Untangle the relationship of muscle mass and bone mineral content on handgrip strength: Results of ELSA-Brasil

Desvendando a relação entre massa muscular e conteúdo mineral ósseo na força de preensão palmar: Resultados do ELSA-Brasil

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Abstract *The study aims to investigate the independent association of muscle mass (MM) and bone mineral content (BMC) in the performance of the handgrip strength (HGS) test and whether there is effect modification by sex and age. In 12,491 participants from the ELSA-Brasil we estimated the associations between MM, BMC and HGS using linear regression models. All the analyses were performed for total population, also stratified for sex and age. For total population an interaction term was included between each explanatory variable of interest with sex and age to verify the presence of effect modification. We observed that the higher quintiles of MM and BMC were associated to an increasing in the mean of HGS compared to the first quintile, with greater magnitudes in men compared to women, also adults compared to elderly. When we estimated the independent effect of each exposure of interest, MM showed stronger effect in HGS in women, men and adults then BMC. In conclusion, we observed that higher amounts of MM and BMC are associated with higher HGS, regardless of sociodemographic characteristics, health conditions and lifestyle, with this effect being greater in men and adults.*

Key words *Muscle mass, Bone mineral content, Handgrip strength, Aging*

Resumo *O estudo tem como objetivo investigar a associação independente da massa muscular (MM) e conteúdo mineral ósseo (CMO) na realização do teste de força de preensão manual (FPM) e se há modificação do efeito por sexo e idade. Em 12.491 participantes do ELSA-Brasil estimamos as associações entre MM, CMO e FPM usando modelos de regressão linear. Todas as análises foram realizadas para a população total, também estratificada por sexo e idade. Para a população total foi incluído um termo de interação entre cada variável explicativa de interesse com sexo e idade para verificar a presença de modificação de efeito. Observamos que os maiores quintis de MM e BMC estiveram associados a um aumento na média da FPM em relação ao primeiro quintil, com maiores magnitudes em homens em relação a mulheres, também em adultos em relação a idosos. Quando estimamos o efeito independente de cada exposição de interesse, MM mostrou efeito mais forte na FPM em mulheres, homens e adultos do que BMC. Em conclusão, observamos que maiores quantidades de MM e BMC estão associadas a maior FPM, independentemente das características sociodemográficas, condições de saúde e estilo de vida, sendo esse efeito maior em homens e adultos.*

Palavras-chave *Massa muscular, Conteúdo mineral ósseo, Força de preensão manual, Envelhecimento*

Introduction

A low handgrip strength (HGS) in adulthood leads to a decrease in functional capacity in aging[1], expressed in the low performance in instrumental activities[2,3] and basic activities of daily living[2,3] and also greater incidences of chronic diseases[4,5] and general mortality[6]. The HGS evaluates the maximum strength that the individual can do with each hand using dynamometer equipment[7], which has the advantages of being simple, fast, and inexpensive[8]. HGS correlates with strength in other body compartments, being an alternative to complex arm and leg strength measurements[9].

Muscle mass (MM) and bone mineral content (BMC) are reached in adulthood and reflect the balance between acquisition, maintenance and loss throughout life[10,11]. This process is influenced by genetic factors, nutrient adequacy, physical exercises, chronic diseases and health behaviors[12].

Skeletal muscle and bone form a functional unit, which interact directly by the mechanical load of muscle contraction on the bone, and indirectly by the secretion of cytokines by the muscle which favor bone maintenance[13]. Previous evidence suggests an isolated relationship between low muscle mass[14-16] and bone mineral density (BMD)[17-19] and low HGS in adulthood, and this effect seems to be stronger with advancing age[17,20,21] and in women[7,21].

Thus, understanding how skeletal muscle and bone act independently on muscle strength can contribute to planning and early interventions that favor bone and muscle health throughout life. In addition, the relationship between muscle and bone mass in HGS in middle-aged and elderly adults seems to estimate whether they have reached the maximum power of development and, consequently, the risk of illness and mortality.

Dual-energy X-ray absorptiometry (DXA) is considered the standard method for detailed assessment of body composition, including bone mass and skeletal muscle mass[22-25]. However, its use in clinical practice has important limitations[22,23], which is why Bioimpedance (BIA) emerges as an alternative method for assessing body composition[26,27], showing evidence of good correlation with the values obtained by DXA[24,25,28,29].

Thus, the present study is innovative for covering a large sample of men and women, adults and elderly, and for investigating the effect of a life course marker, bone mass reserve, and the effect of a current health marker, muscle mass, muscle strength. In clinical practice, this can be useful, as the interpretation of the HGS test can explain the body composition conditions of individuals, allowing for more effective interventions. For public health, it can contribute to support actions and public policies that act throughout life in search of the promotion of healthy aging. Therefore, the objective of the present study is to verify the independent relationship between MM and BMC in the performance of the HGS test and whether this relationship is modified by sex and age.

Methods

Study population and design

This is a cross-sectional study, using data from participants in the second wave (2012-2014) of the Longitudinal Study on Adult Health (ELSA-Brasil), a multicenter cohort composed of 15,105 active and retired civil servants, aged between 35 and 74 years in the baseline (2008-2010), from higher education and research institutions located in six Brazilian cities (Belo Horizonte, Porto Alegre, Rio de Janeiro, São Paulo, Vitória, and Salvador). ELSA-Brasil was approved by the Ethics and Research Committees of the six participating institutions, and all participants signed an informed consent form. Details of the study design and characteristics of the cohort have been described in previous publications[30,31].

