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PEDRO PUGLIESI ABDALLA

Pontos de corte para identificar sarcopenia em idosos a partir da força muscular de membros superiores e inferiores normalizada

RIBEIRÃO PRETO

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Tese desenvolvida no âmbito do Acordo de Doutoramento em Regime de Cotutela internacional entre a Universidade de São Paulo[1] e a Universidade do Porto[2], apresentada ao Programa Interunidades de Doutoramento em Enfermagem da Escola de Enfermagem da Universidade de São Paulo e Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo para obtenção do título de Doutor em Ciências.

Linha de pesquisa: Fundamentos Teóricos e Filosóficos do Cuidar

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ABDALLA, Pedro Pugliesi

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RESUMO

ABDALLA, P. P. **Pontos de corte para identificar sarcopenia em idosos a partir da força muscular de membros superiores e inferiores normalizada**. 2022. 152 f. Tese (Doutorado). Escola de Enfermagem de Ribeirão Preto – Universidade de São Paulo, Ribeirão Preto, 2022.

Essa tese defende a normalização da força e massa muscular pelo tamanho corporal para minimizar o viés das dimensões corporais na funcionalidade de idosos. A tese contemplou três objetivos abordados 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 (Estudos I e II). O Estudo I envolveu 94 idosos e foram medidas a força (preensão manual, extensão de joelhos dinâmica e isocinética), o tamanho corporal e mobilidade. As estratégias de normalização para testar a associação com mobilidade foram força/tamanho corporal e alometria (força/tamanho corporal^b; sendo ^{b} o expoente alométrico). Quarenta e nove modelos válidos foram gerados 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 independente do tamanho corporal, reduzindo o enviesamento para casos extremos. Houve menor risco de diagnóstico falso-positiva/negativo. O Estudo II envolveu idosos de seis países. Os métodos foram similares ao Estudo I, mas somente foi medida 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. Os expoentes alométricos gerados para cada país foram muito próximos, confirmando a efetividade dessa estratégia. Nosso segundo objetivo foi aplicar comparativamente os expoentes alométricos propostos no Estudo I e outros da literatura, a testar sua eficácia em normalizar a força e identificar fraqueza muscular. Assim, no Estudo III, 132 idosos portugueses foram medidos em mobilidade e dimensões corporais para normalizar a força de extensão do joelho. Os pontos de corte (menor quartil de mobilidade) para fraqueza muscular derivaram da força normalizada, ou não. A força absoluta mostrou acurácia insuficiente (AUC<0.70). Expoentes alométricos estrangeiros melhoraram a acurácia na identificação de fraqueza muscular. Normalizar a força, mesmo com expoentes alométricos estrangeiros é melhor do que nenhum ajuste. Nosso terceiro objetivo foi propor estratégia simplificada para identificar a baixa massa muscular, baseada na limitação de mobilidade. Assim, para o Estudo IV foram propostos pontos de corte para o perímetro da panturrilha normalizado pelo tamanho corporal para identificar baixa massa muscular em idosas. Valores do perímetro da panturrilha de mulheres jovens foram a referência para os pontos de corte de baixa massa muscular (-2 desvio padrão). O perímetro da panturrilha normalizado pelo índice de massa corporal identificou baixa massa muscular com maior acurácia do que os valores absolutos. A normalização retirou o viés da relação de U invertido com a mobilidade, geralmente observado em valores absolutos. A precisão obtida suportou o uso do perímetro da panturrilha normalizado pelo índice de massa corporal para identificar baixa massa muscular em mulheres idosas. Por conclusão, a estratégia alométrica evita erros na classificação da baixa força muscular de idosos, decorrentes do viés causado pelo tamanho corporal. Possivelmente, isso poderá reduzir diagnósticos falso positivos e negativos de sarcopenia em idosos com dimensões corporais extremas.

Palavras-chave: Alometricamente normalizado. Avaliação. Incapacidade. Fragilidade. Funcionalidade/Estado funcional.

ABSTRACT

ABDALLA, P. P. **Cut-off points to identify sarcopenia in older adults from normalized upper and lower limbs muscular strength**. 2022. 152 f. Tese (Doutorado). Escola de Enfermagem de Ribeirão Preto – Universidade de São Paulo, Ribeirão Preto, 2022.

This thesis defends the normalization of muscle strength and mass by body size to minimize the body dimensions bias in the functionality of older adults. The thesis contemplated three objectives addressed in four original studies. The first objective was to propose allometric exponents to normalize upper and lower limb strength by body size and generate cut-off points for muscle weakness in older adults (Studies I and II). Study I involved 94 older adults and were measured strength (handgrip, dynamic, and isokinetic knee extension), body size, and mobility. The normalization strategies to test the association with mobility were strength/body size and allometry (strength/body size^b; with ^{b} being the allometric exponent). Forty-nine valid models were generated to identify muscle weakness. Normalization increased the accuracy of cut-offs in women but not in men. However, adjustments in men also made strength independent of body size, reducing the bias for extreme cases. There was a lower risk of false-positive/negative diagnosis. Study II involved older adults from six countries. The methods were similar to Study I, but only grip strength, height, and body mass were measured. The non-linear relationship between strength and body mass was confirmed, except for height. Allometric adjustments made muscle strength independent of body size. The allometric exponents generated for each country were very close, confirming the effectiveness of this strategy. Our second objective was to comparatively apply the allometric exponents proposed in Study I and others in the literature, to test their effectiveness in normalizing strength and identifying muscle weakness. Thus, in Study III, 132 older Portuguese adults were measured in mobility and body dimensions to normalize knee extension strength. Cut-off points (lowest quartile of mobility) for muscle weakness were derived from normalized strength or not. Absolute strength showed insufficient accuracy (AUC<0.70). Foreign allometric exponents improved accuracy in identifying muscle weakness. Normalizing the strength, even with foreign allometric exponents, is better than no adjustment. Our third objective was to propose a simplified strategy to identify low muscle mass, based on mobility limitation. Thus, for Study IV, cut-off points were proposed for calf circumference normalized by body size to identify low muscle mass in older women. Calf circumference values of young women were the reference for low muscle mass cut-off points (-2 standard deviation). The calf circumference normalized by the body mass index identified low muscle mass with greater accuracy than the absolute values. Normalization removed the bias from the inverted U relationship with mobility, usually seen in absolute values. The accuracy obtained supports the use of calf circumference normalized by body mass index to identify low muscle mass in older women. In conclusion, the allometric strategy avoids errors in the classification of low muscle strength in older adults, resulting from the bias caused by body size. Possibly, allometry could reduce false positive and negative diagnoses of sarcopenia in older adults with extreme body dimensions.

Keywords: Allometrically normalized. Assessment. Inability. Frailty. Functionality/Functional state.

RESUMEN

ABDALLA, P. P. **Puntos de corte para rastreo de sarcopenia en ancianos a partir de la fuerza muscular de los miembros superiores e inferiores normalizada**. 2022. 152 f. Tese (Doutorado). Escola de Enfermagem de Ribeirão Preto – Universidade de São Paulo, Ribeirão Preto, 2022.

Esta tesis defiende la normalización de la fuerza y la masa muscular por tamaño corporal para minimizar el sesgo de las dimensiones corporales en la funcionalidad de las personas mayores. La tesis contemplaba tres objetivos en cuatro estudios originales. El primer fue proponer exponentes alométricos para normalizar la fuerza de miembros superiores e inferiores por tamaño corporal y generar puntos de corte para la debilidad muscular (Estudios I y II). El estudio I involucró a 94 personas mayores y se midió la fuerza (agarre, extensión de rodilla dinámica e isocinética), el tamaño corporal y la movilidad. Las estrategias de normalización para probar la asociación con la movilidad fueron fuerza/tamaño corporal y alometría (fuerza/tamaño corporal^b; siendo ^{b} el exponente alométrico). Se generaron cuarenta y nueve modelos válidos para identificar la debilidad muscular. La normalización aumentó la precisión de los puntos de corte en las mujeres pero no en los hombres. Sin embargo, los ajustes en los hombres también hicieron que la fuerza fuera independiente del tamaño del cuerpo, lo que redujo el sesgo para casos extremos. Hubo un menor riesgo de diagnóstico falso positivo/negativo. El estudio II involucró seis países. Los métodos fueron similares a los del Estudio I, pero solo se midieron la fuerza de agarre, la altura y la masa corporal. Se confirmó la relación no lineal entre la fuerza y la masa corporal, a excepción de la altura. Los ajustes alométricos hicieron que la fuerza muscular fuera independiente del tamaño del cuerpo. Los exponentes alométricos generados para cada país fueron muy cercanos, lo que confirma la efectividad de esta estrategia. Nuestro segundo objetivo fue aplicar comparativamente los exponentes alométricos propuestos en el Estudio I y otros en la literatura, para probar su efectividad en la normalización de la fuerza e identificación de la debilidad muscular. Así, en el Estudio III, 132 portugueses fueron medidos en movilidad y dimensiones corporales para normalizar la fuerza de extensión de la rodilla. Los puntos de corte (cuartil más bajo de movilidad) para la debilidad muscular se derivaron o no de la fuerza normalizada. La fuerza absoluta mostró una precisión insuficiente (AUC<0,70). Los exponentes alométricos mejoraron la precisión en la identificación de la debilidad muscular. Normalizar la fuerza es mejor que ningún ajuste. Nuestro tercer objetivo fue proponer una estrategia simplificada para identificar la baja masa muscular, basada en la limitación funcional. Por lo tanto, para el Estudio IV, se propusieron puntos de corte para la circunferencia de la pantorrilla normalizada por el tamaño corporal para identificar la baja masa muscular en mujeres. Los valores de la circunferencia de la pantorrilla de las jóvenes fueron la referencia para los puntos de corte de masa muscular baja (-2 desviación estándar). La circunferencia de la pantorrilla normalizada por el índice de masa corporal identificó baja masa muscular con mayor precisión que los valores absolutos. La normalización eliminó el sesgo de la relación de U invertida con la movilidad. La precisión obtenida apoyó el uso de la circunferencia de la pantorrilla normalizada para identificar la baja masa muscular en mujeres de edad avanzada. En conclusión, la estrategia alométrica evita errores en la clasificación de la baja fuerza muscular en ancianos, resultantes del sesgo causado por el tamaño corporal. Posiblemente, alometria podría reducir los diagnósticos falsos positivos y negativos de sarcopenia en personas mayores con dimensiones corporales extremas.

Palabras clave: Normalizado alométricamente. Evaluación. Incapacidad. Fragilidad. Funcionalidad/Estado funcional.

LISTA DE FIGURAS

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

DISCUSSÃO

4.4 VARIABILIDADE DOS EXPOENTES ALOMÉTRICOS PROPOSTOS PARA NORMALIZAR A FORÇA MUSCULAR: UMA RELAÇÃO AOS ACHADOS DA LITERATURA

LISTA DE TABELAS

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

Estudo Original II - Adjusting grip strength to body size: Analyses from 6 countries

LISTA DE EQUAÇÕES

INTRODUÇÃO

DISCUSSÃO

4.3 DIFERENTES FORMAS DE GERAR E INTERPRETAR OS EXPOENTES ALOMÉTRICOS

LISTA DE ABREVIATURAS

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

_{knee extension}PT^{60º/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

SUMÁRIO

1 INTRODUÇÃO

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 (WHO, 2014). Em países desenvolvidos também haverá aumento do número de idosos, contudo, em menor expressão. Isso ocorrerá porque os países desenvolvidos já envelheceram. 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 visualmente, 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), como aprofundado na discussão da presente tese. No entanto, critérios relacionados a capacidade funcional como a força muscular e o desempenho físico são agora obrigatórios para confirmar a sarcopenia.

Os consensos/consórcios internacionais mais conhecidos para identificar sarcopenia são determinados por *task-force groups*, como demonstrado no Quadro 1.

Quadro 1 - Consensos e consórcios internacionais para identificar sarcopenia e os critérios/valores referenciais para a identificação.

Consenso/consórcio	Critério 1	Critério 2	Critério 3
European Working Group on Sarcopenia in Older People (EWGSOP) (CRUZ-JENTOFT *et al.*, 2010)	MASSA MUSCULAR DXA (massa muscular apendicular/estatura²): ♂: 7,26 kg/m² ♀: 5,5 kg/m² Entre outros valores ou BIA (massa muscular esquelética/estatura² ♂: 8,87 kg/m² ♀: 6,42 kg/m² Entre outros valores ou Outros (tomografia computadorizada, ressonância magnética, potássio corporal).	FORÇA MUSCULAR Força de preensão manual: ♂: 30 kg ♀: 20 kg Entre outros valores por quartis de IMC ou Outros (flexão/extensão de joelho, pico de fluxo expiratório	PERFORMANCE FÍSICA SPPB: ≤8 ou Velocidade usual de marcha: <0,8 m/s (em 4 metros) Entre outros valores ou Outros (TUG, *stair climb power test*)
Presarcopenia	↓		
Sarcopenia	↓	↓	Ou ↓
Sarcopenia severa	↓	↓	↓
European Society for Clinical Nutrition and Metabolism Special Interest Group on cachexia/anorexia in chronic wasting diseases (ESPEN) (MUSCARITOLI *et al.*, 2010)	MASSA MUSCULAR Massa muscular ≥ desvios padrão abaixo da média medida em adultos jovens do mesmo sexo e origem étnica	VELOCIDADE USUAL DE MARCHA <0,8 m/s (em 4 metros) Entre outros valores Pode ser substituído por testes funcionais bem estabelecidos de avaliação geriátrica	-
Sarcopenia	↓	↓	-

