Nutrición Hospitalaria

Trabajo Original

Population specificity affects prediction of appendicular lean tissues for diagnosed sarcopenia: a cross-sectional study

La especificidad de la población impacta en la predicción de los tejidos magros apendiculares para la sarcopenia diagnosticada: un estudio transversal

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Abstract

Introduction: sarcopenia is a disease characterized by reduced musculoskeletal tissue and muscle strength. The estimation of appendicular lean soft tissue by DXA ($ALST_{DXA}$) is one of the criteria for the diagnosis of sarcopenia. However, this method is expensive and not readily avaiable in clinical practice. Anthropometric equations are low-cost and able to accurate predict ALST, but such equations have not been validated for male Brazilian older adults between the ages of 60 to 79 years. To this end, this study sought to validate the existing predictive anthropometric equations for ALST, and to verify its accuracy for the diagnosis of sarcopenia in male Brazilian older adults.

Methods: this cross-sectional study recruited and enrolled 25 male older adults (69.3 ± 5.60 years). $ALST_{DXA}$ and anthropometric measures were determined. ALST estimations with 13 equations were compared to $ALST_{DXA}$. The validity of the equations was established when: $p > 0.05$ (paired t-test); standard error of the estimate (SEE) < 3.5 kg; and coefficient of determination $r^2 > 0.70$.

Results: two Indian equations met the criteria (Kulkarini 1: 22.19 ± 3.41 kg; $p = 0.134$; $r^2 = 0.78$; EPE = 1.3 kg. Kulkarini 3: 22.14 ± 3.52 kg; $p = 0.135$; $r^2 = 0.82$; SEE = 1.2 kg). However, these equations presented an average bias (Bland-Altman: 0.54 and 0.48 kg) and 'false negative' classification for the ALST index. Thus, three explanatory equations were developed. The most accurate equation demonstrated a high level of agreement ($r^2_{adj} = 0.87$) and validity ($r^2_{PRESS} = 0.83$), a low predictive error ($SEE_{PRESS} = 1.53$ kg), and an adequate ALST classification.

Conclusion: anthropometric models for predicting ALST are valid alternatives for the diagnosis and monitoring of sarcopenia in older adults; however, population specificity affects predictive validity, with risks of false positive/negative misclassification.

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POPULATION SPECIFICITY AFFECTS PREDICTION OF APPENDICULAR LEAN TISSUES FOR DIAGNOSED SARCOPENIA: A CROSS-SECTIONAL STUDY

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Resumen

Introducción: la sarcopenia es una enfermedad caracterizada por una reducción del tejido musculoesquelético y la fuerza muscular. Uno de los criterios utilizados para su diagnóstico es la determinación de tejido blando magro apendicular por DXA (TBMA$_{DXA}$), método costoso que no siempre está disponible en la práctica clínica. Las ecuaciones antropométricas suponen un bajo coste y predicen bien el TBMA, pero con una validez desconocida para los varones brasileños de 60 a 79 años. Por lo tanto, nuestro objetivo fue validar las ecuaciones antropométricas existentes predictivas del TBMA y verificar su precisión para el diagnóstico de sarcopenia en varones brasileños de edad avanzada.

Palabras clave:

Composición corporal. Antropometría. DXA. Sarcopenia. Adultos mayores. Ecuación.

Métodos: participaron en este estudio transversal 25 hombres de edad avanzada (69,3 ± 5,60 años). Se determinaron el TBMA$_{DXA}$ y las medidas antropométricas. Las ecuaciones predictivas del TBMA se compararon con el TBMA$_{DXA}$. La validez de las ecuaciones en las comparaciones se confirmó cuando: $p > 0,05$ (prueba de la "t" pareada); error estándar estimado (EEE) < 3,5 kg; coeficiente de determinación $r^2 > 0,70$.

Resultados: dos ecuaciones indias cumplieron los criterios (Kulkarini 1: 22,19 ± 3,41 kg; $p = 0,134$; $r^2 = 0,78$; EEE = 1,3 kg. Kulkarini 3: 22,14 ± 3,52 kg; $p = 0,135$; $r^2 = 0,82$; EEE = 1,2 kg). Sin embargo, presentaron sesgo promedio (Bland-Altman: 0,54 y 0,48 kg) y clasificación de 'falso negativo' para el índice de TBMA. Por lo tanto, se crearon tres ecuaciones explicativas. La ecuación más precisa mostró un alto acuerdo ($r^2_{adj} = 0,87$), uma alta validez ($r^2_{PRESS} = 0,83$), um bajo error predictivo (EEE$_{PRESS}$ = 1,53 kg) y uma clasificación del TBMA adecuada.

Conclusión: los modelos antropométricos para predecir el TBMA son alternativas válidas para el diagnóstico y el seguimiento de la sarcopenia en los ancianos. Pero la especificidad de la población afecta a su validez predictiva, con riesgos de incorrección por clasificación falsa positiva/negativa.

