Universidade do Porto

Faculdade de Desporto

Centro de Investigação em Atividade Física, Saúde e Lazer (CIAFEL)

Pontos de corte para diagnóstico de sarcopenia em idosos a partir da força muscular de membros superiores e inferiores com ajustes alométricos

---

Tese académica com o propósito de obter o grau de doutoramento em Atividade Física e Saúde ao abrigo da lei 74/2006 de 24 de março. Esta tese foi desenvolvida no âmbito do Acordo de Doutoramento em Regime de Cotutela internacional entre a Universidade do Porto[1] e a Universidade de São Paulo[2], concluída no Centro de Pesquisa de Atividade Física, Saúde e Lazer (CIAFEL).

Supervisores: [1]Professor Doutor Jorge Augusto Pinto da Silva Mota

[2]Professor Doutor Dalmo Roberto Lopes Machado

Pedro Pugliesi Abdalla

Porto, 2022

Abdalla, P. P. (2022). *Pontos de corte para diagnóstico de sarcopenia em idosos a partir da força muscular de membros superiores e inferiores com ajustes alométricos.* Tese de Doutoramento em Atividade Física e Saúde. Centro de Investigação em Atividade Física, Saúde e Lazer. Faculdade de Desporto. Universidade do Porto.

Keywords**:** allometrically scaled, disability, evaluation, frailty, function/functional status, measurement, sarcopenia, scaling

Financiamento

O candidato recebeu auxílio do Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) com a referência de bolsa de doutorado 142248/2018–5; da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) com o código de financiamento 001; e bolsa de doutorado sanduíche através do programa CAPES-Print com a referência 88887.593242/2020-00.

Aos meu pais, Neto e Milena

Agradecimentos

Agradeço primeiramente ao meu Orientador do Brasil e Supervisor em Portugal, Prof. Dr. Dalmo Roberto Lopes Machado por ser um excelente orientador, por sempre me incentivar a galgar objetivos maiores, com muita paciência e sempre disposto a auxiliar no que fosse preciso.

Ao Prof. Dr. Jorge Augusto Pinto Silva Mota, Supervisor de Portugal, por não medir esforços para minha vinda até sua terra natal, pelo cuidado e orientações permanentes, por possibilitar todas as vivências que tive no CIAFEL - FADEUP e seu papel fundamental neste processo de Cotutela de Dupla Titulação.

À Profa. Dra. Lucimere Bohn, por possibilitar parcerias acadêmicas incríveis, por me motivar nas horas mais difíceis da vida acadêmica e por toda contribuição e auxílio sempre permanentes.

Ao Prof. Dr. Ricardo Arcêncio que não mediu esforços para concretizar minha candidatura ao Programa CAPES-Print-USP e possibilitar a Dupla Titulação, além de sua incansável dedicação na coordenação e dar o melhor de si ao Programa Interunidades de Doutoramento em Enfermagem da EERP-USP, do qual tenho a honra de fazer parte.

Ao Prof. Nilo César Ramos, por sempre auxiliar nos assuntos acadêmicos internacionais, incentivar o estudo da língua inglesa e participação em congressos internacionais, possibilitando vivências no exterior que foram cruciais para minha trajetória acadêmica.

Ao Prof. Dr. Eduardo Ferriolli pela parceria em toda minha trajetória no mestrado e pelas relevantes contribuições em meu Exame de Qualificação para o doutorado.

Ao Prof. Antônio Rui Silva Gomes, por me receber na Universidade do Minho em Braga e possibilitar parcerias acadêmicas futuras.

A Profa. de inglês Daniela, que me incentivou nos estudos iniciais do idioma inglês para o Exame do TOEFL.

Aos professores e funcionários da EEFERP-USP, EERP-USP, HC-FMRP-USP, UNAERP e FADEUP. Em especial à Flavia Souza (EERP-USP), sempre disposta em auxiliar na resolução das demandas acadêmicas durante minha trajetória na EERP-USP e FADEUP. Também, à Ida Mara, que não mediu esforços para viabilizar o convênio entre a EERP-USP e FADEUP, que possibilitou esta Dupla Titulação em Regime de Cotutela.

Aos professores e funcionários da Bergenline, aos Professores Iremar, Luciana, Marcelo, Silvana e Wilson, por me ajudarem a ultrapassar um dos maiores obstáculos durante a trajetória do doutorado, o exame TOEFL-iTP na língua inglesa, requisito obrigatório do programa CAPES-Print-USP, que apoiaram esta minha Dupla Titulação.

Aos amigos do Grupo de Estudo e Pesquisa em Antropometria, Treinamento e Esporte (GEPEATE-USP), Alcivandro, Anderson, Ana Claudia, André, Eurípedes, Franciane, Giovani, Jéssica, José Augusto, Leonardo, Lisa, Marcio, Pablo, Paulo, Thiago Alves, Thiago Figueira, Thiago Oliveira, Vitor, Rafael e aos Professores Emerson e Gustavo por acompanharem minha trajetória e contribuírem diretamente com os trabalhos e projetos acadêmicos.

Aos amigos do Centro de Investigação em Actividade Física, Saúde e Lazer (CIAFEL) e FADEUP, Alba, Ana Carolina Lage, Ana Catarina, Ana Corrales, Ana Flavia, Andreia, Beshoy, Dona Celeste, Dona Julia, Edigar, Elzier, Florêncio, Giorjines, Lara, Laura, Leonardo, Lucas, Maria, Nicolás, Rodrigo, Tiago e Tomas pelo convívio e motivação.

Aos amigos moradores e agregados da habitação Luz Soriano, Alessandra, Alexandre, Augusto, Bianca Braz, Bianca Flores, Denise, Elif, Felipe, Gaetano, Giulia, Henrique, Irene, Karol, Kica, Luana, Marcelo, Maria, Martina, Paloma, Sofia, Vanilson, Vivian, William pelo apoio, convívio diário e motivação.

À Mariane por acompanhar e incentivar o início de minha trajetória do doutorado.

E de forma muito especial aos meus pais Neto e Milena, minha irmã Julia pelo amor incondicional e por serem minha base permanente não só durante o doutorado, mas em toda minha trajetória de vida.

SUMÁRIO

CAPÍTULO I **1**
INTRODUÇÃO GERAL 2
DELIMITAÇÕES E JUSTIFICATIVAS 10
OBJETIVOS 11
Objetivo Geral 11
Objetivos Específicos 12
ESTRUTURA (apresentação de formato) 12
CAPÍTULO II **14**
ESTUDO ORIGINAL I - Identification of muscle weakness in older adults from normalized upper and lower limbs strength: A cross-sectional study 14
CAPÍTULO III **55**
ESTUDO ORIGINAL II - Allometrically adjusted grip strength to identify low strength from 13,235 older adults of low- and middle-income countries 55
CAPÍTULO IV **77**
ESTUDO ORIGINAL III - Foreign allometric exponents adequately normalize isokinetic knee extension strength to identify muscle weakness and functional limitation in Portuguese older adults: A cross-sectional study 77
CAPÍTULO V **97**
ESTUDO ORIGINAL IV - Normalizing Calf Circumference to identify low Skeletal Muscle Mass in Older Women: A Cross-sectional Study 97
CAPÍTULO VI **112**
DISCUSSÃO GERAL 112
CAPÍTULO VII **127**
CONCLUSÕES 127
REFERÊNCIAS **129**
ANEXOS **140**
ANEXO A – Aprovação do Comitê de Ética e Pesquisa 140
ANEXO B – Comprovativos de Financiamento 141
ANEXO C – Comprovativos de Vínculo Institucional 143

ANEXO D – Acordo de Doutoramento em Regime de Cotutela Internacional entre a Universidade do Porto e a Universidade de São Paulo (Páginas 1 e 9) 145

APÊNDICES 147

APÊNDICE A – Planilha automatizada (hiperlink) para normalizar e avaliar a força de idosos residentes em países de baixa e média renda. 147

Lista de Figuras

CAPÍTULO II

Estudo original I - Identification of muscle weakness in older adults from normalized upper and lower limbs strength: A cross-sectional study

Figure 1. Study phases and data from older adults included, excluded, analyzed and procedure flow 26

Figure 2. Accuracy comparison between non-normalized, ratio standard/muscle quality and allometric scaling of muscle weakness cut-off points of HGS and lower limbs strength (1RM and PT) in older men (letters a, b, c) and older women (letters d, e, f) 31

CAPÍTULO III

Estudo original II - Allometrically adjusted grip strength to identify low strength from 13,235 older adults of low- and middle-income countries

Figure 1. Relationship between grip strength and body mass (a) and height (b) in older females (circles) and older males (triangles) from the SAGE study.. 66

Figure 2. Confusion matrix of low grip strength frequency in the SAGE Study according to allometric normalization (observed in our study) and with the EWGSOP2 and SDOC criteria 69

Figure S1. Study flow chart 76

CAPÍTULO IV

Estudo original III - Foreign allometric exponents adequately normalize isokinetic knee extension strength to identify muscle weakness and functional limitation in Portuguese older adults: A cross-sectional study

Figure 1. Comparison of functional capacity (A) and isokinetic knee extension peak torque at 60º/s ($_{\text{knee extension}}PT^{60º/s}$; B) among Brazilian and Portuguese older adults 89

Figure 2. Accuracy comparison of absolute (non-normalized) and normalized isokinetic knee extension peak torque at 60º/s $_{(\text{knee extension}}PT^{60º/s})$ with international and Brazilian allometric exponents to identify poor functional performance (lowest quartile of six-minute walk test) in Portuguese older adults' women (A) and men (B)... 92

CAPÍTULO V

Estudo original IV - Normalizing Calf Circumference to identify low Skeletal Muscle Mass in Older Women: A Cross-sectional Study

Figure 1. Flowchart of women recruited by age groups 105

Figure 2. Accuracy of absolute and normalized calf circumference (CC) to detect functional limitation (≤400m in six-minute walk test) in older women, represented by the ROC curve and area under the curve (AUC) 107

Figure 3. Comparison of the inverted U-shaped relationship (a) between absolute CC and mobility (six-minute walk test) with the linear (b) of the indicator proposed in this study (CC·BMI-1) in older women (n=67) 108

Lista de Tabelas

CAPÍTULO II

Estudo original I - Identification of muscle weakness in older adults from normalized upper and lower limbs strength: A cross-sectional study

Table 1. Allometric exponents (b) proposed in previous studies 24

Table 2. Descriptive analysis and significant correlations of muscle strength with body-size variables in older men and women (n=94) 27

Table 3. Adequate cut-off points (AUC≥0.70 simultaneously in both sexes and r≤0.30 with body size) of handgrip strength (HGS), one maximum repetition measurement for knee extensors (1RM) and isokinetic knee extension peak torque at 60º/s (PT) to identify muscle weakness 29

Tabela Suplementar A. Body size variables (n=49) to normalize muscle strength 36

Tabela Suplementar B. Linear regressions to obtain allometric exponents for handgrip strength (HGS), one maximum repetition measurement for knee extensors (1RM) and isokinetic knee extension peak torque at 60º/s (PT) in older men and women (n=94) 37

Tabela Suplementar C. Cut-off points to identify muscle weakness in older adults of the handgrip strength (HGS), one maximum repetition measurement for knee extensors (1RM) and isokinetic knee extension peak torque at 60º/s (PT) (non-normalized, ratio standard/muscle quality and allometric scaling), and the correlation of muscle strength with body size 49

CAPÍTULO III

Estudo original II - Allometrically adjusted grip strength to identify low strength from 13,235 older adults of low- and middle-income countries

Table 1. Characteristics of the sample 65

Table 2. Allometric exponents for body-size variables according to countries and gender 67

Table 3. Mean sex-specific, standard deviation (SD) and 95% confidence intervals (CI) for absolute or allometrically adjusted grip strength and cut-off points for low muscle strength........ 68

Table S1. Allometric exponents for body size variables according to countries. Analyzes adjusted for sex 74

Table S2. Correlations between adjusted grip strength and body-size variables 75

CAPÍTULO IV

Estudo original III - Foreign allometric exponents adequately normalize isokinetic knee extension strength to identify muscle weakness and functional limitation in Portuguese older adults: A cross-sectional study

Table 1. Brazilian and North American allometric exponents (b) proposed in previous studies to normalize isokinetic knee extension peak torque at 60°/s ($_{\text{knee extension}}PT^{60°/s}$)........ 86

Table 2. Descriptive and comparative analysis of independent community-dwelling older adults in Brazil and Portugal 88

Table 3. Application of international and Brazilian allometric exponents in Portuguese community-dwelling older adults to normalize isokinetic knee extension peak torque at 60º/s ($_{\text{knee extension}}PT^{60º/s}$), their accuracy and cut-off points to identify poor functional performance (lowest quartile of six-minute walk test) 91

Estudo original IV

Table 1. Descriptive analysis of young and older women, body measurements, cut points of the calf circumference (CC) absolute and normalized to identify low skeletal muscle mass (SMM) and functional performance of the older women........ 106

Table 2. Likelihood of the occurrence of a functional limitation* explained by logistic regression from the absolute and normalized calf circumference (CC) 107

Lista de Equações

CAPÍTULO I

INTRODUÇÃO GERAL

(Equação 1) 9

(Equação 2) 9

(Equação 3) 9

CAPÍTULO VI

DISCUSSÃO GERAL

Diferentes formas de gerar e interpretar os expoentes alométricos

(Equação 4) 117

(Equação 5) 119

(Equação 6) 120

(Equação 7) 120

(Equação 8) 120

(Equação 9) 120

(Equação 10) 120

Resumo

A presente tese defende a normalização da força e da massa muscular pelo tamanho corporal como estratégia eficiente para minimizar o viés das dimensões corporais sobre a funcionalidade de idosos. A tese foi composta de três objetivos específicos respondidos em quatro estudos originais. O primeiro objetivo foi propor expoentes alométricos para normalizar a força de membros superiores e inferiores pelo tamanho corporal e gerar pontos de corte para a fraqueza muscular de idosos, respondido em dois estudos originais. No Estudo I (Identification of muscle weakness in older adults from normalized upper and lower limbs strength: A cross-sectional study), que envolveu 94 idosos (IC 95%: 68,2 a 73,9 anos) de ambos os sexos, foram obtidas medidas de força muscular (preensão manual, extensão de joelhos dinâmica e isocinética), do tamanho corporal (antropometria, dimensões e índices) e mobilidade. Foram aplicadas estratégias de normalização (força/tamanho corporal) e alometria (força/tamanho corporal^b; sendo ^{b} o expoente alométrico) associado à mobilidade dos idosos. Foram gerados 49 modelos válidos para identificar fraqueza muscular. A normalização aumentou a precisão dos pontos de corte em mulheres, mas não em homens. Todavia os ajustes nos homens também tornaram a força muscular independente do tamanho corporal, reduzindo o enviesamento para casos extremos. Isso implicou em menor risco de atribuir um diagnóstico falso-positiva/negativo à fraqueza muscular. E no Estudo II (Allometrically adjusted grip strength to identify low strength from 13,235 older adults of low- and middle-income countries), que envolveu idosos de ambos os sexos oriundos de seis países em desenvolvimento, a normalização da força muscular por dimensões corporais foi replicada em diferentes populações. Os métodos foram similares ao Estudo I, mas envolveu somente medidas da força de preensão manual, estatura e massa corporal. A relação não linear entre força e massa corporal foi confirmada, exceto para estatura. Os ajustes alométricos tornaram a força muscular independente do tamanho corporal e sua variabilidade destacou a necessidade de pontos de corte específicos para cada país. Os valores dos expoentes alométricos gerados para cada país foram muito próximoa, confirmando a efetividade universal dessa estratégia. Nosso segundo objetivo foi aplicar comparativamente os expoentes alométricos propostos no Estudo I e outros relatados na literatura, a testar sua eficácia em normalizar a força e identificar fraqueza muscular. Assim, no Estudo III (Foreign allometric exponents adequately normalize isokinetic knee extension strength to identify muscle weakness and functional limitation in Portuguese older adults: A cross-sectional study) 132 idosos portugueses de ambos os sexos realizaram testes de mobilidade, força isocinética de extensão do joelho e medidas das dimensões corporais para normalizar a força (força/tamanho corporal^b). Foram definidos pontos de corte para fraqueza muscular (curva ROC) a partir da força de extensão isocinética do joelho normalizada, ou não, identificado pelo menor quartil de mobilidade. Os pontos de corte da força absoluta, mostraram acurácia insuficiente (AUC<0.70). Expoentes alométricos, ainda que estrangeiros (três brasileiros e um norte americano), melhoraram a acurácia diagnóstica de fraqueza muscular. Concluímos que normalizar a força muscular isocinética de extensão do joelho, mesmo com o uso de expoentes alométricos estrangeiros é melhor do que nenhum ajuste. Nosso terceiro objetivo foi buscar uma estratégia simplificada para identificar a baixa massa muscular de idosos, baseada na limitação funcional para o risco de sarcopenia. Assim, para o Estudo IV (Normalizing Calf Circumference to identify low Skeletal Muscle Mass in Older Women: A Cross-sectional Study) foram propostos pontos de corte para o perímetro da panturrilha, normalizado pelo tamanho corporal, para identificar baixa massa muscular esquelética em mulheres idosas. Valores do perímetro da panturrilha de mulheres jovens (n=78) foram utilizados como referencia dos pontos de corte de baixa massa muscular (-2 desvio padrão). Os resultados mostraram que o perímetro da panturrilha normalizado pelo IMC identificou baixa massa muscular com maior acurácia do que os valores absolutos. A normalização retirou o costumeiro viés da relação de U invertido com a mobilidade (6MWT), geralmente observado em valores absolutos. A precisão obtida suportou o uso de $PP \cdot IMC^{-1}$ para identificar baixa massa muscular em mulheres idosas. Por conclusão, A estratégia alométrica proposta evita erros na classificação da baixa força muscular de idosos, decorrentes do viés causado pelo tamanho corporal. Possivelmente, isso reduz consideravelmente as chances de diagnósticos de casos falso positivos e negativos de sarcopenia em dimensões corporais de idosos com valores extremos.

Palavras-chave: ajuste, alometricamente normalizado, avaliação, incapacidade, fragilidade, funcionalidade/estado funcional, medida, sarcopenia

Abstract

This thesis defends the normalization of strength and muscle mass by body size as an efficient strategy to minimize the bias of body dimensions on the functionality of the older adults. The thesis consisted of three specific objectives answered in four original studies. The first objective was to propose allometric exponents to normalize the strength of upper and lower limbs by body size and generate cutoff points for muscle weakness in the older adults, which was answered in two original studies. In Study I (Identification of muscle weakness in older adults from normalized upper and lower limbs strength: A cross-sectional study), which involved 94 older people (95% CI: 68.2 to 73.9 years) of both sexes, were muscle strength measurements were obtained (hand grip, dynamic and isokinetic knee extension), body size (anthropometry, dimensions, and indexes) and mobility. Strategies for normalization (strength/body size) and allometry (strength/body size^{b}; ^{b} being the allometric exponent) associated with the mobility of the older adults were applied. Were generated 49 valid models to identify muscle weakness. Normalization increased the precision of the cut-off points in women but not in men. However, adjustments in men also made muscle strength independent of body size, reducing the bias for extreme cases. This implied a lower risk of attributing a false-positive/negative diagnosis to muscle weakness. And in Study II (Allometrically adjusted grip strength to identify low strength from 13,235 older adults of low- and middle-income countries), which involved older adults of both sexes from six developing countries, the normalization of muscle strength by body dimensions was replicated in different populations. The methods were like Study I, but only involved measurements of handgrip strength, height, and body mass. The non-linear relationship between strength and body mass was confirmed, except for height. Allometric adjustments made muscle strength independent of body size, and their variability highlighted the need for country-specific cutoff points. The values of allometric exponents generated for each country were very close to, confirming the universal effectiveness of this strategy. Our second objective was to comparatively apply the allometric exponents proposed in Study I and others reported in the literature, to test their effectiveness in normalizing strength and identifying muscle weakness. Thus, in Study III (Foreign allometric exponents suitably normalize isokinetic knee extension strength to identify muscle weakness and functional limitation in Portuguese older adults: A cross-sectional study) 132 Portuguese older adults of both genders performed tests of mobility, isokinetic strength of breast extension. knee and body dimension measurements to normalize strength (strength/body size^{b}). Cutoff points for muscle weakness (ROC curve) were defined based on the normalized isokinetic knee extension strength, or not, identified by the lowest mobility quartile. The absolute strength cut-off points showed insufficient accuracy (AUC<0.70). Allometric exponents, although foreign (three Brazilians and one North American), improved the diagnostic accuracy of muscle weakness. We conclude that normalizing isokinetic knee extension muscle strength, even with the use of foreign allometric exponents, is better than no adjustment. Our third objective was to seek a simplified strategy to identify low muscle mass during aging, based on functional limitation for the risk of sarcopenia. Thus, for Study IV (Normalizing Calf Circumference to identify low Skeletal Muscle Mass in Older Women: A Cross-sectional Study) cut-off points were proposed for the calf perimeter, normalized by body size, to identify low skeletal muscle mass in older women. Calf circumference values for young women (n=78) were used as a reference for low muscle mass cutoff points (-2 standard deviation). The results showed that the calf perimeter normalized by BMI identified low muscle mass with greater accuracy than the absolute values. Normalization removed the usual bias of the inverted U-to-mobility ratio (6MWT), usually seen in absolute values. The accuracy obtained supported the use of PP·BMI-1 to identify low muscle mass in older women. In conclusion, the proposed allometric strategy avoids errors in the classification of low muscle strength in the older adults, resulting from the bias caused by body size. Possibly, this considerably reduces the chances of diagnosing false positive and negative cases of sarcopenia in body dimensions of older people with extreme values.

Keywords: allometrically scaled, disability, evaluation, frailty, function/functional status, measurement, sarcopenia, scaling

Lista de Abreviações

1RM: uma repetição máxima

6MWT: Teste de caminhada de seis minutos

ADL: atividades instrumentais e básicas de vida diária

AFA: Área gordurosa do braço

ASM ou ASSM: massa muscular apendicular

AST: Área de Secção Transversa

AUC: Área abaixo da curva

AWGS: Asian Working Group for Sarcopenia

^{b}: Expoente alométrico

BIA: Análise de Bioimpedância Elétrica

BMI: Índice de massa corporal

CAMA: Circunferência muscular do braço corrigida

CC: Perímetro da panturrilha

CI: Intervalo de confiança

CID: Classificação Internacional de Doenças

Creatina D_3: Teste de diluição de creatina marcada com deutério

DXA: Absorciometria radiológica de dupla energia

ESCEO: European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases

ESPEN: European Society for Clinical Nutrition and Metabolism Special Interest Group on cachexia/anorexia in chronic wasting diseases

EU: European Union

EuGMS: EU Geriatric Medicine Society

EWGSOP: European Working Group on Sarcopenia in Older People

EWGSOP2: revised European Working Group on Sarcopenia in Older People

FADEUP: Faculdade de Desporto da Universidade do Porto

FFM: massa isenta de gordura

FNIH: Foundation for the National Institutes of Health

GPAQ: Global Physical Activity Questionnaire

HGS: força de preensão manual

IWGS: International Working Group on Sarcopenia

${}_{\text{knee extension}}PT^{60°/s}$: Pico de torque da extensão isocinética de joelho à 60º/s

LL: Margem inferior do intervalo de confiança

ln: Logaritmo natural

LST: tecido mole magro

M=Mean

MAMC: Circunferência muscular do braço

MMSE: Mini-Exame do Estado Mental

NIA: National Institute on Aging

Nm: Newtons-metro

PT: Pico de torque da extensão isocinética de joelho à 60º/s

r: Coeficiente de correlação

SA: Área de superfície corporal humana

SAGE: Study on Global Aging and Adult Health

SCWD: Society of Sarcopenia, Cachexia and Wasting Disorders

SD: Desvio padrão

SDOC: Sarcopenia Definition and Outcomes Consortium

Sens: Sensibilidade

SMM: Massa muscular esquelética

Spe: Especificidade

STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

UL: Margem superior do intervalo de confiança

USP: Universidade de São Paulo

VIF: Fator de inflação da variância

WHO: Organização Mundial de Saúde

χ^2: Qui-quadrado

CAPÍTULO I

INTRODUÇÃO GERAL, DELIMITAÇÕES E JUSTIFICATIVAS, OBJETIVOS E ESTRUTURA

INTRODUÇÃO GERAL

Sarcopenia foi um termo criado pelo autor Irwin Rosenberg (1997), que relacionou-a com a redução da massa muscular que ocorre simultaneamente ao envelhecimento. A origem etimológica da palavra sarcopenia é derivada do grego, sendo "Sarx" ou carne; e "penia" ou perda (Rosenberg, 1997). Devido a sarcopenia ser uma condição mais frequente em idosos comparativamente aos adultos e jovens, passa a ser importante compreendê-la como um fenômeno natural do envelhecimento.

O número de indivíduos idosos no mundo aumenta de forma significativa e a estimativa é que no ano de 2050 o globo terrestre abrigue 1,5 bilhões de pessoas com mais de 65 anos (Higo & Khan, 2015). Nos países em desenvolvimento, como é o caso do Brasil, os idosos perfarão desse total 1,2 bilhões (Higo & Khan, 2015). Ou seja, em 2050 cerca de 80% dos idosos de todo o mundo viverão em países de baixa e média renda (World Health Organization, 2014). Em países desenvolvidos também haverá aumento do número de idosos, contudo, em menor expressão. Em Portugal é esperado um aumento perto de 37% em seis décadas (de 2,2 milhões em 2016 para 3,0 milhões em 2080) (Instituto Nacional de Estatística, 2020).

Com o avanço da idade cronológica ocorrem alterações fisiológicas, morfológicas, sensoriais e motoras no organismo, impactando na função dos diversos sistemas (cardiovascular, digestório, endócrino, esquelético, muscular, nervoso, entre outros). O impacto do envelhecimento sobre os músculos esqueléticos é tão evidente que é notado sem utilizar qualquer método específico para quantificar a composição corporal.

A observação do impacto do envelhecimento sobre a morfologia humana é documentada desde o século XVI, como descreveu o poeta inglês William Shakespeare, na passagem a seguir traduzida, que refere a sexta das sete idades do homem em sua obra "As You Like It":

> "... óculos no nariz, bolsa de lado, calças da mocidade bem poupadas, mundo amplo em demasia para pernas tão mirradas ..." (Marín, 1929).

A partir dos 27 anos de idade, homens e mulheres começam a apresentar sinais de diminuição da massa muscular (Silva et al., 2010), e dos 20 até os 70 anos de idade ocorre uma redução de até 40% (Rogers & Evans, 1993). Mais acentuada ainda é a redução da força muscular, que com o envelhecimento chega a ser três vezes maior do que a massa muscular (Compston et al., 2014). Baixos níveis de força muscular influenciam a funcionalidade de idosos em atividades corriqueiras como andar, subir escadas, sentar e levantar de uma cadeira, dentre outras. No passado, a sarcopenia foi reconhecida somente como uma alteração morfológica, ou seja, como redução estrita da massa muscular (Baumgartner et al., 1998; Rosenberg, 1997). Contudo, mais recentemente, algumas entidades internacionais criaram consensos e consórcios com algoritmos com intuito de identificar a sarcopenia. O parâmetro da massa muscular continua a ser a adotado como critério para identificar sarcopenia (Cruz-Jentoft et al., 2018), mas visto como dúbio por especialistas da área (Bhasin et al., 2020). No entanto, critérios relacionados a capacidade funcional como a força muscular e o desempenho físico são agora obrigatórios para confirmar a sarcopenia.

Os consensos internacionais para sarcopenia são determinados por task-force groups. Dentre os mais conhecidos estão o *European Working Group on Sarcopenia in Older People* (EWGSOP) (Cruz-Jentoft et al., 2010; Cruz-Jentoft et al., 2018), *European Society for Clinical Nutrition and Metabolism Special Interest Group on cachexia/anorexia in chronic wasting diseases* (ESPEN) (Muscaritoli et al., 2010), *International Working Group on Sarcopenia* (IWGS) (Fielding et al., 2011), *Society of Sarcopenia, Cachexia and Wasting Disorders* (SCWD) (J. E. Morley et al., 2011), *Foundation for the National Institutes of Health* (FNIH) (Dam et al., 2014), *Asian Working Group for Sarcopenia* (AWGS) (Chen et al., 2014; Chen et al., 2020) e *Sarcopenia Definition and Outcomes Consortium* (SDOC) (Bhasin et al., 2020). Todas essas entidades consideram parâmetros relacionados a massa muscular esquelética reduzida como um dos critérios para realizar o diagnóstico da sarcopenia, exceto o SDOC (como explicado anteriormente). Embora possa haver alguma variação nos critérios e entendimentos da sarcopenia, em geral essas entidades concordam que a degradação de massa muscular e os impactos na mobilidade e funcionalidade são consensuais. Em 2010, a sarcopenia foi definida pelo EWGSOP como uma síndrome caracterizada por uma progressiva e generalizada redução da massa muscular, da força muscular e da mobilidade (Cruz-Jentoft et al., 2010). Em 2018 foi publicada uma atualização que definia sarcopenia como distúrbio progressivo e generalizado dos músculos esqueléticos caracterizada pela redução da força e da massa muscular, sendo considerada severa quando associada à redução do desempenho físico/mobilidade (Cruz-Jentoft et al., 2018). A consideração da baixa força muscular como primeiro critério se deu por favorecer a identificação precoce da sarcopenia na prática clínica. Isso porque a força muscular apresenta uma redução três vezes maior do que a massa muscular (Compston et al., 2014). Além disso, a força muscular é a medida de maior confiabilidade dentre todas adotadas pelo EWGSOP para o diagnóstico da sarcopenia (Cruz-Jentoft et al., 2018). Portanto, segundo o consenso europeu (EWGSOP), para o idoso ser considerado com sarcopenia, deve apresentar obrigatoriamente dois critérios: *Critério 1*: baixa força muscular; e *Critério 2*: baixa massa muscular (Cruz-Jentoft et al., 2018). O *Critério 3* apenas serve para definição de severidade, quando identificado baixo desempenho físico, medido por teste de mobilidade ou baterias de testes funcionais (Cruz-Jentoft et al., 2018). O consórcio americano (SDOC) (Bhasin et al., 2020) dos grupos *Foundation for the National Institutes of Health* (FNIH) e *National Institute on Aging* (NIA) define sarcopenia semelhante ao consenso europeu, contudo não recomenda utilizar a massa muscular como parâmetro. Assim a identificação da sarcopenia se dá quando há redução conjunta de dois critérios: *Critério 1*: baixa força muscular (i.e., força de preensão manual); e *Critério 2*: baixo desempenho físico (i.e., velocidade usual de marcha). Essa decisão, mediante voto, envolveu especialistas em sarcopenia do consórcio americano. A massa muscular apendicular derivada da absorciometria radiológica de dupla energia (DXA) não teria associação suficiente com eventos adversos do envelhecimento (limitação de mobilidade, fraturas, mortalidade e quedas). Assim, foi decidido que a massa muscular apendicular medida pela DXA não deve ser incluída na definição de sarcopenia e outras variáveis podem ser admitidas pela SDOC como parâmetro de massa muscular futuramente (exemplo: teste de diluição de creatina marcada com deutério [creatina D_3]).

A prevalência da sarcopenia pode variar a depender da população analisada. Por exemplo, um estudo com idosos americanos, italianos e franceses mostrou prevalência entre 5 e 50% dos casos (von Haehling et al., 2010). A sarcopenia acomete cerca de 17% dos idosos do Brasil, sendo a prevalência maior nas mulheres (20%) em comparação aos homens (12%) (Diz et al., 2017). A doença está presente em 10% dos idosos no mundo (Shafiee et al., 2017). Em idosos portugueses com mais de 65 anos, mostrou prevalência de 4,5% (Sousa-Santos et al., 2020). Portanto, independentemente da nacionalidade estudada, a sarcopenia configura um dos principais fatores da perda da independência em idosos (Lauretani et al., 2003; Wu et al., 2014). A sarcopenia aumenta a chance de mortalidade prematura e quedas de idosos (Gadelha et al., 2018; Lauretani et al., 2003; Wu et al., 2014). Esses desfechos de mortalidade prematura e quedas são responsáveis frequentemente por internações e por onerar consideravelmente os sistemas públicos e privados de saúde (Janssen et al., 2004). Idosos com sarcopenia e sarcopenia severa têm maiores chances de terem osteopenia/osteoporose (Lima et al., 2019). O impacto negativo na saúde decorrentes de internações, osteopenia/osteoporose, mortalidade prematura e quedas foi o que deu o reconhecimento para a catalogação da sarcopenia na classificação internacional de doenças (CID) com o código M62.84 (Anker et al., 2016). Diante desse quadro, políticas de intervenção e iniciativas profiláticas de combate e prevenção da sarcopenia são elaboradas.

O exercício físico, principalmente o treinamento com pesos, é uma terapia de custo reduzido e eficiente para aumentar a força e massa muscular além da capacidade funcional (Câmara et al., 2012; Cruz-Jentoft et al., 2014; Mijnarends et al., 2013; Phillips, 2015; Rolland et al., 2008). É comprovada a possibilidade de manutenção da espessura muscular do quadríceps e sua funcionalidade em idosos com a realização de exercício de força (Abe et al., 2014; Welle et al., 1996). O exercício de força promove adaptações positivas em indivíduos com mais de 75 anos (Stewart et al., 2014) até mesmo em nonagenários (Fiatarone et al., 1990), com aumento médio de 148% da força, da área muscular transversa da coxa (9%) e na velocidade da mobilidade (48%). O aumento de força e massa muscular com exercício pode ser potencializado quando realizado em concomitância à nutrição e à suplementação adequadas, a envolver superavit de consumo calórico e de proteínas (Phillips, 2015). Contudo, para isso é preciso contar com parâmaetros de identificação (pontos de corte) específicos para cada população/nacionalidade.

Estudos brasileiros realizaram a proposição de pontos de corte para baixa força de preensão manual para identificar o declínio da força muscular decorrente do envelhecimento. Esses modelos fazem parte da rede FIBRA (Fragilidade em Idosos Brasileiros) com dados de sete municípios brasileiros, totalizando 3478 idosos de ambos os sexos (Bez & Neri, 2014; Moreira & Lourenco, 2013; Neri et al., 2013; Vasconcelos et al., 2016; Vieira et al., 2013). O método adotado para consideração de baixa força muscular foi referenciado no primeiro quintil da força de preensão manual, segundo sexo e intervalos de IMC em kg/m^2 (≤ 24; 24,1 a 26; 26,1 a 28 e >28 para homens e ≤ 23; 23,1 a 26; 26,1 a 29; >29 para mulheres) (Fried et al., 2001). Outro estudo também propôs valores para identificação da sarcopenia em 578 idosos de ambos os sexos (R. A. C. Sampaio et al., 2017) com pontos de corte para baixa força, a considerar o medo de quedas (derivado da questão: *are you afraid of falling?*) como variável dependente (1: sim; 0: não). Obtiveram valores de 30 e 21,7 kg para força de preensão manual absoluta, ou de 1,07 e 0,66 m^2, quando normalizada pelo IMC.

Todavia, pontos de corte da força de preensão manual de forma absoluta, ou de índice pelo tamanho corporal aponta para dois fatores: 1º) valores absolutos são injustos com idosos de tamanho corporal pequeno (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). Esses valores consideram idosos mais leves e de menor estatura como tendo menores níveis de força quando comparados a seus pares mais pesados e mais altos, pois mesmo abaixo do ponto de corte, ainda podem ser independentes fisicamente; e 2º) a força não apresenta relação linear com o tamanho corporal (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020), o que pode induzir a vieses na interpretação da força. Em suma. Simplesmente ao se dividir a força pelo tamanho corporal (i.e. “força muscular/massa corporal”), por um lado superestima a real força dos idosos leves/baixos e, por outro, a força muscular é subestimada em idosos altos/pesados. Portanto, o uso de ajustes matemáticos que considerem as relações não lineares entre a força muscular e o tamanho corporal poderia solucionar esse problema. Considerar a real relação da força muscular com o tamanho corporal evitaria equívocos no diagnóstico de casos de falso positivos e falso negativos da doença. Isso teria impacto relevante nos recursos disponíveis para saúde pública e privada, de países em desenvolvimento e de economias frágeis. Por outro lado, idosos que realmente necessitariam de intervenção seriam excluídos dos possíveis tratamentos diante de tais erros no diagnóstico. Nesse sentido, a alometria seria uma das estratégias matemáticas mais adequada para a correta interpretação.

O termo alometria foi criado na década de 40 (Huxley & Teissier, 1936a, 1936b) e é aplicado a partir da expressão alométrica: $Y = aX^b$. Onde, Y é a variável dependente ou variável a ser predita, a letra "a" é uma constante de correção, X é uma variável independente ou preditor, e ^{b} é o expoente da razão de potência entre as relações, ou ainda, o expoente alométrico (Huxley, 1924). Existe a possibilidade de descrever a relação entre duas variáveis quaisquer pela alometria, desde que estas apresentem uma relação de potência. A relação de potência é caracterizada quando existe a necessidade de um fator de transformação ($^{\mathbf{b}}$), que promove o intercâmbio correto entre as variáveis. Sem esse fator, a relação torna-se espúria, descaracterizando-a. O expoente pode ser necessário, quando: 1) relacionam-se variáveis de diferentes dimensões e/ou 2) relaciona-se variáveis que variam no mesmo tempo, porém apresentam magnitudes de variação distintas. Algumas situações aonde a alometria pode ser aplicada envolve a comparação do desempenho de um indivíduo com valores normativos, comparar o desempenho motor entre grupos, verificar os efeitos do crescimento/treinamento e identificar as relações entre características fisiológicas e de desempenho motor (Winter & Nevill, 2009).

Modelos lineares são insuficientes para explicar relações não lineares entre variáveis, impedindo o correto entendimento de um determinado fenômeno. O tipo de relação entre a variável dependente (Y) e a variável independente (X) é o que determina os valores do expoente alométrico. Caso a variável Y aumente mais lentamente do que a variável X, a inclinação da reta será curvilínea, maior do que zero, mas menor do que um ($^{0 < b < 1}$); se acontece o contrário (X aumenta mais rapidamente na relação) os valores de *b* são maiores do que um ($^{b > 1}$); e no caso do valor obtido ser igual a um ($^{b = 1}$) a relação entre as variáveis é considerada como isométrica ou linear (Calder, 1984). Segundo o princípio das similaridades geométricas (Abernethy et al., 1996), que estabelecem as relações entre áreas ($A=L^2$), volumes ($V=L^3$) e dimensões lineares, de comprimento ($C=L^1$), é esperado que a força seja proporcional à Área de Secção Transversa (AST) de um músculo, que é uma área (L^2). A relação da força com a massa corporal, que é cúbica (L^3), é dada pela seguinte expressão: $L^2/L^3 = L^{2/3}$, expressa, portanto como $L^{0,67}$: isto é, força/massa corporal^{0,67} , onde $^{b = 0,67}$ representa a correção da relação não linear (Jaric, 2003). Estudos realizados com idosos americanos confirmaram a relação não-linear da força de preensão manual com a massa corporal, com valores de 0,63 (Y. H. Pua, 2006) e 0,40 (Foley et al., 1999) propostos para o ajuste do expoente alométrico.

Dessa maneira, parece evidente a necessidade de ajustar força de preensão manual por alguma dimensão corporal, corrigida alometricamente, a isolar a influência do tamanho do corpo sobre esse parâmetro. Um estudo mais recente com idosos brasileiros (Maranhão Neto et al., 2017) confirmou a existência dessa relação, com ligeira variação do expoente dessas variáveis ($^{b = 0,31}$). A mesma relação alométrica foi encontrada entre a força muscular de membros inferiores de idosos e a massa corporal (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020; Davies & Dalsky, 1997). Nesse sentido, a força de extensão do joelho de idosos sedentários (65 a 78 anos) testada em dinamômetro isocinético a 60º/s apresentou relação alométrica ($^{b = 0,74}$) com a massa corporal (Davies & Dalsky, 1997). Sabe-se que a espessura muscular do quadríceps obtida por ultrassonografia (Radaelli et al., 2013) está relacionada à força de extensão de joelho.

Como ilustração, segue um exemplo hipotético de ajuste alométrico da força de preensão manual (45 kg) de um idoso, sendo considerada sua massa corporal (80 kg) como variável de ajuste. Ou seja:

$$\text{Força de preensão manual ajustada alometricamente} = \frac{\text{Força de preensão manual (kg)}}{\left(\text{Massa corporal (kg)}^{\text{Expoente alométroco (b)}}\right)}$$

(Equação 1)

1) O cálculo do expoente alométrico$^{(b)}$ inicialmente é obtido para força de preensão manual, mediante regressão linear simples entre os logaritmos naturais da força muscular e da massa corporal. Em nosso exemplo, o resultado de ^{b} foi determinado em 0,67 ($^{b=0,67}$);

2) Em seguida, aplica-se a equação substituindo os valores da Equação 1 do exemplo hipotético:

$$\text{Força de preensão manual ajustada alometricamente} = \frac{45\ \text{(kg)}}{(80\ \text{kg}^{0,67})}$$

(Equação 2)

3) Dessa forma, o resultado da força de preensão manual normalizada pela massa corporal com ajuste alométrico seria de 0,56 (adimensional/sem unidade, pois houve divisão de kg por kg);

4) Se não quiser utilizar o ajuste alométrico, o valor da força de preensão manual é normalizado por *ratio standard*, assim expresso:

$$\text{Força de preensão manual ajustada com } ratio\ standard = \frac{45\ \text{(kg)}}{80\ \text{(kg)}}$$

(Equação 3)

5) dessa forma, o resultado seria de 2,39 (também adimensional/sem unidade), pois houve divisão de kg por kg).

Outro assunto de importância é a forma de proposição dos pontos de corte da baixa força muscular para identificar a sarcopenia, onde geralmente considera-se a variável dependente de limitação da mobilidade (Cruz-Jentoft et al., 2018). O teste de caminhada de seis minutos (6MWT), uma das recomendações do Consenso proposto por John E Morley et al. (2011), testa o desempenho de mobilidade, ainda sendo este, preditivo de hospitalizações e mortalidade (Agarwala & Salzman, 2020). Sobretudo, quando as distâncias percorridas no teste são abaixo de 400 m (Holland et al., 2010), a caracterizar a limitação de mobilidade. A incapacidade funcional, ou seja, dificuldade para realizar atividades instrumentais e básicas de vida diária-ADL (i.e., limitação de mobilidade) (Santanasto et al., 2020) é mais significativa para prever mortalidade entre idosos do que a multimorbidade (Landi et al., 2010). O mesmo valor limítrofe de risco (< 400 m) foi proposto por um consenso internacional (J. E. Morley et al., 2011) como um dos critérios para identificar a sarcopenia. Por ser capaz de prever resultados adversos na saúde de idosos (hospitalizações, mortalidade prematura e perda da independência funcional), a limitação de mobilidade é utilizada como variável dependente para proposição dos pontos de corte de baixa força muscular (fraqueza muscular) na identificação da sarcopenia.

DELIMITAÇÕES E JUSTIFICATIVAS

Quando idosos sarcopênicos realizam treinamento com pesos para aumento da força geral (Fielding et al., 2011), a força de preensão manual deixa de ser representativa da força dos membros inferiores (Arai et al., 2018; Vlietstra et al., 2018; Yoshimura et al., 2017). Portanto, as adaptações promovidas pelo treinamento físico devem ser identificadas por métodos sensíveis e válidos. Nesse sentido, a força dos membros inferiores parece ser mais representativa, pois associa-se com atividades funcionais que asseguram a independência dos idosos (Hughes et al., 1996; Ploutz-Snyder et al., 2002). Além disso, é sensível ao treinamento físico (Bunout et al., 2001). Contudo, a maior parte dos referenciais de segmentos inferiores são da força isométrica de extensão do joelho (Assantachai et al., 2014; Cruz-Jentoft et al., 2014; Lauretani et al., 2003; Martien et al., 2015), que tendem a subestimar a força quando comparadas à medidas de referência (dinamômetro isocinético) (Martien et al., 2015). Existem ainda referenciais da força em dinamômetro isocinético, (Akpinar et al., 2014; Farinatti et al., 2017; Gadelha et al., 2018; Hofmann et al., 2015; Lima et al., 2019), porém sua utilização têm elevado custo e aplicabilidade clínica limitada (Lesnak et al., 2019). Assim, o teste de uma repetição máxima (1RM) em cadeira extensora parece ter maior aplicabilidade e boa associação com a mobilidade de idosos (Van Roie et al., 2011).

Todavia, os pontos de corte da força de extensão de joelho, ou mesmo da força de preensão manual são consideradas em sua forma absoluta, mas quando tratados de forma relativa à massa corporal (Akpinar et al., 2014; Assantachai et al., 2014; Farinatti et al., 2017; Foley et al., 1999; Fried et al., 2001; Gadelha et al., 2018; Hofmann et al., 2015; Lauretani et al., 2003; Lima et al., 2019; Maranhão Neto et al., 2017; Martien et al., 2015; Y. H. Pua, 2006), consideram equivocadamente uma relação linear, quando essa relação é curvilínea (Maranhão Neto et al., 2017). Dessa forma, a alometria poderia auxiliar na correção de vieses entre variáveis de relação não linear (Winter & Nevill, 2009).

A presente tese defende a ideia de que a normalização da força e da massa muscular pelo tamanho corporal pode ser uma estratégia para minimizar o viés das dimensões corporais sobre a funcionalidade de idosos. Os ajustes alométricos/normalização favoreceriam a proposição de pontos de corte da força muscular justos para identificar sarcopenia, melhorando a previsibilidade da mobilidade, reduzindo a distância dos pontos de corte absolutos entre países desenvolvidos e subdesenvolvidos. Os expoentes alométricos poderiam ser utilizados independentemente da amostra de origem. Além disso, medidas antropométricas simplificadas para estimativa de índices musculares, tem se mostrado eficientes na indicação de limitação funcional de idosos (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). Portanto, normalizar o perímetro da panturrilha pelo tamanho corporal permitiria linearizar a relação de U-invertido com a mobilidade de pessoas idosas, possibilitando estabelecer ponto de corte somente para valores de risco (baixos).

OBJETIVOS

Objetivo Geral

Na defesa desta tese, foram propostos modelos para interpretação da força e da massa muscular normalizados pelo tamanho corporal, com intuito de identificar o risco de sarcopenia em idosos.

Objetivos Específicos

Nomeadamente três objetivos específicos foram delineados:

1) propor expoentes alométricos para normalizar a força de membros superiores e inferiores pelo tamanho corporal; e a partir desses referenciais, gerar os pontos de corte determinantes da fraqueza muscular de idosos;

2) aplicar o modelo proposto comparativamente a outros modelos da literatura numa população terciária de idosos, para testar sua eficácia em normalizar força muscular e identificação de fraqueza muscular;

3) identificar baixa massa muscular esquelética de forma normalizada pelo tamanho corporal, baseada na limitação funcional para o risco de sarcopenia, a envolver medidas de simples aplicação clínica (perímetro da panturrilha).

ESTRUTURA (apresentação de formato)

A presente tese está organizada em sete capítulos. No capítulo I está posta uma introdução geral à temática da tese com respaldo na literatura, destaque ao problema de estudo para justificação desta tese e exposição dos objetivos gerais e específicos. Os capítulos II ao V tratam dos estudos originais realizados para tentar solucionar os problemas específicos destacados. A discussão geral é apresentada no capítulo VI. As principais conclusões da presente tese são apresentadas no capítulo VII. As referências, por opção, estão localizadas no final do documento.

As intenções que levaram a inclusão dos capítulos II ao V (Estudos originais I ao IV), juntamente com a justificação e ordenamento lógico da composição estão dispostas na seguinte lógica: Nenhum dos estudos anteriores aos propostos nessa tese considerou o uso da alometria para estabelecer os pontos de cortes para sarcopenia. Houve somente um estudo que propôs pontos de corte da força muscular de 1RM normalizada pela massa corporal (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). Contudo, existem outras variáveis associadas com a independência física [massa gorda (Bouchard et al., 2007), massa isenta de gordura (Broadwin et al., 2001) e comprimento da perna (Enright, 2003)] ainda não consideradas pela ótica da alometria (objetivo do Estudo Original I). Solvida esta questão, o desafio seguinte se impunha.

Diferenças em relação a fatores biológicos, genéticos e sociais entre países desenvolvidos e os subdesenvolvidos impactam na força (Koopman et al., 2015), sendo necessário propor expoentes alométricos e pontos de corte específicos para países subdesenvolvidos (objetivo do Estudo Original II). Expoentes alométricos oriundos de países desenvolvidos (Davies & Dalsky, 1997; Segal et al., 2008) e subdesenvolvidos (P. P. Abdalla, L. Bohn, et al., 2021) são disponíveis na literatura, mas ainda a validade externa não havia sido testada (objetivo do Estudo Original III).

