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Association between Skeletal Mass Indices and Metabolic Syndrome in Brazilian Adults

Cristiane Junqueira de Carvalho,[1,2,] Giana Zarbato Longo,[2] Adriana Maria Kakehasi,[3] Patrícia Feliciano Pereira,[2] Kátia Josiany Segheto,[2] Leidjaira Lopes Juvanhol,[2] and Andréia Queiroz Ribeiro[2]*

[1] Department of Medicine and Nursing, Federal University of Viçosa (UFV), Viçosa, Minas Gerais, Brazil; [2] Postgraduate Program in Nutrition Science, Department of Nutrition and Health, Federal University of Viçosa (UFV), Viçosa, Minas Gerais, Brazil; and [3] Department of the Locomotor Apparatus, Medical School, Federal University of Minas Gerais (UFMG), Belo Horizonte, Minas Gerais, Brazil

Abstract

Introduction: Skeletal muscle is the primary site of glucose uptake and its reduction would increase insulin resistance, which is a determinant factor for diseases such as type 2 diabetes mellitus, hypertension, and metabolic syndrome. However, the role of low skeletal muscle mass as a risk factor for metabolic syndrome and its association with cardiometabolic risk is still uncertain. We aimed to investigate the association between muscle mass (determined by different skeletal mass indices) and metabolic syndrome in Brazilian adults. *Methodology:* We conducted a cross-sectional population-based study with 689 adults of both sexes aged between 20 and 59 years. Data were collected through questionnaires and assessment of body composition through dual-energy X-ray absorptiometry and anthropometric, clinical, and biochemical measurements. *Results:* Older individuals, obese and those with metabolic syndrome predominated in the highest tertile of skeletal mass index adjusted by height (SMI_{height}), whereas using skeletal mass index adjusted by weight (SMI_{weight}) and skeletal mass index adjusted by body mass index (SMI_{BMI}) these individuals were the majority in the lowest tertile of these indices. In men and women, the adjusted logistic regression model revealed that the highest tertile of SMI_{weight} (odds ratio [OR]: 0.06; 95% confidence interval [CI]: 0.02–0.21 and OR: 0.27, 95% CI: 0.10–0.74) and SMI_{BMI} (OR: 0.14, 95% CI: 0.05–0.37 and OR: 0.34, 95% CI: 0.12–0.94) were negatively associated with metabolic syndrome. On the other hand, the highest tertile of SMI_{height} was positively associated with metabolic syndrome in both sexes (OR: 4.17, 95% CI: 1.80–9.66 and OR: 6.15, 95% CI: 2.31–16.37, respectively in men and women). *Conclusion:* In adults, the muscle mass assessed from the skeletal mass index adjusted for body weight and body mass index is inversely associated with metabolic syndrome in both sexes.

Key Words: body composition; DXA; metabolic syndrome; Sarcopenia; skeletal muscle.

Introduction

Metabolic syndrome (MetS) is cluster of metabolic conditions (abdominal obesity, high blood pressure, high glycemia, dyslipidemia) that increase the risk of cardiovascular diseases and type 2 diabetes mellitus (DM 2), thus increasing morbidity and mortality in adults and older people *(1,2)*. MetS prevalence is increasing around the world and

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*Address correspondence to: Cristiane Junqueira de Carvalho, MD, Phd, Rua Joaquim Ferreira Coelho, 501, casa 192, Jardins do Vale, Viçosa, Minas Gerais CEP: 36570-460, Brazil. E-mail: cristiane.carvalho@ufv.br

sedentary lifestyle and central obesity are among the main modifiable risk factors associated with it (2,3).

Muscle mass loss has been observed with aging and has gained a lot of attention from the researches since the 1990s, when studies have related it to functional capacity reduction, physical frailty, falls, and fractures (4,5). Recently, studies have suggested the relationship between muscle mass deficit and cardiometabolic risk. This assumption is supported by the fact that skeletal muscle is the primary site of glucose uptake and its reduction would increase insulin resistance, which is a determinant factor for diseases such as DM 2, hypertension, and MetS (6–9). However, the role of low skeletal muscle mass as a risk factor for MetS and its association with cardiometabolic risk is still uncertain (10).

The increasing number of studies on body composition and the greater interest in understanding the role of lean mass in cardiometabolic diseases has contributed to dual-energy X-ray absorptiometry (DXA) to become the ideal technique to measure indices of body composition, including skeletal mass indices (SMI) (4,11–15).

In order to estimate these indices, several predictors are suggested, most of them using the appendicular lean mass (ALM) adjusted for height (4), weight, (11) or body mass index (BMI) (14).

Few studies have compared these indices for determining lean mass and most analyzed the outcomes of physical disability in older adults (16). Research with adults addressing the MetS, cardiometabolic or cardiovascular outcomes and muscle mass is uncommon and findings are divergent (1,7,16–18). To the best of our knowledge, no other studies have addressed this topic in the Brazilian population.

