographic characteristics, lifestyle habits, family history of chronic disease, current clinical conditions, and medical treatments. In addition, a three-day 24-hour dietary questionnaire (2 working days and 1 weekend) was recorded to monitor the average intake of dietary nutrients.

Anthropometrical Measurements

Anthropometrical data, including height (m), body weight (kg), waistline (cm) and blood pressure (mmHg), were measured by well-trained physicians using calibrated equipment. Body mass index (BMI, kg/m^2) was calculated as the participant's weight (kg) divided by the square of height (m^2).

Biochemical Measurement

Fasting blood samples were collected into vacuum tubes for laboratory analyses. Serum was separated by centrifugation (4000 rpm for 10 min at 4°C) for biochemical analysis. Meanwhile, assays of serum fasting glucose and lipid profiles (total cholesterol [TC], triglyceride [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C]) were determined by automatic biochemical analyzer (TBA-40FR, Toshiba, Japan).

Measurement Of Muscle Mass

After an overnight fasting, skeletal muscle mass was estimated via bioelectric impedance analysis (BIA, InBody S10, Korea), an effective tool that was widely applied for assessing body composition. The participants rested for at least 10 minutes in order to achieve a regular distribution of fluid. The measurement was carried out in a sitting position. Inbody S10 performed three different frequencies (5KHz, 50KHz and 250kHz) to measure the impedance of five parts of the body (trunk, left and right arms, left and right legs), and calculate the muscle mass of each part. Then, body weight was adopted to standardized regional muscle mass.

Statistical analysis

The Shapiro-Wilk test was adopted to check the normality of continuous variables. The normal variables were expressed as mean \pm standard deviation (SD), whereas the skewed variables were presented as the median (interquartile range [IQR]). The baseline characteristics of study participants were evaluated by the Chi-test for categorical variables and the Wilcoxon rank sum test for continuous variables.

Conditional logistical regression model was implemented to estimate crude odds ratio (OR) with 95% confidence interval (CI) of MetS risk across quintiles, with the lowest quintile serving as the reference. Meanwhile, multivariate-adjusted OR with 95% CI was also implemented by adjustment for age, gender, duration of education, exercise, smoking status, alcohol drinking status, total energy intake, proteins, fats, carbohydrates, serum fasting glucose and lipid profiles. We used a restricted cubic spline model with 4 knots (at 5th, 35th, 65th and 95th) to explore the shape of the association between skeletal muscle mass index and MetS risk, adjusting for confounding factors [15]. Tests for trends were conducted by assigning

the median value for each category and modeling this variable as a continuous variable [16]. All statistical analyses were performed using STATA 15.0 (Stata CORP, College Station, TX). A two-tailed $P < 0.05$ was regarded as statistically significant.

Results

Baseline characteristics of the inclusive participants are presented in Table 1. The prevalence of MetS was 27.17%, 29.50% in females and 24.13% in males, respectively. The proportion of secondary education, overweight and obesity in patients with MetS were significantly higher than that control group ($P < 0.001$). In terms of dietary intake, protein intake in patients with MetS was significantly lower than that in the control group ($P = 0.044$). In addition, the levels of serum triglyceride, fasting blood glucose and blood pressure in the MetS group were significantly higher compared with control group ($P < 0.001$). However, no significant associations were observed with total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol.

Table 1
Baseline characteristics of study participants by metabolic syndrome status