At the end of the second wave, complete follow-up information was available for 14,014 participants (203 deaths, 640 refusals, and 248 incomplete information). For the present analysis, participants who did not perform the HSG (n=747) and the measurement of body composition using electrical bioimpedance (n=776) were excluded, with 12,491 participants being eligible.

Hand grip strength

The response variable was the manual pressure force in kilogram-force (kgf), measured using a hydraulic manual dynamometer (Jamar; Sammons & Preston, USA) according to American Society of Hand Therapists (ASHT)[32]. The participants were instructed to perform the test while seated, with the spine erect, the arm extended along the trunk, the elbow flexed at 90º, the forearm supported on flat support up to the wrist. The participant was instructed to press the device all at once, with as much force as he could

when he heard the command: "STRENGTH" repeatedly for 3 to 4 seconds. The tester read the force to the nearest 1 Kg. Three measurements were performed on each hand alternately, and the highest of all was considered as the maximum force according to the universal standardization of the ASHT.

Muscle mass and bone mineral content

The amount of MM (kg) and BMC (kg) were determined by an electric bioimpedance device (BIA)[33] direct vertical segmental multi-frequency (InBody 230; BioSpace, Seoul, South Korea). MM and BMC information was obtained by the Lookin'Body LBM.1.2.0.16 software version. The participants were instructed to fast overnight for 12 to 15 hours, to empty their bladders previously, to abstain from strenuous exercise and alcoholic beverages 24 hours before the test, and not to use metallic accessories during the test.

Other variables

All the confounders included in this analysis were self-reported through standardized questionnaires or obtained through clinical procedures or laboratory exams measurements[30,34].

The following covariates were considered:

Sociodemographic variables: sex, age (continuous in years), educational attainment (university degree or more, complete high school, complete elementary school, or incomplete elementary school), and self-reported race/skin color (white, brown, black, Asian and Indians descendent and Brazilian indigenous defined in accordance with the Brazilian Institute of Geography and Statistics recommendation).

Health Behaviors: alcohol consumption (no use, moderate drinkers: <210 g of alcohol/week for men and <140 g of alcohol/week for women, and heavy drinkers: >210 g of alcohol/week for men and >140 g of alcohol/week for women)[35]; smoking, categorized as non-smokers (<100 cigarettes over a lifetime), ex-smokers (≥100 cigarettes over a lifetime), life and who no longer smokes) and current smoker (≥100 cigarettes throughout life and who still smokes)[30]; and leisure physical activity (mild: <600 MET-min/week, moderate: 600-3000 MET-min/week, vigorous: ≥3000 MET-min/week) obtained from the leisure-related domain in the long version of the International Physical Activity Questionnaire (IPAQ)[36] and categorized based on the sum of time in each type of activity performed. Alcohol consumption, smoking and physical inactivity are lifestyle factors that are known to influence bone and muscle mass status, and therefore will be considered in this analysis[12,37].

Health conditions: Body mass index (Normal weight: ≤25.0 kg/m², Overweight: ≥25 and ≤29,9 kg/m², Obesity: ≥30 kg/m²). Anthropometric - current weight (kg) being the measurement performed with the participant barefoot, fasting and wearing standard uniform on underwear; gauged by a Toledo® Model 2096PP electronic scale, with a capacity of 200 Kg and a precision of 50 g; current height (meters) measured using Seca® wall stadiometer, Hamburg, BRD, accurate to 1 mm and affixed to the wall; the participant remained supine, barefoot, leaning his head, buttocks and heels on the wall and with his gaze fixed on the horizontal plane and his height was verified during the inspiratory period of the breathing cycle[38,39]. The body mass index (BMI) was calculated as weight divided by height squared (kg/m²); depression symptoms (no and yes), defined as a score 12 obtained in by adapted Brazilian-Portuguese version of the Clinical Interview Schedule - Revised (CIS-R)[34]; and the number of chronic diseases (cardiovascular diseases, diabetes mellitus, hypertension, hypertriglyceridemia, categorized in 0, 1, 2, >3). The presence of cardiovascular disease was considered by the self-report of the following conditions: acute myocardial infarction, unstable angina, congestive heart failure, stroke, and myocardial revascularization. Diabetes was self-reported or based on use of oral hypoglycemic agents and/or insulin therapy, fasting plasma glucose ≥126 mg/dL, 2 hours post-prandial 75 g glucose test ≥200 mg/dL, or glycated hemoglobin ≥6.5%[40]. Hypertension was defined by systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, use of antihypertensive medication, or a previous medical diagnosis of hypertension[41]. For hypertriglyceridemia, the cut-off point for triglycerides (TG) was defined as adequate <150 mg/dL and inadequate ≥150 mg/dL[42], measured by the enzymatic colorimetric assay - glycerol phosphate peroxidase (ADVIA Chemistry; Siemens Healthcare Diagnostics Ltda., São Paulo Brazil).