From the foregoing, therefore, the objective of the present study was to investigate the association between muscle mass (determined by different skeletal mass indices) and metabolic syndrome in Brazilian adults.

Materials and Methods

Subjects and Study Design

This cross-sectional population-based study was carried out in the urban area of the municipality of Viçosa-MG, with adults (20–59 years of age) of both sexes. Pregnant women, bedridden individuals, amputees, and those unable to undergo anthropometric or body composition measurements and having limitation to respond to the questionnaire were not included in the study.

The *OpenEpi* program was used for calculation of the sample, considering the following parameters: reference population of 43,431 people, 95% confidence level, expected prevalence of low lean mass of 15% (4), estimated sampling error of 3%, and effect of the estimated sampling design at 1.0. There was addition of 20% related to losses or refusals and 10% to control of confounding factors. The calculated final sample was 697 adults.

Probabilistic sampling was used without replacement, by double-stage clusters, with census sectors as the first-stage units and the households as the second-stage units. A total of 30 census sectors were selected from the 99 existing in the urban area of Viçosa-MG and in each of them the blocks were identified and numbered to establish the order of the start of the work. After exclude 22 individuals by technical problems in the analysis of the images, the final sample of the present study was composed of 689 individuals. The detailed methodology of the sampling process is described in an earlier publication (19).

This study was conducted according to the declaration of Helsinki. The current study was approved by The Research Ethics Committee of the Federal University of Viçosa (Official Letter 02/2013). An informed written consent was obtained from the subjects.

Study Variables

Socio-demographic Variables, Health Conditions, and Lifestyle

All of the participants underwent a structured interviewer-administered questionnaire about health conditions, current medication use and menstrual history, as well as sociodemographic data and lifestyle, such as age (years), skin color (white and non-white), sex (female and male), marital status, smoking status (never smoker, current smoker, and former smoker) and alcohol consumption (drinks per week: 0; 1–7;> 8) (20).

The International Physical Activity Questionnaire (IPAQ), version-6, long form (21) was used to assess the level of leisure-time physical activity. Leisure-time physical activity was determined from the time spent with leisure physical activities in a normal week (fourth domain). Individuals who scored ≥ 150 min were classified as physically active and those who scored <150 min as insufficiently active or inactive (22).

Anthropometric, Clinical, and Body Composition Variables

Weight and height were measured with participants using as little clothing as possible and barefoot. BMI was calculated as weight (in kilograms) divided by the square of the height (in metres) (23). Waist circumference (WC) was measured in centimetres with an inelastic measuring tape at the mid-point between the last rib and the iliac crest. All antropometric measurements were performed in triplicate by one experienced examiner, considering the average values. Blood pressure (BP) was measured in duplicate, in the same upper arm, using an automatic insufflation blood pressure monitor. The first measure was obtained after 5 min rest and the second 15 min after the first measurement. The mean of the 2 measurements was considered for analysis.

Body composition was assessed by the DXA Lunar Prodigy Advance DXA System (GE Healthcare® Chicago, Illinois, EUA). All evaluations were performed by the same technician using the Incore Users Manual standard procedure. Using the ALM data, we obtained the SMI relative to

the height (SMI_{height}: ALM/height^2, as kg/m^2) as proposed by Baumgartner *(4);* the SMI relative to body weight (SMI_{weight}: ALM/weight × 100, as %) *(11);* and the SMI relative to BMI (SMI_{BMI}: ALM/BMI, as kg/kg/m^2) *(14).*

Biochemical Variables

Blood samples were collected after 12 h of fasting. Fasting glucose (FG) was determined by the enzymatic glucose-oxidase method. Total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) were measured by the enzymatic colorimetric method.

Metabolic Syndrome

MetS was defined in accordance with the harmonized criteria *(2)*. Participants were considered to have MetS when they presented 3 or more of the following components: WC > 90 cm for men and > 80 cm for women (based on recommended cut-off points for non-Europeans) *(24)*; TG ≥ 150 mg/dl or drug treatment for elevated TG; HDL-C < 40 mg/dl for men and < 50 mg/dL for women or drug treatment for reduced HDL-C; elevated BP (systolic BP ≥ 130 mmHg and/or diastolic BP ≥ 85 mmHg) or antihypertensive drug treatment and FG ≥ 100 mg/dl or drug treatment for elevated glucose.

Statistical Analysis

Descriptive analysis was presented as mean ± standard deviation (SD) for continuous variables, and frequency (percent) for categorical variables, after testing the normal distribution of the variables with the Shapiro-Wilk test, skewness coefficient, and graphical analysis. Differences between sexes and between the presence or absence of alterations metabolic were analyzed using Student's *t* test for continuous variables, and Pearson's chi-square for categorical variables. One-factor analysis of variance was used to compare the means of the variables between the tertiles of SMI (with Bonferroni post-hoc test).

