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ANA CLAUDIA ROSSINI-VENTURINI

Estimativa da composição corporal por análise multivariada em idosos

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RESUMO

ROSSINI-VENTURINI, A. C**. Estimativa da composição corporal por análise multivariada em idosos**. 2022. 128 f. Tese (Doutorado). Escola de Enfermagem de Ribeirão Preto – Universidade de São Paulo, Ribeirão Preto, 2022.

Essa tese defende que os modelos preditivos da composição corporal (CC) de idosos deveriam ser capazes de identificar/monitorar sua degeneração natural durante o envelhecimento de forma simultânea. Nesse sentido, os componentes corporais que mais se alteram durante a senescência (músculo, osso e gordura) representam alto risco do acometimento de sarcopenia, osteopenia e obesidade, e, portanto, requerem maior atenção e monitoramento. Componentes reconhecidos por tecido mole magro apendicular (TMMA), indicadores do mineral ósseo e tecido adiposo são identificadores dos agravos corporais acima referidos, deveriam ser facilmente identificados. Se os métodos preditivos da CC convencionais como antropometria e bioimpedância falham nessa tarefa, modelos alternativos de baixo custo, devem ser propostos. A redução nos custos dos serviços de saúde e ampliação das redes de atendimento a idosos sofreria positivo impacto econômico, uma vez que o acesso a equipamentos clínicos mais sofisticados está mais restrito a centros médicos. Diante do exposto, o objetivo geral deste estudo foi inicialmente verificar a precisão de métodos convencionais para identificar riscos a tais agravos, mediante o monitoramento dos componentes corporais em idosos; e caso falhassem, propor modelos de maior precisão e aplicação clínica de campo. Para isso, três objetivos específicos foram considerados e respondidos a partir de artigos originais. O primeiro (Artigo I – *Population specificity affects prediction of apendicular lean soft tissues for diagnosed sarcopenia: a cross-sectional study*) buscou validar e examinar a eficácia das equações antropométricas existentes para predizer o TMMA em idosos brasileiros. As equações foram comparadas com os valores de referência dado por absorciometria de raio-X de dupla energia. Concluiu-se que a especificidade populacional prejudica a validade das equações, implicando em grande parte, no diagnóstico falso positivo/negativo da sarcopenia. O segundo objetivo (Artigo II – *Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: a cross-sectional study*) verificou a capacidade da bioimpedância, por técnica mais acurada em análise vetorial de bioimpedância (BIVA - clássica e específica), identificar as nuances corporais, nomeadamente da sarcopenia em idosos. A análise vetorial mostrou potencial para monitorar hidratação e perdas musculares. Além disso, tanto a BIVA clássica como a específica foram capazes de distinguir sarcopenia nas mulheres, mas não nos homens. Quando os critérios diagnósticos para sarcopenia foram testados individualmente, ambas também foram capazes de detectar as mudanças morfológicas (índice musculoesquelético), mas não as funcionais. Dessa forma, os resultados foram promissores, mas insuficientes para monitorar riscos da sarcopenia durante o envelhecimento. O terceiro objetivo (Artigo III - *Multicompartment body composition analysis in older adults: a cross-sectional study*) retoma a antropometria convencional para propor e validar alternativamente um modelo multicompartimental único, capaz de predizer simultaneamente componentes corporais musculares, ósseos e de gordura. O modelo pôde predizer o TMMA como um dos critérios diagnósticos da sarcopenia, o

conteúdo mineral ósseo como marcador da saúde óssea dos idosos, e a massa gorda para indicar os limiares da obesidade. O modelo foi submetido à validação cruzada, mostrando coeficientes de desempenho válidos e confiáveis. Em conclusão, considerar a especificidade populacional ao selecionar equações para predizer o evita erros no diagnóstico de sarcopenia do componente muscular. A falha da BIVA na identificação e monitoramento satisfatório dos indicadores de sarcopenia para ambos os sexos requer uma alternativa simples, de baixo custo e viável capaz de predizer simultaneamente indicadores de sarcopenia, obesidade e osteoporose. Portanto, o uso do modelo aqui proposto representa uma simples estratégia, capaz de monitorar, identificar e prever precocemente os agravos dessas doenças.

Palavras-chave: DXA. Composição Corporal. Envelhecimento. Sarcopenia. Massa Gorda. Conteúdo Mineral Ósseo.

ABSTRACT

ROSSINI-VENTURINI, A. C**. Estimation of body composition by multivariate analysis in the older adults**. 2022. 128 p. Doctoral Dissertation, University of São Paulo at Ribeirão Preto College of Nursing, Ribeirão Preto, 2022.

This thesis argues that predictive models of body composition (BC) of the older adults should be able to simultaneously identify/monitor your natural degeneration during aging. In this sense, the body components that change most during senescence (muscle, bone and fat) represent a high risk of sarcopenia, osteopenia and obesity, and therefore require greater attention and monitoring. Components recognized by lean soft tissue apendicular (ALST), indicators of bone mineral and adipose tissue are identifiers of the bodily injuries mentioned above, they should be easily identified. If conventional BC predictive methods such as anthropometry and bioimpedance fail in this task, alternative low-cost models should be proposed. The reduction in the costs of health services and the expansion of care networks for the older adults would have a positive economic impact, since access to more sophisticated clinical equipment is more restricted to medicais centers. Given the above, the general objective of this study was initially to verify the accuracy of conventional methods to identify risks to such injuries, by monitoring body components in the older adults; and if they failed, propose more accurate models and clinical application in the field. For this, three specific objectives were considered and answered from original articles. The first (Article I – Population specificity affects prediction of appendicular lean soft tissues for diagnosed sarcopenia: a cross-sectional study) sought to validate and examine the effectiveness of existing anthropometric equations to predict ALST in Brazilians older adults. Equations were compared with reference values given by dual-energy X-ray absorptiometry. It was concluded that the population specificity impairs the validity of the equations, implying the false positive/negative diagnosis of sarcopenia. The second objective (Article II – Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: a cross-sectional study) verified the capacity of bioimpedance, using a more accurate technique in bioimpedance vector analysis (BIVA - classic and specific), identify bodily nuances, namely sarcopenia in the older adults. Vector analysis showed potential to monitor hydration and muscle loss. Furthermore, both classical and specific BIVA were able to distinguish sarcopenia in women but not in men. When the diagnostic criteria for sarcopenia were tested individually, both were also able to detect morphological changes (musculoskeletal index), but not functional ones. Thus, the results were promising, but insufficient to monitor risks of sarcopenia during aging. The third objective (Article III - Multicompartment body composition analysis in older adults: a cross-sectional study) takes up conventional anthropometry to alternatively propose and validate a single multicompartment model, capable of simultaneously predicting muscle, bone and fat body components. The model was able to predict ALST as one of the diagnostic criteria for sarcopenia, bone mineral content as a marker of bone health in the older adults, and fat mass as an indicator of obesity thresholds. The model was submitted to cross-validation, showing valid and reliable coefficients. In conclusion, considering population

specificity when selecting equations to predict ALST avoids errors in diagnosing sarcopenia of the muscular component. BIVA's failure to identify and monitor sarcopenia indicators for both sexes requires a simple, low-cost, and viable alternative capable of simultaneously predicting sarcopenia, obesity, and osteoporosis indicators. Therefore, the use of the model proposed here represents a simple strategy, capable of monitoring, identifying and precociously predicting the aggravations of these diseases.

Keywords: DXA. Body composition. Aging. Sarcopenia. Fat mass. Bone Mineral Content.