Characteristics	Case(n = 250)	Control(n = 750)	P*
Age, y	72.5(69–77)	72(68–77)	0.139
Sex			1.000
Male	100(40%)	300(40%)	
Female	150(60%)	450(60%)	
Educational level			0.029
Primary(≤ 6 y)	64(25.6%)	136(18.1%)	
Secondary(6–12 y)	156(62.4%)	466(62.1%)	
High(> 12 y)	26(10.4%)	108(14.4%)	
Smoke status			0.967
Yes	25(10.0%)	73(9.7%)	
No	220(88.0%)	636(84.8%)	
Alcohol drinking status			0.324
Yes	47(18.8%)	116(15.5%)	
No	199(79.6%)	593(79.1%)	
BMI			< 0.001
Normal(≤ 24 kg/m ²)	10(4%)	306(40.8%)	
Overweight(24–28 kg/m ²)	134(53.6%)	319(42.5%)	
Obesity(> 28 kg/m ²)	106(42.4%)	125(16.7%)	
SBP			< 0.001
Normal(< 140mmHg)	67(26.8%)	537(71.6%)	
High(≥ 140mmHg)	183(73.2%)	213(28.4%)	
Continuous, mmHg	149(138–158)	134(125–141)	< 0.001
DBP			< 0.001
Normal(< 140mmHg)	188(75.2%)	668(89.1%)	

Data are presented as median (interquartile range) for continuous variables with non-normal distributions or participants (percentage) for categorical variables.

P* for difference between groups was tested by chi-square and Wilcoxon rank sum test, respectively.

Characteristics	Case(n = 250)	Control(n = 750)	P*
High(≥ 140 mmHg)	62(24.8%)	82(10.9%)	
Continuous, mmHg	82(75–89)	77(70–84)	< 0.001
FPG			< 0.001
Normal(< 6.1mmol/L)	51(20.4%)	562(74.9%)	
High(≥ 6.1 mmol/L)	199(79.6%)	188(25.1%)	
Continuous, mmol/L	6.99(6.20–8.83)	5.51(5.10–6.11)	< 0.001
TG			< 0.001
Normal(< 1.7mmol/L)	55(22.0%)	578(77.1%)	
High(≥ 1.7 mmol/L)	195(78.0%)	172(22.9%)	
Continuous, mmol/L	2.23(1.74–2.82)	1.19(0.84–1.64)	< 0.001
TC			0.284
Normal(< 5.18mmol/L)	83(33.2%)	222(29.6%)	
High(≥ 5.18 mmol/L)	167(66.8%)	528(70.4%)	
Continuous, mmol/L	5.94(4.96–7.12)	5.95(4.97–6.83)	0.431
LDL-C, mmol/L	2.92(2.35–3.56)	2.85(2.32–3.36)	0.155
HDL-C, mmol/L	1.95(1.58–2.34)	1.92(1.61–2.23)	0.261
Total energy intake, kcal	1762.19(1515.78-2028.13)	1776.72(1514.85-2103.78)	0.534
Proteins, kcal	224.08(182-273.6)	242.88(190.4-297.04)	0.044
Carbohydrates, kcal	842.24(699.04–998.2)	857.9(681.88-1034.36)	0.441
Fats, kcal	680.31(584.64-800.91)	669.56(558.09-806.94)	0.311
Data are presented as median (interquartile range) for continuous variables with non-normal distributions or participants (percentage) for categorical variables.			
P* for difference between groups was tested by chi-square and Wilcoxon rank sum test, respectively.			

The associations between the skeletal muscle mass and MetS risk are listed in Table 2. By using conditional logistic regression analyses, leg muscle mass index (LMI) (OR = 0.13; 95%CI: 0.07, 0.24; P for trend < 0.001), trunk muscle mass index (TMI) (OR = 0.16; 95%CI: 0.09, 0.29; P for trend < 0.001), skeletal muscle mass index (SMI) (OR =

Table 2
Odds ratios with 95% confidence interval for MetS by quintile of relative skeletal muscle mass

