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Think Globally, Act Locally: The Importance of Population-Specific Bioelectrical Impedance Analysis Prediction Equations for Muscle Mass Assessment

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Abstract

Background: Bioelectrical impedance analysis (BIA) is a convenient muscle assessment method, but its accuracy highly depends on population-specific aspects of the adopted equation. We aimed to develop appendicular lean mass (ALM) prediction models for older South Americans and to compare their performances to those of reference equations in the same sample. *Methods:* Cross-sectional evaluation of 192 community-dwelling Brazilian subjects ≥60 years old from the COMO VAI? study. Using measurements from single-frequency and multifrequency devices (BIASF and BIAMF, respectively), new ALM prediction equations were developed (reference method: dual-energy x-ray absorptiometry [DXA]). Validity was assessed by bootstrapping. Four previously established equations were also tested, and the performances were compared using Bland–Altman analysis. *Results:* Stepwise variable selection produced the following equations: $ALM_{SF\text{-}BIA} = (2.08 \times sex) + (0.04 \times weight) + (0.24 \times RI_{50}) + (0.07 \times Xc_{50}) - 0.16$; $ALM_{MF\text{-}BIA} = (1.85 \times sex) + (0.03 \times weight) + (0.31 \times RI_{50}) + (0.04 \times Xc_{50}) + (0.01 \times Z_5) - 8.16$, where ALM is estimated in kg; female sex = 0 and male sex = 1; weight is measured in kg; RI_{50} is the resistance index at 50 kHz measured in cm^2/Ω); Xc_{50} is the reactance at 50 kHz measured in Ω; and Z_5 is impedance at 5 kHz measured in Ω. The equations explained, respectively, 89% and 90% of the variability of ALM_{DXA} in our sample, and their estimates were not significantly different from DXA measurements. Bland–Altman analysis revealed accurate and unbiased performances for both models, with similar limits of agreement (BIA_{SF}: ±2.58 kg; BIA_{MF}: ±2.48 kg), and their validity was considered adequate by the bootstrap method. The reference equations, however, systematically overestimated ALM in our sample. *Conclusion:* The proposed equations might represent practical options to estimate ALM in older noninstitutionalized South Americans. Further external validation, though, is required to verify the reproducibility of our findings. (*JPEN J Parenter Enteral Nutr.* 2019;00:1–9)

Keywords

body composition; geriatric assessment; muscle; sarcopenia

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Clinical Relevancy Statement

Diagnosing sarcopenia in the elderly requires muscle mass assessment. However, the use of body composition methods based on prediction equations, such as bioelectric impedance analysis (BIA), is frequently limited in certain contexts by the lack of available suitable models. In this study, previously developed equations systematically overestimated appendicular lean mass (ALM) in a sample composed of South American older subjects, reinforcing the need for alternative predictive models. The proposed ALM prediction equations for single-frequency and multifrequency BIA produced accurate and unbiased estimates and might represent an important contribution for clinicians and researchers involved in South American elderly care.

Introduction

Muscle mass (MM) is highly affected by the aging process. One of the main consequences of the aging-related muscle loss is represented by sarcopenia, a pathological condition defined by the loss of MM associated with the decrease of muscle functionality.[1] Therefore, unsurprisingly, despite the observed differences among sarcopenia working definitions by special interest groups and societies around the world, they all do seem to agree on the importance of accurately quantifying MM.[1-5]

Unfortunately, MM measurement is usually the most troublesome sarcopenia diagnostic criteria to be evaluated. High precision reference methods, such as dual-energy x-ray absorptiometry (DXA), computerized tomography, or magnetic resonance imaging, might be expensive, time-consuming, and involve radiation or the patient's dislodgement to the device, which is not always an option. Thus, to adequately diagnose the disease in different contexts, the enhancement of alternative feasible methods is needed.

In this sense, bioelectrical impedance analysis (BIA) represents a portable and affordable option that allows providers to perform assessments in a fast and radiation-free fashion. However, its ease of use should not be mistaken with universal applicability. Body shape, temperature, and fluid and electrolyte homeostasis are required assumptions that must be observed, and failing to fulfill such requirements may compromise the obtained results.[6]

Another relevant aspect is that BIA is an indirect body composition estimation method based on prediction equations. The frequency of an electrical current affects its ability to penetrate cell membranes, and therefore single-frequency or multifrequency BIA devices (BIA_{SF} and BIA_{MF}, respectively) may provide different estimates of intracellular and extracellular water. Moreover, even at the same frequency, raw parameters (resistance [R], reactance [Xc], and impedance [Z]) may vary among devices from different manufacturers. In fact, even DXA devices (commonly adopted as the reference method) from different manufacturers may produce distinct results.[7]