INTRODUCTION

The older adult population is increasing in developed and developing countries. The World Health Organization estimates that by 2050 20 % of the world's population will consist of individuals over the age of 65 years (1). This poses a challenge to the society and the healthcare system as aging-related conditions such as sarcopenia, malnutrition or cachexia are on the rise. Such conditions are strongly associated with functional limitations resulting from loss of muscle mass. Among the referred conditions, special attention should be paid to sarcopenia, a disorder (2) registered in the International Classification of Diseases with the code M62.84. Sarcopenia is defined as a generalized, progressive disfunction of skeletal muscle tissue, which is characterized by a reduction of muscle strength and muscular structure (3), with a prevalence of 17 % among Brazilian older adults (4). In older adults the negative consequences associated with sarcopenia include, but are not limited to, motor dependence, increased risk of falls, fractures, cognitive impairment, and premature death (5).

The established consensus for the identification of sarcopenia (3,5-10) takes into consideration morphological aspects and reduced appendicular lean soft tissue (ALST), functional responses with an impact on motor performance (3,6-10) and muscle strength (3,7). Muscle tissue estimation may be measured using imaging techniques such as magnetic resonance imaging, computed tomography, ultrasound, and dual-energy x-ray absorptiometry (DXA) (3). However, these modalities are associated with high costs, high levels of radiation exposure (tomography), requirement of adequate space, specialized personnel, and longer time for evaluation. Thus, their use is restricted to specialist hospital and clinical settings (11). Further, these techniques are not always viable in estimating ALST for the diagnosis of sarcopenia, according to established consensus criteria. However, there are several advantages to the use of DXA, including: observer independence, fast and accurate total body measurements, and lower costs and exposure to radiation (12). With DXA, ALST is measured with great accuracy, as composed of lean mass free of fat and bone from the upper and lower limbs, the use of which by consensus is shown in table I.

Table I. Different approaches to the Appendicular Lean Soft Tissue (ALST) or its Index (ALSTI), according to the international consensus diagnosis of sarcopenia

Institution	Sarcopenia Indicator
FNIH	ALST
	ALST/BMI
IWGS	ALSTI = ALST/stature²
SCWD	ALSTI = ALST/stature²
ESPEN	-
EWGSOP	ALSTI = ALST/stature²

FNIH: Foundation for the National Institutes of Health; IWGS: International Working Group on Sarcopenia; SCWD: Society of Sarcopenia, Cachexia and Wasting Disorders; ESPEN: European Society for Clinical Nutrition and Metabolism Special Interest Group on cachexia/anorexia in chronic wasting diseases; EWGSOP: European Working Group on Sarcopenia in Older People; ALST: appendicular lean soft tissue (kg); ALSTI: appendicular lean soft tissue index (kg/m²); BMI: body mass index (kg/m²). Stature in m².

The first anthropometric equation developed to predict ALST for the diagnosis of sarcopenia was based on the DXA scores of adult-older Americans (13). The idea was to propose a strategy to be used in epidemiological approaches, when DXA was not readily avaiable. Later, predictive equations were proposed for Danish older women (14), for Australian older adults of both sexes (15), and for Indian (16), Chilean (17), and Mexican (18) adults. Brazilian equations for individuals over the age of 60 were developed (19) when the validaty of previous equations failed, such as those by Baumgartner et al. (1998) and Tanko et al. (2002). However, these involved only physically active women, like most studies of this nature. One Brazilian study was found that proposed equations for older adults, but the sample comprised individuals of both sexes over 80 years of age (20). In addition, the study reported a trend ($p < 0.05$) for ALST as compared to DXA. To this end, to the best of our knowledge, no studies were found to verify the validity of such equations for Brazilian male subjects aged 60 to 79 years of age.

The validity of anthropometric equations is important as it represents an alternative method/approach to DXA, which is relatively expensive and involves a greater complexity of execution, thus being impractical for epidemiological studies. On the other hand, anthropometry involves simpler and lower-cost measurements (21). Thus, this study sought to validate and examine the accuracy of the existing anthropometric equations developed to predict ALST in male Brazilian older adults between the ages of 60 and 79 years. Our hypothesis is that the validity of existing anthropometric equations may fail for elderly Brazilians, impacting the appropriate diagnosis of sarcopenia. We believe that early diagnosis and appropriate disease monitoring may favor more efficient interventions and more effective monitoring, thus reducing the condition's adverse effects.

MATERIAL AND METHODS

STUDY POPULATION

This cross-sectional study involved a convenience sample of 25 male older adults. This manuscript followed the guidelines from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) conference list, and the completed checklist follows attached.

Participants in this study were involved in: a) health services at the University of São Paulo Clinical Hospital in Ribeirão Preto, Brazil (HC-FMRP/USP); b) the Physical Activity for Seniors program at the School of Physical Education and Sports in Ribeirão Preto (EEF-ERP/USP); and c) Projeto Fragilidade (Fragility Project) developed by FMRP/USP. Data collection was conducted from July 2016 to August 2017. Inclusion criteria included: a) between 60 and 79 years of age; b) able to walk independently; c) no amputated limbs; d) free of unstable cardiovascular diseases and other conditions such as acute infections, tumors, and back pain; e) no knee or hip prostheses, no body weight loss greater than 3 kg in the previous 3 months; f) able to perform the proposed battery of tests, and g) participants were excluded if unable to complete the testing protocol, presented with uncontrolled chronic diseases, had stroke sequelae, or voluntarily decided to no longer participate in the study.