	Quintiles of muscle mass					P
	Q1	Q2	Q3	Q4	Q5	
AMI						
Range	< 0.0651	0.0651–0.0706	0.0706–0.0769	0.0769–0.0855	≥ 0.0855	
Case/Control	54/146	40/150	63/137	43/157	40/160	
Crude OR(95%CI) ^a	1(Ref.)	0.87(0.56, 1.37)	1.11(0.70, 1.76)	0.57(0.33, 0.98)	0.50(0.28, 0.89)	0.044
Adjusted OR(95%CI) ^b	1(Ref.)	0.63(0.29, 1.36)	0.68(0.31, 1.48)	0.40(0.16, 1.01)	0.41(0.16, 1.04)	0.067
LMI						
Range	< 0.1891	0.1891–0.2063	0.2063–0.2232	0.2232–0.2464	≥ 0.2464	
Case/Control	74/126	58/142	61/149	30/170	27/173	
Crude OR(95%CI)	1(Ref.)	0.58(0.37, 0.91)	0.51(0.32, 0.81)	0.18(0.10, 0.31)	0.13(0.07, 0.24)	< 0.001
Adjusted OR(95%CI)	1(Ref.)	0.40(0.18, 0.87)	0.57(0.27, 1.24)	0.16(0.06, 0.37)	0.12(0.05, 0.32)	< 0.001
TMI						
Range	< 0.2883	0.2883–0.3047	0.3047–0.3207	0.3207–0.3456	≥ 0.3456	
Case/Control	72/127	61/140	54/146	37/163	26/174	
Crude OR(95%CI)	1(Ref.)	0.70(0.46, 1.09)	0.50(0.32, 0.79)	0.27(0.16, 0.46)	0.16(0.09, 0.29)	< 0.001
Adjusted OR(95%CI)	1(Ref.)	0.50(0.23, 1.07)	0.45(0.21, 0.97)	0.22(0.09, 0.54)	0.11(0.04, 0.29)	< 0.001
SMI						

CI = Confidence interval, OR = Odds ratio, Ref = Reference.

^aCrude OR was estimated in initial conditional logistic regression model.

^bAdjusted OR was estimated in a multivariate-adjusted conditional logistic regression model adjusted for age, duration of education, smoking status, alcohol drinking status, physical activity, total energy intake, proteins, fats, carbohydrates, serum fasting glucose and lipid profiles.

	Quintiles of muscle mass					P
	Q1	Q2	Q3	Q4	Q5	
Range	< 0.3484	0.3484–0.3744	0.3744–0.4020	0.4020–0.4397	≥ 0.4397	
Case/Control	67/133	60/140	61/139	32/168	30/170	
Crude OR(95%CI)	1(Ref.)	0.75(0.48, 1.16)	0.69(0.44, 1.08)	0.27(0.16, 0.46)	0.21(0.12, 0.38)	< 0.001
Adjusted OR(95%CI)	1(Ref.)	0.39(0.18, 0.84)	0.41(0.19, 0.91)	0.21(0.08, 0.52)	0.11(0.04, 0.29)	< 0.001
CI = Confidence interval, OR = Odds ratio, Ref = Reference.						
^a Crude OR was estimated in initial conditional logistic regression model.						
^b Adjusted OR was estimated in a multivariate-adjusted conditional logistic regression model adjusted for age, duration of education, smoking status, alcohol drinking status, physical activity, total energy intake, proteins, fats, carbohydrates, serum fasting glucose and lipid profiles.						

0.21; 95%CI: 0.12, 0.38; *P* for trend < 0.001) and arm muscle mass index (AMI) (OR = 0.50; 95%CI: 0.28, 0.89; *P* for trend = 0.044) were inversely associated with MetS risk when comparing the upper quintile with the lowest quintile. After adjusting for potential confounders, these associations only remained significant for LMI (OR = 0.12; 95%CI: 0.05, 0.32; *P* for trend < 0.001), TMI (OR = 0.11; 95%CI: 0.04, 0.29; *P* for trend < 0.001) and SMI (OR = 0.11; 95%CI: 0.04, 0.29; *P* for trend < 0.001) with MetS risk, respectively. By using restricted cube model, significant linear relationships were observed between LMI (*P* for non-linearity = 0.8928, *P* for linearity < 0.001), TMI (*P* for non-linearity = 0.2434, *P* for linearity < 0.001) and SMI (*P* for non-linearity = 0.2879, *P* for linearity < 0.001) and MetS risk, and these associations are presented in Fig. 1–3. Dose-response analysis indicated that per standard deviation increment of LMI, TMI and SMI were associated with 55% (95%CI: 0.34, 0.58; *P* for trend < 0.001), 61% (95%CI: 0.28, 0.53; *P* for trend < 0.001) and 71% (95%CI: 0.19, 0.43; *P* for trend < 0.001) reduction of MetS risk, respectively (Fig. 1–3).