Finally, some considerations concerning the intended outcome should be made. Prediction equations for older subjects usually estimate either skeletal muscle mass (SM) or appendicular skeletal muscle mass (ASM). Whereas the first represents the body's total skeletal muscle amount, the latter is given by the sum of SM from the 4 limbs (≈75% of whole-body SM), and both can only be directly assessed by magnetic resonance imaging. Alternatively, appendicular lean mass (ALM)—the sum of fat and bone-free tissue of the limbs—can be easily assessed by DXA. Though slightly different, ALM and ASM are frequently used as synonyms: ALM is 85% constituted by muscle and therefore stands as a good surrogate for ASM.[7] Currently, ASM (estimated by DXA-obtained ALM) is preferred in the sarcopenia context, given its direct influence over mobility and performing daily life activities.[8]

To our knowledge, there is a lack of suitable equations for South American older subjects. Currently available equations for ALM prediction in the elderly were developed either on North American, European, or Asian subjects,[9-15] which compromises their use in South Americans, given the well-known body composition differences between ethnicities. Additionally, the current variety of BIA and DXA manufacturers (and the lack of agreement between their results) must also be considered, reinforcing the convenience of having diverse prediction equations available for different circumstances.[7]

Given the importance of adequately estimating MM in older subjects and the identified aforementioned gaps, we aimed to develop ALM prediction equations for both BIA_{SF} and BIA_{MF} from a population-based community-dwelling South American elderly sample. Also, our secondary objective was to compare the performance of the developed equations to those of selected previously published equations from distinct contexts.

Materials and Methods

Study Participants

Data were obtained from a body composition sub-study performed on a subsample of the COMO VAI? study (Master's Consortium for Valuation of Elderly Care, or *Consórcio de Mestrado Orientado para a Valorização da Atenção ao Idoso*, in Portuguese). COMO VAI? was a population-based cross-sectional survey performed in 2014 in Pelotas, a southern Brazilian city of ≈330,000 inhabitants,[16] and its methods have been thoroughly discussed elsewhere.[17,18]

Inclusion criteria for the main study were community-dwelling subjects aged 60 years or older living in the urban area of Pelotas. Subjects physically or mentally unable to

answer the questionnaires or perform the required exams were excluded. "Physical limitations" included the presence of metal prostheses or implanted electronic devices, anatomical deformities (such as amputations), and clinically relevant edema.

To ensure random and representative population sampling, a multistep stratified and randomized household and individual selection was performed,[17] which resulted in 1,844 eligible elderlies. After 21.3% of losses and refusals, 1,451 subjects were interviewed in their own houses. Aiming to deterministically select approximately one-sixth of the sample in the occasion, those who were born in the randomly selected months of March and September were also invited to the body composition sub-study. From the 241 invited subjects, 192 (45 losses/refusals and 4 exclusions because of hospitalization or death) were effectively evaluated in the study's clinic in the following weeks.

Measurements and Socioeconomic Data Collection

Socioeconomic data were collected in home interviews. Sex and skin color were observed and registered by the interviewers, and the latter was used as a surrogate for defining race in our sample. Age was based on subjects' self-report, as well as previous medical diagnosis of heart diseases or diabetes. Socioeconomic status was classified according to criteria of the Brazilian Association of Research Companies,[19] which considers the possession of certain consumer goods, the head of household's schooling, and the presence of a maid. According to this scale, the wealthier individuals constitute category A, whereas the least wealthy constitute category E.

All the following measurements were performed in the clinic during the body composition sub-study,[17] with the participants wearing light clothing and no shoes. Body weight was measured using a digital scale (Tanita UM-080; Tanita, Tokyo, Japan); a fixed stadiometer (CMS Weighting Equipment; London, United Kingdom) was used for measuring standing height by a trained researcher, respecting the Frankfurt plane; and posteriorly, body mass index (BMI) was calculated by dividing weight for the squared height (kg/m^2).