Por fim, o desafio final envolvia uma lacuna da literatura, da proposição de métodos alternativos para medição da massa muscular de idosos, uma vez que os recursos de alta precisão (análise por imagem), nem sempre estão disponíveis. O consenso europeu propõe o perímetro da panturrilha como alternativa para identificar baixa massa muscular (Cruz-Jentoft et al., 2018) e pontos de corte absolutos foram propostos (Bahat et al., 2016; Barbosa-Silva et al., 2016; Bonnefoy et al., 2002; Kawakami et al., 2015; Kim et al., 2018; Kusaka et al., 2017; Landi et al., 2014; Pagotto et al., 2018; Rolland et al., 2003; L. S. Sampaio et al., 2017). Apesar de muito bem se associarem com mobilidade (Tsai et al., 2012), a relação se dá na forma de U-invertido (Pérez-Zepeda & Gutiérrez-Robledo, 2016). Pensou-se então em se ao normalizar o perímetro da panturrilha pelo tamanho corporal, poderia se linearizar essa relação (objetivo do Estudo Original IV).

CAPÍTULO II

ESTUDO ORIGINAL I - Identification of muscle weakness in older adults from normalized upper and lower limbs strength: A cross-sectional study

Identification of muscle weakness in older adults from normalized upper and lower limbs strength: A cross-sectional study

Pedro Pugliesi Abdalla[12], Lucimere Bohn[2], Leonardo Santos Lopes da Silva[3], André Pereira dos Santos[1], Marcio Fernando Tasinafo Junior[3], Ana Claudia Rossini Venturini[1], Anderson dos Santos Carvalho[4], David Martinez Gomez[5], Jorge Mota[2], Dalmo Roberto Lopes Machado[123].

[1] University of São Paulo, College of Nursing at Ribeirão Preto, Ribeirão Preto, Brazil.

[2] University of Porto, Faculty of Sports, Porto, Portugal.

[3] University of São Paulo, School of Physical Education and Sport of Ribeirão Preto, Ribeirão Preto, Brazil.

[4] Paulista University, Physical Education Course, São José do Rio Preto, Brazil.

[5] Autonomous University of Madrid, School of Medicine, Madrid, Spain.

Publicado em *BMC Sports Science, Medicine and Rehabilitation* (ISSN: 2052-1847; Fator de impacto: 1,934).

DOI: https://doi.org/10.1186/s13102-021-00390-1

BMC Sports Sci Med Rehabil. 2021 Dec 18;13(1):161.

Abstract

Background: To propose cut-off points for older adults' weakness for upper and lower limbs muscle strength normalized by body size with the ratio standard/muscle quality and allometric scaling. Methods: Ninety-four community-dwelling older adults (69.1% women) were assessed for 49 body-size variables (anthropometry, body composition and body indexes), handgrip strength (HGS), one maximum repetition measurement for knee extensors (1RM), isokinetic knee extension peak torque at 60°/s (PT), and six-minute walk test (6MWT). Ratio standard or muscle quality (muscle strength/body size) and allometric scaling (muscle strength/body size^{b}; when ^{b} is the allometric exponent) were applied for body-size variables significantly correlated with HGS, 1RM and PT. Cut-off points were computed according to sex based on mobility limitation (6MWT<400m) with ROC curve and Youden index. Results: Absolute HGS, 1RM and PT cut-off points were not adequate because they were associated with body size (r>0.30). But it was corrected with muscle strength normalization according to body size-variables: HGS (n=1); 1RM (n=24) and PT (n=24). The best cut-off points, with the highest area under the curve (AUC), were found after normalization for men: HGS/forearm circumference (1.33 kg/cm, AUC=0.74), 1RM/triceps skinfold (4.22 kg/mm, AUC=0.81), and PT/body mass*height$^{0.43}$ (13.0 Nm/kg*m$^{0.43}$, AUC=0.94); and for women: HGS/forearm circumference (1.04 kg/cm, AUC=0.70), 1RM/body mass (0.54 kg/kg, AUC=0.76); and PT /body mass$^{0.72}$ (3.14 Nm/kg$^{0.72}$; AUC=0.82). Conclusions: Upper and lower limbs muscle weakness cut-off points standardized according to body size were proposed for older adults of both sexes. Normalization removes the effect of extreme body size on muscle strength (both sexes) and improves the accuracy to identify weakness at population level (for women, but not in men), reducing the risk of false-positive cases.

Keywords: allometrically scaled, disability, evaluation, frailty, function/functional status, measurement, sarcopenia, scaling

1. Introduction

Muscle weakness is a natural muscle strength loss occurring along aging, and it predicts older adults' increased risk of hospital admissions, depression, fractures and premature mortality (Bohannon, 2008, 2019; Teng et al., 2021). Muscle weakness can predict functional disability (i.e., difficulty to perform instrumental and basic activities of daily living-ADL) like as mobility limitation (Santanasto et al., 2020), which is even more important than multimorbidity to forecast mortality amongst older adults (Landi et al., 2010). As a consequence of its predictive ability, muscle weakness was used to identify geriatric syndromes such as dynapenia (Clark & Manini, 2008), frailty (Fried et al., 2001) and sarcopenia (Cruz-Jentoft et al., 2018).

Muscle weakness is normally measured using muscle strength tests such as handgrip (HGS) or leg extension strength (Cruz-Jentoft et al., 2018). The current values to identify muscle weakness are based on absolute (non-normalized) muscle strength results (Akpinar et al., 2014; Albrecht et al., 2021; Dodds et al., 2014; Farinatti et al., 2017; Fried et al., 2001; Gadelha et al., 2018; Hofmann et al., 2015; Lauretani et al., 2003; Lima et al., 2019; Wang et al., 2018) or dividing absolute results by a body-size variable (ratio standard) such as body mass (Manini et al., 2007; McGrath et al., 2020) or by some body composition component, like lean tissue (muscle quality) (de Mello et al., 2019; Sardeli et al., 2018; Strasser et al., 2018). The identification of weakness based on absolute muscle strength cut-off points may be inaccurate for lighter body mass and shorter height older adults (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). In fact, the absolute values characterize lighter and shorter body size older adults as having muscle weakness, even if they sustain their instrumental and basic ADL (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). This is a false positive muscle weakness diagnostic, that frequently leads to an unnecessarily utilization of public health resources, contributing to health burden (P. P. Abdalla, A. C. R. Venturini, et al., 2021). Another topic that merits consideration is the inaccuracy of the ratio standard/muscle quality procedure because it overestimates the real strength of light/short older adults and underestimates it for tall/heavy ones (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). These limitations are a consequence of the nonlinear relationship between muscle strength and body-size variables (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). To overcome these constraints, the utilization of allometric scaling, that contemplates power and sensitivity in the nonlinear relationship between muscle strength and body size with the allometric exponent (^{b}) might represent an adequate option (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020; Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006).

Previous studies reported already the power function ratio in older adults between HGS and body-size variables as body mass ($^{b=0.63}$ or $^{0.40}$ or $^{0.31}$) (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006), height ($^{b=1.84}$) (Maranhão Neto et al., 2017) and fat-free mass (FFM) ($^{b=0.46}$) (Maranhão Neto et al., 2017) and between leg extension strength and body mass ($^{b=0.67}$ or $^{0.69}$ or $^{0.72}$ or $^{0.74}$ or $^{0.96}$) (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020; Davies & Dalsky, 1997). Indeed, scaling HGS by body size (example: HGS/heigth$^{1.84}$) removes the effect of body size on muscle strength (Maranhão Neto et al., 2017), but the scaling muscle strength by body size to determine muscle weakness cut-off points has not been considered from HGS and knee extension in isokinetic dynamometer, excepting the one maximum repetition measurement for knee extensors (1RM) scaled to body mass (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). Besides, important body-size variables related to mobility and ADL [e.g. fat mas (Bouchard et al., 2007), FFM (Broadwin et al., 2001) and leg length (Enright, 2003)] were not utilized to scaling muscle strength and create muscle weakness cut-off points.

Thus, our objective is to propose cut-off points for older adults' weakness with upper and lower limbs muscle strength normalized by body-size with the ratio standard/muscle quality and allometric scaling. We hypothesize that the normalization of muscle strength by ratio standard/muscle quality and allometry can be a way to approach muscle strength regardless of body size, which should reduce the risk of bias in identifying false-positive cases of vulnerable older people.

2. Materials and Methods

Design and Study population

This is a cross-sectional study conducted from October 2016 to May 2017 at the University Hospital of Ribeirao Preto School of Medicine, University of São Paulo, Brazil (HC-FMRP-USP). The study was approved by the HC-FMRP-USP institutional review board (CAAE: 54345016.6.3001.5440). Older adults were voluntarily recruited and assigned an informed consent. This manuscript followed the guidelines from The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) conference list (Cuschieri, 2019).

The sample consisted of 94 community-dwelling older adults (≥60 years old, 69.1% women) recruited in projects for older adults of USP and in health community services. Inclusion criteria were ≥60 years old, walk independently, absent limitation to execute all procedures, acute infections, cancer diagnosis, hip or knee prostheses, unstable cardiovascular condition, stroke sequelae, tumors, and weight loss >3 kg in the last three months. The exclusion criteria were discontinuity in the study and cognition impairment (assessed by Mini Mental State Examination).

A sample size calculation ($n=[ZySD/\varepsilon]^2$) (Bolfarine & Bussab, 2005) with trust level (Zy=0,95), greater compatible population variability founded in the literature (SD of 1RM: ±19.96 kg) (Binder et al., 2005; Cruz-Jentoft et al., 2014) and maximum desired error ($\varepsilon \leq 8.0$ kg) was performed and identified a minimum sample size of n=24 for each sex.

Procedures

A multidisciplinary health team (nurses, nutritionists, pharmacists, physical educators, physicians, and physiotherapists) performed data collection. The appraisers were the same in each test. Data collection occurred on three non-consecutive days: 1st) recruitment: inclusion criteria verification by phone calls; 2nd) cognition assessment, anthropometrics, body composition, HGS, mobility and physical activity level assessment; and 3rd) lower limbs muscle strength assessment. These procedures are resumed in Figure 1.

Cognition Assessment

The validated Mini Mental State Examination (MMSE) was used to assess participants' cognition status and to ensure that participants understood the other tests executed in the present study (Finney et al., 2016). The MMSE was executed in a quiet room, face to face with the researcher. Those who have MMSE≤12 were considered with dementia and were excluded (Icaza & Albala, 1999).

Measure of Body-Size Variables

Forty-nine body-size variables (SUPPLEMENT A in Additional file 1) were collected to propose allometric exponents and to normalize performance in muscle strength tests. The selection of these variables were based on those previously used to calculate body indexes (Bailey & Briars, 1996; Baumgartner et al., 1991; Baumgartner et al., 1998; George et al., 1977; Heymsfield et al., 1982; Jelliffe & Jelliffe, 1969; Lean et al., 1996; Segal et al., 2008; WHO Expert Consultation, 2004), and involved anthropometric measurements (Timothy G Lohman et al., 1988) and body composition (Dual Energy X-ray Absorptiometry-DXA and bioelectrical impedance analysis-BIA), as briefly detailed below (body indexes).

Measures and instruments utilized were: body mass (Filizola® digital scale, model Personal, Brazil), height (Sanny® wall-mounted aluminum stadiometer, Professional model ES2020, Brazil), circumferences (Sanny® inelastic and inextensible measuring tape, Brazil), skinfolds (Lange scientific skinfold caliper, Cambridge Scientific Instruments, Cambridge, Maryland), bone breadths (Sanny® anthropometer and small sliding caliper, Brazil), and segment lengths (Sanny® segmometer, Brazil), lean soft tissue (LST) components, appendicular skeletal muscle mass (ASM) and FFM (DXA, Hologic®, model QDR4500W, software version 11.2, Bedford, MA), FFM (Baumgartner et al., 1991)

(Bioimpedance Imp DF50 Body Composition Analysis, ImpediMed®, Brisbane, Queensland, Australia).

Anthropometry (body mass, height, circumferences, skinfold and bone breadths) was collected according to a standardized procedure published elsewhere (Timothy G Lohman et al., 1988). DXA involved a full body scan performed (according to the manufacturer's recommended procedures) and interpreted always by the same technician. BIA exam was conducted in controlled temperature room (23 ºC) with the older adults backed on a litter in comfortable position after rest for 10 minutes in supine position, without footwear and adornments (rings and earrings), with legs separated and opened hands. Older adults were previously oriented (24 hours before the exam) to avoid the consumption of alcohol and caffeine (coffee, tea, chocolate), diuretic medication, intense physical activity and meal four hours before the exam.

Body Indexes

The body indexes derived from anthropometry were body mass index (BMI, kg/m²) (WHO Expert Consultation, 2004), body mass*height (Segal et al., 2008), human body surface area (SA, m²) (Bailey & Briars, 1996), absolute mid-arm muscle circumference (MAMC, cm) (Jelliffe & Jelliffe, 1969), corrected arm muscle area (CAMA, cm) (Heymsfield et al., 1982), arm fat area (AFA,cm²) (George et al., 1977), FFM (Lean et al., 1996) and fat mass (obtained by body mass difference). The body indexes derived from body composition were LST of arms and legs, ASM, ASM/height (m)² (Baumgartner et al., 1998), FFM (estimated from BIA) (Baumgartner et al., 1991) and DXA, when fat mass were estimated by body mass difference.

Mobility Measurement

The cut-off points for muscle weakness were established based on the main outcome (mobility limitation). Mobility was verified based on the six-minute walk test (6MWT) carried out in a corridor 30-meter length. Along this path, at every three meters there was a cone to help researcher to precisely identify the walked distance (Enright, 2003). Participants were instructed to cover the longest distance walking as faster as they could during the six-minute time. Nevertheless, participants could slow down, interrupt the walking, and resume the test whenever desired, although time was not paused. Total walked distance was recorded and mobility limitation was characterized when the 6MWT<400 m (J. E. Morley et al., 2011).

Muscle Strength Measurements

Muscle strength was measured using HGS, one maximum repetition measurement for knee extensors (1RM) and isokinetic knee extension peak torque at a velocity of 60°/s (PT). The maximum HGS was measured with a manual dynamometer (Jamar®, model 5030J1) using a previously published protocol (Massy-Westropp et al., 2011). Three attempts were performed, one minute apart, with the dominant hand and the highest result was recorded in kg as HGS (Alexandre et al., 2014; Lourenco et al., 2014). The 1RM was estimated in a leg extension machine (Lion Fitness® model LFS) with a submaximal repetition protocol: 1RM=weight lifted/(1.0278-[0.0278*nº of reps]) (Brzycki, 1993). The detailed protocol was published elsewhere (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). Briefly, a warm-up with lowest load was executed with 10 repetitions. After two-min resting, the load was doubled and eight repetitions were performed. After three-min resting, the test started and initial load was based on participants body mass (45% for women and 64% for men). The goal was to perform a maximum of 10 repetitions in three possible attempts (separate with three minutes intervals). Therefore, depending on older adults' muscle strength level, these initial loads could be increased or decreased to estimate 1RM. The PT of the right lower limb was recorded with the Biodex (model System 4 Pro) isokinetic dynamometer and results are in newton-meter (Nm) according to standardized protocol (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, & Machado, 2020). Briefly, a warm-up with 10 submaximal repetitions in angular speed of 60°/s was performed. After three-min resting, the test was started with executing five maximum repetitions verbally encouraged by researchers without visual feedback. 1RM was executed prior to the PT, and the time interval between these tests was at least 30 minutes.

Physical Activity Level Measurement

The International Physical Activity Questionnaire - Short Version was used to get physical activity level (Matsudo et al., 2012). Physical activity level was dichotomized into sedentary (0) and irregularly active, active or very active (1). These two categories were introduced in the models to provide allometric exponents.

Muscle Strength Normalization Procedures (Ratio Standard/Muscle Quality and Allometric Scaling)

HGS, 1RM and PT were considered in three different ways: 1) absolute (non-normalized); 2) ratio standard or muscle quality (muscle strength/body-size variable); and 3) allometrically adjusted (muscle strength/body-size variable^b).

Allometric exponents (^{b}) were proposed only for body-size variables that showed significant correlation (Pearson's correlation) with muscle strength. To generate the allometric exponents, muscle strength (Y) and body-size variables (X) were converted to natural logarithm (ln) and the slope of regression line is allometric exponent (^{b}), according to more detail previously published (Maranhão Neto et al., 2017). Therefore, allometric exponents were discarded when the interaction (ln body-size variable*age*sex*physical activity level) was significant or when there was multicollinearity in the linear regression (variance inflation factor [VIF]>10) (Myers, 1990).

We also consider other allometric exponents (^{b}) of the literature, as described in Table 1.

Table 1. Allometric exponents (b) proposed in previous studies

Authors	Normalized muscle strength for body-size variable
Jaric (2003)	General muscle strength/body mass$^{0.67}$
Foley et al., (1999)	HGS/body mass$^{0.40}$
Pua (2006)	HGS/body mass$^{0.63}$
Maranhão Neto et al., (2017)	HGS/body mass$^{0.31}$
	HGS/height$^{1.84}$
Abdalla et al., 2020	1RM/body mass$^{0.69}$
	1RM/body mass$^{0.96}$
Davies and Dalsky (1997)	PT/body mass$^{0.67}$
	PT/body mass$^{0.72}$
	PT/body mass$^{0.74}$
Segal et al., (2008)	PT/body mass*height$^{0.97}$

HGS=handgrip strength; 1RM=one maximum repetition measurement for knee extensors; PT =isokinetic knee extension peak torque at 60º/s.

In order to verify whether normalization removed the influence of body size on muscle strength, the correlation between normalized muscle strength and body-size variables (body mass, height and body-size used) should be negligible (r≤30) (Mukaka, 2012).

Statistical Analysis

We recorded and reviewed the data by double typing, followed by an exploratory analysis for error detection. We use parametric statistics for continuous variables considering the central limit theorem (Kwak & Kim, 2017).

Proposition of Cut-off Points for Muscle Weakness

Absolute muscle strength and normalized by ratio standard/muscle quality or allometric scaling had their area under the curve (AUC) quantified by the ROC curve. The Youden index (Schisterman et al., 2005) selected the most appropriate cut-off points with the best relationship between sensitivity and specificity for the primary main outcome (functional limitation: 6MWD<400) (J. E. Morley et al., 2011).

The cut-off points were considered adequate when they have AUC≥0.70 (Hosmer & Lemeshow, 2000) simultaneously for both sexes ($p<0.05$) and when the correlation between muscle strength and body-size variables (body mass, height and body-size used) were negligible ($r\leq0.30$) (Mukaka, 2012).

For each muscle strength test (HGS, 1RM and PT), way (non-normalized, ratio standard/muscle quality and allometric scaling) and for each and sex was selected the adequate cut-off point according the superior accuracy. When there was a tie in accuracy, the variable with the greatest sensitivity or specificity was chosen. Finally, the AUC - ROC curves of non-normalized and normalized muscle strength were compared with each other to decide the best cut-off point.

The analyzes were performed using the SPSS 25.0 statistical package, and the ROC curves and Youden index in MedCalc 15.2 with a previously established level of significance (α=5%).

3. Results

Sample was encompassed by 100 older adults (69 women) who agreed to participate in the study. From those, 6 were excluded for different reasons, as the stages of the study proceeded, as detailed in Figure 1. Therefore, the final sample comprised 29 older men (31%) and 65 older women (69%).

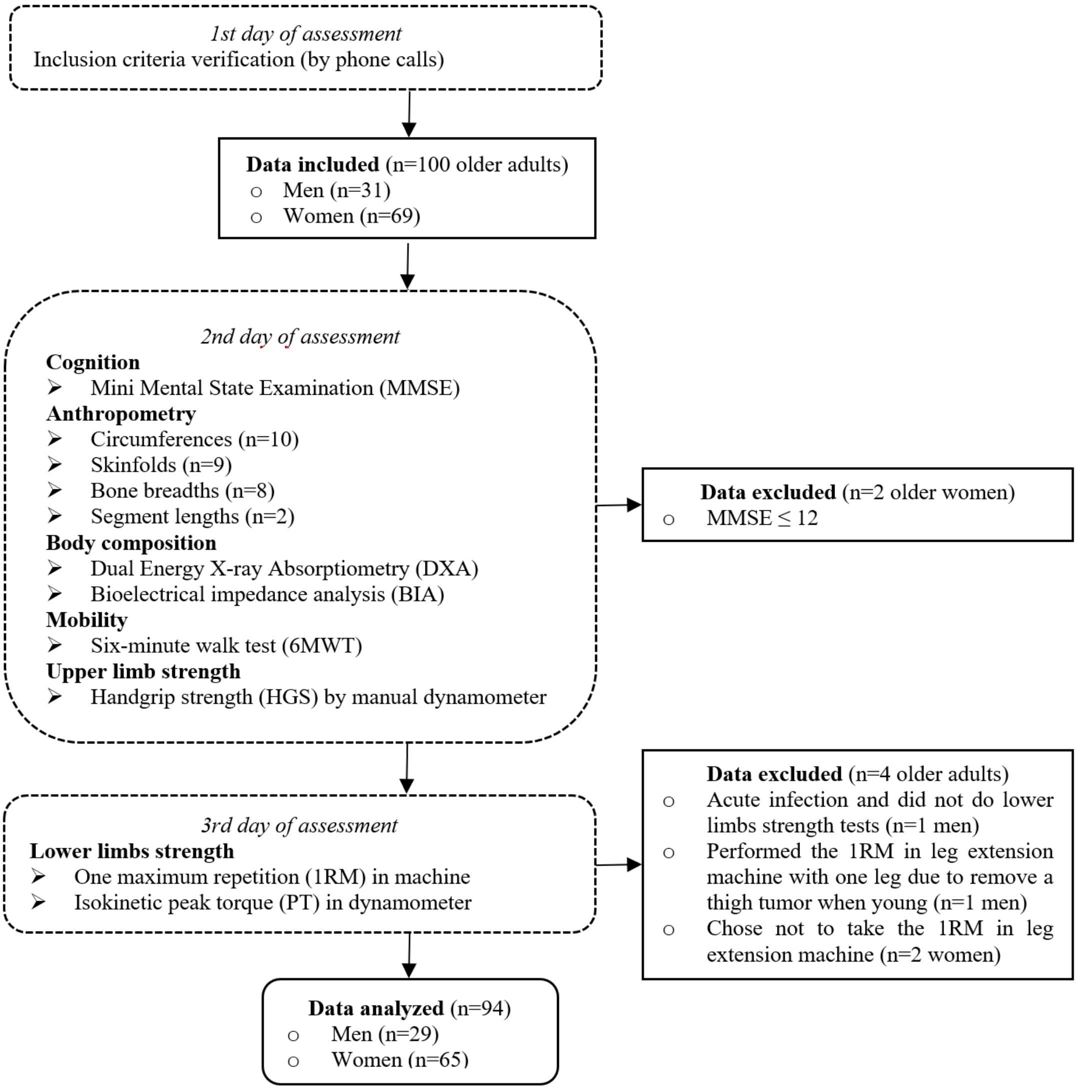


Figure 1. Study phases and data from older adults included, excluded, analyzed and procedure flow

Sample characterization according to sex is shown in Table 2. About main outcome of the study, twenty-five women (38.5%) and seven men (24.1%) had functional limitation (6MWT<400 m).

The correlations between muscle strength and body-size variables are also shown in Table 2. Most of the body-size variables showed a significant correlation with muscle strength (r=-0.41 to 0.75; p<0.05). Non-significant correlations between body-size variables and muscle strength tests are shown in SUPPLEMENT B (Additional file 1).

Table 2. Descriptive analysis and significant correlations of muscle strength with body-size variables in older men and women (n=94)

Variables	Older Men (n=29)				Older Women (n=65)				Correlation (r) with Muscle Strength		
	M	95% CI		SD	M	95% CI		SD	HGS (kg)	Knee Extension	
		LL	UL			LL	UL			1RM (kg)	PT (Nm)
Age (years)	71.2	68.5	73.9	7.1	69.7	68.2	71.2	6.1			
Mini-Mental State Examination (0-19)	17.6	16.9	18.2	1.8	17.4	16.9	17.8	1.8			
Body-size variables											
Anthropometry											
Body mass (kg)	73.0	67.7	78.3	13.9	66.9	64.0	69.8	11.6	0.37†	0.39†	0.40†
Height (m)	1.7	1.6	1.7	0.1	1.6	1.5	1.6	0.1	0.71†	0.62†	0.68†
Circumferences (cm)											
Forearm	26.0	25.2	26.8	2.0	23.8	23.3	24.4	2.2	0.50†	0.40†	0.46†
Calf	35.8	34.4	37.1	3.5	34.8	34.1	35.5	2.9	0.34*	0.37†	0.37†
Chest	97.8	94.3	101.4	9.4	93.2	91.3	95.1	7.7	0.26*	0.32*	0.36†
Waist	92.1	87.8	96.5	11.4	86.5	84.0	89.0	10.0		0.26*	0.30*
Skinfold thickness (mm)											
Triceps	15.2	12.9	17.5	6.0	25.8	24.1	27.4	6.7	-0.39†	-0.22*	-0.25*
Biceps	8.0	6.7	9.4	3.5	15.4	14.0	16.7	5.4	-0.40†	-0.28*	-0.31*
Midaxillary	18.5	15.5	21.5	7.8	23.9	22.2	25.6	6.9	-0.26*		
Pectoral	16.8	14.7	18.9	5.5	14.6	13.0	16.2	6.4	0.21*		
Suprailiac	19.7	15.8	23.5	10.1	29.7	27.8	31.7	7.8	-0.29*		
Abdominal (vertical)	26.2	23.1	29.3	8.1	33.7	31.5	35.9	8.8	-0.22*		
Thigh (midline)	17.9	15.0	20.8	7.6	32.1	29.5	34.8	10.7	-0.35*	-0.27*	-0.38†
Medial calf	11.8	9.3	14.3	6.6	23.8	21.9	25.7	7.6	-0.41†	-0.28*	-0.33*
Bone breadths (mm)											
Biacromial	39.9	38.9	41.0	2.8	37.1	36.6	37.6	2.1	0.63†	0.58†	0.60†
Bitrochanteric	33.7	33.1	34.3	1.7	33.4	32.8	34.0	2.3		0.20*	0.22*
Ankle (bimalleolar)	7.0	6.8	7.2	0.5	6.3	6.2	6.4	0.4	0.59†	0.47†	0.52†
Elbow	6.7	6.5	6.9	0.5	5.8	5.7	6.0	0.5	0.53†	0.40†	0.44†
Wrist	5.7	5.6	5.9	0.4	5.1	5.0	5.1	0.4	0.52†	0.37†	0.44†
Chest	30.9	29.9	31.9	2.6	27.8	27.4	28.3	1.8	0.58†	0.49†	0.59†
Segment lenghts (cm)											
Knee height	53.5	52.4	54.5	2.7	49.5	49.0	50.0	2.1	0.62†	0.55†	0.58†
Half arm span	87.3	85.5	89.2	4.8	80.8	79.8	81.7	3.8	0.71†	0.62†	0.58†
Body indexes											
Derived from anthropometry											
Body mass*height (kg*m)	123.3	112.6	134.1	28.2	104.7	99.8	109.7	20.0	0.49†	0.49†	0.52†

Variables	Older Men (n=29)				Older Women (n=65)				Correlation (r) with Muscle Strength		
	M	95% CI		SD	M	95% CI		SD	HGS (kg)	Knee Extension	
		LL	UL			LL	UL			1RM (kg)	PT (Nm)
SA (m^2)	1.9	1.8	1.9	0.2	1.7	1.7	1.8	0.2	0.47†	0.48†	0.50†
MAMC (cm)	24.2	23.0	25.3	2.9	21.9	21.3	22.5	2.6	0.45†	0.39†	0.45†
CAMA (cm^2)	37.1	32.7	41.6	11.7	32.2	29.9	34.5	9.2	0.37†	0.33†	0.40†
AFA (cm^2)	16.3	14.0	18.6	6.0	22.9	21.3	24.6	6.6	-0.23*		
$FFM_{(LEAN\ et\ al.,\ 1996)}$ (kg)	52.1	49.6	54.6	6.6	37.1	36.0	38.2	4.6	0.75†	0.66†	0.67†
Fat $mass_{(LEAN\ et\ al.,\ 1996)}$ (kg)	20.9	17.7	24.0	8.2	29.8	27.9	31.7	7.8	-0.22*		
Derived from body composition											
Left arm LST (kg)	2.4	2.1	2.6	0.6	1.5	1.4	1.6	0.3	0.72†	0.62†	0.66†
Right arm LST (kg)	2.8	2.5	3.0	0.6	1.8	1.7	1.9	0.4	0.72†	0.61†	0.60†
Left leg LST (kg)	7.7	7.1	8.3	1.6	5.5	5.3	5.8	1.0	0.67†	0.64†	0.64†
Right leg LST (kg)	8.0	7.4	8.6	1.6	5.7	5.4	5.9	1.0	0.70†	0.64†	0.65†
Arms LST (kg)	5.1	4.7	5.6	1.2	3.3	3.2	3.5	0.7	0.74†	0.63†	0.64†
Legs LST (kg)	15.7	14.6	16.9	3.1	11.2	10.7	11.6	1.9	0.69†	0.65†	0.66†
ASM (kg)	20.9	19.3	22.5	4.2	14.5	13.9	15.1	2.5	0.72†	0.65†	0.66†
ASM/height^2 (kg/m^2)	7.3	7.0	7.7	1.0	6.0	5.7	6.2	0.9	0.55†	0.51†	0.48†
$FFM_{(BAUMGARTNER\ et\ al.,\ 1991)}$ (kg)	54.3	51.3	57.3	7.7	45.5	44.0	47.0	6.1	0.60†	0.55†	0.57†
$FFM_{(DXA)}$ (kg)	51.5	47.9	55.0	9.4	38.8	37.4	40.3	5.8	0.68†	0.59†	0.61†
Fat $mass_{(DXA)}$ (kg)	21.5	18.8	24.2	7.1	28.1	26.3	29.9	7.2	-0.20*		
Mobility											
Six-minute walk test (6MWT)	464.7	431.1	498.3	88.3	412.7	389.9	435.5	92.0			
Functional limitation (6MWT<400m); %	24.1%				38.5%						
Muscle strength											
HGS (kg)	36.4	33.1	39.7	8.6	24.1	23.0	25.2	4.5			
1RM (kg)	66.8	56.9	76.7	26.0	40.8	36.9	44.8	15.9			
nº of reps to estimate 1RM	7.2	6.3	8.1	2.3	6.6	6.0	7.2	2.4			
PT (Nm)	119.8	102.4	137.2	45.6	73.2	66.8	79.6	25.9			

$^*p<0.05$ and $^†p<0.001$ (statistically significant correlation).

Note: M=mean; CI=confidence interval; LL=lower limit; UL=upper limit; SD=standard deviation; HGS=handgrip strength; 1RM=one maximum repetition measurement for knee extensors; PT=isokinetic knee extension peak torque at 60º/s; Nm=Newton meter; SA=human body surface area; MAMC=mid-arm muscle circumference; CAMA=corrected arm muscle area; AFA=arm fat area; FFM=fat-free mass; LST=lean soft tissue; ASM=appendicular skeletal muscle mass; DXA=Dual-energy X-ray absorptiometry.

Allometric exponents were proposed for those body-size variables that showed a significant relationship with muscle strength (Table 2). Linear regressions to obtain allometric exponents are shown in SUPPLEMENT C in Additional file 1. All regressions were significant to explain muscle strength ($p<0.05$), with adjusted R^2 ranging from 0.39 to 0.61. The regression coefficients (β) obtained for each body-size variable represent the allometric exponents obtained. For HGS, the allometric exponents of triceps, pectoral, abdominal and thigh skinfolds were discarded because the interaction terms were statistically significant ($p<0.05$) and have accentuated multicollinearity (VIF>10). The remaining allometric exponents were used to perform normalization (for example, 1RM/body mass$^{0.44}$).

The sex-specific cut-off points proposed for HGS, 1RM and PT (non-normalized, ratio standard/muscle quality and allometric scaling) to identify muscle weakness are presented in the SUPPLEMENT D in Additional file 1. In the same supplement there are also presented correlations between muscle strength and body size (body mass, height and body-size variable used in normalization).

Non-normalized HGS, 1RM and PT^s cut-off points to identify muscle weakness were not adequate for both sexes or because they did not present AUC≥0.70 ($p<0.05$) or because they had a significant association with body size ($r>0.30$; $p<0.05$) (SUPPLEMENT D in Additional file 1).

Table 3 shows the cut-off points based on the ratio standard/muscle quality and allometric scaling classified as adequate.

Table 3. Adequate cut-off points (AUC≥0.70 simultaneously in both sexes and r≤0.30 with body size) of handgrip strength (HGS), one maximum repetition measurement for knee extensors (1RM) and isokinetic knee extension peak torque at 60º/s (PT) to identify muscle weakness

Variable	Unit	Men (n=29)				Women (n=65)			
		AUC	Cut-off point (≤)	Sens (%)	Spe (%)	AUC	Cut-off point (≤)	Sens (%)	Spe (%)
HGS (kg)									
/forearm circumference	(cm)	0.74*	1.33	86	59	0.70*	1.04	84	58
1RM (kg)									
/body mass	(kg)	0.77*	0.85	86	68	0.76†	0.54	68	78
/forearm circumference	(cm)	0.75*	2.16	86	77	0.70*	1.38	60	75
/calf circumference	(cm)	0.74*	1.65	86	77	0.70*	1.06	72	68

Variable	Unit	Men (n=29) AUC	Cut-off point (≤)	Sens (%)	Spe (%)	Women (n=65) AUC	Cut-off point (≤)	Sens (%)	Spe (%)
/chest circumference		0.76*	0.64	86	73	0.71*	0.4	72	65
/waist circumference		0.78*	0.73	100	59	0.72*	0.37	60	80
/triceps skinfold	(mm)	0.81†	4.22	86	68	0.70*	1.40	60	75
/bitrochanteric breadth		0.73*	1.72	86	77	0.70*	1.16	76	60
/bimalleolar breadth		0.73*	8.77	86	77	0.70*	5.77	76	65
/elbow breadth		0.73*	9.36	86	73	0.70*	6.57	76	63
/SA	(m²)	0.75*	31.6	86	77	0.72*	21.2	72	68
/MAMC	(cm)	0.77*	2.42	86	73	0.72*	1.54	64	75
/CAMA	(cm²)	0.71*	2.03	100	41	0.73*	0.90	52	93
/FFM (LEAN et al., 1996)	(kg)	0.76*	1.11	86	77	0.72*	1.00	72	68
/FFM (BAUMGARTNER et al., 1991)	(kg)	0.78*	1.13	83	73	0.75†	0.83	76	64
/body mass$^{0.44}$	(kg)	0.75*	9.04	86	77	0.71*	6.03	76	63
/body mass^{0,67} (JARIC, 2003)		0.78*	3.40	86	77	0.73†	2.28	76	65
/body mass$^{0.96}$ (ABDALLA et al., 2020)		0.77*	1.00	86	68	0.75†	0.45	44	100
/body mass$^{0.69}$ (ABDALLA et al., 2020)		0.78*	3.06	86	77	0.73*	1.48	44	98
/calf circumference$^{1.10}$	(cm)	0.75*	1.14	86	77	0.71*	0.70	68	73
/bimalleolar breadth$^{1.20}$	(mm)	0.71*	6.01	86	68	0.70*	3.93	76	65
/(body mass*height)$^{0.48}$	(kg*m)	0.75*	5.83	86	77	0.72*	4.06	76	65
/SA$^{0.93}$	(m²)	0.75*	33	86	77	0.72*	22.7	76	65
/FFM$^{0.88}$ (LEAN et al., 1996)	(kg)	0.75*	1.77	86	77	0.71*	1.53	76	65
/FFM$^{0.67}$ (BAUMGARTNER et al., 1991)		0.76*	3.94	83	77	0.72*	2.91	76	64
$_{s}$PT (Nm)									
/height	(m)	0.93†	54.1	86	95	0.74†	44.1	64	75
/knee height	(cm)	0.94†	1.83	100	86	0.75†	1.44	68	73
/SA	(m²)	0.94†	56.9	100	82	0.81†	36.3	64	88
/FFM (LEAN et al., 1996)	(kg)	0.93†	1.79	86	95	0.81†	1.84	76	80
/left leg LST	(g)	0.82†	0.015	100	55	0.76†	0.012	68	80
/right leg LST		0.77*	0.015	100	50	0.78†	0.013	76	78
/legs LST		0.81*	0.0063	71	82	0.77†	0.0065	76	78
/ASM	(kg)	0.81*	4.66	71	86	0.77†	5.01	76	78
/FFM (BAUMGARTNER et al., 1991)		0.93†	1.63	83	95	0.85†	1.60	88	77
/FFM (DXA)		0.84†	2.08	100	59	0.79†	1.89	76	75
/body mass$^{0.67}$ (DAVIES; DALSKY, 1997)	(kg)	0.93†	5.06	86	95	0.82†	3.71	68	88
/body mass$^{0.72}$ (DAVIES; DALSKY, 1997)		0.94†	4.1	86	95	0.82†	3.14	72	85
/body mass$^{0.74}$ (DAVIES; DALSKY, 1997)		0.93†	3.77	86	95	0.82†	2.87	72	85
/body mass$^{0.67}$ (JARIC, 2003)		0.93†	5.06	86	95	0.82†	3.71	68	88
/height$^{3.27}$	(m)	0.86†	19.2	100	77	0.74†	17.4	72	65
/knee height$^{1.82}$	(cm)	0.90†	0.068	100	86	0.74†	0.053	64	75
/half arm span$^{1.62}$		0.88†	0.076	100	73	0.75†	0.066	84	58
/biacromial breadth$^{2.15}$	(mm)	0.82†	0.038	86	68	0.77†	0.03	76	73
/bimalleolar breadth$^{1.54}$		0.81*	5.04	86	73	0.80†	4.64	92	60
/(body mass*height)$^{0.43}$	(kg*m)	0.94†	13	100	82	0.80†	10.5	84	65
/SA$^{0.83}$	(m²)	0.94†	53.8	86	95	0.80†	50	84	65
/left leg LST$^{0.43}$	(g)	0.92†	2.26	100	77	0.77†	1.83	76	70
/right leg LST$^{0.48}$		0.90†	1.39	100	73	0.78†	1.16	80	70
/legs LST$^{0.47}$		0.92†	1.07	100	73	0.77†	0.87	76	70

$^{*}p<0.05$ and $^{\dagger}p<0.001$ (statistically significant AUC)

Dependent variable (primary outcome): functional limitation (6MWT<400 m)

Note: AUC=area under the curve; *p*=significance; Sens=sensibility; Spe=specificity; SA= human body surface area; MAMC=mid-arm muscle circumference; CAMA=corrected arm muscle area; FFM=Fat-free mass; LST=lean soft tissue; ASM=appendicular skeletal muscle mass; DXA=Dual-energy X-ray absorptiometry; 6MWT=six-minute walk test.

A comparison of the most accurate ROC curves is presented in Figure 2 to support the decision for the best cut-off point between non-normalized, ratio standard/muscle quality and allometric scaling of HGS and lower limbs strength (1RM and PT) for each sex.

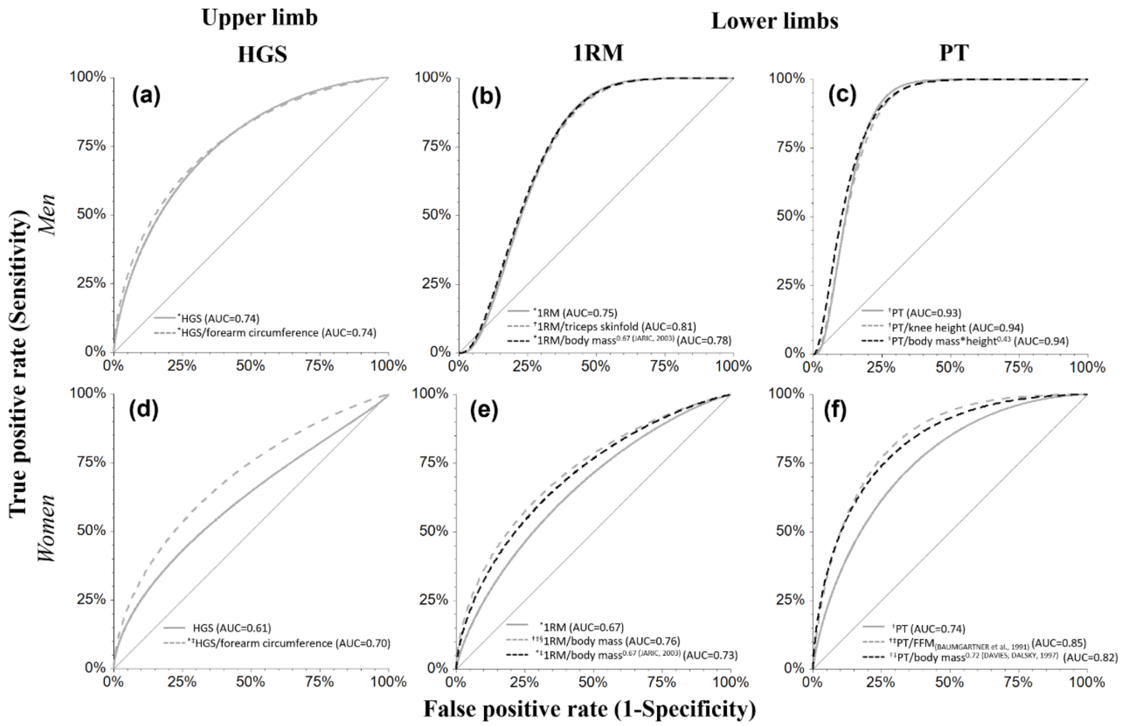


Figure 2. Accuracy comparison between non-normalized, ratio standard/muscle quality and allometric scaling of muscle weakness cut-off points of HGS and lower limbs strength (1RM and PT) in older men (letters a, b, c) and older women (letters d, e, f)

*$p<0.05$ and †$p<0.001$ (statistically significant AUC).
‡$p<0.05$ (greater than the AUC of non-normalized muscle strength).
§$p<0.05$ (greater than the AUC of the allometric scaling).
Dependent variable (primary outcome): functional limitation (6MWT<400 m).
Note: HGS=handgrip strength; 1RM=one maximum repetition measurement for knee extensors; PT=isokinetic knee extension peak torque at 60º/s; 6MWT=six-minute walk test.

For men, there were no differences in accuracy (AUC) to identify functional limitation between absolute muscle strength, normalized by ratio standard/muscle quality or by allometric scaling (p>0.05; Figure 2 a, b, c). However, the absolute muscle strengths (HGS, 1RM and PT) previously indicated great dependence (r>0.30) on body size (SUPPLEMENT D in Additional file 1), suggesting the need for normalization to avoid errors in the classification of weakness. The normalized muscle strength increased the AUC and made it possible to classify muscle weakness of older adults with extreme body sizes, independently.

For women, only after normalizing muscle strength the AUC values perform acceptable to identify functional limitation (AUC>0.70; Figure 2 d, e). The exception was PT, when the absolute values already had adequate accuracy (AUC>0.70), although without the desirable independence of body size. All the normalizations increased (‡) the AUC (p<0.001).

4. Discussion

Cut-off points based on upper and lower limbs muscle strength were proposed to identify muscle weakness in older adults of both sexes. The non-normalized cut-off points for HGS and lower limbs strength were significantly associated with body size, which involves biases to assess older adults with extreme body size (e.g., heavy or short). After normalizing HGS and lower limbs strength by the ratio standard/muscle quality or by the allometry, the association with body size was no longer relevant. In addition, for women, the accuracy to predict mobility limitation/muscle weakness from normalized muscle strength cut-off points become acceptable when compared to non-normalized strategy. In men, muscle strength normalization did not increase accuracy. However, all normalized models of both sexes avoided biases in the assessment of muscle weakness/mobility limitation, to isolate the natural interdependence between muscle strength and body size (Maranhão Neto et al., 2017).

To the best of our knowledge, this is the first study to propose muscle weakness cut-off points for the HGS and PT allometrically adjusted in older adults. In a previous study, 1RM was allometrically adjusted for body mass (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020), but not according to all other potential body size variables. Indeed, we expanded the number of variables that can be used to normalize 1RM with allometry (n=8) in order to augment model´s accuracy for identifying muscle weakness regardless of extreme body sizes. Other studies proposed muscle weakness cut-off points with HGS normalized by ratio standard (body mass or BMI) (Alley et al., 2014; Cawthon et al., 2020; McGrath et al., 2020) or stratified by BMI quartiles (Fried et al., 2001). There are also muscle weakness cut-off points for PT normalized by body mass (Manini et al., 2007). However, these studies did not compare the accuracy of normalized with non-normalized muscle strength to identify muscle weakness. Furthermore, they did not explore other body-size variables to normalize muscle strength.

Previous studies have proposed allometric exponents to normalize muscle strength, including HGS (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006), 1RM (2020), PT (Davies & Dalsky, 1997; Segal et al., 2008), and they are comparable with the ones found in the present study. Curvilinear (allometric) relationship variables is confirmed when allometric coefficient (^{b}) is between 0.00 and 0.99 (Owings et al., 2002), while the linear relationship is characterized when the exponent is ≥1.00 (Owings et al., 2002). In the literature, body mass generally presents an allometric relationship with muscle strength independently of the test (HGS, 1RM or PT; Table 1), confirming our findings (SUPPLEMENT C in Additional file 1), when ^{b} exponents were 0.22 (HGS), 0.44 (1RM) and 0.37 (PT). Contrarily, height tends to have a linear relationship (^{b}≥1.00) with muscle strength (Maranhão Neto et al., 2017), what was also confirmed by our proposed allometric exponents (SUPPLEMENT C in Additional file 1), that were between 1.87 and 3.27.

Some strengths of our study are noteworthy. We proposed muscle weakness cut-off points for isokinetic dynamometer, considered as a "gold standard" resource to assess lower limbs strength. The estimated 1RM obtained with submaximal repetition protocol and the HGS are valid for older adults, even for those with muscle weakness (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, & Machado, 2020; Ramírez-Vélez et al., 2021). An extensive number of body-size variables (n=49) were tested in our study, expanding the possibilities to promote the normalization of performance in muscle strength tests. Furthermore, regardless of the chosen muscle strength test to evaluate weakness, our findings can be applied with sufficient accuracy (AUC>0.70) both for scientific research (PT) and population-based monitoring (HGS and 1RM). Nevertheless, this study is not without limitations. The individual muscle strength decline along aging may have been underestimated with the cross-sectional design. The small and local sample size of our study, requiring caution to extrapolate these findings inferentially to other populations. Another limitation is the utilization of open kinetic chain test in the case of 1RM in a leg extension machine, a movement far to the natural comportment during daily living. Our suggestion for future studies is to establish allometric exponents and cut-off points for a close kinetic chain exercise like leg press or squat, which require movements more closely associated with daily live.

We found greater accuracy (AUC) for normalized lower limbs strength (isokinetic dynamometer and leg extension machine) than manual dynamometer (normalized upper extremity strength), usually adopted to predict mobility limitations/muscle weakness (Cruz-Jentoft et al., 2018). However, the isokinetic dynamometer is expensive and generally more available in terms of research. Even though, our normalized models are also applicable in clinical practice from manual dynamometers (widely available in geriatric environments) and leg extension machines (available in most fitness centers, adequate environment for intervention against aged-related muscle weakness) (Cruz-Jentoft et al., 2014). The assessment of HGS and 1RM and proper classification of muscle weakness amongst older adults should be frequent in clinical practice to better target health expending, avoiding unnecessary expenditures. Future research should observe if proposed allometric exponents can be utilized to normalize muscle strength for different older adults' population, with other ethnicity/race characteristics.

As an applied example to avoid false positive diagnosis for muscle weakness, we hypothesize one older man with extreme lower values of body mass (42 kg), 1.57 m of height, who performed PT of 85.2 Nm. If we consider our absolute cut-off point (≤85.4 Nm), this older man has muscle weakness confirmed. However, when considered the normalized PT/([body mass*height]$^{0.43}$), the adjusted value (14.1 Nm/kg*m) is above of the cut-off point (13.0 Nm/kg*m; Table 3). Normalization would also avoid false negative cases, for large body size of older adults. For example, if an older woman with 90 kg performs 1RM of 38.2 kg and considering our absolute cut-off point (≤38.1 kg), this older woman does not have weakness. However, when considered the normalized (1RM/body mass$^{0.67}$), the adjusted value (1.87 kg/kg) is below of the cut-off point (2.28 kg/kg; Table 3), characterizing weakness and a false negative case if non-normalized cut-off point were considered. The mistaken framing of false weakness cases could greatly impact the financial resources in the health and older people care systems. Especially in low- and middle-income countries, where these resources are scarcer.