Bivariate logistic regression was used to estimate the association between each SMI (independent variable) and MetS (dependent variable). Adjustment variables (age, schooling, marital status, alcohol consumption, smoking, leisure-time physical activity, and menopausal status) were considered for the multivariable regression after bivariate analysis and analysis of clinical/epidemiological relevance. Men and Women were analyzed separately. It was decided to analyze SMI in tertiles due to the lack of a cutoff point in this population and the little explanatory power of it in a continuous way. The same adjustment variables were chosen to favor the comparability of results between the different indices. Odds ratio (OR) with 95% confidence interval (95% CI) was used as a measure of association. The Hosmer and Lemeshow test and the likelihood ratio test were used to verify the fit of the final model. For the first test a p value of > 0.05 indicated a good fit of the model, and, for the second test, a p value < 0.05 indicated that the explanatory variable significantly predicts the dependent variable.

Statistical significance was analyzed by using STATA 13.1 statistical program at 5% significance level.

Results

Table 1 shows the sample characteristics according to sex. Men were significantly younger (34.4 vs 37.3 years), often white and with higher schooled. Men had a higher frequency of alcohol consumption per week and a higher prevalence of overweight (38.0% vs 25.5%). The prevalence of obesity was higher in women than in men (16.7% and 10.8%, respectively) and the prevalence of MetS was 21.9% among men and 20.3% among women. Women had the lowest means of the 3 SMI assessed (p < 0.001).

Tables 2 and 3 present the characteristics of men and women according to the skeletal mass indices tertiles.

The analysis of SMI_{height} showed that the highest tertile of women and men contained the oldest individuals, the majority of the obese individuals, and those with MetS. Individuals with higher schooling predominated in the lowest tertile. Among women, those with partners predominated in the highest tertile.

In contrast, the analysis of SMI_{weight} and SMI_{BMI} for both sexes showed that the oldest, obese, and MetS subjects predominated in the lowest tertile. For women, those with higher schooling predominated in the 2 highest tertiles of these indices. In the highest tertile of SMI_{weight} and SMI_{BMI}, the majority of the subjects assessed of both sexes had no partners.

The level of physical activity and alcohol consumption were not significantly different between the SMI tertiles, but in both men and women a large proportion of the active individuals were in the group with the highest values of SMI_{weight} and SMI_{BMI}. With regard to smoking, nonsmokers were predominant in the highest tertile of SMI_{weight} and SMI_{BMI}, for both sexes and among women, respectively.

Menopausal women were prevalent in the group with the lowest SMI_{weight} and SMI_{BMI}, whereas the analysis of SMI_{heght} showed that most of them were among the highest value of this index.

Figs. 1 and 2 shows the means and the confidence intervals for the SMI according to the presence of MetS and its components in men and women, respectively. In both sexes, the highest means of SMI_{weight} and SMI_{BMI} were observed among subjects without MetS and their components. On the other hand, the analysis of SMI_{heght} showed that their means were higher in the presence of MetS and its components.

Crude odds ratios, adjusted odds ratios and their respective 95% confidence intervals for the association between the SMI tertiles and MetS are presented in Table 4. In men and women, the adjusted model showed that the highest tertile of SMI_{weight} (OR: 0.06; 95% CI: 0.02−0.21 and OR: 0.27, 95% CI: 0.10−0.74) and SMI_{BMI}

Table 1
Characteristics of women and men who participated in the study. Viçosa, MG, Brasil, 2012−2014.

Variable	Total	Men	Women	*p* value
Sex		43,8	56,1	
Age (years)	36.1 ± 12.2	34.4 ± 11.9	37.3 ± 12.3	<0.01
Skin color				<0.05
White	41.6	46.7	37.7	
Non-white	58.4	53.3	62.3	
Menopause				
Not	——	——	73.6	
Yes			26.4	
Marital status				0.49
Without partner	52.8	54.3	51.7	
With partner	47.2	45.7	48.3	
Schooling (years)	11.7 ± 4.4	12.2 ± 4.4	11.3 ± 4.4	<0.01
LTPA				0.73
Active	29.5	30.1	28.9	
Inactive	70.5	69.9	71.1	
Smoking				0.25
Never smoker	71.1	68.2	73.4	
Current smoker	12.2	14.2	10.6	
Former smoker	16.7	17.6	16.0	
Alcohol use (drinks/week)				<0.01
0	47.9	29.8	62.0	
1−7	40.9	50.3	33.6	
≥8	11.2	19.9	4.4	
Metabolic syndrome				0.60
Not	79.0	78.1	79.7	
Yes	21.0	21.9	20.3	
Nutritional status				<0.01
Eutrophy	54.9	51.2	57.8	
Overweight	31.0	38.0	25.5	
Obesity	14.1	10.8	16.7	
SMI_{height} (kg/m^2)	7.1 ± 1.3	8.2 ± 0.9	6.2 ± 0.8	<0.001
SMI_{weight} (%)	28.7 ± 5.0	33.0 ± 3.8	25.4 ± 3.1	<0.001
SMI_{BMI} ($Kg/m^2/m^2$)	0.8 ± 0.2	1.0 ± 0.1	0.6 ± 0.1	<0.001

Values are means ± standard deviation or proportion (%).
Abbr: LTPA, leisure-time physical activity; SMI, skeletal mass index; BMI, body mass index.