Sub-study participants underwent whole-body DXA (Lunar Prodigy, enCORE software, v15; GE Healthcare, Little Chalfont, United Kingdom) evaluations for ALM estimation. As recommended by the manufacturer, the device was calibrated once a week using the provided phantom. Exams were performed after bladder voiding and a fasting period of at least 2 hours, with the participants lying relaxed on the device's table without jewelry or metallic accessories. Bone landmarks and regions of interest were automatically determined by the device (and checked by a trained technician). In addition, the few subjects unable to be entirely accommodated within the 60-cm-wide scanning region of the examination table had their right sides measured, and such values were systematically duplicated by the software as surrogates for full body assessments. The measurements took about 10–15 minutes, and the participants were oriented not to move during the whole period in order to achieve the required resting period prior to BIA examination. The appendicular lean mass index (ALMI) was obtained by dividing ALM by the squared height. Subjects with ALMI values <7.76 kg/m^2 (males) or <5.62 kg/m^2 (females) were classified as presenting low muscularity, according to previously established cutoffs for the studied population.[17]

Following DXA measurements, the right hand and feet of the resting supine subjects were cleansed with alcohol, and 4 BIA electrodes (Bodystat 0525; Bodystat, UK) were placed on the following conventional sites: (1) dorsal surface of the right hand, over the third metatarsal; (2) dorsal surface of the right wrist, between the distal prominences of the radius and the ulna; (3) dorsal surface of the right foot, over the third metacarpal; and (4) dorsal surface of the ankle, between the medial and lateral malleoli.[20] Single-frequency (BIA_{SF}) 50-kHz (RJL Quantum II; RJL Systems, USA) and multifrequency (BIA_{MF}) 5–200-kHz (Bodystat Quadscan 4000; Bodystat, UK) BIA assessments were then performed. First, 3 alternate BIA_{SF} measurements of R and Xc—at a 50-kHz frequency (R_{50} and Xc_{50})—were performed, and then the higher value of each parameter was selected. Next, from a single BIA_{MF} assessment, the following parameters were obtained: R and Xc at a 50-kHz frequency (R_{50} and Xc_{50}) and Z at 5, 50, 100, and 200-kHz frequencies (Z_5, Z_{50}, Z_{100}, and Z_{200}, respectively). Periodical calibration was performed according to the manufacturers' instructions (RJL: supplied 500-Ω resistor, 2% precision; Bodystat: supplied 500-Ω resistor, 1% precision). Both devices were phase sensitive.

Statistical Analysis and Ethical Concerns

Exploratory analysis of the preselected variables (sex, weight, height, age, R_{50}, Xc_{50}, Z_5, Z_{50}, Z_{100}, and Z_{200}) was performed to define the need for transformation prior to the ALM prediction model. Also, R_{50} and height were combined in the resistance index (RI_{50}),[21] whose formula is $RI = height^2/R$. Establishing ALM as the dependent variable, prediction equations of BIA_{SF} and BIA_{MF} were developed through backward stepwise regression analysis, with the significance level set at 5%.

To assess their performance against selected previously published equations (Table 1), we have also applied the latter to our sample and tested all the estimates against ALM_{DXA} by Bradley–Blackwood's *F*-test. Pearson's correlation coefficient and Lin's concordance correlation coefficient (CCC) were also determined, and Bland–Altman

Table 1. Selected Previously Published BIA ALM/ASM Prediction Equations.

Author	BIA/DXA	Equation[a]
Kyle[11,b]	Xitron 4000B (MF)[c]/Hologic	$ASM = (0.267 \times RI_{50}) + (0.095 \times weight) + (1.909 \times sex) + (0.058 \times Xc_{50}) - (0.012 \times age) - 4.211$
Rangel Peniche[12,d]	RJL Quantum X (SF)/Hologic	$ASM = (0.2394 \times RI_{50}) + (0.065 \times weight) + (2.708 \times sex) - 0.05376$
Sergi[14,e]	Akern (RJL) 101 (SF)/Hologic	$ASM = (0.227 \times RI_{50}) + (0.095 \times weight) + (1.384 \times sex) + (0.064 \times Xc_{50}) - 3.964$
Scafoglieri[13,f]	Akern (RJL) 101 (SF)/Lunar[g]	$ALM = (0.168 \times RI_{50}) + (0.132 \times weight) - (1.931 \times sex) + (0.017 \times Xc_{50}) + 1.821$

ALM, appendicular lean mass; ASM, appendicular skeletal muscle mass; BIA, bioelectrical impedance analysis; DXA, dual-energy x-ray absorptiometry; MF, multifrequency; RI_{50}, resistance index with resistance at 50 kHz; SF, single-frequency; Xc_{50}, reactance at 50 kHz.
[a]For all equations: age (in whole years); ASM/ALM (in kg); RI, height/resistance (in cm^2/Ω); sex, 0 for women and 1 for men (except for Scafoglieri, who adopted 0 for men, 1 for women); weight (in kg); Xc (in Ω).
[b]Healthy Swiss outpatient volunteers, 22–94 years.
[c]Even though the authors report having used only 50-kHz-obtained parameters.
[d]Healthy community-dwelling Mexican volunteers (outpatients) ≥60 years.
[e]Healthy physically active community-dwelling Italian volunteers ≥65 years.
[f]Sarcopenic European (inpatients/outpatients from 19 centers in 6 countries) volunteers ≥65 years.
[g]For comparison and analytic purposes (to match the device used in the current paper), only the Lunar-specific equation was selected.

distribution was examined to identify possible biases and the limits of agreement (LOA). Finally, the validity of the developed equations was tested by the bootstrap method, which consists in random resampling and replacement of the participants to simulate the equations' application in N different software-generated samples. Analysis was performed using the statistical software program Stata, version 14.2 (StataCorp, College Station, TX, USA).