RESUMEN

ROSSINI-VENTURINI, A. C**. Estimación de la composición corporal por análisis multivariado en ancianos**. 2022. 128 h. Tesis (Doctorado) – Escuela de Enfermería de Ribeirão Preto, Universidad de São Paulo, Ribeirão Preto, 2022.

Esta tesis argumenta que los modelos predictivos de composición corporal (CC) de las personas mayores deberían ser capaces de identificar/monitorizar simultáneamente su degeneración natural durante el envejecimiento. En este sentido, los componentes del organismo que más se modifican durante la senescencia (músculo, hueso y grasa) representan un alto riesgo de sarcopenia, osteopenia y obesidad, y por tanto requieren mayor atención y seguimiento. Los componentes reconocidos por tejido blando magro apendicular (TBMA), indicadores de mineral óseo y tejido adiposo son identificadores de las lesiones corporales mencionadas anteriormente, deben identificarse fácilmente. Si los métodos predictivos de CC convencionales, como la antropometría y la bioimpedancia, fallan en esta tarea, se deben proponer modelos alternativos de bajo costo. La reducción de los costos de los servicios de salud y la ampliación de las redes de atención al adulto mayor tendrían un impacto económico positivo, ya que el acceso a equipos clínicos más sofisticados está más restringido a los centros médicos. Dado lo anterior, el objetivo general de este estudio fue inicialmente verificar la precisión de los métodos convencionales para identificar riesgos de este tipo de lesiones, mediante el monitoreo de componentes corporales en ancianos; y si fracasaron, proponer modelos más precisos y de aplicación clínica en el campo. Para ello, se consideraron tres objetivos específicos y se respondieron a partir de artículos originales. La primera (Artículo I - *Population specificity affects prediction of apendicular lean soft tissues for diagnosed sarcopenia: a cross-sectional study*) buscó validar y examinar la efectividad de las ecuaciones antropométricas existentes para predecir el TBMA en ancianos brasileños. Las ecuaciones se compararon con valores de referencia dados por absorciometría de rayos X de energía dual. Se concluyó que la especificidad poblacional perjudica la validez de las ecuaciones, lo que implica en gran medida el diagnóstico falso positivo/negativo de sarcopenia. El segundo objetivo (Artículo II - *Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: a cross-sectional study*) verificó la capacidad de la bioimpedancia, utilizando una técnica más precisa en el análisis de vectores de bioimpedancia (BIVA - clásica y específica), para identificar matices corporales, a saber, la sarcopenia en los ancianos. El análisis de vectores mostró potencial para controlar la hidratación y la pérdida de masa muscular. Además, tanto el BIVA clásico como el específico pudieron distinguir la sarcopenia en mujeres pero no en hombres. Cuando los criterios diagnósticos de sarcopenia se probaron individualmente, ambos también pudieron detectar cambios morfológicos (índice musculoesquelético), pero no funcionales. Por lo tanto, los resultados fueron prometedores, pero insuficientes para monitorear los riesgos de sarcopenia durante el envejecimiento. El tercer objetivo (Artículo III - *Multicompartment body composition analysis in older adults: a cross-sectional study*) retoma la antropometría convencional para proponer y validar alternativamente un modelo multicompartimental único, capaz de predecir simultáneamente los componentes musculares, óseos y grasos del cuerpo. El modelo pudo

predecir el TBMA como uno de los criterios de diagnóstico de la sarcopenia, el contenido mineral óseo como marcador de la salud ósea en los ancianos y la masa grasa como indicador de los umbrales de obesidad. El modelo fue sometido a validación cruzada, mostrando coeficientes de desempeño válidos y confiables. En conclusión, considerar la especificidad de la población al seleccionar ecuaciones para predecir evita errores en el diagnóstico de sarcopenia del componente muscular. El fracaso de BIVA para identificar y monitorear satisfactoriamente indicadores de sarcopenia para ambos sexos requiere una alternativa simple, de bajo costo y viable capaz de predecir simultáneamente indicadores de sarcopenia, obesidad y osteoporosis. Por lo tanto, el uso del modelo aquí propuesto representa una estrategia simple, capaz de monitorear, identificar y predecir precozmente los agravamientos de estas enfermedades.

Palabras-clave: DXA. Composición corporal. Envejecimiento. Sarcopenia. Grasa corporal. Contenido mineral óseo.

LISTA DE FIGURAS

Artigo Original I

Artigo Original II

Artigo Original III

LISTA DE TABELAS

Artigo Original I

Artigo Original II

Artigo Original III

LISTA DE ABREVIATURAS

2-C – Modelo de dois compartimentos

3-C – Modelo de três compartimentos

AF – Ângulo de fase

BIA – Análise de impedância bioelétrica

BIVA – Análise vetorial de impedância bioelétrica

CC – Composição corporal

CMO – Conteúdo mineral ósseo

DMO – Densidade mineral óssea

DXA – Absorciometria de raios X de dupla energia

IMC – Índice de massa corporal

MG – Massa gorda

MIG – Massa isenta de gordura

MM – Massa muscular

OMS – Organização mundial de saúde

R – Resistência

TME – Tecido muscular esquelético

TMMA – Tecido mole magro apendicular

Xc – Reatância

Z – Impedância

SUMÁRIO

1. INTRODUÇÃO

A composição corporal (CC) e o fenótipo corporal são os indicadores fisiológicos que mais se alteram durante o processo do envelhecimento. Nesta fase ocorre redução da massa muscular (MM) e conteúdo mineral ósseo (CMO), bem como acréscimo da massa gorda (MG) que impactam na funcionalidade do idoso (JAFARINASABIAN et al., 2017a). Essas alterações refletem agravos na CC durante os processos degenerativos do envelhecimento. Por isso essa tese defende que os modelos preditivos da CC de idosos devem ser capazes de identificar/monitorar sua degeneração natural durante o envelhecimento de forma simultânea.

A quantidade de MM regula a saúde metabólica de todo o organismo (WILKINSON; PIASECKI; ATHERTON, 2018). Por volta dos 27 anos de idade, homens e mulheres começam apresentar indícios de redução da MM (SILVA et al., 2010), e dos 20 até aos 70 anos ocorre um declínio desta, de até 40% (ROGERS; EVANS, 1993). Estudos longitudinais reportam que em idosos com ≅75 anos, a MM reduz, aproximadamente de 0.64 a 0.7% ao ano em mulheres e de 0.8 a 0.98% em homens (MITCHELL et al., 2012). Essa redução decorre do processo de envelhecimento, que provoca um desequilíbrio entre as vias anabólicas e catabólicas das proteínas musculares, causando redução da musculatura (CRUZ-JENTOFT; SAYER, 2019). Essas alterações provocam redução no tamanho e número de miofibrilas, impactando principalmente nas dimensões de fibras do tipo II. Isso acontece, devido à transição das fibras musculares do tipo II para o tipo I durante a senescência (FRONTERA; ZAYAS; RODRIGUEZ, 2012). Além disso, há também redução no número de células satélites de fibras musculares do tipo II (FRONTERA; ZAYAS; RODRIGUEZ, 2012; VERDIJK et al., 2014). Outras importantes mudanças fisiológicas também impactam a função muscular. Por exemplo, infiltração de gordura intramuscular e intermuscular (FRONTERA; ZAYAS; RODRIGUEZ, 2012) e diminuição da influência anabólica do sistema endócrino. No sistema nervoso, ocorre redução de neurônios motores, remodelação de unidades motoras e comprometimento da ativação neuromuscular. Embora essas mudanças não ocorram no tipo de fibras musculares, impactam nas suas respostas funcionais (FRONTERA; ZAYAS; RODRIGUEZ, 2012). Essas mudanças observadas em ambos os sexos durante o envelhecimento, configuram-se em consequências fisiológicas e funcionais atingindo sobremodo a saúde do idoso (FRONTERA; ZAYAS; RODRIGUEZ, 2012). Fraqueza muscular, redução da força muscular e capacidade de andar são alguns dos prejuízos associados às alterações musculares (CAWTHON et al., 2009). Além disso, vários