(OR: 0.14, 95% CI: 0.05−0.37 and OR: 0.34, 95% CI: 0.12−0.94) were negatively associated with MetS, when compared to the lowest tertile of these indices. On the other hand, the highest of SMI_{height} was positively associated with MetS in both sexes (OR: 4.17, 95% CI: 1.80-9.66 and OR: 6.15, 95% CI: 2.31−16.37, respectively in men and women).

Discussion

This population-based study compared 3 SMI in relation to their association with MetS. The main findings show that the muscle mass evaluated from the ratio of ALM to body weight and to BMI was significantly and inversely associated with MetS, corroborating with evidence of the protective role of muscle mass in metabolic disorders *(6−9)*. Conversely, the study found a direct association when the index that relates ALM to height was considered.

Tertiles of SMI were used to examine the difference between the 3 indices most commonly used in the assessment of lean mass and to identify which best relates to MetS. Our findings showed that, using the initially proposed method of muscle mass analysis *(4)*, which adjusts ALM to height, the majority of obese and overweight individuals were in the highest tertile of SMI_{height}. This result suggests that this index may have overestimated muscle mass in this portion of the sample, since it does not consider the fat mass in its adjustment *(25)*. This fact may make it impossible the identification of individuals

Table 2
Distribution of socio-demographic and lifestyle, nutritional status and metabolic syndrome, according to SMI tertiles for men. Viçosa, MG, Brasil, 2012−2014, n = 302.

	T1	T2	T3	T1	T2	T3	T1	T2	T3
Age (years)	33.3 ± 11.9	34.3 ± 11.9	35.7 ± 11.9	38.2 ± 12.2 **	35.0 ± 11.5	30.1 ± 10.6	39.3 ± 11.7 **	34.8 ± 12.1	29.2 ± 9.7
Skin color									
White	36.8*	36.8	26.2	33.3	32.6	34.0	31.9	32.6	35.4
Non-white	29.8	30.4	39.7	32.9	34.1	32.9	33.5	34.7	31.6
Marital status									
Without partner	35.4	36.6	28.0	26.8 **	31.1	42.0	22.5 **	33.5	43.9
With partner	30.4	29.7	39.9	40.5	36.2	23.1	44.9	34.0	21.0
Schooling (years)	12.7 ± 4.5*	12.6 ± 4.4	11.2 ± 4.2	12.2 ± 4.7	12.0 ± 4.3	12.2 ± 4.1	11.4 ± 5.0	12.3 ± 4.5	11.8 ± 3.6
LTPA									
Active	36.2	30.7	32.9	30.7	30.7	38.4	34.0	25.3	40.6
Inactive	31.7	34.6	33.6	34.1	34.6	31.2	32.2	37.4	30.3
Smoking									
Never smoker	35.4	33.5	31.0	32.5*	30.5	36.8	29.6 **	35.4	34.9
Current smoker	34.8	32.5	32.5	20.9	48.8	30.2	20.9	44.1	34.8
Former smoker	22.6	33.9	43.4	45.2	32.0	22.6	54.7	18.8	26.4
Alcohol use (drinks/week)									
0	33.3	30.0	36.6	35.5	27.7	36.6	33.3	36.6	30.0
1−7	36.8	34.2	28.9	30.2	34.2	35.5	30.9	32.2	36.8
≥8	23.3	36.6	40.0	36.6	40.0	23.3	36.6	33.3	30.0
Nutritional status									
Eutrophy	50.9 **	34.4	14.5	13.9 **	33.1	52.9	15.8 **	37.7	46.3
Overweight	13.3	39.2	47.3	46.4	40.1	13.3	44.6	33.0	22.3
Obesity	3.13	15.6	81.2	84.3	15.6	0	75.0	25.0	0
MetS	18.4 **	30.7	50.7	66.1 **	27.6	6.1	61.5 **	29.2	9.2

Values are means ± standard deviation or proportion (%).
Abbr: SMI, skeletal mass index; BMI, body mass index; SD, standard deviation; LTPA, leisure-time physical activity; MetS, metabolic syndrome. Tertiles: SMI_{height} Kg/m^2 (T1: < 7.89; T2: 7.90−8.63; T3: 8.64−12.27) SMI_{weight} % (T1: < 31.37; T2: 31.38−34.61; T3: 34.62−42.59) SMI_{BMI} $kg/m^2/m^2$ (T1: < 0.93; T2: 1.05, T3: 1.06−1.48) p (one-way analysis of variance or Pearson's chi-square test): * < 0.05, ** < 0.01.