Both projects (the COMO VAI? study and the body composition sub-study) were approved by the Research Ethics Committee of the School of Medicine of Federal University of Pelotas (*Universidade Federal de Pelotas*—mUFPel, Pelotas, Brazil) under the register CAAE-24538513.1.0000.5317, and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Participation was voluntary, and informed consent was obtained from all participants.

Table 2. Descriptive Analysis of Study Participants' Characteristics.

Variable		BIA_{SF} (N = 181); N (%)	BIA_{MF} (N = 178); N (%)
Sex	Male	70 (38.7)	67 (37.6)
	Female	111 (61.3)	111 (62.4)
Age, years	60–69	96 (53.0)	96 (53.9)
	≥70	85 (47.0)	82 (46.1)
Race	Caucasian	147 (81.2)	143 (80.3)
	Non-Caucasian[d]	34 (18.8)	35 (19.7)
Heart diseases[a]	No	117 (65.0)	116 (65.5)
	Yes	63 (35.0)	61 (34.5)
Diabetes mellitus	No	128 (70.7)	124 (69.7)
	Yes	53 (29.3)	54 (30.3)
Economic status[b,c]	A/B	66 (38.4)	67 (39.2)
	C	91 (52.9)	90 (52.6)
	D/E	15 (8.7)	14 (8.2)

BIA_{MF}, multifrequency bioelectrical impedance analysis; BIA_{SF}, single-frequency bioelectrical impedance analysis.
[a]Missing self-reported heart diseases data for 1 BIA_{SF} and 1 BIA_{MF} subject.
[b]Ranging from the wealthier individuals (A) to the least wealthy (E), based on a scale of possessed consumer goods.
[c]Missing economic status data for 9 BIA_{SF} and 7 BIA_{MF} subjects.
[d]Twenty-one and 22 African-American subjects in the BIA_{SF} and BIA_{MF} groups, respectively; 13 mixed-race subjects in both BIA groups.

Results

Participants' Characteristics

From the 192 sub-study participants, 1 was not able to perform DXA evaluation, and 2 were excluded because of metal hip prostheses ($N_{DXA} = 189$). Concerning BIA evaluation, because of technical issues, complete BIA_{SF} data was obtained for 181 of them and for BIA_{MF}, 178. The coefficient of variation for R and Xc measurements by BIA_{SF} in our sample was 0.65% and 1.18%, respectively.

Females, Caucasians, and middle-class subjects constituted the majority of the sample. Twenty-four participants were 80 or older (age range: 60–90 years old). Most individuals were free of heart conditions or glucose disorders. Mean BMI was ≈28 kg/m^2 (SD 4.43 kg/m^2), ranging from 18.7 to 43.7 kg/m^2 in the whole sample. Concerning ALMI, there was a significant difference between sexes: low muscularity was found on 31.5% and 6.8% of men and women, respectively. Complete descriptive and anthropometric characteristics of both groups are presented in Tables 2 and 3.

Table 3. Descriptive Analysis of Study Participants' Body Composition.

Variable	BIA_{SF} (N = 181); Mean (SD)		BIA_{MF} (N = 178); Mean (SD)	
	Males (N = 70)	Females (N = 111)	Males (N = 67)	Females (N = 111)
Height, cm	166.8 (6.23)	154.6 (6.75)	166.7 (6.18)	154.8 (6.78)
Weight, kg	75.1 (11.77)	69.1 (12.34)	74.8 (11.55)	69.2 (12.32)
BMI, kg/m^2	27.0 (3.66)	28.9 (4.72)	26.9 (3.64)	28.9 (4.73)
R_{50}, Ω	409.9 (50.98)	480.4 (53.14)	422.4 (52.90)	490.6 (53.22)
RI_{50}, $cm^2/Ω$	69.0 (9.85)	50.5 (7.19)	66.9 (9.59)	49.5 (6.96)
Xc_{50}, Ω	46.8 (7.91)	48.8 (7.86)	48.2 (8.76)	48.8 (8.40)
Z_5, Ω	–	–	489.2 (61.52)	554.9 (58.72)
Z_{50}, Ω	–	–	425.3 (53.00)	488.7 (67.46)
Z_{100}, Ω	–	–	399.5 (48.91)	468.2 (51.77)
Z_{200}, Ω	–	–	379.0 (67.03)	450.3 (50.22)
ALM_{DXA}, kg	22.5 (2.87)	15.9 (2.30)	22.5 (2.91)	15.9 (2.26)
$ALMI_{DXA}$, kg/m^2	8.1 (0.81)	6.6 (0.71)	8.1 (0.82)	6.6 (0.69)