Consenso/consórcio	Critério 1	Critério 2	Critério 3
International Working Group on Sarcopenia (IWGS) (FIELDING *et al.*, 2011)	MASSA MUSCULAR DXA (Massa muscular apendicula/estatura²: ♂: 7,23 kg/m² e ♀: 5,67 kg/m² ou Massa isenta de gordura/estatura² abaixo do 20º percentil de adultos jovens)	PERFOMANCE FÍSICA Velocidade usual de marcha: <1,0 m/s (em 4 metros)	-
Sarcopenia	↓	↓	-
Society of Sarcopenia, Cachexia and Wasting Disorders (SCWD) (MORLEY *et al.*, 2011)	MASSA MUSCULAR DXA (Massa muscular apendicular/estatura² ≤2 desvios padrão em comparação com jovens saudáveis de 20 a 30 anos): ♂: 7,26 kg/m² ♀: 5,45 kg/m² ou Outros (tomografia computadorizada, ressonância magnética, ultrasom)	MOBILIDADE Velocidade usual de marcha: <1,0 m/s (4 a 6 metros) ou Teste de caminhada de seis minutos: <400 m	-
Sarcopenia	↓	↓	-
Foundation for the National Institutes of Health (FNIH) (DAM *et al.*, 2014)	PERFORMANCE FÍSICA Velocidade usual de marcha: ≤0,8 m/s (4 a 6 metros)	FORÇA MUSCULAR Força de preensão manual: ♂: 26 kg ♀: 16 kg	MASSA MUSCULAR DXA: Massa muscular apendicular/IMC: ♂: 0,789 ♀: 0,512 Massa muscular apendicular: ♂: 19,75 kg ♀: 15,02 kg
Sarcopenia	↓	↓	↓
Sarcopenia	-	↓	↓
Asian Working Group for Sarcopenia (AWGS) (CHEN *et al.*, 2014)	MASSA MUSCULAR DXA (massa muscular apendicular/estatura²): ♂: 7,0 kg/m² ♀: 5,4 kg/m² ou BIA (massa muscular apendicular/estatura² ♂: 7,0 kg/m² ♀: 5.7 kg/m²	FORÇA MUSCULAR Força de preensão manual: ♂: <26 kg ♀: <18 kg	PERFORMANCE FÍSICA Velocidade usual de marcha: ≤0,8 m/s (em 6 metros) Entre outros valores
Sarcopenia	↓	↓	ou ↓
European Working Group on Sarcopenia in Older People (EWGSOP2) (CRUZ-JENTOFT *et al.*, 2018)	FORÇA MUSCULAR Força de preensão manual: ♂: 27 kg ♀: 16 kg ou Teste de levantar da cadeira (5 repetições):	MASSA MUSCULAR DXA (massa muscular apendicular/estatura²): ♂: 7,0 kg/m² ♀: 5,5 kg/m² massa muscular apendicular: ♂: 20,0 kg/m² ♀: 15,0 kg/m²	PERFORMANCE FÍSICA Velocidade usual de marcha: <0,8 m/s (em 4 metros) Entre outros valores ou SPPB:

Consenso/consórcio	Critério 1	Critério 2	Critério 3
	>15 s ou Outros (torque isométrico dos membros inferiores)	Entre outros valores ou Perímetro da panturrilha: <31 cm Outros (BIA, tomografia computadorizada, ressonância magnética, teste de diluição de creatina, ultrasom, biomarcadores)	≤8 ou TUG: ≥20 s ou Teste de caminhada de 400 m: Não conclusão ou ≥6 min para conclusão Outros
Provável sarcopenia	↓		
Sarcopenia	↓	↓	
Sarcopenia severa	↓	↓	↓
Asian Working Group for Sarcopenia (AWGS) (CHEN *et al.*, 2020)	MASSA MUSCULAR DXA (massa muscular apendicular/estatura²): ♂: 7,0 kg/m² ♀: 5,4 kg/m² ou Massa muscular apendicular/IMC: ♂: 0,789 ♀: 0,512 ou BIA (massa muscular apendicular/estatura²): ♂: 7,0 kg/m² ♀: 5,7 kg/m²	FORÇA MUSCULAR Força de preensão manual: ♂: <28 kg ♀: <18 kg	PERFORMANCE FÍSICA Velocidade usual de marcha: <1,0 m/s (em 6 metros) Entre outros valores ou Teste de levantar da cadeira (5 repetições): ≥12 s ou SPPB: ≤9
Possível sarcopenia		↓	ou ↓
Sarcopenia	↓	↓	ou ↓
Sarcopenia severa	↓	↓	↓
Sarcopenia Definition and Outcomes Consortium (SDOC) (BHASIN *et al.*, 2020)	FORÇA DE PREENSÃO MANUAL Absoluta: ♂: <35,5 kg ♀: <20,0 kg ou Normalizada pelo IMC: ♂: <1,05 ♀: <0,79 ou Normalizada pelo peso corporal: ♂: <0,45 ♀: <0,34	VELOCIDADE USUAL DE MARCHA <0,8 m/s	-
Sarcopenia	↓	↓	-

DXA: absorciometria radiológica de dupla energia; BIA: Bioimpedância elétrica; ♂: homens; ♀: mulheres; IMC: índice de massa corporal; SPBB: *Short Physical Performance Battery*; TUG: *timed-up and go test*;

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).

A prevalência da sarcopenia pode variar a depender da população analisada e do critério/consórcio adotado, bem como os valores referenciais utilizados para identificação. Por exemplo, um estudo com idosos americanos, italianos e franceses mostrou prevalência entre 5 e 50% dos casos (VON HAEHLING; MORLEY; ANKER, 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 (KITAMURA *et al.*, 2021; LAURETANI *et al.*, 2003; WU *et al.*, 2014). Indivíduos com sarcopenia tem maiores riscos de perda da independência (razão de riscos em homens de 1,6; e em mulheres de 1,7) (KITAMURA *et al.*, 2021). 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; MORLEY; VON HAEHLING, 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; BASTOS; VOLPE, 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; TOTTERMAN; THORNTON, 1996). O exercício de força promove adaptações positivas em indivíduos com mais de 75 anos (STEWART; SAUNDERS; GREIG, 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 parâmetros 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 ($\leq$ 24; 24,1 a 26; 26,1 a 28 e >28 para homens e $\leq$ 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 (SAMPAIO, R. A. C. *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; 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 *et al.*, 2020b), 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. A alometria é um modelo matemático que descreve como as características dos seres vivos mudam de acordo com seu tamanho. É utilizada para entender a relação entre o tamanho de uma parte do corpo e o corpo total, mas também entre uma característica fisiológica (força muscular) e o tamanho corporal.

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 (^{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 (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 *et al.*, 2020b; 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:

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

(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 2,39 (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 0,56 (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 pela SCWD (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 (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.

1.1 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; HENDRICKX; WATERS, 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; MYERS; SCHENKMAN, 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; 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 em desenvolvimento. 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 de mobilidade de idosos (ABDALLA *et al.*, 2020b). 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).

2 OBJETIVOS

2.1 OBJETIVO GERAL

Propor modelos para força e a massa muscular normalizadas pelo tamanho corporal para identificar sarcopenia em idosos.

2.2 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 da força normalizada pelo tamanho corporal proposto comparativamente a outros modelos da literatura numa população estrangeira de idosos, para testar sua eficácia em identificar a fraqueza muscular;

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

3 ORGANIZAÇÃO LÓGICA DO CONJUNTO DE ARTIGOS PUBLICADOS (n=3) E SUBMETIDO (n=1)

As intenções que levaram a inclusão dos 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 *et al.*, 2020b). Contudo, existem outras variáveis associadas com a funcionalidade física [massa gorda (BOUCHARD *et al.*, 2007), massa isenta de gordura (BROADWIN; GOODMAN-GRUEN; SLYMEN, 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 (e.g., tamanho corporal), genéticos e sociais (e.g., renda) entre países desenvolvidos e em desenvolvimento impactam na força (KOOPMAN *et al.*, 2015), sendo necessário propor expoentes alométricos e pontos de corte específicos para países em desenvolvimento (objetivo do Estudo Original II). Expoentes alométricos oriundos de países desenvolvidos (DAVIES; DALSKY, 1997; SEGAL *et al.*, 2008) e em desenvolvimento (ABDALLA *et al.*, 2021a) 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; BIELEMANN; GONZALEZ, 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; SAMPAIO, L. S. *et al.*, 2017). Apesar de se associarem com mobilidade (TSAI; LAI; CHANG, 2012), a relação se dá na forma de U-invertido (PÉREZ-ZEPEDA; GUTIÉRREZ-ROBLEDO, 2016), o que exigiria ponto de corte duplo (um para valores baixos, como já existente, e outro para valores elevados). Pensou-se então em se ao normalizar o perímetro da panturrilha pelo tamanho corporal, poderia se linearizar essa relação (objetivo do Estudo Original IV).

3.1 Estudo original I - IDENTIFICATION OF MUSCLE WEAKNESS IN OLDER ADULTS FROM NORMALIZED UPPER AND LOWER LIMBS STRENGTH: A CROSS-SECTIONAL STUDY

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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; STALLING; BAMMANN, 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) (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; 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 *et al.*, 2020b). This is a false positive muscle weakness diagnostic, that frequently leads to an unnecessarily utilization of public health resources, contributing to health burden (ABDALLA *et al.*, 2021b). 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 *et al.*, 2020b). These limitations are a consequence of the nonlinear relationship between muscle strength and body-size variables (ABDALLA *et al.*, 2020b; FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; 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 *et al.*, 2020b; FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; 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; 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 *et al.*, 2020b; 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 *et al.*, 2020b). Besides, important body-size variables related to mobility and ADL [e.g. fat mas (BOUCHARD *et al.*, 2007), FFM (BROADWIN; GOODMAN-GRUEN; SLYMEN, 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 (CAAE: 54345016.6.3001.5440) and EERP-USP (CAAE: 23987519.5.0000.5393). 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; MINAGAR; HEILMAN, 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; HAN; DEURENBERG, 1996; SEGAL $et\ al.$, 2008; WHO EXPERT CONSULTATION,

2004), and involved anthropometric measurements (LOHMAN; ROCHE; MARTORELL, 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 (LOHMAN; ROCHE; MARTORELL, 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; HAN; DEURENBERG, 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 (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: $1RM = weight\ lifted/(1.0278 - [0.0278 * n^o\ of\ reps])$ (BRZYCKI, 1993). The detailed protocol was published elsewhere (ABDALLA *et al.*, 2020b). 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 *et al.*, 2020a). 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) (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≤0.30) (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
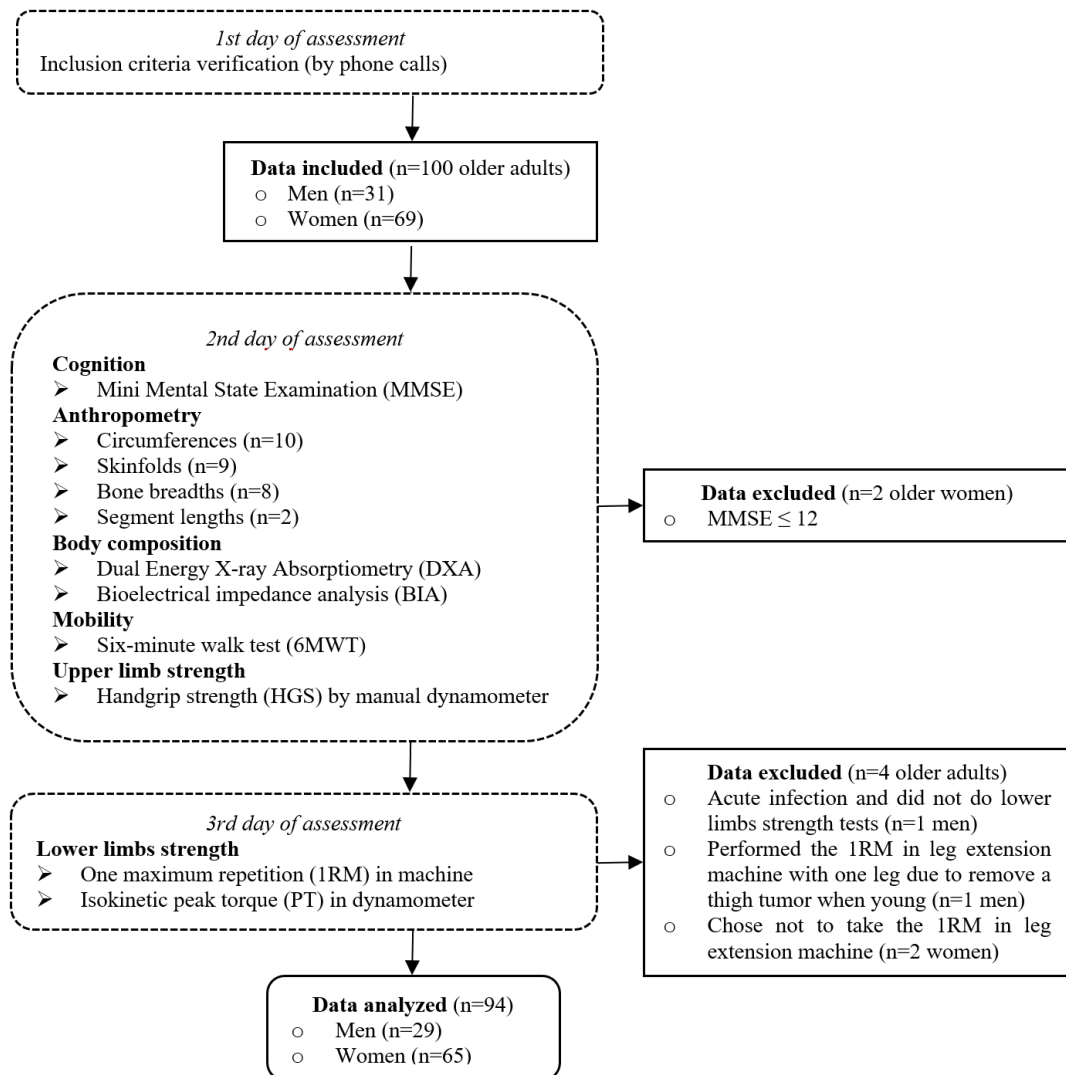
Sample characterization according to sex is shown in Table 2. About main outcome of the study, twenty-five women (38.5%) and seven men (24.1%) had functional limitation (6MWT<400 m).