Statistical analysis

The characteristics of the study population were presented using means (standard deviation - SD) for quantitative variables with normal distribution and absolute and relative frequencies for qualitative variables. The difference of the

means (SD) of HGS were presented according the quintiles of MM and BMC were estimated through Analysis of Variance (ANOVA) with a significance level of 95% (p-value<0,05).

The spearman correlation coefficients regarding the explanatory variables of interest were moderate (data not shown). We tested for possible multicollinearity between the variables included in the final multivariate model by calculating the variance inflation factor (VIF). In order to avoid multicolinearity between BMC and MM, for the regression analysis they were included in quintile.

Linear regression was used to investigate the associations between MM and BMC with performance in the HGS. The associations magnitudes were estimated by differences in means and their 95% confidence intervals. Initially, the association between exposures (BMC and MM) and the outcome (HGS) (Model 1) was estimated. Next, sequential adjustments were made, considering potential confounders including sociodemographic factors[14]: continuous age and self-reported race/color (Model 2), education (Model 3), as well as behaviors and health conditions[9,17]: alcohol consumption, smoking, physical activity (Model 4), BMI, depressive symptoms and the number of chronic diseases (Model 5). Afterwards, we further adjusted for the other exposures of interest (Model 6), whenever they were also associated with the response variable at the level of p<0.05 in Model 5. In order to test for possible heterogeneity in the effect of every variable of interest (BMC and MM) according to sex and age we created and added interaction terms to the final model (Models 5 and 6) for total population, retaining the ones that were statistically significant. All the analysis were performed for total population and stratified by sex (Women/Men) and age (<65/≥65 years old, since we observe effect modification between theses age groups in the multivariate analysis). Regression diagnostics were run to verify whether the full models violated the assumptions for linear regression (i.e., normality of error distribution, linearity, homoscedasticity). Analyzes were performed using Stata 13.0 (Stata Corporation, College Station, EUA).

Results

From of 12,491 individuals, the mean age was 55.56±8.95 years and most participants were women (54.48%). In total population, also strat-

ified by sex and age stratus, most self-reported the race skin/color as white, had completed higher education, are moderate drinkers of alcohol, nonsmoker/former smoker, practice mild intensity of physical activity, had at least one chronic disease and non-depression symptoms. Furthermore, we observed higher mean values of MM, BMC, weight, height, and HGS in men and adults. However, higher BMI were observed in women and adults (Table 1).

We observed an increasing in the mean values of HGS according to higher quintiles of MM and BMC with greater values in men compared to women, also in adults compared to the elderly (Table 2).

In total population, also stratified for women and men, and adults and elderly, after adjustments for race/skin color, educational attainment, physical activity, alcohol consumption, smoking, BMI, depressive symptoms and the number of chronic diseases (Model 5), we observed that the higher quintiles of MM and BMC were dose-respond associated to an increasing in the mean of HGS compared to the first quintile. Higher associations magnitudes between MM, BMC and HGS were found in men compared to women (P-value of interaction term for 3rd, 4th and 5th quintile <0.001), also in adults compared to elderly (P-value of interaction term for 5th quintile <0.001). After mutual adjustment for MM and BMC (Model 6) we verify a significant reduction in the association's magnitudes for BMC, and only total population and adults remained associated to HGS (Table 3).

Discussion

We observed in a large sample of men and women, middle-aged adults and older, that individuals with higher amounts of MM and BMC performed better on HGS, even after adjusting for sociodemographic characteristics, health conditions and lifestyle. Concerning the effect modification, higher MM and BMC seems to be more related to greater HSG in men compared to women and adults compared to elderly. Although, when we estimated the independent effect of each exposure of interest, MM showed stronger effect in HGS in women, men and adults then BMC.

Previous studies that investigated the effect only of the amount of muscle[21,43] or bone mass[17] have been performed restricted in older adults. Some studies have found a stronger association

Table 1. Sociodemographic, lifestyle and health conditions of the study population, data from second wave of Brazilian Longitudinal Study of Adult Health. ELSA-Brasil, 2012-2014 (n=12,491).