Discussion

On the basis of present study, higher TMI, LMI and SMI were associated with a lower prevalence of MetS after adjustment for confounding factors. However, even non-significant association was found between AMI and MetS. The findings of this study supported the hypothesis that lower muscle mass was positively associated with MetS risk, and that different regions of muscle mass might perform different physiological functions.

Three studies have investigated the association between region muscle and MetS (two for trunk muscle and one for arm and leg muscle). Of these, two studies were conducted in Japan showed that trunk

muscle quality as well as quantity were associated with MetS, however, the cross-sectional area of trunk skeletal muscle was only evaluated by computed tomography at the third lumbar vertebrae [17, 18]. In addition, a low arm and leg muscle mass to body weight ratio was associated with a higher prevalence of MetS after adjusting for age, physical activity, frequency of smoking, and frequency of alcohol consumption in the Korea National Health and Nutrition Examination Survey [19]. Previous epidemiological studies in other countries have assessed the relationship between skeletal muscle and MetS, but these studies focused on cross-sectional studies in adults. Therefore, this study was first to comprehensively investigate regional skeletal muscle mass and MetS risk in a case-control study among Chinese elders. Consistent with previous studies, the results had also reported similar associations of TMI and LMI with MetS risk, indicating that low muscle mass was strongly associated with MetS risk [17, 18, 20]. However, our finding did not support that AMI was an independent risk factor for MetS, as compared with previous study [19]. Additionally, no studies had investigated the relationship between total skeletal muscle mass and MetS.

Skeletal muscle is a primary tissue responsible for insulin-mediated glucose disposal. However, individuals tend to gradually lose muscle mass in older adulthood, which contribute to problems associated with frailty or sarcopenia [21]. Insulin resistance was regarded as a central link in the development of MetS. Decrease in glucose uptake caused by the loss of skeletal muscle mass might result in insulin resistance. Low muscle mass may increase the risk of MetS through several mechanisms as follows: 1) Mitochondria converts energy stored in nutrients to adenosine triphosphate (ATP) through oxidative phosphorylation. Thus, the number and function of mitochondria are major determinants of glucose and lipid oxidation in skeletal muscle [22]. However, the progression of metabolic disease was associated with a decline in mitochondrial functions of skeletal muscle through oxidative stress and lipid peroxidation [23]. Similarly, observed by electron microscopy, muscle mitochondria from patients with type 2 diabetes were smaller in size compared with controls [24]. 2) Central obesity was one of the characteristics of metabolic syndrome. In addition, as muscle mass decreases, older people tend to have a higher fat mass. The infiltration of fat into muscle causes muscle inflammation, leading to increased secretion of pro-inflammatory factors such as interleukin 1, interleukin 6 and tumor necrosis factor [25]. The pro-inflammatory factors can negatively affect skeletal muscle by stimulating muscle protein degradation, resulting in muscle atrophy and reduced muscle protein synthesis, ultimately leading to insulin resistance [26].