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[†]
SA (m²)	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[†]

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)
CAMA (cm²)	37.1	32.7	41.6	11.7	32.2	29.9	34.5	9.2	0.37[†]	0.33[†]	0.40[†]
AFA (cm²)	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/height² (kg/m²)	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		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
/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		0.81[†]	4.22	86	68	0.70[*]	1.40	60	75
/bitrochanteric breadth	(mm)	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

Variable	Unit	Men (n=29)				Women (n=65)			
		AUC	Cut-off point ($\leq$)	Sens (%)	Spe (%)	AUC	Cut-off point ($\leq$)	Sens (%)	Spe (%)
/FFM[BAUMGARTNER et al., 1991]	(kg)	0.78^*	1.13	83	73	$0.75^\dagger$	0.83	76	64
/body mass$^{0.44}$		0.75^*	9.04	86	77	0.71^*	6.03	76	63
/body mass$^{0.67}$ [JARIC, 2003]	(kg)	0.78^*	3.40	86	77	$0.73^\dagger$	2.28	76	65
/body mass$^{0.96}$ [ABDALLA et al., 2020]		0.77^*	1.00	86	68	$0.75^\dagger$	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)	$0.93^\dagger$	54.1	86	95	$0.74^\dagger$	44.1	64	75
/knee height	(cm)	$0.94^\dagger$	1.83	100	86	$0.75^\dagger$	1.44	68	73
/SA	(m²)	$0.94^\dagger$	56.9	100	82	$0.81^\dagger$	36.3	64	88
/FFM [LEAN et al., 1996]	(kg)	$0.93^\dagger$	1.79	86	95	$0.81^\dagger$	1.84	76	80
/left leg LST		0.82^*	0.015	100	55	$0.76^\dagger$	0.012	68	80
/right leg LST	(g)	0.77^*	0.015	100	50	$0.78^\dagger$	0.013	76	78
/legs LST		0.81^*	0.0063	71	82	$0.77^\dagger$	0.0065	76	78
/ASM		0.81^*	4.66	71	86	$0.77^\dagger$	5.01	76	78
/FFM [BAUMGARTNER et al., 1991]	(kg)	$0.93^\dagger$	1.63	83	95	$0.85^\dagger$	1.60	88	77
/FFM [DXA]		$0.84^\dagger$	2.08	100	59	$0.79^\dagger$	1.89	76	75
/body mass$^{0.67}$ [DAVIES; DALSKY, 1997]		$0.93^\dagger$	5.06	86	95	$0.82^\dagger$	3.71	68	88
/body mass$^{0.72}$ [DAVIES; DALSKY, 1997]		$0.94^\dagger$	4.1	86	95	$0.82^\dagger$	3.14	72	85
/body mass$^{0.74}$ [DAVIES; DALSKY, 1997]	(kg)	$0.93^\dagger$	3.77	86	95	$0.82^\dagger$	2.87	72	85
/body mass$^{0.67}$ [JARIC, 2003]		$0.93^\dagger$	5.06	86	95	$0.82^\dagger$	3.71	68	88
/height$^{3.27}$	(m)	$0.86^\dagger$	19.2	100	77	$0.74^\dagger$	17.4	72	65
/knee height$^{1.82}$	(cm)	$0.90^\dagger$	0.068	100	86	$0.74^\dagger$	0.053	64	75
/half arm span$^{1.62}$		$0.88^\dagger$	0.076	100	73	$0.75^\dagger$	0.066	84	58
/biacromial breadth$^{2.15}$	(mm)	$0.82^\dagger$	0.038	86	68	$0.77^\dagger$	0.03	76	73
/bimalleolar breadth$^{1.54}$		0.81^*	5.04	86	73	$0.80^\dagger$	4.64	92	60
/(body mass*height)$^{0.43}$	(kg*m)	$0.94^\dagger$	13	100	82	$0.80^\dagger$	10.5	84	65
/SA$^{0.83}$	(m²)	$0.94^\dagger$	53.8	86	95	$0.80^\dagger$	50	84	65
/left leg LST$^{0.43}$		$0.92^\dagger$	2.26	100	77	$0.77^\dagger$	1.83	76	70
/right leg LST$^{0.48}$	(g)	$0.90^\dagger$	1.39	100	73	$0.78^\dagger$	1.16	80	70
/legs LST$^{0.47}$		$0.92^\dagger$	1.07	100	73	$0.77^\dagger$	0.87	76	70

*p<0.05 and †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)

Upper limb   **Lower limbs**

HGS   **1RM**   **PT**

(a) *HGS (AUC=0.74); *HGS/forearm circumference (AUC=0.74)

(b) *1RM (AUC=0.75); †1RM/triceps skinfold (AUC=0.81); *†1RM/body mass$^{0.67}$ (JARIC, 2003) (AUC=0.78)

(c) †PT (AUC=0.93); †PT/knee height (AUC=0.94); †PT/body mass*height$^{0.43}$ (AUC=0.94)

(d) HGS (AUC=0.61); *†HGS/forearm circumference (AUC=0.70)

(e) *1RM (AUC=0.67); *†§1RM/body mass (AUC=0.76); *†1RM/body mass$^{0.67}$ (JARIC, 2003) (AUC=0.73)

(f) †PT (AUC=0.74); *†§PT/FFM (BAUMGARTNER et al., 1991) (AUC=0.85); *†PT/body mass$^{0.72}$ (DAVIES; DALSKY, 1997) (AUC=0.82)

True positive rate (Sensitivity) — *Men* / *Women*

False positive rate (1-Specificity)

*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 et al., 2020b), 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; PUA, 2006), 1RM (2020b), 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; PAVOL; GRABINER, 2002), while the linear relationship is characterized when the exponent is ≥1.00 (OWINGS; PAVOL; GRABINER, 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 ($^b \geq 1.00$) 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 *et al.*, 2020a; 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 ($\leq$85.4 Nm), this older man has muscle weakness confirmed. However, when considered the normalized PT/([body mass*height]$^{0.43}$), the adjusted value (14.1 Nm/kg*m) is above of the cut-off point (13.0 Nm/kg*m; Table 3). Normalization would also avoid false negative cases, for large body size of older adults. For example, if an older woman with 90 kg performs 1RM of 38.2 kg and considering our absolute cut-off point ($\leq$38.1 kg), this older woman does not have weakness. However, when considered the normalized (1RM/body mass$^{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.

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 R²
		β	Standard error	LL	UL		
	Dependent variable: HGS (ln kg)						
1	Constant	3.040[†]	0.669	1.711	4.368		
	Sex	0.407[†]	0.046	0.315	0.499	1.129	
	Age	-0.012[*]	0.003	-0.019	-0.005	1.181	0.53
	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		
	Sex	0.282[†]	0.057	0.169	0.395	1.919	
	Age	-0.010[*]	0.003	-0.017	-0.004	1.143	0.58
	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		
	Sex	0.381[†]	0.050	0.281	0.480	1.334	
	Age	-0.012[†]	0.003	-0.019	-0.006	1.128	0.54
	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		
	Sex	0.413[†]	0.045	0.323	0.502	1.084	
	Age	-0.012[*]	0.003	-0.018	-0.005	1.186	0.54
	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		
	Sex	0.424[†]	0.047	0.329	0.518	1.143	
	Age	-0.014[†]	0.003	-0.021	-0.007	1.110	0.52
	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		
	Sex	0.323[†]	0.057	0.210	0.435	1.779	
	Age	-0.013[†]	0.003	-0.019	-0.006	1.061	0.56
	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		
	Sex	0.283[†]	0.052	0.179	0.387	1.705	
	Age	-0.010[*]	0.003	-0.016	-0.003	1.161	0.61
	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		
	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	0.54
	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		
	Sex	0.413[†]	0.059	0.296	0.53	1.752	
	Age	-0.015[†]	0.003	-0.021	-0.008	1.041	0.52
	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		
	Sex	0.425[†]	0.049	0.329	0.522	1.197	
	Age	-0.015[†]	0.003	-0.021	-0.008	1.035	0.52
	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	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	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		
	Sex	0.431†	0.053	0.327	0.536	1.412	
	Age	-0.014†	0.003	-0.021	-0.008	1.085	0.52
	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		
	Sex	1.253†	0.312	0.632	1.874	53.064	
	Age	-0.010*	0.004	-0.017	-0.003	1.302	0.55
	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		
	Sex	1.059†	0.284	0.495	1.624	42.851	
	Age	-0.011*	0.004	-0.018	-0.004	1.246	0.54
	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		
	Sex	0.403†	0.058	0.287	0.519	1.737	
	Age	-0.015†	0.003	-0.021	-0.008	1.041	0.52
	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		
	Sex	0.348†	0.052	0.244	0.452	1.506	
	Age	-0.010*	0.004	-0.017	-0.003	1.295	0.56
	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	
17	Constant	0.536	1.234	-1.917	2.988		
	Sex	0.414†	0.044	0.327	0.501	1.072	
	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	
18	Constant	2.339*	0.669	1.009	3.668		
	Sex	0.337†	0.054	0.231	0.444	1.593	
	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	
19	Constant	3.443†	0.565	2.32	4.566		
	Sex	0.375†	0.059	0.259	0.492	1.792	
	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	
20	Constant	3.190†	0.528	2.141	4.239		
	Sex	0.355†	0.057	0.242	0.468	1.715	
	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	
21	Constant	2.929*	0.855	1.230	4.628		
	Sex	0.384†	0.054	0.278	0.491	1.504	
	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	
22	Constant	2.709†	0.656	1.407	4.012		
	Sex	0.384†	0.048	0.289	0.479	1.243	
	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	
23	Constant	3.641†	0.345	2.955	4.327		
	Sex	0.388†	0.048	0.293	0.483	1.222	
	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	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	ln SA (m²)	0.489*	0.214	0.064	0.915	1.317	
24	Constant	3.417†	0.696	2.035	4.799		
	Sex	0.405†	0.050	0.306	0.504	1.276	
	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	
25	Constant	3.773†	0.427	2.925	4.622		
	Sex	0.414†	0.047	0.321	0.508	1.141	
	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	
26	Constant	4.087†	0.375	3.342	4.832		
	Sex	0.432†	0.051	0.331	0.532	1.299	
	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 (cm²)	0.010	0.058	-0.106	0.126	1.353	
27	Constant	1.747	0.897	-0.036	3.530		
	Sex	0.242*	0.080	0.083	0.401	3.528	
	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(LEAN et al., 1996) (kg)	0.531*	0.191	0.152	0.910	3.814	
28	Constant	3.934†	0.391	3.157	4.711		
	Sex	0.447†	0.053	0.342	0.551	1.414	
	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(LEAN et al., 1996) (kg)	0.048	0.067	-0.085	0.180	1.415	
29	Constant	1.774*	0.861	0.063	3.485		
	Sex	0.298†	0.063	0.174	0.423	2.181	
	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	
30	Constant	1.864*	0.917	0.042	3.685		
	Sex	0.310†	0.063	0.184	0.436	2.187	
	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	
31	Constant	1.314	1.213	-1.096	3.723		
	Sex	0.326†	0.062	0.203	0.448	2.049	
	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	
32	Constant	1.202	1.271	-1.324	3.728		
	Sex	0.319†	0.064	0.192	0.446	2.211	
	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	
33	Constant	1.418	0.995	-0.559	3.394		
	Sex	0.295†	0.064	0.167	0.422	2.287	
	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	
34	Constant	0.879	1.365	-1.835	3.592		
	Sex	0.317†	0.064	0.190	0.443	2.194	
	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	
35	Constant	2.917†	0.534	1.856	3.979		
	Sex	0.303†	0.065	0.174	0.432	2.299	
	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	
36	Constant	3.808†	0.463	2.888	4.729		
	Sex	0.400†	0.056	0.288	0.511	1.601	
	Age	-0.013†	0.003	-0.02	-0.007	1.179	0.52
	Physical activity level	0.061	0.146	-0.23	0.352	1.070	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	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		
	Sex	0.375†	0.051	0.273	0.477	1.503	
	Age	-0.009*	0.003	-0.016	-0.002	1.235	0.58
	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		
	Sex	0.325†	0.060	0.205	0.445	1.979	
	Age	-0.011*	0.003	-0.018	-0.004	1.231	0.55
	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		
	Sex	0.438†	0.050	0.338	0.537	1.268	
	Age	-0.014†	0.003	-0.021	-0.008	1.077	0.52
	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		
	Sex	0.501†	0.083	0.336	0.666	1.129	
	Age	-0.027†	0.006	-0.039	-0.015	1.181	0.43
	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		
	Sex	0.305*	0.104	0.098	0.512	1.919	
	Age	-0.025†	0.006	-0.037	-0.013	1.143	0.48
	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		
	Sex	0.506†	0.092	0.323	0.688	1.334	
	Age	-0.03†	0.006	-0.042	-0.018	1.128	0.41
	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		
	Sex	0.511†	0.080	0.352	0.671	1.084	
	Age	-0.026†	0.006	-0.038	-0.014	1.186	0.45
	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		
	Sex	0.513†	0.085	0.345	0.681	1.143	
	Age	-0.029†	0.006	-0.041	-0.017	1.110	0.42
	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		
	Sex	0.524†	0.084	0.356	0.692	1.128	
	Age	-0.031†	0.006	-0.042	-0.019	1.045	0.41
	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		
	Sex	0.360*	0.102	0.157	0.563	1.779	
	Age	-0.028†	0.006	-0.04	-0.017	1.061	0.46
	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		
	Sex	0.324*	0.097	0.130	0.517	1.705	
	Age	-0.024†	0.006	-0.036	-0.012	1.161	0.49
	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		
	Sex	0.647†	0.101	0.447	0.847	1.640	
	Age	-0.03†	0.006	-0.041	-0.018	1.058	0.43
	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	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	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	
	Constant	5.74[†]	0.650	4.448	7.033		
	Sex	0.563[†]	0.103	0.358	0.767	1.660	
11	Age	-0.031[†]	0.006	-0.043	-0.02	1.026	0.41
	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	
	Constant	5.806[†]	0.604	4.606	7.007		
	Sex	0.556[†]	0.105	0.347	0.765	1.737	
12	Age	-0.031[†]	0.006	-0.043	-0.02	1.041	0.41
	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	
	Constant	-0.722	2.76	-6.207	4.763		
	Sex	0.417[†]	0.095	0.228	0.605	1.506	
13	Age	-0.024[†]	0.006	-0.037	-0.012	1.295	0.45
	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	
	Constant	3.329	2.313	-1.267	7.924		
	Sex	0.532[†]	0.082	0.369	0.695	1.072	
14	Age	-0.03[†]	0.006	-0.042	-0.018	1.101	0.42
	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	
	Constant	3.52[*]	1.23	1.076	5.965		
	Sex	0.423[†]	0.098	0.228	0.619	1.593	
15	Age	-0.03[†]	0.006	-0.041	-0.018	1.043	0.44
	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	
	Constant	5.702[†]	1.028	3.660	7.744		
	Sex	0.529[†]	0.107	0.316	0.741	1.792	
16	Age	-0.031[†]	0.006	-0.043	-0.02	1.037	0.41
	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 (m²)	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 (cm²)	0.082	0.137	-0.19	0.353	1.18	
23	Constant	1.932	1.625	-1.297	5.161		0.45
	Sex	0.234	0.145	-0.054	0.522	3.528	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
	Age	-0.021[*]	0.007	-0.035	-0.008	1.529	
	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	
24	Constant	3.787[*]	1.603	0.603	6.972		0.42
	Sex	0.427[†]	0.117	0.195	0.659	2.181	
	Age	-0.028[†]	0.006	-0.041	-0.016	1.174	
	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	
25	Constant	3.986[*]	1.698	0.613	7.359		0.42
	Sex	0.444[†]	0.117	0.211	0.677	2.187	
	Age	-0.028[†]	0.006	-0.041	-0.015	1.258	
	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	
	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	
	ln height (m)	3.268[*]	0.908	1.465	5.071	1.891	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
3	Constant	3.966*	1.631	0.725	7.206		
	Sex	0.499†	0.093	0.314	0.684	1.334	
	Age	-0.026†	0.006	-0.039	-0.014	1.128	0.40
	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		
	Sex	0.522†	0.082	0.360	0.683	1.084	
	Age	-0.023†	0.006	-0.035	-0.010	1.186	0.43
	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		
	Sex	0.517†	0.086	0.347	0.687	1.143	
	Age	-0.026†	0.006	-0.038	-0.014	1.110	0.40
	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		
	Sex	0.528†	0.086	0.358	0.698	1.128	
	Age	-0.028†	0.006	-0.04	-0.016	1.045	0.40
	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		
	Sex	0.409†	0.106	0.199	0.620	1.779	
	Age	-0.026†	0.006	-0.038	-0.015	1.061	0.42
	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		
	Sex	0.425†	0.104	0.219	0.632	1.705	
	Age	-0.025†	0.006	-0.037	-0.012	1.161	0.41
	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		
	Sex	0.643†	0.103	0.438	0.848	1.640	
	Age	-0.027†	0.006	-0.039	-0.015	1.058	0.40
	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		
	Sex	0.596†	0.108	0.382	0.809	1.752	
	Age	-0.028†	0.006	-0.04	-0.016	1.041	0.39
	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		
	Sex	0.492†	0.104	0.285	0.700	1.660	
	Age	-0.030†	0.006	-0.041	-0.018	1.026	0.39
	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		
	Sex	0.557†	0.107	0.344	0.770	1.737	
	Age	-0.029†	0.006	-0.041	-0.017	1.041	0.39
	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		
	Sex	0.393†	0.095	0.205	0.582	1.506	
	Age	-0.020*	0.006	-0.032	-0.007	1.295	0.45
	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		
	Sex	0.547†	0.084	0.38	0.714	1.072	
	Age	-0.028†	0.006	-0.040	-0.015	1.101	0.39
	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		
	Sex	0.402†	0.099	0.206	0.599	1.593	
	Age	-0.026†	0.006	-0.038	-0.015	1.043	0.43
	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	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
16	Constant	5.825†	1.047	3.744	7.906		
	Sex	0.541†	0.109	0.324	0.757	1.792	
	Age	-0.029†	0.006	-0.041	-0.017	1.037	0.39
	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		
	Sex	0.453†	0.105	0.244	0.662	1.715	
	Age	-0.029†	0.006	-0.04	-0.017	1.018	0.40
	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		
	Sex	0.405†	0.100	0.206	0.603	1.616	
	Age	-0.023†	0.006	-0.035	-0.011	1.178	0.43
	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		
	Sex	0.480†	0.088	0.304	0.656	1.243	
	Age	-0.023†	0.006	-0.036	-0.011	1.207	0.42
	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		
	Sex	0.487†	0.088	0.313	0.662	1.222	
	Age	-0.024†	0.006	-0.036	-0.011	1.203	0.41
	Physical activity level	0.252	0.261	-0.267	0.772	1.057	
	ln SA (m²)	0.830*	0.394	0.047	1.613	1.317	
21	Constant	5.163†	1.281	2.618	7.708		
	Sex	0.528†	0.092	0.345	0.710	1.276	
	Age	-0.028†	0.006	-0.040	-0.015	1.129	0.39
	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		
	Sex	0.537†	0.087	0.365	0.709	1.141	
	Age	-0.027†	0.006	-0.04	-0.015	1.134	0.39
	Physical activity level	0.218	0.268	-0.313	0.750	1.063	
	ln CAMA (cm²)	0.107	0.139	-0.17	0.383	1.180	
23	Constant	3.606*	1.695	0.239	6.973		
	Sex	0.367*	0.151	0.067	0.667	3.528	
	Age	-0.023*	0.007	-0.037	-0.008	1.529	0.40
	Physical activity level	0.274	0.266	-0.254	0.802	1.067	
	ln FFM(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		
	Sex	0.410*	0.118	0.175	0.645	2.181	
	Age	-0.025†	0.006	-0.038	-0.013	1.174	0.41
	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		
	Sex	0.513†	0.120	0.274	0.752	2.187	
	Age	-0.028†	0.007	-0.041	-0.014	1.258	0.39
	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		
	Sex	0.407*	0.114	0.18	0.634	2.049	
	Age	-0.024*	0.007	-0.037	-0.010	1.275	0.41
	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		
	Sex	0.383*	0.118	0.147	0.618	2.211	
	Age	-0.023*	0.007	-0.036	-0.010	1.288	0.41
	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		
	Sex	0.460†	0.122	0.217	0.703	2.287	
	Age	-0.026†	0.007	-0.039	-0.013	1.237	0.39
	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	