	Total Population	Women	Men	<65 Years old	≥65 years old
	n (%)	n (%)	n (%)	n (%)	n (%)
Sex					
Men	5,686 (45.52)			4,666 (45.13)	1,020 (47.38)
Women	6,805 (54.48)			5,672 (54.87)	1,133 (52.62)
Age in years, mean (SD)	55.56 (8.95)	55.52 (8.74)	55.62 (9.21)	52.63 (6.62)	69.67 (3.80)
Self-reported race/skin color					
White	6,675 (54.04)	2,409 (52.30)	3,070 (54.77)	5,394 (52.73)	1,281 (60,40)
Brown	3,361 (27.21)	1,430 (31.05)	1,623 (28.96)	2,901 (28.36)	460 (21.69)
Black	1,859 (15.05)	629 (13.66)	725 (12.93)	1,587 (15.51)	272 (12.82)
Asian Descendent	325 (2.63)	77 (1.67)	112 (2.00)	241 (2.36)	84 (3.96)
Brazilian Indigenous	131 (1.06)	61 (1.32)	75 (1.34)	107 (1.05)	24 (1.13)
Educational Attainment					
University Degree or more	7,229 (57.90)	4,082 (59.99)	3,147 (55.40)	5,951 (57.59)	1,278 (59.41)
High School Degree	3,856 (30.89)	2,145 (31.53)	1,711 (30.12)	3,401 (32.91)	455 (21.15)
Elementary School Degree	763 (6.11)	344 (5.06)	419 (7.38)	554 (5.36)	209 (9.72)
Incomplete Elementary School	637 (5.10)	233 (3.42)	404 (7.11)	428 (4.14)	209 (9.72)
Alcohol consumption					
No use	4,311 (34,56)	2,750 (40.47)	1,561 (27.49)	3,511 (34.56)	800 (37.31)
Moderate drinkers	7,159 (57.40)	3,760 (55.33)	3,399 (59.86)	5,958 (57.68)	1,201 (56.02)
Heavy drinkers	1,003 (8.04)	285 (4.19)	718 (12.65)	860 (8.33)	143 (6.67)
Smoking					
Nonsmoker	7,260 (58.16)	4,323 (63.55)	2,937 (51.71)	6,084 (58.87)	1,176 (54.72)
Former smoker	3,839 (30.75)	1,768 (25.99)	2,071 (36.46)	3,013 (29.16)	826 (38.44)
Current smoker	1,384 (11.09)	712 (10.47)	672 (11.83)	1,237 (11.97)	147 (6.84)
Leisure-time physical activity					
Vigorous	998 (8.00)	396 (5.83)	602 (10.60)	862 (8.34)	136 (6.34)
Moderate	2,238 (17.94)	1,152 (16.95)	1,086 (19.13)	1,706 (16.51)	532 (24.81)
Mild	9,239 (74.06)	5,249 (77.23)	3,990 (70.27)	7,763 (75.14)	1,476 (68.84)
Depressive symptoms					
Yes	593 (4.75)	435 (6.40)	158 (2.78)	519 (5.02)	74 (3.45)
Number of chronic diseases					
0	4,528 (36.25)	2,861 (47.29)	1,667 (32.71)	4,069 (44.33)	459 (23.32)
1	3,735 (29.90)	1,948 (32.20)	1,787 (35.07)	3,024 (32.95)	711 (36.13)
2	2,044 (16.37)	907 (14.99)	1,137 (22.31)	1,518 (16.54)	526 (26.73)
>3	2,184 (17.48)	304 (5.53)	505 (9.91)	567 (6.17)	272 (13.82)
Muscle Mass (kg), mean (SD)	27.28 (6.39)	22.89 (3.59)	32.53 (4.92)	27.67 (6.45)	25.43 (5.74)
Bone Mineral Content (kg), mean (SD)	2.78 (0.57)	2.43 (0.35)	3.20 (0.49)	2.81 (0.57)	2.63 (0.52)
Weight (kg), mean (SD)	74.88 (15.29)	69.81 (13.96)	80.96 (14.59)	75.51 (15.49)	71.90 (13.92)
Height (m), mean (SD)	164.62 (9.44)	158.62 (6.48)	171.79 (7.14)	165.15 (9.35)	162.03 (9.41)
BMI (Kg/m²), mean (SD)	27.57 (4.86)	27.73 (5.24)	27.38 (4.35)	27.62 (4.93)	27.33 (4.52)
Handgrip Strength (HGS), mean (SD)	29.82 (10.80)	22.73 (6.15)	38.34 (8.85)	30.43 (10.96)	26.90 (9.46)

Abbreviation: n = number of observations; % = percentage; SD = Standard Deviation; BMI = Body Mass Index.

Source: Authors.

of MM with HGS in women[7,21], or in men[20]. In a longitudinal study[17] with individuals aged 50 years or more, over a 10-year follow-up period, it was observed that men and women present a reduction in bone mass, as well as a reduction in HGS in both sexes, although stronger decline were observed among women. In addition, for MM, in the elderly in Sweden, after 5 years of fol-

Table 2. Handgrip strength according to quintiles of muscle muss and bone mineral content, data from second wave of Brazilian Longitudinal Study of Adult Health. ELSA-Brasil, 2012-2014.

	Handgrip Strength, Mean (SD)				
	Total Population	Women	Men	<65 Years old	≥65 years old
Muscle Mass (kg)*					
1º	20.60 (5.32)	19.66 (4.98)	33.54 (7.48)	20.91 (5.37)	19.64 (5.06)
2º	23.58 (6.05)	21.69 (5.38)	36.96 (7.90)	23.69 (6.00)	23.05 (6.27)
3º	28.32 (8.30)	22.94 (5.64)	38.14 (7.67)	28.24 (8.35)	28.68 (8.03)
4º	35.76 (8.68)	23.95 (5.79)	40.39 (8.94)	36.10 (8.77)	34.10 (8.03)
5º	41.08 (9.30)	25.54 (7.09)	42.77 (9.24)	41.43 (9.29)	37.42 (8.58)
Bone Mineral Content (kg)*					
1º	21.18 (5.93)	19.93 (5.04)	34.06 (7.65)	21.50 (5.99)	20.17 (5.64)
2º	24.22 (6.77)	21.91 (5.75)	36.97 (7.87)	24.30 (6.75)	23.89 (6.87)
3º	28.59 (8.94)	22.55 (5.63)	38.40 (8.03)	28.69 (8.93)	28.09 (8.97)
4º	34.90 (9.19)	23.98 (5.82)	39.98 (9.17)	35.15 (9.35)	33.50 (8.12)
5º	40.49 (9.56)	25.38 (6.95)	42.41 (9.17)	41.01 (9.56)	36.25 (8.47)

Abbreviation: SD = Standard Deviation; Kg = Kilograms. *Analysis of Variance (ANOVA) with a significance level of 95% (p-value<0,05) to estimate the differences between sex and age groups.