Table 3
Distribution of socio-demographic and lifestyle, nutritional status and metabolic syndrome, according to SMI tertiles for women. Viçosa, MG, Brasil, 2012–2014, n = 387.

	T1	T2	T3	T1	T2	T3	T1	T2	T3
Age (years)	33.4 ± 11.8**	38.4 ± 12.6	40.2 ± 11.7	42.6 ± 10.5 **	37.2 ± 12.1	32.2 ± 12.1	44.6 ± 9.9 **	36.2 ± 12.0	31.4 ± 11.3
Skin color									
White	39.0	31.5	29.4	34.9	28.7	36.3	33.5	30.1	36.3
Non-white	29.8	34.4	35.6	32.3	36.1	31.5	32.7	35.2	31.9
Menopause									
Not	39.1*	28.9	31.8	25.3**	34.2	40.4	21.2**	37.5	41.2
Yes	21.5	39.7	38.6	52.2	31.8	15.9	59.0	28.4	12.5
Marital status									
Without partner	39.5*	32.0	28.5	24.5**	30.5	45.0	23.5**	31.5	45.0
With partner	26.7	34.7	38.5	42.7	36.3	20.8	43.3	35.2	21.3
Schooling (years)	13.0 ± 3.6**	10.9 ± 4.5	10.0 ± 4.6	10.0 ± 4.7 **	11.3 ± 4.5	12.6 ± 3.7	9.5 ± 4.6 **	11.4 ± 4.5	13.0 ± 3.3
LTPA									
Active	35.7	38.3	35.8	30.3	31.2	38.3	36.9	29.4	36.6
Inactive	32.3	31.2	36.3	34.5	34.1	31.2	32.7	34.9	32.3
Smoking									
Never smoker	38.7**	33.1	28.1	28.5**	35.5	35.9	29.5	33.4	36.9
Current smoker	24.3	41.4	34.1	46.3	17.0	36.5	39.0	29.2	31.7
Former smoker	14.5	29.0	56.4	46.7	36.8	19.3	45.1	35.4	19.3
Alcohol use (drinks/week)									
0	32.0	32.5	35.4	31.6	37.5	30.8	34.1	33.3	32.5
1-7	36.1	33.0	30.7	34.6	26.1	39.2	30.7	33.8	35.3
≥8	29.4	47.0	23.5	47.0	29.4	23.5	35.2	29.4	35.2
Nutritional status									
Eutrophy	47.4**	38.5	13.0	11.1**	39.0	49.7	14.8**	35.8	49.3
Overweight	13.6	37.8	48.4	62.1	30.5	7.3	56.8	32.6	10.5
Obesity	1.6	9.6	88.7	74.1	24.1	1.6	67.7	29.0	3.23
MetS	10.2**	33.3	56.4	53.8**	35.9	10.2	55.1**	34.6	10.2

Values are means ± standard deviation or proportion (%).
Abbr: SMI, skeletal mass index; BMI, body mass index; SD, standard deviation; LTPA, leisure-time physical activity; MetS, metabolic syndrome. Tertiles: SMI_{height} Kg/m^2 (T1: < 5.77; T2: 5.78–6.49; T3: 6.50–10.74) SMI_{weight} (T1: < 23.92; T2: 23.93–26.89; T3: 26.90–36.09) SMI_{BM} $Kg/m^2/m^2$ (T1: < 0.60; T2: 0.61–0.69; T3: 0.70–1.02) p (one-way analysis of variance or Pearson's chi-square test): * < 0.05, ** < 0.01.