ALM_{DXA}, appendicular lean mass from dual-energy x-ray absorptiometry; $ALMI_{DXA}$, appendicular lean mass index from dual-energy x-ray absorptiometry; BIA_{MF}, multifrequency bioelectrical impedance analysis; BIA_{SF}, single-frequency bioelectrical impedance analysis; BMI, body mass index; R_{50}, resistance at 50-kHz frequency; RI_{50}, resistance index with resistance at 50 kHz; Xc_{50}, reactance at 50 kHz; Z_5, impedance at 5 kHz; Z_{50}, impedance at 50 kHz; Z_{100}, impedance at 100 kHz; Z_{200}, impedance at 200 kHz.

Development and Validation of $ALM_{SF\text{-}BIA}$ and $ALM_{MF\text{-}BIA}$ Equations

Stepwise analysis was performed to establish statistically significant variables for ALM prediction through the evaluated BIA devices. The following variables reached the preestablished level of significance ($P < .05$) and therefore were selected for the final prediction equations (Table 4):

- $ALM_{SF\text{-}BIA} = (2.08 \times \text{sex}) + (0.04 \times \text{weight}) + (0.24 \times RI_{50}) + (0.07 \times Xc_{50}) - 0.16$;
- $ALM_{MF\text{-}BIA} = (1.85 \times \text{sex}) + (0.03 \times \text{weight}) + (0.31 \times RI_{50}) + (0.04 \times Xc_{50}) + (0.01 \times Z_5) - 8.16$,

where ALM is estimated in kg, female sex = 0 and male sex = 1, weight is measured in kg, RI_{50} is measured in $cm^2/Ω$, Xc_{50} is measured in Ω, and Z_5 is measured in Ω. The BIA_{SF} equation was able to explain 89% of ALM_{DXA}'s variability, with an estimated root mean square error (RMSE) of 1.34 kg (SD 0.014 kg). For BIA_{MF}, the adjusted R^2 was 0.90, and the estimated RMSE was 1.29 kg (SD 0.015 kg).

Both equations were highly correlated with ALM_{DXA} (r = 0.95 for both $ALM_{SF\text{-}BIA}$ and $ALM_{MF\text{-}BIA}$) and presented an excellent CCC (0.95 for both). Observed and measured ALM estimates were not proven statistically different for either BIA_{SF} ($P = 0.08$; LOA −2.58, 2.58 kg) or BIA_{MF} ($P = 0.10$; LOA −2.48, 2.48 kg) (Table 5). Bland–Altman plot and concordance distribution analysis did not reveal significant biases for either equation (Figure 1).

The new equations' performance was compared with selected previously published ones. With that purpose, Rangel Peniche's,[12] Scafoglieri's,[13] and Sergi's[14] BIA_{SF} and Kyle's[11] BIA_{MF} equations were applied in the current sample. Our proposed equations presented superior performances than the chosen previous equations, with high CCCs, null average differences, and no systematic biases in relation to ALM_{DXA} (Table 5). Among the reference BIA_{SF} equations, ALM was systematically overestimated by all: ≈1 kg for both Rangel

Table 4. Multiple Linear Regression Models and Explanatory Values of the Predictor Variables Included in the $ALM_{SF\text{-}BIA}$ and $ALM_{MF\text{-}BIA}$ Prediction Equations.

Variable	Coefficient	SE	Adjusted R^2	*P*
$ALM_{SF\text{-}BIA}$ [a]			0.89	
Intercept	−0.16	1.32		0.904
Sex	2.08	0.34		<0.001
Weight	0.04	0.01		0.001
RI_{50}	0.24	0.02		<0.001
Xc_{50}	0.07	0.01		<0.001
$ALM_{MF\text{-}BIA}$ [b]			0.90	
Intercept	−8.16	2.28		<0.001
Sex	1.85	0.33		<0.001
Weight	0.03	0.01		0.003
RI_{50}	0.31	0.02		<0.001
Xc_{50}	0.04	0.01		0.004
Z_5	0.01	<0.01		<0.001