estudos tem mostrado associação inversa entre MM e mortalidade (SZULC et al., 2010; LEE et al., 2011; MURPHY et al., 2014; ABRAMOWITZ et al., 2018; LIU et al., 2022), favorecendo evidências para a manutenção de níveis mais altos de MM (LIU et al., 2022). Os desfechos de mortalidade prematura e risco de quedas aumentam o risco de hospitalização e oneram os sistemas públicos e privados de saúde (CAWTHON et al., 2017). Dessa forma, a quantificação da MM deve ser precisa, como forma profilática de doenças como a sarcopenia (BAUMGARTNER et al., 1995; GALLAGHER et al., 2000), a comprometer a mobilidade, aumento do número de quedas e fragilidade do idoso (CRUZ-JENTOFT; SAYER, 2019), nomeadamente em decorrência da sarcopenia.

Sarcopenia é definida como um distúrbio progressivo e generalizado do músculo esquelético e envolve redução acelerada de massa e função muscular (CRUZ-JENTOFT; SAYER, 2019). Em 2016, foi reconhecida como doença na Classificação Internacional de Doenças (CID-10M62.84) (ANKER; MORLEY; VON HAEHLING, 2016). A sarcopenia é classificada como severa quando a presença de baixo desempenho físico/mobilidade é identificada (CRUZ-JENTOFT et al., 2019). No Brasil, a prevalência é de 17% na população idosa, sendo maior nas mulheres (20%) do que nos homens (DIZ et al., 2017). Atualmente, a MM é o indicador da CC mais aceito entre os consensos (GONZALEZ; BARBOSA-SILVA; HEYMSFIELD, 2018). Diversos consensos estabelecidos para identificação da sarcopenia (CRUZ-JENTOFT et al., 2010a; MUSCARITOLI et al., 2010; FIELDING et al., 2011; MORLEY et al., 2011; CHEN et al., 2014; DAM et al., 2014; CRUZ-JENTOFT et al., 2019) levam em consideração aspectos morfológicos e redução do tecido mole magro apendicular (TMMA), nas respostas funcionais com impactos no desempenho motor (MUSCARITOLI et al., 2010; FIELDING et al., 2011; MORLEY et al., 2011; CHEN et al., 2014; DAM et al., 2014; CRUZ-JENTOFT et al., 2019) e na força muscular (DAM et al., 2014; CRUZ-JENTOFT et al., 2019). As consequências negativas estão associadas à dependência motora, aumento do risco de quedas, fraturas, comprometimentos cognitivos, morte prematura em idosos (CRUZ-JENTOFT et al., 2010b; BEAUDART et al., 2014), depressão e isolamento social, aumento do risco de doenças crônicas, sedentarismo (WILKINSON; PIASECKI; ATHERTON, 2018) e está associada à doenças respiratórias (BONE et al., 2017). Os gastos com sarcopenia impactam de forma significativa nos sistemas de saúde (BEAUDART et al., 2014). Em 2000, os gastos públicos decorrentes da sarcopenia foram de US$ 18,5 bilhões nos EUA. Uma redução de 10% na prevalência de sarcopenia

reduziria os custos com assistência médica em aproximadamente US$ 1,1 bilhões por ano (JANSSEN et al., 2004).

Além da sarcopenia, marcada pela redução da MM, o envelhecimento provoca diminuição do CMO e densidade mineral óssea (DMO) aumentando o risco de quedas e fraturas (JÄRVINEN et al., 2008). Após a terceira década ocorre uma diminuição progressiva do CMO (LIM et al., 2004), que se agrava com o avançar da idade. Isto ocorre devido ao desequilíbrio entre a formação e mudanças na absorção óssea (BURCKHARDT; MICHEL, 1989). Esse declínio ao longo da fase adulta pode ser influenciado pelo meio (OHNAKA, 2017), por fatores genéticos (MOAYYERI et al., 2012) e uso prolongado de contraceptivos (KANG et al., 2016). Além disso, as mulheres apresentam menores valores de CMO em relação aos homens (SEGHETO et al., 2019). Essa diferença está relacionada as questões hormonais (HEIDARI et al., 2015) e se intensifica após a menopausa, quando ocorre uma redução significativa dos níveis de estrogênio. Esse declínio drástico pode desencadear a osteoporose, conhecida mundialmente como a mais prevalente doença óssea, caracterizada pela diminuição da massa óssea, deterioração da microarquitetura do tecido ósseo e por conseguinte, a força óssea (COUGHLAN; DOCKERY, 2014). Essas inúmeras alterações podem aumentar o risco de fratura. Estima-se que 137 milhões de mulheres e 21 milhões de homens apresentem alto risco de fraturas osteoporóticas em todo o mundo. É esperado que essa prevalência dobre nos próximos 40 anos (ODÉN et al., 2015). Diante do exposto, o monitoramento da saúde óssea é imprescindível, para isso o CMO e DMO são importantes determinantes no agravo desta doença (NGUYEN et al., 2005).

Outra preocupação que acomete a saúde do idoso é a obesidade, caracterizada por um acúmulo excessivo de gordura corporal que afeta negativamente sua saúde (KALYANI; CORRIERE; FERRUCCI, 2014). Além disso, é considerada uma doença complexa e multifatorial que se tornou uma pandemia mundial (BRAY et al., 2017). A MG, principal determinante da obesidade, apresenta um aumento progressivo em ambos os sexos até a 7ª década de vida. Após os 70 anos, a MG tende a declinar (SANTANASTO et al., 2017). Este acréscimo pode ser parcialmente explicado pela diminuição do gasto energético total e alterações hormonais durante a senescência (KALISH, 2016). O controle dos níveis de gordura nos idosos merece atenção e cuidado, uma vez que a obesidade impacta negativamente na qualidade de vida e desempenho físico (MATHUS-VLIEGEN, 2012; HAN; WU; LEAN, 2013). Além disso, está associada a mais de 200 complicações médicas e risco aumentado de morbidade e mortalidade, representando a

quinta principal causa de morte no mundo (BRAY et al., 2017; LEE et al., 2018; BLÜHER, 2019). Esses agravos impactam os cofres públicos e refletem nos gastos com saúde (COLDITZ, 1999; CAWLEY; MEYERHOEFER, 2012) visto que o custo médico anual para um indivíduo obeso em média, é cerca de US$ 1,429 maior do que para um sujeito saudável (REILLY; KELLY, 2011). A obesidade pode ser identificada quando o IMC ≥ 30 kg/m^2 (NEWMAN et al., 2003), ou quando se observa aumento nos limiares de % gordura (>28% em homens e >40% em mulheres) (BAUMGARTNER et al., 2004) ou circunferência da cintura > 98 cm (SCHRAGER et al., 2007). No entanto, a Associação Americana de Endocrinologia Clínica recomenda o uso dos limites de gordura da OMS, para definir obesidade com %MG > 25% e > 35% para homens e mulheres, respectivamente (GARVEY et al., 2016).