In conclusion, upper and lower limbs muscle weakness cut-off points standardized according to body size were proposed for older adults of both sexes. The normalization has increased accuracy for identify women with muscle weakness; but not in men, whose absolute muscle strength values have an acceptable accuracy. However, normalization made muscle strength independent of body size, confirming our hypothesis and preventing bias in the evaluation of older adults with extreme body size (e.g., very low or very heavy). Forty-nine valid models were proposed for older adults of both sexes, with different possibilities of body's normalization of muscle strength, which broadens the interpretation of muscle strength with less risk of attributing a false-positive diagnosis to muscle weakness.

Acknowledgements

Not applicable.

Material Suplementar A

Tabela Suplementar A. Body size variables (n=49) to normalize muscle strength

Anthropometry		
Body mass (kg)		
Height (m)		
Circumferences (cm)	*Skinfold site (mm)*	*Bone breadths (mm)*
Arm	Subescapular	Biacromial
Forearm	Triceps	Biiliac
Midthigh	Biceps	Bitrochanteric
Calf	Midaxillary	Ankle (bimalleolar)
Chest	Pectoral (chest)	Elbow
Waist	Suprailiac	Wrist
Abdomen	Abdominal (vertical)	Knee
Buttocks (hip)	Thigh (midline)	Chest
	Medial calf	
Segment lenghts (cm)		
Knee height		
Half arm span		

Body indexes	
Derived from anthropometry	*Derived from body composition*
BMI (kg/m²)	Left arm LST (g)
Body mass*height (kg*m)	Right arm LST (g)
SA (m²)	Left leg LST (g)
MAMC (cm)	Right leg LST (g)
CAMA (cm²)	Arms LST (g)
AFA (cm²)	Legs LST (g)
FFM(LEAN et al., 1996) (kg)	ASM (kg)
Fat mass(LEAN et al., 1996) (kg)	ASM/height² (kg/m²)
	FFM(BAUMGARTNER et al., 1991) (kg)
	FFM(DXA) (kg)
	Fat mass(BAUMGARTNER et al., 1991) (kg)
	Fat mass(DXA) (kg)

Note: BMI=body mass index; SA=surface area of human body; MAMC=mid-arm muscle circumference; CAMA=corrected arm muscle area; AFA=arm fat area; FFM=fat-free mass; LST=lean soft tissue; ASM=appendicular skeletal muscle mass.

.

Material Suplementar B

Tabela Suplementar B. Linear regressions to obtain allometric exponents for handgrip strength (HGS), one maximum repetition measurement for knee extensors (1RM) and isokinetic knee extension peak torque at 60º/s (PT) in older men and women (n=94)

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R^2
		β	Standard error	LL	UL		
Dependent variable: HGS (ln kg)							
1	Constant	3.040†	0.669	1.711	4.368		0.53
	Sex	0.407†	0.046	0.315	0.499	1.129	
	Age	-0.012*	0.003	-0.019	-0.005	1.181	
	Physical activity level	0.061	0.144	-0.225	0.347	1.059	
	ln body mass (kg)	0.219	0.122	-0.024	0.462	1.218	
2	Constant	3.069†	0.380	2.314	3.823		0.58
	Sex	0.282†	0.057	0.169	0.395	1.919	
	Age	-0.010*	0.003	-0.017	-0.004	1.143	
	Physical activity level	-0.009	0.136	-0.279	0.262	1.068	
	ln height (m)	1.875†	0.491	0.899	2.85	1.891	
3	Constant	2.393*	0.877	0.651	4.135		0.54
	Sex	0.381†	0.050	0.281	0.480	1.334	
	Age	-0.012†	0.003	-0.019	-0.006	1.128	
	Physical activity level	0.044	0.143	-0.239	0.328	1.056	
	ln forearm circumference (cm)	0.501*	0.240	0.023	0.978	1.349	
4	Constant	1.992	1.002	<0.001	3.984		0.54
	Sex	0.413†	0.045	0.323	0.502	1.084	
	Age	-0.012*	0.003	-0.018	-0.005	1.186	
	Physical activity level	0.084	0.143	-0.200	0.368	1.071	
	ln calf circumference (cm)	0.536*	0.242	0.056	1.017	1.195	
5	Constant	3.728*	1.227	1.289	6.167		0.52
	Sex	0.424†	0.047	0.329	0.518	1.143	
	Age	-0.014†	0.003	-0.021	-0.007	1.110	
	Physical activity level	0.048	0.146	-0.242	0.338	1.057	
	ln chest circumference (cm)	0.084	0.248	-0.409	0.576	1.162	
6	Constant	-1.116	1.815	-4.722	2.489		0.56
	Sex	0.323†	0.057	0.210	0.435	1.779	
	Age	-0.013†	0.003	-0.019	-0.006	1.061	
	Physical activity level	0.02	0.140	-0.258	0.297	1.061	
	ln knee height (cm)	1.318*	0.451	0.422	2.213	1.708	
7	Constant	-4.217*	1.867	-7.927	-0.507		0.61
	Sex	0.283†	0.052	0.179	0.387	1.705	
	Age	-0.010*	0.003	-0.016	-0.003	1.161	
	Physical activity level	0.086	0.132	-0.176	0.349	1.061	
	ln half arm span (cm)	1.813†	0.402	1.015	2.611	1.752	
8	Constant	2.942†	0.659	1.633	4.251		0.54

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	Sex	1.070*	0.298	0.478	1.663	47.067	
	Age	-0.011*	0.004	-0.018	-0.004	1.279	
	Physical activity level	0.647*	0.308	0.035	1.258	4.896	
	ln triceps skinfold (mm)	0.114	0.079	-0.043	0.270	3.147	
	Interaction	-0.003*	0.001	-0.006	<0.001	36.925	
9	Constant	4.213†	0.343	3.530	4.895		0.52
	Sex	0.413†	0.059	0.296	0.53	1.752	
	Age	-0.015†	0.003	-0.021	-0.008	1.041	
	Physical activity level	0.037	0.148	-0.257	0.331	1.086	
	ln biceps skinfold (mm)	-0.021	0.053	-0.126	0.083	1.706	
10	Constant	4.160†	0.343	3.478	4.843		0.52
	Sex	0.425†	0.049	0.329	0.522	1.197	
	Age	-0.015†	0.003	-0.021	-0.008	1.035	
	Physical activity level	0.044	0.147	-0.247	0.336	1.067	
	ln midaxillary skinfold (mm)	-0.007	0.050	-0.106	0.091	1.158	
11	Constant	2.809†	0.523	1.769	3.848		0.56
	Sex	1.055†	0.256	0.546	1.564	36.193	
	Age	-0.011*	0.003	-0.018	-0.005	1.154	
	Physical activity level	0.769*	0.307	0.160	1.378	5.064	
	ln pectoral skinfold (mm)	0.141*	0.055	0.032	0.249	1.384	
	Interaction	-0.003*	0.001	-0.006	-0.001	36.287	
12	Constant	4.098†	0.370	3.363	4.833		0.52
	Sex	0.431†	0.053	0.327	0.536	1.412	
	Age	-0.014†	0.003	-0.021	-0.008	1.085	
	Physical activity level	0.049	0.147	-0.243	0.341	1.069	
	ln suprailiac skinfold (mm)	0.007	0.050	-0.093	0.106	1.432	
13	Constant	2.458*	0.682	1.101	3.814		0.55
	Sex	1.253†	0.312	0.632	1.874	53.064	
	Age	-0.010*	0.004	-0.017	-0.003	1.302	
	Physical activity level	0.891*	0.346	0.203	1.578	6.352	
	ln abdominal skinfold (mm)	0.148*	0.071	0.008	0.289	1.86	
	Interaction	-0.004*	0.001	-0.006	-0.001	47.986	
14	Constant	2.951†	0.619	1.720	4.181		0.54
	Sex	1.059†	0.284	0.495	1.624	42.851	
	Age	-0.011*	0.004	-0.018	-0.004	1.246	
	Physical activity level	0.676*	0.314	0.052	1.300	5.107	
	ln thigh skinfold (mm)	0.092	0.064	-0.034	0.219	2.412	
	Interaction	-0.003*	0.001	-0.006	<0.001	35.064	
15	Constant	4.256†	0.335	3.590	4.921		0.52
	Sex	0.403†	0.058	0.287	0.519	1.737	
	Age	-0.015†	0.003	-0.021	-0.008	1.041	
	Physical activity level	0.041	0.146	-0.249	0.331	1.06	
	ln medial calf skinfold (mm)	-0.031	0.046	-0.121	0.060	1.711	
16	Constant	-0.060	1.519	-3.077	2.958		0.56

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	Sex	0.348†	0.052	0.244	0.452	1.506	
	Age	-0.010*	0.004	-0.017	-0.003	1.295	
	Physical activity level	0.091	0.141	-0.189	0.371	1.07	
	ln biacromial breadth (mm)	1.059*	0.378	0.308	1.810	1.689	
	Constant	0.536	1.234	-1.917	2.988		
	Sex	0.414†	0.044	0.327	0.501	1.072	
17	Age	-0.012†	0.003	-0.018	-0.005	1.101	0.56
	Physical activity level	0.053	0.139	-0.224	0.329	1.056	
	ln bitrochanteric breadth (mm)	0.971*	0.325	0.324	1.617	1.091	
	Constant	2.339*	0.669	1.009	3.668		
	Sex	0.337†	0.054	0.231	0.444	1.593	
18	Age	-0.013†	0.003	-0.019	-0.007	1.043	0.56
	Physical activity level	0.050	0.139	-0.228	0.327	1.056	
	ln bimalleolar breadth (mm)	0.915*	0.313	0.292	1.537	1.538	
	Constant	3.443†	0.565	2.32	4.566		
	Sex	0.375†	0.059	0.259	0.492	1.792	
19	Age	-0.014†	0.003	-0.020	-0.007	1.037	0.53
	Physical activity level	0.029	0.145	-0.260	0.317	1.065	
	ln elbow breadth (mm)	0.375	0.269	-0.159	0.908	1.704	
	Constant	3.190†	0.528	2.141	4.239		
	Sex	0.355†	0.057	0.242	0.468	1.715	
20	Age	-0.014†	0.003	-0.021	-0.008	1.018	0.54
	Physical activity level	0.036	0.143	-0.248	0.319	1.058	
	ln wrist breadth (mm)	0.576*	0.277	0.026	1.125	1.638	
	Constant	2.929*	0.855	1.230	4.628		
	Sex	0.384†	0.054	0.278	0.491	1.504	
21	Age	-0.013†	0.003	-0.02	-0.007	1.068	0.53
	Physical activity level	0.049	0.144	-0.238	0.336	1.056	
	ln chest breadth (mm)	0.338	0.228	-0.114	0.791	1.468	
	Constant	2.709†	0.656	1.407	4.012		
	Sex	0.384†	0.048	0.289	0.479	1.243	
22	Age	-0.011*	0.003	-0.018	-0.004	1.207	0.55
	Physical activity level	0.056	0.142	-0.226	0.337	1.057	
	ln body mass*height (kg*m)	0.256*	0.108	0.042	0.470	1.339	
	Constant	3.641†	0.345	2.955	4.327		
	Sex	0.388†	0.048	0.293	0.483	1.222	
23	Age	-0.011*	0.003	-0.018	-0.005	1.203	0.54
	Physical activity level	0.057	0.142	-0.225	0.339	1.057	
	ln SA (m²)	0.489*	0.214	0.064	0.915	1.317	
	Constant	3.417†	0.696	2.035	4.799		
	Sex	0.405†	0.050	0.306	0.504	1.276	
24	Age	-0.013†	0.003	-0.020	-0.007	1.129	0.52
	Physical activity level	0.034	0.145	-0.255	0.323	1.062	
	ln MAMC (cm)	0.208	0.186	-0.162	0.579	1.292	
	Constant	3.773†	0.427	2.925	4.622		
	Sex	0.414†	0.047	0.321	0.508	1.141	
25	Age	-0.013†	0.003	-0.020	-0.007	1.134	0.52
	Physical activity level	0.034	0.145	-0.255	0.323	1.063	
	ln CAMA (cm²)	0.083	0.076	-0.067	0.233	1.180	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	Constant	4.087†	0.375	3.342	4.832		
	Sex	0.432†	0.051	0.331	0.532	1.299	
26	Age	-0.014†	0.003	-0.021	-0.008	1.105	0.52
	Physical activity level	0.047	0.146	-0.243	0.337	1.057	
	ln AFA (cm^2)	0.010	0.058	-0.106	0.126	1.353	
	Constant	1.747	0.897	-0.036	3.530		
	Sex	0.242*	0.080	0.083	0.401	3.528	
27	Age	-0.008*	0.004	-0.016	-0.001	1.529	0.56
	Physical activity level	0.086	0.141	-0.194	0.366	1.067	
	ln FFM$_{\text{(LEAN et al., 1996)}}$ (kg)	0.531*	0.191	0.152	0.910	3.814	
	Constant	3.934†	0.391	3.157	4.711		
	Sex	0.447†	0.053	0.342	0.551	1.414	
28	Age	-0.014†	0.003	-0.021	-0.008	1.059	0.52
	Physical activity level	0.050	0.146	-0.239	0.339	1.057	
	ln fat mass$_{\text{(LEAN et al., 1996)}}$ (kg)	0.048	0.067	-0.085	0.180	1.415	
	Constant	1.774*	0.861	0.063	3.485		
	Sex	0.298†	0.063	0.174	0.423	2.181	
29	Age	-0.011*	0.003	-0.018	-0.004	1.174	0.56
	Physical activity level	0.036	0.140	-0.241	0.314	1.057	
	ln left arm LST (g)	0.290*	0.101	0.090	0.490	2.182	
	Constant	1.864*	0.917	0.042	3.685		
	Sex	0.310†	0.063	0.184	0.436	2.187	
30	Age	-0.011*	0.003	-0.018	-0.004	1.258	0.55
	Physical activity level	0.065	0.141	-0.215	0.345	1.059	
	ln right arm LST (g)	0.264*	0.102	0.061	0.467	2.282	
	Constant	1.314	1.213	-1.096	3.723		
	Sex	0.326†	0.062	0.203	0.448	2.049	
31	Age	-0.011*	0.004	-0.018	-0.004	1.275	0.55
	Physical activity level	0.053	0.142	-0.228	0.334	1.056	
	ln left leg LST (g)	0.296*	0.124	0.049	0.543	2.149	
	Constant	1.202	1.271	-1.324	3.728		
	Sex	0.319†	0.064	0.192	0.446	2.211	
32	Age	-0.011*	0.004	-0.018	-0.004	1.288	0.54
	Physical activity level	0.077	0.142	-0.205	0.360	1.065	
	ln right leg LST (g)	0.305*	0.129	0.048	0.562	2.351	
	Constant	1.418	0.995	-0.559	3.394		
	Sex	0.295†	0.064	0.167	0.422	2.287	
33	Age	-0.010*	0.003	-0.017	-0.004	1.237	0.56
	Physical activity level	0.053	0.140	-0.225	0.331	1.056	
	ln arms LST (g)	0.299*	0.106	0.089	0.509	2.346	
	Constant	0.879	1.365	-1.835	3.592		
	Sex	0.317†	0.064	0.190	0.443	2.194	
34	Age	-0.011*	0.004	-0.018	-0.003	1.298	0.55
	Physical activity level	0.067	0.142	-0.215	0.348	1.06	
	ln legs LST (g)	0.317*	0.130	0.058	0.576	2.324	
	Constant	2.917†	0.534	1.856	3.979		
	Sex	0.303†	0.065	0.174	0.432	2.299	
35	Age	-0.010*	0.004	-0.017	-0.003	1.302	0.55
	Physical activity level	0.064	0.141	-0.216	0.344	1.058	
	ln ASM (kg)	0.335*	0.127	0.082	0.588	2.422	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
36	Constant	3.808†	0.463	2.888	4.729		0.52
	Sex	0.400†	0.056	0.288	0.511	1.601	
	Age	-0.013†	0.003	-0.02	-0.007	1.179	
	Physical activity level	0.061	0.146	-0.23	0.352	1.070	
	ln ASM/height² (kg/m²)	0.130	0.149	-0.167	0.426	1.685	
37	Constant	2.112*	0.764	0.593	3.631		0.58
	Sex	0.375†	0.051	0.273	0.477	1.503	
	Age	-0.009*	0.003	-0.016	-0.002	1.235	
	Physical activity level	0.114	0.137	-0.159	0.386	1.074	
	ln FFM$_{(BAUMGARTNER\ et\ al.,\ 1991)}$ (kg)	0.412*	0.157	0.099	0.724	1.665	
38	Constant	2.569†	0.680	1.218	3.920		0.55
	Sex	0.325†	0.060	0.205	0.445	1.979	
	Age	-0.011*	0.003	-0.018	-0.004	1.231	
	Physical activity level	0.059	0.141	-0.222	0.339	1.057	
	ln FFM$_{(DXA)}$ (kg)	0.356*	0.142	0.073	0.638	2.054	
39	Constant	3.988†	0.408	3.177	4.799		0.52
	Sex	0.438†	0.050	0.338	0.537	1.268	
	Age	-0.014†	0.003	-0.021	-0.008	1.077	
	Physical activity level	0.052	0.146	-0.238	0.343	1.063	
	ln fat mass$_{(DXA)}$ (kg)	0.034	0.070	-0.105	0.172	1.28	
Dependent variable: 1RM (ln kg)							
1	Constant	3.703*	1.198	1.322	6.083		0.43
	Sex	0.501†	0.083	0.336	0.666	1.129	
	Age	-0.027†	0.006	-0.039	-0.015	1.181	
	Physical activity level	-0.018	0.257	-0.530	0.493	1.059	
	ln body mass (kg)	0.436	0.219	0.001	0.871	1.218	
2	Constant	4.152†	0.693	2.774	5.530		0.48
	Sex	0.305*	0.104	0.098	0.512	1.919	
	Age	-0.025†	0.006	-0.037	-0.013	1.143	
	Physical activity level	-0.137	0.249	-0.631	0.357	1.068	
	ln height (m)	3.047*	0.897	1.266	4.829	1.891	
3	Constant	4.546*	1.609	1.35	7.743		0.41
	Sex	0.506†	0.092	0.323	0.688	1.334	
	Age	-0.03†	0.006	-0.042	-0.018	1.128	
	Physical activity level	-0.049	0.262	-0.569	0.471	1.056	
	ln forearm circumference (cm)	0.384	0.441	-0.492	1.260	1.349	
4	Constant	1.472	1.788	-2.081	5.025		0.45
	Sex	0.511†	0.080	0.352	0.671	1.084	
	Age	-0.026†	0.006	-0.038	-0.014	1.186	
	Physical activity level	0.03	0.255	-0.477	0.538	1.071	
	ln calf circumference (cm)	1.104*	0.431	0.247	1.962	1.195	
5	Constant	3.186	2.190	-1.166	7.538		0.42
	Sex	0.513†	0.085	0.345	0.681	1.143	
	Age	-0.029†	0.006	-0.041	-0.017	1.110	
	Physical activity level	-0.038	0.261	-0.555	0.48	1.057	
	ln chest circumference (cm)	0.558	0.442	-0.32	1.436	1.162	
6	Constant	4.581*	1.553	1.496	7.667		0.41
	Sex	0.524†	0.084	0.356	0.692	1.128	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	Age	-0.031†	0.006	-0.042	-0.019	1.045	
	Physical activity level	-0.046	0.262	-0.566	0.474	1.056	
	ln waist circumference (cm)	0.277	0.315	-0.347	0.902	1.088	
7	Constant	-3.215	3.276	-9.725	3.295		0.46
	Sex	0.360*	0.102	0.157	0.563	1.779	
	Age	-0.028†	0.006	-0.04	-0.017	1.061	
	Physical activity level	-0.094	0.252	-0.595	0.408	1.061	
	ln knee height (cm)	2.284*	0.814	0.667	3.901	1.708	
8	Constant	-6.682	3.473	-13.584	0.219		0.49
	Sex	0.324*	0.097	0.130	0.517	1.705	
	Age	-0.024†	0.006	-0.036	-0.012	1.161	
	Physical activity level	0.013	0.246	-0.475	0.501	1.061	
	ln half arm span (cm)	2.728†	0.747	1.243	4.213	1.752	
9	Constant	5.136†	0.651	3.842	6.430		0.43
	Sex	0.647†	0.101	0.447	0.847	1.640	
	Age	-0.03†	0.006	-0.041	-0.018	1.058	
	Physical activity level	-0.022	0.259	-0.536	0.492	1.059	
	ln triceps skinfold (mm)	0.179	0.103	-0.025	0.383	1.637	
10	Constant	5.585†	0.616	4.360	6.809		0.41
	Sex	0.596†	0.105	0.387	0.805	1.752	
	Age	-0.031†	0.006	-0.043	-0.019	1.041	
	Physical activity level	-0.011	0.265	-0.538	0.516	1.086	
	ln biceps skinfold (mm)	0.077	0.095	-0.111	0.265	1.706	
11	Constant	5.74†	0.650	4.448	7.033		0.41
	Sex	0.563†	0.103	0.358	0.767	1.660	
	Age	-0.031†	0.006	-0.043	-0.02	1.026	
	Physical activity level	-0.031	0.267	-0.561	0.499	1.091	
	ln thigh skinfold (mm)	0.032	0.095	-0.158	0.222	1.595	
12	Constant	5.806†	0.604	4.606	7.007		0.41
	Sex	0.556†	0.105	0.347	0.765	1.737	
	Age	-0.031†	0.006	-0.043	-0.02	1.041	
	Physical activity level	-0.044	0.263	-0.566	0.479	1.06	
	ln medial calf skinfold (mm)	0.018	0.082	-0.146	0.181	1.711	
13	Constant	-0.722	2.76	-6.207	4.763		0.45
	Sex	0.417†	0.095	0.228	0.605	1.506	
	Age	-0.024†	0.006	-0.037	-0.012	1.295	
	Physical activity level	0.023	0.256	-0.486	0.532	1.070	
	ln biacromial breadth (mm)	1.668*	0.687	0.304	3.033	1.689	
14	Constant	3.329	2.313	-1.267	7.924		0.42
	Sex	0.532†	0.082	0.369	0.695	1.072	
	Age	-0.03†	0.006	-0.042	-0.018	1.101	
	Physical activity level	-0.043	0.261	-0.561	0.476	1.056	
	ln bitrochanteric breadth (mm)	0.688	0.610	-0.523	1.900	1.091	
15	Constant	3.52*	1.23	1.076	5.965		0.44
	Sex	0.423†	0.098	0.228	0.619	1.593	
	Age	-0.03†	0.006	-0.041	-0.018	1.043	
	Physical activity level	-0.043	0.257	-0.553	0.467	1.056	
	ln bimalleolar breadth (mm)	1.204*	0.576	0.059	2.349	1.538	
16	Constant	5.702†	1.028	3.660	7.744		0.41
	Sex	0.529†	0.107	0.316	0.741	1.792	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R^2
		β	Standard error	LL	UL		
	Age	-0.031†	0.006	-0.043	-0.02	1.037	
	Physical activity level	-0.052	0.264	-0.576	0.472	1.065	
	ln elbow breadth (mm)	0.096	0.489	-0.874	1.067	1.704	
	Constant	5.159†	0.969	3.234	7.083		
	Sex	0.486†	0.104	0.279	0.693	1.715	
17	Age	-0.031†	0.006	-0.043	-0.02	1.018	0.41
	Physical activity level	-0.056	0.262	-0.576	0.465	1.058	
	ln wrist breadth (mm)	0.440	0.508	-0.568	1.449	1.638	
	Constant	3.383	2.075	-0.74	7.506		
	Sex	0.469†	0.101	0.269	0.669	1.616	
18	Age	-0.029†	0.006	-0.041	-0.016	1.178	0.42
	Physical activity level	-0.024	0.261	-0.543	0.494	1.061	
	ln chest breadth (mm)	0.684	0.552	-0.413	1.781	1.679	
	Constant	3.212*	1.176	0.875	5.55		
	Sex	0.460†	0.086	0.289	0.631	1.243	
19	Age	-0.025†	0.006	-0.038	-0.013	1.207	0.45
	Physical activity level	-0.030	0.254	-0.535	0.475	1.057	
	ln body mass*height (kg*m)	0.480*	0.193	0.097	0.863	1.339	
	Constant	4.952†	0.619	3.722	6.183		
	Sex	0.467†	0.086	0.297	0.637	1.222	
20	Age	-0.026†	0.006	-0.038	-0.013	1.203	0.45
	Physical activity level	-0.027	0.255	-0.533	0.479	1.057	
	ln SA (m^2)	0.925*	0.384	0.163	1.688	1.317	
	Constant	5.277†	1.258	2.777	7.777		
	Sex	0.523†	0.090	0.344	0.702	1.276	
21	Age	-0.031†	0.006	-0.043	-0.018	1.129	0.41
	Physical activity level	-0.058	0.263	-0.581	0.465	1.062	
	ln MAMC (cm)	0.176	0.337	-0.494	0.846	1.292	
	Constant	5.528†	0.772	3.993	7.062		
	Sex	0.529†	0.085	0.359	0.698	1.141	
22	Age	-0.030†	0.006	-0.043	-0.018	1.134	0.41
	Physical activity level	-0.059	0.263	-0.582	0.463	1.063	
	ln CAMA (cm^2)	0.082	0.137	-0.19	0.353	1.18	
	Constant	1.932	1.625	-1.297	5.161		
	Sex	0.234	0.145	-0.054	0.522	3.528	
23	Age	-0.021*	0.007	-0.035	-0.008	1.529	0.45
	Physical activity level	0.018	0.255	-0.489	0.525	1.067	
	ln $FFM_{(LEAN\ et\ al.,\ 1996)}$ (kg)	0.879*	0.346	0.192	1.566	3.814	
	Constant	3.787*	1.603	0.603	6.972		
	Sex	0.427†	0.117	0.195	0.659	2.181	
24	Age	-0.028†	0.006	-0.041	-0.016	1.174	0.42
	Physical activity level	-0.056	0.260	-0.573	0.460	1.057	
	ln left arm LST (g)	0.257	0.188	-0.115	0.630	2.182	
	Constant	3.986*	1.698	0.613	7.359		
	Sex	0.444†	0.117	0.211	0.677	2.187	
25	Age	-0.028†	0.006	-0.041	-0.015	1.258	0.42
	Physical activity level	-0.032	0.261	-0.550	0.487	1.059	
	ln right arm LST (g)	0.22	0.189	-0.155	0.596	2.282	
26	Constant	-0.207	2.151	-4.481	4.066		0.46
	Sex	0.322*	0.109	0.105	0.539	2.049	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	Age	-0.023†	0.006	-0.036	-0.011	1.275	
	Physical activity level	-0.033	0.251	-0.532	0.466	1.056	
	ln left leg LST (g)	0.639*	0.220	0.202	1.077	2.149	
27	Constant	0.338	2.280	-4.192	4.868		0.45
	Sex	0.336*	0.115	0.108	0.564	2.211	
	Age	-0.024†	0.006	-0.037	-0.012	1.288	
	Physical activity level	0.011	0.255	-0.496	0.518	1.065	
	ln right leg LST (g)	0.577*	0.232	0.116	1.037	2.351	
28	Constant	3.537	1.851	-0.142	7.215		0.42
	Sex	0.427*	0.120	0.189	0.665	2.287	
	Age	-0.028†	0.006	-0.041	-0.015	1.237	
	Physical activity level	-0.042	0.260	-0.559	0.475	1.056	
	ln arms LST (g)	0.258	0.197	-0.132	0.649	2.346	
29	Constant	-0.695	2.435	-5.534	4.144		0.46
	Sex	0.317*	0.114	0.092	0.543	2.194	
	Age	-0.023†	0.006	-0.036	-0.011	1.298	
	Physical activity level	-0.006	0.253	-0.508	0.495	1.060	
	ln legs LST (g)	0.641*	0.233	0.178	1.103	2.324	
30	Constant	3.848†	0.966	1.929	5.768		0.45
	Sex	0.333*	0.117	0.100	0.566	2.299	
	Age	-0.024†	0.006	-0.037	-0.012	1.302	
	Physical activity level	-0.018	0.255	-0.524	0.488	1.058	
	ln ASM (kg)	0.560*	0.231	0.102	1.018	2.422	
31	Constant	5.305†	0.834	3.648	6.961		0.41
	Sex	0.492†	0.101	0.292	0.692	1.601	
	Age	-0.030†	0.006	-0.042	-0.017	1.179	
	Physical activity level	-0.021	0.263	-0.545	0.502	1.070	
	ln ASM/height² (kg/m²)	0.231	0.268	-0.302	0.764	1.685	
32	Constant	2.917*	1.443	0.05	5.785		0.45
	Sex	0.415†	0.097	0.222	0.607	1.503	
	Age	-0.027†	0.006	-0.039	-0.014	1.235	
	Physical activity level	0.012	0.259	-0.502	0.526	1.074	
	ln $FFM_{(BAUMGARTNER\ et\ al.,\ 1991)}$ (kg)	0.671*	0.297	0.081	1.262	1.665	
33	Constant	4.193*	1.251	1.709	6.678		0.42
	Sex	0.431†	0.111	0.21	0.652	1.979	
	Age	-0.028†	0.006	-0.040	-0.015	1.231	
	Physical activity level	-0.034	0.260	-0.550	0.482	1.057	
	ln $FFM_{(DXA)}$ (kg)	0.384	0.261	-0.136	0.903	2.054	
	Dependent variable: PT^{s} (ln Nm)						
1	Constant	4.174*	1.230	1.731	6.618		0.40
	Sex	0.520†	0.085	0.351	0.689	1.129	
	Age	-0.025†	0.006	-0.038	-0.013	1.181	
	Physical activity level	0.259	0.264	-0.267	0.784	1.059	
	ln body mass (kg)	0.367	0.225	-0.08	0.814	1.218	
2	Constant	4.153†	0.702	2.759	5.548		0.46
	Sex	0.301*	0.105	0.091	0.510	1.919	
	Age	-0.022†	0.006	-0.034	-0.010	1.143	
	Physical activity level	0.138	0.252	-0.362	0.638	1.068	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	ln height (m)	3.268*	0.908	1.465	5.071	1.891	
3	Constant	3.966*	1.631	0.725	7.206		0.40
	Sex	0.499†	0.093	0.314	0.684	1.334	
	Age	-0.026†	0.006	-0.039	-0.014	1.128	
	Physical activity level	0.232	0.265	-0.295	0.759	1.056	
	ln forearm circumference (cm)	0.588	0.447	-0.300	1.476	1.349	
4	Constant	1.299	1.816	-2.308	4.907		0.43
	Sex	0.522†	0.082	0.360	0.683	1.084	
	Age	-0.023†	0.006	-0.035	-0.010	1.186	
	Physical activity level	0.317	0.259	-0.198	0.832	1.071	
	ln calf circumference (cm)	1.179*	0.438	0.309	2.05	1.195	
5	Constant	2.509	2.220	-1.901	6.920		0.40
	Sex	0.517†	0.086	0.347	0.687	1.143	
	Age	-0.026†	0.006	-0.038	-0.014	1.110	
	Physical activity level	0.247	0.264	-0.278	0.771	1.057	
	ln chest circumference (cm)	0.724	0.448	-0.166	1.614	1.162	
6	Constant	4.120*	1.576	0.990	7.251		0.40
	Sex	0.528†	0.086	0.358	0.698	1.128	
	Age	-0.028†	0.006	-0.04	-0.016	1.045	
	Physical activity level	0.236	0.265	-0.291	0.763	1.056	
	ln waist circumference (cm)	0.403	0.319	-0.231	1.037	1.088	
7	Constant	-1.243	3.396	-7.991	5.504		0.42
	Sex	0.409†	0.106	0.199	0.620	1.779	
	Age	-0.026†	0.006	-0.038	-0.015	1.061	
	Physical activity level	0.197	0.262	-0.322	0.717	1.061	
	ln knee height (cm)	1.820*	0.843	0.144	3.496	1.708	
8	Constant	-1.433	3.711	-8.807	5.940		0.41
	Sex	0.425†	0.104	0.219	0.632	1.705	
	Age	-0.025†	0.006	-0.037	-0.012	1.161	
	Physical activity level	0.270	0.262	-0.252	0.791	1.061	
	ln half arm span (cm)	1.615*	0.799	0.029	3.202	1.752	
9	Constant	5.377†	0.667	4.051	6.702		0.40
	Sex	0.643†	0.103	0.438	0.848	1.640	
	Age	-0.027†	0.006	-0.039	-0.015	1.058	
	Physical activity level	0.256	0.265	-0.271	0.782	1.059	
	ln triceps skinfold (mm)	0.152	0.105	-0.057	0.361	1.637	
10	Constant	5.780†	0.629	4.530	7.030		0.39
	Sex	0.596†	0.108	0.382	0.809	1.752	
	Age	-0.028†	0.006	-0.04	-0.016	1.041	
	Physical activity level	0.262	0.271	-0.277	0.800	1.086	
	ln biceps skinfold (mm)	0.059	0.097	-0.133	0.251	1.706	
11	Constant	6.422†	0.660	5.111	7.733		0.39
	Sex	0.492†	0.104	0.285	0.700	1.660	
	Age	-0.030†	0.006	-0.041	-0.018	1.026	
	Physical activity level	0.186	0.271	-0.351	0.724	1.091	
	ln thigh skinfold (mm)	-0.096	0.097	-0.288	0.096	1.595	
12	Constant	5.993†	0.616	4.77	7.217		0.39
	Sex	0.557†	0.107	0.344	0.770	1.737	
	Age	-0.029†	0.006	-0.041	-0.017	1.041	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R^2
		β	Standard error	LL	UL		
	Physical activity level	0.235	0.268	-0.298	0.768	1.060	
	ln medial calf skinfold (mm)	0.003	0.084	-0.164	0.169	1.711	
13	Constant	-2.485	2.757	-7.964	2.994		0.45
	Sex	0.393†	0.095	0.205	0.582	1.506	
	Age	-0.020*	0.006	-0.032	-0.007	1.295	
	Physical activity level	0.325	0.256	-0.183	0.833	1.070	
	ln biacromial breadth (mm)	2.146*	0.686	0.783	3.509	1.689	
14	Constant	4.151	2.365	-0.548	8.851		0.39
	Sex	0.547†	0.084	0.38	0.714	1.072	
	Age	-0.028†	0.006	-0.040	-0.015	1.101	
	Physical activity level	0.238	0.267	-0.293	0.768	1.056	
	ln bitrochanteric breadth (mm)	0.500	0.624	-0.739	1.739	1.091	
15	Constant	2.982*	1.236	0.527	5.438		0.43
	Sex	0.402†	0.099	0.206	0.599	1.593	
	Age	-0.026†	0.006	-0.038	-0.015	1.043	
	Physical activity level	0.239	0.258	-0.273	0.751	1.056	
	ln bimalleolar breadth (mm)	1.543*	0.579	0.393	2.693	1.538	
16	Constant	5.825†	1.047	3.744	7.906		0.39
	Sex	0.541†	0.109	0.324	0.757	1.792	
	Age	-0.029†	0.006	-0.041	-0.017	1.037	
	Physical activity level	0.230	0.269	-0.304	0.764	1.065	
	ln elbow breadth (mm)	0.098	0.498	-0.891	1.087	1.704	
17	Constant	4.697†	0.978	2.754	6.640		0.40
	Sex	0.453†	0.105	0.244	0.662	1.715	
	Age	-0.029†	0.006	-0.04	-0.017	1.018	
	Physical activity level	0.219	0.264	-0.306	0.744	1.058	
	ln wrist breadth (mm)	0.800	0.513	-0.218	1.819	1.638	
18	Constant	0.890	2.058	-3.200	4.980		0.43
	Sex	0.405†	0.100	0.206	0.603	1.616	
	Age	-0.023†	0.006	-0.035	-0.011	1.178	
	Physical activity level	0.281	0.259	-0.234	0.795	1.061	
	ln chest breadth (mm)	1.402*	0.548	0.314	2.490	1.679	
19	Constant	3.591*	1.208	1.191	5.990		0.42
	Sex	0.480†	0.088	0.304	0.656	1.243	
	Age	-0.023†	0.006	-0.036	-0.011	1.207	
	Physical activity level	0.250	0.261	-0.268	0.769	1.057	
	ln body mass*height (kg*m)	0.435*	0.198	0.041	0.828	1.339	
20	Constant	5.174†	0.636	3.911	6.438		0.41
	Sex	0.487†	0.088	0.313	0.662	1.222	
	Age	-0.024†	0.006	-0.036	-0.011	1.203	
	Physical activity level	0.252	0.261	-0.267	0.772	1.057	
	ln SA (m^2)	0.830*	0.394	0.047	1.613	1.317	
21	Constant	5.163†	1.281	2.618	7.708		0.39
	Sex	0.528†	0.092	0.345	0.710	1.276	
	Age	-0.028†	0.006	-0.040	-0.015	1.129	
	Physical activity level	0.219	0.268	-0.313	0.752	1.062	
	ln MAMC (cm)	0.246	0.343	-0.436	0.928	1.292	
22	Constant	5.547†	0.786	3.985	7.108		0.39
	Sex	0.537†	0.087	0.365	0.709	1.141	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R^2
		β	Standard error	LL	UL		
	Age	-0.027†	0.006	-0.04	-0.015	1.134	
	Physical activity level	0.218	0.268	-0.313	0.750	1.063	
	ln CAMA (cm^2)	0.107	0.139	-0.17	0.383	1.180	
23	Constant	3.606*	1.695	0.239	6.973		0.40
	Sex	0.367*	0.151	0.067	0.667	3.528	
	Age	-0.023*	0.007	-0.037	-0.008	1.529	
	Physical activity level	0.274	0.266	-0.254	0.802	1.067	
	ln FFM$_{\text{(LEAN et al., 1996)}}$ (kg)	0.534	0.36	-0.182	1.250	3.814	
24	Constant	3.378*	1.624	0.151	6.606		0.41
	Sex	0.410*	0.118	0.175	0.645	2.181	
	Age	-0.025†	0.006	-0.038	-0.013	1.174	
	Physical activity level	0.223	0.264	-0.301	0.746	1.057	
	ln left arm LST (g)	0.323	0.19	-0.054	0.701	2.182	
25	Constant	5.207*	1.741	1.747	8.666		0.39
	Sex	0.513†	0.120	0.274	0.752	2.187	
	Age	-0.028†	0.007	-0.041	-0.014	1.258	
	Physical activity level	0.241	0.268	-0.291	0.773	1.059	
	ln right arm LST (g)	0.093	0.194	-0.292	0.478	2.282	
26	Constant	1.938	2.25	-2.533	6.409		0.41
	Sex	0.407*	0.114	0.18	0.634	2.049	
	Age	-0.024*	0.007	-0.037	-0.010	1.275	
	Physical activity level	0.244	0.263	-0.278	0.766	1.056	
	ln left leg LST (g)	0.427	0.23	-0.031	0.885	2.149	
27	Constant	1.383	2.35	-3.286	6.052		0.41
	Sex	0.383*	0.118	0.147	0.618	2.211	
	Age	-0.023*	0.007	-0.036	-0.010	1.288	
	Physical activity level	0.283	0.263	-0.240	0.805	1.065	
	ln right leg LST (g)	0.481*	0.239	0.006	0.956	2.351	
28	Constant	4.074*	1.893	0.313	7.835		0.39
	Sex	0.460†	0.122	0.217	0.703	2.287	
	Age	-0.026†	0.007	-0.039	-0.013	1.237	
	Physical activity level	0.239	0.266	-0.29	0.768	1.056	
	ln arms LST (g)	0.213	0.201	-0.187	0.612	2.346	
29	Constant	1.137	2.531	-3.892	6.167		0.41
	Sex	0.388*	0.118	0.154	0.623	2.194	
	Age	-0.023*	0.007	-0.036	-0.010	1.298	
	Physical activity level	0.264	0.263	-0.257	0.786	1.060	
	ln legs LST (g)	0.474	0.242	-0.006	0.955	2.324	
30	Constant	4.476†	0.999	2.491	6.462		0.41
	Sex	0.397*	0.121	0.156	0.638	2.299	
	Age	-0.023*	0.007	-0.037	-0.010	1.302	
	Physical activity level	0.257	0.263	-0.267	0.780	1.058	
	ln ASM (kg)	0.422	0.238	-0.052	0.896	2.422	
31	Constant	5.959†	0.853	4.263	7.654		0.39
	Sex	0.551†	0.103	0.346	0.755	1.601	
	Age	-0.029†	0.006	-0.042	-0.016	1.179	
	Physical activity level	0.236	0.269	-0.299	0.772	1.070	
	ln ASM/height^2 (kg/m^2)	0.019	0.274	-0.527	0.564	1.685	
32	Constant	3.261*	1.486	0.306	6.215		0.41
	Sex	0.443†	0.100	0.245	0.642	1.503	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	Age	-0.024*	0.007	-0.037	-0.011	1.235	
	Physical activity level	0.294	0.266	-0.236	0.823	1.074	
	ln $FFM_{(BAUMGARTNER\ et\ al.,\ 1991)}$ (kg)	0.612*	0.306	0.004	1.220	1.665	
33	Constant	4.617*	1.280	2.074	7.160		0.40
	Sex	0.463†	0.114	0.237	0.689	1.979	
	Age	-0.026†	0.007	-0.039	-0.013	1.231	
	Physical activity level	0.245	0.266	-0.283	0.773	1.057	
	ln $FFM_{(DXA)}$ (kg)	0.316	0.268	-0.216	0.848	2.054	

*p<0,05 and †p<0,001 (statistically significant β)

Note: sex=0 for women and 1 for men; age in years; physical activity level=0 for inactive and 1 for active; ln=natural logarithm; β=coefficient of regression; CI=confidence interval; LL=lower limit; UL=upper limit; VIF=variance inflation factor; R²=coefficient of determination; BMI=body mass index; SA=surface area of human body; MAMC=mid-arm muscle circumference; CAMA=corrected arm muscle area; AFA=arm fat area; FFM=Fat-free mass; LST=lean soft tissue; ASM=appendicular skeletal muscle mass; DXA=Dual-energy X-ray absorptiometry.

