Author's response to reviews

Title: Development and validation of anthropometric equations to estimate appendicular muscle mass in elderly women.

Authors:

  Piettra MG Pereira (piettra_galvao@hotmail.com)
  Giselma A Silva (gisalcantara@gmail.com)
  Gilberto M Santos Jr. (moreirasjr@hotmail.com)
  Édio L Petroski (petroski@cds.ufsc.br)
  Amandio AR Geraldes (amandioargeraldes@gmail.com)

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Author's response to reviews: see over
Dear Editor,

Initially, we would like to thank the comments made regarding this manuscript, which undoubtedly contributed to its improvement. In order to facilitate the reviewers' task, their comments, as well as the changes and justifications are below. It should be noted that virtually all requests were met. Thank you for your attention.

Respectfully,

The author
**Title:** Development and validation of anthropometric equations to estimate appendicular muscle mass in elderly women.

**Version:** 3  **Date:** 26 February 2013

**Respostas ao revisor:** Cassiano Ricardo Rech

**Major Compulsory Revisions**

**Abstract**

**Observação 1:** Display summary in the two study objectives. Propose predictive models is not presented.

**Answer:** The abstract presents two goals as well as their results.

**Objective:** This study aimed to examine the cross validity of two anthropometric equations commonly used and propose simple anthropometric equations to estimate appendicular muscle mass (AMM) in elderly women. **Methods:** Among 234 physically active and functionally independent elderly women, 101 (60 to 89 years) were selected through simple drawing to compose the study sample. The paired t test and the Pearson correlation coefficient were used to perform cross-validation and concordance was verified by intraclass correction coefficient (ICC) and by the Bland and Altman technique. To propose predictive models, multiple linear regression analysis, anthropometric measures of body mass (BM), height, girth, skinfolds, body mass index (BMI) were used, and muscle perimeters were included in the analysis as independent variables. Dual-Energy X-ray Absorptiometry (AMM\textsubscript{DXA}) was used as criterion measurement. The sample power calculations were carried out by *Post Hoc Compute Achieved Power*. Sample power values from 0.88 to 0.91 were observed. **Results:** When compared, the two equations tested differed significantly from the AMM\textsubscript{DXA} (p <0.001 and p = 0.001). Ten population / specific anthropometric equations were developed to estimate AMM, among them, three equations achieved all validation criteria used: AMM \textsubscript{(E2)} = 4.150 +0.251 [bodymass (BM)] - 0.411 [bodymass index (BMI)] + 0.011 [Right forearm perimeter (PANTd) \textsuperscript{2}]; AMM \textsubscript{(E3)} = 4.087 + 0.255 (BM) - 0.371 (BMI) + 0.011 (PANTd) \textsuperscript{2} - 0.035 [thigh skinfold (DCCO)]; MMA \textsubscript{(E6)} = 2.855 + 0.298 (BM) + 0.019 (Age) - 0.082 [hip circumference (PQUAD)] + 0.400 (PANTd) - 0.332 (BMI). The equations estimated the criterion method (p = 0.056 p = 0.158), and explained from 0.69% to 0.74% of variations observed in AMM\textsubscript{DXA} with low standard errors of the estimate (1.36 to 1.55 kg), and high concordance (ICC between 0.90 and 0.91 and concordance limits from 2.33 to 2.93 kg). **Conclusion:** The equations tested were not valid for use in physically active and functionally independent elderly women. The simple anthropometric equations developed in this study showed good practical applicability and high validity to estimate AMM in elderly women.
**Introduction:**

**Observação 2:** Its way not explored the arguments and evidence of validity of DXA to estimate the AMM. What is the validity of DXA for this estimate?

**Answer:** Seeking to meet the reviewer’s suggestions, we presented evidence on the validity of DXA to estimate AMM. The change can be seen in the following text:

Among the various techniques available to assess AMM in humans, MRI is the current gold standard [22,23], however, it has high cost, which limits its use in research and clinical practice [24]. An alternative technique is the Dual-energy X-ray absorptiometry (DXA), which allows measuring the AMM validly when compared with other techniques such as total body nitrogen [25] Nuclear Magnetic Resonance [26] and Computed Tomography (27). In addition, for being a rapid and practical technique, DXA has been increasingly used in laboratory studies [28, 29, 30]. However, using DXA in field studies or on a large scale is impractical due to its high cost and logistics required to perform the measurements [31].

**Methods**

**Observação 3:** The number of subjects for the study is based on other research. The authors are able to calculate the sample size to verify that it is suitable for the statistical tests proposed. It is suggested to perform a calculation of power of the sample afterwards.

**Answer:** Seeking to meet the reviewer’s suggestions, we have performed calculations of the sample power with post hoc analysis. The change can be verified in the following texts:

After checking the validation criteria adopted, the calculations of the sample power were performed by post hoc Compute Achieved Power analysis using the G * Power software version 3.0.10
The post hoc test to calculate the sample power of valid equations was conducted by adopting an error probability of 5% for the sample size used. The sample power (1-β err prob) was 0.91 (for E2 with three explanatory variables), 0.88 (for E3 with four explanatory variables) and 0.85 (for E6 with five explanatory variables).