Na literatura, o comprometimento funcional mais agravante relacionado a músculo, osso e gordura é a obesidade osteosarcopênica, que consiste na presença concomitante de sarcopenia, osteoporose e obesidade (JAFARINASABIAN et al., 2017b). Outra complicação é a coexistência de obesidade e sarcopenia, definida como obesidade sarcopênica. Esse *cross-talk* entre músculo e gordura leva a um risco cumulativo derivado das duas situações clínicas individuais (DONINI et al., 2022). Além disso, outro problema para a saúde global do idoso envolve a combinação da redução óssea e muscular é denominada osteosarcopenia (KIRK; ZANKER; DUQUE, 2020). Com o tempo, ambas as condições, provavelmente, resultarão em obesidade osteosarcopênica (ABIDIN; MITRA, 2021). Diante do exposto, os três componentes (músculo, osso e gordura) estão intimamente relacionados durante o envelhecimento, portanto, devem ser avaliados concomitantemente (JAFARINASABIAN et al., 2017a).

1.1 Massa muscular: critério morfológico no diagnóstico de sarcopenia

A MM é o critério utilizado para confirmar o diagnóstico de sarcopenia (CRUZ-JENTOFT et al., 2019). Nesse contexto, a variável mais utilizada para representar a quantidade de MM é o TMMA (CRUZ-JENTOFT et al., 2010a; FIELDING et al., 2011; MORLEY et al., 2011; GOULD et al., 2014; DIZ et al., 2017; SHAFIEE et al., 2017; CRUZ-JENTOFT et al., 2019; CHEN et al., 2020; PETERMANN-ROCHA et al., 2022). O TMMA é composto, principalmente, por quatro componentes: tecido músculo esquelético (TME) dos membros, gordura intramuscular e uma pequena quantidade de pele e tecidos conectivos (GEISLER et al., 2017). Nesse sentido, o TMMA é considerado

um bom indicador do TME, uma vez que representa 75% do TME total do adulto (KIM et al., 2002). Por esse motivo, o TMMA é também chamado de TME apendicular (KAWAKAMI et al., 2021). No entanto, os termos representam diferentes compartimentos, uma vez que o TMMA pertence ao nível II (molecular) e o TME apendicular ao nível IV (órgão tecidual) do modelo dos cinco níveis da CC proposto por Wang, Pierson e Heymsfield (1992). A quantidade muscular apresenta correlação positiva com o tamanho corporal, ou seja, indivíduos com maior tamanho corporal, normalmente apresentam maior quantidade muscular (KIM; JANG; LIM, 2016). Portanto, os valores absolutos de TMMA podem ser ajustados para peso corporal de diferentes formas (i.e., TMMA/altura^2; TMMA/peso corporal; TMMA/IMC) (BAUMGARTNER et al., 1998; JANSSEN; HEYMSFIELD; ROSS, 2002; CAWTHON et al., 2014). Nesse sentido, o método amplamente disponível para medir a quantidade muscular (TMMA) é a absorciometria de raios X de dupla energia (DXA) (CRUZ-JENTOFT; SAYER, 2019).

A DXA é considerada um modelo de 3 compartimento (3-C) para avaliar a CC (TOOMEY et al., 2015) e utilizada como método de referência para o CMO. Além disso, é precisa para determinar MG e tecido mole magro de corpo total e regional (KAMINSKY et al., 2014). Atualmente, a DXA está se tornando preferência tanto na pesquisa como na pratica clínica para medir a quantidade muscular (BUCKINX et al., 2018). Pois é capaz de estimar os principais componentes corporais, incluindo o TMMA, de forma rápida e precisa. Todavia, a DXA não é um método portátil para uso em estudos epidemiológicos (CRUZ-JENTOFT et al., 2019). Assim, seu uso é restrito a pratica clínica e grandes centros de pesquisa (GONZALEZ; HEYMSFIELD, 2017). Diante do exposto, análise de impedância bioelétrica (BIA) pode ser uma alternativa no contexto da sarcopenia (GONZALEZ; HEYMSFIELD, 2017; CRUZ-JENTOFT et al., 2019) e composição corporal dos idosos.

1.2 Análise de impedância bioelétrica, sarcopenia e composição corporal

Análise de impedância bioelétrica (BIA) também é utilizada para identificar baixa quantidade muscular no contexto da sarcopenia (GONZALEZ; HEYMSFIELD, 2017; GONZALEZ; BARBOSA-SILVA; HEYMSFIELD, 2018), uma vez que é um método rápido, seguro e não invasivo (MARINI et al., 2020). Diferentes dos outros métodos para estimar a CC, a BIA não estima um componente específico (i.e., gordura, músculo e osso) (GONZALEZ; HEYMSFIELD, 2017), e é considerada um método duplamente indireto (GONZALEZ; BARBOSA-SILVA; HEYMSFIELD, 2018). Dessa forma, a utilização da

BIA carece de equações específicas para uma determinada população. Por isso, os avaliadores utilizam os valores gerados pelo equipamento, ou seja, equações embutidas no aparelho, e na maioria das vezes, não apresentada pelo fabricante (BUCKINX et al., 2018).

Como alternativa, a análise pode ser realizada usando dados brutos como na abordagem de análise vetorial de impedância bioelétrica (BIVA) (PICCOLI et al., 1994; BUFFA et al., 2013; MARINI et al., 2013). A impedância bioelétrica (Z, ohm) é composta pela resistência (R, ohm) e reatância (Xc, ohm) [$Z=(R^2+Xc^2)^{0.5}$]. R representa a oposição que o corpo oferece ao fluxo de uma corrente elétrica alternada e está inversamente relacionado ao conteúdo de água e eletrólitos dos tecidos. Enquanto que a Xc está relacionada às propriedades de capacitância da membrana celular e às variações que podem ocorrer dependendo de sua integridade, função e composição (BAUMGARTNER; CHUMLEA; ROCHE, 1988). O ângulo de fase (AF) [$AF=\text{arctn } Xc/R\ 180/\pi$] é uma medida segura, não invasiva e de baixo custo, e é determinado pelo tempo que a corrente elétrica passa pela membrana celular (NORMAN et al., 2012). Vários estudos destacam o AF como um indicador da saúde celular, massa celular corporal, integridade da membrana celular e melhor função muscular (LUKASKI; KYLE; KONDRUP, 2017; MATIAS et al., 2015; NORMAN et al., 2012). Além disso, o AF apresenta uma associação com massa muscular (KILIC et al., 2017), qualidade muscular (MARINI et al. 2020) e força muscular (BASILE et al.; 2014). Além disso, maiores valores de AF estão relacionados a altos níveis de atividade física em idosos não institucionalizados (NORMAN et al., 2012).

Nesse sentido, como as variáveis utilizadas na BIVA são indicadores de saúde muscular e celular, a BIVA pode ser uma estratégia interessante para identificar sarcopenia. Durante a revisão de literatura, apenas um estudo verificou o uso da BIVA (clássica e específica) para identificar sarcopenia em idosos de ambos os sexos (MARINI et al., 2012). No entanto, eles usaram apenas o critério de quantidade muscular. Nesse sentido, nosso Artigo Original II avançou na área do conhecimento e classificou os idosos com sarcopenia considerando os três critérios (qualidade e quantidade muscular e desempenho físico) (CRUZ-JENTOFT et al., 2019). Além disso, verificamos as associações entre as BIVAs com os componentes da CC, hidratação e desempenho físico de idosos com e sem sarcopenia.