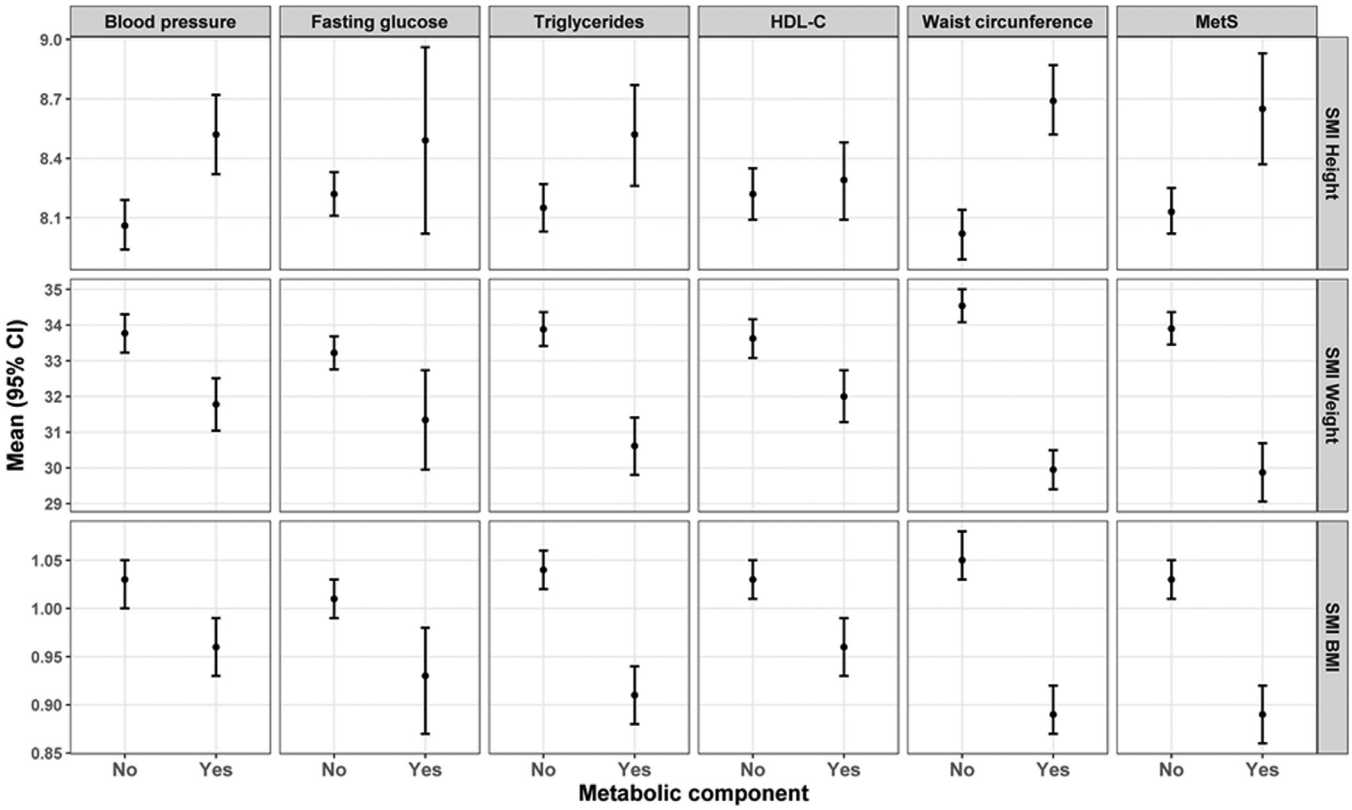

Fig. 1. Means and confidence intervals of SMI according to presence or absence of MetS and its components for men. Abbr: 95% CI, confidence interval; HDL-C, HDL cholesterol; MetS, metabolic syndrome; SMI, skeletal mass index; BMI, body mass index.

with higher risk of MetS associated with lower muscle mass in this population *(17)*.

In 2003, Newman and colleagues reported that, adjusting the ALM by height, more individuals with underweight and normal weight were classified as having low muscle mass than obese individuals. Therefore, they proposed adjusting the ALM for body fat and height, to better identify low muscle mass in overweight and obese individuals *(25)*. Overestimation of muscle mass in obese individuals is less likely when using the methods adjusted for body weight *(11)* and for BMI *(14)*. In this context, *two studies based on* the São Paulo Ageing & Health Study (SPAH) data with Brazilian elderly population, also identified that ALM should be adjusted for fat mass, since this definition has a higher sensitivity to recognize low muscle mass in obese individuals than the definition proposed by Baumgartner *(4,26,27)*.

In our study, in the adjusted logistic regression analysis, the muscle mass tertiles evaluated by SMI_{weight} and SMI_{BMI} had an inverse and significant association with MetS in both sexes. This finding are in agreement with previous international studies that analyzed the association and correlation between muscle mass and MetS or other cardiometabolic diseases, which demonstrated the superiority of SMI_{weight} and SMI_{BMI} in comparison with SMI_{height} for the identification of this inverse association *(18,28–30)*. A recent meta-analysis that included data from 12 studies (10 performed in Asia, one in North America, and one in Asia and Oceania) revealed that low muscle mass was positively associated with MetS in middle-aged and elderly nonobese individuals. It also showed that the most used method to define low muscle mass was SMI_{BMI}, as well as it was considered the best predictor of metabolic instability in this population *(1)*. Also, in australian adults, lower values of SMI_{BMI} were significantly associated with a higher likelyhood of MetS *(7)*.

A recent 7-year follow-up study with Korean subjects aged 20–80 years found that increasing muscle mass over the years (assessed by SMI_{weight}) had a protective effect against the development of MetS (*adjusted hazard ratio*[*AHR*] 0.87, 95% CI: 0.78–0.97) and this effect was not restricted to the older population. Protection was present at all ages, indicating the importance of muscle mass and its gain in young adults as well *(31)*. In this same study, the relationship between the baseline values of SMI_{weight} and SMI_{BMI} and the incidence of MetS was examined. Individuals in the highest tertile of these indices had a significant reduction in the incidence of MetS (*AHR* 0.60 and 0.71, 95% CI: 0.54–0.68 and 0.64–0.78, respectively).