Observação 4: Report values technical error of measurement for anthropometric measurements.

Answer: The section methods already described four appraisers and the values of correlation coefficients observed, as can be seen in the following text:

Anthropometric measurements were performed by four trained appraisers. The inter-rater and intra-rater reproducibility, respectively, for the anthropometric variables held in a group of 17 subjects showed intraclass correlation coefficients from 0.83 to 0.98 for measurements of skinfold thickness and from 0.76 to 0.98 for measurements of body perimeters.

Observação 5: In related text anthropometric measurements is missing a piece of text.

Answer: The incomplete sentence has been removed.

Discussion

Observação 6: The discussion is appropriate. However, authors should discuss the limitations of predictive models proposed. Changes in predictor variables can promote change in estimated muscle mass? What is the expected error for the model of individuals presenting infiltrações intramuscular fat tissue. This fact is not mentioned. But can increase the error in the estimates.

Answer: The limitations of predictive models have been described in section discussion in the following paragraphs:
Despite the limitations noted in this study such as the fact that the elderly in the sample showed homogeneity in relation to anthropometric characteristics, habits, and physical fitness, the three equations showed the best conditions, therefore E2, E3 and E6 were selected for use, because besides showing high validity, they used variables of easy access and high convenience for measurement, which are characteristics necessary for the development of strategies to maintain or improve health, independence and quality of life in subjects with sarcopenia.

The use of valid equations in combination with simple anthropometric models for the verification of BF % in the elderly as a strategy is recommended to identify subjects with sarcopenia, obesity and sarcopenic obesity, caused by the accumulation of intramuscular fat.

**Discretionary Essential revisions**

**Observação 7:** It is suggested that to be inserted in the tables the abbreviations explanatory labels. Thus, as the ratings statistics.

**Answer:** The labels of tables are inserted in the text, along with the titles of tables as requested by the submission rules.

**Observação 8:** Quality of written English: Needs some language corrections before being published

**Answer:** A review of all language was performed.

**Observação 9:** Declaration of competing interests

**Answer:** The statement was rephrased to

There are no conflicts of interest among authors
Abstract

Observação 1: Please restructure the results section in the abstract. It is not quite clear what has been made unless one has read the manuscript. Abstract should be self standing.

Answer: the abstract has been rewritten.

Objective: This study aimed to examine the cross validity of two anthropometric equations commonly used and propose simple anthropometric equations to estimate appendicular muscle mass (AMM) in elderly women.

Methods: Among 234 physically active and functionally independent elderly women, 101 (60 to 89 years) were selected through simple drawing to compose the study sample. The paired t test and the Pearson correlation coefficient were used to perform cross-validation and concordance was verified by intraclass correction coefficient (ICC) and by the Bland and Altman technique. To propose predictive models, multiple linear regression analysis, anthropometric measures of body mass (BM), height, girth, skinfolds, body mass index (BMI) were used, and muscle perimeters were included in the analysis as independent variables. Dual-Energy X-ray Absorptiometry (AMM_{DXA}) was used as criterion measurement. The sample power calculations were carried out by Post Hoc Compute Achieved Power. Sample power values from 0.88 to 0.91 were observed.

Results: When compared, the two equations tested differed significantly from the AMM_{DXA} (p <0.001 and p = 0.001). Ten population / specific anthropometric equations were developed to estimate AMM, among them, three equations achieved all validation criteria used: AMM \(_{(E2)} = 4.150 +0.251 [\text{bodymass (BM)}] - 0.411 [\text{bodymass index (BMI)}] + 0.011 [\text{Right forearm perimeter (PANTd)}]^{2} + 0.035 [\text{thigh skinfold (DCCO)}] + 0.019 [\text{Age}] - 0.082 [\text{hip circumference (PQUAD)}] + 0.400 (\text{PANTd}) - 0.332 (\text{BMI})

Conclusion: The equations tested were not valid for use in physically active and functionally independent elderly women. The simple anthropometric equations developed in this study showed good practical applicability and high validity to estimate AMM in elderly women.
Observação 2: In order to support your work it would be nice to justify more extensively in your introduction why estimating appendicular muscle mass is better than estimating total muscle mass in elderly subjects. For example has it been linked better to sarcopenia? Why is it better than estimating muscle mass from equations estimating fat mass? A few models have been proposed lately estimating fat mass in the elderly from Manios et al and Kanellakis et all. Please discuss this a little.

Answer: we have improved the discussion about the importance of estimating appendicular muscle mass and the use of a model for estimating body fat as mentioned above. These changes can be seen in the following paragraphs:

(Introduction)

Evans and Rosenberg [14] highlight that no decline with age is so dramatic and potentially more significant than the decline in muscle mass. Although the highest losses of skeletal muscle mass are verified in men, it has been suggested that for women, sarcopenia is a major public health problem [15,16]. This assertion has been justified by the fact that women have lower muscle mass and strength when young and higher life expectancy, which implies the high rates of functional limitations in this gender [5,17]. Additionally, females exhibit greater vulnerability related to aging, due to physiologic exhaustion of the ovarian function (menopause) and hence reduced estrogen, thus enhancing the effects of sarcopenia [18,19].