Material Suplementar C

Tabela Suplementar C. Cut-off points to identify muscle weakness in older adults of the handgrip strength (HGS), one maximum repetition measurement for knee extensors (1RM) and isokinetic knee extension peak torque at 60º/s (PT) (non-normalized, ratio standard/muscle quality and allometric scaling), and the correlation of muscle strength with body size

Variable	Unit	Men					Women					Correlation (r) with body size		
		AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	Body mass	Height	Variable for normalization
HGS (kg)														
Non-normalized		0.74^{*}	0.548 to 0.886	36	86	59	0.61	0.477 to 0.725	22	52	70	0.17	$0.39^{\S}$	-
/body mass	(kg)	0.66	0.464 to 0.826	0.54	86	45	$0.76^{\dagger}$	0.634 to 0.854	0.38	88	63	$-0.57^{\S}$	-0.03	$-0.57^{\S}$
/body mass$^{0.22}$		0.73^{*}	0.538 to 0.880	14.4	86	59	0.65^{*}	0.523 to 0.765	9.5	68	65	-0.02	$0.29^{\ddagger}$	-0.02
/body mass$^{0.40}$ (FOLEY et al., 1999)		0.70	0.504 to 0.856	6.7	86	50	0.68^{*}	0.556 to 0.793	4.41	72	68	-0.18	$0.22^{\ddagger}$	-0.18
/body mass$^{0.67}$ (JARIC, 2003)		0.70	0.504 to 0.856	2.15	86	50	0.73^{*}	0.607 to 0.833	1.46	80	65	$-0.39^{\S}$	0.10	$-0.39^{\S}$
/body mass$^{0.63}$ (PUA, 2006)		0.70	0.504 to 0.856	2.55	86	50	0.73^{*}	0.600 to 0.829	1.77	84	60	$-0.36^{\S}$	0.11	$-0.36^{\S}$
/body mass$^{0.31}$ (MARANHÃO NETO et al., 2017)		0.71^{*}	0.517 to 0.865	10.9	100	41	0.67^{*}	0.540 to 0.780	6.5	68	65	-0.10	$0.26^{\ddagger}$	-0.10
/height	(m)	0.70	0.504 to 0.856	23.5	100	45	0.60	0.474 to 0.722	15.8	72	50	0.09	0.17	0.17
/height$^{1.87}$		0.65	0.451 to 0.816	14.8	86	50	0.60	0.466 to 0.715	10.2	60	63	0.01	-0.03	-0.03
/height$^{1.84}$ (MARANHÃO NETO et al., 2017)		0.65	0.451 to 0.816	15.1	86	50	0.60	0.467 to 0.716	10.4	60	63	0.01	-0.02	-0.02
/forearm circumference	(cm)	0.74^{*}	0.548 to 0.886	1.33	86	59	0.70^{*}	0.570 to 0.805	1.04	84	58	-0.17	$0.27^{\ddagger}$	-0.19
/forearm circumference$^{0.50}$		0.75^{*}	0.552 to 0.889	6.91	86	68	0.67^{*}	0.537 to 0.777	4.84	68	65	0.01	$0.34^{\ddagger}$	0.02
/calf circumference		0.73^{*}	0.531 to 0.875	0.92	57	82	0.67^{*}	0.544 to 0.783	0.69	72	63	-0.14	$0.25^{\ddagger}$	-0.21
/calf circumference$^{0.54}$		0.73^{*}	0.531 to 0.875	5.35	86	59	0.64^{*}	0.515 to 0.758	3.54	64	60	0.01	$0.32^{\ddagger}$	0.01
/chest circumference		0.69	0.490 to 0.846	0.37	86	55	0.68^{*}	0.551 to 0.789	0.28	84	58	-0.20	$0.24^{\ddagger}$	$-0.39^{\S}$
/chest circumference$^{0.08}$		0.75^{*}	0.552 to 0.889	24.6	86	68	0.62	0.487 to 0.734	16.4	60	68	0.14	$0.37^{\S}$	-0.02
/knee height		0.71	0.510 to 0.861	0.72	100	45	0.61	0.478 to 0.726	0.44	44	75	0.05	0.19	0.03
/knee height$^{1.32}$		0.70	0.504 to 0.856	0.21	100	50	0.61	0.482 to 0.729	0.13	44	78	0.01	0.13	-0.05
/half arm span		0.69	0.490 to 0.846	0.47	100	36	0.59	0.464 to 0.713	0.28	48	75	0.11	0.21	0.19
/half arm span$^{1.81}$		0.65	0.451 to 0.816	0.012	100	32	0.58	0.453 to 0.703	0.0086	72	45	0.04	0.04	-0.03
/triceps skinfold	(mm)	0.71^{*}	0.514 to 0.863	2.25	86	59	0.65	0.519 to 0.762	0.93	64	68	$-0.30^{\ddagger}$	0.15	$-0.55^{\S}$
/biceps skinfold		0.63	0.428 to 0.798	6.67	100	36	0.73^{*}	0.605 to 0.832	1.29	56	85	$-0.35^{\S}$	0.16	$-0.53^{\S}$
/biceps skinfold$^{-0.02}$		0.75^{*}	0.552 to 0.889	41.6	100	45	0.59	0.459 to 0.709	23.2	48	78	$0.21^{\ddagger}$	$0.38^{\S}$	-0.05
/midaxillary skinfold		0.62	0.419 to 0.790	0.86	29	100	0.52	0.395 to 0.648	1.23	80	33	$-0.34^{\ddagger}$	0.12	$-0.65^{\S}$
/midaxillary skinfold$^{-0.01}$		0.75^{*}	0.552 to 0.889	40.7	100	45	0.61	0.479 to 0.727	22.5	48	78	0.19	$0.38^{\S}$	-0.07
/pectoral skinfold		0.58	0.388 to 0.763	1.13	29	100	$0.74^{\dagger}$	0.618 to 0.843	1.64	76	73	$-0.31^{\ddagger}$	$0.21^{\ddagger}$	$-0.70^{\S}$
/suprailiac skinfold		0.61	0.413 to 0.785	1.88	71	55	0.62	0.488 to 0.735	0.77	64	73	$-0.34^{\ddagger}$	0.12	$-0.60^{\S}$
/suprailiac skinfold$^{0.01}$		0.74^{*}	0.545 to 0.884	35.3	86	68	0.62	0.486 to 0.733	23.4	64	68	0.17	$0.38^{\S}$	-0.07
/abdominal skinfold		0.66	0.464 to 0.826	1.13	57	73	0.69^{*}	0.564 to 0.800	0.62	56	85	$-0.29^{\ddagger}$	0.12	$-0.58^{\S}$
/thigh skinfold		0.78^{*}	0.584 to 0.909	1.82	71	77	$0.81^{\dagger}$	0.694 to 0.897	0.67	72	80	-0.16	$0.25^{\ddagger}$	$-0.46^{\S}$
/medial calf skinfold		$0.80^{\dagger}$	0.609 to 0.924	2.91	100	64	$0.76^{\dagger}$	0.632 to 0.853	0.93	64	78	-0.15	0.16	$-0.42^{\S}$

Variable	Unit	Men					Women					Correlation (r) with body size		
		AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	Body mass	Height	Variable for normalization
/medial calf skinfold$^{-0.03}$		0.73*	0.538 to 0.880	39.1	86	59	0.59	0.457 to 0.706	24.5	52	70	0.21	0.38§	0.04
/biacromial breadth	(mm)	0.68	0.484 to 0.841	1.02	100	36	0.62	0.493 to 0.739	0.67	76	50	0.01	0.26‡	0.01
/biacromial breadth$^{1.06}$		0.67	0.470 to 0.831	0.82	100	36	0.63	0.496 to 0.742	0.54	76	50	0.01	0.25‡	-0.01
/bitrochanteric breadth		0.71	0.510 to 0.861	1.06	86	59	0.67*	0.538 to 0.778	0.7	68	60	-0.02	0.29‡	-0.05
/bitrochanteric breadth$^{0.97}$		0.71	0.510 to 0.861	1.18	86	59	0.67*	0.537 to 0.777	0.78	68	60	-0.02	0.29‡	-0.04
/bimalleolar breadth		0.65	0.454 to 0.819	6.25	100	32	0.66*	0.529 to 0.770	3.85	68	58	0.04	0.21‡	-0.10
/bimalleolar breadth$^{0.91}$		0.68	0.480 to 0.839	6.78	86	50	0.65*	0.525 to 0.767	4.51	68	58	0.05	0.23‡	-0.07
/elbow breadth		0.70	0.497 to 0.851	4.86	71	68	0.68*	0.550 to 0.788	4.18	76	58	-0.04	0.31‡	-0.26‡
/elbow breadth$^{0.37}$		0.73*	0.531 to 0.875	20.4	100	41	0.64	0.506 to 0.751	12.1	64	65	0.10	0.36§	-0.03
/wrist breadth		0.80*	0.605 to 0.922	7.02	100	50	0.61	0.478 to 0.726	4.71	64	63	0.01	0.31‡	-0.19
/wrist breadth$^{0.58}$		0.76*	0.562 to 0.896	14.7	100	45	0.60	0.474 to 0.722	9.5	64	60	0.08	0.35§	-0.04
/chest breadth		0.67	0.470 to 0.831	1.32	100	45	0.60	0.466 to 0.716	0.88	64	63	-0.03	0.28‡	-0.20
/chest breadth$^{0.34}$		0.71*	0.517 to 0.865	11.5	86	59	0.61	0.476 to 0.725	7.53	56	70	0.04	0.31‡	-0.08
/body mass*height	(kg*m)	0.60	0.400 to 0.774	0.17	29	100	0.74†	0.616 to 0.841	0.23	76	68	-0.63§	-0.19	-0.60§
/(body mass*height)$^{0.26}$		0.70	0.497 to 0.851	12	100	36	0.66*	0.533 to 0.774	7.63	76	55	-0.08	0.23‡	-0.03
/SA	(m²)	0.69	0.490 to 0.846	20.8	86	50	0.70*	0.574 to 0.807	14.1	80	63	-0.32‡	0.08	-0.28‡
/SA$^{0.49}$		0.71	0.510 to 0.861	30.2	100	36	0.66*	0.529 to 0.770	18.3	68	63	-0.07	0.24‡	-0.02
/MAMC	(cm)	0.77*	0.573 to 0.902	1.39	71	77	0.70*	0.568 to 0.803	1.02	64	78	-0.21‡	0.23‡	-0.37§
/MAMC$^{0.21}$		0.75*	0.552 to 0.889	18.3	86	68	0.63	0.505 to 0.750	12.3	60	70	0.09	0.36§	0.08
/CAMA	(cm²)	0.70	0.504 to 0.856	0.83	71	73	0.71*	0.588 to 0.819	0.66	60	80	-0.49§	0.01	-0.74§
/CAMA$^{0.08}$		0.75*	0.552 to 0.889	26.3	86	68	0.63	0.504 to 0.749	17.6	60	70	0.10	0.36§	0.10
/AFA		0.71	0.517 to 0.865	2.17	86	55	0.70*	0.572 to 0.806	0.95	60	78	-0.42§	0.08	-0.59§
/AFA$^{0.01}$		0.74*	0.545 to 0.884	34.9	86	68	0.63	0.497 to 0.743	23.2	60	70	0.16	0.38§	-0.01
/FFM$_{\text{(LEAN et al., 1996)}}$	(kg)	0.68	0.477 to 0.836	0.75	86	45	0.70*	0.577 to 0.810	0.68	84	63	-0.32‡	0.06	-0.27‡
/FFM$^{0.53}_{\text{(LEAN et al., 1996)}}$		0.71	0.510 to 0.861	4.96	100	36	0.67*	0.544 to 0.783	3.63	76	58	-0.09	0.22‡	0.01
/fat mass$_{\text{(LEAN et al., 1996)}}$		0.64	0.438 to 0.806	2.69	100	32	0.76†	0.638 to 0.857	0.8	76	78	-0.62§	-0.08	-0.63§
/fat mass$^{0.05}_{\text{(LEAN et al., 1996)}}$		0.75*	0.552 to 0.889	31.3	86	68	0.62	0.494 to 0.740	20.3	64	65	0.10	0.35§	0.02
/left arm LST	(g)	0.53	0.333 to 0.713	0.01	29	100	0.69*	0.558 to 0.795	0.016	72	73	-0.42§	0.01	-0.58§
/left arm LST$^{0.29}$		0.70	0.497 to 0.851	4.31	100	36	0.66*	0.528 to 0.769	2.93	72	63	-0.02	0.29‡	0.05
/right arm LST		0.56	0.363 to 0.741	0.012	57	73	0.70*	0.576 to 0.809	0.013	68	80	-0.4§	0.06	-0.57§
/right arm LST$^{0.26}$		0.70	0.497 to 0.851	4.21	71	68	0.66*	0.531 to 0.772	3.3	68	65	0.01	0.32‡	0.08
/left leg LST		0.57	0.375 to 0.752	0.0027	29	100	0.65*	0.522 to 0.764	0.0041	60	75	-0.41§	-0.09	-0.50§
/left leg LST$^{0.30}$		0.70	0.504 to 0.856	2.88	100	45	0.63	0.498 to 0.744	1.9	72	60	-0.02	0.24‡	0.01
/right leg LST		0.53	0.333 to 0.713	0.0026	29	100	0.66*	0.530 to 0.771	0.0044	76	58	-0.37§	-0.01	-0.47§
/right leg LST$^{0.30}$		0.68	0.477 to 0.836	2.65	100	36	0.63	0.504 to 0.749	1.72	64	63	0.01	0.27‡	0.05
/arms LST		0.54	0.345 to 0.725	0.0045	29	100	0.70*	0.573 to 0.807	0.0068	68	80	-0.42§	0.04	-0.55§
/arms LST$^{0.30}$		0.68	0.484 to 0.841	2.68	71	68	0.66*	0.528 to 0.769	2.09	64	68	-0.03	0.30‡	0.07
/legs LST		0.55	0.357 to 0.736	0.0013	29	100	0.65*	0.518 to 0.761	0.002	60	75	-0.39§	-0.05	-0.46§
/legs LST$^{0.32}$		0.68	0.477 to 0.836	1.91	100	36	0.64	0.506 to 0.751	1.25	68	63	-0.02	0.25‡	0.03
/ASM	(kg)	0.54	0.345 to 0.725	1.03	29	100	0.66*	0.535 to 0.776	1.59	64	75	-0.41§	-0.03	-0.46§
/ASM$^{0.33}$		0.66	0.464 to 0.826	14.9	100	32	0.65*	0.517 to 0.760	9.87	72	63	-0.04	0.25‡	0.04
/ASM/height²	(kg/m²)	0.67	0.467 to 0.829	4.74	71	68	0.67*	0.538 to 0.778	4.17	76	65	-0.23‡	0.34‡	-0.50§
/ASM/height$^{2(0.13)}$		0.73*	0.531 to 0.875	31.3	100	41	0.63	0.499 to 0.745	18.9	64	65	0.12	0.38§	0.06
/FFM$_{\text{(BAUMGARTNER et al., 1991)}}$	(kg)	0.64	0.434 to 0.808	0.71	83	50	0.74†	0.619 to 0.845	0.56	88	59	-0.4§	0.10	-0.39§
/FFM$^{0.41}_{\text{(BAUMGARTNER et al., 1991)}}$		0.69	0.488 to 0.849	7.11	83	59	0.68*	0.546 to 0.787	5.29	84	51	-0.07	0.28‡	-0.02
/FFM$_{\text{(DXA)}}$		0.60	0.406 to 0.779	0.41	29	100	0.73*	0.600 to 0.829	0.65	84	63	-0.43§	-0.04	-0.44§
/FFM$^{0.36}_{\text{(DXA)}}$		0.70	0.504 to 0.856	10.1	100	36	0.65*	0.526 to 0.768	6.71	72	60	-0.06	0.24‡	0.02
/fat mass$_{\text{(DXA)}}$		0.71	0.517 to 0.865	1.01	43	95	0.77†	0.643 to 0.861	0.9	80	68	-0.53§	0.03	-0.66§

Variable	Unit	Men					Women					Correlation (r) with body size		
		AUC	**95% CI**	**Cut-off point (≤)**	**Sens (%)**	**Spe (%)**	**AUC**	**95% CI**	**Cut-off point (≤)**	**Sens (%)**	**Spe (%)**	**Body mass**	**Height**	**Variable for normalization**
/fat mass$^{0.03}_{(DXA)}$		0.74*	0.545 to 0.884	32.3	86	68	0.62	0.490 to 0.737	21.3	60	65	0.13	0.37§	-0.04
1RM (kg)														
Non-normalized		0.75*	0.555 to 0.891	56.1	86	77	0.67*	0.545 to 0.784	38.1	72	60	0.18	0.33‡	-
/body mass	(kg)	0.77*	0.580 to 0.907	0.85	86	68	0.76†	0.634 to 0.854	0.54	68	78	-0.28‡	0.13	-0.28‡
/body mass$^{0.44}$		0.75*	0.559 to 0.893	9.04	86	77	0.71*	0.586 to 0.818	6.03	76	63	-0.03	0.24‡	-0.03
/body mass$^{0.67}$ (JARIC, 2003)		0.78*	0.587 to 0.911	3.4	86	77	0.73†	0.604 to 0.832	2.28	76	65	-0.13	0.20	-0.13
/body mass$^{0.96}$ (ABDALLA et al., 2020)		0.77*	0.573 to 0.902	1.00	86	68	0.75†	0.629 to 0.851	0.45	44	100	-0.26‡	0.13	-0.26‡
/body mass$^{0.69}$ (ABDALLA et al., 2020)		0.78*	0.587 to 0.911	3.06	86	77	0.73*	0.606 to 0.833	1.48	44	98	-0.15	0.19	-0.15
/height	(m)	0.73*	0.531 to 0.875	33	86	77	0.69*	0.584 to 0.779	33	88	48	0.12	0.21‡	0.21‡
/height$^{3.05}$ (m)		0.68	0.484 to 0.841	12.2	86	64	0.68*	0.557 to 0.794	8.44	60	83	0.02	-0.03	-0.03
/forearm circumference	(cm)	0.75*	0.552 to 0.889	2.16	86	77	0.70*	0.577 to 0.810	1.38	60	75	0.01	0.27‡	-0.16
/forearm circumference$^{0.38}$		0.75*	0.552 to 0.889	16.1	86	77	0.69*	0.560 to 0.796	11.2	76	58	0.11	0.3‡	-0.02
/calf circumference		0.74*	0.545 to 0.884	1.65	86	77	0.70*	0.573 to 0.807	1.06	72	68	0.02	0.26‡	-0.02
/calf circumference$^{1.10}$		0.75*	0.552 to 0.889	1.14	86	77	0.71*	0.580 to 0.813	0.7	68	73	0.01	0.26‡	-0.04
/chest circumference		0.76*	0.566 to 0.898	0.64	86	73	0.71*	0.580 to 0.813	0.4	72	65	-0.03	0.26‡	-0.15
/chest circumference$^{0.56}$		0.75*	0.552 to 0.889	4.62	86	77	0.69*	0.566 to 0.801	3.06	76	60	0.06	0.29‡	-0.05
/waist circumference		0.78*	0.587 to 0.911	0.73	100	59	0.72*	0.591 to 0.821	0.37	60	80	-0.11	0.26‡	-0.24‡
/waist circumference$^{0.28}$		0.75*	0.552 to 0.889	16.5	86	77	0.69*	0.563 to 0.799	11.4	76	58	0.09	0.31‡	0.01
/knee height		0.73*	0.538 to 0.880	1.02	86	77	0.68*	0.554 to 0.792	0.78	76	60	0.10	0.22‡	0.15
/knee height$^{2.28}$		0.71	0.510 to 0.861	0.0065	86	77	0.68*	0.554 to 0.792	0.0041	52	83	0.01	0.09	0.24‡
/half arm span		0.72*	0.524 to 0.870	0.65	86	77	0.68*	0.547 to 0.786	0.48	76	60	0.13	0.23‡	0.26‡
/half arm span$^{2.73}$		0.64	0.438 to 0.806	0.48	76	60	0.67*	0.545 to 0.784	0.00026	76	58	0.05	0.05	0.14
/triceps skinfold	(mm)	0.81†	0.624 to 0.932	4.22	86	68	0.70*	0.575 to 0.809	1.4	60	75	-0.24‡	0.26‡	0.07
/triceps skinfold$^{0.18}$		0.77*	0.580 to 0.907	36.5	86	77	0.69*	0.564 to 0.799	21.6	76	60	0.09	0.34‡	0.10
/biceps skinfold		0.71	0.507 to 0.858	7.24	71	68	0.76†	0.637 to 0.856	2.5	80	65	-0.25‡	0.24‡	-0.38§
/biceps skinfold$^{0.08}$		0.77*	0.573 to 0.902	48.9	86	77	0.69*	0.566 to 0.801	31.3	76	60	0.12	0.32‡	-0.17
/thigh skinfold		0.81*	0.624 to 0.932	2.95	71	86	0.79†	0.668 to 0.879	1.18	76	73	-0.09	0.31‡	-0.26‡
/thigh skinfold$^{0.03}$		0.75*	0.559 to 0.893	51.1	86	77	0.68*	0.553 to 0.790	34.1	72	63	0.16	0.33‡	-0.04
/medial calf skinfold		0.83†	0.646 to 0.944	4.61	86	73	0.77†	0.646 to 0.863	1.6	76	70	-0.09	0.23‡	-0.38§
/medial calf skinfold$^{0.02}$		0.75*	0.559 to 0.893	53.6	86	77	0.68*	0.551 to 0.789	37.1	76	60	0.17	0.32‡	-0.02
/biacromial breadth	(mm)	0.73*	0.531 to 0.875	1.42	86	77	0.68*	0.552 to 0.789	1.07	76	58	0.08	0.27‡	0.13
/biacromial breadth$^{1.67}$		0.71	0.510 to 0.861	0.12	86	77	0.68*	0.550 to 0.788	0.11	84	50	0.02	0.22‡	0.26‡
/bitrochanteric breadth		0.73*	0.538 to 0.880	1.72	86	77	0.70*	0.572 to 0.806	1.16	76	60	0.08	0.27‡	0.01
/bitrochanteric breadth$^{0.69}$		0.74*	0.545 to 0.884	5.1	86	77	0.69*	0.567 to 0.802	3.48	76	60	0.11	0.28‡	-0.04
/bimalleolar breadth		0.73*	0.531 to 0.875	8.77	86	77	0.70*	0.575 to 0.808	5.77	76	65	0.10	0.24‡	0.12
/bimalleolar breadth$^{1.20}$		0.71*	0.517 to 0.865	6.01	86	68	0.70*	0.577 to 0.810	3.93	76	65	0.08	0.22‡	0.13
/elbow breadth		0.73*	0.538 to 0.880	9.36	86	73	0.70*	0.569 to 0.804	6.57	76	63	0.05	0.28‡	-0.09
/elbow breadth$^{0.10}$		0.75*	0.559 to 0.893	47.2	86	77	0.68*	0.548 to 0.786	32.7	76	60	0.16	0.32‡	-0.10
/wrist breadth		0.79*	0.602 to 0.919	11.5	100	64	0.66*	0.536 to 0.776	7.33	72	58	0.07	0.29‡	-0.05
/wrist breadth$^{0.44}$		0.75*	0.559 to 0.893	26.1	86	77	0.67*	0.542 to 0.782	18.4	72	63	0.13	0.31‡	0.03
/chest breadth		0.73*	0.538 to 0.880	1.85	86	77	0.66*	0.532 to 0.773	1.44	76	55	0.05	0.27‡	0.02
/chest breadth$^{0.68}$		0.73*	0.531 to 0.875	5.45	86	77	0.66*	0.536 to 0.776	4.06	76	58	0.09	0.29‡	0.06
/body mass*height	(kg*m)	0.73*	0.538 to 0.880	0.52	86	64	0.75†	0.627 to 0.849	0.33	68	78	-0.33‡	0.02	0.10
/(body mass*height)$^{0.48}$		0.75*	0.552 to 0.889	5.83	86	77	0.72*	0.589 to 0.820	4.06	76	65	-0.07	0.18	0.14
/SA	(m²)	0.75*	0.552 to 0.889	31.6	86	77	0.72*	0.593 to 0.823	21.2	72	68	-0.09	0.18	-0.29‡
/SA$^{0.93}$		0.75*	0.559 to 0.893	33	86	77	0.72*	0.589 to 0.820	22.7	76	65	-0.07	0.19	-0.03
/MAMC	(cm)	0.77*	0.573 to 0.902	2.42	86	73	0.72*	0.592 to 0.822	1.54	64	75	-0.03	0.26‡	-0.11

Variable	Unit	Men AUC	Men 95% CI	Men Cut-off point (≤)	Men Sens (%)	Men Spe (%)	Women AUC	Women 95% CI	Women Cut-off point (≤)	Women Sens (%)	Women Spe (%)	Correlation (r) with body size: Body mass	Correlation (r) with body size: Height	Correlation (r) with body size: Variable for normalization
/MAMC$^{0.18}$		0.75*	0.559 to 0.893	32	86	77	0.68*	0.557 to 0.794	22.5	76	60	0.14	0.31‡	-0.09
/CAMA	(cm²)	0.71*	0.517 to 0.865	2.03	100	41	0.73*	0.602 to 0.830	0.9	52	93	-0.26‡	0.14	-0.24‡
/CAMA$^{0.08}$		0.75*	0.559 to 0.893	41.7	86	77	0.69*	0.558 to 0.795	28.5	72	63	0.13	0.31‡	0.04
/FFM$_{(LEAN\ et\ al.,\ 1996)}$	(kg)	0.76*	0.566 to 0.898	1.11	86	77	0.72*	0.592 to 0.822	1	72	68	-0.09	0.18	-0.18
/FFM$^{0.88}_{(LEAN\ et\ al.,\ 1996)}$		0.75*	0.559 to 0.893	1.77	86	77	0.71*	0.583 to 0.815	1.53	76	65	-0.06	0.20	0.20
/left arm LST	(g)	0.64	0.438 to 0.806	0.026	86	59	0.70*	0.568 to 0.803	0.021	52	88	-0.18	0.14	0.05
/left arm LST$^{0.26}$		0.72*	0.524 to 0.870	7.77	86	77	0.69*	0.560 to 0.796	5.86	72	63	0.08	0.28‡	0.07
/right arm LST		0.62	0.425 to 0.795	0.026	100	45	0.70*	0.578 to 0.811	0.013	40	98	-0.17	0.18	-0.30‡
/right arm LST$^{0.22}$		0.73*	0.538 to 0.880	10.1	86	77	0.69*	0.559 to 0.795	7.44	72	63	0.09	0.3‡	0.07
/left leg LST		0.68	0.477 to 0.836	0.0079	86	64	0.68*	0.553 to 0.790	0.0048	44	93	-0.18	0.08	-0.15
/left leg LST$^{0.64}$		0.72*	0.524 to 0.870	0.19	86	77	0.69*	0.560 to 0.796	0.12	44	88	-0.05	0.17	0.19
/right leg LST		0.65	0.451 to 0.816	0.0079	86	55	0.69*	0.561 to 0.797	0.005	44	93	-0.15	0.13	-0.14
/right leg LST$^{0.58}$		0.73*	0.531 to 0.875	0.33	86	77	0.69*	0.562 to 0.798	0.21	48	83	-0.01	0.21‡	0.01
/arms LST		0.63	0.432 to 0.801	0.012	86	55	0.70*	0.572 to 0.806	0.009	52	85	-0.18	0.17	-0.18
/arms LST$^{0.26}$		0.72*	0.524 to 0.870	6.38	86	77	0.69*	0.561 to 0.797	4.76	72	63	0.08	0.29‡	0.01
/legs LST		0.68	0.477 to 0.836	0.0039	86	59	0.68*	0.556 to 0.793	0.0024	44	93	-0.16	0.10	-0.17
/legs LST$^{0.64}$		0.73*	0.531 to 0.875	0.12	86	77	0.69*	0.559 to 0.795	0.08	44	88	-0.04	0.18	0.18
/ASM	(kg)	0.66	0.457 to 0.821	2.99	86	55	0.69*	0.561 to 0.797	1.74	44	93	-0.17	0.12	-0.17
/ASM$^{0.56}$		0.72*	0.524 to 0.870	10.7	86	77	0.69*	0.565 to 0.801	5.68	36	98	-0.02	0.21‡	-0.01
/ASM/height²	(kg/m²)	0.73*	0.538 to 0.880	8.47	86	73	0.70*	0.568 to 0.803	4.88	48	88	-0.06	0.34‡	-0.28‡
/ASM/height²$^{(0.23)}$		0.73*	0.538 to 0.880	36.3	86	77	0.68*	0.554 to 0.791	22.4	60	73	0.12	0.33‡	-0.10
/FFM$_{(BAUMGARTNER\ et\ al.,\ 1991)}$	(kg)	0.78*	0.584 to 0.914	1.13	83	73	0.75†	0.620 to 0.845	0.83	76	64	-0.14	0.20	-0.03
/FFM$^{0.67}_{(BAUMGARTNER\ et\ al.,\ 1991)}$		0.76*	0.559 to 0.898	3.94	83	77	0.72*	0.592 to 0.823	2.91	76	64	-0.03	0.24‡	0.16
/FFM$_{(DXA)}$		0.70	0.504 to 0.856	1.16	86	73	0.70*	0.575 to 0.808	0.67	44	93	-0.17	0.11	-0.08
/FFM$^{0.38}_{(DXA)}$		0.72*	0.524 to 0.870	12.7	86	77	0.69*	0.562 to 0.798	9.48	72	60	0.04	0.24‡	0.02
PT (Nm)														
Non-normalized		0.93†	0.769 to 0.991	85.4	86	95	0.74†	0.619 to 0.843	66.6	64	75	0.20	0.42§	-
/body mass	(kg)	0.90†	0.734 to 0.981	1.26	86	91	0.84†	0.726 to 0.918	0.93	72	88	-0.32‡	0.17	-0.32‡
/body mass$^{0.37}$		0.93†	0.769 to 0.991	18.2	86	95	0.80†	0.677 to 0.885	16.2	80	68	0.01	0.33‡	0.01
/body mass$^{0.67}$ (DAVIES; DALSKY, 1997)		0.93†	0.769 to 0.991	5.06	86	95	0.82†	0.704 to 0.904	3.71	68	88	-0.15	0.26‡	-0.15
/body mass$^{0.72}$ (DAVIES; DALSKY, 1997)		0.94†	0.778 to 0.993	4.1	86	95	0.82†	0.710 to 0.907	3.14	72	85	-0.18	0.24‡	-0.18
/body mass$^{0.74}$ (DAVIES; DALSKY, 1997)		0.93†	0.769 to 0.991	3.77	86	95	0.82†	0.710 to 0.907	2.87	72	85	-0.19	0.24‡	-0.19
/body mass$^{0.67}$ (JARIC, 2003)		0.93†	0.769 to 0.991	5.06	86	95	0.82†	0.704 to 0.904	3.71	68	88	-0.15	0.26‡	-0.15
/height	(m)	0.93†	0.769 to 0.991	54.1	86	95	0.74†	0.620 to 0.843	44.1	64	75	0.14	0.30‡	0.30‡
/height$^{3.27}$		0.86†	0.677 to 0.958	19.2	100	77	0.74†	0.617 to 0.842	17.4	72	65	0.01	0.01	0.01
/forearm circumference	(cm)	0.94†	0.787 to 0.995	3.88	100	82	0.80†	0.683 to 0.890	2.59	60	88	0.01	0.36§	-0.09
/forearm circumference$^{0.59}$		0.95†	0.796 to 0.996	14.9	100	86	0.78†	0.664 to 0.876	12.8	92	55	0.08	0.38§	0.02
/calf circumference		0.90†	0.734 to 0.981	2.46	86	91	0.79†	0.676 to 0.884	2.13	84	65	0.02	0.34‡	-0.01
/calf circumference$^{1.18}$		0.90†	0.734 to 0.981	1.31	86	91	0.80†	0.686 to 0.891	1.2	88	63	-0.01	0.32‡	-0.05
/chest circumference		0.90†	0.726 to 0.978	0.9	86	91	0.79†	0.676 to 0.884	0.67	64	83	-0.03	0.34‡	-0.12
/chest circumference$^{0.72}$		0.90†	0.734 to 0.981	3.16	86	91	0.78†	0.663 to 0.876	2.27	60	85	0.03	0.36§	-0.04
/waist circumference		0.90†	0.726 to 0.978	0.93	86	91	0.79†	0.670 to 0.880	0.71	68	83	-0.13	0.33‡	-0.23‡
/waist circumference$^{0.40}$		0.93†	0.769 to 0.991	13.8	86	95	0.77†	0.648 to 0.865	11.4	72	73	0.07	0.38§	-0.01
/knee height		0.94†	0.778 to 0.993	1.83	100	86	0.75†	0.624 to 0.847	1.44	68	73	0.12	0.30‡	0.14
/knee height$^{1.82}$		0.90†	0.734 to 0.981	0.068	100	86	0.74†	0.617 to 0.842	0.053	64	75	0.05	0.21‡	0.02
/half arm span		0.91†	0.743 to 0.984	1.04	86	91	0.75†	0.627 to 0.849	0.9	68	70	0.15	0.31‡	0.11
/half arm span$^{1.62}$		0.88†	0.709 to 0.972	0.076	100	73	0.75†	0.631 to 0.852	0.066	84	58	0.11	0.24‡	0.01

Variable	Unit	Men					Women					Correlation (r) with body size		
		AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	Body mass	Height	Variable for normalization
/triceps skinfold		0.86†	0.677 to 0.958	5.26	86	86	0.78†	0.660 to 0.873	2.45	64	85	-0.25‡	0.26‡	-0.57§
/triceps skinfold$^{0.15}$		0.93†	0.769 to 0.991	55.6	86	95	0.76†	0.641 to 0.860	47.6	80	63	0.12	0.42§	-0.12
/biceps skinfold		0.79*	0.602 to 0.919	16.8	100	59	0.82†	0.704 to 0.904	5.3	92	63	-0.27‡	0.25‡	-0.56§
/biceps skinfold$^{0.06}$	(mm)	0.93†	0.769 to 0.991	76.1	86	95	0.75†	0.631 to 0.852	71.9	88	53	0.16	0.41§	-0.14
/thigh skinfold		0.92†	0.751 to 0.986	5.31	100	86	0.82†	0.708 to 0.907	1.85	72	83	-0.11	0.32‡	-0.57§
/thigh skinfold$^{-0.10}$		0.90†	0.734 to 0.981	115	86	91	0.73†	0.601 to 0.829	105	76	60	0.23‡	0.39§	-0.06
/medial calf skinfold		0.92†	0.760 to 0.988	7.21	86	95	0.83†	0.720 to 0.914	2.5	72	85	-0.10	0.25‡	-0.51§
/medial calf skinfold$^{0.003}$		0.93†	0.769 to 0.991	84.8	86	95	0.74†	0.620 to 0.843	66	64	75	0.20	0.41§	-0.04
/biacromial breadth		0.90†	0.726 to 0.978	2.56	100	73	0.76†	0.642 to 0.861	2.04	84	60	0.1	0.35§	0.15
/biacromial breadth$^{2.15}$		0.82†	0.631 to 0.936	0.038	86	68	0.77†	0.647 to 0.864	0.03	76	73	-0.01	0.27‡	-0.04
/bitrochanteric breadth		0.93†	0.769 to 0.991	2.56	86	95	0.79†	0.666 to 0.877	2.13	76	73	0.08	0.35§	-0.08
/bitrochanteric breadth$^{0.50}$		0.93†	0.769 to 0.991	14.8	86	95	0.77†	0.647 to 0.864	14.1	88	58	0.14	0.38§	0.01
/bimalleolar breadth		0.88†	0.701 to 0.969	13.6	86	86	0.79†	0.666 to 0.877	12.0	84	65	0.10	0.31‡	0.03
/bimalleolar breadth$^{1.54}$		0.81*	0.616 to 0.928	5.04	86	73	0.80†	0.681 to 0.888	4.64	92	60	0.06	0.26‡	-0.07
/elbow breadth	(mm)	0.90†	0.726 to 0.978	14	86	86	0.79†	0.674 to 0.884	13.9	88	63	0.07	0.37§	-0.20
/elbow breadth$^{0.10}$		0.93†	0.769 to 0.991	70.6	86	95	0.75†	0.624 to 0.847	56.6	64	75	0.18	0.41§	0.01
/wrist breadth		0.93†	0.769 to 0.991	15.9	86	95	0.76†	0.636 to 0.856	14.2	68	73	0.09	0.38§	-0.07
/wrist breadth$^{0.80}$		0.93†	0.769 to 0.991	22.1	86	95	0.76†	0.635 to 0.855	19.7	72	73	0.11	0.38§	-0.03
/chest breadth		0.89†	0.718 to 0.975	3.33	100	73	0.75†	0.625 to 0.848	2.2	56	83	0.07	0.37§	0.05
/chest breadth$^{1.40}$		0.88†	0.701 to 0.969	0.85	100	73	0.74†	0.611 to 0.837	0.77	84	55	0.02	0.34‡	-0.04
/body mass*height	(kg*m)	0.84†	0.654 to 0.947	0.8	86	77	0.84†	0.729 to 0.920	0.6	72	88	-0.38§	0.04	-0.32‡
/(body mass*height)$^{0.43}$		0.94†	0.787 to 0.995	13	100	82	0.80†	0.681 to 0.888	10.5	84	65	-0.06	0.26‡	0.01
/(body mass*height)$^{0.97}$ (SEGAL et al., 2008)		0.86†	0.677 to 0.958	0.9	86	77	0.84†	0.729 to 0.920	0.68	72	88	-0.37§	0.05	-0.31‡
/SA	(m²)	0.94†	0.787 to 0.995	56.9	100	82	0.81†	0.692 to 0.896	36.3	64	88	-0.10	0.24‡	-0.04
/SA$^{0.83}$		0.94†	0.778 to 0.993	53.8	86	95	0.80†	0.680 to 0.887	50	84	65	-0.05	0.28‡	0.01
/MAMC	(cm)	0.95†	0.796 to 0.996	4.11	100	86	0.80†	0.677 to 0.885	2.82	68	88	-0.04	0.34‡	-0.21‡
/MAMC$^{0.25}$		0.94†	0.778 to 0.993	45.9	100	82	0.77†	0.643 to 0.861	32.9	72	70	0.14	0.40§	0.08
/CAMA	(cm²)	0.96†	0.806 to 0.998	2.66	100	82	0.80†	0.685 to 0.891	2.49	84	73	-0.31‡	0.18	-0.58§
/CAMA$^{0.11}$		0.94†	0.778 to 0.993	68.5	100	82	0.77†	0.643 to 0.861	48.7	72	70	0.14	0.40§	0.10
/FFM(LEAN et al., 1996)	(kg)	0.93†	0.769 to 0.991	1.79	86	95	0.81†	0.697 to 0.899	1.84	76	80	-0.11	0.23‡	-0.10
/FFM$^{0.53}$(LEAN et al., 1996)		0.94†	0.778 to 0.993	10.7	86	95	0.79†	0.674 to 0.884	11.2	84	65	0.04	0.32‡	0.06
/left arm LST		0.81*	0.616 to 0.928	0.047	86	68	0.76†	0.641 to 0.860	0.047	76	75	-0.20	0.19	-0.35§
/left arm LST$^{0.32}$		0.91†	0.743 to 0.984	7.65	86	91	0.77†	0.646 to 0.863	6.72	72	70	0.07	0.36§	0.09
/right arm LST		0.80*	0.609 to 0.924	0.034	71	86	0.78†	0.662 to 0.875	0.036	68	83	-0.18	0.21‡	-0.44§
/right arm LST$^{0.09}$		0.93†	0.769 to 0.991	41.8	86	95	0.76†	0.635 to 0.855	38.8	80	63	0.16	0.40§	0.10
/left leg LST		0.82†	0.631 to 0.936	0.015	100	55	0.76†	0.636 to 0.856	0.012	68	80	-0.19	0.13	-0.25‡
/left leg LST$^{0.43}$		0.92†	0.760 to 0.988	2.26	100	77	0.77†	0.648 to 0.865	1.83	76	70	0.03	0.30‡	0.05
/right leg LST	(g)	0.77*	0.580 to 0.907	0.015	100	50	0.78†	0.662 to 0.875	0.013	76	78	-0.16	0.18	-0.21
/right leg LST$^{0.48}$		0.90†	0.734 to 0.981	1.39	100	73	0.78†	0.656 to 0.870	1.16	80	70	0.02	0.31‡	0.05
/arms LST		0.81*	0.616 to 0.928	0.018	71	82	0.78†	0.656 to 0.870	0.022	76	78	-0.19	0.21	-0.38§
/arms LST$^{0.21}$		0.92†	0.751 to 0.986	14.8	86	95	0.77†	0.651 to 0.867	14.0	80	63	0.11	0.38§	0.10
/legs LST		0.81*	0.616 to 0.928	0.0063	71	82	0.77†	0.651 to 0.867	0.0065	76	78	-0.18	0.15	-0.21‡
/legs LST$^{0.47}$		0.92†	0.751 to 0.986	1.07	100	73	0.77†	0.652 to 0.868	0.87	76	70	0.02	0.30‡	0.05
/ASM	(kg)	0.81*	0.624 to 0.932	4.66	71	86	0.77†	0.652 to 0.868	5.01	76	78	-0.18	0.17	-0.23‡
/ASM$^{0.42}$		0.91†	0.743 to 0.984	27.2	86	86	0.77†	0.646 to 0.863	23.9	76	70	0.03	0.32‡	0.07
/ASM/height²	(kg/m²)	0.88†	0.701 to 0.969	11.9	71	95	0.78†	0.656 to 0.870	11.5	72	78	-0.06	0.39§	-0.35§
/ASM/height$^{2(0.02)}$		0.93†	0.769 to 0.991	82.3	86	95	0.74†	0.620 to 0.843	64.6	64	75	0.19	0.41§	0.06
/FFM(BAUMGARTNER et al., 1991)	(kg)	0.93†	0.769 to 0.992	1.63	83	95	0.85†	0.734 to 0.924	1.6	88	77	-0.16	0.25‡	-0.15

Variable	Unit	Men					Women					Correlation (r) with body size		
		AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	AUC	95% CI	Cut-off point (≤)	Sens (%)	Spe (%)	Body mass	Height	Variable for normalization
/$FFM^{0.61}$$_{(BAUMGARTNER\ et\ al.,\ 1991)}$		0.92†	0.759 to 0.990	7.54	83	95	0.81†	0.694 to 0.898	7.2	88	67	-0.02	0.32‡	0.01
/$FFM_{(DXA)}$		0.84†	0.654 to 0.947	2.08	100	59	0.79†	0.672 to 0.882	1.89	76	75	-0.19	0.17	-0.23‡
/$FFM^{0.32}_{(DXA)}$		0.93†	0.769 to 0.991	26.1	86	95	0.77†	0.652 to 0.868	25.9	88	55	0.07	0.34‡	0.09

*p<0.05 and †p<0.001 (statistically significant AUC)

‡p<0.05 and §p<0.001 (statistically significant correlation)

Dependent variable (primary outcome): functional limitation (6MWT<400 m)

Note: AUC=area under the curve; CI=confidence interval; *p*=significance; Sens=sensibility; Spe=specificity; SA=surface area of human body; MAMC=mid-arm muscle circumference; CAMA=corrected arm muscle area; AFA=arm fat area; FFM=Fat-free mass; LST=lean soft tissue; ASM=appendicular skeletal muscle mass; DXA=Dual-energy X-ray absorptiometry; 6MWT=six-minute walk test.

CAPÍTULO III

ESTUDO ORIGINAL II - Allometrically adjusted grip strength to identify low strength from 13,235 older adults of low- and middle-income countries

Allometrically adjusted grip strength to identify low strength from 13,235 older adults of low- and middle-income countries

Pedro P. Abdalla[1,2,3], Lucimere Bohn[2,3], André Pereira dos Santos[1], Marcio Fernando Tasinafo Junior[4], Leonardo Santos Lopes da Silva[4], José Augusto Gonçalves Marini[4], Ana Claudia Rossini Venturini[1], Anderson dos Santos Carvalho[5], Gustavo André Borges[6], Nilo Cesar Ramos[7], Jorge Mota[1,2], Dalmo Roberto Lopes Machado[1,2,3,4].

[1] University of São Paulo, College of Nursing at Ribeirão Preto, Ribeirão Preto, Brazil.

[2] University of Porto, Faculty of Sports, Porto, Portugal.

[3] Research Center in Physical Activity, Health and Leisure, Faculty of Sport, University of Porto, Porto, Portugal.

[4] University of São Paulo, School of Physical Education and Sport of Ribeirão Preto, Ribeirão Preto, Brazil.

[5] Paulista University, Physical Education Course, São José do Rio Preto, Brazil.

[6] The Western Paraná State University, Physical Education Course, Marechal Cândido Rondon, Brazil.

[7] Coastal Carolina University, Graduate and Specialty Studies, Conway, United States.

Under review in *Journal of the American Medical Directors Association* (ISSN: 1525-8610; Fator de Impacto: 4,669).

Abstract

OBJECTIVES: Absolute handgrip strength or adjusted by body mass index are useful to identify geriatric syndromes. However, these values are not accurate for older adults with extreme body size because the nonlinear relationship between strength, height and body mass. The purpose was to determine cut-off points for geriatric syndromes of older adults using allometric coefficients to normalize grip strength by body size. METHODS: Data from 13,235 older adults of Study on Global Aging and Adult Health (SAGE) conducted in six low- and middle-income countries were analyzed. Country- and sex-specific allometric exponents for body-size variables (mass and height) were computed with log-linear models. Partial correlation was used to observe whether allometric normalization removed the effect of body size on grip strength. Cut-off points (first quintile) for low allometrically adjusted grip strength were established. RESULTS: Allometric exponents for normalization of grip strength were provided for body-size variables, ranging from 0.19 to 2.45. Allometric normalization removed the effect of body size on grip strength. Overall, frequencies of low muscle strength according to international criteria (absolute grip strength) and the cut-off points proposed in this study were significantly different. CONCLUSIONS: The proposed allometric exponents normalized grip strength according to body-size variables. These exponents improved the accuracy in identifying geriatric syndromes in older adults with extreme body size. The variability between

strength reveals the need for developing specific cut-off points for low- and middle-income countries.

Keywords: allometric models, body composition, frailty, geriatric assessment, physical function.

1. Introduction

Grip strength performed with a hand dynamometer (Kim & Jeon, 2018) estimates fractures, mobility limitations, physical functioning, poor health outcomes, in-hospital complications, increased health-related costs, long-term care admission and premature mortality in older adults (Beaudart et al., 2014; Bohannon, 2008, 2019; Hendin et al., 2020; Santanasto et al., 2020; Sieber, 2017; Teng et al., 2021). The assessment is simple, inexpensive and reliable (Cruz-Jentoft et al., 2018) and has been widely used to identify geriatric syndromes, such as dynapenia, frailty and sarcopenia (Clark & Manini, 2008; Cruz-Jentoft et al., 2018; Fried et al., 2001). In 2050, 80% (1.2 billion) of the world's older adult population (1.5 billion) will be living in low- or middle-income countries (Higo & Khan, 2015) and the prevalence of geriatric syndromes is expected to increase.

Current grip strength reference values used to identify geriatric syndromes are based on absolute results (Albrecht et al., 2021; Dodds et al., 2014; Fried et al., 2001; Lauretani et al., 2003; Wang et al., 2018), dividing grip strength by body mass index (BMI) (McGrath et al., 2020) or by stratifying strength in ranges according to sex and BMI quartiles (Fried et al., 2001). Absolute values may be inaccurate in older adults with lighter body weight and shorter body sizes (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). These reference values characterize lighter and shorter older adults as having a low level of strength when compared to their heavier and taller peers, even though they are able to sustain their motor independence (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). Furthermore, there are limitations in the stratification of the grip strength according to BMI quartiles or ratio standard (i.e., by simple division by body mass or BMI). This ratio standard overestimates the real strength of light/short older adults and underestimates tall/heavy older adults.(Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020) Previous studies have demonstrated a nonlinear relationship between grip strength and body size (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). To overcome this methodological constraint, proposed mathematical models contemplate power in the nonlinear relationship between grip strength and body size (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006).

Allometry or power scaling ratio is a mathematical model ($Y=aX^b$) that characterize the nonlinear relationship between two variables (Huxley & Teissier, 1936b). Y is the dependent variable (grip strength), X is the independent variable (body size) and ^{b} is the exponent of the power ratio between then (allometric exponent or coefficient) (Huxley, 1924). The power function ratio between grip strength and body-size variables as body mass ($^{b=0.31 \text{ to } 0.63}$), height ($^{b=1.84}$) and fat-free mass ($^{b=0.46}$) was reported in older adults (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). However, the use of allometry to determine cut-off points of low grip strength has not been considered.

Thus, the purpose of this study was to a) establish allometric coefficients to normalize grip strength according to body-size variables for older adults from low- and middle-income countries and b) determine the minimal threshold for low muscle strength of the allometrically adjusted grip strength of this population.

2. Materials and methods

The Survey

Publicly available data from the Study on Global Aging and Adult Health (SAGE) were analyzed (WHO.). This survey was conducted with participants (n=47,443) over 18 years old in China, Ghana, India, Mexico, Russian Federation and South Africa between 2007 and 2010. According to the World Bank classification (normalizing GDP per capita) at that time, Ghana was a low-income, China and India were lower-middle-income and Mexico, Russia Federation and South Africa were upper middle-income countries. The research protocol involved nationally representative samples using a multistage, clustered sampling method and was published previously (Kowal et al., 2012). Ethical approval was obtained from the World Health Organization (WHO) ethical review committee and the local ethic research council. Participants signed a written informed consent.

Sample

In the current study, data analysis was restricted to older adults aged 60 or more (n=24,212). The exclusion criteria was: cognitive limitations, inability to maintain an orthostatic position, wheelchair use, some type of paralysis, limb amputation, any pain or recent surgery (in the last three months), and arthritis in the dominant hand or wrist. Data from participants with answers of implausible values for the physical activity questionnaire were also excluded.

Anthropometry

Height (m) and weight (kg) were measured using a stadiometer and a scale, respectively (Ramlagan et al., 2014).

Grip Strength

Maximum grip strength was measured twice in both hands using a Smedley's handgrip dynamometer (Scandidact Aps, Denmark) (Ramlagan et al., 2014). Participants were seated with elbow flexed at 90 degrees and palm facing inward. Measurements were taken alternately, starting with the left hand. A verbal stimulus was provided by evaluators during assessments (Ramlagan et al., 2014). Handedness was confirmed with the question "which hand do you consider your dominant hand?". The highest value between the two attempts of the dominant hand was considered in the analysis. In ambidextrous participants, the highest of the four measures was adopted (Ramlagan et al., 2014).

Physical Activity Level

Physical activity level was estimated by the Global Physical Activity Questionnaire (GPAQ) (Armstrong & Bull, 2006). Participants were classified as active or inactive according to whether or not they performed weekly physical activity: 150 minutes of moderate-intensity; or 75 minutes of vigorous-intensity; or an equivalent combination of moderate and vigorous-intensity, achieving 600 metabolic equivalent task per minute (MET-min) (Armstrong & Bull, 2006). Participants was excluded if implausible values were reported according to the

GPAQ guidelines (>16 hours of moderate or vigorous physical activity in a 24h/day period and/or "zero days" of moderate or vigorous physical activity but reported duration was greater than zero minutes in a corresponding time domain) (Armstrong & Bull, 2006).

Low muscle strength

Low grip strength was classified with cut-off points adopted by revised consensus of the European Working Group on Sarcopenia in Older People (EWGSOP2) (Dodds et al., 2014) (<16 kg for older females; <27 kg for older males) and proposed by Sarcopenia Definitions and Outcomes Consortium (SDOC) (<20 kg, 0.34 and 0.79 for older females; <35.5 kg, 0.45 and 1.05 for older males, being absolute, normalized by body mass and BMI, respectively) (Manini et al., 2020).

Statistical analyses

Descriptive statistics for the sample characteristics were calculated and normality of distributions checked. Outliers were identified and excluded from the analyzes if values of grip strength, body mass and height were outside of the 1.5 interquartile range (IQR) according to sex and country (Wang et al., 2018). Grip strength were compared between countries with ANOVA and LSD post hoc test. The relationship between grip strength and body mass and between height were gathered with dispersion plots and smoothing splines (MedCalc v. 15.2, Ostend, Belgium). Other procedures were carried out with IBM SPSS v. 23 (Chicago, USA).

Log-linear regression models generated allometric exponents (*i.e.,* regression coefficient). The transformation of each body-size expression (independent variables) and grip strength (dependent variable) in its natural logarithm (ln) was performed to develop their specific allometric exponent (ln grip strength, ln body mass and ln height). The variable considered to be confounding was sex (females=0, males=1) and an interaction variable (for example, for the allometric exponent "body mass": ln body mass*sex) was computed in each model. The same was done for ln height. The enter method sustains the independent variables entry in the models (all models are shown in the Table S1 in the Supplementary Material).

Additional models without interaction variable (when possible) reduced the number of independent variables considering two scenarios: 1st) when the interaction variable was not statistically significant, the interaction was excluded from the model, which allowed application of allometric exponents regardless of sex; 2nd) when the interaction variable was statistically significant, allometric exponents for females and males were generated. Multicollinearity was confirmed if Variance Inflation Factor (VIF)>5 (Myers, 1990) and models were discarded. The allometric coefficients were used to adjust grip strength according to each body-size variable through the following equation (Equation 1):

$$\text{Allometrically Adjusted Grip Strength} = \frac{\text{Absolute Grip Strength (kg)}}{(\text{BodySize Variable}^{\text{allometric coefficient}})} \qquad \text{(Equation 1)}$$

The partial correlation analysis (between normalized grip strength and body-size variables) was performed to verify the ability of allometric normalization to remove the effect of body size on grip strength (Mukaka, 2012), controlling sex, age and physical activity effects. Pearson correlation of the product moment was negligible ($r<0.30$) (Mukaka, 2012), meaning that the normalization was able to isolate the effect of body-size variables on grip strength (Maranhão Neto et al., 2017). The cut-off points for low muscle strength of absolute and allometrically adjusted grip strength was fixed at the 20th percentile of the distribution (lowest quintile) (Bez & Neri, 2014; Fried et al., 2001; Moreira & Lourenco, 2013; Neri et al., 2013; Vasconcelos et al., 2016; Vieira et al., 2013). Finally, the difference between classifications of low grip strength with EWGSOP2, SDOC and this study's criteria (allometrically adjusted) were checked with Confusion Matrix. Statistical significance level was fixed at $p<0.05$.

3. Results

The data cleaning process is illustrated by the Figure S1 (in the Supplementary Material), after applying inclusion and exclusion criteria. From the initial 47,443 participants, data from 13,235 participants (aged between 60 and 114 years old) were included for analysis.