Linear regression	Independent variables	Regression coefficients		95% CI of β		VIF	Adjusted R²
		β	Standard error	LL	UL		
29	Constant	1.137	2.531	-3.892	6.167		
	Sex	0.388*	0.118	0.154	0.623	2.194	
	Age	-0.023*	0.007	-0.036	-0.010	1.298	0.41
	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		
	Sex	0.397*	0.121	0.156	0.638	2.299	
	Age	-0.023*	0.007	-0.037	-0.010	1.302	0.41
	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		
	Sex	0.551†	0.103	0.346	0.755	1.601	
	Age	-0.029†	0.006	-0.042	-0.016	1.179	0.39
	Physical activity level	0.236	0.269	-0.299	0.772	1.070	
	ln ASM/height² (kg/m²)	0.019	0.274	-0.527	0.564	1.685	
32	Constant	3.261*	1.486	0.306	6.215		
	Sex	0.443†	0.100	0.245	0.642	1.503	
	Age	-0.024*	0.007	-0.037	-0.011	1.235	0.41
	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		
	Sex	0.463†	0.114	0.237	0.689	1.979	
	Age	-0.026†	0.007	-0.039	-0.013	1.231	0.40
	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§	-
/body mass	(kg)	0.66	0.464 to 0.826	0.54	86	45	0.76†	0.634 to 0.854	0.38	88	63	-0.57§	-0.03	-0.57§
/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‡	-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‡	-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§	0.10	-0.39§
/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§	0.11	-0.36§
/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‡	-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‡	-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‡	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‡	-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‡	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‡	-0.39§
/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§	-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‡	0.15	-0.55§
/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§	0.16	-0.53§
/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‡	0.38§	-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‡	0.12	-0.65§
/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§	-0.07
/pectoral skinfold		0.58	0.388 to 0.763	1.13	29	100	0.74†	0.618 to 0.843	1.64	76	73	-0.31‡	0.21‡	-0.70§
/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‡	0.12	-0.60§
/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§	-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‡	0.12	-0.58§
/thigh skinfold		0.78*	0.584 to 0.909	1.82	71	77	0.81†	0.694 to 0.897	0.67	72	80	-0.16	0.25‡	-0.46§
/medial calf skinfold		0.80†	0.609 to 0.924	2.91	100	64	0.76†	0.632 to 0.853	0.93	64	78	-0.15	0.16	-0.42§
/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

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
/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[(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][(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[(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][(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		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	(g)	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/height²[(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[(BAUMGARTNER et al., 1991)]		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][(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[(DXA)]	(kg)	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][(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[(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[§]
/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		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]	(kg)	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[‡]

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
/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
/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

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
/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$_{(BAUMGARTNER\ et\ al.,\ 1991)}$		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}$$_{(BAUMGARTNER\ et\ al.,\ 1991)}$	(kg)	0.76[*]	0.559 to 0.898	3.94	83	77	0.72[*]	0.592 to 0.823	2.91	76	64	-0.03	0.24[‡]	0.16
/FFM$_{(DXA)}$		0.70	0.504 to 0.856	1.16	86	73	0.70[*]	0.575 to 0.808	0.67	44	93	-0.17	0.11	-0.08
/FFM$^{0.38}$$_{(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		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$^{0.67\ (DAVIES;\ DALSKY,\ 1997)}$	(kg)	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		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$^{0.72}$	(cm)	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
/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	(mm)	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

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
/elbow breadth		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$^{0.43}$	(g)	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		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/height²$^{(0.02)}$		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$_{(BAUMGARTNER et al., 1991)}$		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
/FFM$^{0.61}_{(BAUMGARTNER et al., 1991)}$	(kg)	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.

3.2 Estudo original II - ADJUSTING GRIP STRENGTH TO BODY SIZE: ANALYSES FROM 6 COUNTRIES

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ABSTRACT

OBJECTIVES: Absolute handgrip strength and adjusted by body mass index are useful to identify age-related conditions. However, these values are not accurate for older adults with extreme body size because of the nonlinear relationship between strength, height, and body mass. The purpose of this study was to determine cut-off points for age-related conditions of older adults using allometric coefficients to normalize grip strength by body size. DESIGN: Cross-sectional SETTING AND PARTICIPANTS: Data from 13,235 older adults of Study on Global Aging and Adult Health conducted in 6 low- and middle-income countries were analyzed. METHODS: Country- and sex-specific allometric exponents for body-size variables (mass and height) were computed with log-linear models. Partial correlation verified whether allometric normalization removed the effect of body size on grip strength. Cut-off points were established (<20th percentile) for low allometrically adjusted grip strength. 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 ($r < 0.30$). Overall, frequencies of low muscle strength were overestimated with international criteria (absolute grip strength) compared with the cut-off points proposed in this study. CONCLUSIONS AND IMPLICATIONS: The proposed allometric exponents normalized grip strength according to body-size variables. These exponents improved the accuracy in identifying age-related conditions 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. New cut-off points of low normalized grip strength with automatized applicability were proposed for health care providers use in clinical practice.

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

1. INTRODUCTION

Grip strength used to identify age-related conditions are based on absolute results (ALBRECHT; STALLING; BAMMANN, 2021; DODDS *et al.*, 2014; FRIED *et al.*, 2001; LAURETANI *et al.*, 2003; WANG *et al.*, 2018), dividing by body mass index (BMI) (MCGRATH *et al.*, 2020) or by stratifying in ranges according to sex and BMI quartiles (FRIED *et al.*, 2001). Grip strength is strongly and positively associated with body size (NEVILL *et al.*, 2022). Absolute values may be inaccurate in older adults with small body size (FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; PUA, 2006). Absolute values characterize lighter and shorter older adults as having a low strength when compared to their heavier and taller peers, even sustaining their motor independence (ABDALLA *et al.*, 2020b). Heavy and tall older adults, despite having an adequate strength, might be at greater health risk (ABDALLA *et al.*, 2021b). Furthermore, stratify grip strength to BMI or ratio standard (simple division by body mass or BMI) overestimates the real strength of light/short older adults and underestimates tall/heavy older adults (ABDALLA *et al.*, 2020b). A nonlinear relationship between grip strength and body size exists (FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; PUA, 2006).

To overcome this methodological constraint, allometry or power scaling/function ratio characterize the nonlinear relationship between variables (FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; PUA, 2006). The power function ratio between grip strength and body-size (body mass and height) was reported in older adults (FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; PUA, 2006). However, the use of allometry to determine cut-off points of low grip strength has not been considered.

Thus, the aim was to determine low allometrically adjusted grip strength cut-off points for older adults from low- and middle-income countries.

2 MATERIALS AND METHODS

The Survey

Data from the Study on Global Aging and Adult Health (SAGE) were analyzed (WHO, 2010). SAGE was conducted with participants (n=47,443) over 18 years old in households from China, Ghana, India, Mexico, Russian Federation and South Africa between 2007 and 2010 with response rate >55% in 60+ participants (WHO, 2010). The research protocol and ethical approval were published previously (KOWAL *et al.*, 2012).

Sample

In this study, data analysis was restricted to older adults aged 60 or more (n=24,212). The exclusion criteria (n=9,262) involved cognitive limitations (judged by the interviewer), not maintain orthostatic position, wheelchair use, 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 implausible values for the Global Physical Activity Questionnaire (GPAQ) were also excluded (n=86).

Anthropometry

Height (m) and weight (kg) were measured using a stadiometer and a scale, respectively (RAMLAGAN; PELTZER; PHASWANA-MAFUYA, 2014).

Grip Strength

Maximum grip strength was measured twice in both hands using a Smedley's handgrip dynamometer (Scandidact Aps, Denmark) and the protocol was published previously (RAMLAGAN; PELTZER; PHASWANA-MAFUYA, 2014).