Source: Authors

low-up, the lowest amount of muscle mass was associated with worse performance on five tests of muscle strength, including HGS, but the decline in strength was more prominent in men[20]. In our study, the greater amount reserve of BMC and MM were associated with greater performance on HGS, especially in men and adults (Models 5), since the higher amount of HSG were expressed in all quintiles of BMC and MM compared respectively to women and elderly.

During the life-course, skeletal muscle undergoes constant modifications resulting from the synthesis and degradation of proteins, and in advancing age, the increase in catabolism leads to muscle loss. Several factors are involved in this process, such as cell senescence, reduction in the number and regenerative capacity of muscle cells, resistance to anabolic stimuli, impaired mitochondrial function, changes in gene expression, resistance to insulin, and impaired neuromuscular signaling[44]. Muscle gain, on the other hand, is supported by testosterone, a growth factor similar to insulin-1 (IGF1), interleukins IL-4 and IL-6, while muscle loss is supported by the ubiquitin-proteasome-dependent ATP system, caspase activity, and increased autophagy[44].

Regarding BMC, bone quantity and quality reflect a large set of events that happened to an individual from intrauterine life to adulthood, when peak bone mass is reached[8]. The process of obtaining and maintaining peak bone mass is influenced by several factors, including gender, genetic factors, physical activity, diet (calcium and vitamin D), endocrine status (sex hormones, growth hormone, insulin as a growth factor 1), alcohol consumption, smoking, chronic diseases, and medications[12]. During puberty, there are different patterns of bone acquisition between the sexes, due to the action of sex steroids[45], explaining the lower net bone loss in men during aging[46]. As for the loss of BMC, this occurs mainly in postmenopausal women, due to the imbalance between the processes of bone resorption (osteoclasts action) and bone formation (osteoblasts action). Osteoclasts, in women, have receptors for alpha estrogens (ERα), so these hormones would act by decreasing their resorption activity, which seems to be minimized after menopause[11].

Our findings point to a stronger independent effect of MM on HGS in women, men and adults. We aimed to analyze the independent effects of MM and BMC to understand how these parameters influence muscle strength. BMC, as it is formed from the fetal period and reaches its formation peak in young adulthood, already has its status defined in middle-aged and elderly adults, where the process of bone loss already begins[8]. In turn, although muscle mass decreases with age, it can be continuously stimulated even in the elderly, such as by strength exercises[47]. Thus, this may explain why MM had a stronger effect when compared to BMC.

Table 3. Associations of Muscle Mass and Bone Mineral Content with handgrip strength, data from second wave of Brazilian Longitudinal Study of Adult Health. ELSA-Brasil, 2012-2014.