Sample characteristics is presented in Table 1. China was the country with the largest number of participants (n: 5,349; 40%) and female sex frequency (53%) was higher compared to men. Overall, the age-group 60-64 yrs. had the highest number of participants, with a progressive decrease in number as age increased. The exception was females from Ghana and Russia Federation, with a superior frequency in the 70-74 age-group strata. Except for South Africa, the frequency of males without any education was lower compared to their female pairs. Additionally, males had a higher percentage of less education (<8 years) compared to women in all countries, except for Russia Federation and South Africa. Physical inactivity was present in 25% of males and 30% of females, with South Africa being the country with the highest percentage for both sexes. Considering the whole sample, overweight and obesity were more frequent in females than in males. Conversely, underweight was more frequent in males and participants from India. In all countries, men had higher scores compared to women for grip strength ($p<0.001$). Grip strength was different among all countries ($F_{ANOVA}=255.1$; $p<0.001$ for women and $F_{ANOVA}=195.9$; $p<0.001$ for men; data not shown), except between China and Ghana for women ($p=0.143$) and between Russian Federation and South Africa for men ($p=0.473$).

Associations of grip strength with body mass (a) and height (b) of older women and men are presented in Figure 1. For both sexes, the smoothing splines highlight a nonlinear relationship between grip strength and body mass. On the other hand, there was a linear relationship between grip strength and height.

Table 1. Characteristics of the sample

	China (n: 5,349; 40%)		Ghana (n: 1,805; 14%)		India (n: 2,808; 21%)		Mexico (n: 1,076; 8%)		Russia Federation (n: 1,084; 8%)		South Africa (n: 1,113; 8%)		All countries (n: 13,235; 100%)	
	Female n: 2775	Male n: 2574	Female n: 875	Male n: 930	Female n: 1289	Male n: 1519	Female n: 657	Male n: 419	Female n: 733	Male n: 351	Female n: 649	Male n: 464	Female n: 6978	Male n: 6257
Mean age, yrs ± sd	68.9 ± 6.4	69.0 ± 6.6	70.8 ± 8.1	70.1 ± 8.2	67.2 ± 6.6	67.8 ± 6.4	69.1 ± 7.1	69.9 ± 7.2	70.4 ± 7.0	69.4 ± 6.8	69.9 ± 7.7	68.6 ± 7.1	69.1 ± 7.0	68.9 ± 7.0
Age Group (years)														
60-64	31%	31%	23%	27%	38%	33%	33%	28%	24%	27%	28%	35%	30%	31%
65-69	26%	25%	22%	25%	29%	31%	24%	28%	23%	29%	26%	27%	26%	27%
70-74	23%	22%	27%	21%	19%	20%	19%	16%	26%	22%	20%	19%	22%	21%
75-79	14%	15%	14%	12%	7%	9%	14%	17%	16%	13%	14%	8%	13%	13%
80-84	5%	5%	8%	7%	4%	5%	6%	7%	9%	7%	6%	7%	6%	6%
85+	1%	2%	7%	7%	3%	2%	3%	4%	3%	3%	5%	3%	3%	3%
Years of Education														
None	45%	18%	81%	55%	75%	38%	26%	15%	2%	0%	40%	42%	48%	29%
<8	34%	46%	10%	13%	18%	34%	59%	69%	26%	21%	33%	28%	29%	37%
≥8	21%	36%	9%	32%	7%	28%	15%	16%	72%	79%	27%	30%	22%	34%
Physical activity level (GPAQ)														
Moderate (min/week), mean ± sd	631.2 ± 805.8	702.1 ± 903.3	864.1 ± 855.8	932.8 ± 819.4	767.9 ± 807.1	787.1 ± 867.2	709.5 ± 973.8	799.7 ± 1103.8	1157.5 ± 1049.4	1069.6 ± 960.6	422.9 ± 724.6	527.4 ± 926.4	728.9 ± 870.7	771.2 ± 910.9
Vigorous (min/week), mean ± sd	72.8 ± 362	171.9 ± 547.6	303.3 ± 579.7	631.4 ± 821.5	102.8 ± 353.2	254.7 ± 637.7	44.2 ± 303.5	315.3 ± 794.5	140.4 ± 472.2	307 ± 585.5	40.1 ± 175.7	138.9 ± 488.2	108.6 ± 398	275 ± 652.8
MET-min, mean ± sd	3106.9 ± 4776.6	4183.7 ± 6442.6	5882.5 ± 5997.7	8782.1 ± 7467.2	3894.2 ± 4627.5	5185.7 ± 6896.8	3191.3 ± 4850.2	5721.2 ± 8034.1	5753.5 ± 6189.9	6734.1 ± 6841	2012.2 ± 3418.1	3220.6 ± 5515.3	3784.5 ± 5130	5285 ± 6988.7
Physical inactivity	32%	28%	24%	14%	24%	21%	38%	30%	14%	15%	54%	47%	30%	25%
Body mass index, km/m^2														
< 18.5 (underweight)	6%	6%	18%	20%	39%	41%	1%	1%	1%	1%	4%	6%	12%	16%
18.5 - 24.9 (normal weight)	59%	66%	55%	66%	49%	52%	22%	32%	19%	29%	25%	34%	46%	56%
25 - 29.9 (overweight)	30%	26%	20%	13%	10%	7%	39%	46%	39%	51%	29%	33%	27%	23%
≥ 30 (obese)	5%	2%	7%	1%	1%	0%	38%	21%	41%	19%	42%	27%	15%	5%
Grip strength (kg), mean ± sd	20.5 ± 8.0	31.6 ± 9.9	21 ± 8.7	28.3 ± 10.8	15.5 ± 5.2	23.8 ± 7.2	17 ± 5.7	26.5 ± 7.4	21.9 ± 7.1	35.9 ± 9.8	28.7 ± 13.9	36.4 ± 18.2	20.2 ± 8.9	29.5 ± 11
Low grip strength														
EWGSOP2														
Absolute	26%	29%	22%	38%	51%	65%	35%	52%	21%	18%	13%	34%	29%	40%
SDOC														
Absolute	40%	65%	34%	74%	77%	94%	62%	87%	35%	49%	22%	63%	46%	74%
Grip strength/Body mass	40%	34%	36%	39%	48%	47%	77%	77%	64%	47%	43%	49%	47%	43%
Grip strength/BMI	39%	23%	32%	27%	53%	33%	80%	57%	53%	24%	38%	38%	46%	30%

Note. MET-min: metabolic equivalent task per minute (combination of moderate and vigorous-intensity) from GPAQ: Global Physical Activity Questionnaire. EWGSOP2: revised European Working Group on Sarcopenia in Older People). SDOC: Sarcopenia Definitions and Outcomes Consortium. BMI: Body mass index.

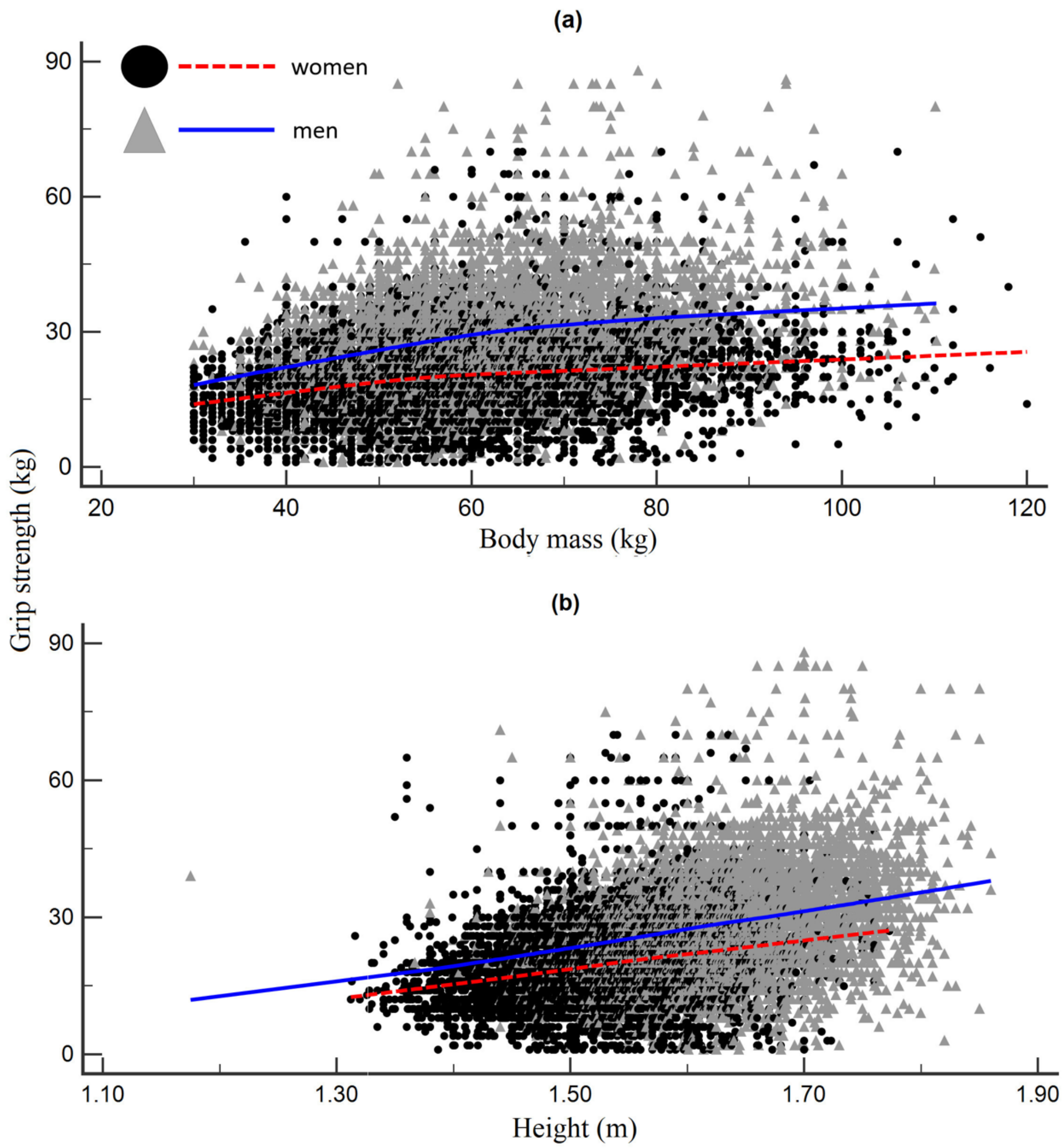


Figure 1. Relationship between grip strength and body mass (a) and height (b) in older females (circles) and older males (triangles) from the SAGE study

Table 2 shows allometric coefficients for ln grip strength according to the independent variables (ln body mass and ln height). The allometric exponents (regression coefficient) varied between 0.19 and 0.61 for body mass and between 1.46 and 2.45 for height were all statistically significant (except for height of older Ghanaian women) (Table 2). When the 95% CI of generated allometric exponents were analyzed, there was similarity between all countries. The coefficients 0.40 for body mass and 1.70 for height are contemplated inside the 95% CI of the six countries (except for body mass of older men from China). Therefore, we proposed the cut-off points based on these coefficients.

Table 2. Allometric exponents for body-size variables according to countries and gender

Country	Independent variable	Female				Male			
		Regression Coefficient*	SE	95% CI		Regression Coefficient*	SE	95% CI	
				Lower to upper				Lower to upper	
China	ln body mass (kg)	0.19	0.06	0.1	0.3	0.46	0.04	0.4	0.5
	ln height (m)	1.65	0.25	1.2	2.1	2.34	0.18	2.0	2.7
Ghana	ln body mass (kg)	0.45	0.12	0.2	0.7	0.50	0.12	0.3	0.7
	ln height (m)	0.53	0.58	-0.6	1.7	1.98	0.45	1.1	2.9
India	ln body mass (kg)	0.40	0.05	0.3	0.5	0.54	0.05	0.4	0.6
	ln height (m)	1.92	0.25	1.4	2.4	1.96	0.21	1.5	2.4
Mexico	ln body mass (kg)	0.61	0.09	0.4	0.8	0.54	0.09	0.4	0.7
	ln height (m)	2.17	0.42	1.4	3.0	1.56	0.39	0.8	2.3
Russian Federation	ln body mass (kg)	0.29	0.08	0.1	0.4	0.31	0.10	0.1	0.5
	ln height (m)	1.46	0.38	0.7	2.2	1.58	0.37	0.9	2.3
South Africa	ln body mass (kg)	0.22	0.08	0.1	0.4	0.32	0.11	0.1	0.5
	ln height (m)	1.48	0.37	0.7	2.2	2.45	0.37	1.7	3.2

Note.
SE: standard error
CI: confidence interval
lower: lower band
upper: upper band
ln: natural logarithm
*All are statistically significant (p<0.05; except for height of older Ghanaian women)

Correlations between allometrically adjusted grip strength and body-size variables fluctuated between -0.06 and 0.01, as shown in Table S2 (in the Supplementary Material). Although some correlations were statistically significant, all were negligible (Mukaka, 2012). These results confirm the adequate procedure of allometric normalization for each country and for all body-size variables (even when normalizing grip strength by body mass of older men from China and by height of older women from Ghana).

Mean sex-specific values±SD and 95% CI for absolute or allometrically adjusted grip strength are shown in Table 3. The cut-off points for low muscle strength (<20th percentile) according to each country are also presented.

Table 3. Mean sex-specific, standard deviation (SD) and 95% confidence intervals (CI) for absolute or allometrically adjusted grip strength and cut-off points for low muscle strength

Country		Female					Male				
		Mean	SD	95% CI Lower to upper		Cut-off points (< 20th percentile)	Mean	SD	95% CI Lower to upper		Cut-off points (< 20th percentile)
China	Absolute Grip Strength	20.5	8.0	20.2	20.8	**14.0**	31.6	9.9	31.2	32.0	**23.0**
	Grip Strength/Body Mass$^{0.40}$	4.14	1.6	4.8	4.2	**2.74**	6.17	1.9	6.0	6.1	**4.46**
	Grip Strength/Height$^{1.70}$	9.97	3.8	9.8	10.1	**6.64**	13.62	4.1	13.5	13.8	**10.09**
Ghana	Absolute Grip Strength	21	8.7	20.4	21.6	**14.0**	28.3	10.8	27.6	29.0	**20.0**
	Grip Strength/Body Mass$^{0.40}$	4.24	1.8	4.1	4.4	**2.85**	5.57	2.1	5.4	5.7	**3.95**
	Grip Strength/Height$^{1.70}$	9.81	4.1	9.5	10.1	**6.68**	11.97	4.5	11.7	12.3	**8.49**
India	Absolute Grip Strength	15.5	5.2	15.2	15.8	**11.0**	23.8	7.2	23.4	24.2	**18.0**
	Grip Strength/Body Mass$^{0.40}$	3.41	1.1	3.3	3.5	**2.42**	4.92	1.4	4.8	5.0	**3.73**
	Grip Strength/Height$^{1.70}$	7.85	2.6	7.7	8.0	**5.67**	10.41	3.1	10.3	10.6	**7.94**
Mexico	Absolute Grip Strength	17.0	5.7	16.6	17.5	**12.0**	26.5	7.4	25.8	27.2	**20.0**
	Grip Strength/Body Mass$^{0.40}$	3.23	1.1	3.1	3.3	**2.29**	4.81	1.3	4.7	4.9	**3.53**
	Grip Strength/Height$^{1.70}$	8.56	2.8	8.3	8.8	**6.14**	11.47	3.2	11.2	11.8	**8.62**
Russian Federation	Absolute Grip Strength	21.9	7.1	21.4	22.5	**15.0**	35.9	9.8	34.8	36.9	**27.0**
	Grip Strength/Body Mass$^{0.40}$	3.93	1.3	3.8	4.0	**2.81**	6.31	1.7	6.1	6.5	**4.80**
	Grip Strength/Height$^{1.70}$	9.93	3.1	9.7	10.1	**7.19**	14.61	4.0	14.2	15.0	**11.01**
South Africa	Absolute Grip Strength	28.7	13.9	27.6	29.8	**18.0**	36.4	18.2	34.7	38.0	**22.0**
	Grip Strength/Body Mass$^{0.40}$	5.31	2.6	5.1	5.5	**3.37**	6.65	3.3	6.3	6.9	**4.06**
	Grip Strength/Height$^{1.70}$	13.62	6.6	13.1	14.1	**8.45**	15.79	7.5	15.1	16.5	**9.71**
All countries	Absolute Grip Strength	20.2	8.9	20.0	20.5	**13.0**	29.5	11.0	29.2	29.7	**20.0**
	Grip Strength/Body Mass$^{0.40}$	4.01	1.7	4.0	4.1	**2.64**	5.7	2.0	5.6	5.7	**4.06**
	Grip Strength/Height$^{1.70}$	9.76	4.1	9.7	9.9	**6.43**	12.7	4.6	12.5	12.8	**9.00**

Note.
SD: standard deviation
CI: confidence interval
lower: lower band
upper: upper band

Figure 2 presents a confusion matrix of participants' low grip strength frequency according to cut-off points with allometric normalization proposed in this study (observed) and predicted by cut-off points of EWGSOP2 and SDOC.

			Grip strength/height$^{1.70}$		EWGSOP2 (absolute grip strength)		SDOC (absolute grip strength)		SDOC (grip strength/body mass)		SDOC (grip strength/BMI)	
			Predicted									
			Normal	Low	Normal	Low	Normal	Low	Normal	Low	Normal	Low
Grip strength/body mass$^{0.40}$	Observed	Normal	10342	237	8591	1988	5395	5184	7271	3308	8148	2431
		Low	252	2404	75	2581	12	2644	4	2652	32	2624
		Accuracy	96.3		84.4		60.7		75.0		81.4	
		Sensibility	90.5		97.2		99.5		99.8		98.8	
		Specificity	97.8		81.2		51.0		68.7		77.0	
Grip strength/height$^{1.70}$		Normal	-	-	8600	1994	5405	5189	7230	3364	8039	2555
		Low	-	-	66	2575	2	2639	45	2596	141	2500
		Accuracy	-		84.4		60.8		74.2		79.6	
		Sensibility	-		97.5		99.9		98.3		94.7	
		Specificity	-		81.2		51.0		68.2		75.9	

Figure 2. Confusion matrix of low grip strength frequency in the SAGE Study according to allometric normalization (observed in our study) and with the EWGSOP2 and SDOC criteria

Accuracy (96%), sensibility (90%) and specificity (98%) were high in our cut-off points classifications (grip strength/body mass$^{0.40}$ vs. grip strength/height$^{1.70}$) of low grip strength (Figure 2). When compared to our classifications, EWGSOP2 presented the highest numbers of accuracy (84%) and specificity (81%). All SDOC cut-off points presented elevated sensibility (≥95%). Absolute SDOC cut-off points had the lowest accuracy (≅61%) and specificity (51%), which were improved with normalization by body mass and BMI.

4. Discussion

To the best of our knowledge, this is the first study that proposed allometric coefficients for grip strength normalization and established the minimal threshold for low muscle strength to identify geriatric syndromes in older adults. Results indicated that allometric normalization removed the effect of body size on the expressions of grip strength. This was confirmed by the negligible correlations between the allometrically adjusted grip strength and body size. Thus, the identification of older adults with geriatric syndromes from country-specific cut-off points are more precise, regardless of body-size variability. Older adults with extreme body size (i.e., light and short or tall and heavy) living in low- and middle-income countries can be evaluated with less chance of error.

From the cut-off points proposed in this study, the classification of older adults with low muscle strength was significantly lower when compared to the EWGSOP2 criteria, which considered absolute values of grip strength (Cruz-Jentoft et al., 2018; Dodds et al., 2014). The EWGSOP2 cut-off points were proposed based on the combination of data from 12 studies, encompassing approximately 50,000 United Kingdom citizens (Dodds et al., 2014). Older adults from high-income countries have superior grip strength compared to low- and middle-income countries (Dodds et al., 2016), which may explain why the EWGSOP2 cut-off points overestimated the frequency of low muscle strength in this study's sample. The two exceptions (older Russia males and older South Africa females) may be explained by the fact that these two countries are closer to UK's economic classification (as they are upper middle-income countries) compared to low-income (Ghana) and lower middle-income countries in this study's sample (China and India). The cut-off points proposed by the SDOC were also derived from a high-income country (United States of America),(Manini et al., 2020) and likewise, overestimated the frequency of low muscle strength in this study's sample. However, when grip strength was normalized by body mass or BMI (as also proposed by the SDOC), overestimates of low muscle strength were reduced (as shown in Figure 2). Therefore, we hypothesize that the normalization of grip strength decreases the disagreements of the cut-off points when classifying low grip strength between countries of different incomes.

Some studies have proposed allometric exponents to normalize grip strength (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006), which may be comparable with this study's exponents. When allometric exponents vary from 0.00 to 0.99, the allometric (curvilinear) power relationship between the two variables is confirmed (Owings et al., 2002). However, if the exponent is ≥1.00, the linear relationship between variables is assumed (Owings et al., 2002). Allometric relationship between handgrip strength and body mass was confirmed in previous studies, with exponents of 0.33 (95% CI=0.14 to 0.48) (Maranhão Neto et al., 2017), 0.40 (95% CI=0.26 to 0.78) (Foley et al., 1999) and 0.63 (95% CI=0.31 to 0.91) (Y.-H. Pua, 2006). Following the same logic, the allometric relationship (Figure 1a) between body mass and handgrip in this study was assumed once the exponents ranged from 0.19 to 0.61 (Table 2). On the other hand, height had a linear relationship with handgrip strength (Figure 1b), given that the exponents exceeded the limit unit (≥1.00), varying between 1.46 and 2.45. Likewise, attempts of allometric adjustments for height in the literature were also unsuccessful, where the allometric exponent was 1.84 (95% CI: 1.23 to 2.45) (Maranhão Neto et al., 2017), indicating a quadratic relationship between handgrip strength and height. Our proposed generalized allometric exponents (0.40 for body mass and 1.70 for height) were always within or close to the 95% CI of all six countries studied. They were also within all confidence intervals indicated by the literature for body mass (95% CI=0.14 to 0.91) (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006) and height (95% CI=1.23 to 2.45) (Maranhão Neto et al., 2017). Although one of these studies used a sample of high-income country (Foley et al., 1999), it had a small sample (n=104). Therefore, the generalization of the allometric exponents proposed for high-income countries need to be tested in large and representative samples. The economic situation of each country/geographical region and the direct influence of the morphological characteristics on variability of grip strength must be taken into account in the development of specific low strength cut-off points (Dodds et al., 2016).

Future research should longitudinally observe the proposed allometrically adjusted strength cut-off points to test efficiency in predicting poor health outcomes (e.g., disability, falls, hospitalization or mortality factor risks). Since aging leads to reductions in strength, body mass and height it is likely that adjustments in grip strength will improve the predictability of adverse outcomes compared to absolute strength.

To the best of our knowledge, this is the first study that proposed values of grip strength with allometric adjustments in representative samples of older adults living in low- and middle-income countries. The literature supports that allometry techniques remove body-size effects on grip strength (Kara et al., 2019; Maranhão Neto et al., 2017; Y.-H. Pua, 2006), since strength itself is a physical fitness index related to body mass and height (Dodds et al., 2014; McGrath, 2019). The sample size, in this study, from six low- and middle-income countries covered a large range of ages and characteristics not always covered in studies with older adults. There were people over 85 years old (≅9%), with extreme ages of up to 114 years old. There was a wide diversity of nutritional status, with cases of extreme classifications of underweight (16%) and obese (5%).

This study also has limitations. It is worth indicating that the cross-sectional design could have underestimated the individual decline of grip strength with age. Indeed, future studies should consider prospective cohorts with multiple waves. Additionally, the proposed method to generate cut-off points in this study (lowest quintile) was performed when there was no data on young people to propose references for low muscle strength (Bez & Neri, 2014; Fried et al., 2001; Moreira & Lourenco, 2013; Neri et al., 2013; Vasconcelos et al., 2016; Vieira et al., 2013). Similarly to bone mineral density and osteopenia/osteoporosis, the utilization of a life course trajectory and determination of T-scores (Dodds et al., 2014) could represent a better alternative (Kanis, 2002).

The suggested reference exponents can be easily used to estimate grip strength indexes in older adults in epidemiological studies, from simple resources and accessible variables. The allometric models of low muscle strength adjusted by the expressions of body size (body mass and height) can be found in the link: http://posgraduacao.eerp.usp.br/files/Routine_Models_Men_and_Women_HGS.xlsx. As a practical example, consider an Indian older man with 70 years old, 55 kg, 1.70 m, who performed maximum grip strength of 20 kg. According to the adopted EWGSOP2 criteria (low grip strength: <27 kg), this person would be classified as having low grip strength. However, if this study's proposed allometric normalization is applied, by body mass ($20/55^{[0.40]}$) or height ($20/1.70^{[1.70]}$), his grip strength would be 4.03 kg/kg and 8.11 kg/m, respectively. These values would be above the cut-off points proposed in this study (3.73 and 7.94 kg/m), considering this person with no low muscle strength. In this way, the identification of a false positive case was prevented, as by the EWGSOP2 criteria. This strategy becomes important in developing countries where financial resources for healthcare are limited. Incorrect allocation for treatment of geriatric syndromes can be avoided with a simple, appropriate control of body-size bias.

In conclusion, allometry found a nonlinear relationship between grip strength and body mass and a linear relationship with height. Variability between strength of different countries highlights the need for cut-off points according to geographical area and population specificity. Grip strength allometrically adjusted for lighter/heavier and shorter/taller older adults may be more accurate in identifying dynapenia, sarcopenia and frailty. It is a simple, inexpensive and reliable way of diagnosis including the variability of body size of older adults living in low- and middle-income countries.

The implications of these findings for research include that the cut-off points for low grip strength should be correctly chosen since those proposed for high-income countries overestimate the presence of low grip strength in samples from low- and middle-income countries (Dodds et al., 2016). In addition, it is necessary to review the cut-off points for absolute low grip strength in developed countries and test the allometric normalization on their data.

Material Suplementar 1

Table S1. Allometric exponents for body size variables according to countries. Analyzes adjusted for sex

Model	Independent variables	Regression coefficients			t	*p*	95.0% CI		VIF
		β	SE	Standardized β			Lower to upper		
China									
Body mass	Constant	1.85	0.15		12.5	<0.001	1.56	2.15	
	ln body mass (kg)	0.27	0.04	0.09	7.1	<0.001	0.19	0.34	1.1
	Interaction: ln body mass*sex	0.11	0.00	0.43	33.0	<0.001	0.10	0.11	1.1
Height	Constant	2.15	0.07		31.4	<0.001	2.01	2.28	
	ln height (m)	1.81	0.16	0.18	11.3	<0.001	1.50	2.13	1.9
	Interaction: ln height*sex	0.21	0.01	0.34	20.5	<0.001	0.19	0.23	1.9
Ghana									
Body mass	Constant	1.11	0.33		3.3	0.001	0.45	1.77	
	ln body mass (kg)	0.44	0.08	0.12	5.3	<0.001	0.28	0.61	1.0
	Interaction: ln body mass*sex	0.08	0.01	0.22	9.7	<0.001	0.06	0.09	1.0
Height	Constant	2.36	0.17		14.0	<0.001	2.03	2.70	
	ln height (m)	1.14	0.38	0.08	3.0	0.002	0.41	1.88	1.5
	Interaction: ln height*sex	0.17	0.02	0.20	7.2	<0.001	0.12	0.21	1.5
India									
Body mass	Constant	1.09	0.13		8.4	<0.001	0.84	1.34	
	ln body mass (kg)	0.42	0.03	0.21	12.3	<0.001	0.35	0.49	1.2
	Interaction: ln body mass*sex	0.10	0.00	0.44	26.0	<0.001	0.09	0.10	1.2
Height	Constant	1.96	0.07		29.0	<0.001	1.83	2.09	
	ln height (m)	1.80	0.17	0.25	10.7	<0.001	1.47	2.13	2.3
	Interaction: ln height*sex	0.17	0.01	0.33	14.1	<0.001	0.15	0.20	2.3
Mexico									
Body mass	Constant	0.47	0.27		1.7	0.087	-0.07	1.00	
	ln body mass (kg)	0.55	0.07	0.22	8.4	<0.001	0.42	0.68	1.1
	Interaction: ln body mass*sex	0.10	0.01	0.44	16.4	<0.001	0.08	0.11	1.1
Height	Constant	2.02	0.12		16.2	<0.001	1.78	2.27	
	ln height (m)	1.83	0.31	0.23	6.0	<0.001	1.23	2.44	2.3
	Interaction: ln height*sex	0.19	0.02	0.33	8.4	<0.001	0.14	0.23	2.3
Russian Federation									
Body mass	Constant	1.88	0.27		7.0	<0.001	1.35	2.40	
	ln body mass (kg)	0.27	0.06	0.11	4.3	<0.001	0.14	0.39	1.0
	Interaction: ln body mass*sex	0.12	0.01	0.53	21.0	<0.001	0.11	0.13	1.0
Height	Constant	2.39	0.13		18.2	<0.001	2.13	2.65	
	ln height (m)	1.35	0.28	0.15	4.8	<0.001	0.80	1.90	1.6
	Interaction: ln height*sex	0.25	0.02	0.46	14.5	<0.001	0.22	0.29	1.6
South Africa									
Body mass	Constant	2.25	0.27		8.4	<0.001	1.72	2.78	
	ln body mass (kg)	0.24	0.06	0.11	3.7	<0.001	0.11	0.36	1.0
	Interaction: ln body mass*sex	0.05	0.01	0.22	7.7	<0.001	0.04	0.07	1.0
Height	Constant	2.42	0.12		20.3	<0.001	2.19	2.66	
	ln height (m)	1.87	0.27	0.22	6.9	<0.001	1.33	2.40	1.2
	Interaction: ln height*sex	0.09	0.02	0.15	4.6	<0.001	0.05	0.13	1.2

Note.
SE: standard error
CI: confidence interval
lower: lower band
upper: upper band
VIF: Variance Inflaction Factor

Material Suplementar 2

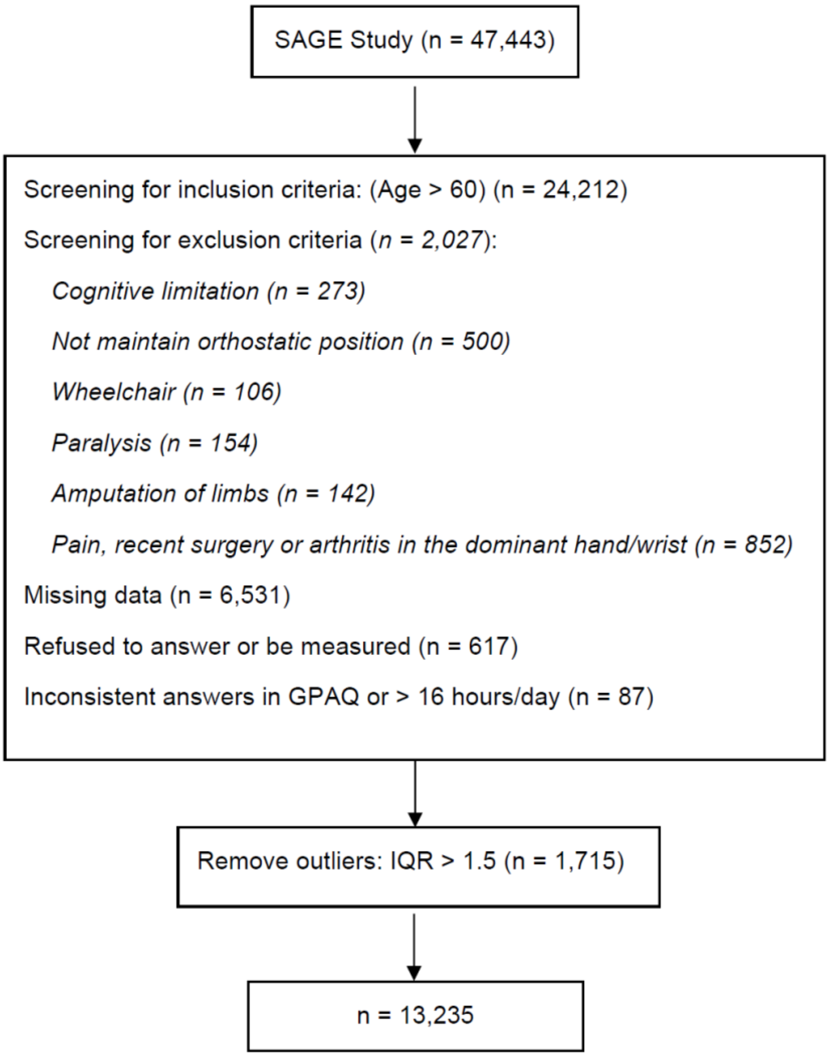
Table S2. Correlations between adjusted grip strength and body-size variables

Country	Variable	Body mass (kg)	Height (m)
China	Grip strength/body mass$^{0.40}$	-0.05**	
	Grip strength/height$^{1.70}$		0.01
Ghana	Grip strength/body mass$^{0.40}$	-0.05*	
	Grip strength/height$^{1.70}$		-0.07*
India	Grip strength/body mass$^{0.40}$	-0.01	
	Grip strength/height$^{1.70}$		-0.01
Mexico	Grip strength/body mass$^{0.40}$	-0.03	
	Grip strength/height$^{1.70}$		-0.05
Russian Federation	Grip strength/body mass$^{0.40}$	-0.14**	
	Grip strength/height$^{1.70}$		-0.09*
South Africa	Grip strength/body mass$^{0.40}$	-0.08*	
	Grip strength/height$^{1.70}$		0.03

Note. Correlations adjusted for sex and age
*p<0.05 and **p<0.001

Material Suplementar 3

Figure S1. Study flow chart



Note. GPAQ: Global Physical Activity Questionnaire; IQR: interquartile range

CAPÍTULO IV

ESTUDO ORIGINAL III - Foreign allometric exponents adequately normalize isokinetic knee extension strength to identify muscle weakness and functional limitation in Portuguese older adults: A cross-sectional study

Foreign allometric exponents adequately normalize isokinetic knee extension strength to identify muscle weakness and functional limitation in Portuguese older adults: A cross-sectional study

Dalmo Roberto Lopes Machado[1,2,3,4,5], Pedro Pugliesi Abdalla[1,3,4,5], Lucimere Bohn[3,4,5,6], Jorge Mota[3,4,5]

[1] University of São Paulo, College of Nursing at Ribeirão Preto, Ribeirão Preto, Brazil.

[2] University of São Paulo, School of Physical Education and Sport of Ribeirão Preto, Ribeirão Preto, Brazil.

[3] University of Porto, Faculty of Sports, Porto, Portugal.

[4] Research Center in Physical Activity, Health and Leisure, Faculty of Sport, University of Porto, Porto, Portugal

[5] Laboratory for Integrative and Translational Research in Population Health (ITR), Porto, Portugal.

[6] Lusófona University of Porto, Faculty of Psychology, Education and Sport, Porto, Portugal.

Under review

Abstract

INTRODUCTION: The accuracy to identify muscle weakness/functional limitation is improved with allometrically adjusted muscle strength, meaning the removing of body size influence. Although there are Brazilian and North American allometric exponents normalizing isokinetic knee extension strength, these have not yet been tested in Portuguese older adults. The study aims to compare functional capacity according to birthplace, and to test Brazilian and North American allometric exponents for normalize isokinetic knee extension strength in Portuguese older adults to identify muscle weakness/functional limitation. METHODS: This is a cross-sectional study encompassing 226 older Brazilian (n=94) and Portuguese (n=132) adults. Samples were assessed for anthropometry, body composition, mobility (six-minute walk test), and knee extension isokinetic strength at 60º/s. Independent t-test was applied to identify between nationalities comparisons on mobility and muscle strength. The Brazilian and North American allometric exponents (^{b}) were used to normalize Portuguese isokinetic knee extension strength (strength/body-size variables^{b}). Non-normalized and normalized isokinetic knee extension strength were compared by the ROC curve to decide the best cut-off point to muscle weakness/functional limitation (lowest quartile of mobility performance). RESULTS: Older Brazilian and Portuguese adults were not different for chronological age ($p>0.05$). Conversely, older Portuguese adults (both sexes) had a better mobility compared to the Brazilian ones. Older Portuguese women had also a superior muscle strength comparing against Brazilian's women. Non-normalized cut-off points presented an insufficient accuracy (AUC≤0.70) to identify muscle weakness/functional limitation. After normalizing muscle strength (e.g., isokinetic knee extension strength/[body mass*height]$^{0.43}$) the cut-off points performed acceptable accuracy (AUC≥0.70). CONCLUSION: Portuguese older adult women are stronger and have a superior functional capacity compared to

Brazilian ones. Nevertheless, some available international allometric exponents were supported to normalize knee extension strength of older Portuguese community, improving the accuracy to identify muscle weakness/functional limitation in both sexes.

Keywords: functional performance, geriatric assessment, geriatric medicine, health science, longevity, physical function, public health, scaling, sports medicine

1. Introduction

Muscle weakness occurs along aging and predicts clinically relevant health outcomes in older adults (Bohannon, 2008, 2019; Teng et al., 2021) such as disability (e.g. mobility limitation) (Santanasto et al., 2020) which, in turn, is more important than multimorbidity to forecast older adults mortality (Landi et al., 2010). Therefore, muscle weakness, diagnosed via muscle strength tests assessments (Cruz-Jentoft et al., 2018), is used to identify geriatric syndromes including dynapenia (Clark & Manini, 2008), frailty (Fried et al., 2001) and sarcopenia (Cruz-Jentoft et al., 2018). With aging, muscle strength declines three folds faster than skeletal muscle mass (Compston et al., 2014), and the leg extension strength presents an earlier decline compared to the upper limbs muscle strength lessening (Samuel et al., 2012).

Amongst muscle strength tests, the isokinetic knee extension was the one better associated with mobility limitation (Pedro Pugliesi Abdalla et al., 2021; Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). The available isokinetic strength indexes to identify muscle weakness are based on absolute (non-normalized) results (Akpinar et al., 2014; Farinatti et al., 2017; Gadelha et al., 2018; Hofmann et al., 2015; Lima et al., 2019) or normalized by body mass (ratio standard) (Manini et al., 2007). However, the muscle weakness phenotype may be incorrectly applied to older adults with a lighter body mass and shorter stature using absolute cutoff points (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006), even if they sustain their mobility (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). This false positive muscle weakness diagnostic can lead to an unnecessarily use of health resources (P. P. Abdalla, A. C. R. Venturini, et al., 2021). The other available strategy is the ratio standard, that overestimates the real strength of light/short older adults and underestimates it for tall/heavy ones (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). These misclassifications of the condition ´mobility limitation´ result from the nonlinear relationship between muscle strength and body-size variables (Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). Because allometric scaling contemplates power and sensitivity in these nonlinear relationship with the allometric exponent (^{b}), it overcomes the after mentioned constraints (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020; Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006).

The nonlinear relationship between isokinetic leg extension strength and body mass ($^{b=0.67}$ or $^{0.69}$ or $^{0.72}$ or $^{0.74}$ or $^{0.96}$) in older adults was previously reported (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020; Davies & Dalsky, 1997). Indeed, scaling isokinetic knee extension strength by body size (example: muscle strength/[body mass*height]$^{0.43}$) removes the effect of body size on muscle strength (Pedro Pugliesi Abdalla et al., 2021). Furthermore, when muscle strength was allometrically adjusted, the accuracy to identify muscle weakness and functional limitation was improved compared to non-normalized values in older adults (Pedro Pugliesi Abdalla et al., 2021; Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020). Brazilian (Pedro Pugliesi Abdalla et al., 2021) and North American (Davies & Dalsky, 1997; Segal et al., 2008) allometric exponents are already available to normalize isokinetic knee extension strength, however they external validity were not tested in any other population. To tests these exponents in Portuguese older adults should be an initial step in their internationalization and understanding of muscle weakness in aging as a universal phenomenon.

The study aims are 1) to compare functional capacity and muscle strength between older adults from Portugal and Brazil; 2) to identify muscle weakness/functional limitation in older Portuguese adults applying allometric exponents to normalize isokinetic knee extension strength developed with Brazilian and North American older adults. Our hypothesis is that the muscle strength normalized accordioning to Brazilian and North American allometric exponent shows muscle strength independently of body size and it should improve the accuracy to identify muscle weakness/functional limitation.

2. Methods

Design and Study population

This is a cross-sectional study with data of two samples, one from Brazil (measured at University Hospital of Ribeirao Preto School of Medicine, University of Sao Paulo, Brazil (HC-FMRP-USP) and another from Portugal (measured in Faculty of Sport, University of Porto, Portugal [FADEUP]). Both studies obeyed the Helsinki Declaration and were approved by their respective institutional review board. Older adults were voluntarily recruited, and all of them have assigned an informed consent. This manuscript still followed the guidelines from The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) conference list.

Both Brazilian and Portuguese samples consisted of community-dwelling older adults (>60 years old). Brazilian sample was recruited from social projects on behalf of older adults of USP and from health community services of the same institution and city. The Portuguese sample was recruited through advertisements into newspaper from Porto metropolitan area. Inclusion criteria for Brazilian sample were walk independently, absent limitation to execute all procedures, inexistence of acute infections, cancer diagnosis, hip or knee prostheses, unstable cardiovascular condition, stroke sequelae, tumors, and weight loss >3 kg in the last three months, and for Portuguese sample were aged 60–85 years, community-dwelling status, lack of use of bone-acting drugs and nutritional supplements known to affect bone metabolism (such as vitamin D and calcium), lack of and significant sensory/cognitive impairment or medical conditions. The exclusion criterion was cognition impairment for Brazilian sample.

Procedures

A multidisciplinary health team (Brazilian sample) and researchers of Faculty of Sport (Portuguese sample) performed data collection.

Cognition assessment

The validated Mini Mental State Examination (MMSE) was used to assess participants´ cognition status in Brazilian sample and those who have MMSE≤12 were excluded (Icaza & Albala, 1999).

Measure of Body-Size variables

Body-size variables were collected to compare anthropometric profile of Portuguese and Brazilian older adults and to normalize their performance in muscle strength tests. The selection of these variables were based on those previously used to calculate body indexes (Bailey & Briars, 1996), and involved the anthropometric measurements body mass [digital medical scales Filizola® (model Personal, MS, Brazil) for Brazilian sample; and Seca (GmbH, model 708, Germany) for Portuguese sample], height (using the stadiometer Sanny® Professional (model ES2020, Brazil) for Brazilian sample, and Seca 220 (Germany) for Portuguese sample], waist circumference (T. G.; LOHMAN et al., 1988) with tape measure (both samples) and body composition by Dual Energy X-ray Absorptiometry (DXA; QDR 4500A, Hologic, Bedford, MA for both samples), as briefly detailed below.

Body indexes

The body indexes derived from anthropometry were body mass index (BMI, kg/m²) (WHO Expert Consultation, 2004), body mass*height (Segal et al., 2008) and human body surface area (SA, m²) (Bailey & Briars, 1996). Body indexes derived from body composition were LST of arms and legs, ASM, ASM/height (m)² (Baumgartner et al., 1998), FFM by DXA, when fat mass were estimated from body mass difference.

Mobility Measurement

The cut-off points for muscle weakness were established based on poor mobility (lowest quartile of mobility performance) (McDermott et al., 2007). Mobility performance was verified based on the six-minute walk test (6MWT) executed in a corridor 30-meter length (Brazilian sample) and 45-meter length (Portuguese sample). Along this path, there were positioned signaling cones at each five meters to help researchers to identify the walked distance (Enright, 2003). Participants were instructed to cover the longest distance walking as faster they could during the six-minute time. Participants could slow down, interrupt the walking, and resume the test whenever desired, although time was not paused. Total walked distance was recorded.

Muscle Strength Measurements

The isokinetic knee extension peak torque at 60°/s (${}_{\text{knee extension}}PT^{60°/s}$) of the right lower limb was recorded with the isokinetic dynamometer (Biodex System 4 Pro; Biodex, Shirley, NY in both samples). Result is in newton-meter (Nm). Detailed protocols are previously published on Brazilian (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, & Machado, 2020) and Portuguese sample (Marques et al., 2011). The major differences were in the warm-up: 10 submaximal repetitions at velocity 60º/s for Brazilian sample and five minutes on a bicycle ergometer (Bike-Max; Tectrix, Irvine, CA) at 45–60 W for Portuguese sample; and in the maximal efforts to obtain ${}_{\text{knee extension}}PT^{60°/s}$: five repetitions at 60º/s for Brazilian sample and three repetitions for Portuguese sample (but executed two minutes after five repetitions in maximal effort at 180º/s).

Muscle Strength Normalization Procedures (allometric scaling)

${}_{\text{knee extension}}PT^{60º/s}$ were considered in two different ways: 1) absolute (non-normalized) and 2) allometrically adjusted (muscle strength/body-size variables^{b}). Allometric exponents (^{b}) were considered from the literature, as described in Table 1.

Table 1. Brazilian and North American allometric exponents (b) proposed in previous studies to normalize isokinetic knee extension peak torque at 60°/s ($_{\text{knee extension}}PT^{60°/s}$)

Authors	Nationality	Normalized $_{\text{knee extension}}PT^{60°/s}$ for body-size variable
Abdalla et al. (2021)	São Paulo, Brazil	/height$^{3.27}$ /(body mass*height)$^{0.43}$ /SA$^{0.83}$ /left leg LST$^{0.43}$ /right leg LST$^{0.48}$ /legs LST$^{0.47}$
Davies and Dalsky (1997)	New Mexico, USA	/body mass$^{0.67}$ /body mass$^{0.72}$ /body mass$^{0.74}$
Segal et al., (2008)	Iowa, USA	/body mass*height$^{0.97}$

In order to verify whether normalization ($_{\text{knee extension}}PT^{60°/s}$/body-size variable^{b}) removed the influence of body size on muscle strength, the correlation between normalized muscle strength and body-size variables (body mass, height and body-size used) should be negligible (r≤30) (Mukaka, 2012).

Statistical analysis

Descriptive statistics (mean, 95% CI and standard deviation) were used as appropriate. Functional capacity (mobility and muscle strength) differences between nationalities were examined by independent samples t-test.

Proposition of cut-off points for muscle weakness

Absolute muscle strength and normalized with allometric scaling had their area under the curve (AUC) quantified by ROC curve. The Youden index (Schisterman et al., 2005) selected the most appropriate cut-off points with the best relationship between sensitivity and specificity for the primary outcome (poor mobility).

For each body-size variable and sex, the ROC curves of non-normalized (n=1) and normalized muscle strength (n=2) were compared to each other to decide the best cut-off point.

Analyzes were carried out using the SPSS 25.0 statistical package, and the ROC curves and Youden index with NCSS 2021 with a previously established level of significance (α=5%).

3. Results

The Brazilian sample encompassed 94 older adults (69 women, 69.1%) and the Portuguese one, 132 (94 women, 71.2% women). Sample characterization according to nationality and sex is shown in Table 2. Between nationalities comparisons according to sex, show that Portuguese men present a higher body mass, BMI, and SA than the Brazilian ones, while the Brazilian women present a higher stature than Portuguese women. For both sexes, older Portuguese adults present higher ASM, ASM/height^2 and mobility in 6MWT (Figure 1) than the Brazilians. Differences for muscle strength (${}_{\text{knee extension}}PT^{60°/s}$) were noted for women (Figure 1) and these differences were preserved after normalization by body size-variables (except when ${}_{\text{knee extension}}PT^{60°/s}$ was normalized by the left leg $LST^{0.43}$; Table 1). Twenty-four Portuguese women (25.5%) and twenty-eight Portuguese men (26.3%) had poor mobility performance (6MWT<lowest quartile) (McDermott et al., 2007).