Since appendicular muscle mass (AMM) is closely related to ambulation, mobility, and functional independence [15] and consequently with the performance of daily activities [8], the most important and significant muscle losses associated with aging are observed in the appendicular skeleton [7] and may show declines from 1 to 2% per year [20]. Thus, the maintenance of the AMM structure and function in the elderly is necessary to preserve mobility and functional independence [21].

Among the various techniques available to assess AMM in humans, MRI is the current gold standard [22,23], however, it has high cost, which limits its use in research and clinical practice [24]. An alternative technique is the Dual-energy X-ray absorptiometry (DXA), which allows measuring the AMM validly when compared with other techniques such as total body nitrogen [25] Nuclear Magnetic Resonance [26] and Computed Tomography (27). In addition, for being a rapid and practical
technique, DXA has been increasingly used in laboratory studies [28, 29, 30]. However, using DXA in field studies or on a large scale is impractical due to its high cost and logistics required to perform the measurements [31].

On the other hand, due to its characteristics, the anthropometric method has been a valid, accurate, innocuous and inexpensive alternative to measure body composition [32,33]. Recently, Kanellaris and Manios [33] performed the validation of simple anthropometric models to estimate body fat in postmenopausal women, which provides us with a two-compartment model for assessing body composition (fat mass and lean mass). However, for being a two-compartment model for assessing body composition, the predictive equations of body fat do not allow a specific measurement of the amount of muscle mass and especially the AMM for diagnosing sarcopenia. Therefore, several models of predictive equations to assess AMM have been developed in samples composed of individuals with specific characteristics [34,35,36]; therefore for use in a general way or in other populations, these models must be validated [34,37,38,39].

(Discussion)

The use of valid equations in combination with simple anthropometric models to assess BF % in older women is suggested as a strategy to identify subjects with sarcopenia, obesity and sarcopenic obesity, caused by the accumulation of intramuscular fat.

Methods

Observação 3: Why didn’t the authors validated the equations from the literature and those developed in the same cohort? This would increase the sample size and statistical power of the validation cohort.

Answer: Seeking to meet the questions of the author, we have shown evidence of the need for differentiated groups for the development and validation of predictive equations as shown in the paragraph below:
The sample was distributed by three different groups: two validation groups (GV1 and GV2) and one estimate group (GE). Authors like Maroco [43] and Snee [44] suggested that when attempting to validate a model, one should always use a set of data different from that used for its development, where 60% of the sample data should be used in model adjustment and the other 40% in its validation.

**Observação 4:** In the developed models have you checked for co-linearity between independent variables? It is likely that BM and BMI are highly correlated. Please provide VIF and Tolerance for all variables.

**Answer:** The evaluation and interpretation of VIF and Tolerance values have been described in the text below.

The collinearity between variables was verified by the variance inflation factors (VIF) and tolerance (T) values. Thus, VIF values lower than 5 or even 10 were considered acceptable, as well as tolerance values above 0.1 [43,44].

In addition, the values in Table 4 are described.

Anthropometric measurements were performed by four trained evaluators. The inter-rater and intra-rater reproducibility, respectively, for anthropometric variables held in a group of 17 subjects showed intraclass correlation coefficients from 0.83 to 0.98 for skinfold thickness measurements and from 0.76 to 0.98 for body perimeter measures.

**Observação 5:** It would be nice to apply ICC additionally to Bland – Altman for validation of the developed equations.

**Answer:** The ICC was calculated to assess the concordance of the ten equations developed with the criterion method. The values are given in Table 5.

*Discussion*
Observação 6: How do you explain that the 6th predictive equation of AMM which seems to be the best has as an independent variable hip circumference?

Answer: the following paragraph was inserted in section discussion

Moreover, the explanatory variables of AMM\textsubscript{DXA} (BM, BMI, age, DCCO, PANTd, PQUAD) are easily measured. Given the capacity of, PQUAD in explaining AMM, we can assume that this fact is related to the volume of muscles that make up the hip joint and responsible for the movements of the lower limbs (flexors, extensors, adductors, abductors and medial and lateral rotators of the hip).

Minor essential revisions:

Observação 7: Is there really a stadiometer with accuracy of 0.1mm? Probably the authors mean to say 0.1cm.

Answer: It really was a typing error and has been corrected. The stadiometer sensitivity is 0.1 cm

Observação 8: The manuscript should be checked for correct English usage.

Answer: A review of all language was performed.

Observação 9: Declaration of competing interests

Answer: The statement was rewritten to: there are no conflicts of interest among the authors

Hoping to have met the Reviewer’s demands,

Best regards

The authors