	Total Population Mean difference (95%CI)	Women Mean difference (95%CI)	Men Mean difference (95%CI)	<65 years old Mean difference (95%CI)	≥65 years old Mean difference (95%CI)
Muscle mass (kg)					
Model 1					
1º	Reference	Reference	Reference	Reference	Reference
2º	2.98 (2.56; 3.41)*	2.02 (1.59; 2.46)*	3.42 (2.74; 4.10)*	2.78 (2.29; 3.26)*	3.41 (2.55; 4.27)*
3º	7.75 (7.29; 8.15)*	3.28 (2.85; 3.71)*	4.60 (3.91; 5.28)*	7.33 (6.84; 7.82)*	9.04 (8.18; 9.90)*
4º	15.16 (14.73; 15.59)*	4.28 (3.85; 4.72)*	6.85 (6.16; 7.53)*	15.19 (14.70; 15.68)*	14.46 (13.59; 15.33)*
5º	20.48 (20.05; 20.90)*	5.88 (5.44; 6.32)*	9.23 (8.54; 9.91)*	20.51 (20.04; 20.99)*	17.78 (16.69; 18.87)*
Model 2					
1º	Reference	Reference	Reference	Reference	Reference
2º	2.05 (1.66; 2.44)*	1.84 (1.40; 2.28)*	2.84 (2.16; 3.51)*	2.25 (1.80; 2.69)*	1.69 (0.90; 2.49)*
3º	3.48 (3.06; 3.90)*	2.95 (2.51; 3.38)*	3.84 (3.15; 4.53)*	3.68 (3.21; 4.16)*	3.27 (2.32; 4.22)*
4º	5.98 (5.46; 6.51)*	3.86 (3.42; 4.30)*	5.65 (4.95; 6.35)*	5.94 (5.35; 6.53)*	6.18 (5.06; 7.31)*
5º	9.46 (8.89; 10.04)*	5.26 (4.81; 5.71)*	7.67 (6.96; 8.38)*	9.38 (8.73; 10.02)*	9.08 (7.76; 10.40)*
Model 3					
1º	Reference	Reference	Reference	Reference	Reference
2º	2.04 (1.65; 2.43)*	1.83 (1.39; 2.26)*	2.85 (2.17; 3.52)*	2.23 (1.79; 2.68)*	1.70 (0.91; 2.50)*
3º	3.47 (3.05; 3.89)*	2.93 (2.50; 3.37)*	3.92 (3.23; 4.61)*	3.68 (3.20; 4.15)*	3.17 (2.22; 4.12)*
4º	5.96 (5.43; 6.49)*	3.85 (3.40; 4.29)*	5.74 (5.03; 6.44)*	5.93 (5.34; 6.53)*	6.04 (4.91; 7.17)*
5º	9.46 (8.88; 10.04)*	5.24 (4.79; 5.69)*	7.78 (7.06; 8.49)*	9.38 (8.74; 10.03)*	8.92 (7.60; 10.25)*
Model 4					
1º	Reference	Reference	Reference	Reference	Reference
2º	2.02 (1.63; 2.40)*	1.83 (1.39; 2.27)*	2.82 (2.14; 3.49)*	2.20 (1.75; 2.64)*	1.76 (0.96; 2.56)*
3º	3.47 (3.05; 3.90)*	2.93 (2.49; 3.36)*	3.87 (3.17; 4.56)*	3.68 (3.20; 4.15)*	3.21 (2.25; 4.17)*
4º	5.97 (5.44; 6.49)*	3.84 (3.39; 4.28)*	5.66 (4.95; 6.36)*	5.94 (5.35; 6.53)*	6.08 (4.94; 7.21)*
5º	9.42 (8.85; 10.00)*	5.29 (4.84; 5.76)*	7.69 (6.97; 8.41)*	9.32 (8.68; 9.97)*	8.99 (7.66; 10.32)*
Model 5					
1º	Reference	Reference	Reference	Reference	Reference
2º	2.44 (2.03; 2.86)*	2.18 (1.71; 2.65)*	3.21 (2.48; 3.93)*	2.60 (2.12; 3.08)*	2.28 (1.41; 3.14)*
3º	4.38 (3.91; 4.86)*	3.44 (2.97; 3.91)*	4.71 (3.95; 5.46)*	4.55 (4.01; 5.09)*	4.25 (3.19; 5.30)*
4º	7.22 (6.61; 7.83)*	4.65 (4.15; 5.14)*	6.65 (5.85; 7.45)*	7.13 (6.44; 7.82)*	7.45 (6.16; 8.74)*
5º	11.12 (10.42; 11.82)*	6.51 (5.97; 7.05)*	9.47 (8.61; 10.33)*	10.92 (10.13; 11.71)*	11,10 (9.54; 12.65)*
Model 6					
1º	Reference	Reference	Reference	Reference	Reference
2º	1.96 (1.40; 2.52)*	2.03 (1.45; 2,60)*	2.79 (1.81; 3.76)*	2.11 (1.47; 2.76)*	1.78 (0.67; 2.88)*
3º	3.64 (2.88; 4.41)*	3.45 (2.74; 4.15)*	4.41 (3.20; 5.62)*	3.79 (2.92; 4.67)*	3.44 (1.88; 4.99)*
4º	6.09 (5.08; 7.10)*	4.61 (3.77; 5.44)*	6.57 (5.14; 8.01)*	5.88 (4.72; 7.04)*	6.34 (4.33; 8.34)*
5º	9.21 (7.98; 10.43)*	6.34 (5.34; 7.34)*	9.23 (7.52; 10.94)*	8.60 (7.20; 10.00)*	10.26 (7.74; 12.78)*

In terms of sex differences and in agreement with our results, Orsatti et al.[48] found in a sample of Brazilian women (n=52) lower MM and muscle strength values in the fifth decade of life, with lower MM a probable factor for these findings. One explanation would be that, in general, the fifth decade of life is marked by the advent of menopause, which seems to be related to the decline of MM[48]. On the other hand, men are favored by the androgenic action of testosterone, and when muscle strength is considered in absolute values, men are generally stronger than women, with this difference being more pronounced in the muscle groups of the trunk and upper limbs[49].

Table 3. Associations of Muscle Mass and Bone Mineral Content with handgrip strength, data from second wave of Brazilian Longitudinal Study of Adult Health. ELSA-Brasil, 2012-2014.