To ensure data quality a sample size calculation was performed to define the desired maximum error (ε) and degree of confidence (Zy), with previous knowledge of the population's variability (σ^2) (22). The variability of the ALST index was used as a reference in a multiethnic study of different populations (23). The highest variance used was observed for the ALST index of men over the age of 18 (SD = 2.35 kg). From the predetermined estimated error ($\varepsilon \leq 1.0$ %) and confidence interval ($\gamma = 0.95$), the ideal sample size for our study (n = 22) was defined by the equation: n = [ZySD / ε]^2 (22). The minimum number of participants was reached (n = 25) even after applying the exclusion criteria.

Our study is in agreement with the Helsinki declaration. All participants were informed about the objectives of the study, and signed an inform consent form prior to data collection. The study protocol was approved by the Ethics Committee of EEFERP/USP (CAAE nº 54345016.6.0000.5659).

DETERMINATION OF APPENDICULAR LEAN SOFT TISSUE (ALST) USING DXA

Appendicular lean soft tissue was measured using DXA (ALST$_{DXA}$; Hologic® scanner, model QDR4500W; software version 11.2, Bedford, MA, USA). ALST$_{DXA}$ was treated as a dependent variable, and was obtained by summing upper and lower limb LSTs as obtained by a total and regional body scan. The equipment was calibrated every morning before measurements by the same technician, in accordance with the manufacturer's instructions. Participants were instructed to remove metallic objects (e.g., earrings, bracelets, rings, removable piercings) and wear a hospital gown, when necessary. They were positioned in a supine position, centered on the scanner table, with their lower limbs secured by Velcro strips. Their hands remained open, with palms resting laterally on the examination table, and arms extended along the body (within the sweep lines of the table). Image alignment adjustments were made following the anatomical references of the body regions. The entire procedure was performed by a specialized technician following the manufacturer's recommendations (24).

MEASUREMENTS

Anthropometric and muscle strength measures were necessary for the equations in order to predict ALST. Measures included: body mass (kg); stature (cm); girth (cm) of the arm, calf, waist and hip; skinfolds (mm) of biceps, triceps, subscapular, and suprailiac, and knee height (cm). All measurements followed conventional international standardization (25).

BMI (kg/m^2) was calculated and classified according to Lipschitz (26). The corrected arm muscle area (AMA$_C$) in cm² was calculated using the equation proposed by Heymsfield, McManus, Smith, Stevens and Nixon (27). To predict the ALST from the American, Chilean and Mexican equations, it was also necessary to determine handgrip strength (HS). This was measured using an analogic handheld dynamometer (Jamar®, model 5030J1). HS assessment procedures were conducted according to the recommendations proposed by the American Society of Hand Therapists, provided by Massy-Westropp et al. (28). Thus, the largest of three attempts at one-minute intervals was recorded.

PREDICTIVE ANTHROPOMETRIC EQUATIONS OF ALST

Thirteen ALST predictive equations developed for American (BAUMGARTNER et al., 1998; SANTOS et al., 2019), Australian (VISVANATHAN et al., 2012), Brazilian (GOMES et al., 2013), Indian (KULKARNI et al., 2013), Chilean (LERA et al., 2014), and Mexican (RAMIREZ et al., 2015) individuals were compared against the obtained ALST$_{DXA}$. The search to include these equations met the following criteria: studies published between 1998 and 2019; studies using older adults in their sample. Of note, studies involving only young individuals were not included. We further adopted the following keywords during the search: equations, appendicular lean soft tissue, older, aging, DXA. The equations used in our study are described in table II.

Table II. Predictive equations of appendicular lean soft tissue (ALST) found in the literature for older men