Table 2. Descriptive and comparative analysis of independent community-dwelling older adults in Brazil and Portugal

	Unit	Women									Men								
		Brazil (n=65)				Portugal (n=94)				*p*	Brazil (n=29)				Portugal (n=38)				*p*
		M	95% CI		SD	M	95% CI		SD		M	95% CI		SD	M	95% CI		SD	
			LL	UL			LL	UL				LL	UL			LL	UL		
Age	Years	69.7	68.2	71.2	6.1	68.5	67.4	69.6	5.3	0.197	71.2	68.5	73.9	7.1	69.4	67.5	71.3	5.9	0.267
Body mass	kg	66.9	64.0	69.8	11.6	65.8	63.7	67.9	10.1	0.519	73	67.7	78.3	13.9	81	77.5	84.4	10.5	0.009
Height	m	1.6	1.5	1.6	0.1	1.5	1.5	1.5	0.1	<0.001	1.7	1.6	1.7	0.1	1.7	1.7	1.7	0.1	0.627
BMI	kg/m²	27.4	26.3	28.5	4.4	28.3	27.5	29.1	4.1	0.194	25.7	24.3	27.2	3.8	28.9	27.9	30.0	3.3	<0.001
Waist circumference	cm	86.5	84.0	89.0	10	89.7	87.4	92.0	8.6	0.068	92.1	87.8	96.5	11.4	91.1	88.5	93.7	5	0.738
SA	m²	1.7	1.7	1.8	0.2	1.7	1.7	1.7	0.1	0.212	1.9	1.8	1.9	0.2	2.0	1.9	2.0	0.1	0.024
ASM (kg)	kg	14.5	13.9	15.1	2.5	15.3	14.8	15.9	2.1	0.048	20.9	19.3	22.5	4.2	23.5	22.1	24.9	3.3	0.016
ASM/height²	kg/m²	5.95	5.7	6.2	0.95	6.58	6.4	6.8	0.77	<0.001	7.34	7.0	7.7	0.99	8.45	8.0	8.9	1.01	<0.001
Six-minute walk test (6MWT)	m	412.7	389.9	435.5	92	536	521.6	550.4	70.2	<0.001	464.7	431.1	498.3	88.3	588.8	565.7	611.9	70.2	<0.001
Non-normalized $_{\text{knee extension}}PT^{60º/s}$	Nm	73.2	66.8	79.6	25.9	83.8	80.2	87.5	17.4	0.003	119.8	102.4	137.2	45.6	131.4	118.9	143.9	37.5	0.262
Normalized $_{\text{knee extension}}PT^{60º/s}$																			
/body mass$^{0.74}$ (DAVIES; DALSKY, 1997)	Nm/kg	3.3	3.0	3.6	1.1	3.9	3.7	4.0	0.9	0.001	5.0	4.4	5.6	1.6	5.1	4.7	5.5	1.3	0.776
/body mass$^{0.72}$ (DAVIES; DALSKY, 1997)	Nm/kg	3.6	3.3	3.9	1.2	4.2	4.0	4.4	0.9	0.001	5.4	4.8	6.1	1.8	5.5	5.1	6.0	1.4	0.754
/body mass$^{0.67}$ (DAVIES; DALSKY, 1997)	Nm/kg	4.4	4.0	4.8	1.5	5.2	4.9	5.4	1.1	0.001	6.7	5.9	7.6	2.2	6.9	6.3	7.5	1.7	0.702
/(body mass*height)$^{0.97}$ (SEGAL et al., 2008)	Nm/kg*m	0.8	0.7	0.9	0.3	1	0.9	1.0	0.2	<0.001	1.1	1.0	1.2	0.3	1.1	1.0	1.2	0.3	0.736
/height$^{3.27}$ (ABDALLA et al., 2021)	Nm/m	16.9	15.6	18.3	5.4	21.2	20.3	22.1	4.3	<0.001	21.5	19.0	24.0	6.6	24.3	22.2	26.4	6.3	0.082
/(body mass*height)$^{0.43}$ (ABDALLA et al., 2021)	Nm/kg*m	9.7	8.9	10.5	3.3	11.7	11.2	12.2	2.4	<0.001	14.7	12.8	16.5	4.9	15.9	14.5	17.2	4.1	0.283
/SA$^{0.83}$ (ABDALLA et al., 2021)	Nm/m²	42.6	39.0	46.2	14.4	54.7	52.3	57.0	11.3	<0.001	63.8	55.9	71.8	20.9	75	68.6	81.5	19.3	0.028
/left leg LST$^{0.43}$ (ABDALLA et al., 2021)	Nm/g	1.8	1.7	2.0	0.6	2	1.9	2.1	0.4	0.085	2.6	2.3	2.9	0.9	2.8	2.4	3.1	0.7	0.507
/right leg LST$^{0.48}$ (ABDALLA et al., 2021)	Nm/g	1.1	1.1	1.2	0.4	1.3	1.2	1.4	0.3	0.011	1.6	1.4	1.8	0.5	1.8	1.5	2.0	0.4	0.215
/legs LST$^{0.47}$ (ABDALLA et al., 2021)	Nm/g	0.9	0.8	1.0	0.3	1.0	1.0	1.1	0.2	0.002	1.2	1.1	1.4	0.4	1.4	1.2	1.6	0.3	0.134

Note: M=mean; CI=confidence interval; LL=lower limit; UL=upper limit; SD=standard deviation; SA=human body surface area; LST=lean soft tissue; ASM=appendicular skeletal muscle mass; Nm: Newtons-meter.

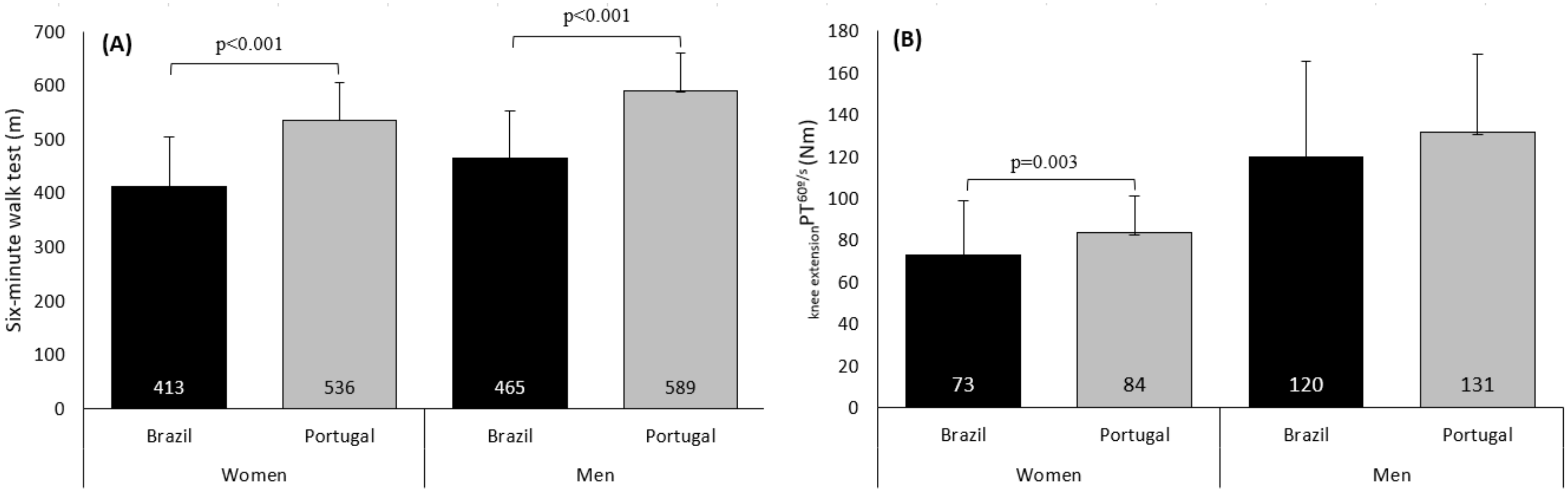


Figure 1. Comparison of functional capacity (A) and isokinetic knee extension peak torque at 60º/s ($_{\text{knee extension}}PT^{60º/s}$; B) among Brazilian and Portuguese older adults

The sex-specific cut-off points proposed for $_{knee\ extension}PT^{60º/s}$ (non-normalized and allometrically adjusted) to identify muscle weakness are presented in Table 3. Table 3 also shows correlations between muscle strength and body size (body mass, height and body-size variable used in normalization). When $_{knee\ extension}PT^{60º/s}$ was normalized, some derived cut-off points presented adequate accuracy (AUC≥0.70) to identify muscle weakness in both sexes, however only one of them [/(body mass*height)$^{0.97}$ (SEGAL et al., 2008)] present dependency of body size (with r>0.30). Non-normalized $_{knee\ extension}PT^{60º/s}$ cut-off points were not adequate for both sexes because they did not present sufficient accuracy (AUC≥0.70) to identify muscle weakness (Hosmer & Lemeshow, 2000). To support the decision of best cut-off point selection to identify muscle weakness, we compared the cut-off points with higher accuracy and negligible correlation (r≤30) with body size-variables (Figure 2). Only after normalizing muscle strength, the AUC perform acceptable values to identify functional limitation (≥0.70; Figure 2).

Table 3. Application of international and Brazilian allometric exponents in Portuguese community-dwelling older adults to normalize isokinetic knee extension peak torque at 60º/s ($_{\text{knee extension}}PT^{60º/s}$), their accuracy and cut-off points to identify poor functional performance (lowest quartile of six-minute walk test)

$_{\text{knee extension}}PT^{60º/s}$	**Unit**	**Portuguese women**				**Portuguese men**				**Correlation (r) with body size**		
		AUC	**Cut-off point (≤)**	**sens (%)**	**spec (%)**	**AUC**	**Cut-off point (≤)**	**sens (%)**	**spec (%)**	**Body mass**	**Height**	**Normalization**
Non-normalized	Nm	0.68	87.4	86	51	0.67	132.4	90	48	0.28*	0.29*	
/body mass$^{0.74}$ (DAVIES; DALSKY, 1997)	Nm/kg	0.75	4.10	100	47	0.69	4.46	70	74	-0.19	0.08	
/body mass$^{0.72}$ (DAVIES; DALSKY, 1997)	Nm/kg	0.75	4.46	100	47	0.69	4.89	70	74	-0.18	0.08	
/body mass$^{0.67}$ (DAVIES; DALSKY, 1997)	Nm/kg	0.74	5.51	100	46	0.68	6.15	70	74	-0.15	0.10	
/(body mass*height)$^{0.97}$ (SEGAL et al., 2008)	Nm/kg*m	0.78	1.00	90	60	0.71	0.98	70	74	-0.41*	-0.15	-0.38*
/height$^{3.27}$ (ABDALLA et al., 2021)	Nm/m	0.74	21.0	86	63	0.69	18.8	60	85	-0.01	-0.26*	
/(body mass*height)$^{0.43}$ (ABDALLA et al., 2021)	Nm/kg*m	0.75	12.5	100	49	0.69	13.2	60	78	-0.03	0.11	0.02
/SA$^{0.83}$ (ABDALLA et al., 2021)	Nm/m²	0.74	58.7	100	47	0.69	62.5	60	78	-0.02	0.12	0.01
/left leg LST$^{0.43}$ (ABDALLA et al., 2021)	Nm/g	0.69	2.14	93	49	0.72	2.83	100	50	0.07	0.15	0.11
/right leg LST$^{0.48}$ (ABDALLA et al., 2021)	Nm/g	0.70	1.40	93	46	0.73	1.67	80	75	0.04	0.14	0.10
/legs LST$^{0.47}$ (ABDALLA et al., 2021)	Nm/g	0.70	1.10	93	46	0.73	1.31	80	75	0.05	0.14	0.10

*p<0.05: statistically significant correlation

Note. AUC=area under the curve; sens=sensibility; specificity; Nm=Newtons meter; SA=human body surface estimated by Bailey and Briars (1996) equation; LST=lean soft tissue.

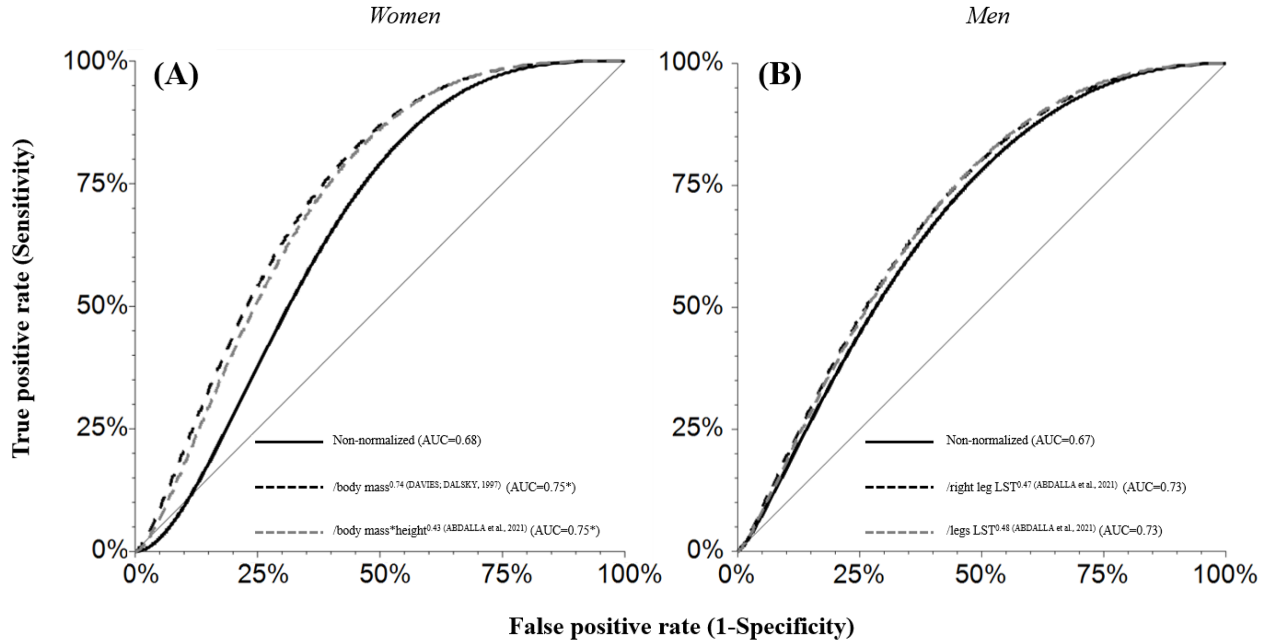


Figure 2. Accuracy comparison of absolute (non-normalized) and normalized isokinetic knee extension peak torque at 60º/s ($_{\text{knee extension}}PT^{60º/s}$) with international and Brazilian allometric exponents to identify poor functional performance (lowest quartile of six-minute walk test) in Portuguese older adults' women (A) and men (B)

*p<0.001 (greater than the AUC of non-normalized)

4. Discussion

Cut-off points were tested to identify muscle weakness in older Portuguese adults based on lower limbs muscle strength normalized with allometric exponents from other countries (from Brazil and North America). The non-normalized cut-off points for lower limbs strength did not present sufficient accuracy (AUC≥0.70) to identify muscle weakness and thus they seem not adequate for both sexes. Our intention was to validate international allometric exponents to older Portuguese adults. After normalizing lower limbs strength by allometric exponents there were find eleven valid models (women=8; men=3) with acceptable accuracy to identify false negative cases of muscle weakness. In addition, after normalization the association with body size was reduced for non-significant levels, excepting for "(body mass*height)$^{0.97\ (SEGAL\ et\ al.,\ 2008)}$" and "height$^{3.27\ (ABDALLA\ et\ al.,\ 2021)}$". Normalized models of both sexes, without correlation with body size, isolate the natural interdependence between muscle strength and body size (Maranhão Neto et al., 2017). The comparison of functional capacity according to birthplace shows that older Portuguese adults have better mobility (both sexes) and superior muscle strength against older Brazilian's women.

To the best of our knowledge, this is the first study testing muscle weakness cut-off points for $_{knee\ extension}PT^{60°/s}$ allometrically adjusted with international allometric exponents in older Portuguese adults. In the literature there are also muscle weakness cut-off points for $_{knee\ extension}PT^{60°/s}$ linearly normalized (ratio standard) by body mass (Manini et al., 2007). However, that study did not compare the accuracy of allometrically adjusted with non-normalized muscle strength to identify mobility limitation/muscle weakness. Furthermore, the authors did not explore the natural interdependence between muscle strength and body size. When $_{knee\ extension}PT^{60°/s}$ was linearly normalized by body mass, this variable presented correlation (r≥0.30) with body size (Pedro Pugliesi Abdalla et al., 2021), what prevents recommending its use.

The normalization of $_{knee\ extension}PT^{60°/s}$ with North American allometric exponents did not result in acceptable accuracy to identify muscle weakness in Portuguese men. There were no considerable differences reported in the literature in the six-minute walk test between Portuguese and North Americans older men (Gouveia et al., 2013). Furthermore, differences for some anthropometric variables of North American men [29.6±4.6 kg/m² (Davies & Dalsky, 1997); 80.8±10.2 kg and 174.4±7.0 cm (Segal et al., 2008)] didn't show considerable differences compared to Portuguese men (Δ of +0.2 kg; and -0.7 kg/m²), but not-negligible difference for height (Δ of -7.0 cm) was found and can somehow explain the lack of accuracy of the North American allometric exponents applied for Portuguese samples. Therefore, in addition to the anthropometric difference influencing accuracy, other factors still need to be studied and may require test across countries the necessity for specific allometric exponents. There are differences between countries of different incomes (e.g., Portugal vs USA) in regard of biological, early growth, nutrition and genetic factors (ethnicity differences) that impacts in muscle strength (Koopman et al., 2015).

Previous studies have proposed allometric exponents to normalize $_{\text{knee extension}}PT^{60°/s}$ by body mass, height, body mass*height, SA and DXA derived LST (Pedro Pugliesi Abdalla et al., 2021; Davies & Dalsky, 1997; Segal et al., 2008). All allometric exponents were tested in our sample and most of them were accurate enough to identify muscle weakness. Although the variables "(body mass*height)$^{0.97\ \text{(SEGAL et al., 2008)}}$" and "height$^{3.27\ \text{(ABDALLA et al., 2021)}}$" are accurate enough to identify muscle weakness, they were correlated with body size (Table 2). This results from the linear relationship between height and strength (when ^{b}≥1.00) (Owings et al., 2002) where ^{b} varies between 1.84 and 3.27 (Pedro Pugliesi Abdalla et al., 2021; Maranhão Neto et al., 2017); and by the non-linearity tendence (when ^{b}≤1.00) of the variable "body mass*height", showing ^{b} of 0.974 (Segal et al., 2008), previously observed in the literature. Despite a curvilinear (allometric) relationship is confirmed when ^{b} is between 0.00 and 0.99 (Owings et al., 2002), the dependency of "$_{\text{knee extension}}PT^{60°/s}$/(body mass*height)$^{0.97\ \text{(SEGAL et al., 2008)}}$" with body size (r>0.30) can be possibly explained by confidence interval. The authors (Segal et al., 2008) did not report the confidence interval, but certainly upper limit of 95% CI exceeds unity (^{b}≥1.00), featuring a linear relationship with body size, which justifies the interdependence between muscle strength and body size. Notwithstanding, when an allometric scaling (^{b}=0.43;

(Pedro Pugliesi Abdalla et al., 2021)) is used for body mass*height, independence of body size (r between -0.03 and 0.11; Table 2) was reached, demonstrating the usefulness of allometry.

Some strengths of our study are noteworthy. We tested muscle weakness cut-off points from the “gold standard” passive device to assess lower limbs strength (isokinetic dynamometer). A considerable number of allometric exponents (n=10) were tested in our study, expanding the normalization possibilities of knee extension strength performed in isokinetic dynamometer. Our findings can be applied to identify muscle weakness in clinical practice for both sexes with sufficient accuracy (AUC>0.70), independently of body size (negligible correlation). Nonetheless, this study has limitations such as the cross-sectional design, which may underestimate the decline in the individual muscle strength because of the naturally aging process. Additionally, because sample size was small and constituted mostly for women, the extrapolation of our findings to other populations must be with caution.

The isokinetic dynamometer is expensive and generally available in research settings rather than clinical settings. Even though, our idea to normalize muscle strength can be also applicable in clinical practice with widely available in geriatric environments through other instruments like manual dynamometers. For this, allometric exponents proposed (Pedro Pugliesi Abdalla et al., 2021; Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006) to normalize performed handgrip strength need to be tested for Portuguese older adults. The assessment of older adult’s muscle strength and muscle weakness classification should be frequent in clinical practice, to avoid unnecessary expenditures from false-positive cases election. Future studies can test allometric exponents to normalize muscle strength for different ethnicity/race of older adults.

As an applied example to avoid false positive diagnosis for muscle weakness, we hypothesize one older Portuguese man, with extreme lower values of height (1.53 m) and right leg LST_{DXA} (6700 g), who performed ${}_{knee\ extension}PT^{60º/s}$ of 130.0 Nm. If considered our absolute cut-off point (≤132.4 Nm), this person has “muscle weakness” confirmed. However, when considered the normalized $_{knee}$

$_{extension}PT^{60°/s}$/(right leg $LST^{0.48}$), the adjusted value (1.89 Nm/g) is above of the cut-off point (1.67 Nm/g; Table 2). For older people with large body sizes, normalizing strength would also prevent muscle weakness false negative diagnosis. Mistakenly classified cases of muscle weakness can impact on the financial resources of the healthcare and older adults care systems.

In conclusion, community-dwelling Portuguese older adults are stronger (women) and have better functional capacity (both sexes) compared to the Brazilian ones. Despite that, some foreign allometric exponents (Brazilian and North American) can be utilized to normalize knee extension strength of these Portuguese older adults, when this normalization strategy improves the accuracy to identify muscle weakness/functional limitation for both sexes. Normalizing muscle strength, even with foreign allometric exponents, is better than using it in an absolute form (non-normalized) to identify muscle weakness/functional limitation, against cases of false-positive diagnosis.

CAPÍTULO V

ESTUDO ORIGINAL IV - Normalizing Calf Circumference to identify low Skeletal Muscle Mass in Older Women: A Cross-sectional Study

Normalizing Calf Circumference to identify low Skeletal Muscle Mass in Older Women: A Cross-sectional Study

Pedro Pugliesi Abdalla[124], Ana Claudia Rossini Venturini[12], André Pereira dos Santos[12], Marcio Tasinafo[23], José Augusto Gonçalves Marini[23], Thiago Cândido Alves[2], Alcivandro de Sousa Oliveira[2], Jorge Mota[24], Gareth Stratton[5], Dalmo Roberto Lopes Machado[1234].

[1] College of Nursing of the University of Sao Paulo at Ribeirao Preto, Sao Paulo, Brazil

[2] Anthropometry, Training and Sport Study and Research Group (GEPEATE), University of Sao Paulo at Ribeirao Preto, SP, Brazil.

[3] School of Physical Education and Sport of Ribeirao Preto at the University of Sao Paulo at Ribeirao Preto, Sao Paulo, Brazil

[4] Center for Research in Physical Activity, Health and Leisure (CIAFEL), University of Porto, Porto, Portugal.

[5] School of Sport Science, Swansea University, Swansea, United Kingdom.

Publicado em Nutrition Hospitalaria (ISSN: 1699-5198; Fator de impacto: 1,057).

DOI: https://doi.org/10.20960/nh.03572

Nutr Hosp. 2021 Jul 29;38(4):729-735.

Abstract

Introduction: Functional limitation is a result of sarcopenia and is associated with loss of skeletal muscle mass (SMM). Cost-effective methods are important for identification of sarcopenia. Objective: to propose cut points for normalized calf circumference (CC) to identify low SMM in older women based on their functional limitation. Methods: in this descriptive and cross-sectional study, young female sample CC values (n=78) were used to establish the cut points (-2SD) of low SMM in older women (n=67). Functional limitation was identified by six-minute walk test (≤400m). CC was normalized by body mass, height and BMI. The diagnostic accuracy of CC was calculated with ROC curve, using functional limitation as standard. Results: Cut points and area under curve (AUC) were: CC (≤28.5; 0.62); CC·body mass^{-1} (≤0.40; 0.63); CC·height^{-2} (≤8.52; 0.55) and CC·BMI^{-1} (≤1.10; 0.73). Only the CC·BMI^{-1} achieved desirable accuracy (AUC>0.7) to distinguish functional limitation. Conclusion: The accuracy attained support the use of PP·IMC^{-1} to identify low SMM in older women. In clinical context is possible to predict the risk of sarcopenia when sophisticated methods for determining SMM are not available.

Keywords: aged; anthropometry; frail elderly; mobility disability; muscle mass

1. Introduction

Functional limitation caused by reduced mobility is an age-related phenomenon that negatively affects the physical independence of older adults (J. E. Morley et al., 2011). One of the main consequences of this limitation is sarcopenia, a disease characterized by low muscle strength and reduced amount of skeletal muscle mass (SMM) (Cruz-Jentoft et al., 2018). Sarcopenia affects 10 percent of older adults worldwide (Shafiee et al., 2017) and 60 percent of older women in Brazil (Diz et al., 2017). When untreated, sarcopenia exposes older adults to functional impairment, mobility disorders, increased risk of falls, loss of functional independence, physical frailty, increases of hospitalization, decreases quality of life and increases the risk of premature death (Mijnarends et al., 2018). Therefore, the early identification of the disease considerably reduces the economic impact on health systems and on the personal and social burdens of care for older adults (Abdalla, Dos Santos Carvalho, et al., 2020).

For diagnostic confirmation of sarcopenia, two conditions are required: reduced muscle strength and decreased SMM (Cruz-Jentoft et al., 2018). SMM parameters can be obtained from Dual-energy X-ray absorptiometry (DXA), Bioelectrical impedance analysis, Magnetic Resonance Imaging, Computed Tomography, Muscle Biopsy or Magnetic resonance Spectroscopy (Cruz-Jentoft et al., 2018). However, these require skilled health professionals, are high cost, and difficult to access in the context of the regular clinical practice, particularly in low and middle-income countries (dos Santos et al., 2018). Although the measurement of SMM by DXA is one of the most used procedures (Diz et al., 2017), these do not have a good relationship with reduced mobility that is associated with sarcopenia (Bhasin et al., 2020) and thus limited diagnostic validity (Bhasin et al., 2020). On the other hand, calf circumference (CC) is a cost effective and expedient alternative for estimating SMM, a clinically relevant outcome in community-dwelling older adults (Cruz-Jentoft et al., 2018; Pérez-Zepeda & Gutiérrez-Robledo, 2016).

Although the CC has a good association with mobility in older adults (Tsai et al., 2012), this relationship is characterized in an inverted U-shaped form (Pérez-Zepeda & Gutiérrez-Robledo, 2016). Normalizing the CC by body size as recommended will correct this non-linear relationship (Cruz-Jentoft et al., 2018). Normalization of SMM is already performed on selected DXA variables, such as the appendicular skeletal muscle mass (ASMM), usually corrected by relative to body size ($ASMM \cdot height^{-2}$, $ASMM \cdot body\ mass^{-1}$ or $ASMM \cdot BMI^{-1}$) (Kim et al., 2016). Unfortunately, these variables have weak associations with clinically relevant outcomes in older adults (Bhasin et al., 2020; Evans et al., 2019). Moreover, the identification of low SMM index ($ASMM \cdot height^{-2}$) includes the absolute value of CC (Chart 1) (Bahat et al., 2016; Barbosa-Silva et al., 2016; Bonnefoy et al., 2002; Kawakami et al., 2015; Kim et al., 2018; Kusaka et al., 2017; Landi et al., 2014; Pagotto et al., 2018; Rolland et al., 2003; L. S. Sampaio et al., 2017) for generating cut points, which will penalize older adults with smaller body size.

Chart I. Studies that proposed cut points to identify low skeletal muscle mass (SMM) by the calf circumference (CC), identified from the Receiver Operating Characteristic (ROC) curve analysis.

Authors	Origin of older adults	n	Dependent variable	Cut points (≤) of absolute CC (cm)	AUC	Sens. (%)	Spec. (%)
Pagotto et al. (2018) (Pagotto et al., 2018)	Brazilians	132	ASMM·height^{-2}	34 for men 33 for women	0.75 0.84	71 80	77 85
Kim et al. (2018) (Kim et al., 2018)	South koreans	657	ASMM·height^{-2}	35 for men 33 for women	0.81 0.72	92 83	59 50
Sampaio et al. (2017) (Sampaio et al., 2017)	Brazilians	316	Frailty(Fried et al., 2001)	32 for both sexes	0.67	54	73
Kusaka et al. (2017) (Kusaka et al., 2017)	Japanese women	116	Sarcopenia(Chen et al., 2014)	32.8 for women	0.79	73	80
Bahat et al. (2016) (Bahat et al., 2016)	Turks	406	SMM*·height^{-2}	33 for both sexes	- -	100 100	74 69
Kawakami et al. (2015) (Kawakami et al., 2015)	Japanese (40-89 years old)	526	Sarcopenia(Chen et al., 2014)	34 for men 33 for women	0.94 0.84	89 78	88 72
Barbosa-Silva et al. (2015) (Barbosa-Silva et al., 2016)	Brazilians	189	ASMM·height^{-2}	34 for men 33 for women	0.76 0.91	61 100	76 76
Rolland et al. (2003) (Rolland, Lauwers-Cances, et al., 2003)	French women	1458	ASMM·height^{-2}	31 for women	-	44	91
Bonnefoy et al. (2002) (Bonnefoy et al., 2002)	French	911	ASMM·height^{-2}	30.5 for both sexes	0.81 0.78	73 79	73 61

ASMM: appendicular skeletal muscle mass; SMM: Skeletal Muscle Mass; *calculated from the fat-free mass obtained by Bioelectrical impedance analysis; †Serum albumin<30g·l^{-1} or BMI<19 kg·m^{-2}; Sens.: Sensitivity; Spec: Specificity.

Given the limitations evident in quantifying SMM, the objective of this study was to propose cut points for CC normalized by body size to identify low SMM in older women with reference to functional limitation. Our hypothesis is that the normalization of the CC is a pragmatic indicator of functional limitation which in turn indicates a risk of sarcopenia. Therefore, the monitoring of functional limitation could alert to the degenerative consequences resulting from the ageing process in women at a public health level.

2. Materials and Methods

Participants and Settings (age, gender, country socioeconomic status and so on)

For this descriptive and cross-sectional study, a sample was comprised of two age groups from the same population who attended our laboratory between October 2016 and June 2017: The first group consisted of 79 young women aged between 18 and 30 years old (23.9 ± 3.4 years); and the second group 69 older women aged between 60 and 85 years old (69.8 ± 6.0 years). A sample size calculation was previously performed ($n= [ZySD/\varepsilon]^2$) from the maximum desired error ($\varepsilon \leq 1\%$), trust level (Zy=0,95) and population variability (SD). The main variable (CC) of the age group of women with greater variability obtained from a compatible population was adopted as a reference (SD=4.29 cm) (Bonnefoy et al., 2002). The minimum sample size was calculated (n=142).

The voluntary recruitment of participants took place through personal invitations, electronic and printed dissemination in the community. Young women met the following criteria: not taking antidepressants or stimulants that affect the central nervous system, self-declared to be in good health, not having amputated body parts, not performing more than 10 hours/week of physical training. Older women should be able to walk independently, not have uncontrolled chronic illnesses, acute infections, tumors, back pain, hip and knee prosthesis, unintentional weight loss of more than three kg in the last three months. Criteria for discontinuing the study, were reports of serious balance problems, and sequelae of stroke and cognitive impairment. All participants gave their full and informed consent to take part and the study was designed and conducted in accordance with the Declaration of Helsinki and was approved by the Institution's Ethics Committees (CAAE: 57511516.5.0000.5659 and 54345016.6.0000.5659).

Instruments and Procedures

All measurements were taken individually at University Hospital of Ribeirao Preto School of Medicine, University of Sao Paulo, Brazil (HC-FMRP-USP) in the morning from 9am to 11am). Data collection took place in a single session, by the same examiners trained in each measure. The older women cognitive deficit was verified by a questionnaire. Anthropometric measurements of height to the nearest 0.01 m, body weight (kg) were performed (T. Lohman et al., 1988) for all women and BMI was calculated (kg·m^{-2}). Other measures performed are descried below.

Cognitive assessment

To ensure the aptitude and cognitive capacity of older women, the Mini Mental State Examination (MMSE) was used in the reduced version of 19 points (Icaza & Albala, 1999). Participants who scored 12 or less were considered to have a cognitive deficit and were excluded from the analysis.

Anthropometric assessments

From the measurements of body mass in kg and height in cm, the body mass index (BMI; kg·m^{-2}) was determined. CC was measured according to a standardized procedure,(T. Lohman et al., 1988) with recording of the median from 3 measurements. For analyses, CC was considered as absolute (cm) and normalized: CC·body mass^{-1} in cm·kg^{-1}, CC·height^{-2} in cm·m^{-2} and CC·BMI^{-1} in cm·kg^{-1}·m^{-2}.

Six-minute walk test

To assess physical functional, the six-minute walk test was performed on a flat, non-slip surface, 30 meters in length with calibrated markings once every three meters. Older women were asked to walk as fast as possible for six minutes and were allowed to rest during the test without stopping the clock. Total distance covered was recorded to the nearest 3 meters. Functional limitation was identified when the walking distance was ≤400m (J. E. Morley et al., 2011).

Statistical analysis

Descriptive statistics included were central tendency and confidence interval (95% CI). The cut points were established for absolute or normalized CC considering -2 SD compared to the mean CC of young and healthy women, as recommended by the EWGSOP for SMM parameters (Cruz-Jentoft et al., 2018). The likelihood of different CC expressions to explain the occurrence of functional limitation was confirmed by logistic regression. Additionally, significance in statistical models were verified using chi-square (χ^2) and their coefficients of logistic regression. Finally, the ability of the CC to discriminate functional limitation was illustrated using area under the ROC curve (AUC) value >0.70 (Hosmer & Lemeshow, 2000). For this analyzes we adopted a dichotomous classification for the presence (1) or absence (0) of a functional limitation. All analyzes were performed on SPSS 25.0 and MedCalc 15.2, with a previously established level of significance (α=5%).

3. Results

Figure 1 shows the flowchart for recruiting study participants. One hundred and forty-eight women were initially eligible for studies. After applying the exclusion criteria, the analyzes were carried out with 145 women (78 young people).

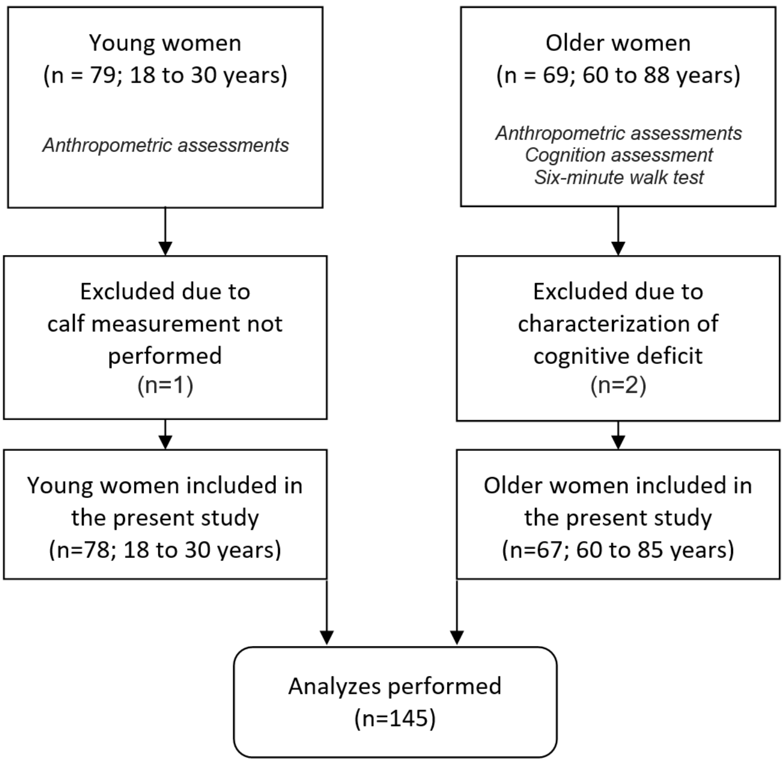


Figure 1. Flowchart of women recruited by age groups

Descriptive statistics of the MMSE score, chronological age, anthropometric variables, and walking distance are shown in Table 1. Older women were older, and had greater body mass, BMI and absolute CC. Younger women were taller (10 cm) and weighed less (6 kg) than their older counterparts. The higher BMI found in older (≅27kg·m^{-2}) compared to younger women (≅21 kg·m^{-2}) illustrates greater weight gain with age. Likewise, the highest normalized CC values observed in young women showed an inverse relationship with absolute CC according to age. From a functional perspective nearly two thirds of older women (39%; n=26), did not achieve a good functional score on the walk test.

Table 1. Descriptive analysis of young and older women, body measurements, cut points of the calf circumference (CC) absolute and normalized to identify low skeletal muscle mass (SMM) and functional performance of the older women

variables	unit	young women (n=78)					cut point (≤) of CC	older women (n=67)				
		mean	95% CI lower		95% CI upper	SD		mean	95% CI lower		95% CI upper	SD
MMSE score	(0-19)							17.4	17.0	to	17.8	1.7
Age	(years)	23.9	23.2	to	24.7	3.4		69.8	68.3	to	71.2	6.0
Body mass	(kg)	60.0	58.1	to	61.9	8.5		66.6	63.8	to	69.4	11.6
Height	(m)	1.7	1.6	to	1.7	0.1		1.6	1.5	to	1.6	0.1
BMI	(kg·m^{-2})	21.8	21.1	to	22.4	2.8		27.3	26.2	to	28.4	4.4
CC	(cm)	34.0	33.4	to	34.6	2.7	28.50	34.8	34.1	to	35.5	2.9
CC·body mass^{-1}	(cm·kg^{-1})	0.6	0.5	to	0.6	0.1	0.40	0.5	0.5	to	0.6	0.1
CC·height^{-2}	(cm·m^{-2})	12.2	11.8	to	12.6	1.8	8.52	11.3	12.0	to	11.7	1.4
CC·BMI^{-1}	(cm·kg^{-1}·m^{-2})	1.6	1.5	to	1.6	0.2	1.10	1.3	1.3	to	1.33	0.2
Walking distance§	(m)							413.6	391.1	to	436.1	92.2
Functional limitation¶	(*f*)							39%				

CI: confidence interval; SD: standard deviation; MMSE: Mini Mental State Examination; BMI: body mass index; CC: calf circumference; §: in the six-minute walk test; ¶: walking distance ≤400m.

Normalized CC cut points showed an inverse relationship with age when compared to absolute CC (Table 1). CC values normalized by body mass (0.40 cm·kg^{-1}), height squared (8.52 cm·m^{-2}) or BMI (1.10 cm·kg^{-1}·m^{-2}) also had different relationship for each age group. All mean CC values were within the 95% confidence threshold, which suggests high reliability even when replicated to other samples of the same population.

The accuracy of detecting a functional limitation using different CC expressions are shown in Table 2. The p-values of the regressions originating from CC normalized by body mass (p=0.027) and BMI (p=0.001) demonstrate the likelihood of significantly accounting for the occurrence of functional limitation. In fact, only the CC·BMI^{-1} presented an acceptable accuracy (AUC>0.70), as shown in Figure 2. There is statistical significance in the chi-quadratic distribution (Wald=8.72; p=0.001). From the beta exponent (b=0.002) of the variable CC·BMI^{-1} (Table 2), it was possible to calculate the likelihood of decreasing functional limitation (i.e., 0.002-1=-0.998). That is, for every increased tenth of unit (0.1 cm·kg^{-1}·m^{-2}) of CC·BMI^{-1}, there is a reduction in the chance of functional limitation by ≅10%. As example from our findings (Table 2), the mean CC·BMI^{-1} in young women (1.6 cm·kg^{-1}·m^{-2}) compared to older women (1.3 cm·kg^{-1}·m^{-2}) has a difference of 0.3 cm·kg^{-1}·m^{-2}. This represents a reduction in the chances of functional limitation for young women, by around 30%.

Table 2. Likelihood of the occurrence of a functional limitation* explained by logistic regression from the absolute and normalized calf circumference (CC)

variable					
dependent	**independent**	**χ^2**	***P-value***	**Wald**	**OR**
Dichotomous walking distance (1: ≤ 400m and 0: > 400m)	CC	2.79	0.095	2.56	1.166
	CC·body mass^{-1}	4.89	0.027	4.33	<0.001
	CC·height^{-2}	0.28	0.595	0.28	1.102
	CC·BMI^{-1}	10.77	0.001	8.72	0.002

*: walking distance ≤400m in six-minute walk test; BMI: body mass index; χ^2: chi-square; OR: odds ratio.

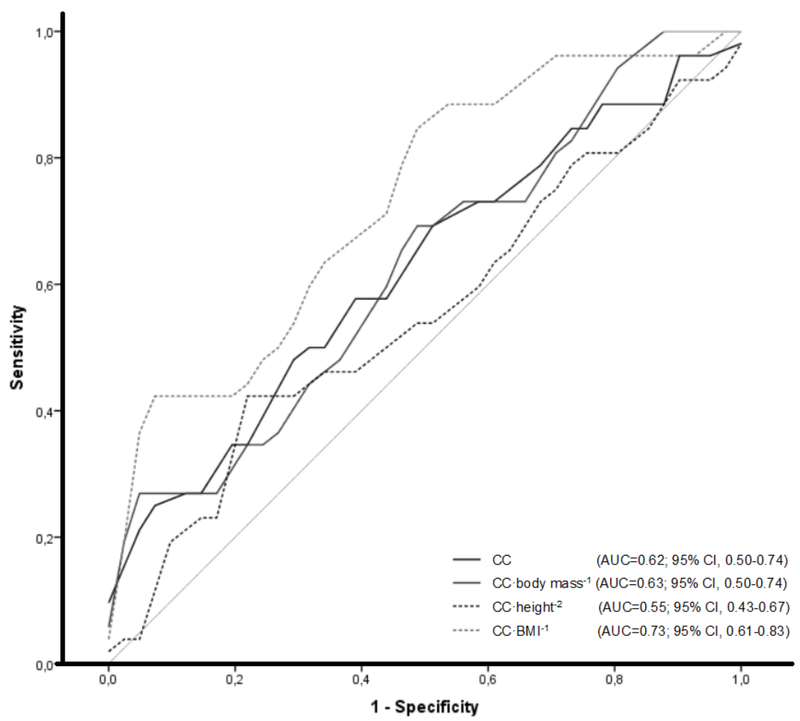


Figure 2. Accuracy of absolute and normalized calf circumference (CC) to detect functional limitation (≤400m in six-minute walk test) in older women, represented by the ROC curve and area under the curve (AUC)

Although the adjustment of CC by body mass (Table 2) was significant (χ^2=4.89; p=0.027), the extremely low odds ratio value (<0.001) did not sufficiently explain the occurrence of functional limitation. This finding was confirmed when the analysis of the ROC curve for CC·body mass^{-1} showed insufficient sensitivity (27%), specificity (98%) and AUC (0.63) values. On the other hand, the CC·BMI^{-1} cut point presented acceptable AUC (0.73), even though its sensitivity (85%) was greater than its specificity (54%).

After applying the cut point of the CC·BMI^{-1} (≤1.10 cm·kg^{-1}·m^{-2}) in our sample, about 12% of older women were classified with low SMM (n=7/60). Figure 3 further illustrates the relationship between CC and the mobility of older women, expressed by the distance covered in the six-minute walk test. It is possible to observe the inverted U-shaped relationship expressed by absolute CC (a) versus the resulting linearity when normalized by BMI (b).

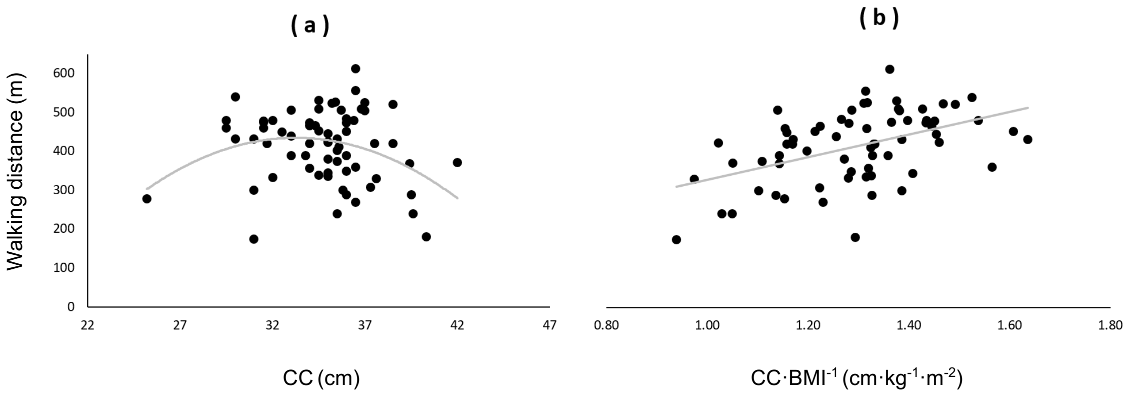


Figure 3. Comparison of the inverted U-shaped relationship (a) between absolute CC and mobility (six-minute walk test) with the linear (b) of the indicator proposed in this study (CC·BMI-1) in older women (n=67)

Our model (CC·BMI^{-1}), in addition to correcting the non-linear relationship between CC and mobility, showed a positive and significant correlation between adjusted CC and mobility (r=0.48; p<0.001).

4. Discussion

Our aim was to develop cut points for CC normalized by body size to identify low SMM in older women with reference to functional limitation. The cut points of the CC when normalized by body size were more effective than absolute CC in identifying low SMM in older women. The CC·body mass^{-1} and CC·BMI^{-1} explained ($p<0.05$) the likelihood of occurrence of functional limitation (walking ≤400m in six minutes). But only the CC normalized BMI (1.10 cm·kg^{-1}·m^{-2}) achieved acceptable sensitivity (85%) and accuracy (AUC>0.70)(Hosmer & Lemeshow, 2000) to identify low SMM associated with functional limitation. Furthermore, this model (CC·BMI^{-1}) was able to linearize the inverted U-shaped relationship usually observed in absolute CC expressions.

Absolute CC is accurate to estimate and identify low level of SMM in older women(Barbosa-Silva et al., 2016), however, when normalized by body size, particularly BMI(Cruz-Jentoft et al., 2018) avoid false negatives for functional limitation and sarcopenia. The absolute CC value below 27 cm alert to care-need for older women to perform their daily activities (Hsu et al., 2016). However, when the absolute CC is high (i.e.>38 cm) also predict the risk of impaired mobility,(Tsai et al., 2012) suggesting the need to create double cutoff points for the absolute CC (one for high values and another for low values), due a non-linear relationship between absolute CC and mobility (Tsai et al., 2012). This was confirmed in this study when all of our older women with elevated CC (>38 cm) have functional limitations (walking distance ≤400m), as seen in Figure 3a.

A multiple linear regression model proposed from NHANES data (Santos & Gonzalez, 2019), including CC measure in combination with sex, race and age, was able to predict up to 90% of ASMM measured by DXA. This approach could be adequate to identify SMM deficit in older women, were it not for its weak relationship with functional limitation (Bhasin et al., 2020). Absolute CC values could result in prediction errors (Figure 3a) over time, since higher CCs are generally related to overweight and obesity (BMI >25 kg·m^{-2}) characterizing a negative impact on functional performance (Tsai et al., 2012).

One of the strengths of the study involves the normalization of the CC that had not yet been proposed as a predictor of SMM, although it has long been recommended (Cruz-Jentoft et al., 2018). Another positive finding was that alternate to most studies that used ASMM·height^{-2} derived from DXA as an SMM indicator, our model was able to discriminate functional limitation using normalized CC, in an linear expression approach. The procedure to generate cut point at -2SD of mean of young women is a recommended method to parameters of SMM (Cruz-Jentoft et al., 2018). This study also has its limitations, for example sample was not random or stratified. Another limitation in terms of muscle function and quality, was not analyzed in present study. These limitations as well as other such as perceptual-motor factors affect the relationship between CC and performance, and thus can be aims for future studies. Nevertheless, the application of the model to other populations has an unconfirmed predictive validity and requires further development before being adopted into clinical practice.

One implications of our findings for clinical practice supports the use of normalized CC by BMI as a simple and inexpensive indicator for monitoring SMM losses associated with the functional capacity of older women. Another implication involves choosing variables that predict incident adverse health-related outcomes in older adults to identify potential sarcopenia by CC allowing intervention or prophylactic decisions to be made when monitoring the health of older women. Our CC·BMI^{-1} model classified 12% of older women with reduced SMM and 39% of older women as having functional limitation (walking ≤400m). The cut point at -2SD of mean CC·BMI^{-1} of young women (≤1.10 cm·kg^{-1}·m^{-2}) was lower than the cut point based on functional limitation (≤1.33 cm·kg^{-1}·m^{-2}) estimated by ROC curve (data not shown), which would classify older women with mobility problems. This corrects the distortion of overestimating the functional limitation (39%) of the actual classification of SMM deficit (12%), closer to the worldwide prevalence of sarcopenia (≅10%) (Shafiee et al., 2017) but still below the prevalence of Brazilian older women (≅20%) (Diz et al., 2017). But we emphasize that we did not consider muscle strength here, the first criterion for the diagnosis of sarcopenia; but only the second criterion (low SMM) (Cruz-Jentoft et al., 2018). May it should be recommendations for further researches.