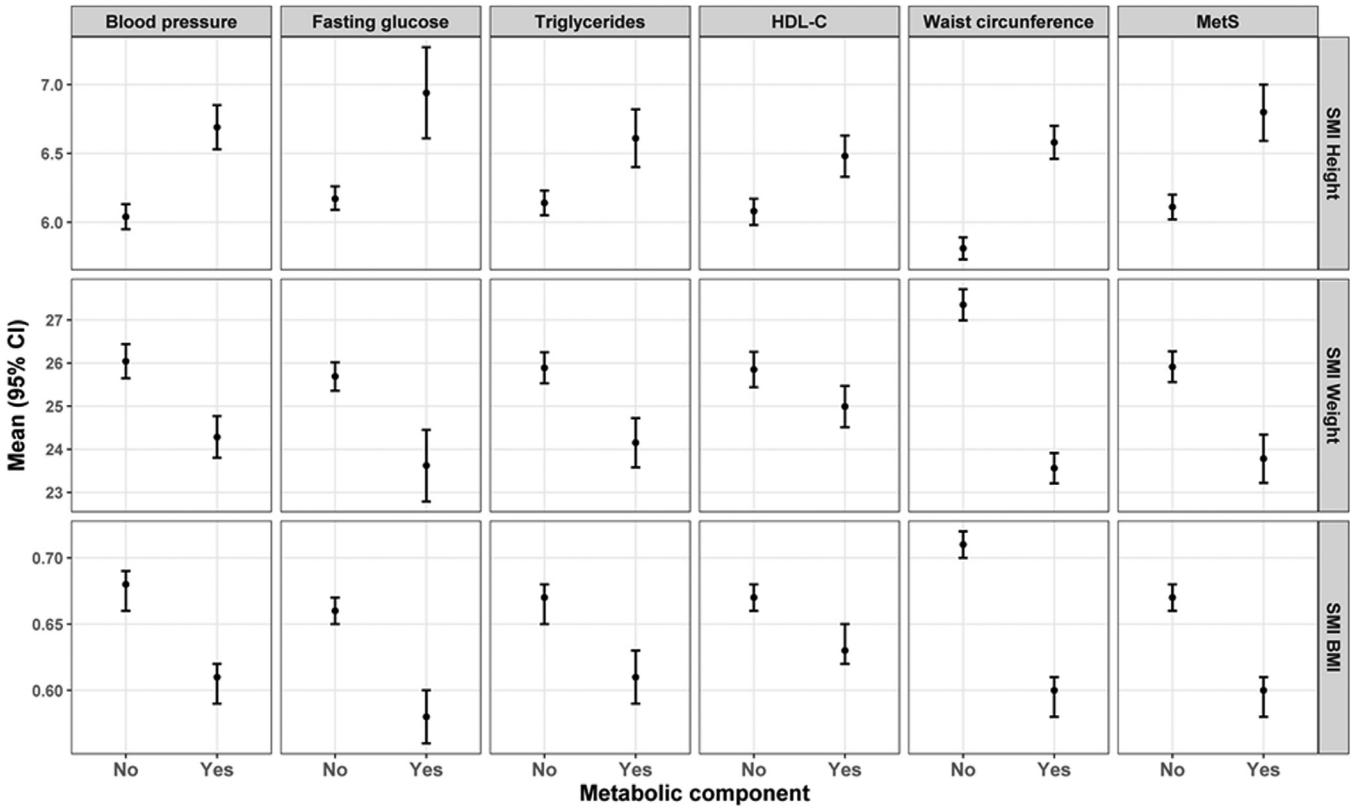

Fig. 2. Means and confidence intervals of SMI according to presence or absence of MetS and its components for women. Abbr: 95% CI, confidence interval; HDL-C, HDL cholesterol; MetS, metabolic syndrome; SMI, skeletal mass index; BMI, body mass index.

Table 4
Crude and adjusted model for the association between SMI tertiles and metabolic syndrome in adults. Viçosa, MG, Brasil, 2012–2014.

	MEN						WOMEN					
	Crude Model			Adjusted Model[a]			Crude Model			Adjusted Model[b]		
	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
SMI_{height}												
T1	1.00			1.00			1.00			1.00		
T2	1.83	0.84–3.99	0.12	1.71	0.71–4.07	0.22	3.75	1.62–8.65	<0.01	2.46	0.90–6.66	0.07
T3	3.62	1.73–7.55	<0.01	4.17	1.80–9.66	<0.001	7.68	3.44–17.18	<0.001	6.15	2.31–16.37	<0.001
SMI_{weight}												
T1	1.00			1.00			1.00			1.00		
T2	0.28	0.14–0.54	<0.001	0.28	0.14–0.59	0.001	0.58	0.33–1.01	0.05	0.89	0.44–1.78	0.75
T3	0.05	0.01–0.15	<0.001	0.06	0.02–0.19	<0.001	0.13	0.06–0.30	<0.001	0.27	0.10–0.74	0.01
SMI_{BMI}												
T1	1.00			1.00			1.00			1.00		
T2	0.33	0.17–0.62	<0.01	0.36	0.17–0.76	<0.01	0.52	0.30–0.92	0.02	1.10	0.54–2.21	0.78
T3	0.09	0.03–0.23	<0.001	0.14	0.05–0.37	<0.001	0.13	0.05–0.29	<0.001	0.34	0.12–0.94	<0.05

Abbr: OR, odds ratio; 95%CI, confidence interval; SMI, skeletal mass index.
[a]Model adjusted for age (years), schooling (years), marital status, leisure activity level, smoking, and alcohol consumption.
[b]Model adjusted for age (years), schooling (years), marital status, leisure activity level, smoking, alcohol consumption, and menopausal status.