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; <16 kg for older females; <27 kg for older males) (DODDS *et al.*, 2014) 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).

Physical Activity Level

Physical activity level was estimated by the GPAQ (ARMSTRONG; BULL, 2006). Participants were classified as active or inactive according to WHO GPAQ analysis guide and implausible values were checked in the same guide (https://www.who.int/ncds/surveillance/steps/resources/GPAQ_Analysis_Guide.pdf).

Statistical analyses

Descriptive statistics and normality were checked. Grip strength, body mass and height outliers (outside of the 1.5 interquartile range-IQR according to sex and country) were excluded (n=1,715) (WANG *et al.*, 2018). Grip strength were compared between countries and sex (ANOVA-two way with LSD post hoc test; p<0.05). The relationship between grip strength and body size was gathered with dispersion plots and smoothing splines.

Log-linear regression models generated allometric exponents (*i.e.,* regression coefficient). 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 (Table S2 in the Supplementary Material) and generated the allometric coefficients utilized in the Equation 1 to normalize grip strength.

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

The partial correlation (controlling sex, age and physical activity) between normalized grip strength and body-size variables verify the remotion of body-size effect on grip strength with normalization (negligible r: <0.30) (MUKAKA, 2012).

The cut-off points for low muscle strength was fixed at the lowest quintile (BEZ; NERI, 2014; FRIED *et al.*, 2001; MOREIRA; LOURENCO, 2013; NERI *et al.*, 2013; VASCONCELOS *et al.*, 2016; VIEIRA *et al.*, 2013).

Confusion matrix verified difference between low grip strength classifications with EWGSOP2, SDOC and this study's criteria.

3 RESULTS

The data cleaning process is shown in Figure S1. Data from 13,235 participants (aged between 60 and 114 years old) were included.

Table 1 presents sample characteristics. In all countries, men had higher grip strength compared to women (Δ=+9.3±2.1; p<0.001). Grip strength was different among all countries (p<0.001 for women and men; data not shown), except between China and Ghana for women (p=0.143) and between Russia 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/m²														
< 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[w] ± 9.9	21 ± 8.7	28.3[w] ± 10.8	15.5 ± 5.2	23.8[w] ± 7.2	17 ± 5.7	26.5[w] ± 7.4	21.9 ± 7.1	35.9[w] ± 9.8	28.7 ± 13.9	36.4[w] ± 18.2	20.2 ± 8.9	29.5[w] ± 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
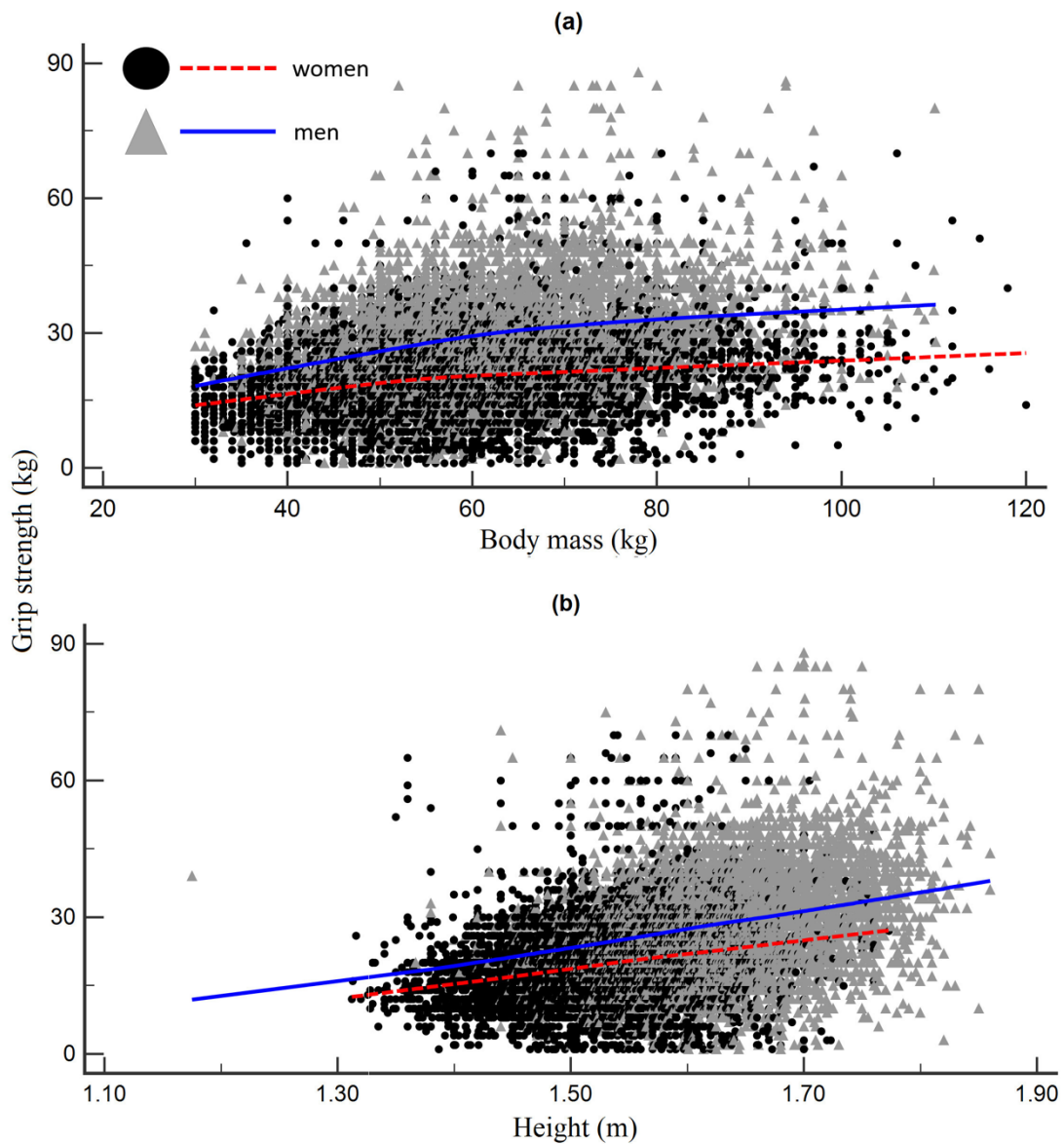

Table S2 shows allometric coefficients for natural logarithm (ln) grip strength according to the independent variables (ln body mass and ln height). Coefficients varied between 0.19 and 0.61 for body mass and between 1.46 and 2.45 for height. When the 95% CI of generated allometric exponents were analyzed, 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 China women[1]). Therefore, we proposed the cut-off points based on these coefficients.

Correlations between normalized grip strength and body size were negligible (MUKAKA, 2012) fluctuating between -0.06 and 0.01 (Table S3), isolating body-size effect on grip strength (MARANHÃO NETO *et al.*, 2017), which confirms the adequate normalization for each country.

Mean, 95% CI and cut-off points for absolute or allometrically adjusted low grip strength are shown in Table 2 according to sex and each country.

Table 2 - 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				
				95% CI		Cut-off points (< 20th percentile)			95% CI		Cut-off points (< 20th percentile)
		Mean	SD	Lower to upper			Mean	SD	Lower to upper		
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**

Figure S2 presents a confusion matrix of participants' low grip strength frequency according to our study normalized cut-off points and predicted by EWGSOP2 and SDOC. Agreement between our proposed cut-off points for low normalized grip strength classification

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[1] Notwithstanding grip strength ranking classification for Chinese women did not differ regardless of the body mass exponent used for normalization ($^{0.19}$ vs $^{0.40}$; Wilcoxon test=-1.852; p=0.064)

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

4. DISCUSSION

This study established cut-off points of low normalized muscle strength to identify age-related conditions in older adults of six low- and middle-income countries. Normalization removed the body-size effect on grip strength expression, confirmed by the negligible correlations between the normalized grip strength and body size. Thus, the geriatric syndromes identification is more precise with country-specific cut-off points, regardless of body-size variability and extreme body sizes (i.e., light and short or tall and heavy).

The cut-off points proposed in our study (with 60+ adults) classify less cases of low muscle strength when compared to the EWGSOP2 criteria (-2SD of average absolute grip strength of whole population) (CRUZ-JENTOFT *et al.*, 2018; DODDS *et al.*, 2014; LAURETANI *et al.*, 2003; SANTANASTO *et al.*, 2020). The EWGSOP2 cut-off points were proposed based on $\cong$50,000 UK 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 our sample. The two exceptions (older Russian 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- (Ghana) and lower middle-income countries (China and India) in our sample. 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 our study's sample. However, normalization by body-size (as also proposed by the SDOC) reduce overestimates of low muscle strength (Figure S2), decreasesing the disagreements between countries of different incomes.

Allometric mathematical model (Y=aX^{b}), being Y the grip strength, X the body size-variable and ^{b} allometric exponent, was previously utilized to normalize grip strength (FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; PUA, 2006). Allometric relationship (allometric exponents varying from 0.00 to 0.99) (OWINGS; PAVOL; GRABINER, 2002) 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) (PUA, 2006). Following the same logic, our study present exponents below the unit (<1.00).

On the other hand, height had a linear relationship with handgrip strength in our study (≥1.00) (OWINGS; PAVOL; GRABINER, 2002). 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) or 1.75 (95% CI: 1.67 to 1.83) (NEVILL *et al.*, 2022), indicating a quadratic relationship between handgrip strength and height (NEVILL *et al.*, 2022). 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, including those indicated by the literature for body mass (95% CI=0.14 to 0.91) (FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; PUA, 2006) and height (95% CI=1.23 to 2.45) (MARANHÃO NETO *et al.*, 2017).

The sample size of our study covered a large range of ages and characteristics not always covered in studies with older adults, amplifying the generalizability of our findings. There were people over 85 years old ($\cong$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 (data are old, cross-sectional design, and lowest quintile method to generate cut-off points, although performed when there was no data on young people to propose cut-off points) (BEZ; NERI, 2014; FRIED *et al.*, 2001; MOREIRA; LOURENCO, 2013; NERI *et al.*, 2013; VASCONCELOS *et al.*, 2016; VIEIRA *et al.*, 2013). Another limitation is the generalizability of the allometric exponents and cut-off points, that need to be tested for older adults from higher income countries and institutionalized settings. Longitudinally test our cut-off points to predict survival or poor health outcomes is necessary.

The suggested reference exponents can be easily used to estimate grip strength indexes in older adults in epidemiological studies, from simple resources, accessible variables and automatized routine excel model (http://posgraduacao.eerp.usp.br/files/Routine_Models_Men_and_Women_HGS.xlsx). We exemplified a prevention of a false positive case utilizing our proposal. 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 an appropriate control of body-size bias.

5. CONCLUSIONS AND IMPLICATIONS

Allometry reveals a nonlinear relationship between grip strength and body mass and a linear relationship with height. Variability between strength levels of different countries highlights the need for cut-off points according to geographical area and population specificity. Normalized grip strength for lighter/heavier and shorter/taller older adults may be more accurate in identifying dynapenia, sarcopenia and frailty. Normalized grip strength 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.

Clinical implications includes 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. We proposed new cut-off points of low normalized grip strength with automatized applicability for healthcare providers utilize in clinical practice.

Material Suplementar 1

Table S1 - Log-linear regression models that generated 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.
*Log-linear regression models methods: 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 In height. The enter method sustains the independent variables entry in the models
SE: standard error
CI: confidence interval
lower: lower band
upper: upper band
VIF: Variance Inflation Factor

Material Suplementar 2

Table S2 - 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.
†Generated 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 (not occurred in our study); 2nd) when the interaction variable was statistically significant, allometric exponents for females and males were generated (occurred in our study). Multicollinearity was confirmed if Variance Inflation Factor (VIF)>5(MYERS, 1990) and models were discarded (not occurred in our study).
Regression Coefficient: equivalent to unstandardized beta-coefficient
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)

Material Suplementar 3

Table S3 - 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 **$p < 0.001$

Figure S1 - Study flow chart
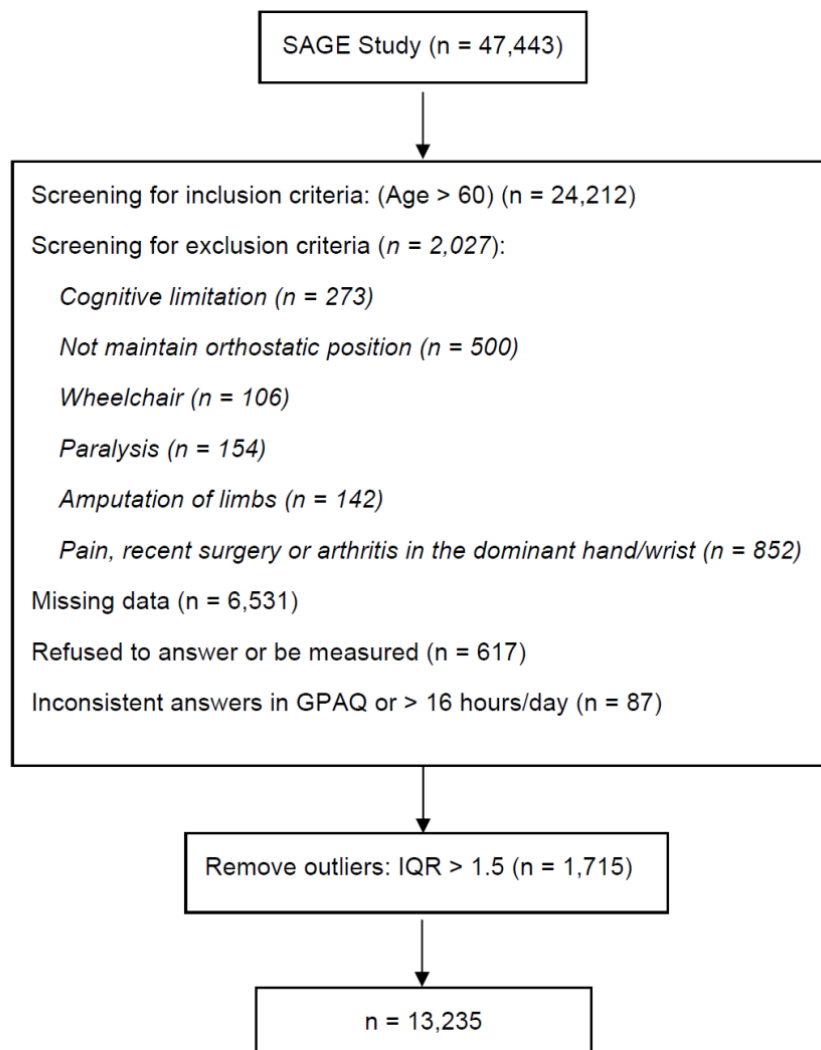
Note. GPAQ: Global Physical Activity Questionnaire; IQR: interquartile range

Figure S2 - 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.