In conclusion, our hypothesis of normalized CC helps to identify functional limitation as a prognostic tool to estimate the risk of sarcopenia, has been confirmed. Our findings support the use of the normalized CC by the BMI to identify low SMM as an expression of functional limitation in older women, without an inverted U-shaped relationship bias. Monitoring the functional limitations resulting from ageing in women may be feasible using this simple and inexpensive approach, particularly given the high prevalence of sarcopenia in older women in low to middle income countries. Its use can be a viable alternative in the clinical practice, when sophisticated methods for identifying low SMM associated with functional limitation are not available.

CAPÍTULO VI

DISCUSSÃO GERAL

Principais achados

A presente tese teve três objetivos específicos integrados. O primeiro, consistiu em propor expoentes alométricos para normalizar a força de membros superiores e inferiores pelo tamanho corporal e gerar pontos de corte para a fraqueza muscular de idosos. Assim, nos Estudos I e II, o tamanho corporal ajustado alometricamente tornou a força muscular independentemente do tamanho corporal. Logo, o risco de atribuir um diagnóstico falso-positivo/negativo à fraqueza muscular foi minimizado. Essa estratégia mostrou-se adequada para diferentes populações. Isso possibilita evitar intervenções desnecessárias para combater síndromes geriátricas, poupando os recursos escassos da saúde em países menos favorecidos economicamente (Gheorghe et al., 2018). O segundo objetivo específico, consistiu na aplicação dos expoentes alométricos (do Estudo I) para normalizar a força e identificar fraqueza muscular a uma amostra independente de idosos portugueses. Adicionalmente, sua efetividade foi comparada a outros modelos da literatura. Os achados mostraram que os expoentes alométricos, ainda que derivados de uma população estrangeira, melhoram a precisão para identificar fraqueza muscular e limitação funcional de idosos. O terceiro objetivo foi propor modelos de simples aplicação para identificar baixa massa muscular esquelética, baseada na limitação funcional para o risco de sarcopenia. A normalização do perímetro da panturrilha de idosas, retirou o viés da relação de U invertido com a mobilidade, sendo propostos os pontos de corte para baixa massa muscular esquelética. Dessa forma, essa simples estratégia antropométrica permite prever atempadamente o risco de sarcopenia em idosas. Intervir precocemente pode evitar o agravamento da doença de sarcopenia, aumentando as chances de ganho de força e massa muscular, contribuindo para melhor qualidade de vida no envelhecimento (Xie et al., 2020).

Limitações na definição consensual de sarcopenia

A discussão da metodologia conveniente para definição e identificação da sarcopenia é tema de relevante fundamentação desta tese. A sarcopenia, apesar de ter sido reconhecida como doença na Classificação Internacional de Doenças (CID) (Anker et al., 2016), ainda não tem uma definição unânime na literatura (Sanchez-Rodriguez et al., 2020). O termo “sarcopenia” foi criado por Irving Rosenberg em 1988 para descrever a redução de massa muscular relacionada ao envelhecimento, que estaria associada à mobilidade e independência de movimentos (Rosenberg, 1989). Posteriormente em 1998 (Baumgartner et al., 1998) e 2007 (Delmonico et al., 2007) estudiosos apontaram que a redução da massa muscular está mais bem associada com a redução de força muscular. Devido à importância da sarcopenia como fator determinante na prevenção de resultados adversos à saúde, o interesse em melhor compreender esse fenômeno, aumentou (Sanchez-Rodriguez et al., 2020).

Ainda não há uma definição unânime, critérios de diagnósticos uniformes e *guidelines* de tratamentos para sarcopenia, universalmente aceitos (Sanchez-Rodriguez et al., 2020). As tentativas dos consensos nessa direção a partir de 2010 com o *European Society for Clinical Nutrition and Metabolism* (ESPEN) (Muscaritoli et al., 2010); em 2011 com o *International Working Group on Sarcopenia* (IWGS) por Fielding e colaboradores (Fielding et al., 2011) e a *Society of Sarcopenia, Cachexia and Wasting Disorders* (SCWD) de Morley e colegas (Morley et al., 2011). O consenso da *European Union* (EU) *Geriatric Medicine Society* (EuGMS) em conjunto com a ESPEN, foi denominado de *European Working Group on Sarcopenia in Older People* (EWGSOP) (Cruz-Jentoft et al., 2010), mais adiante replicado para população asiática do *Asian Working Group for Sarcopenia* (AWGS) (Chen et al., 2014). Tempos depois a houve o consenso proposto pelo *Foundation for the National Institutes of Health* (FNIH) (Dam et al., 2014) que trazia alteração dos valores de de pontos de corte para o diagnóstico. Após 10 anos da sua proposta original, o EWGSOP se reuniu para criar o EWGSOP2, endossado pelo *International Osteoporosis Foundation*, o *European Society for Clinical and Economic Aspects of Osteoporosis,* *Osteoarthritis and Musculoskeletal Diseases* (ESCEO) para o ESPEN e o EuGMS (Cruz-Jentoft et al., 2018), que motivou a atualização do AWGS (Chen et al., 2020). Todos, até então, entendiam que a massa muscular era critério necessário para identificar a sarcopenia. Mesmo que o EWGSOP2 tenha a estabelecido como segundo critério a ser considerado (sendo a força muscular como o primeiro), ainda era essencial para a identificação da doença. Mais recentemente, o grupo FNIH e o *National Institute on Aging* (NIA) criou o *Sarcopenia Definition and Outcomes Consortium* (SDOC) (Bhasin et al., 2020), que propôs temporariamente excluir a baixa massa muscular do consenso de sarcopenia. Isso foi decidido por especialistas do SDOC uma vez que a massa muscular apendicular derivada da DXA (mais utilizada e recomendada por outros consensos) não ter associação suficiente com eventos adversos do envelhecimento (limitação de mobilidade, fraturas, mortalidade e quedas). Portanto, não justificaria ser incluída na definição de sarcopenia. Vale destacar que a DXA faz varredura dos componentes corporais no nível molecular (WANG et al., 2002) e, portanto, parece haver alguma confusão conceitual do que efetivamente está a medir. Da mesma forma que lipídeos contém gordura, mas não a representa quantitativamente, tecido mole magro contém massa muscular, mas ambas estruturas não devem ser confundidas. Não haverá aqui aprofundamento do tema neste momento, mas a abordagem metodológica deveria ser uma discussão pertinente no estabelecimento de critérios para definição da sarcopenia.

Uma vez que a sarcopenia tem um laço histórico com o aspecto morfológico do tecido muscular, o grupo SDOC lembrou de alternativas metodológicas que no futuro podem ser parâmetros referenciais de boa representatividade da massa muscular. Um exemplo é o teste de diluição de creatina marcada com deutério [creatina D_3]), que mostra uma associação mais significativa com a massa muscular. Quando comparada a métodos de referência (ressonância magnética e tomografia computadorizada) e funcionalidade de idosos, demonstra maiores coeficientes de correlação do que com as medidas da DXA (Evans et al., 2019). Contudo o método da creatina D_3 ainda tem custo elevado limitando sua aplicação na prática clínica. Nesse sentido, pensando em redução de custos, facilidade de aplicação, eficácia de indicadores da baixa massa muscular associados à funcionalidade de idosas, propusemos pontos de corte para identificar risco de sarcopenia a partir do perímetro da panturrilha, normalizado pelo índice de massa corporal (P. P. Abdalla et al., 2021).

Ainda sobre a definição conceitual de sarcopenia, evidências anteriores colocaram em dúvida a relação da redução da massa muscular de forma associada à redução da força muscular no envelhecimento (Clark & Manini, 2008). Esses investigadores tratam do termo “sarcopenia” como uma “banana verde” (uma possível aposta errônea em utilizar essa nomenclatura ou não para o futuro). A ideia dos autores foi dissociar a redução da força muscular da definição de sarcopenia. Ou seja, o conceito de sarcopenia se manteria como o proposto por Irwin Rosenberg, tão somente como redução morfológica. A redução da força seria tratada distintivamente, como dinapenia (Clark & Manini, 2012; Manini & Clark, 2011). Sustentam essa ideia, uma vez que a redução da massa muscular pode explicar menos de 5% da redução da força muscular (Hughess et al., 2001). Logo, a diminuição da força muscular não é explicada exclusivamente pela morfologia e arquitetura da massa muscular, mas sim por fatores neurais (impulso excitatório dos centros supraespinhais, excitabilidade do motoneurônio, atividade muscular antagônica, recrutamento de unidades motoras e codificação de taxa, transmissão neuromuscular e processos de acoplamento E-C) e de alteração nas propriedades de contração muscular (Clark & Manini, 2008).

Portanto, ainda é necessária uma iniciativa nos consensos internacionais para discussão e aprofundamento das ideias e conceitos, a uniformizar as definições de sarcopenia e proposituras de metodologias mais adequadas, quer para sua caracterização (Sanchez-Rodriguez et al., 2020), quer para seu tratamento. Um contributo desta tese nessa questão, impõe-se que a força muscular seria mais bem interpretada, caso fosse concebida sem o viés do tamanho corporal, mediante a estratégia de ajustamento/normalização alométrica.

Diferentes formas de gerar e interpretar os expoentes alométricos

A forma de gerar, comparar ou mesmo de unificar os expoentes alométricos é um tema que julgamos relevante para discussões futuras. Tanto quanto a conceituação da sarcopenia, acreditamos que uma padronização de uso dos expoentes alométricos seria relevante e necessária.

Em síntese, existem duas formas de **gerar** os modelos alométricos; outras duas maneiras de **comparar** os modelos alométricos; e ainda uma forma para **unificar** expoentes entre diferentes grupos, ou quando estes apresentam interação significativa.

As duas formas para **gerar** os expoentes são:

1ª) considerando somente a relação existente entre a variável dependente (i.e., força muscular) e independente (i.e., tamanho corporal); resultando em um expoente específico dessa relação;

Ou ainda,

2ª) a mesma relação entre variáveis que a anterior, porém incluindo outras características (covariáveis independentes: sexo, idade, nível de atividade física, atletas ou não-atletas, doentes ou não-doentes etc.); o que pode resultar em um expoente único para todas essas características (covariáveis).

Em ambas, o procedimento para geração dos expoentes alométricos é o mesmo: A variável dependente e a independente são convertidas em seu logaritmo natural (ln), seguidas da regressão linear simples:

$$\ln Y = \ln(a) + \ln(X) * b \quad \text{(Equação 4)}$$

> Onde Y é a variável dependente; X a variável independente; b é o expoente alométrico ou expoente da relação de potência entre variáveis (coeficiente alométrico); e “a” é uma constante.

Portanto, a única diferença da primeira é que na segunda forma, os expoentes gerados incluem as covariáveis, como idade, dimensões corporais (em unidades contínuas) ou características dicotômicas, como sexo (mulheres=0, homens=1) e nível de atividade física (inativo=0; ativo=1). Cada covariável também é incluída na regressão, acrescida de uma variável de interação, ou seja, multiplicação entre as covariáveis (i.e., ln variável independente*idade*sexo*nível de atividade física).

Caso essa interação apresente significância estatística, seria necessário realizar regressões independentes para gerar os expoentes alométricos correspondentes para cada condição/característica (i.e., um expoente para atletas e outro para sedentários; um expoente para homens e outro para mulheres, e assim por diante). Contudo, se a interação não apresenta significância estatística, a regressão deve ser repetida, mas desta vez sem a "variável" de interação. Abaixo (Quadro 1) está um exemplo da primeira regressão (sem significância estatística da interação), e em seguida a segunda regressão, onde o beta representa o expoente alométrico gerado ($^{b=0,24}$).

Quadro 1. Resultado de regressões sem interação significativa, a considerar exemplo de variável dependente força de preensão manual na segunda forma de gerar expoente alométrico (destacado: $^{b=0,24}$).

Regressão 1				
Variável independente	**Coeficientes da regressão**	***p***	**IC 95%**	
	β		Inferior a superior	
Constante	1.85	<0.001	1.56	2.15
ln massa corporal (kg)	0.27	<0.001	0.19	0.34
sexo (0=mulher; homen=1)	0.50	0.450	0.25	0.60
Interação: ln massa corporal*sexo	0.11	0.456	0.10	0.11
Regressão 2				
Variável independente	**Coeficientes da regressão**	***p***	**IC 95%**	
	β		Inferior a superior	
Constante	1.89	<0.001	1.59	2.20
ln massa corporal (kg)	$\boxed{0.24}$	<0.001	0.17	0.32
sexo (0=mulher; homen=1)	0.55	0.500	0.30	0.65

Assim, teoricamente, a força muscular padronizada pelo tamanho corporal, elevada a um expoente alométrico (no exemplo $^{b=0,24}$ do Quadro 1), permitiria comparações entre características muito distintas (sendo o mesmo expoente para todos os sujeitos). Seria possível, por exemplo, comparar a força de uma mulher mais velha e inativa com a força de um homem mais jovem e fisicamente ativo. Tal é o poder da sensibilidade da alometria.

Há exemplos na literatura dessas formas de geração de expoentes alométricos, tanto da primeira forma (Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020; Külkamp et al., 2020) como da segunda (P. P. Abdalla, L. Bohn, et al., 2021; Maranhão Neto et al., 2017).

Cada forma de **comparar** a variável dependente entre sujeitos de diferentes características/grupos, depende da forma como os expoentes foram gerados. Na primeira forma, são criados expoentes específicos para cada grupo. Como exemplo, citamos um estudo que comparou a força muscular de judocas atletas e praticantes recreacionais (Külkamp et al., 2020). Os autores propuseram valores específicos de expoentes alométricos para o grupo de atletas ($^{b=0.68}$) e para o grupo de praticantes recreacionais ($^{b=0.56}$). Vale ressaltar que a comparação entre sujeitos de diferentes grupos só é possível se o índice de cada indivíduo for considerado com base na média de seu próprio grupo (índice percentual) (Külkamp et al., 2020), expresso da seguinte forma:

$$\text{índice percentual de força} = \left(\frac{\left(\frac{\text{força individual}}{\text{massa corporal}^{\text{b}}}\right)}{\left(\frac{\text{força média do grupo}}{\text{massa corporal média do grupo}^{\text{b}}}\right)} - 1\right) \text{x } 100$$

(Equação 5)

Nesse exemplo (Külkamp et al., 2020), a força de preensão manual individual foi ajustada alometricamente pela média da massa corporal de cada grupo (atletas e praticantes recreacionais). Para além da massa corporal individual, foi possível comparar a força de um atleta (i.e., força: 60 kg; massa corporal: 75 kg; força ajustada pela massa corporal média do grupo: 3,086) com força de um praticante recreacional (força: 45 kg; massa corporal: 70 kg; força ajustada pela massa corporal média do grupo: 4,794).

Os cálculos para estimar a força desse atleta, podem ser expressos por:

$$\text{índice percentual de força do atleta} = \left(\frac{\left(\frac{60}{75^{0,68}}\right)}{3{,}086} - 1\right) \text{x } 100 \therefore = 3{,}2$$

(Equação 6)

E para o praticante recreacional, seria:

$$\text{índice percentual de força do prat. recreacional} = \left(\frac{\left(\frac{45}{70^{0,56}}\right)}{4{,}794} - 1\right) \text{x } 100 \therefore = -13{,}0$$

(Equação 7)

Por fim, se conclui que uma vez isolada a influência do tamanho corporal (massa corporal), o índice percentual de força do atleta (3,21) é comparativamente maior do que o praticante recreacional (-13,0). Se for utilizada a classificação proposta por Külkamp et al. (2020) para o índice percentual de força: ≤-15 (inferior); entre -15 e 0 (média inferior); entre 0 e 15 (media-superior) e ≥15 (superior), o atleta e o praticante recreacional apresentaram forças médias-superior e inferior, respectivamente.

A comparação é mais simples, caso seja utilizada a segunda forma, de gerar o expoente (único para todo o grupo). A interação não é significativa, permitindo geração de um expoente único aplicável a diferentes grupos. Nesse mesmo exemplo com judocas, caso a interação não fosse significativa, um único expoente seria gerado para a amostra total ($^{b=0,64}$). Os sujeitos seriam comparados sem a necessidade do índice percentual ou valores normativos. O cálculo então seria:

$$\text{força alometricamente ajustada} = \frac{\text{força individual}}{\text{massa corporal individual}^{\text{b}}}$$

(Equação 8)

Utilizando os mesmos valores individuais do exemplo anterior, a força do atleta seria:

$$\text{força alometricamente ajustada do atleta} = \frac{60}{75^{0,64}} \therefore = 3{,}79$$

(Equação 9)

E a do praticante recreacional seria:

$$\text{força alometricamente ajustada do praticante recreacional} = \frac{45}{70^{0,64}} \therefore = 2{,}97$$

(Equação 10)

Portanto, após ajustar alometricamente a força, o atleta apresenta maior força (3,79) se comparado ao praticante recreacional (2,97).

Quando a interação for significativa (na segunda forma) ou quando o expoente foi gerado pela primeira forma (expoentes específicos para cada condição), para comparação entre dois grupos distintos, uma opção facilitada seria a **unificação** dos expoentes alométricos. Tal procedimento consiste em trocar os expoentes entre dois grupos e calcular o coeficiente de correlação produto-momento entre a variável dependente (i.e., força) ajustada pela variável independente (i.e., massa corporal) (Vanderburgh et al., 1995). Caso os valores de correlação sejam próximos de zero, existe a possibilidade de proposição de expoente único para os dois grupos (Vanderburgh et al., 1995). A partir do exemplo anterior entre judocas atletas e recreacionais simulamos o processo de unificação do expoente alométrico que obteve êxito (r≅0,0) no Quadro 2.

Quadro 2. Procedimentos para unificação de expoentes alométricos.

1º: troca dos expoentes								
	Grupo de atletas				**Grupo de praticantes recreacionais**			
Indivíduo	*Força (kg)*	*Massa corporal (kg)*	*Ajuste com expoente original*	*Ajuste com expoente trocado*	*Força (kg)*	*Massa corporal (kg)*	*Ajuste com expoente original*	*Ajuste com expoente trocado*
1	60	75	$60/75^{0,68}$	$60/75^{0,56}$ = 5,35	45	70	$40/70^{0,56}$	$40/70^{0,68}$ = 2,50
2	55	72	$55/72^{0,68}$	$55/72^{0,56}$ = 5,01	30	65	$30/65^{0,56}$	$30/65^{0,68}$ = 1,76
3	57	73	$57/73^{0,68}$	$57/73^{0,56}$ = 5,16	22	60	$22/60^{0,56}$	$22/60^{0,68}$ = 1,36
.	.	.	.	. . .	.	.	.	. . .
.	.	.	.	. . .	.	.	.	. . .
.	.	.	.	. . .	.	.	.	. . .
k	Y	X	$Y/X^{b\ atleta}$	$Y/X^{b\ prat.\ recr.}$	Y	X	$Y/X^{b\ prat.\ recr.}$	$Y/X^{b\ atleta}$
2º: cáculo do coeficiente de correlação								
1		75		5,35		70		2,50
2		72		5,01		65		1,76
3		73		5,16		60		1,36
.		.		.		.		.
.		.		.		.		.
.		.		.		.		.
k		X		$Y/X^{b\ prat.\ recr.}$		X		$Y/X^{b\ atleta}$
			r = 0,01				r = -0,02	

Dessa forma, é possível utilizar, por exemplo, somente o expoente ^{0,56}, normalizar a força de ambos os grupos e comparar os sujeitos entre os diferentes grupos.

Portanto, não há ainda na literatura uma forma padronizada para gerar os expoentes e nem para unificá-los no caso de comparar sujeitos de diferentes grupos. As duas formas apresentadas para gerar expoentes alométricos precisariam ser comparadas em futuros estudos para prever variáveis importantes longitudinalmente (quedas, hospitalização, mortalidade) para decidir qual a melhor. A previsibilidade dessas ocorrências importantes para saúde de idosos também precisa ser testada com a unificação dos expoentes alométricos para diferentes grupos. Isso poderia explicar se os ajustes com expoentes únicos se relacionam mais com esses desfechos ou se expoentes específicos por grupo são mais precisos nessa previsibilidade.

Variabilidade dos expoentes alométricos propostos para normalizar a força muscular: uma relação aos achados da literatura

Expoentes alométricos para normalizar diferentes expressões da força muscular pela massa corporal ou estatura foram propostos na literatura (P. P. Abdalla, L. Bohn, et al., 2021; Abdalla, Carvalho, Santos, Venturini, Alves, Mota, Oliveira, et al., 2020; Davies & Dalsky, 1997; Foley et al., 1999; Maranhão Neto et al., 2017; Y.-H. Pua, 2006). No Quadro 3, são exibidos exemplos encontrados para normalização da força de membros superiores e inferiores, medida nos testes de força de preensão manual, 1RM de extensão de joelho e o pico de torque a 60º/s da extensão de joelho normalizados por estatura ou massa corporal.

Quadro 3. Diferentes expoentes alométricos das variáveis de massa corporal e estatura para normalizar força de preensão manual, 1RM e pico de torque da extensão de joelho com respectivos Intervalos de Confiança (IC-95%).

Variável	Autor	Expoente alométrico	IC-95%
Força de preensão manual			
Massa corporal	Maranhao Neto et al. (2017)	0,33	0,14 a 0,48
	Foley et al., (1999)	0,40	0,26 a 0,78
	Pua (2006)	0,63	0,31 a 0,91
	Abdalla et al. (2021)	0,22	-0,02 a 0,46
	Estudo Oritinal II	0,19 a 0,61	-
	Nevill et al. (2022)	0,58	0,53 a 0,62
Estatura	Maranhao Neto et al. (2017)	1,84	1,23 a 2,45
	Abdalla et al. (2021)	1,86	0,90 a 2,85
	Estudo Oritinal II	1,46 a 2,45	-

Variável	Autor	Expoente alométrico	IC-95%
	Nevill et al. (2022)	1,75	
1RM da extensão de joelho			
Massa corporal	Abdalla et al. (2020)	0,70 ou 0,96	0,11 a 1,28 ou 0,28 a 1,64
	Abdalla et al. (2021)	0,44	0,01 a 0,87
Estatura	Abdalla et al. (2021)	3,05	1,27 a 4,83
Pico de torque à 60º/s da extensão de joelho			
Massa corporal	Abdalla et al. (2021)	0,37	-0,08 a 0,814
	Davies & Dalsky (1997)	0,67 ou 0,72 ou 0,74	-
Estatura	Abdalla et al. (2021)	3,27	1,47 a 5,07

Outras variáveis são encontradas na literatura para normalizar força muscular a partir desses mesmos testes, como por exemplo, multiplicação do peso pela estatura (Segal et al., 2008), área de superfície corporal (P. P. Abdalla, L. Bohn, et al., 2021), espessura muscular por ultrassonografia (Radaelli et al., 2013), dentre outros. Contudo, essas propostas não encontram grande reprodutibilidade na literatura como a estatura e a massa corporal, que lhes atribua um caráter de análise comparativa.

Dos expoentes alométricos encontrados na literatura para ajustar a força muscular, nota-se que há sempre uma relação alométrica (curvilínea) entre força muscular (independente do teste realizado) e a massa corporal (Quadro 3), quando os expoentes variam entre 0,33 e 0,96. Essa relação não linear pode ser observada na Figura 1a do Capítulo III. Por outro lado, para a estatura, também independente do teste de força abordado, a relação mais observável entre a força e a estatura é linear (Quadro 1), quando os expoentes variaram de 1,46 a 3,27). A Figura 1b do Capítulo III retrata essa relação linear. Recentemente, Nevill et al. (2022) confirmaram a relação linear entre estatura e a força de preensão manual utilizando dados de 8690 pessoas do *National Health and Nutrition Examination Survey* (NHANES). Devido o expoente encontrado (1,752) ser próximo da relação quadrática, os autores sugeriram ajustar a força de preensão manual por estatura^2 (em metros). Os autores também confirmaram a relação não linear entre massa corporal e a força de preensão manual (com expoente de 0,577), confirmando a necessidade da alometria para ajustar a força pela massa corporal.

Pontos fortes

Propusemos pontos de corte para identificar fraqueza muscular em idosos com o dinamômetro isocinético (padrão ouro para avaliar força de membros inferiores). Adicionalmente, pontos de corte de 1RM de extensão de joelhos e força de preensão manual foram validados (P. P. Abdalla, L. Bohn, et al., 2021). Diversas variáveis (n = 49) foram utilizadas para normalizar a força muscular e algumas também foram validadas para uma amostra portuguesa. Além disso, independentemente do teste de força, a fraqueza muscular foi identificada com precisão suficiente (AUC> 0,70) tanto no contexto acadêmico da investigação científica (dinamômetro isocinético), como clínico da prática de campo (1RM e força de preensão manual). A validade da força de preensão manual normalizada pela massa corporal e estatura foi ampliada para seis países subdesenvolvidos. Houve amplitude etária e diversidade étnica e cerca de 9% dos idosos tinham mais de 85 anos, chegando alguns a 114 anos. Adicionalmente, houve casos de baixo peso (16%) ou de obesidade (5%). Assim nossos modelos se mostraram aplicáveis a pessoas de diferentes nacionalidades, idades e estados nutricionais.

Outro contributo considerado como ponto forte do presente estudo, foi a proposição do perímetro da panturrilha normalizado pelo tamanho corporal que ainda não havia sido proposta como alternativa para estimar a massa muscular esquelética na identificação ao risco de sarcopenia (Estudo Original IV). Muito embora essa normalização tenha sido previamente recomendada pelo EWGSOP (Cruz-Jentoft et al., 2018).

Pontos fracos

Como limitações de nossos achados, identificamos ao menos duas questões principais: a ampla variabilidade de formas para gerar e interpretar os expoentes alométricos para normalização da força muscular, deixa dúvidas de qual o melhor método a ser utilizado. Não conseguimos no presente estudo realizar uma comparação metodológica para elucidar essa questão. Outra questão envolve a variedade de consensos para identificação de sarcopenia, que dificultam comparações de estudos conduzidos sob diferentes critérios. Não conseguimos também indicar qual o melhor referencial (consenso) a ser seguido. Os idosos do sexo masculino também foram minoria em nossos estudos, tal como usualmente ocorre nos estudos dessa natureza. Além disso, o caráter transversal dos nossos quatro estudos limita a completa compreensão das relações entre força e massa muscular com o tamanho corporal durante o processo de envelhecimento. Estudos longitudinais futuros com maior equilíbrio entre os sexos, a partir de amostras representativas devem esclarecer melhor essas associações.

Aplicabilidade para área acadêmica e prática clínica

No que se refere à aplicabilidade para área acadêmica e prática clínica, foi encontrada maior precisão (AUC) para se prever limitações de mobilidade/fraqueza muscular com a força normalizada de membros inferiores (dinamômetro isocinético e cadeira extensora) do que o método geralmente adotado para estimativa da força de membros superiores (dinamômetro de preensão manual) para esse fim (Cruz-Jentoft et al., 2018). No entanto, o dinamômetro isocinético tem custo mais elevado e, portanto, mais disponível no contexto investigativo dos laboratórios. Desse modo, nossos modelos normalizados de força de preensão manual e de 1RM da extensão de joelho também são aplicáveis na prática clínica. Uma vez que os instrumentos dessas medidas (dinamômetros manuais e a cadeira extensora) seriam mais disponíveis em ambientes geriátricos para intervir na fraqueza muscular relacionada ao envelhecimento (Cruz-Jentoft et al., 2014).

Os expoentes alométricos que propusemos para os seis países de baixa e média renda (África do Sul, China, Ghana, Índia, México e Rússia) podem ser facilmente usados para normalizar a força de preensão em idosos nos estudos epidemiológicos, por se tratar de recursos automatizados (http://posgraduacao.eerp.usp.br/files/Routine_Models_Men_and_Women_HGS.xlsx). Adicionalmente, envolvem medidas simples com certa frequência em idosos (massa corporal e estatura). Se forem utilizados os critérios referenciais do EWGSOP2 em países de baixa e média renda, uma parcela significativa de sujeitos seriam classificados como falso positivos, uma vez que foram derivados a partir de dados de países de alta renda (Dodds et al., 2016). A estratégia de normalização da força muscular torna-se importante em países em desenvolvimento, muito embora esse tema ainda seja inscipiente na literatura, inviabilizando uma discussão mais enriquecedora. O fato importante é que a alocação incorreta para o tratamento de síndromes geriátricas pode ser evitada com um controle simples e apropriado, do mero controlo de viés que envolve o tamanho corporal.

CAPÍTULO VII

CONCLUSÕES

Foram propostos expoentes alométricos para normalizar o desempenho em diferentes testes de força muscular pelo tamanho corporal. Ainda é preciso testar uma generalização dos expoentes alométricos dos mesmos testes (força de preensão manual, extensão de joelho a partir de teste de 1RM e isocinético) e variáveis de tamanho corporal utilizadas para normalização de diferentes amostras populacionais. Nesse sentido, avançamos com a aplicação dos expoentes brasileiros em amostra portuguesa com aceitável efetividade. Não houve decréscimo da capacidade de acurácia para identificar limitação funcional após normalizar a variável da força muscular pelo tamanho corporal. Adicionalmente houve melhora da previsibilidade da funcionalidade. Também verificamos que expoentes genéricos podem ser utilizados, desde que a população estudada esteja dentro do intervalo de confiança. Normalizar a força (^{b}) tornou-a independente do tamanho do corporal, implicando em menores vieses na baixa força muscular de idosos com tamanhos corporais extremos. Nesse sentido é preciso realizar mais testes entre amostras com diferentes perfis antropométricos, econômicos e genéticos, na tentativa de testar modelos generalistas, mais abrangentes, independente de características populacionais.

Em suma, a partir dos desígnios gerais desta tese, foram propostos referenciais da força e da massa muscular de idosos, normalizados pelo tamanho corporal para identificar o risco de sarcopenia. Os modelos de normalização da força para identificar fraqueza muscular, independentemente da amostra utilizada para gerá-los, mostraram potencial de serem replicáveis a outras populações. A normalização é uma estratégia simples, viável e de baixo custo pois envolve medidas de tamanho corporal facilmente obtidas, amplamente conhecidas e utilizadas pelos profissionais da saúde. Além disso, o link com planilhas automatizada foi disponibilizado (APÊNDICE A), para rapidamente classificar os idosos com baixa força muscular, sem a preocupação com cálculos e números exponenciais. A estratégia alométrica proposta evita erros na classificação da baixa força muscular de idosos, decorrentes do viés causado pelo tamanho corporal. Isso deve reduzir consideravelmente as chances de diagnósticos de casos falso positivos e negativos de sarcopenia em idosos com valores extremos nas dimensões corporais.

REFERÊNCIAS

Abdalla, P. P., Bohn, L., da Silva, L. S. L., dos Santos, A. P., Tasinafo Junior, M. F., Venturini, A. C. R., Carvalho, A. d. S., Gomez, D. M., Mota, J., & Machado, D. R. L. (2021). Identification of muscle weakness in older adults from normalized lower and upper limbs strength. *MedRxiv*, 2021.2007.2028.21261230. https://doi.org/10.1101/2021.07.28.21261230

Abdalla, P. P., Bohn, L., da Silva, L. S. L., Dos Santos, A. P., Tasinafo Junior, M. F., Venturini, A. C. R., Dos Santos Carvalho, A., Gomez, D. M., Mota, J., & Machado, D. R. L. (2021). Identification of muscle weakness in older adults from normalized upper and lower limbs strength: a cross-sectional study. *BMC sports science, medicine & rehabilitation*, *13*(1), 161. https://doi.org/10.1186/s13102-021-00390-1

Abdalla, P. P., Carvalho, A. S., Santos, A. P., Venturini, A. C. R., Alves, T. C., Mota, J., & Machado, D. R. L. (2020). One-repetition submaximal protocol to measure knee extensor muscle strength among older adults with and without sarcopenia: a validation study. *BMC Sports Science, Medicine and Rehabilitation*, *12*(1), 29. https://doi.org/10.1186/s13102-020-00178-9

Abdalla, P. P., Carvalho, A. S., Santos, A. P., Venturini, A. C. R., Alves, T. C., Mota, J., Oliveira, A. S., Ramos, N. C., Marini, J. A. G., & Machado, D. R. L. (2020). Cut-off points of knee extension strength allometrically adjusted to identify sarcopenia risk in older adults: A cross-sectional study. *Arch Gerontol Geriatr*, *89*, 104100. https://doi.org/10.1016/j.archger.2020.104100

Abdalla, P. P., Dos Santos Carvalho, A., Dos Santos, A. P., Venturini, A. C. R., Alves, T. C., Mota, J., de Sousa Oliveira, A., Ramos, N. C., Marini, J. A. G., & Machado, D. R. L. (2020). Cut-off points of knee extension strength allometrically adjusted to identify sarcopenia risk in older adults: A cross-sectional study. *Arch Gerontol Geriatr*, *89*, 104100. https://doi.org/10.1016/j.archger.2020.104100

Abdalla, P. P., Venturini, A. C. R., Santos, A. P. D., Tasinafo, M., Marini, J. A. G., Alves, T. C., de Sousa Oliveira, A., Mota, J., Stratton, G., & Machado, D. R. L. (2021). Normalizing calf circumference to identify low skeletal muscle mass in older women: a cross-sectional study. *Nutr Hosp*, *38*(4), 7. https://doi.org/10.20960/nh.03572 (Normalización de la circunferencia de la pantorrilla para identificar la masa muscular esquelética baja en las mujeres mayores: un estudio transversal.)

Abe, T., Nahar, V. K., Young, K. C., Patterson, K. M., Stover, C. D., Lajza, D. G., Tribby, A. C., Geddam, D. A., Ford, M. A., Bass, M. A., & Loftin, M. (2014). Skeletal muscle mass, bone mineral density, and walking performance in masters cyclists. *Rejuvenation research*, *17*(3), 291-296. https://doi.org/10.1089/rej.2013.1538

Abernethy, B., Mackinnon, L., Neal, R., Kippers, V., & Hanrahan, S. (1996). *Biophysical foundations of human movement*. Macmillan.

Agarwala, P., & Salzman, S. H. (2020). Six-Minute Walk Test: Clinical Role, Technique, Coding, and Reimbursement. *Chest*, *157*(3), 603-611. https://doi.org/10.1016/j.chest.2019.10.014

Akpinar, T. S., Tayfur, M., Tufan, F., Sahinkaya, T., Kose, M., Ozsenel, E. B., Bahat Ozturk, G., Saka, B., Erten, N., Yildiz, S., & Karan, M. A. (2014). Uncomplicated diabetes does not accelerate age-related sarcopenia. *Aging Male*, *17*(4), 205-210. https://doi.org/10.3109/13685538.2014.963040

Albrecht, B. M., Stalling, I., & Bammann, K. (2021). Sex- and age-specific normative values for handgrip strength and components of the Senior Fitness Test in community-dwelling older adults aged 65-75 years in Germany: results from the OUTDOOR ACTIVE study. *BMC Geriatr*, *21*(1), 273. https://doi.org/10.1186/s12877-021-02188-9

Alexandre, S., Duarte, Y. A., Santos, J. L., Wong, R., & Lebrao, M. L. (2014). Prevalence and associated factors of sarcopenia among elderly in Brazil: findings from the SABE study. *The journal of nutrition, health & aging*, *18*(3), 284-290. https://doi.org/10.1007/s12603-013-0413-0

Alley, D. E., Shardell, M. D., Peters, K. W., McLean, R. R., Dam, T.-T. L., Kenny, A. M., Fragala, M. S., Harris, T. B., Kiel, D. P., Guralnik, J. M., Ferrucci, L., Kritchevsky, S. B., Studenski, S. A., Vassileva, M. T., & Cawthon, P. M. (2014). Grip Strength Cutpoints for the Identification of Clinically Relevant Weakness. *The Journals of Gerontology: Series A*, *69*(5), 559-566. https://doi.org/10.1093/gerona/glu011

Anker, S. D., Morley, J. E., & von Haehling, S. (2016). Welcome to the ICD-10 code for sarcopenia. *Journal of cachexia, sarcopenia and muscle*, *7*(5), 512-514. https://doi.org/10.1002/jcsm.12147

Arai, H., Wakabayashi, H., Yoshimura, Y., Yamada, M., Kim, H., & Harada, A. (2018). Chapter 4 Treatment of sarcopenia. *Geriatr Gerontol Int*, *18 Suppl 1*, 28-44. https://doi.org/10.1111/ggi.13322

Armstrong, T., & Bull, F. (2006). Development of the world health organization global physical activity questionnaire (GPAQ). *Journal of Public Health*, *14*(2), 66-70.

Assantachai, P., Muangpaisan, W., Intalapaporn, S., Sitthichai, K., & Udompunturak, S. (2014). Cut-off points of quadriceps strength, declines and relationships of sarcopenia-related variables among Thai community-dwelling older adults. *Geriatrics & gerontology international*, *14*(S1), 61-68. https://doi.org/10.1111/ggi.12207

Bahat, G., Tufan, A., Tufan, F., Kilic, C., Akpinar, T. S., Kose, M., Erten, N., Karan, M. A., & Cruz-Jentoft, A. J. (2016). Cut-off points to identify sarcopenia according to European Working Group on Sarcopenia in Older People (EWGSOP) definition. *Clin Nutr*, *35*(6), 1557-1563. https://doi.org/10.1016/j.clnu.2016.02.002

Bailey, B. J., & Briars, G. L. (1996). Estimating the surface area of the human body. *Stat Med*, *15*(13), 1325-1332.

Barbosa-Silva, T. G., Bielemann, R. M., & Gonzalez, M. C. (2016). Prevalence of sarcopenia among community-dwelling elderly of a medium-sized South American city: results of the COMO VAI? study. *J Cachexia Sarcopenia Muscle*, *7*(2), 136-143. https://doi.org/10.1002/jcsm.12049

Baumgartner, R. N., Heymsfield, S. B., Lichtman, S., Wang, J., & Pierson, R. N., Jr. (1991). Body composition in elderly people: effect of criterion estimates on predictive equations. *Am J Clin Nutr*, *53*(6), 1345-1353. https://doi.org/10.1093/ajcn/53.6.1345

Baumgartner, R. N., Koehler, K. M., Gallagher, D., Romero, L., Heymsfield, S. B., Ross, R. R., Garry, P. J., & Lindeman, R. D. (1998). Epidemiology of sarcopenia among the elderly in New Mexico. *American journal of epidemiology*, *147*(8), 755-763.

Beaudart, C., Rizzoli, R., Bruyère, O., Reginster, J.-Y., & Biver, E. (2014). Sarcopenia: burden and challenges for public health. *Archives of Public Health*, *72*(45), 1-8. https://doi.org/10.1186/2049-3258-72-45

Bez, J. P. d. O., & Neri, A. L. (2014). Velocidade da marcha, força de preensão e saúde percebida em idosos: dados da rede FIBRA Campinas, São Paulo, Brasil. *Ciência & Saúde Coletiva*, *19*(8), 3343-3353.

Bhasin, S., Travison, T. G., Manini, T. M., Patel, S., Pencina, K. M., Fielding, R. A., Magaziner, J. M., Newman, A. B., Kiel, D. P., Cooper, C., Guralnik, J. M., Cauley, J. A., Arai, H., Clark, B. C., Landi, F., Schaap, L. A., Pereira, S. L., Rooks, D., Woo, J., . . . Cawthon, P. M. (2020). Sarcopenia Definition: The Position Statements of the Sarcopenia Definition and Outcomes Consortium. *J Am Geriatr Soc*. https://doi.org/10.1111/jgs.16372

Binder, E. F., Yarasheski, K. E., Steger-May, K., Sinacore, D. R., Brown, M., Schechtman, K. B., & Holloszy, J. O. (2005). Effects of progressive resistance training on body composition in frail older adults: results of a randomized, controlled trial. *The Journals of Gerontology: Series A*, *60*(11), 1425-1431.

Bohannon, R. W. (2008). Hand-grip dynamometry predicts future outcomes in aging adults. *J Geriatr Phys Ther*, *31*(1), 3-10. https://doi.org/10.1519/00139143-200831010-00002

Bohannon, R. W. (2019). Grip Strength: An Indispensable Biomarker For Older Adults. *Clin Interv Aging*, *14*, 1681-1691. https://doi.org/10.2147/cia.s194543

Bolfarine, H., & Bussab, W. d. O. (2005). *Elementos de amostragem* (Vol. 1). Edgard Blücher

Bonnefoy, M., Jauffret, M., Kostka, T., & Jusot, J. F. (2002). Usefulness of calf circumference measurement in assessing the nutritional state of hospitalized elderly people. *Gerontology*, *48*(3), 162-169. https://doi.org/10.1159/000052836

Bouchard, D. R., Beliaeff, S., Dionne, I. J., & Brochu, M. (2007). Fat Mass But Not Fat-Free Mass Is Related to Physical Capacity in Well-Functioning Older Individuals: Nutrition as a Determinant of Successful Aging (NuAge)—The Quebec Longitudinal Study. *The Journals of Gerontology: Series A*, *62*(12), 1382-1388. https://doi.org/10.1093/gerona/62.12.1382
Broadwin, J., Goodman-Gruen, D., & Slymen, D. (2001). Ability of Fat and Fat-Free Mass Percentages to Predict Functional Disability in Older Men and Women. *Journal of the American Geriatrics Society*, *49*(12), 1641-1645. https://doi.org/https://doi.org/10.1111/j.1532-5415.2001.49273.x
Brzycki, M. (1993). Strength testing—predicting a one-rep max from reps-to-fatigue. *Journal of Physical Education, Recreation & Dance*, *64*(1), 88-90.
Bunout, D., Barrera, G., de la Maza, P., Avendano, M., Gattas, V., Petermann, M., & Hirsch, S. (2001). The impact of nutritional supplementation and resistance training on the health functioning of free-living Chilean elders: results of 18 months of follow-up. *J Nutr*, *131*(9), 2441s-2446s.
Calder, W. A. (1984). *Size, function, and life history*. Courier Corporation.
Câmara, L. C., Bastos, C. C., & Volpe, E. F. T. (2012). Exercício resistido em idosos frágeis: uma revisão da literatura. *Fisioterapia em Movimento*, *25*(2), 435-443.
Cawthon, P. M., Manini, T., Patel, S. M., Newman, A., Travison, T., Kiel, D. P., Santanasto, A. J., Ensrud, K. E., Xue, Q.-L., Shardell, M., Duchowny, K., Erlandson, K. M., Pencina, K. M., Fielding, R. A., Magaziner, J., Kwok, T., Karlsson, M., Ohlsson, C., Mellström, D., . . . Bhasin, S. (2020). Putative Cut-Points in Sarcopenia Components and Incident Adverse Health Outcomes: An SDOC Analysis. *Journal of the American Geriatrics Society*, *68*(7), 1429-1437. https://doi.org/https://doi.org/10.1111/jgs.16517
Chen, L.-K., Liu, L.-K., Woo, J., Assantachai, P., Auyeung, T.-W., Bahyah, K. S., Chou, M.-Y., Chen, L.-Y., Hsu, P.-S., Krairit, O., Lee, J. S. W., Lee, W.-J., Lee, Y., Liang, C.-K., Limpawattana, P., Lin, C.-S., Peng, L.-N., Satake, S., Suzuki, T., . . . Arai, H. (2014). Sarcopenia in Asia: Consensus Report of the Asian Working Group for Sarcopenia. *Journal of the American Medical Directors Association*, *15*(2), 95-101. https://doi.org/10.1016/j.jamda.2013.11.025
Chen, L. K., Woo, J., Assantachai, P., Auyeung, T. W., Chou, M. Y., Iijima, K., Jang, H. C., Kang, L., Kim, M., Kim, S., Kojima, T., Kuzuya, M., Lee, J. S. W., Lee, S. Y., Lee, W. J., Lee, Y., Liang, C. K., Lim, J. Y., Lim, W. S., . . . Arai, H. (2020). Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. *J Am Med Dir Assoc*, *21*(3), 300-307.e302. https://doi.org/10.1016/j.jamda.2019.12.012
Clark, B. C., & Manini, T. M. (2008). Sarcopenia ≠ Dynapenia. *The Journals of Gerontology: Series A*, *63*(8), 829-834. https://doi.org/10.1093/gerona/63.8.829
Clark, B. C., & Manini, T. M. (2012). What is dynapenia? *Nutrition (Burbank, Los Angeles County, Calif.)*, *28*(5), 495-503. https://doi.org/10.1016/j.nut.2011.12.002
Compston, J. E., Flahive, J., Hosmer, D. W., Watts, N. B., Siris, E. S., Silverman, S., Saag, K. G., Roux, C., Rossini, M., & Pfeilschifter, J. (2014). Relationship of weight, height, and body mass index with fracture risk at different sites in postmenopausal women: the global longitudinal study of osteoporosis in women (GLOW). *Journal of Bone and Mineral Research*, *29*(2), 487-493.
Cruz-Jentoft, A. J., Baeyens, J. P., Bauer, J. M., Boirie, Y., Cederholm, T., Landi, F., Martin, F. C., Michel, J.-P., Rolland, Y., & Schneider, S. M. (2010). Sarcopenia: European consensus on definition and diagnosis Report of the European Working Group on Sarcopenia in Older People. *Age and ageing*, *39*(4), 412-423.
Cruz-Jentoft, A. J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A. A., Schneider, S. M., Sieber, C. C., Topinkova, E., Vandewoude, M., Visser, M., Zamboni, M., Writing Group for the European Working Group on Sarcopenia in Older People 2 , & EWGSOP2, t. E. G. f. (2018). Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*, *48*(1), 16-31. https://doi.org/10.1093/ageing/afy169
Cruz-Jentoft, A. J., Landi, F., Schneider, S. M., Zuniga, C., Arai, H., Boirie, Y., Chen, L. K., Fielding, R. A., Martin, F. C., Michel, J. P., Sieber, C., Stout, J. R., Studenski, S. A., Vellas, B., Woo, J., Zamboni, M., & Cederholm, T. (2014). Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the

International Sarcopenia Initiative (EWGSOP and IWGS). *Age and ageing*, *43*(6), 748-759. https://doi.org/10.1093/ageing/afu115
Cuschieri, S. (2019). The STROBE guidelines. *Saudi journal of anaesthesia*, *13*(Suppl 1), S31-S34. https://doi.org/10.4103/sja.SJA_543_18
Dam, T. T., Peters, K. W., Fragala, M., Cawthon, P. M., Harris, T. B., McLean, R., Shardell, M., Alley, D. E., Kenny, A., Ferrucci, L., Guralnik, J., Kiel, D. P., Kritchevsky, S., Vassileva, M. T., & Studenski, S. (2014). An evidence-based comparison of operational criteria for the presence of sarcopenia. *The Journals of Gerontology: Series A*, *69*(5), 584-590. https://doi.org/10.1093/gerona/glu013
Davies, M. J., & Dalsky, G. P. (1997). Normalizing strength for body size differences in older adults. *Medicine & Science in Sports & Exercise*, *29*(5), 713-717. http://journals.lww.com/acsm-msse/Fulltext/1997/05000/Normalizing_strength_for_body_size_differences_in.20.aspx
de Mello, R. G. B., Dalla Corte, R. R., Gioscia, J., & Moriguchi, E. H. (2019). Effects of Physical Exercise Programs on Sarcopenia Management, Dynapenia, and Physical Performance in the Elderly: A Systematic Review of Randomized Clinical Trials. *Journal of Aging Research*, *2019*, 1959486. https://doi.org/10.1155/2019/1959486
Delmonico, M. J., Harris, T. B., Lee, J. S., Visser, M., Nevitt, M., Kritchevsky, S. B., Tylavsky, F. A., & Newman, A. B. (2007). Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women. *Journal of the American Geriatrics Society*, *55*(5), 769-774.
Diz, J. B. M., Leopoldino, A. A. O., Moreira, B. d. S., Henschke, N., Dias, R. C., Pereira, L. S. M., & Oliveira, V. C. (2017). Prevalence of sarcopenia in older Brazilians: A systematic review and meta‐analysis. *Geriatr Gerontol Int*, *17*(1), 5-16.
Dodds, R. M., Syddall, H. E., Cooper, R., Benzeval, M., Deary, I. J., Dennison, E. M., Der, G., Gale, C. R., Inskip, H. M., Jagger, C., Kirkwood, T. B., Lawlor, D. A., Robinson, S. M., Starr, J. M., Steptoe, A., Tilling, K., Kuh, D., Cooper, C., & Sayer, A. A. (2014). Grip strength across the life course: normative data from twelve British studies. *PLoS One*, *9*(12), e113637. https://doi.org/10.1371/journal.pone.0113637
Dodds, R. M., Syddall, H. E., Cooper, R., Kuh, D., Cooper, C., & Sayer, A. A. (2016). Global variation in grip strength: a systematic review and meta-analysis of normative data. *Age Ageing*, *45*(2), 209-216. https://doi.org/10.1093/ageing/afv192
dos Santos, A. P., Navarro, A. M., Schwingel, A., Alves, T. C., Abdalla, P. P., Venturini, A. C. R., de Santana, R. C., & Machado, D. R. L. (2018). Lipodystrophy diagnosis in people living with HIV/AIDS: prediction and validation of sex-specific anthropometric models. *BMC Public Health*, *18*(1), 806. https://doi.org/10.1186/s12889-018-5707-z
Enright, P. L. (2003). The Six-Minute Walk Test. *Respiratory Care*, *48*(8), 783-785. http://rc.rcjournal.com/content/respcare/48/8/783.full.pdf
Evans, W. J., Hellerstein, M., Orwoll, E., Cummings, S., & Cawthon, P. M. (2019). D3-Creatine dilution and the importance of accuracy in the assessment of skeletal muscle mass. *Journal of cachexia, sarcopenia and muscle*, *10*(1), 14-21. https://doi.org/10.1002/jcsm.12390
Farinatti, P., Paes, L., Harris, E. A., Lopes, G. O., & Borges, J. P. (2017). A Simple Model to Identify Risk of Sarcopenia and Physical Disability in HIV-Infected Patients. *J Strength Cond Res*, *31*(9), 2542-2551. https://doi.org/10.1519/jsc.0000000000002070
Fiatarone, M. A., Marks, E. C., Ryan, N. D., Meredith, C. N., Lipsitz, L. A., & Evans, W. J. (1990). High-intensity strength training in nonagenarians. Effects on skeletal muscle. *Journal of the American Medical Association*, *263*(22), 3029-3034.
Fielding, R. A., Vellas, B., Evans, W. J., Bhasin, S., Morley, J. E., Newman, A. B., Abellan van Kan, G., Andrieu, S., Bauer, J., & Breuille, D. (2011). Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *Journal of the American Medical Directors Association*, *12*(4), 249-256.
Finney, G. R., Minagar, A., & Heilman, K. M. (2016). Assessment of Mental Status. *Neurol Clin*, *34*(1), 1-16. https://doi.org/10.1016/j.ncl.2015.08.001
Foley, K. T., Owings, T. M., Pavol, M. J., & Grabiner, M. D. (1999). Maximum grip strength is not related to bone mineral density of the proximal femur in older adults. *Calcified tissue international*, *64*(4), 291-294.