This study has several strengths to be highlighted. First, this is the first to investigate the associations between regional skeletal muscle and MetS risk among Chinese elders, suggesting that different parts of the muscle perform differential physiological functions. Second, the community-based case-control design was reliable compared with the hospital-based case-control design, because the participants represented general population. Simultaneously, the limitations of this study should be considered. First, the potential confounding factors cannot be identified and adjusted, and that might mask the true relationship by using case-control design. Hence, additional prospective longitudinal studies are worthy to obtain a reliable relationship between regional skeletal muscle mass and MetS risk. In addition, the error of recall bias was inevitable. Second, only the relationship between muscle mass and MetS was studied

in this study, but the function of skeletal muscle (grip strength, gait speed) was not explored. In future studies, skeletal muscle mass and its function can be combined to explore their correlation with MetS. Third, this study included the elders aged 65 years and above, so the current results cannot be generalized to the entire Chinese population. Fourth, although demographic characteristics, multiple lifestyles, and clinical factors were adjusted to reduce potential confounding factors, we cannot rule out the possibility of residual confounding caused by inaccurate or unmeasured risk factors.

Conclusion

The present results provide substantial evidence that higher trunk muscle, leg muscle, and total skeletal muscle mass are associated with a lower risk of MetS. Therefore, interventions to maintain and build muscle mass and strength will contribute to achieve the goal of reducing the risk of MetS in Chinese elders.

Abbreviations

MetS: Metabolic Syndrome; LMI: Leg Muscle Mass Index; TMI: Trunk Muscle Mass Index; SMI: Skeletal Muscle Mass Index; AMI: Arm Muscle Mass Index; NCEP ATP III: The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III); IDF: International Diabetes Federation; CDS: The Chinese Medical Association; SD: Standard Deviation; IQR: Interquartile Range; ATP: Adenosine Triphosphate; BMI = Body mass index, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, FBG = Fasting blood glucose, TG = Triglyceride, TC = Total cholesterol, LDL-C = Low density lipoprotein cholesterol, HDL-C = High density lipoprotein cholesterol; CI = Confidence interval, OR = Odds ratio, Ref = Reference.

Declarations

Ethics approval and consent to participate

The study was carried out in line with the Declaration of Helsinki. All study participants provided written informed consent. This study was approved by the Ethics Committee of Qingdao University Affiliated Hospital, Qingdao, China (QYFY WZLL 25548).

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests whether financial and nonfinancial.

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Authors' contributions: TY and XFG contributed to data collection, data analysis and writing manuscript. CW and TZ participated in the collection of anthropometric parameters and body composition data. DL and XFG conceived and designed the research, and contributed to reviewing or revising the paper. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

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Figures

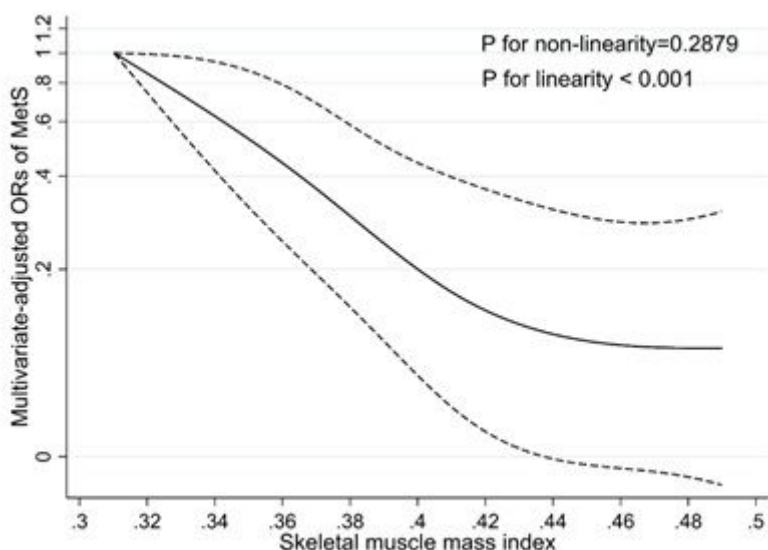


Figure 1

Examination of the dose-response relationship between SMI and MetS by restricted cubic splines model. The solid line and dashed line represent the estimated ORs and the corresponding 95% CIs, respectively. OR, odds ratio; CI, confidence interval.