Regarding SMI_{height}, similar to our study, a research with Caucasians and Asians also showed that muscle mass, when evaluated by this index, was directly associated with MetS. In addition, individuals with the lowest values of lean mass had lower values of FG, TG, and WC *(7,17)*. In the study with older German adults, the authors concluded that, when using SMI_{height}, overweight may make it impossible the early detection of inadequate muscle mass *(17)*.

Analyzing the components of the MetS separately, in both sexes, the means of SMI_{weight} and SMI_{BMI} were significantly lower in the presence of each of the metabolic alterations (central obesity, hypertriglyceridemia, low HDL-C, hypertension, or hyperglycemia) and in the presence of MetS when compared to individuals without their changes. In contrast, when the SMI_{height} was evaluated, the means were higher in the presence of metabolic changes. These findings reflect the direct association observed between SMI_{height} and MetS and the inversely between the indices adjusted for body weight and BMI and MetS.

Kim et al (2017) had already indicated the positive relationship between SMI_{height}, MetS components and BMI even after adjusting for sex and age, as well as the inverse relationship of several MetS components with SMI_{BMI} *(29)*. Likewise, a study on the prevalence of sarcopenic obesity and its association with MetS found that SMI_{height} was positively associated with BMI, visceral fat and insulin resistance, whereas SMI_{weight} correlated negatively with these factors *(28)*. This positive association of SMI_{height} has also been observed in a study with older Brazilian postmenopausal women, which did not show a favorable association between muscle mass evaluated by this index and lipid profile, glucose metabolism, and blood pressure *(12)*.

Several mechanisms may explain the relationship between muscle mass and metabolic profile. One of the most relevant of these is that the skeletal muscle is the most abundant insulin-sensitive tissue in our body and is the primary site of glucose utilization from the insulin-regulated glucose transporter (GLUT4), thus having a protective role against insulin resistance and DM 2 *(32–34)*. In addition, it is believed that myokine secretion, from the skeletal muscle mass, may also interfere positively in the prevention of insulin resistance and inflammation *(34)*.

A limitation of this study is the lack of data on muscle strength and physical performance, which made it impossible for us to assess the current definition of sarcopenia *(15),* and its relationship with MetS. In addition, the cross-sectional approach used does not allow us to draw a causal relationship between muscle mass and MetS. Finally, although our study was carried out with a representative sample of adults from a city of Minas Gerais, caution should be taken in extrapolating the results to the whole Brazilian population, taking into account the size of our country and the different characteristics of each region.

Despite these limitations, in the Brazilian population, there is no knowledge of population-based studies comparing the different indices of muscle mass assessment in relation to cardiometabolic diseases. As far as we aware, this is the first population-based study with Brazilian subjects that suggests that SMI adjusted for body weight or BMI are the most suitable for analyzing the association of lean mass with cardiometabolic risk in adults. Moreover, the SMI adjusted for body weight and BMI had the advantage of avoiding muscle mass overestimation in obese individuals, as is the case with SMI_{height}, making those indices ideal for the study of lean mass, especially in adults with higher degrees of adiposity.

The findings of this study indicate that the muscle mass assessed from the appendicular lean mass adjusted for weight and BMI is inversely associated with the metabolic syndrome in both sexes. Corroborating these results, when the components of MetS were considered separately, the muscle mass means assessed by these indices were lower in the presence of metabolic abnormalities. Additionally, SMI_{weight} and SMI_{BMI} proved to be more suitable for evaluating the association between muscle mass and cardiometabolic alterations.

Our data highlight the importance of body composition by DXA as a promising tool for the evaluation of muscle mass. Although a causal relationship with the MetS could not be established based on the present results, low SMI could be a potential therapeutic target for reducing adverse clinical outcomes in patients with cardiometabolic changes. Since muscle mass deficit is affected by multifactorial etiologies, a comprehensive multidisciplinary approach including both pharmacological and non-pharmacological interventions should be considered, like an exercise program and an adequate nutritional intervention to increase protein intake.

Data Availability Statement

Availability of data and materials data are from the "Estudo Sobre Saúde e Alimentação" (ESA). Data are available upon request to coordinators of the study – Giana Zarbato Longo (giana.zarbato@gmail.com).

Declaration of Competing Interest

The authors declare no conflict of interest.

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