2. DELIMITAÇÕES E JUSTIFICATIVAS

Durante o envelhecimento mudanças importantes ocorrem nas proporções de músculo, gordura e osso. Essas alterações impactam na saúde, qualidade de vida e capacidade funcional dos idosos. Para monitorar a variabilidade entre os componentes corporais, é importante o desenvolvimento de métodos simples capazes de monitorar os agravos do envelhecimento (SAARELAINEN et al., 2012). Dessa forma, a avaliação da CC é uma ferramenta importante nesse processo (NORMAN et al., 2015). As técnicas para avaliar os componentes corporais em ambientes clínicos e em campo devem utilizar métodos seguro, não invasivo, acessível e que necessite do mínimo possível de colaboração do paciente idoso.

Várias equações para predizer a CC, a partir de medidas antropométricas, têm sido desenvolvidas através de modelo de dois compartimentos (2-C) que determinam a MG e massa isenta de gordura (MIG). Essas equações utilizaram a pesagem hidrostática como método de referência e estimaram a gordura corporal a partir da densidade corporal (SIRI, 1961; BROZEK et al., 1963; DURNIN; WOMERSLEY, 1974; TRAN; WELTMAN, 1988; 1989). Porém, esses modelos apresentam limitações (detalhadas no Artigo III) ao considerar densidade comum a todos componentes corporais (FIDANZA; KEYS; ANDERSON, 1953; BROZEK et al., 1963), desmineralização óssea progressiva (KUK et al., 2009) e alterações na hidratação da MIG (BRODIE; MOSCRIP; HUTCHEON, 1998), modificações típicas da senescência.

Com o aumento do envelhecimento na população mundial, a incidência de sarcopenia aumentará significativamente e resultará em consequências adversas (XIE et al., 2020). Por isso, a sarcopenia ganhou maior visibilidade na pesquisa e pratica clínica (BUCKINX et al., 2018), uma vez que as mudanças no TMMA decorrentes do envelhecimento estão associadas a desfechos clínicos adversos, como fraturas ósseas e até mesmo a morte (FILIPPIN et al., 2015). Nesse contexto, estabelecer um consenso internacional sobre um método preciso, confiável e de baixo custo para avaliar o TMMA em pesquisa, pratica clínica e estudos epidemiológicos é importante (BUCKINX et al., 2018). Além disso, como os desfechos patológicos associados à sarcopenia frequentemente resultam nas combinações da quantidade e qualidade da musculatura, osso e gordura (STENHOLM et al., 2008; CRUZ-JENTOFT et al., 2010a).

O uso de modelos antropométricos para estimar a CC de forma multicompartimental vêm se apresentando como alternativa válida para jovens de ambos os sexos (MACHADO; OIKAWA; BARBANTI, 2013; MACHADO et al., 2017), e em

pacientes com HIV/Aids (DOS SANTOS et al., 2018), mostrando-se uma adequada abordagem para outros seguimentos populacionais. Para idosos, a máxima deveria contemplar os componentes corporais na forma que expressam os agravos crônico-degenerativos que ocorrem na CC durante o envelhecimento. Dessa forma, a abordagem para monitoramento da saúde do idoso, deve envolver uma estratégia prática, simples e não invasiva. Logo, esta tese pretende trazer avanço científico à área, com uma discussão dos meios convencionais de monitoramento da CC durante o envelhecimento.

3. OBJETIVOS

3.1 Objetivo Geral

Verificar a precisão de métodos convencionais para a estimativa dos componentes corporais em idosos; e propor modelos de maior precisão e aplicação clínica de campo.

3.2 Objetivos Específicos

Especificamente três objetivos foram descritos:

1. Validar equações antropométricas para predizer tecido mole magro apendicular e sua precisão para o diagnóstico de sarcopenia em idosos Brasileiros;

2. Avaliar a associação entre análise vetorial de impedância bioelétrica clássica e específica com composição corporal, hidratação e desempenho físico em idosos com e sem sarcopenia; e verificar qual análise vetorial (clássica ou específica) é mais precisa para distinguir sarcopenia em idosos de ambos os sexos.

3. Propor e validar um modelo antropométrico multicompartimental para predizer simultaneamente tecido mole magro apendicular, massa gorda e conteúdo mineral ósseo com altos níveis de acurácia e baixos erros de estimativa;

4. RESULTADOS

Os resultados dessa tese estão apresentados em três artigos. O primeiro deles contempla o objetivo específico 1, através da comparação das equações existentes (TMMA) com o método de referência (DXA). O segundo objetivo específico foi alcançado através do Artigo II que verificou o uso da BIVA como meio para identificar sarcopenia, composição corporal e hidratação dos idosos. Por fim, uma vez que os métodos convencionais falharam na identificação monitoramento dos componentes corporais de interesse para o idoso, o objetivo específico 3 foi considerado com a proposição de um modelo antropométrico multicompartimental, capaz de predizer simultaneamente os componentes corporais que mais se alteram durante o envelhecimento (TMMA, MG e CMO). As contribuições dos autores para cada artigo estão apresentadas no Apêndice C.

4.1 Artigo Original I – Population specificity affects prediction of appendicular lean tissues for diagnosed sarcopenia: a cross-sectional study.

Esse tópico apresenta uma comparação de equações existentes na literatura para predizer o TMMA com o método de referência DXA. Este trabalho foi realizado durante a disciplina "Redação Científica para Ciências da Saúde" na Faculdade de Medicina de Ribeirão Preto – Universidade de São Paulo no ano de 2019. O artigo intitulado: *Population specificity affects prediction os appendicular lean tissues for diagnosed sarcopenia: a cross-sectional study* foi publicado no *Journal Nutrición Hospitalaria*, em 2020 [http://dx.doi.org/10.20960/nh.02929] (VENTURINI et al., 2020). O *Journal Nutrición Hospitalaria* é uma revista internacional, que no momento da publicação tinha um fator de impacto de 1.057 (2020), atualmente indica 1.169 (2022).

Referência: VENTURINI, A.C.R. et al. Population specificity affects prediction of appendicular lean tissues for diagnosed sarcopenia: a cross-sectional study. **Nutr Hosp**. 2020, v. 37, n. 4, p.776-785, 27 aug. 2020. doi: http://dx.doi.org/10.20960/nh.02929.

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

RESUMEN

Introducción: la sarcopenia es una enfermedad caracterizada por la reducción del tejido musculoesquelético y la fuerza muscular. Uno de los criterios utilizados para su diagnóstico es la determinación de tejido blando magro apendicular por DXA ($TBMA_{DXA}$), método costoso que no siempre está disponible en la práctica clínica. Las ecuaciones antropométricas suponen un bajo coste y predicen bien el TBMA, pero con una validez desconocida para los varones brasileños de 60 a 79 años. Por lo tanto, nuestro objetivo fue validar las ecuaciones antropométricas existentes predictivas del TBMA y verificar su precisión para el diagnóstico de sarcopenia en varones brasileños de edad avanzada; **Métodos:** participaron en este estudio transversal 25 hombres de edad avanzada (69,3 ± 5,60años). Se determinaron el $TBMA_{DXA}$ y las medidas antropométricas. Las ecuaciones predictivas del TBMA se compararon com el $TBMA_{DXA}$. La validez de las ecuaciones en las comparaciones se confirmó cuando: p>0.05 (prueba de la "t" pareada); error estándar estimado (EEE) < 3.5kg; coeficiente de determinación $r^2 > 0.70$. **Resultados:** dos ecuaciones indias cumplieron los criterios (Kulkarini 1: 22.19 ± 3.41 kg; $p = 0.134$; $r^2 = 0.78$; EEE = 1.3 kg; Kulkarini 3: 22.14 ± 3.52 kg; $p = 0.135$; $r^2 = 0.82$; EEE = 1.2 kg). Sin embargo, presentaron sesgo promedio (Bland-Altman: 0.54 y 0.48 kg) y clasificación de 'falso negativo' para el índice TBMA. Por lo tanto, se crearon tres ecuaciones explicativas. La ecuación más precisa mostró un alto acuerdo ($r^2_{adj} = 0.87$), validez ($r^2_{PRESS} = 0.83$), bajo error predictivo ($EEE_{PRESS} = 1.53$ kg) y clasificación del TBMA adecuada. **Conclusión:** los modelos antropométricos para predecir el TBMA son alternativas válidas para el diagnóstico y seguimiento de sarcopenia en los ancianos. Pero la especificidad de la población afecta a su validez predictiva, con riesgos de incorrección por clasificación falsa positiva/negativa.