Author (year)	Sample country of origin	n for proposition	Age[years] mean (SD) or range	Eq.	ALST predictive equations	Original study r²	Original study SEE
Baumgartner et al. (1998)	USA	149 (male/female)	73.6 (5.8)	1	$0.2487 * Weight_{[kg]} + 0.0483 * Stature_{[cm]} - 0.1584 * Hip\ circumference_{[cm]} + 0.0732 * HS_{[kg]} + 2.5843 * sex_{[\male=1;\female=0]} + 5.8828$	0.91	1.58
Visvanathan et al. (2012)	Australia	188 (male/female)	18 to 83	1	$9.11472 + 0.36992 * Weight_{[kg]} - 0.67551 * BMI_{[kg/m^2]} + 5.00840 * sex_{[\male=1;\female=0]}$	0.90*	1.89
				2	$-27.879919 + 0.129727 * Weight_{[kg]} + 22.122674 * Stature_{[m]} + 4.980820 * sex_{[\male=1;\female=0]}$	0.90*	1.93
				3	$10.047427 + 0.353307 * Weight_{[kg]} - 0.621112 * BMI_{[kg/m^2]} - 0.022741 * Age_{[years]} + 5.096201 * sex_{[\male=1;\female=0]}$	0.91*	1.87
Gomes et al. (2013)	Brazil	106 (male = 35; female = 71)	> 80	1	$0.074 * Stature_{[m]} + 0.277 * Weight_{[kg]} - 0.144 * TS_{[mm]} - 0.103 * waist\ circumference_{[cm]} + 1.831 * sex_{[\male=1;\female=0]} - 0.966$	0.82*	1.67
				2	$0.138 * Stature_{[m]} + 0.103 * Weight_{[kg]} + 3.061 * sex_{[\male=1;\female=0]} - 12.489$	0.75*	1.94
Kulkarni et al. (2013)	India	851 (male)	18 to 79	1†	$-13.432 - 0.0445 * age_{[years]} + 0.200 * Weight_{[kg]} + 0.140 * Stature_{[cm]}$	0.78*	1.28
				2	$-12.81 - 0.029 * age_{[years]} + 0.211 * Weight_{[kg]} + 0.153 * Stature_{[cm]} + 0.255 * Calf\ circumference_{[cm]} + 0.141 * Arm\ circumference_{[cm]} - 0.178 * Hip\ circumference_{[cm]}$	0.82*	1.17
				3†	$-16.270 - 0.037 * age_{[years]} + 0.143 * Weight_{[kg]} + 0.159 * Stature_{[cm]} + 0.087 * AMAc$	0.82*	1.18
				4	$-0.996 - 0.023 * age_{[years]} + 0.274 * Weight_{[kg]} + 0.090 * Stature_{[cm]} + 0.223 * Calf\ circumference_{[cm]} + 0.143 * Arm\ circumference_{[cm]} - 0.104 * Hip\ circumference_{[cm]} - 3.163 * LOG$	0.86*	1.02
Lera et al. (2014)	Chile	308 (male = 109; female = 199)	69.9 (5.2)	1	$0.107 * Weight_{[kg]} + 0.251 * Knee\ height_{[cm]} + 0.197 * Calf\ circumference_{[cm]} + 0.047 * HS_{[kg]} - 0.034 * Hip\ circumference_{[cm]} + 3.417 * sex_{[\male=1;\female=0]} - 0.020 * age_{[years]} - 7.646$	0.89	1.35
Ramirez et al. (2015)	Mexico	171 (male/female)	60 a 86	1	$0.215 * Calf\ circumference_{[cm]} + 0.093 * HS_{[kg]} + 0.061 * Weight_{[kg]} + 3.637 * sex_{[\male=1;\female=0]} + 0.112 * Stature_{[cm]} - 16.449$	0.92	1.25
Santos et al. (2019)	USA	15,293 (male = 7810; female = 7,483)	≥ 18	1	$-10.427 + (Calf\ circumference_{[cm]} * 0.768) - (age_{[years]} * 0.029) + (sex * 7.523) + (white * 0\ or\ black * 2.203\ or\ mexican\ american * -0.540\ or\ others * -0.402)$	0.88	1.95

r²: determination coefficient; SEE: standard error of the estimate; *Adjusted; ♂: men; HS: handgrip strength; BMI: body mass index: $weight_{[kg]} / Stature^2_{[m]}$; TS: triceps skinfold; AMAc: arm muscle area, corrected: $[arm\ circumference_{[cm]} - (\pi * TS_{[cm]})]^2 / 4 * \pi - 10[27]$; π: 3.14; LOG: logarithm of the sum of the biceps, triceps, subscapular, and suprailiac skinfolds, all in mm; Sex: 0 for females, 1 for males; Sex: 0 for females, 1 for males; ♀=0 or 1: white, black, Mexican American and others; †Valid equation (p < 0.05) vs DXA.

STATISTICAL ANALYSIS

A descriptive analysis was used to describe the sample and ALST estimates by predictive equations. A confidence interval (95 % CI) was used to indicate the estimate reliability (%). The normality of the data was verified using the Shapiro-Wilk test. The validity of the equations was tested based on the criteria proposed by Lohman (29): a) no statistically significant differences ($p > 0.05$) from the ALST values referenced in the DXA using a paired t-test; b) standard error of the estimate (SEE) < 3.5 kg between predicted (equations) and measured (DXA) values; and c) coefficient of determination r² > 0.70 in the estimates. Because the diagnosis of sarcopenia requires an adequate estimation of ALST, a Bland-Altman plot (30) was used to identify the degree of agreement between measured and predicted values. Valid predictive models of the ALST index (ALSTI) were tested for the diagnosis of sarcopenia (< 7 kg/m²) according to the current cutoff points proposed by the EWGSOP (3). The cases of sarcopenia diagnosed by DXA were compared with the diagnoses made with the valid equations to verify predictive accuracy. In case of disagreement an explanatory regression model would be proposed using stepwise multiple regression. If the new equation demonstrated predictive potential for ALST, the assumptions of reduced multi-colinearity and variance inflation factor (VIF) lower than 10 would be considered (31). Statistical analyses were performed using the SPSS software, version 20 (Chicago, IL, USA). The plots were created using MedCalc® 2015 (v.15.2) and the PRESS statistics using Minitab® (v.17.3.1). Statistical significance was set at α = 5 %.