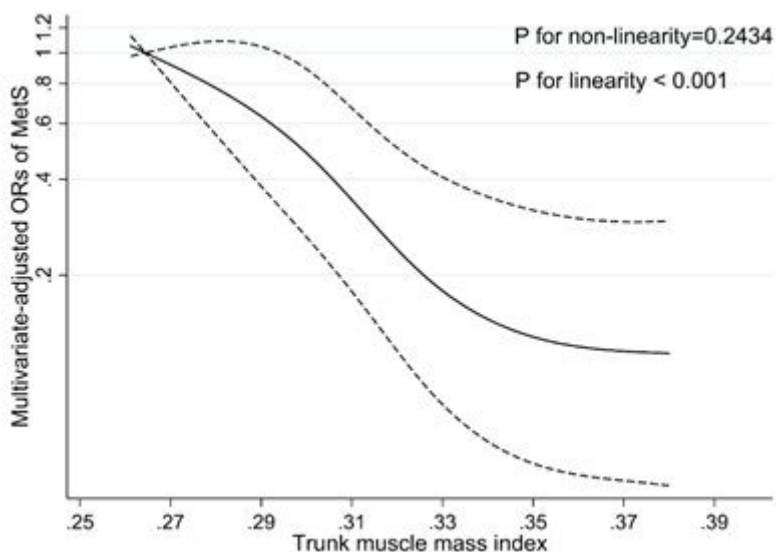


Figure 2

Examination of the dose-response relationship between TMI and MetS by restricted cubic splines model. The solid line and dashed line represent the estimated ORs and the corresponding 95% CIs, respectively. OR, odds ratio; CI, confidence interval.

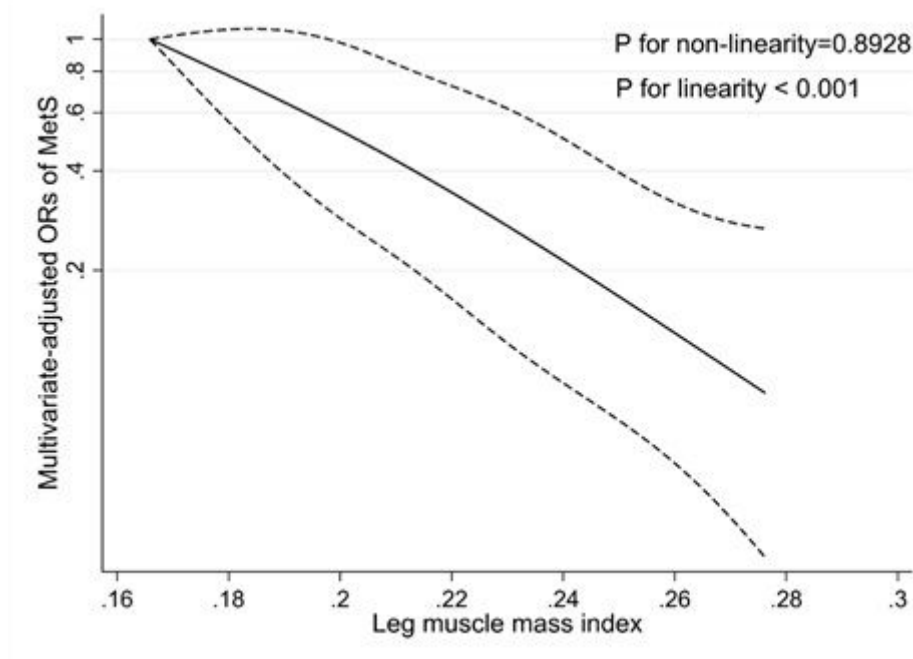


Figure 3

Examination of the dose-response relationship between LMI and MetS by restricted cubic splines model. The solid line and dashed line represent the estimated ORs and the corresponding 95% CIs, respectively. OR, odds ratio; CI, confidence interval.