$ALM_{MF\text{-}BIA}$, appendicular lean mass estimated by multifrequency bioelectrical impedance analysis; $ALM_{SF\text{-}BIA}$, appendicular lean mass estimated by single-frequency bioelectrical impedance analysis; BIA_{MF}, multifrequency bioelectrical impedance analysis; BIA_{SF}, single-frequency bioelectrical impedance analysis; RI_{50}, resistance index with resistance at 50 kHz; RMSE, root mean square error; Xc_{50}, reactance at 50 kHz; Z_5, impedance at 5 kHz.
[a] $ALM_{SF\text{-}BIA}$ RMSE, 1.34 kg (SD 0.014 kg); bootstrap-corrected RMSE, 1.31 kg (SD 0.080 kg).
[b] $ALM_{MF\text{-}BIA}$ RMSE, 1.29 kg (SD 0.015 kg); bootstrap-corrected RMSE, 1.25 kg (SD 0.076 kg).

Table 5. Performance of the Proposed and Previously Published Prediction Equations by BIA Against DXA Evaluation to Determine ALM.

Method	Performance in the Current Sample				
	r	CCC	ALM ± SD, kg	Mean difference; LOA, kg	*P*
BIA_{SF} equations[a]					
New BIA_{SF} equation	0.95	0.95	18.4 ± 3.88	0.01; −2.58, 2.58	0.079
Rangel Peniche[12]	0.94	0.91	19.4 ± 4.49	−1.01; −4.08, 2.06	<0.001
Sergi[14]	0.93	0.90	19.5 ± 3.94	−1.1; −4.00, 1.82	<0.001
Scafoglieri[13]	0.91	0.80	20.6 ± 3.90	−2.1; −5.47, 1.19	<0.001
BIA_{MF} equations[b]					
New BIA_{MF} equation	0.95	0.95	18.4 ± 3.85	0.01; −2.48, 2.48	0.095
Kyle[11]	0.93	0.85	20.2 ± 4.46	−1.8; −4.99, 1.31	<0.001

ALM, appendicular lean mass; BIA_{MF}, multifrequency bioelectrical impedance analysis; BIA_{SF}, single-frequency bioelectrical impedance analysis; CCC, concordance correlation coefficient; DXA, dual-energy x-ray absorptiometry; LOA, limits of agreement.
[a]ALM measured by DXA for the 181 BIA_{SF} evaluated subjects (mean ± SD), 18.4 ± 4.10 kg.
[b]ALM measured by DXA for the 178 BIA_{MF} evaluated subjects (mean ± SD), 18.4 ± 4.05 kg.

Peniche's and Sergi's and 2 kg by Scafoglieri's. Concerning BIA_{MF}, Kyle's equation has also presented systematic error in its estimations, compromising its performance in our sample (Figure 1).

Finally, to validate the proposed equations and access their performance in simulated external scenarios, bootstrap optimism analysis was performed (set at 10,000 replications). For $ALM_{SF\text{-}BIA}$, bootstrap-corrected RMSE was 1.31 kg (SD 0.080 kg), and for $ALM_{MF\text{-}BIA}$, it was 1.25 kg (SD 0.076 kg); neither were statistically different from the original RMSEs. These findings suggest both equations' adequacy and support their validity for ALM estimation.

Discussion

The main objective of this study was to develop new ALM prediction equations for different BIA devices from a South American community-dwelling elderly sample. To our knowledge, these are the first population-representative equations in such molds to be proposed in the scientific literature.

The validity of the proposed equations was accessed by the bootstrap method. This approach has been used previously in the BIA context[22,23] and is considered a viable alternative to estimate the reliability of prediction equations' appliance to samples different from the ones they were developed. Bootstrap estimates remained not significantly different from the originals after the 10,000 replications' adopted threshold, which suggests the validity of the proposed equations in outer samples.

The parameters included in our final models are usually reported in similar equations: sex, weight, RI (which combines R and height), and Xc. Together, they were able to explain 90% of the ALM variability in our sample. Additionally, in the BIA_{MF} equation, Z_5 was also found to be a significant parameter, which has already been reported in Yamada and colleagues' segmental BIA prediction equation.[24] Impedance is a parameter derived from R and Xc, and its inclusion in our preliminary MF model is justified as a surrogate for the basic parameters in different frequencies (5, 50, 100, and 200 kHz). Different frequencies have diverse penetrability in the cell membrane, and although higher frequencies are able to estimate intracellular and extracellular water, lower frequency estimates relate mainly to extracellular water.[25] The coefficient for Z_5 was found to have a low, but significant, impact (0.01) in the overall result and therefore was included in the final MF model. Since different frequencies can only be accessed by BIA_{MF}, the fact that estimates from this kind of BIA were marginally more accurate than the ones from BIA_{SF} do not come as a surprise.