RESULTS

The mean values of the variables were within the 95 % CI (Table III) with small amplitude. This suggests more reliable val-

Table III. Descriptive analysis and normality test (Shapiro-Wilk) of body composition, anthropometric variables, and handgrip strength of Brazilian older males

Variables	Mean (SD)	95 % CI	Shapiro-Wilk	
				p-value
Characterization				
Age (years)	69.28 (5.6)	66.97 to 71.59	0.967	0.562
ALST (kg)	21.65 (3.8)	20.08 to 23.23	0.926	0.071
ALSTI (kg/m²)	7.98 (1.0)	7.57 to 8.38	0.963	0.473
Fat mass (kg)	21.92 (6.9)	19.07 to 24.77	0.973	0.715
Weight (kg)	74.98 (13.2)	69.55 to 80.41	0.970	0.638
Stature (cm)	169.36 (7.4)	166.31 to 172.41	0.945	0.190
BMI (kg/m²)	26.08 (3.7)	24.53 to 27.63	0.937	0.127
HS (kg)	37.32 (8.8)	33.68 to 40.96	0.991	0.998
Circumferences (cm)				
Arm	29.18 (3.3)	27.81 to 30.55	0.972	0.701
Waist	92.38 (11.8)	87.51 to 97.25	0.963	0.477
Hip	97.24 (6.4)	94.59 to 99.89	0.971	0.662
Calf	36.42 (3.1)	35.13 to 37.71	0.980	0.894
Knee height (cm)	53.94 (2.6)	52.87 to 55.01	0.922	0.058
Skin folds (mm)				
Biceps	8.40 (3.4)	7.02 to 9.78	0.950	0.248
Triceps	15.08 (5.9)	12.64 to 17.52	0.979	0.862
Subscapular	23.56 (8.6)	20.00 to 27.12	0.949	0.235
Suprailiac	19.64 (9.7)	15.63 to 23.65	0.947	0.216
Derivatives				
LOG (mm)	1.79 (0.2)	1.71 to 1.87	0.890	0.011
AMBc (cm²)	38.16 (11.6)	33.37 to 42.95	0.908	0.027

*SD: standard deviation; CI: confidence interval; ALST: appendicular lean soft tissue; ALSTI: appendicular lean soft tissue index: ALST$_{[kg]}$/Stature²$_{[m]}$; BMI: body mass index: Weight$_{[kg]}$/Stature²$_{[m]}$; TS: triceps skinfold; LOG: logarithm of the sum of the biceps, triceps, subscapular and suprailiac skinfolds, all in mm; AMBc: arm muscle area, corrected: [Arm Circumference$_{[cm]}$ − (π *; TS:$_{[cm]}$)]² / 4 * π − 10[27]; π: 3.14; HS: handgrip strength.*

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ues of the parameters. BMI values indicated that, in general, the 25 older adults presented with adequate body weight, and normal weight (between 22 and 27 kg/m²). However, the minimum (17.48 kg/m²) and maximum (31.08 kg/m²) values indicated the presence of older adults being classified as below (BMI ≤ 22 kg/m²) and above (BMI ≥ 27 kg/m²) the normal weight limits. The data normality trend (Shapiro-Wilk) showed well-centered residual values, with high potential for the use of linear regression or other empirical interpretation analyses.

The predicted ALST mean values and criteria for validation of the equations (difference test [t-test], standard error of the estimate [SEE] and coefficient of determination [r²]) are shown in table IV.

The Indian equations Kulkarni 1 and Kulkarni 3 met the criteria proposed by Lohman (29) (Table IV). However, agreement with the reference (ALST$_{DXA}$) indicated some degree of bias by overestimating the ALST prediction (Fig. 1A and 1B).

For ALST values below 21 kg, the equations tended to overestimate the reference values (as measured by DXA). For older adults with higher ALST (> 21 kg), the tendency of underestimation of the reference values was greater. To ensure the practical application of the equations, a simulation with the older adults data from this study was performed. We consider the ALSTI cutoff point proposed by the EWGSOP of 7.0 kg/m² for men to identify low muscle quantify (3). The Kulkarni 1 and Kulkarni 3 equations misclassified 33 % of the tested cases (4 cases) as compared to ALST$_{DXA}$ (6 cases). Thus, although the equations met the criteria

proposed by Lohman (29) they indicated a bias in the estimate, compromising the diagnosis.

Given this problem, anthropometric equations were proposed to predict ALST (Table V). The assumptions for proposing and validating new models considered: analysis of the accuracy of explanatory variables, statistical and biological relationships within and between variables (explanatory and response variables), structuring of the statistical methods used to formulate the equation from sample size, and inter-colinearity between response variables and homoscedasticity of results (32). Once these recommendations were met, three new anthropometric equations were generated using linear regression analyses. The new equations were able to explain the variance of the ALST with high significance ($^{*}p < 0.01$ and $^{**}p < 0.001$).