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W. J., & Burke, G. (2001). Frailty in older adults evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*, *56*(3), M146-M157.
Gadelha, A. B., Vainshelboim, B., Ferreira, A. P., Neri, S. G. R., Bottaro, M., & Lima, R. M. (2018). Stages of sarcopenia and the incidence of falls in older women: A prospective study. *Arch Gerontol Geriatr*, *79*, 151-157. https://doi.org/10.1016/j.archger.2018.07.014
George, L. B., Bruce, R. B., Baltej, S. M., Haran, T. S., & Michael, F. S. (1977). Nutritional and metabolic assessment of the hospitalized patient. *Journal of Parenteral and Enteral Nutrition*, *1*(1), 11-21. https://doi.org/10.1177/014860717700100101
Gheorghe, A., Griffiths, U., Murphy, A., Legido-Quigley, H., Lamptey, P., & Perel, P. (2018). The economic burden of cardiovascular disease and hypertension in low- and middle-income countries: a systematic review. *BMC Public Health*, *18*(1), 975. https://doi.org/10.1186/s12889-018-5806-x
Gouveia, É. R., Maia, J. A., Beunen, G. P., Blimkie, C. J., Fena, E. M., & Freitas, D. L. (2013). Functional Fitness and Physical Activity of Portuguese Community-Residing Older Adults. *Journal of Aging and Physical Activity*, *21*(1), 1-19. https://doi.org/10.1123/japa.21.1.1
Hendin, A., Tanuseputro, P., McIsaac, D. I., Hsu, A. T., Smith, G. A., Begum, J., Thompson, L. H., Stelfox, H. T., Reardon, P., Herritt, B., Chaudhuri, D., Rosenberg, E., & Kyeremanteng, K. (2020). Frailty Is Associated With Decreased Time Spent at Home After Critical Illness: A Population-Based Study. 885066620939055. https://doi.org/10.1177/0885066620939055
Heymsfield, S. B., McManus, C., Smith, J., Stevens, V., & Nixon, D. W. (1982). Anthropometric measurement of muscle mass: revised equations for calculating bone-free arm muscle area. *Am J Clin Nutr*, *36*(4), 680-690.
Higo, M., & Khan, H. T. (2015). Global population aging: Unequal distribution of risks in later life between developed and developing countries. *Global Social Policy*, *15*(2), 146-166. https://doi.org/10.1177/1468018114543157
Hofmann, M., Halper, B., Oesen, S., Franzke, B., Stuparits, P., Tschan, H., Bachl, N., Strasser, E. M., Quittan, M., Ploder, M., Wagner, K. H., & Wessner, B. (2015). Serum concentrations of insulin-like growth factor-1, members of the TGF-beta superfamily and follistatin do not reflect different stages of dynapenia and sarcopenia in elderly women. *Exp Gerontol*, *64*, 35-45. https://doi.org/10.1016/j.exger.2015.02.008
Holland, A. E., Hill, C. J., Rasekaba, T., Lee, A., Naughton, M. T., & McDonald, C. F. (2010). Updating the minimal important difference for six-minute walk distance in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil*, *91*(2), 221-225. https://doi.org/10.1016/j.apmr.2009.10.017
Hosmer, D., & Lemeshow, S. (2000). *Applied logistic regression* (2 ed.). John Wiley & Sons.
Hsu, W. C., Tsai, A. C., & Wang, J. Y. (2016). Calf circumference is more effective than body mass index in predicting emerging care-need of older adults - Results of a national cohort study. *Clin Nutr*, *35*(3), 735-740. https://doi.org/10.1016/j.clnu.2015.05.017
Hughes, M. A., Myers, B. S., & Schenkman, M. L. (1996). The role of strength in rising from a chair in the functionally impaired elderly. *Journal of biomechanics*, *29*(12), 1509-1513.
Hughess, V. A., Frontera, W. R., Wood, M., Evans, W. J., Dallal, G. E., Roubenoff, R., & Fiatarone Singh, M. A. (2001). Longitudinal muscle strength changes in older adults: influence of muscle mass, physical activity, and health. *The Journals of Gerontology: Series A*, *56*(5), B209-8217.
Huxley, J. S. (1924). Constant Differential Growth-Ratios and their Significance. *Nature*, *114*(2877), 895-896. https://doi.org/10.1038/114895a0
Huxley, J. S., & Teissier, G. (1936a). Terminologie et notation dans la description de la croissance relative. *Comptes Rendus des Séances de la Société de Biologie et ses filiales*, *121*, 934-937.
Huxley, J. S., & Teissier, G. (1936b). Terminology of Relative Growth. *Nature*, *137*(3471), 780-781. https://doi.org/10.1038/137780b0
Icaza, M. C., & Albala, C. (1999). Projeto SABE. *Minimental State Examination (MMSE) del estudio de dementia en Chile: análisis estatístico. Brasília: OPAS*, 1-18.
Instituto Nacional de Estatística. (2020). *Projeções de População Residente em Portugal*. Retrieved 29 Mar from

https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_destaques&DESTAQUESdest_boui=406534255&DESTAQUESmodo=2&xlang=pt
Janssen, I., Shepard, D. S., Katzmarzyk, P. T., & Roubenoff, R. (2004). The healthcare costs of sarcopenia in the United States. *Journal of the American Geriatrics Society*, *52*(1), 80-85.
Jaric, S. (2003). Role of body size in the relation between muscle strength and movement performance. *Exercise and sport sciences reviews*, *31*(1), 8-12.
Jelliffe, D. B., & Jelliffe, E. P. (1969). The arm circumference as a public health index of protein-calorie malnutrition of early childhood. 20. Current conclusions. *Journal of tropical pediatrics*, *15*, 253-260.
Kanis, J. A. (2002). Diagnosis of osteoporosis and assessment of fracture risk. *Lancet*, *359*(9321), 1929-1936. https://doi.org/10.1016/s0140-6736(02)08761-5
Kara, M., Ata, A. M., Çakır, B., Kaymak, B., & Özçakar, L. (2019). The Impact of Cut-Off Values and Adjustments for Muscle Mass and Strength on Diagnosis of Sarcopenia. *J Am Med Dir Assoc*, *20*(12), 1653. https://doi.org/10.1016/j.jamda.2019.07.014
Kawakami, R., Murakami, H., Sanada, K., Tanaka, N., Sawada, S. S., Tabata, I., Higuchi, M., & Miyachi, M. (2015). Calf circumference as a surrogate marker of muscle mass for diagnosing sarcopenia in Japanese men and women. *Geriatr Gerontol Int*, *15*(8), 969-976. https://doi.org/10.1111/ggi.12377
Kim, C. R., & Jeon, Y. J. (2018). Reference values for hand grip strength in the South Korean population. *13*(4), e0195485. https://doi.org/10.1371/journal.pone.0195485
Kim, K. M., Jang, H. C., & Lim, S. (2016). Differences among skeletal muscle mass indices derived from height-, weight-, and body mass index-adjusted models in assessing sarcopenia. *Korean J Intern Med*, *31*(4), 643-650. https://doi.org/10.3904/kjim.2016.015
Kim, S., Kim, M., Lee, Y., Kim, B., Yoon, T. Y., & Won, C. W. (2018). Calf Circumference as a Simple Screening Marker for Diagnosing Sarcopenia in Older Korean Adults: the Korean Frailty and Aging Cohort Study (KFACS). *Journal of Korean medical science*, *33*(20), e151-e151. https://doi.org/10.3346/jkms.2018.33.e151
Koopman, J. J., van Bodegom, D., van Heemst, D., & Westendorp, R. G. (2015). Handgrip strength, ageing and mortality in rural Africa. *Age Ageing*, *44*(3), 465-470. https://doi.org/10.1093/ageing/afu165
Kowal, P., Chatterji, S., Naidoo, N., Biritwum, R., Fan, W., Lopez Ridaura, R., Maximova, T., Arokiasamy, P., Phaswana-Mafuya, N., Williams, S., Snodgrass, J. J., Minicuci, N., D'Este, C., Peltzer, K., Boerma, J. T., & the, S. C. (2012). Data Resource Profile: The World Health Organization Study on global AGEing and adult health (SAGE). *International Journal of Epidemiology*, *41*(6), 1639-1649. https://doi.org/10.1093/ije/dys210
Külkamp, W., Ache-Dias, J., Kons, R. L., Detanico, D., & Dal Pupo, J. (2020). The ratio standard is not adequate for scaling handgrip strength in judo athletes and nonathletes. *Journal of exercise rehabilitation*, *16*(2), 175-182. https://doi.org/10.12965/jer.2040108.054
Kusaka, S., Takahashi, T., Hiyama, Y., Kusumoto, Y., Tsuchiya, J., & Umeda, M. (2017). Large calf circumference indicates non-sarcopenia despite body mass. *Journal of physical therapy science*, *29*(11), 1925-1928. https://doi.org/10.1589/jpts.29.1925
Kwak, S. G., & Kim, J. H. (2017). Central limit theorem: the cornerstone of modern statistics. *Korean J Anesthesiol*, *70*(2), 144-156. https://doi.org/10.4097/kjae.2017.70.2.144
Landi, F., Liperoti, R., Russo, A., Capoluongo, E., Barillaro, C., Pahor, M., Bernabei, R., & Onder, G. (2010). Disability, more than multimorbidity, was predictive of mortality among older persons aged 80 years and older. *J Clin Epidemiol*, *63*(7), 752-759. https://doi.org/10.1016/j.jclinepi.2009.09.007
Landi, F., Onder, G., Russo, A., Liperoti, R., Tosato, M., Martone, A. M., Capoluongo, E., & Bernabei, R. (2014). Calf circumference, frailty and physical performance among older adults living in the community. *Clin Nutr*, *33*(3), 539-544. https://doi.org/10.1016/j.clnu.2013.07.013
Lauretani, F., Russo, C. R., Bandinelli, S., Bartali, B., Cavazzini, C., Di Iorio, A., Corsi, A. M., Rantanen, T., Guralnik, J. M., & Ferrucci, L. (2003). Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *Journal of Applied Physiology*, *95*(5), 1851-1860.

Lean, M., Han, T. S., & Deurenberg, P. (1996). Predicting body composition by densitometry from simple anthropometric measurements. *The American journal of clinical nutrition*, *63*(1), 4-14.
Lesnak, J., Anderson, D., Farmer, B., Katsavelis, D., & Grindstaff, T. L. (2019). VALIDITY OF HAND-HELD DYNAMOMETRY IN MEASURING QUADRICEPS STRENGTH AND RATE OF TORQUE DEVELOPMENT. *Int J Sports Phys Ther*, *14*(2), 180-187.
Lima, R. M., de Oliveira, R. J., Raposo, R., Neri, S. G. R., & Gadelha, A. B. (2019). Stages of sarcopenia, bone mineral density, and the prevalence of osteoporosis in older women. *Arch Osteoporos*, *14*(1), 38. https://doi.org/10.1007/s11657-019-0591-4
Lohman, T., Roche, A., & Martorell, R. (1988). *Anthropometric standardization reference manual*. Human Kinetics.
Lohman, T. G., Roche, A. F., & Martorell, R. (1988). *Anthropometric standardization reference manual*. Human kinetics books.
LOHMAN, T. G., ROCHE, A. F., & MARTORELLI, R. (1988). Anthropometric standardization reference manual. *Champaing human kinects*, *1*(1).
Lourenco, R., Perez-Zepeda, M., Gutierrez-Robledo, L., Rodriguez Manas, L., & Garcia-Garcia, F. (2014). Performance of the European Working Group on Sarcopenia in Older People algorithm in screening older adults for muscle mass assessment. *Age and ageing*, *44*(2), 334-338. https://doi.org/10.1093/ageing/afu192
Manini, T. M., & Clark, B. C. (2011). Dynapenia and Aging: An Update. *The Journals of Gerontology: Series A*, *67A*(1), 28-40. https://doi.org/10.1093/gerona/glr010
Manini, T. M., Patel, S. M., Newman, A. B., Travison, T. G., Kiel, D. P., Shardell, M. D., Pencina, K. M., Wilson, K. E., Kelly, T. L., Massaro, J. M., Fielding, R. A., Magaziner, J., Correa-de-Araujo, R., Kwok, T. C. Y., Hirani, V., Karlsson, M. K., D'Agostino, R. B., Mellström, D., Ohlsson, C., . . . Cawthon, P. M. (2020). Identification of Sarcopenia Components That Discriminate Slow Walking Speed: A Pooled Data Analysis. *Journal of the American Geriatrics Society*, *68*(7), 1419-1428. https://doi.org/10.1111/jgs.16524
Manini, T. M., Visser, M., Won-Park, S., Patel, K. V., Strotmeyer, E. S., Chen, H., Goodpaster, B., De Rekeneire, N., Newman, A. B., Simonsick, E. M., Kritchevsky, S. B., Ryder, K., Schwartz, A. V., & Harris, T. B. (2007). Knee extension strength cutpoints for maintaining mobility. *J Am Geriatr Soc*, *55*(3), 451-457. https://doi.org/10.1111/j.1532-5415.2007.01087.x
Maranhão Neto, G. A., Oliveira, A. J., Pedreiro, R. C., Pereira-Junior, P. P., Machado, S., Marques Neto, S., & Farinatti, P. T. (2017). Normalizing handgrip strength in older adults: An allometric approach. *Archives of gerontology and geriatrics*, *70*, 230-234. https://doi.org/10.1016/j.archger.2017.02.007
Marín, L. A. (1929). *Obras completas de William Shakespeare*. Aguilar.
Marques, E. A., Wanderley, F., Machado, L., Sousa, F., Viana, J. L., Moreira-Gonçalves, D., Moreira, P., Mota, J., & Carvalho, J. (2011). Effects of resistance and aerobic exercise on physical function, bone mineral density, OPG and RANKL in older women. *Exp Gerontol*, *46*(7), 524-532. https://doi.org/10.1016/j.exger.2011.02.005
Martien, S., Delecluse, C., Boen, F., Seghers, J., Pelssers, J., Van Hoecke, A. S., & Van Roie, E. (2015). Is knee extension strength a better predictor of functional performance than handgrip strength among older adults in three different settings? *Archives of gerontology and geriatrics*, *60*(2), 252-258. https://doi.org/10.1016/j.archger.2014.11.010
Massy-Westropp, N. M., Gill, T. K., Taylor, A. W., Bohannon, R. W., & Hill, C. L. (2011). Hand Grip Strength: age and gender stratified normative data in a population-based study. *BMC research notes*, *4*(127), 1-5.
Matsudo, S., Araújo, T., Matsudo, V., Andrade, D., Andrade, E., Oliveira, L. C., & Braggion, G. (2012). Questionário internacional De atividade física (ipaq): estupo De validade e reprodutibilidade No Brasil. *Revista Brasileira de Atividade Física & Saúde*, *6*(2), 5-18.
McDermott, M. M., Guralnik, J. M., Tian, L., Ferrucci, L., Liu, K., Liao, Y., & Criqui, M. H. (2007). Baseline functional performance predicts the rate of mobility loss in persons with peripheral arterial disease. *J Am Coll Cardiol*, *50*(10), 974-982. https://doi.org/10.1016/j.jacc.2007.05.030

McGrath, R. (2019). Comparing absolute handgrip strength and handgrip strength normalized to body weight in aging adults. *Aging clinical and experimental research*, *31*(12), 1851-1853. https://doi.org/10.1007/s40520-019-01126-5

McGrath, R., Hackney, K. J., Ratamess, N. A., Vincent, B. M., Clark, B. C., & Kraemer, W. J. (2020). Absolute and Body Mass Index Normalized Handgrip Strength Percentiles by Gender, Ethnicity, and Hand Dominance in Americans. *Adv Geriatr Med Res*, *2*(1). https://doi.org/10.20900/agmr20200005

Mijnarends, D. M., Luiking, Y. C., Halfens, R. J. G., Evers, S., Lenaerts, E. L. A., Verlaan, S., Wallace, M., Schols, J., & Meijers, J. M. M. (2018). Muscle, Health and Costs: A Glance at their Relationship. *J Nutr Health Aging*, *22*(7), 766-773. https://doi.org/10.1007/s12603-018-1058-9

Mijnarends, D. M., Meijers, J. M., Halfens, R. J., ter Borg, S., Luiking, Y. C., Verlaan, S., Schoberer, D., Cruz Jentoft, A. J., van Loon, L. J., & Schols, J. M. (2013). Validity and reliability of tools to measure muscle mass, strength, and physical performance in community-dwelling older people: a systematic review. *Journal of the American Medical Directors Association*, *14*(3), 170-178.

Moreira, V. G., & Lourenco, R. A. (2013). Prevalence and factors associated with frailty in an older population from the city of Rio de Janeiro, Brazil: the FIBRA-RJ Study. *Clinics (Sao Paulo)*, *68*(7), 979-985. https://doi.org/10.6061/clinics/2013(07)15

Morley, J. E., Abbatecola, A. M., Argiles, J. M., Baracos, V., Bauer, J., Bhasin, S., Cederholm, T., Coats, A. J., Cummings, S. R., Evans, W. J., Fearon, K., Ferrucci, L., Fielding, R. A., Guralnik, J. M., Harris, T. B., Inui, A., Kalantar-Zadeh, K., Kirwan, B. A., Mantovani, G., . . . Anker, S. D. (2011). Sarcopenia with limited mobility: an international consensus. *J Am Med Dir Assoc*, *12*(6), 403-409. https://doi.org/10.1016/j.jamda.2011.04.014

Morley, J. E., Abbatecola, A. M., Argiles, J. M., Baracos, V., Bauer, J., Bhasin, S., Cederholm, T., Stewart Coats, A. J., Cummings, S. R., & Evans, W. J. (2011). Sarcopenia with limited mobility: an international consensus. *Journal of the American Medical Directors Association*, *12*(6), 403-409.

Mukaka, M. M. (2012). Statistics corner: A guide to appropriate use of correlation coefficient in medical research. *Malawi medical journal : the journal of Medical Association of Malawi*, *24*(3), 69-71. https://pubmed.ncbi.nlm.nih.gov/23638278
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3576830/

Muscaritoli, M., Anker, S. D., Argiles, J., Aversa, Z., Bauer, J. M., Biolo, G., Boirie, Y., Bosaeus, I., Cederholm, T., Costelli, P., Fearon, K. C., Laviano, A., Maggio, M., Rossi Fanelli, F., Schneider, S. M., Schols, A., & Sieber, C. C. (2010). Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics". *Clinical Nutrition*, *29*(2), 154-159. https://doi.org/10.1016/j.clnu.2009.12.004

Myers, R. (1990). Classical and modern regression with applications. Boston: PWS and Kent Publishing Company. In: Inc.

Neri, A. L., Yassuda, M. S., Araújo, L. F. d., Eulálio, M. d. C., Cabral, B. E., Siqueira, M. E. C. d., Santos, G. A. d., & Moura, J. G. d. A. (2013). Metodologia e perfil sociodemográfico, cognitivo e de fragilidade de idosos comunitários de sete cidades brasileiras: Estudo FIBRA. *Cadernos de Saude Publica*, *29*(4), 778-792.

Nevill, A. M., Tomkinson, G. R., Lang, J. J., Wutz, W., & Myers, T. D. (2022). How Should Adult Handgrip Strength Be Normalized? Allometry Reveals New Insights and Associated Reference Curves. *Med Sci Sports Exerc*, *54*(1), 162-168. https://doi.org/10.1249/mss.0000000000002771

Owings, T. M., Pavol, M. J., & Grabiner, M. D. (2002). Lower extremity muscle strength does not independently predict proximal femur bone mineral density in healthy older adults. *Bone*, *30*(3), 515-520.

Pagotto, V., Santos, K. F. D., Malaquias, S. G., Bachion, M. M., & Silveira, E. A. (2018). Calf circumference: clinical validation for evaluation of muscle mass in the elderly. *Rev Bras Enferm*, *71*(2), 322-328. https://doi.org/10.1590/0034-7167-2017-0121

Pérez-Zepeda, M. U., & Gutiérrez-Robledo, L. M. (2016). Calf circumference predicts mobility disability: A secondary analysis of the Mexican health and ageing study. *European geriatric medicine*, *7*(3), 262-266. https://doi.org/10.1016/j.eurger.2016.01.004

Phillips, S. M. (2015). Nutritional Supplements in Support of Resistance Exercise to Counter Age-Related Sarcopenia. *Advances in Nutrition: An International Review Journal*, *6*(4), 452-460.

Ploutz-Snyder, L. L., Manini, T., Ploutz-Snyder, R. J., & Wolf, D. A. (2002). Functionally relevant thresholds of quadriceps femoris strength. *The Journals of Gerontology: Series A*, *57*(4), B144-B152.

Pua, Y.-H. (2006). Allometric analysis of physical performance measures in older adults. *Physical therapy*, *86*(9), 1263-1270.

Pua, Y. H. (2006). Allometric analysis of physical performance measures in older adults. *Physical therapy*, *86*(9), 1263-1270. https://doi.org/10.2522/ptj.20060034

Radaelli, R., Botton, C. E., Wilhelm, E. N., Bottaro, M., Lacerda, F., Gaya, A., Moraes, K., Peruzzolo, A., Brown, L. E., & Pinto, R. S. (2013). Low- and high-volume strength training induces similar neuromuscular improvements in muscle quality in elderly women. *Exp Gerontol*, *48*(8), 710-716. https://doi.org/10.1016/j.exger.2013.04.003

Ramírez-Vélez, R., Sáez de Asteasu, M. L., Martínez-Velilla, N., Zambom-Ferraresi, F., García-Hermoso, A., & Izquierdo, M. (2021). Handgrip Strength as a Complementary Test for Mobility Limitations Assessment in Acutely Hospitalized Oldest Old. *Rejuvenation Res*. https://doi.org/10.1089/rej.2020.2344

Ramlagan, S., Peltzer, K., & Phaswana-Mafuya, N. (2014). Hand grip strength and associated factors in non-institutionalised men and women 50 years and older in South Africa. *BMC Res Notes*, *7*, 8. https://doi.org/10.1186/1756-0500-7-8

Rogers, M. A., & Evans, W. J. (1993). Changes in skeletal muscle with aging: effects of exercise training. *Exercise and sport sciences reviews*, *21*(1), 65-102.

Rolland, Y., Czerwinski, S., Van Kan, G. A., Morley, J. E., Cesari, M., Onder, G., Woo, J., Baumgartner, R., Pillard, F., & Boirie, Y. (2008). Sarcopenia: its assessment, etiology, pathogenesis, consequences and future perspectives. *The Journal of Nutrition Health & Aging*, *12*(7), 433-450.

Rolland, Y., Lauwers-Cances, V., Cournot, M., Nourhashémi, F., Reynish, W., Rivière, D., Vellas, B., & Grandjean, H. (2003). Sarcopenia, Calf Circumference, and Physical Function of Elderly Women: A Cross-Sectional Study. *J Am Geriatr Soc*, *51*(8), 1120-1124. https://doi.org/10.1046/j.1532-5415.2003.51362.x

Rosenberg, I. H. (1997). Sarcopenia: origins and clinical relevance. *J Nutr*, *127*(S5), 990s-991s.

Sampaio, L. S., Carneiro, J. A. O., Coqueiro, R. d. S., & Fernandes, M. H. (2017). Indicadores antropométricos como preditores na determinação da fragilidade em idosos. *Cien Saude Colet*, *22*, 4115-4124. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-81232017021204115&nrm=iso

Sampaio, R. A. C., Sampaio, P. Y. S., Castano, L. A. A., Barbieri, J. F., Coelho, H. J. J., Arai, H., Uchida, M. C., & Gutierrez, G. L. (2017). Cutoff values for appendicular skeletal muscle mass and strength in relation to fear of falling among Brazilian older adults: cross-sectional study. *Sao Paulo Medical Journal*, *135*(5), 434-443. https://doi.org/10.1590/1516-3180.2017.0049030517

Samuel, D., Wilson, K., Martin, H. J., Allen, R., Sayer, A. A., & Stokes, M. (2012). Age-associated changes in hand grip and quadriceps muscle strength ratios in healthy adults. *Aging Clin Exp Res*, *24*(3), 245-250.

Sanchez-Rodriguez, D., Marco, E., & Cruz-Jentoft, A. J. (2020). Defining sarcopenia: some caveats and challenges. *Curr Opin Clin Nutr Metab Care*, *23*(2), 127-132. https://doi.org/10.1097/mco.0000000000000621

Santanasto, A. J., Miljkovic, I., Cvejkus, R. K., Wheeler, V. W., & Zmuda, J. M. (2020). Sarcopenia Characteristics Are Associated with Incident Mobility Limitations in African Caribbean Men: The Tobago Longitudinal Study of Aging. *J Gerontol A Biol Sci Med Sci*, *75*(7), 1346-1352. https://doi.org/10.1093/gerona/glz233

Santos, L. P., & Gonzalez, M. C. (2019). New Prediction Equations to Estimate Appendicular Skeletal Muscle Mass Using Calf Circumference: Results From NHANES 1999-2006. *43*(8), 998-1007. https://doi.org/10.1002/jpen.1605

Sardeli, A. V., Komatsu, T. R., Mori, M. A., Gáspari, A. F., & Chacon-Mikahil, M. P. T. (2018). Resistance Training Prevents Muscle Loss Induced by Caloric Restriction in Obese

Elderly Individuals: A Systematic Review and Meta-Analysis. *Nutrients*, *10*(4), 423. https://www.mdpi.com/2072-6643/10/4/423
Schisterman, E. F., Perkins, N. J., Liu, A., & Bondell, H. (2005). Optimal cut-point and its corresponding Youden Index to discriminate individuals using pooled blood samples. *Epidemiology*, *16*(1), 73-81.
Segal, N. A., Torner, J. C., Yang, M., Curtis, J. R., Felson, D. T., & Nevitt, M. C. (2008). Muscle mass is more strongly related to hip bone mineral density than is quadriceps strength or lower activity level in adults over age 50 year. *Journal of Clinical Densitometry*, *11*(4), 503-510. https://doi.org/10.1016/j.jocd.2008.03.001
Shafiee, G., Keshtkar, A., Soltani, A., Ahadi, Z., Larijani, B., & Heshmat, R. (2017). Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies. *J Diabetes Metab Disord*, *16*, 21. https://doi.org/10.1186/s40200-017-0302-x
Sieber, C. C. (2017). Frailty - From concept to clinical practice. *Exp Gerontol*, *87*(Pt B), 160-167. https://doi.org/10.1016/j.exger.2016.05.004
Silva, A. M., Shen, W., Heo, M., Gallagher, D., Wang, Z., Sardinha, L. B., & Heymsfield, S. B. (2010). Ethnicity-related skeletal muscle differences across the lifespan. *American Journal of Human Biology*, *22*(1), 76-82. https://doi.org/10.1002/ajhb.20956
Sousa-Santos, A. R., Afonso, C., Borges, N., Santos, A., Padrão, P., Moreira, P., & F Amaral, T. (2020). Sarcopenia, physical frailty, undernutrition and obesity cooccurrence among Portuguese community-dwelling older adults: results from Nutrition UP 65 cross-sectional study. *BMJ Open*, *10*(6), e033661. https://doi.org/10.1136/bmjopen-2019-033661
Stewart, V. H., Saunders, D. H., & Greig, C. A. (2014). Responsiveness of muscle size and strength to physical training in very elderly people: a systematic review. *Scand J Med Sci Sports*, *24*(1), e1-10. https://doi.org/10.1111/sms.12123
Strasser, E. M., Hofmann, M., Franzke, B., Schober-Halper, B., Oesen, S., Jandrasits, W., Graf, A., Praschak, M., Horvath-Mechtler, B., Krammer, C., Ploder, M., Bachl, N., Quittan, M., Wagner, K. H., & Wessner, B. (2018). Strength training increases skeletal muscle quality but not muscle mass in old institutionalized adults: a randomized, multi-arm parallel and controlled intervention study. *Eur J Phys Rehabil Med*, *54*(6), 921-933. https://doi.org/10.23736/s1973-9087.18.04930-4
Teng, Z., Zhu, Y., Yu, X., Liu, J., Long, Q., Zeng, Y., & Lu, S. (2021). An analysis and systematic review of sarcopenia increasing osteopenia risk. *PLoS One*, *16*(4), e0250437. https://doi.org/10.1371/journal.pone.0250437
Tsai, A. C., Lai, M. C., & Chang, T. L. (2012). Mid-arm and calf circumferences (MAC and CC) are better than body mass index (BMI) in predicting health status and mortality risk in institutionalized elderly Taiwanese. *Arch Gerontol Geriatr*, *54*(3), 443-447. https://doi.org/10.1016/j.archger.2011.05.015
Van Roie, E., Verschueren, S. M., Boonen, S., Bogaerts, A., Kennis, E., Coudyzer, W., & Delecluse, C. (2011). Force-velocity characteristics of the knee extensors: an indication of the risk for physical frailty in elderly women. *Archives of physical medicine and rehabilitation*, *92*(11), 1827-1832. https://doi.org/10.1016/j.apmr.2011.05.022
Vanderburgh, P. M., Mahar, M. T., & Chou, C. H. (1995). Allometric scaling of grip strength by body mass in college-age men and women. *Research quarterly for exercise and sport*, *66*(1), 80-84.
Vasconcelos, K. S., Dias, J. M., Bastone Ade, C., Vieira, R. A., Andrade, A. C., Perracini, M. R., Guerra, R. O., & Dias, R. C. (2016). Handgrip Strength Cutoff Points to Identify Mobility Limitation in Community-dwelling Older People and Associated Factors. *The journal of nutrition, health & aging*, *20*(3), 306-315. https://doi.org/10.1007/s12603-015-0584-y
Vieira, R. A., Guerra, R. O., Giacomin, K. C., Vasconcelos, K. S. d. S., Andrade, A. C. d. S., Pereira, L. S. M., Dias, J. M. D., & Dias, R. C. (2013). Prevalência de fragilidade e fatores associados em idosos comunitários de Belo Horizonte, Minas Gerais, Brasil: dados do estudo FIBRA. *Cadernos de Saude Publica*, *29*(8), 1631-1643.
Vlietstra, L., Hendrickx, W., & Waters, D. L. (2018). Exercise interventions in healthy older adults with sarcopenia: A systematic review and meta-analysis. *Australas J Ageing*. https://doi.org/10.1111/ajag.12521

von Haehling, S., Morley, J. E., & Anker, S. D. (2010). An overview of sarcopenia: facts and numbers on prevalence and clinical impact. *Journal of cachexia, sarcopenia and muscle*, *1*(2), 129-133.
Wang, Y. C., Bohannon, R. W., Li, X., Sindhu, B., & Kapellusch, J. (2018). Hand-Grip Strength: Normative Reference Values and Equations for Individuals 18 to 85 Years of Age Residing in the United States. *J Orthop Sports Phys Ther*, *48*(9), 685-693. https://doi.org/10.2519/jospt.2018.7851
Welle, S., Totterman, S., & Thornton, C. (1996). Effect of age on muscle hypertrophy induced by resistance training. *The Journals of Gerontology: Series A*, *51*(6), M270-M275.
WHO Expert Consultation. (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*, *363*(9403), 157-163. https://doi.org/10.1016/s0140-6736(03)15268-3
WHO. *WHO Study on Global AGEing and Adult Health (SAGE).* Retrieved 3 Aug from http://www.who.int/healthinfo/sage/en/
Winter, E. M., & Nevill, A. M. (2009). Scaling: adjusting for differences in body size. In R. Eston & T. Reilly (Eds.), *Kinanthropometry and exercise physiology laboratory manual* (Vol. 1, pp. 300-320). Routledge.
World Health Organization. (2014). *10 FACTS ON AGEING AND THE LIFE COURSE*. Retrieved 2 Mar from http://www.who.int/features/factfiles/ageing/ageing_facts/en/
Wu, I., Lin, C. C., Hsiung, C. A., Wang, C. Y., Wu, C. H., Chan, D. C. D., Li, T. C., Lin, W. Y., Huang, K. C., & Chen, C. Y. (2014). Epidemiology of sarcopenia among community‐dwelling older adults in Taiwan: A pooled analysis for a broader adoption of sarcopenia assessments. *Geriatrics & gerontology international*, *14*(S1), 52-60.
Xie, W. Q., Xiao, G. L., Hu, P. W., He, Y. Q., Lv, S., & Xiao, W. F. (2020). Possible sarcopenia: early screening and intervention-narrative review. *Ann Palliat Med*, *9*(6), 4283-4293. https://doi.org/10.21037/apm-20-967
Yoshimura, Y., Wakabayashi, H., Yamada, M., Kim, H., Harada, A., & Arai, H. (2017). Interventions for Treating Sarcopenia: A Systematic Review and Meta-Analysis of Randomized Controlled Studies. *J Am Med Dir Assoc*, *18*(6), 553.e551-553.e516. https://doi.org/10.1016/j.jamda.2017.03.019

ANEXOS

ANEXO A – Aprovação do Comitê de Ética e Pesquisa

UNIVERSIDADE DE SÃO PAULO
ESCOLA DE ENFERMAGEM DE RIBEIRÃO PRETO

Centro Colaborador da OPAS/OMS para o Desenvolvimento da Pesquisa em Enfermagem

Avenida Bandeirantes, 3900 - Ribeirão Preto - São Paulo - Brasil - CEP 14040-902
Fone: 55 16 3315.3382 - 55 16 3315.3381 - Fax: 55 16 3315.0518
www.eerp.usp.br - eerp@usp.br

Ofício CEP-EERP/USP nº 021/2020, de 31/01/2020

Prezado Senhor,

Comunicamos que o projeto de pesquisa abaixo especificado foi analisado e considerado **aprovado** ***"ad referendum"*** pelo Comitê de Ética em Pesquisa da Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo (CEP-EERP/USP) em 31 de janeiro de 2020.

Protocolo CAAE: 23987519.5.0000.5393

Projeto: Pontos de Corte para diagnóstico de Sarcopenia em Idosos a partir da Força Muscular de Membros Superiores e Inferiores com Ajustes Alométricos

Pesquisadores: Pedro Pugliesi Abdalla (doutorado)
Dalmo Roberto Lopes Machado (orientador)

Em atendimento às normativas éticas vigentes, em especial as Resoluções CNS nº 466/2012 e nº 510/2016, deverão ser encaminhados ao CEP o relatório final da pesquisa e a publicação de seus resultados, para acompanhamento, bem como comunicada qualquer intercorrência ou a sua interrupção.

Atenciosamente,

Prof. Dr. Ronildo Alves dos Santos
Coordenador do CEP-EERP/USP

Ilmo. Sr.
Prof. Dr. Dalmo Roberto Lopes Machado
Professor Associado da Escola de Educação Física e Esporte de Ribeirão Preto - USP

ANEXO B – Comprovativos de Financiamento

5492161531537853

TERMO DE ACEITAÇÃO DE INDICAÇÃO DE BOLSISTA
DOUTORADO - GD
PROGRAMA DE POS GRADUAÇÃO

PROJETO:
870282/1997-2 -

COORDENADOR:
Regina Szylit
CPF: 05640645806

ORIENTADOR:
Dalmo Roberto Lopes Machado
CPF: 02715901810

Eu, **Pedro Pugliesi Abdalla**, CPF número **40750483814**, declaro conhecer e atender integralmente às exigências do edital/chamada **Cotas do Programa de Pós-Graduação** e às normas específicas do CNPq que regem a concessão da bolsa especificada abaixo:

BOLSA:
Processo: 142248/2018-5
Modalidade - Categoria: Doutorado - GD -
Vigência: De 01/07/2018 a 30/06/2022

Declaro ainda que me comprometo a cumpri-las, não podendo, em nenhuma hipótese, delas alegar desconhecimento.

DATA:
04 de Julho de 2018

ACEITE:

Ao enviá-lo ao CNPq, o BENEFICIÁRIO declara que leu e aceitou integralmente os termos deste documento.

BENEFICIÁRIO:

Pedro Pugliesi Abdalla

Termo de indicação registrado eletronicamente por meio da internet junto ao CNPq, pelo agente receptor 10.0.2.20(srv256.cnpq.br), mediante uso de senha pessoal do Beneficiário em 04/07/2018, originário do número IP 200.130.33.73(200.130.33.73) e número de controle 8617693686176936:1791842557-1433361746.

TERMO DE ACEITAÇÃO DE BOLSA

PRINT - PROGRAMA INSTITUCIONAL DE INTERNACIONALIZAÇÃO

Por este Termo de Aceitação de Bolsa, eu, PEDRO PUGLIESI ABDALLA, residente e domiciliado a Rua José Salomoni, na cidade de Franca, CEP 14.401-298, portador do CPF nº 407.504.838-14, aceito a bolsa de estudos concedida pela CAPES no âmbito do Programa Capes PRINT - PROGRAMA INSTITUCIONAL DE INTERNACIONALIZAÇÃO, na modalidade de DOUTORADO SANDUÍCHE , de 01/2021 a 12/2021 com o apoio da Capes, assumindo, irrevogavelmente, os compromissos e obrigações a seguir:

1. Fornecer à CAPES os documentos e informações necessários a implementação da bolsa.

2. Reconhecer que, ao aceitar esta bolsa, alguns custos podem ser gerados em meu benefício à CAPES ou ao(s) parceiro(s) internacional(is) no presente Programa, mesmo antes de minha chegada à instituição de destino.

3. Ressarcir a CAPES, ou seu(s) parceiro(s) internacional(is) no presente Programa, quaisquer recursos eventualmente recebidos por mim, ou pagos em meu benefício a terceiras partes, em caso de minha desistência da bolsa ou seu cancelamento, devidamente fundamentado, pela CAPES.

4. Respeitar todos os termos, compromissos e obrigações do Programa, descritos no Regulamento de bolsas, no edital/chamada de seleção, no Termo de Compromisso por mim assinado e em quaisquer outros instrumentos normativos aplicáveis ao Programa, como o manual do bolsista, regulamentos do programa e portarias da CAPES.

5. O(A) candidato(a) não poderá acumular bolsa ou auxílios simultaneamente à bolsa concedida pela Capes, independentemente do tipo ou finalidade dos benefícios preexistentes, devendo o(a) candidato(a) declarar a recepção de outras bolsas concedidas por órgãos ou entidades da Administração Pública federal, estadual ou municipal e, na ocasião de aprovação da bolsa, requerer a suspensão ou cancelamento do benefício preexistente, de modo que não haja acúmulo benefícios durante o período de estudos no exterior

6. Somente depois de atendidos todos os requisitos do Edital e suspensa qualquer bolsa concedida por agências de fomento no país, será realizada a implementação da bolsa concedida.

7. Estar ciente de que, conforme Portaria Capes nº 23, de 30 de janeiro de 2017, o tempo de bolsa percebido no exterior será considerado na apuração do limite de duração das bolsas, bem como considerar-se-ão também as parcelas ou mensalidades recebidas anteriormente pelo(a) bolsista, advindas de outro programa de bolsas da Capes e demais agências para o mesmo nível de curso ou modalidade de bolsa, assim como qualquer outro período subsidiado por qualquer agência ou organismo nacional ou estrangeiro para o mesmo nível de formação, mesmo em outros programas de bolsa.

8. Retornar ao Brasil em até sessenta dias após o término da concessão ou da conclusão dos trabalhos inicialmente previstos e aprovados pela Capes, o que ocorrer primeiro, sendo que esses sessenta dias serão sem ônus adicional para a Capes, sempre mantendo seus endereços e dados de contato atualizados

Ao assinar eletronicamente este documento, declare ter ciência de que a bolsa poderá ser suspensa ou cancelada no caso de infrações aos seus termos.

ANEXO C – Comprovativos de Vínculo Institucional

Universidade de São Paulo
Brasil

Janus
Sistema administrativo da Pós-graduação

Interunidades em Enfermagem

DECLARAÇÃO

Declaro, para os devidos fins que o(a) senhor(a) Pedro Pugliesi Abdalla, número USP 7126455, na presente data, é aluno(a) regularmente matriculado(a) no curso de Doutorado, no programa Enfermagem, sob a orientação do(a) Prof(a). Dr(a). Dalmo Roberto Lopes Machado.

Este documento eletrônico dispensa carimbo e assinatura. Sua autenticidade pode ser comprovada fornecendo-se o código de controle na seguinte página da Universidade de São Paulo: **https://uspdigital.usp.br/iddigital**

Documento emitido às 22:34:09 horas do dia 14/12/2021 (hora e data de Brasília).
Código de controle: DSZY - X1ZT - CFNF - 9G7N
Código de controle válido até: 13/03/2022

U. PORTO
FACULDADE DE DESPORTO
UNIVERSIDADE DO PORTO

CERTIDÃO

Matrícula

Paula Raquel Bravo de Sousa Marques, Diretora de Serviços da Faculdade de Desporto da Universidade do Porto:
Certifico, em face de arquivo respetivo que

Pedro Pugliesi Abdalla
titular do numero de identificação civil 47.751.139-9 (Brasil), de nacionalidade brasileira, se matriculou em vinte e três de novembro de dois mil e vinte no ciclo de estudos conducente ao grau de Doutor em Atividade Física e Saúde desta Faculdade, no ano letivo de dois mil e vinte a dois mil e vinte e um.
Mais se certifica que, na presente data, a matrícula se encontra válida.
A presente vai firmada com o selo branco desta Faculdade.
Esta certidão destina-se exclusivamente para efeito de concessão de residência a estudantes estrangeiros.

Faculdade de Desporto da Universidade do Porto, em 27 de novembro de 2020.

FACULDADE DE DESPORTO

mlrodrigues
N.º Cert 19766

ANEXO D – Acordo de Doutoramento em Regime de Cotutela Internacional entre a Universidade do Porto e a Universidade de São Paulo (Páginas 1 e 9)

U.PORTO

USP
Universidade de São Paulo

U.PORTO
Validado pelo SAJ
SERVIÇOS PARTILHADOS

ACORDO DE DOUTORAMENTO EM REGIME DE COTUTELA INTERNACIONAL
ENTRE
A UNIVERSIDADE DO PORTO
E A
UNIVERSIDADE DE SÃO PAULO

A **Universidade do Porto (UPorto)**, Portugal, representada pelo Prof. Dr. António Sousa Pereira, Reitor, e a Faculdade de Desporto (FADEUP), representada pelo Prof. Dr. António Manuel Fonseca, Diretor,

e

a **Universidade de São Paulo (USP)**, Brasil, representada pelo Prof. Dr. Vahan Agopyan, Reitor, a Escola de Enfermagem (EE/USP), representada pela Profª Dra. Regina Szylit, Diretora e a Escola de Enfermagem de Ribeirão Preto (EERP/USP), representada pela Profª. Dra. Maria Helena Palucci Marziale, Diretora,

celebram o presente acordo de coorientação de tese de doutoramento, relativo ao seguinte estudante de doutoramento:

Nome completo: Pedro Pugliesi Abdalla

Documento de identificação: Passaporte FO 462068, expedido pela Polícia Federal do Brasil, com data de emissão em 10/09/1990 e com validade até 09/09/2025.

Nacionalidade: Brasileira

SECÇÃO I
Condições gerais para o estabelecimento do presente acordo

ENQUADRAMENTO LEGISLATIVO
ARTIGO 1º – Diplomas legais

Ao presente acordo são aplicáveis as normas relativas aos acordos de cotutela vigentes em cada uma das instituições signatárias, designadamente:

Na Universidade do Porto:

- *Regulamento de Doutoramento em regime de Cotutela Internacional da Universidade do Porto*, de 08 de fevereiro de 2019, Regulamento Geral dos Terceiros Ciclos da Universidade do Porto, alterado por Despacho Reitoral, de 3 de outubro de 2018 e, em termos gerais, o DL nº 74/2006, na redação dada pelo DL nº 65/2018, de 16 de agosto.

Na Universidade de São Paulo:

ASSINATURAS

Aceitando na integra as condições constantes dos artigos acima referidos, as partes assinam o presente acordo em 5 (cinco) cópias de igual teor e forma, em língua portuguesa, com 2 (duas) cópias para cada instituição e 1 (uma) cópia para o estudante de doutoramento.

Declaro que li e aceito os termos deste acordo:

O estudante:

Pedro Pugliese Abdalla

Prof. Dr. Jorge Mota
Orientador de Tese

Prof. Dr. Dalmo Roberto Lopes Machado
Orientador de Tese

Prof. Dr. José Carlos Ribeiro
Diretor do Programa Doutoral

Prof. Dr. Ricardo Alexandre Arcêncio
Coordenador do Programa Doutoral

As Instituições outorgantes:

Pela Faculdade de Desporto da Universidade do Porto
Porto, 26 / 10 / 2020

Prof. Dr. António Manuel Fonseca
Diretor

Pela Escola de Enfermagem da Universidade de São Paulo
São Paulo, ____ / _______ / 2020

Profª Dra. Regina Szylit
Diretora

Pela Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo
Ribeirão Preto, 14 / 05 / 2020

Profª Dra. Maria Helena Palucci Marziale
Diretora

Pela Universidade do Porto
Porto, 02 / 11 / 2020

Prof. Dr. António Sousa Pereira
Reitor

U.PORTO Validado pelo SAJ SERVIÇOS PARTILHADOS

Pela Universidade de São Paulo
Porto, 08 / 04 / 2020.

Prof. Dr. Vahan Agopyan
Reitor

9

APÊNDICES

APÊNDICE A – Planilha automatizada (hiperlink) para normalizar e avaliar a força de idosos residentes em países de baixa e média renda.

Reference values of low allometrically adjusted grip strength to identify risk of dynapenia, frailty and sarcopenia from 13,235 older adults of low- and middle-income countries

Subject ID	Sex	Country of Birth	Body Mass (kg)	Height (m)	Grip Strength (kg)	Choose Variable to Perform Allometric Adjustment of Grip Strength	Allometrically Adjusted Grip Strength	Cut-off Point (<)	Grip Strength Classification

Authors: Pedro Pugliesi Abdalla[1256], Lucimere Bohn[56], André Pereira dos Santos[12], Marcio Fernando Tasinafo Junior[2], Leonardo Santos Lopes da Silva[2], José Augusto Gonçalves Marini[2], Ana Claudia Rossini Venturini[12], Anderson dos Santos Carvalho[3], Gustavo André Borges[4], Nilo Cesar Ramos[7], Jorge Mota[56], Dalmo Roberto Lopes Machado[1256].