Palabras Clave: Composición Corporal; Antropometría; DXA; Sarcopenia; Adultos mayores; Ecuación.

ABSTRACT

Introduction: sarcopenia is a disease characterized by reduced musculoskeletal tissue and muscle strength. The estimation of appendicular lean soft tissue by DXA ($ALST_{DXA}$) is one of the criteria for the diagnosis of sarcopenia. However, this method is expensive and not readily available in clinical practice. Anthropometric equations are low-cost and able to accurate predict ALST, but such equations have not been validated for male Brazilian older adults between the ages of 60 to 79 years. To this end, this study sought to validate the existing predictive anthropometric equations for ALST, and to verify its accuracy for the diagnosis of sarcopenia in male Brazilian older adults. **Methods:** this cross-sectional study recruited and enrolled 25 male older adults (69.3 ± 5.60 years). $ALST_{DXA}$ and anthropometric measures were determined. ALST estimations with 13 equations were compared to $ALST_{DXA}$. The validity of the equations was established when: $p > 0.05$ (paired t-test); standard error of the estimate (SEE) < 3.5 kg; and coefficient of determination $r^2 > 0.70$. **Results:** two Indian equations met the criteria (Kulkarini 1: 22.19 ± 3.41 kg; $p = 0.134$; $r^2 = 0.78$; EPE = 1.3 kg. Kulkarini 3: 22.14 ± 3.52 kg; $p = 0.135$; $r^2 = 0.82$; SEE = 1.2 kg). However, these equations presented an average bias (Bland-Altman: 0.54 and 0.48 kg) and 'false negative' classification for the ALST index. Thus, three explanatory equations were developed. The most accurate equation demonstrated a high level of agreement ($r^2_{adj} = 0.87$) and validity ($r^2_{PRESS} = 0.83$), a low predictive error ($SEE_{PRESS} = 1.53$ kg), and an adequate ALST classification. **Conclusion:** anthropometric models for predicting ALST are valid alternatives for the diagnosis and monitoring of sarcopenia in older adults; however, population specificity affects predictive validity, with risks of false positive/negative misclassification.

Keywords: Body Composition; Anthropometry; DXA; Sarcopenia; Older Adults; Equation.

INTRODUCTION

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

The established consensus for the identification of sarcopenia (3,5-10) takes into consideration morphological aspects and reduced appendicular lean soft tissue (ALST), functional responses with an impact on motor performance (3,6-10) and muscle strength (3,7). Muscle tissue estimation may be measured using imaging techniques such as magnetic resonance imaging, computed tomography, ultrasound, and dual-energy x-ray absorptiometry (DXA) (3). However, these modalities are associated with high costs, high levels of radiation exposure (tomography), requirement of adequate space, specialized personnel, and longer time for evaluation. Thus, their use is restricted to specialist hospital and clinical settings (11). Further, these techniques are not always viable in estimating ALST for the diagnosis of sarcopenia, according to established consensus criteria. However, there are several advantages to the use of DXA, including: observer independence, fast and accurate total body measurements, and lower costs and exposure to radiation (12). With DXA, ALST is measured with great accuracy, as composed of lean mass free of fat and bone from the upper and lower limbs, the use of which by consensus is shown in Table 1.

Table 1. Different approaches of Appendicular Lean Soft Tissue (ALST) or its Index (IALST), according to the international consensus diagnosis of sarcopenia.

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

FNIH=Foundation for the National Institutes of Health; IWGS=International Working Group on Sarcopenia; SCWD=Society of Sarcopenia, Cachexia and Wasting Disorders; ESPEN=European Society for Clinical Nutrition and Metabolism Special Interest Group on cachexiaanorexia in chronic wasting diseases; EWGSOP=European Working Group on Sarcopenia in Older People.
ALST=apendicular lean soft tissue (kg); IALST=index apendicular lean soft tissue (kg/m^2). BMI = body mass index (kg/m^2). Stature in m^2.

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

The validity of anthropometric equations is important as it represents an alternative method/approach to DXA, which is relatively expensive and involves a greater complexity of execution, thus being impractical for epidemiological studies. On the other hand, anthropometry involves simpler and lower-cost measurements (21). Thus, this study sought to validate and examine the accuracy of the existing anthropometric

equations developed to predict ALST in male Brazilian older adults between the ages of 60 and 79 years. Our hypothesis is that the validity of existing anthropometric equations may fail for elderly Brazilians, impacting the appropriate diagnosis of sarcopenia. We believe that early diagnosis and appropriate disease monitoring may favor more efficient interventions and more effective monitoring, thus reducing the condition's adverse effects.

MATERIALS AND METHODS

Study population

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

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

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

minimum number of participants was reached (n = 25) even after applying the exclusion criteria.

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

Determination of appendicular lean soft tissue (ALST) using DXA

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

Predictive anthropometric equations of ALST

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

BMI (kg/m^2) was calculated and classified according to Lipschitz (26). The corrected arm muscle area (AMA_C) in cm^2 was calculated using the equation proposed by Heymsfield, McManus, Smith, Stevens and Nixon (27). To predict the ALST from the American, Chilean and Mexican equations, it was also necessary to determine handgrip strength (HS). This was measured using an analogic handheld dynamometer (Jamar®, model 5030J1). HS assessment procedures were conducted according to the

recommendations proposed by the American Society of Hand Therapists, provided by Massy-Westropp et al. (28). Thus, the largest of three attempts at one-minute intervals was recorded.

Predictive anthropometric equations of ALST

Thirteen ALST predictive equations developed for Americans [13], Australians [15], Brazilian [20], Indians [16], Chilean [17] and Mexicans [18] individuals were compared against $ALST_{DXA}$. The search to include these equations met the following criteria: studies published between 1998 and 2019; studies using older adults in their sample. Of note, studies involving only young individuals were not included. We further adopted the following keywords during the search: equations, appendicular lean soft tissue, older, aging, DXA. The equations used in our study are described in Table 2.

Table 2. Predictive equations of Appendicular Lean Soft Tissue (ALST) found in the literature for elderly men.