The cross validation method was applied to the new equations using PRESS statistics (sum of the squares of the residuals) (33). This method has been shown to be effective in these comparisons (34,35). Only equations 2 and 3 met the proposed criteria (p > 0.05; SEE < 3.5 kg; r² > 0.70) as observed in table V. Furthermore, these equations did not present multi-colinearity (VIF < 10) or average polarization in the Bland-Altman plot (Fig. 1C and 1D).

The practical simulation was again tested for our equations 2 and 3 using the same cut-point (ALSTI < 7.0 kg/m²) (3) previously adopted. Equation 2 presented the same classification error of Kulkarni 1 and Kulkarni 3, in identical inverse proportion (-33 %) of misclassification. That is, there was a misdiagnosis with the result (i.e., 'false positive'). In the other hand, for equation 3 the

Table IV. Validity of appendicular lean soft tissue (ALST)-predictive anthropometric equations for males aged 60 to 79 years

ALST predictive equation (kg)	Mean (SD)	Validation for this study sample		
		t paired (*p*)	SEE (kg)	r²
Baumgartner 1	22.6 (2.8)	-2.948 (0.007)	1.96	0.71
Visvanathan 1	24.2 (3.0)	-7.131 (< 0.001)	3.27	0.61
Visvanathan 2	24.3 (2.9)	-7.167 (< 0.001)	3.33	0.6
Visvanathan 3	23.8 (3.0)	-6.234 (< 0.001)	2.93	0.63
Gomes 1	22.4 (2.9)	-2.360 (0.027)	1.98	0.71
Gomes 2	21.6 (2.1)	-0.028 (0.978)	2.23	0.48
Kulkarni 1†	22.1 (3.4)	-1.549 (0.134)	1.86	0.78
Kulkarni 2	23.0 (3.6)	-4.603 (< 0.001)	2.06	0.79
Kulkarni 3†	22.1 (3.5)	-1.545 (0.135)	1.67	0.83
Kulkarni 4	29.7 (4.0)	-24.244 (< 0.001)	8.59	0.54
Lera 1	21.5 (2.3)	0.225 (0.824)	1.92	0.62
Ramirez 1	22.0 (2.3)	-0.967 (0.343)	2.03	0.59
Santos 1	23.1 (0.5)	0.238 (0.814)	2.94	0.50
ALST$_{DXA}$	21.6 (3.8)	-	-	-

SD: standard deviation; r²: determination coefficient; SEE: standard error of the estimate; †Valid equation (p > 0.05) vs. DXA; r² > 0.70; SEE < 3.5 kg).
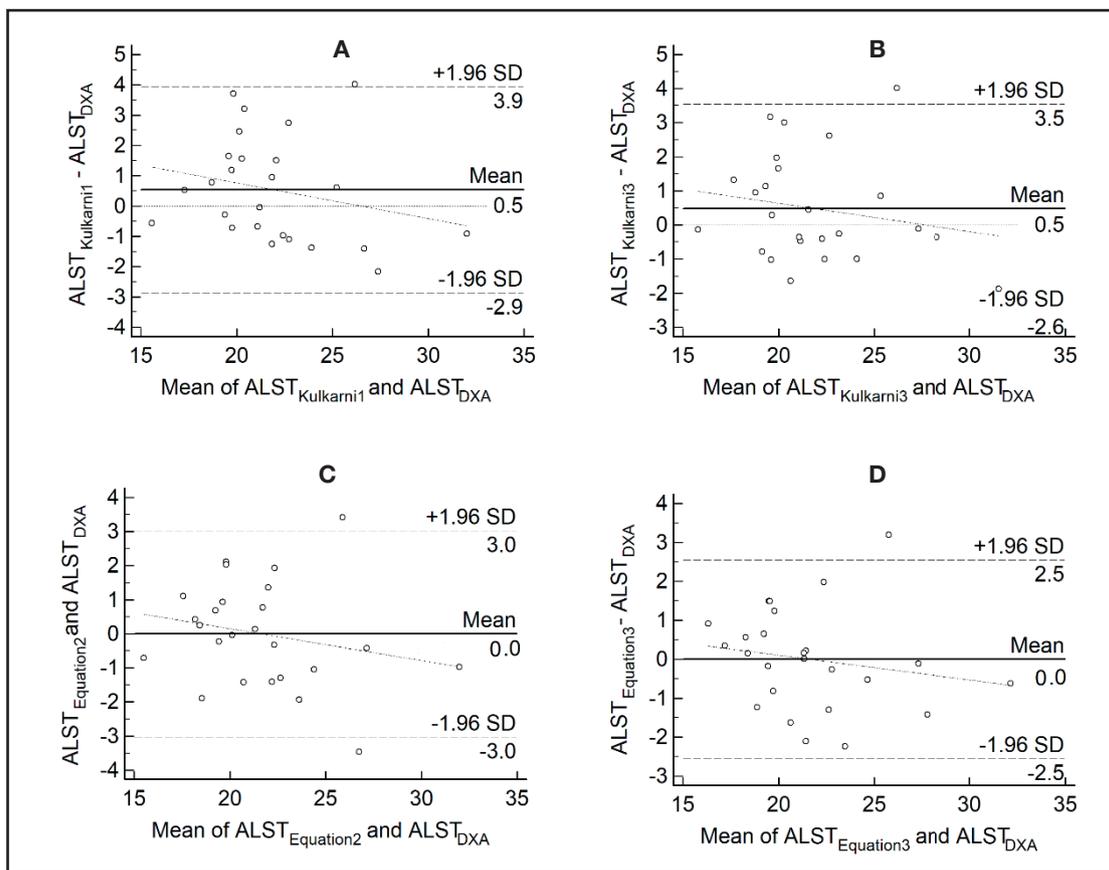
Figure 1.