This paper's secondary objective was to compare the performance of such equations to the newly developed ones by applying alternative previous equations derived from other populations to the present sample. Previous equations were chosen for the possible similarity, and, consequently, comparability, to the developed ones. Sergi's equation[14] is currently referenced by the European Working Group on Sarcopenia in Older People as the reference for older healthy European subjects.[1] Scafoglieri's,[13] despite having included only sarcopenic subjects, was obtained from a multicentric European sample, which could minimize ethnic differences from our population. Also, it was the only available equation that used Lunar DXA as a reference method, which theoretically could provide more similar estimates to ours[7]. Kyle's[11] is not only a well-established BIA reference equation but also the only available BIA_{MF} equation suitable for comparison. Even though the authors have only included parameters in the 50-kHz frequency, the

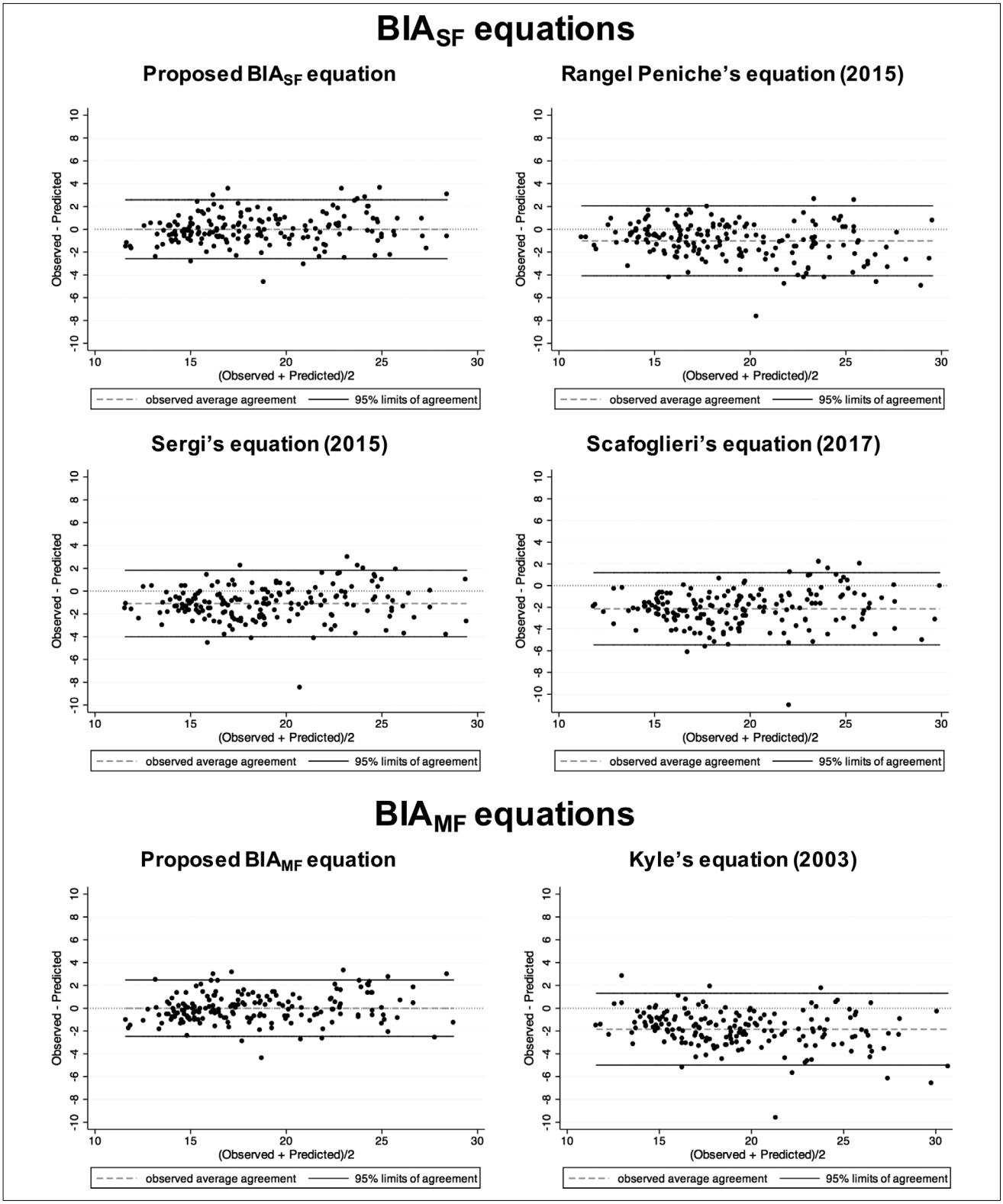

Figure 1. Bland–Altman plots for the proposed and previously published BIA appendicular lean mass prediction equations applied to our sample, with DXA as the reference method. Solid lines represent 95% limits of agreement and dashed lines represent observed average agreement. BIA, bioelectrical impedance analysis; BIA_{MF}, multifrequency bioelectrical impedance analysis; BIA_{SF}, single-frequency bioelectrical impedance analysis; DXA, dual-energy x-ray absorptiometry.