			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	

3.3 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

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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 60°/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 (ABDALLA *et al.*, 2021a). 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; PUA, 2006), even if they sustain their mobility (ABDALLA *et al.*, 2020b). This false positive muscle weakness diagnostic can lead to an unnecessarily use of health resources (ABDALLA *et al.*, 2021b). 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 *et al.*, 2020b). 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; 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 *et al.*, 2020b; FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; 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 *et al.*, 2020b; 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 (ABDALLA *et al.*, 2021a). 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 (ABDALLA *et al.*, 2021a; ABDALLA *et al.*, 2020b; DAVIES; DALSKY, 1997). Brazilian (ABDALLA *et al.*, 2021a) 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 (LOHMAN; ROCHE; MARTORELL, 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 ($_{knee\ extension}PT^{60°/s}$) 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 *et al.*, 2020a) and Portuguese sample (MARQUES *et al.*, 2011). The major differences were in the warm-up: 10 submaximal repetitions at velocity 60°/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 $_{knee\ extension}PT^{60°/s}$: five repetitions at 60°/s for Brazilian sample and three repetitions for Portuguese sample (but executed two minutes after five repetitions in maximal effort at 180°/s).

Muscle Strength Normalization Procedures (allometric scaling)

$_{knee\ extension}PT^{60°/s}$ 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 ($_{\text{knee extension}}\text{PT}^{60°/s}$)

Authors	Nationality	Normalized $_{\text{knee extension}}\text{PT}^{60°/s}$ 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 ($_{\text{knee extension}}\text{PT}^{60°/s}$/body-size variable$^{\text{b}}$) 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 ($r \leq 30$) (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/height² and mobility in 6MWT (Figure 1) than the Brazilians. Differences for muscle strength ($_{knee\ extension}PT^{60°/s}$) were noted for women (Figure 1) and these differences were preserved after normalization by body size-variables (except when $_{knee\ extension}PT^{60°/s}$ 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$^{60°/s}$	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$^{60°/s}$																			
/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
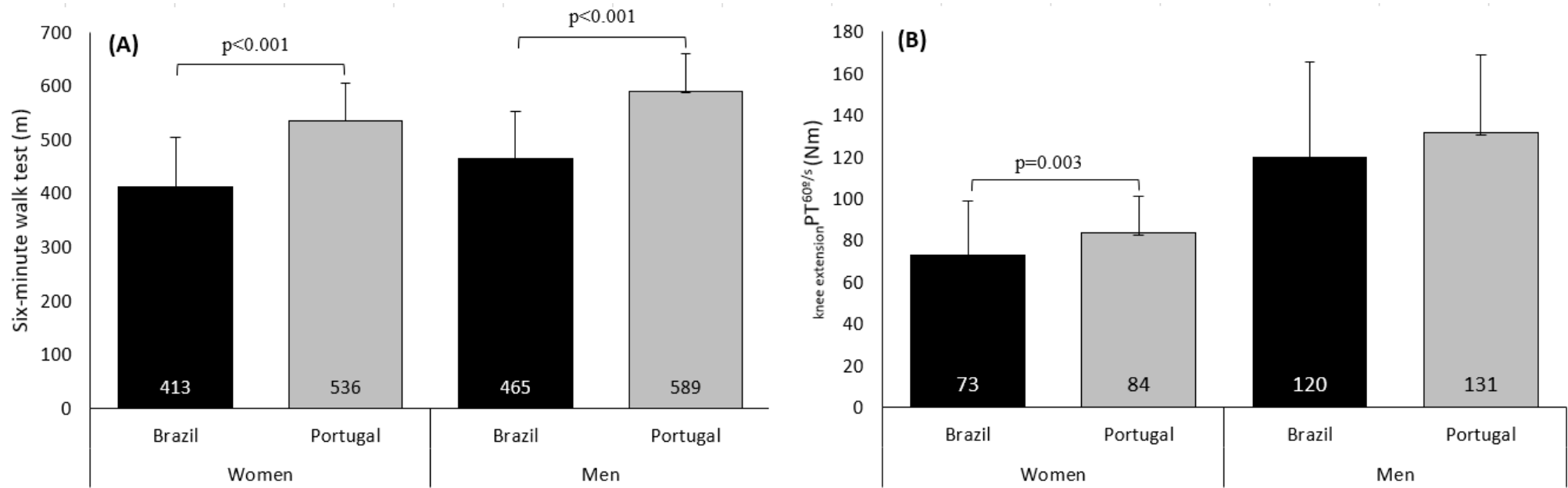
The sex-specific cut-off points proposed for $_{\text{knee extension}}PT^{60°/s}$ (non-normalized and allometrically adjusted) to identify muscle weakness are presented in Table 3. Table 3 also shows correlations between muscle strength and body size (body mass, height and body-size variable used in normalization). When $_{\text{knee extension}}PT^{60°/s}$ 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)$^{0.97 \text{ (SEGAL et al., 2008)}}$] present dependency of body size (with r>0.30). Non-normalized $_{\text{knee extension}}PT^{60°/s}$ 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 ($_{knee\ extension}PT^{60º/s}$), their accuracy and cut-off points to identify poor functional performance (lowest quartile of six-minute walk test)

$_{knee\ extension}PT^{60º/s}$	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 $_{(knee}$ $_{extension}$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)
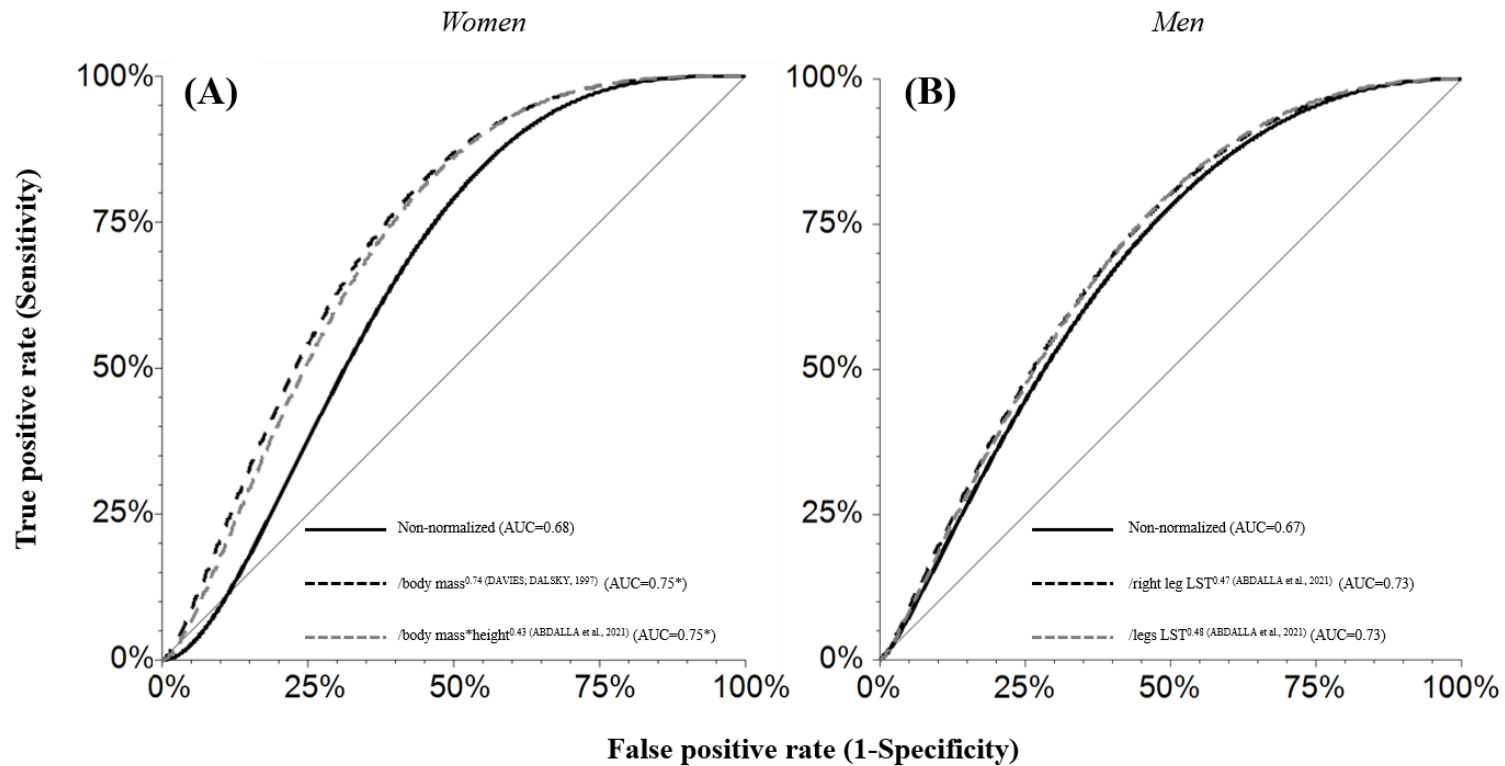
*p<0.001 (greater than the AUC of non-normalized)

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)$^{0.97 \text{ (SEGAL et al.,}}$ $^{2008)}$" and "height$^{3.27 \text{ (ABDALLA et al., 2021)}}$". 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 $_{\text{knee extension}}\text{PT}^{60º/s}$ allometrically adjusted with international allometric exponents in older Portuguese adults. In the literature there are also muscle weakness cut-off points for $_{\text{knee extension}}\text{PT}^{60º/s}$ 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 $_{\text{knee extension}}\text{PT}^{60º/s}$ was linearly normalized by body mass, this variable presented correlation (r≥0.30) with body size (ABDALLA *et al.*, 2021a), what prevents recommending its use.

The normalization of $_{\text{knee extension}}\text{PT}^{60º/s}$ 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 $_{knee\ extension}PT^{60^{o}/s}$ by body mass, height, body mass*height, SA and DXA derived LST (ABDALLA *et al.*, 2021a; 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)$^{0.97\ (SEGAL\ et\ al.,\ 2008)}$" and "height$^{3.27\ (ABDALLA\ et\ al.,\ 2021)}$" 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 $^{b}\geq 1.00$) (OWINGS; PAVOL; GRABINER, 2002) where ^{b} varies between 1.84 and 3.27 (ABDALLA *et al.*, 2021a; MARANHÃO NETO *et al.*, 2017); and by the non-linearity tendence (when $^{b}\leq 1.00$) 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; PAVOL; GRABINER, 2002), the dependency of "$_{knee\ extension}PT^{60^{o}/s}$/(body mass*height)$^{0.97\ (SEGAL\ et\ al.,\ 2008)}$" 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 ($^{b}\geq 1.00$), featuring a linear relationship with body size, which justifies the interdependence between muscle strength and body size. Notwithstanding, when an allometric scaling ($^{b}=0.43$; (ABDALLA *et al.*, 2021a)) 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 (ABDALLA *et al.*, 2021a; FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; 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 $_{knee\ extension}PT^{60°/s}$ of 130.0 Nm. If considered our absolute cut-off point ($\leq$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.

3.4 Estudo Original IV - NORMALIZING CALF CIRCUMFERENCE TO IDENTIFY LOW SKELETAL MUSCLE MASS IN OLDER WOMEN: A CROSS-SECTIONAL STUDY

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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 CC·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 (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 *et al.*, 2020b).

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 (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; LAI; CHANG, 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·height^{-2}, ASMM·body mass^{-1} or ASMM·BMI^{-1}) (KIM; JANG; LIM, 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·height^{-2}) includes the absolute value of CC (Chart 1) (BAHAT *et al.*, 2016; BARBOSA-SILVA; BIELEMANN; GONZALEZ, 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; SAMPAIO, L. S. *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)	Brazilians	132	ASMM·height^{-2}	34 for men	0.75	71	77
				33 for women	0.84	80	85
Kim et al. (2018)	South koreans	657	ASMM·height^{-2}	35 for men	0.81	92	59
				33 for women	0.72	83	50
Sampaio et al. (2017)	Brazilians	316	Frailty(Fried et al., 2001)	32 for both sexes	0.67	54	73
Kusaka et al. (2017)	Japanese women	116	Sarcopenia(Chen et al., 2014)	32.8 for women	0.79	73	80
Bahat et al. (2016)	Turks	406	SMM*·height^{-2}	33 for both sexes	-	100	74
					-	100	69
Kawakami et al. (2015)	Japanese (40-89 years old)	526	Sarcopenia(Chen et al., 2014)	34 for men	0.94	89	88
				33 for women	0.84	78	72
Barbosa-Silva et al. (2015)	Brazilians	189	ASMM·height^{-2}	34 for men	0.76	61	76
				33 for women	0.91	100	76
Rolland et al. (2003)	French women	1458	ASMM·height^{-2}	31 for women	-	44	91
Bonnefoy et al. (2002)	French	911	ASMM·height^{-2}	30.5 for both sexes	0.81	73	73
					0.78	79	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 (LOHMAN; ROCHE; MARTORELL, 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; $kg \cdot m^{-2}$) was determined. CC was measured according to a standardized procedure (LOHMAN; ROCHE; MARTORELL, 1988), with recording of the median from 3 measurements. For analyses, CC was considered as absolute (cm) and normalized: $CC \cdot body$ $mass^{-1}$ in $cm \cdot kg^{-1}$, $CC \cdot height^{-2}$ in $cm \cdot m^{-2}$ and $CC \cdot BMI^{-1}$ in $cm \cdot kg^{-1} \cdot m^{-2}$.