Bland-Altman plot of the reference appendicular lean soft tissue (ALST) measurement (DXA), as estimated by the Indian predictive anthropometric equations Kulkarni 1 (A) and Kulkarni 3 (B), and that estimated by the new predictive anthropometric equations 2 (C) and 3 (D).

Table V. New anthropometric predictive equations of appendicular lean soft tissue (ALST) for 60- to 79-year-old males

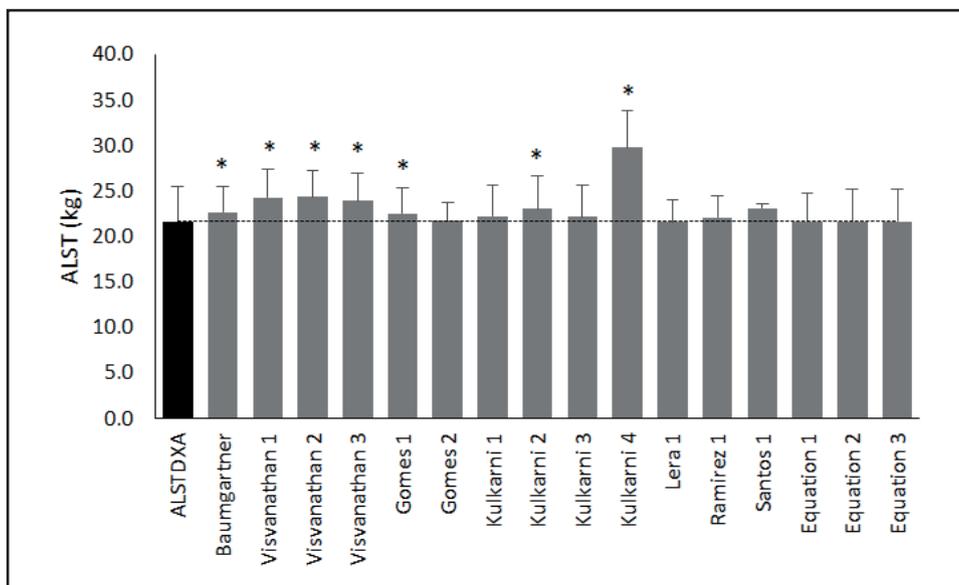| Equation	Independent variables			β	r² adjust.	SEE	VIF	PRESS	r²$_{PRESS}$	SEE$_{PRESS}$
	Weight	**Waist circumference**	**Hip circumference**							
1	0.238 ± 0.03**			3.793 ± 2.61	0.66	2.21	1.000	134.969	0.61	2.32
2[†]	0.469 ± 0.06**	−0.288 ± 0.06**		13.087 ± 2.77**	0.82	1.61	4.990	75.338	0.78	1.74
3[†]	0.603 ± 0.07**	−0.223 ± 0.06*	−0.407 ± 0.14*	36.568 ± 8.38**	0.87	1.39	9.903	58.524	0.83	1.53

Weight in kg, circumference in cm. β: constant; r² adjust.: adjusted coefficient of determination; SEE: standard error of the estimate (kg); VIF: variance ilnflation factor;
[*]p < 0.01; [**]p < 0.001; [†]Valid equation (p < 0.05 vs. DXA; r²$_{PRESS}$ > 0.70; SEE$_{PRESS}$ < 3.5 kg).

diagnosis showed 100 % agreement with the reference method (ALST$_{DXA}$).

Figure 2 presents the means and SD of the ALST measured by the 13 anthropometric equations, the new proposed three equations, and the difference (*) comparisons (t-test; p < 0.05) with the reference values (ALST$_{DXA}$).

DISCUSSION

Our results suggest that of the 13 equations tested to evaluate the ALST of male elderly Brazilians, only two Indian equations (Kulkarni 1 and Kulkarni 3) met the validity criteria adopted in this study, confirming the predictive potential of anthropometric

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Figure 2.

Mean and standard deviation of the reference appendicular lean soft tissue DXA measurement (ALST$_{DXA}$) (black bar) and values estimated by anthropometric equations (gray bars). *Different from ALST$_{DXA}$ ($p < 0.05$).

equations. However, they presented biases (Bland-Altman) and failed to identify low muscle quantity, a fundamental criterion for the diagnosis of sarcopenia (3). A diagnostic simulation of the Indian equations to identify low muscle quantity resulted in the misclassification of 33 % of false-negative cases, as it considered EWGSOP cutoff points (ALSTI < 7.0 kg/m²) (3). Thus, new explanatory equations that met the criteria (29) were developed. However, only one (equation 3) showed adequate agreement with the reference (DXA). This was demonstrated by lack of bias and non-polarization of the means (Bland-Altman plot). The referred equation identified cases of low muscle quantity with 100 % agreement with DXA (3).