Author (year)	Sample Country of Origin	n for proposition	$Age_{[years]}$: mean (SD) or range	Eq.	ALST predictive equations	Original study	
						r^2	SEE
Baumgartner et al. (1998)	EUA	149 (male/ fem.)	73.6 (5.8)	1	$0.2487*Weight_{[kg]} + 0.0483*Stature_{[cm]} – 0.1584*$ Hip $circumference_{[cm]} + 0.0732*HS_{[kg]} + 2.5843*sex_{[♂=1;♀=0]} + 5.8828$	0.91	1.58
Visvanathan et al. (2012)	Australia	188 (male /fem.)	18 a 83	1	$9.11472 + 0.36992*$ $Weight_{[kg]} – 0.67551*BMI_{[kg/m²]} + 5.00840*sex_{[♂=1;♀=0]}$	0.90*	1.89
				2	$–27.879919 + 0.129727*$ $Weight_{[kg]} + 22.122674*Stature_{[m]} + 4.980820*sex_{[♂=1;♀=0]}$	0.90*	1.93
				3	$10.047427 + 0.353307*$ $Weight_{[kg]} – 0.621112*BMI_{[kg/m²]} – 0.022741*Age_{[years]} + 5.096201*sex_{[♂=1;♀=0]}$	0.91*	1.87
Gomes et al. (2013)	Brazil	106 (male=35; fem.=71)	> 80	1	$0.074*Stature_{[m]} + 0.277*$ $Weight_{[kg]} – 0.144*TS_{[mm]} – 0.103*$ waist $circumference_{[cm]} + 1.831*sex_{[♂=1;♀=0]} – 0.966$	0.82*	1.67
				2	$0.138*$ $Stature_{[m]} + 0.103*$ $Weight_{[kg]} + 3.061*sex_{[♂=1;♀=0]} – 12.489$	0.75*	1.94
Kulkarni et al. (2013)	Índia	851 (male)	18 a 79	1†	$– 13.432 – 0.0445*age_{[years]} + 0.200*$ $Weight_{[kg]} + 0.140*Stature_{[cm]}$	0.78*	1.28

				2	– 12.81 – 0.029*age$_{[years]}$ + 0.211* Weight$_{[kg]}$ + 0.153*Stature$_{[cm]}$ + 0.255*Calf circumference$_{[cm]}$ + 0.141*Arm circumference $_{[cm]}$ – 0.178*Hip circumference$_{[cm]}$	0.82*	1.17
				3†	– 16.270 – 0.037*age$_{[years]}$ + 0.143*Weigth$_{[kg]}$ + 0.159*Stature$_{[cm]}$ + 0.087*AMAc	0.82*	1.18
				4	– 0.996 – 0.023*age$_{[years]}$ + 0.274*Weight$_{[kg]}$ + 0.090*Stature$_{[cm]}$ + 0.223*Calf circumference$_{[cm]}$ + 0.143* Arm circumference$_{[cm]}$ – 0.104*Hip circumference$_{[cm]}$ – 3.163*LOG	0.86*	1.02
Lera et al. (2014)	Chile	308 (male=109; fem.=199)	69.9 (5.2)	1	0.107*Weight$_{[kg]}$ + 0.251* Knee height[cm] + 0.197* Calf circumference$_{[cm]}$ + 0.047*HS$_{[kg]}$ – 0.034* Hip circumference$_{[cm]}$ + 3.417*sex$_{[♂=1;♀=0]}$ – 0.020*age$_{[years]}$ – 7.646	0.89	1.35
Ramirez et al. (2015)	Mexico	171 (male /fem.)	60 a 86	1	0.215*Calf circumference$_{[cm]}$ + 0.093*HS$_{[kg]}$ + 0.061*Weight$_{[kg]}$ + 3.637*sex$_{[♂=1;♀=0]}$ + 0.112*Stature$_{[cm]}$ – 16.449	0.92	1.25
Santos et al. (2019)	EUA	15.293 (male =7810; fem.=7483)	≥ 18	1	-10.427 + (Calf circumference$_{[cm]}$ * 0.768) – (age$_{[years]}$* 0.029) + (sex* 7.523) + (white * 0 ou black * 2.203 ou mexican american * -0.540 or others* -0.402)	0.88	1.95

r^2= determination coefficient; SEE=Standard Error of the Estimate; *=adjusted; ♂=men; HS=Handgrip strength; BMI=Body mass index: Weight$_{kg}$/Stature$^2_{[m]}$; TS= Triceps Skinfold; AMAc= Arm Muscle Area Corrected: [Arm Circumference $_{[cm]}$ – (π*DCT$_{[cm]}$)]^2/4*π – 10 [27]; π= 3.14; LOG= Logarithm of the sum of the biceps, triceps, subscapular and supra iliac skinfolds, all in mm; Sex=0 for females, 1 for males; White, black, mexican american and others = 1; †= valid equation (p<0.05) *vs* DXA.

Statistical analysis

A descriptive analysis was used to describe the sample and ALST estimates by predictive equations. A confidence interval (95 % CI) was used to indicate the estimate reliability (%). The normality of the data was verified using the Shapiro-Wilk test. The validity of the equations was tested based on the criteria proposed by Lohman (29): a) no statistically significant differences ($p > 0.05$) from the ALST values referenced in the DXA using a paired t-test; b) standard error of the estimate (SEE) < 3.5 kg between predicted (equations) and measured (DXA) values; and c) coefficient of determination $r^2 > 0.70$ in the estimates. Because the diagnosis of sarcopenia requires an adequate estimation of ALST, a Bland-Altman plot (30) was used to identify the degree of agreement between measured and predicted values. Valid predictive models of the ALST index (ALSTI) were tested for the diagnosis of sarcopenia (< 7 kg/m^2) according to the

current cutoff points proposed by the EWGSOP (3). The cases of sarcopenia diagnosed by DXA were compared with the diagnoses made with the valid equations to verify predictive accuracy. In case of disagreement an explanatory regression model would be proposed using stepwise multiple regression. If the new equation demonstrated predictive potential for ALST, the assumptions of reduced multi-colinearity and variance inflation factor (VIF) lower than 10 would be considered (31). Statistical analyses were performed using the SPSS software, version 20 (Chicago, IL, USA). The plots were created using MedCalc® 2015 (v.15.2) and the PRESS statistics using Minitab® (v.17.3.1). Statistical significance was set at $\alpha = 5$ %.

RESULTS

The mean values of the variables were within the 95 % CI (Table 3) with small amplitude. This suggests more reliable values of the parameters. BMI values indicated that, in general, the 25 older adults presented with adequate body weight, and normal weight (between 22 and 27 kg/m²). However, the minimum (17.48 kg/m²) and maximum (31.08 kg/m²) values indicated the presence of older adults being classified as below ($BMI \leq 22$ kg/m²) and above ($BMI \geq 27$ kg/m²) the normal weight limits. The data normality trend (Shapiro-Wilk) showed well-centered residual values, with high potential for the use of linear regression or other empirical interpretation analyses.

Table 3. Descriptive analysis and normality test (Shapiro-Wilk) of body composition, anthropometric variables and handgrip strength of Brazilian older male.