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 (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
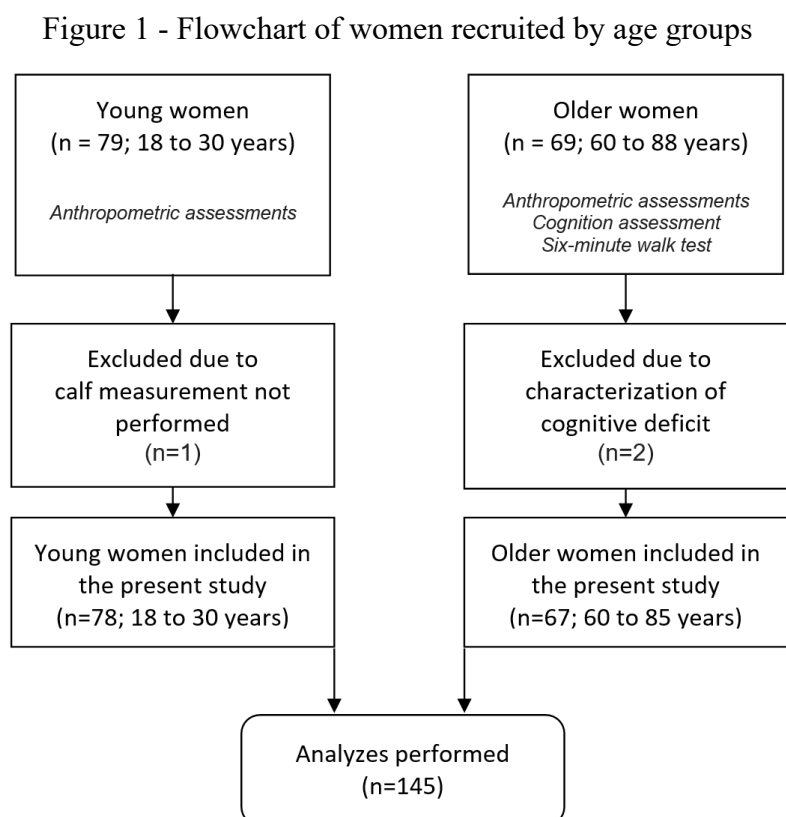
Descriptive statistics of the MMSE score, chronological age, anthropometric variables, and walking distance are shown in Table 1. Older women were older, and had greater body mass, BMI and absolute CC. Younger women were taller (10 cm) and weighed less (6 kg) than their older counterparts. The higher BMI found in older ($\cong$27kg·m^{-2}) compared to younger women ($\cong$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 one third 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 ($\leq$) of CC	older women (n=67)				
		mean	95% CI			SD		mean	95% CI			SD
			lower		upper				lower		upper	
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		χ^2	P-value	Wald	OR
dependent	independent				
	CC	2.79	0.095	2.56	1.166
Dichotomous walking distance	CC·body mass^{-1}	4.89	0.027	4.33	<0.001
(1: ≤ 400m and 0: > 400m)	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)
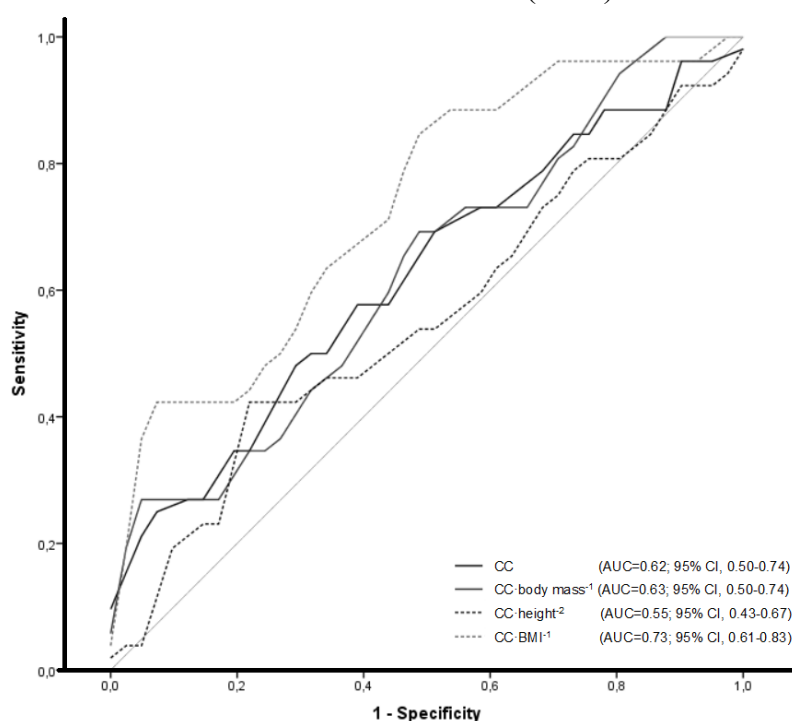
Although the adjustment of CC by body mass (Table 2) was significant (χ^2=4.89; p=0.027), the extremely low odds ratio value (<0.001) did not sufficiently explain the occurrence of functional limitation. This finding was confirmed when the analysis of the ROC curve for CC·body mass^{-1} showed insufficient 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)
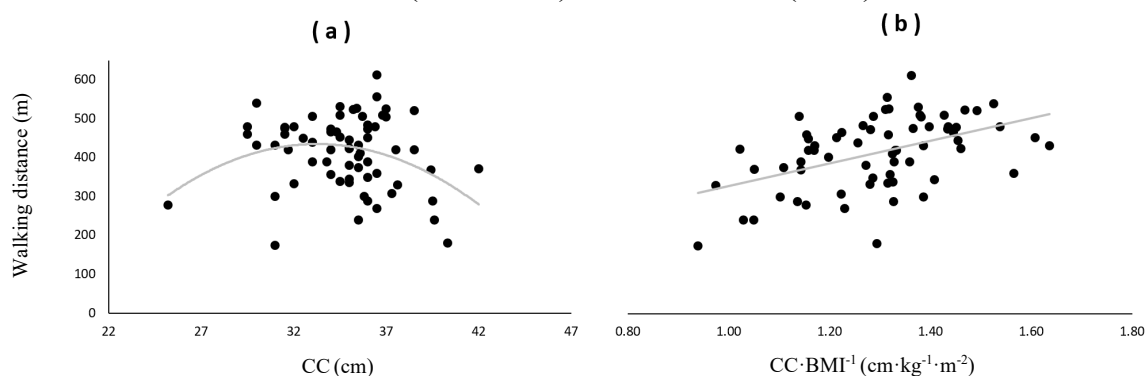
Our model (CC·BMI^{-1}), in addition to correcting the non-linear relationship between CC and mobility, showed a positive and significant correlation between adjusted CC and mobility (r=0.48; p<0.001).

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; BIELEMANN; GONZALEZ, 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; TSAI; WANG, 2016). However, when the absolute CC is high (i.e.>38 cm) also predict the risk of impaired mobility,(TSAI; LAI;

CHANG, 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; LAI; CHANG, 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 $kg \cdot m^{-2}$) characterizing a negative impact on functional performance (TSAI; LAI; CHANG, 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 $ASMM \cdot height^{-2}$ 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 $CC \cdot BMI^{-1}$ 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 $CC \cdot BMI^{-1}$ of young women (≤1.10 $cm \cdot kg^{-1} \cdot m^{-2}$) was lower than the cut point based on functional limitation (≤1.33 $cm \cdot kg^{-1} \cdot m^{-2}$) 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 ($\cong$10%) (SHAFIEE *et al.*, 2017) but still below the prevalence of Brazilian older women ($\cong$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.

4 DISCUSSÃO GERAL

4.1 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 condições relacionadas ao envelhecimento, 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 (Estudo III). 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 de mobilidade de idosos. O terceiro objetivo foi propor modelos de simples aplicação para identificar baixa massa muscular esquelética, baseada na limitação de mobilidade para 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 a 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).

4.2 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; MORLEY; VON HAEHLING, 2016), ainda não tem uma definição unânime na literatura (SANCHEZ-

RODRIGUEZ; MARCO; CRUZ-JENTOFT, 2020). O termo "sarcopenia" foi criado por Irving Rosenberg (1997) para descrever a redução de massa muscular relacionada ao envelhecimento, que estaria associada à mobilidade e independência de movimentos. 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; MARCO; CRUZ-JENTOFT, 2020).

Ainda não há uma definição unânime, critérios de diagnósticos uniformes e *guidelines* de tratamentos para sarcopenia universalmente aceitos (SANCHEZ-RODRIGUEZ; MARCO; CRUZ-JENTOFT, 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 *et al.* (2011) e a *Society of Sarcopenia, Cachexia and Wasting Disorders* (SCWD) de 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 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 para identificar sarcopenia. Essa decisão, mediante voto, envolveu especialistas em sarcopenia do consórcio americano. A massa muscular apendicular derivada da absorciometria radiológica de dupla energia (DXA), que é a mais utilizada e recomendada por outros consensos, 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. Uma vez que a sarcopenia tem um laço histórico com o aspecto morfológico do tecido muscular, o grupo SDOC citou 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 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 mobilidade de idosas, propusemos pontos de corte para identificar sarcopenia a partir do perímetro da panturrilha, normalizado pelo índice de massa corporal (ABDALLA *et al.*, 2021b). Vale destacar que a DXA faz varredura dos componentes corporais no nível molecular (WANG; PIERSON; HEYMSFIELD, 1992) 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.

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). 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; MARCO; CRUZ-JENTOFT, 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.

4.3 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:

$$\ln Y = \ln (a) + \ln (X)*b$$

(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)	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 *et al.*, 2020b; KÜLKAMP *et al.*, 2020) como da segunda (ABDALLA *et al.*, 2021a; 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:

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

(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:

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

(Equação 6)

E para o praticante recreacional, seria:

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

(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:

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

(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; MAHAR; CHOU, 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 ($r \cong 0,0$) 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.

4.4 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 (ABDALLA *et al.*, 2021a; ABDALLA *et al.*, 2022; ABDALLA *et al.*, 2020b; DAVIES; DALSKY, 1997; FOLEY *et al.*, 1999; MARANHÃO NETO *et al.*, 2017; 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	Maranhão 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.* (2021a)	0,22	-0,02 a 0,46
	Abdalla *et al.* (2022)	0,19 a 0,61	-
	Nevill *et al.* (2022)	0,58	0,53 a 0,62
Estatura	Maranhão Neto *et al.* (2017)	1,84	1,23 a 2,45
	Abdalla *et al.* (2021a)	1,86	0,90 a 2,85
	Abdalla *et al.* (2022)	1,46 a 2,45	-
	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.* (2021a)	0,44	0,01 a 0,87
Estatura	Abdalla *et al.* (2021a)	3,05	1,27 a 4,83
Pico de torque à 60º/s da extensão de joelho			
Massa corporal	Abdalla *et al.* (2021a)	0,37	-0,08 a 0,814
	Davies e Dalsky (1997)	0,67 ou 0,72 ou 0,74	-
Estatura	Abdalla *et al.* (2021a)	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 (ABDALLA *et al.*, 2021a), 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) estudaram a relação entre estatura e a força de preensão manual utilizando dados de 8690 pessoas do *National Health and Nutrition Examination Survey* (NHANES), como demonstrado na Figura 1. 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.

Figura 1 - Associação entre a força de preensão manual e a estatura de 8690 adultos e idosos participantes do National Health and Nutrition Examination Survey (NHANES).
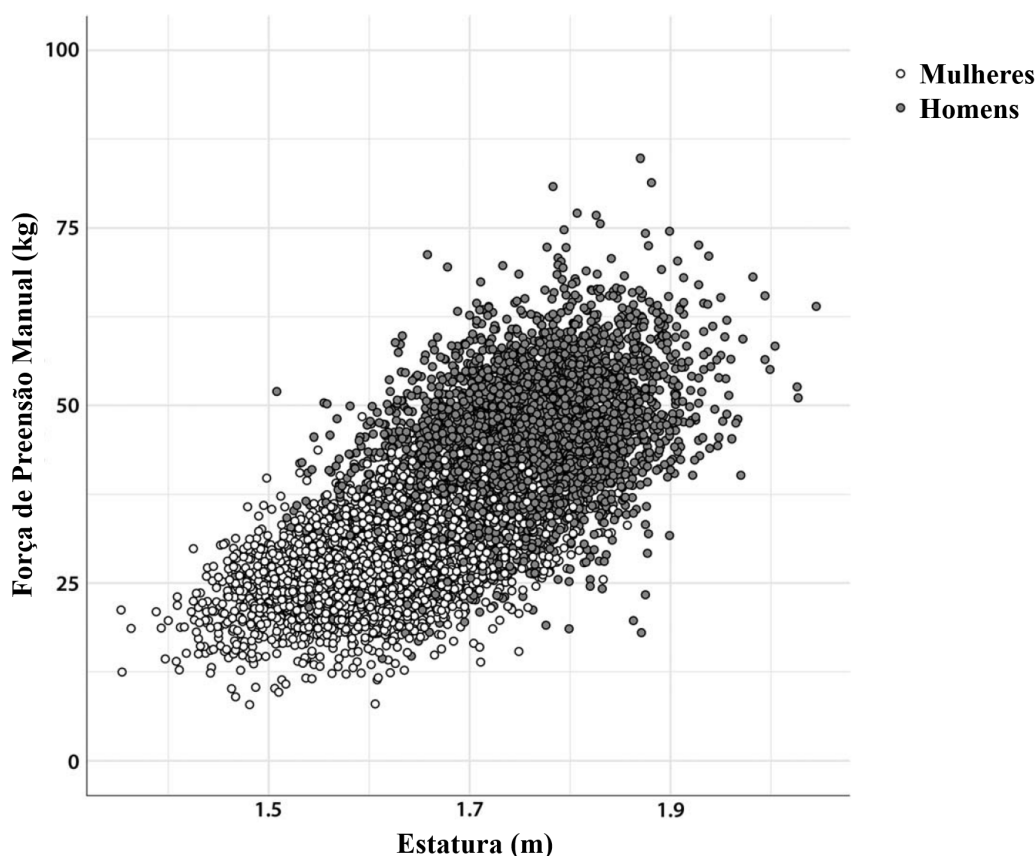
Fonte: Traduzido de Nevill *et al.* (2022) com autorização dos respectivos autores (Anexo E).