Our hypothesis that populational nonspecific equations fail to predict ALST was confirmed. The use of equations generated in a population other than their origin may result in overestimation of ALST, since they are generated based on the body tissue of individuals from different nationalities (19,34). Part of these differences is explained because ALST has great variability in regard to gender and ethnicity. In terms of sex, the quantitative ALST peak in young adults occurs at 27 years for both sexes, but muscle volumes are very different among them. Men have an average of 28.6 kg of muscle tissue while women have 19.2 kg (a 9.4-kg difference) (36). This distinction may be accentuated over time when age-relative decrease in ALST is greater for men (0.8 kg/decade) than women (0.4 kg/decade) (37). Regarding the ethnic factor, the difference in ALST can be up to 10 % when comparing, for example, African American and Asian populations (36). Understanding the interdependent influence of age and ethnicity on older people's muscle mass can be helpful for improving functional capacity and decreasing health risks, especially in older

people of different ethnic groups (36). Therefore, the specificity of the referentials specific to each population must obey well-established criteria and diagnostic thresholds based on their young (3). Considering the various factors when predicting ALST, it can ensure the reliability and adequate diagnosis of our elderly (38).

Our developed equation 3 (Table V) proved its validity (r²$_{adjust}$, SEE, PRESS, r²$_{PRESS}$ and SEE$_{PRESS}$), allowing for an adequate diagnosis of low muscle quantity among older adults. Sophisticated imaging methods for ALST determination are not always available in clinical settings. Thus, alternative methods (e.g., anthropometric equations) may greatly reduce monitoring costs and allow for more frequent measurements and more accurate estimations of low muscle quantity. This would vastly favor interventions. The assumptions of reduced multi-colinearity and variance inflation factor (VIF) less than 10 were considered for the development of the equation (31,39). The predictive validation criteria adopted in this study to test the anthropometric equations are often adopted in studies of this nature (19,20). The PRESS internal validation method (33) confirmed the efficacy of equation 3 to predict ALST with high internal validity, high determination coefficient (r²$_{press}$ = 0.83) and low prediction error (SEE$_{PRESS}$ = 1.53 kg) (Table V). Therefore, the use of the equation developed for older Brazilian males with similar characteristics may avoid bias in the diagnosis of sarcopenia. However, it is important to conduct validation studies in other regions of the country, as well as to define the specific ALSTI cutoff points as recommended by the EWSOP (3).

Our study comes with limitations. One limitation is the small sample size. However, exposure of older adults to unnecessary travel and procedures should be avoided. A prior statistical plan

based on the known variance of ALST among older adults was adopted and met. The challenges of recruiting volunteers for this type of study is not exclusive of the present study. A study with similar purposes to ours but conduted in older Brazilians over the age of 80 years used a similar sample size (n = 35) (20). The strengths of this study include our findings that anthropometry can effectively reduce ALST monitoring costs, favoring interventions. Early interventions designed to counteract and prevent sarcopenia provide better results (40), besides reducing hospitalization and care costs for older adults. Thus, the equation 3 developed in this study from simple measures (weight, waist and hip circumferences) easily obtainable by health professionals does not require high investments or highly specialized training.

The EWGSOP (3) establishes well-defined criteria for diagnosing sarcopenia from low muscle strength (HS < 27 kg), low muscle quantity (ALSTI < 7.0 kg/m^2) and low functional performance (gait speed test ≤ 0.8 m/s). Sarcopenia is considered severe if If all factors are present. In our study, only the second EWGSOP criterion for estimating ALST was met. ALSTI values of 6.20 kg/m² and HS values of 19 kg configured the presence of sarcopenic older adults in our sample. The imminent increase in older population in developing countries is expected to reach around 1.2 billion older people by 2050. This will require simple methods for future use in clinical settings in order to monitor the risk of sarcopenia in the older population. These actions should be intended to identify and prevent sarcopenia, a chronic public health problem with considerable economic impact. There was a gap in the literature for younger older Brazilians. Existing valid equations to predict ALST have been developed for male older Brazilians over the age of 80 years (20). To this end, our equation 3 may enable health professionals to monitor and diagnose sarcopenia earlier. This is important for disease management, prevention and treatment.

In summary, this study sought to test the validity of equations to predict ALST among younger older Brazilians.The use of anthropometry to predict ALST was confirmed as equations from other populations met the criteria adopted for the Brazilian population. However, when applied to the diagnosis of sarcopenia, the values were biased because they were not generated from this specific population. Thus, we can conclude that anthropometric models to predict ALST are valid alternatives for diagnosing and monitoring sarcopenia among older individuals. However, the specificity of the population affects predictive validity, with risk for a false-positive diagnosis. Therefore, the validation of nonspecific equations is still possible, but their precision for the diagnosis of sarcopenia is reduced in older Brazilian males.

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