comparison was justified to evaluate if parameters obtained through an MF device would be somehow different than SF ones. At last, Rangel Peniche's equation[12] was included as the only available American (North American, though) equation, and the comparison should reinforce the differences between Mexican North Americans and their South American counterparties (frequently ethnically grouped as "Latinos"). Asian-derived segmental or whole-body lean mass BIA prediction equations,[9,10,15,24] despite considered, were not found by the authors to be suitable for comparison and were therefore not included in this study.

Among the evaluated equations, ours presented the best performance and were the only ones that achieved unbiased estimates for the whole-sample analysis. Such findings should not come as a surprise, considering that previous studies have reported similar results. Sergi's, Kyle's, and Scafoglieri's studies have also reported biased estimates for other equations when applied to their samples.[11,13,14] Also, the performance of the newly developed equations was always better than the previous ones, which can be partially explained by differences between developmental and reference populations or ALM estimation devices (BIA and/or DXA models, manufacturers, or software versions), as seen in the present paper.

The accuracy of estimates from a specific equation may be influenced by several factors, and better estimates tend to be found when all of these factors are adequately matched to the population from which the equation was derived from.[6,7] However, even when all the factors are not perfectly matched, estimates are usually more accurate when the most similar available equation is selected, as demonstrated, for example, by Yu's report of the appliance of different equations to an Australian sample,[26] or Reiter's similar evaluation on Austrian subjects.[27] Yu attributes Sergi's and Kyle's best performance (although far from ideal) because of similarities between the evaluated populations (both equations came from Caucasian subjects, whereas the others came from Mexican or Asian subjects) and BIA devices (both used BIA_{SF}, whereas the 2 evaluated Asian studies have used BIA_{MF}).[26] Reiter and colleagues, when applying different equations to an older geriatric inpatients sample (≥ 70 years, mean age 80.7 ± 5.6 years), have not surprisingly found that the most suitable equation for ALM estimation was Scafoglieri's, generated from a sarcopenic and functionally limited sample, in comparison with equations obtained from healthy community-dwelling samples.[27] Therefore, one may conclude that better or worse performances in different contexts should not disqualify a prediction equation; in fact, they only reinforce the importance of establishing distinct equations for distinct circumstances, as reinforced by the latest European Working Group on Sarcopenia in Older People consensus paper.[1]

The current work has limitations that should be considered. Despite acceptable and common in similar studies, the use of DXA as a reference method (particularly in older subjects) may overestimate MM, especially because of intramuscular fat infiltration.[7] Even though favorably accessed by the bootstrap method, the validity of the suggested models remains to be confirmed in outer samples, particularly for groups of individuals somewhat underrepresented in our sample, such as those over 80 or with a very high BMI (>35 kg/m^2). On the other hand, the presented findings may be considered unmatched in the current scientific literature, since, to our knowledge, the proposed models represent the first available options for BIA ALM estimation in community-dwelling South American older subjects. The fact that the presented solutions approach both BIA_{SF} and BIA_{MF} devices must be valued as well. Finally, the population representativeness of the evaluated sample, carefully approached by multistep random selection, contributes to ensure the epidemiological accuracy of our findings.

Conclusions

To our knowledge, this is the first population-representative study to approach ALM prediction by BIA in South American community-dwelling elderly people. The developed equations produced more accurate results than previously published counterparts and were also able to generate unbiased estimates, whereas all the reference equations systematically overestimated ALM in our sample. Further external validation, though, is required to verify the reproducibility of our findings.

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Statement of Authorship

T. G. Barbosa-Silva, M. C. Gonzalez, and A. M. B. Menezes contributed to the conception and design of the research; R. M. Bielemann contributed to the design of the research; T. G. Barbosa-Silva, M. C. Gonzalez, R. M. Bielemann and A. M. B. Menezes contributed to the acquisition of the data; T. G. Barbosa-Silva, M. C. Gonzalez, R. M. Bielemann and L. P. Santos contributed to the analysis; all authors contributed to the interpretation of the data; and T. G. Barbosa-Silva drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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