4.5 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 (ABDALLA *et al.*, 2021a). 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 em desenvolvimento. 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 de sarcopenia (Estudo Original IV). Muito embora essa normalização tenha sido previamente recomendada pelo EWGSOP (Cruz-Jentoft et al., 2018).

4.6 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. Outra ressalva é quanto a caracterização da amostra de idosos da comunidade do Estudo original I, pois a maioria foram convidados a partir de projetos envolvendo exercício físico em execução na EEFERP-USP. Poucos deles foram convidados em serviços de saúde. Todavia, os expoentes alométricos foram gerados considerando a variável nível atividade física (dicotomizada em sedentário ou não sedentário). Isso contribui para minimizar o fator de confundimento do nível de atividade física sobre a relação (demonstrada pelo expoente alométrico) entre a força e as variáveis de tamanho corporal. O Estudo III também envolveu idosos participantes de um programa de exercício multicomponente, onde o treinamento tem potencial para alterar positivamente os diferentes componentes da aptidão física e funcional de idosos. Todos os participantes portugueses estavam envolvidos no programa multicomponente. Portanto, é ainda preciso testar a aplicabilidade dos expoentes de forma cruzada em amostras sedentárias, para confirmar a utilidade dos expoentes alométricos para normalizar a força independentemente do nível de atividade física.

4.7 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 seria classificada como falso positiva, 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 incipiente na literatura, inviabilizando uma discussão mais enriquecedora. O fato importante é que a alocação incorreta para o tratamento de problemas relacionados ao envelhecimento pode ser evitada com um controle simples e apropriado, do viés que envolve o tamanho corporal.

5 CONSIDERAÇÕES FINAIS

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 de mobilidade após normalizar a variável da força muscular pelo tamanho corporal. Adicionalmente houve melhora da previsibilidade da mobilidade. 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. 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 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 pode evitar erros na classificação da baixa força muscular de idosos, decorrentes do viés causado pelo tamanho corporal.

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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

CNPq
Conselho Nacional de Desenvolvimento
Científico e Tecnológico

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

PROJETO:
870282/1997-2 -

COORDENADOR:
Regina Szylit

ORIENTADOR:
Dalmo Roberto Lopes Machado

Eu, **Pedro Pugliesi Abdalla**, 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
CPF:

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 n°   , 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 n° 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

USP 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   , 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:
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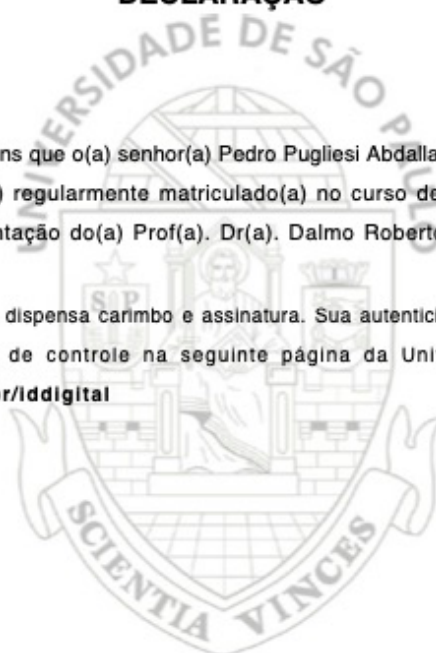
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Código de controle: DSZY - X1ZT - CFNF - 9G7N

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 número 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.

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

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.*
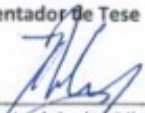
Na Universidade de São Paulo:

ASSINATURAS

Aceitando na íntegra 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

_____
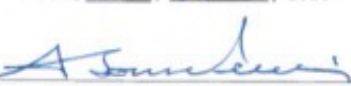Prof. Dr. António Manuel Fonseca
Diretor

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
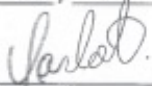Universidade de São Paulo
Ribeirão Preto, _14_ / _05_ / 2020

_____
Profª Dra. Maria Helena Palucci Marziale
Diretora

Pela Universidade do Porto
Porto, _02_ / _11_ / 2020

_____
Prof. Dr. António Sousa Pereira
Reitor

Pela Universidade de São Paulo
Porto, _08_ / _04_ / 2020.

_____
Prof. Dr. Vahan Agopyan
Reitor

ANEXO E – AUTORIZAÇÃO PARA UTILIZAÇÃO DE REPRODUÇÃO E TRADUÇÃO DE FIGURA

M Gmail

Pedro Abdalla <pedroabdalla11@gmail.com>

Figure - Authorisation for replication and translation
5 messages

Pedro Abdalla <pedroabdalla11@gmail.com>   Sun, Jan 23, 2022 at 3:23 AM
To: "Tomkinson, Grant" <grant.tomkinson@und.edu>, a.m.nevill@wlv.ac.uk
Cc: Dalmo Machado <dalmo@usp.br>

Dear Nevill and Tomkinson, my name is Pedro and I am a dual degree doctoral student at the University of São Paulo (Brazil) and the University of Porto (Portugal).

I would like to request permission to replicate a Figure from a recent study written by you ("How Should Adult Handgrip Strength Be Normalized? Allometry Reveals New Insights and Associated Reference Curves").

My subject of study is allometry (normalization of muscle strength in older adults). When reading your article, I became very interested in Figure 1 of your study:
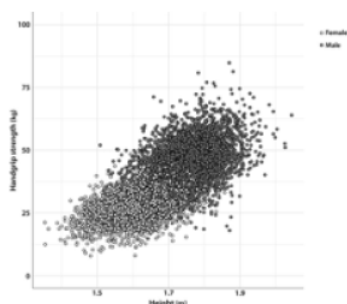

FIGURE 1—Association between HGS (in kilograms; average of the maximum score attained for each hand) and height (in meters) by gender.

This Figure helps in understanding my discussion in the thesis. I would like to be able to use it (translated into Portuguese, the thesis writing language) to properly explain the linear relationship between height and handgrip strength. If you authorize, I will obviously quote the reference of your article saying that the figure has been translated and adapted into Portuguese.

I thank you sir for your attention.

Best regards,
Pedro.

--
Pedro Pugliesi Abdalla

Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo (EERP-USP)
Faculdade de Desporto da Universidade do Porto (FADEUP)
Doutorando no Programa Interunidades de Doutoramento em Enfermagem (EERP-USP) e no Programa de Doutoramento em Atividade Física e Saúde (FADEUP)

Nevill, Alan M. (Prof) <a.m.nevill@wlv.ac.uk>   Sun, Jan 23, 2022 at 7:30 PM
To: Pedro Abdalla <pedroabdalla11@gmail.com>, "Tomkinson, Grant" <grant.tomkinson@und.edu>
Cc: Dalmo Machado <dalmo@usp.br>

Yes go ahead and use the figure. Note that this statement below is incorrect "properly explain the linear relationship between height and handgrip strength" The relationship is curvilinear (see the allometric association) as described in the paper

Prof Alan M Nevill

Faculty of Education, Health and Wellbeing

University of Wolverhampton

Walsall Campus,

Gorway Road,

Walsall WS1 3BD

UK

From: Pedro Abdalla <pedroabdalla11@gmail.com>
Sent: 23 January 2022 06:23
To: Tomkinson, Grant <grant.tomkinson@und.edu>; Nevill, Alan M. (Prof) <a.m.nevill@wlv.ac.uk>
Cc: Dalmo Machado <dalmo@usp.br>
Subject: Figure - Authorisation for replication and translation

Dear Nevill and Tomkinson, my name is Pedro and I am a dual degree doctoral student at the University of São Paulo (Brazil) and the University of Porto (Portugal).

I would like to request permission to replicate a Figure from a recent study written by you ("How Should Adult Handgrip Strength Be Normalized? Allometry Reveals New Insights and Associated Reference Curves").

My subject of study is allometry (normalization of muscle strength in older adults). When reading your article, I became very interested in Figure 1 of your study:
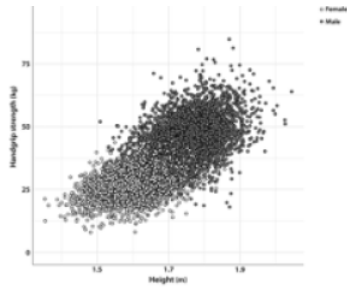
FIGURE 1—Association between HGS (in kilograms; average of the maximum score attained for each hand) and height (in meters) by gender.

This Figure helps in understanding my discussion in the thesis. I would like to be able to use it (translated into Portuguese, the thesis writing language) to properly explain the linear relationship between height and handgrip strength. If you authorize, I will obviously quote the reference of your article saying that the figure has been translated and adapted into Portuguese.

I thank you sir for your attention.

Best regards,

Pedro.

--

Pedro Pugliesi Abdalla

Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo (EERP-USP)

Faculdade de Desporto da Universidade do Porto (FADEUP)

Doutorando no Programa Interunidades de Doutoramento em Enfermagem (EERP-USP) e no Programa de Doutoramento em Atividade Física e Saúde (FADEUP)

Pedro Abdalla <pedroabdalla11@gmail.com>   Sun, Jan 23, 2022 at 7:42 PM
To: "Nevill, Alan M. (Prof)" <a.m.nevill@wlv.ac.uk>
Cc: "Tomkinson, Grant" <grant.tomkinson@und.edu>, Dalmo Machado <dalmo@usp.br>

Dear Nevill,
Thanks for your proper response and authorization. Sorry for the error.

Have a good week!

Best regards,
Pedro.

[Quoted text hidden]
[Quoted text hidden]

Tomkinson, Grant <grant.tomkinson@und.edu>   Mon, Jan 24, 2022 at 6:11 PM
To: "Nevill, Alan M. (Prof)" <a.m.nevill@wlv.ac.uk>, Pedro Abdalla <pedroabdalla11@gmail.com>
Cc: Dalmo Machado <dalmo@usp.br>

Hi Pedro

I too am OK with you reproducing the figure for your thesis.

With gratitude

Grant

Grant Tomkinson *PhD*

Professor

Department of Education, Health and Behavior Studies

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Grand Forks ND 58202

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From: "Nevill, Alan M. (Prof)" <a.m.nevill@wlv.ac.uk>
Date: Sunday, January 23, 2022 at 4:30 PM
To: Pedro Abdalla <pedroabdalla11@gmail.com>, "Tomkinson, Grant" <grant.tomkinson@und.edu>
Cc: Dalmo Machado <dalmo@usp.br>
Subject: RE: Figure - Authorisation for replication and translation

Yes go ahead and use the figure. Note that this statement below is incorrect "properly explain the linear relationship between height and handgrip strength" The relationship is curvilinear (see the allometric association) as described in the paper

Prof Alan M Nevill

Faculty of Education, Health and Wellbeing

University of Wolverhampton

Walsall Campus,

Gorway Road,

Walsall WS1 3BD

UK

From: Pedro Abdalla <pedroabdalla11@gmail.com>
Sent: 23 January 2022 06:23
To: Tomkinson, Grant <grant.tomkinson@und.edu>; Nevill, Alan M. (Prof) <a.m.nevill@wlv.ac.uk>
Cc: Dalmo Machado <dalmo@usp.br>
Subject: Figure - Authorisation for replication and translation

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My subject of study is allometry (normalization of muscle strength in older adults). When reading your article, I became very interested in Figure 1 of your study:

FIGURE 1—Association between HGS (in kilograms; average of the max-
imum score attained for each hand) and height (in meters) by gender.

[Quoted text hidden]

Pedro Abdalla <pedroabdalla11@gmail.com>   Mon, Jan 24, 2022 at 11:00 PM
To: "Tomkinson, Grant" <grant.tomkinson@und.edu>
Cc: "Nevill, Alan M. (Prof)" <a.m.nevill@wlv.ac.uk>, Dalmo Machado <dalmo@usp.br>

Dear Grant,
Thanks for your email and authorization.

With king regards,
Pedro.

[Quoted text hidden]
[Quoted text hidden]

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[3], 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].

APÊNDICE B – CONTRIBUIÇÕES DE CADA AUTOR NOS ARTIGOS.

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

Conceituação e Papéis/Redação - rascunho original (PPA), Curadoria e Visualização de Dados (JM), Metodologia (LB), Análises formais (PPA), Software (DRLM), Aquisição de fundos (JM), Supervisião (APS, ACRV), Investigação (ASC), Redação - revisão e edição (LB, DMG, LSLS e MFTJ), Validação (DRLM), Administração de projetos e recursos (JM).

Estudo Original II - Adjusting grip strength to body size: Analyses from 6 countries

Concepção (PPA, LB, DRLM) e design (JM), Aquisição de dados (APS, ACRV, ASC), Análises (PPA) e interpretação de dados (MFTJ, LSLS), redação do artigo (JAGM), revisando-o criticamente para conteúdo intelectual importante (GAB, NCR) e aprovação final da versão a ser publicada (PPA, LB, APS, MFTJ, LSLS, JAGM, ACRV, ASC, GAB, NCR, JM, DRLM).

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

Concepção (PPA, DRLM) e design (PPA), Aquisição de dados (JM, LB), Análises e interpretação de dados (PPA), redação do artigo (DRLM), revisando-o criticamente para conteúdo intelectual importante (DRLM, LB, GS) e aprovação final da versão a ser publicada (PPA, DRLM, LB, GS, JM).

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

Concepção, design, aquisição, análises e interpretação de dados (PPA; ACRV; APS; TCA; DRLM), Elaborar o trabalho e revisão crítica (MT; JAGM; TCA; JM; GS; ASO), Aprovar a versão a ser publicada (PPA; ACRV; APS; MT; JAGM; TCA; ASO; JM; GS; DRLM).