	Total Population Mean difference (95%CI)	Women Mean difference (95%CI)	Men Mean difference (95%CI)	<65 years old Mean difference (95%CI)	≥65 years old Mean difference (95%CI)
Bone Mineral Content (kg)					
Model 1					
1º	Reference	Reference	Reference	Reference	Reference
2º	3.04 (2.58; 3.49)*	1.97 (1.53; 2.42)*	2.91 (2.21; 3.60)*	2.80 (2.27; 3.32)*	3.72 (2.81; 4.63)*
3º	7.40 (6.95; 7.86)*	2.61 (2.17; 3.05)*	4.34 (3.65; 5.03)*	7.18 (6.67; 7.70)*	7.92 (6.98; 8.85)*
4º	13.72 (13.26; 14.17)*	4.04 (3.60; 4.48)*	5.92 (5.23; 6.61)*	13.65 (13.14; 14.16)*	13.33 (12.37; 14.28)*
5º	19.31 (18.85; 19.76)*	5.44 (5.00; 5.88)*	8.35 (7.65; 9.04)*	19.51 (19.00; 20.02)*	16.08 (15.00; 17.16)*
Model 2					
1º	Reference	Reference	Reference	Reference	Reference
2º	1.77 (1.37; 2.16)*	1.81 (1.36; 2.25)*	2.52 (1.83; 3.20)*	1.92 (1.46; 2.37)*	1. 70 (0.90; 2.49)*
3º	2.95 (2.54; 3.36)*	2.38 (1.94; 2.82)*	3.65 (2.97; 4.33)*	3.06 (2.60; 3.52)*	3.04 (2.15; 3.92)*
4º	4.80 (4.33; 5.27)*	3.66 (3.22; 4.10)*	5.01 (4.31; 5.70)*	4.86 (4.33; 5.38)*	4.94 (3.89; 5.98)*
5º	7.76 (7.24; 8.28)*	4.83 (4.38; 5.28)*	6.95 (6.25; 7.66)*	7.82 (7.24; 8.40)*	7.08 (5.91; 8.25)*
Model 3					
1º	Reference	Reference	Reference	Reference	Reference
2º	1.79 (1.39; 2.18)*	1.81 (1.37; 2.25)*	2.61 (1.93; 3.29)*	1.93 (1.48; 2.38)*	1.69 (0.89; 2.49)*
3º	2.98 (2.57; 3.39)*	2.37 (1.93; 3.81)*	3.80 (3.12; 4.49)*	3.09 (2.63; 3.55)*	2.96 (2.07; 3.84)*
4º	4.86 (4.38; 5.33)*	3.65 (3.21; 4.10)*	5.22 (4.51; 5.92)*	4.92 (4.39; 5.44)*	4.8 (3.81; 5.92)*
5º	7.86 (7.33; 8.38)*	4.82 (4.37; 5.27)*	7.20 (6.48; 7.91)*	7.93 (7.35; 8.52)*	6.98 (5.80; 8.17)*
Model 4					
1º	Reference	Reference	Reference	Reference	Reference
2º	1.78 (1.38; 2.17)*	1.79 (1.35; 2.23)*	2.64 (1.96; 3.32)*	1.90 (1.45; 2.35)*	1.76 (0.96; 2.56)*
3º	2.95 (2.54; 3.36)*	2.38 (1.94; 2.82)*	3.78 (3.09; 4.47)*	3.06 (2.60; 3.52)*	2.97 (2.08; 3.86)*
4º	4.85 (4.38; 5.32)*	3.63 (3.18; 4.08)*	5.16 (4.46; 5.87)*	4.92 (4.39; 5.44)*	4.90 (3.84; 5.96)*
5º	7.82 (7.29; 8.34)*	4.83 (4.38; 5.29)*	7.13 (6.41; 7.86)*	7.87 (7.29; 8.46)*	7.04 (5.85; 8.22)*
Model 5					
1º	Reference	Reference	Reference	Reference	Reference
2º	1.98 (1.56; 2.40)*	1.97 (1.50; 2.44)*	2.74 (2.00; 3.47)*	2.16 (1.67; 2.64)*	1.69 (0.85; 2.54)*
3º	3.29 (2.84; 3.73)*	2.54 (2.07; 3.02)*	4.13 (3.38; 4.89)*	3.44 (2.93; 3.94)*	3.19 (2.23; 4.15)*
4º	5.28 (4.75; 5.80)*	3.92 (3.43; 4.41)*	5.60 (4.82; 6.39)*	5.33 (4.74; 5.92)*	5.41 (4.24; 6.57)*
5º	8.47 (7.87; 9.08)*	5.29 (4.78; 5.81)*	8.03 (7.19; 8.87)*	8.54 (7.86; 9.22)*	7.73 (6.41; 9.05)*
Model 6					
1º	Reference	Reference	Reference	Reference	Reference
2º	0.68 (0.14; 1.23)*	0.56 (0.00; 1.13)	0.71 (-0.25; 1.67)	0.69 (-0.58; 1.32)	0.71 (-0.33; 1.75)
3º	0.78 (0.08; 1.48)*	-0.12 (-0.80; 0.56)	0.46 (-0.71; 1.64)	0.78 (-0.19; 1.58)	0.89 (-0.48; 2.27)
4º	1.13 (0.27; 1.98)*	0.18 (-0.60; 0.98)	0.70 (-1.31; 1.45)	1.22 (0.24; 2.21)	1.38 (-0.32; 3.09)
5º	2.08 (1.04; 3.12)*	0.32 (-0.60; 1.25)	0.42 (-1.20; 2.06)	2.51 (1.32; 3.70)*	0.88 (-1.22; 3.00)

Model 1: without adjustment; Model 2: Model 1 + adjustment for age, sex and color/skin race; Model 3: Model 2 + educational attainment; Model 4: Model 3 + Leisure-time physical activity, alcohol consumption, and smoking; Model 5: Model 4 + BMI, depressive symptoms, and the number of chronic diseases; and Model 6: Model 5 + mutual adjustment for bone mineral content and muscle mass. Abbreviations: 95%CI: confidence interval 95%; BMI: Body Mass Index. *P-value significance <0.05.

Source: Authors.

As far as we know, this is the first study with a sample of men and women to investigate independent associations between the amounts of MM and BMC in the performance of the HGS in middle-aged and older Brazilians (Models 6). It is important to understand the influence

of these two markers in parallel, since MM represents a current marker and BMC a life course marker[44,50]. Another study that investigated MM and Bone Mineral Density (BMD) exposures, in 97 American overweighted and obese women at the beginning of menopause, found that higher amounts of MM and BMD were associated with higher HGS[18].

Some studies indicate that, with aging, reductions in muscle strength are seen more quickly than a reduction in muscle mass[51], by a neurological mechanism, such as deficits in neural activation and reductions in the capacity to generate intrinsic strength muscle[51-53]. In addition, losing muscle mass is not always associated with reduced muscle strength, and gaining mass alone may not be a predictor of strength gain[51-53]. However, our findings indicate the greater amount of MM as an important predictor of HGS in men, women and adults, reinforcing that having more muscle mass in adulthood impacts strength, but longitudinal studies are needed to better understand this relationship. As for the elderly, the BMC appears as an important component to predict muscle strength along with the MM, pointing to the need to promote an adequate accumulation of bone mass throughout life with a view to better muscle quality.

Some studies show that excess weight, measured by BMI, may also be influencing BMD[54,55], due to the effect of mechanical overload on the bone[55]. In relation to the MM, aging alone causes part of the muscle mass to be replaced by fat mass, and these changes in body composition are potentiated by hormonal differences between the sexes, so that women have a greater proportional amount of fat than men[56]. However, to remove the effect of body mass on HGS, we adjusted our analyzes by BMI, a factor that is sometimes overlooked[57].

Bone mineral content is a parameter that helps in the assessment and monitoring of bone mass, and corresponds to the amount in grams or kilograms of bone tissue. Bone mineral density, on the other hand, takes into account the size of the bone, and is projected by the importance of the amount in its size in grams of tissue in square centimeters (g/cm²)[58,59]. Dual energy X-ray absorptiometry (DXA) is considered the standard method for detailed assessment of body composition, including bone mass. However, its use in clinical practice has important limitations, such as high cost, low accessibility, need for trained operators, in addition to not being portable, making field evaluations difficult; and exposes participants to a certain amount of ionizing radiation[22,23]. Thus, Bioelectrical Impedance (BIA) emerges as an alternative method for assessing body composition[26,27]. BIA is a simpler, cheaper and non-invasive technique, suitable for use in field studies and larger research, as well as being valid and accurate in the assessment of body composition in healthy individuals[60].

Some studies have already reported a high correlation between BMC values obtained by DXA and multifrequency BIA[28,29]. Although some studies show unfavorable results regarding the use of BIA in the assessment of BMC[61,62] this method has received attention as it can be effective in longitudinally monitoring changes in bone mass. Likewise, BIA was presented as a valid method for the assessment of fat-free mass and skeletal muscle mass in Brazilians[24,25]. However, further studies are needed in this area, especially in countries where access to DXA is more difficult[22].

Some limitations need to be considered in our study. First, because it is a cross-sectional analysis, factors that interfere in the peak and accumulation of bone mass or muscle mass may not have been considered, such as maternal factors, growth trajectory, poverty conditions, behaviors and health and diet conditions were not considered. Additionally, MM and BMC were measured by bioelectrical impedance rather than DXA, but studies already show good correlation with DXA[24,25,28,29]. However, the strength of is the large sample of a multicenter study including individuals with different physiological characteristics and biotypes. In addition, we stratified the analysis by sex and age to better understand the differences in the relationship between HGS and MM and BMC between men and women and adults and elderly. We also tried to remove some of the potential confounding effects of this relationship, such as sociodemographic characteristics, lifestyle and health conditions. Finally, this study was carried out in a developing country, which is undergoing a process of demographic transition, but with difficulties in addressing active aging, mainly due to unfavorable socioeconomic conditions.

Conclusion

In our study, we observed that higher amounts of MM and BMC are associated with higher HGS, regardless of sociodemographic characteristics, health conditions and lifestyle, with this effect being greater in men and adults. When we investigated the independent effect of each expo-

sure, the MM seems to be more related to HGS in women, men and adults then BMC. Our results contribute to and reinforce the importance of a lifelong approach in public health promotion policies, from the fetal period to aging, as an incentive to adequate nutrition and good physical health. This can impact bone and muscle health, with a view to maintaining a good status of these parameters. We also reinforce the importance of strategies that prioritize the maintenance and gain of muscle mass at the current age, to positively impact muscle strength. In clinical practice, our results indicate that HGS, a simple and inexpensive method, can be useful in assessing the individual's body composition conditions, enabling more effective health interventions.

Collaborations

BC Rodrigues, SPM Arruda and LF Araújo contributed to the conception or design of the work. BC Rodrigues, NHC Tavares, C Szlejf, CK Suemoto, RHG, MFHS Diniz, L Giatti, SM Barreto and LF Araújo contributed to the acquisition, analysis, or interpretation of data for the work. BC Rodrigues and NHC Tavares drafted the manuscript. All authors critically revised the manuscript and gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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