Variables	Mean (SD)	CI 95%	Shapiro-Wilk	
			Value	*p*
Characterization				
Age (years)	69.28 (5.6)	66.97 a 71.59	0.967	0.562
ALST (kg)	21.65 (3.8)	20.08 a 23.23	0.926	0.071
IALST (kg/m²)	7.98 (1.0)	7.57 a 8.38	0.963	0.473
Fat mass (kg)	21.92 (6.9)	19.07 a 24.77	0.973	0.715
Weight (kg)	74.98 (13.2)	69.55 a 80.41	0.970	0.638
Stature (cm)	169.36 (7.4)	166.31 a 172.41	0.945	0.190
BMI (kg/m²)	26.08 (3.7)	24.53 a 27.63	0.937	0.127
HS (kg)	37.32 (8.8)	33.68 a 40.96	0.991	0.998
Circumferences (cm)				
Arm	29.18 (3.3)	27.81 a 30.55	0.972	0.701
Waist	92.38 (11.8)	87.51 a 97.25	0.963	0.477
Hip	97.24 (6.4)	94.59 a 99.89	0.971	0.662
Calf	36.42 (3.1)	35.13 a 37.71	0.980	0.894

Knee height (cm)	53.94 (2.6)	52.87 a 55.01	0.922	0.058
Skin folds (mm)				
Biceps	8.40 (3.4)	7.02 a 9.78	0.950	0.248
Triceps	15.08 (5.9)	12.64 a 17.52	0.979	0.862
Subscapular	23.56 (8.6)	20.00 a 27.12	0.949	0.235
Supra iliac	19.64 (9.7)	15.63 a 23.65	0.947	0.216
Derivatives				
LOG (mm)	1.79 (0.2)	1.71 a 1.87	0.890	0.011
AMBc (cm^2)	38.16 (11.6)	33.37 a 42.95	0.908	0.027

Legend: SD=standard deviation; CI=confidence interval; ALST=Appendicular Lean Soft Tissue; IALST=Índex Appendicular Lean Soft Tissue: $ALST_{[kg]}/Estatura^2_{[m]}$; BMI=body mass index: $Weight_{[kg]}/Stature^2_{[m]}$; Logarithm of the sum of the biceps, triceps, subscapular and supra iliac skinfolds, all in mm; AMBc=Arm Muscle Area Corrected: $[Arm\ Circumference_{[cm]} - (\pi * DCT_{[cm]})]^2/4*\pi - 10$[27]; π= 3.14; HS= handgrip strength.

The predicted ALST mean values and criteria for validation of the equations (difference test [t-test], standard error of the estimate [SEE] and coefficient of determination [r^2]) are shown in Table 4.

Table 4. Validity of Appendicular Lean Soft Tissue (ALST) predictive anthropometric equations for males aged 60 to 79 years.

ALST predictive equation (kg)	**Mean (SD)**	**Validation for this study sample**		
		t paired (*p*)	**SEE (kg)**	**r^2**
Baumgartner 1	22.62 (2.80)	-2.948 (0.007)	1.96	0.71
Visvanathan 1	24.24 (3.06)	-7.131 (< 0.001)	3.27	0.61
Visvanathan 2	24.30 (2.95)	-7.167 (< 0.001)	3.33	0.6
Visvanathan 3	23.86 (3.01)	-6.234 (< 0.001)	2.93	0.63
Gomes 1	22.48 (2.90)	-2.360 (0.027)	1.98	0.71
Gomes 2	21.67 (2.10)	-0.028 (0.978)	2.23	0.48
Kulkarni 1†	22.19 (3.41)	-1.549 (0.134)	1.86	0.78
Kulkarni 2	23.01 (3.63)	-4.603 (< 0.001)	2.06	0.79
Kulkarni 3†	22.14 (3.52)	-1.545 (0.135)	1.67	0.83
Kulkarni 4	29.73 (4.06)	-24.244 (< 0.001)	8.59	0.54
Lera 1	21.57 (2.38)	0.225 (0.824)	1.92	0.62
Ramirez 1	22.03 (2.36)	-0.967 (0.343)	2.03	0.59
Santos 1	23.11 (0.50)	0.238 (0.814)	2.94	0.50
$ALST_{DXA}$	21.65 (3.81)	-	-	-

SD=standard deviation; r^2=determination coefficient; SEE=standard error of the estimate; †= valid equation (p>0.05) *vs* DXA; r^2>0.70; SEE<3.5kg).

The Indian equations Kulkarni 1 and Kulkarni 3 met the criteria proposed by Lohman (29) (Table 4). However, agreement with the reference ($ALST_{DXA}$) indicated some degree of bias by overestimating the ALST prediction (Figure 1a and 1b).

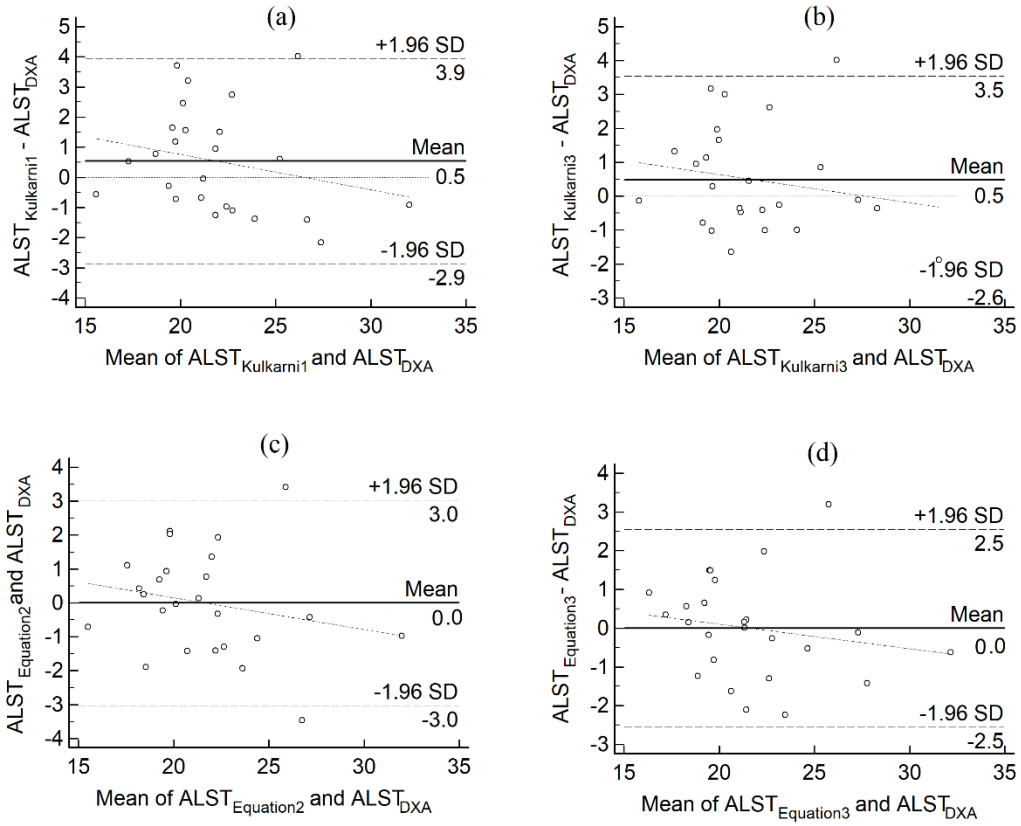

Figure 1. Bland-Altman plot of reference Appendicular Lean Soft Tissue (ALST) measurement (DXA), estimated by the Indian predictive anthropometric equations Kulkarini 1 (a) and Kulkarini 3 (b) and that estimated by the new predictive anthropometric equations 2 (c) and 3 (d).

For ALST values below 21 kg, the equations tended to overestimate the reference values (as measured by DXA). For older adults with higher ALST (> 21 kg), the tendency of underestimation of the reference values was greater. To ensure the practical application of the equations, a simulation with the older adults' data from this study was performed. We consider the ALSTI cutoff point proposed by the EWGSOP of 7.0 kg/m^2 for men to identify low muscle quantify (3). The Kulkarni 1 and Kulkarni 3 equations misclassified 33 % of the tested cases (4 cases) as compared to $ALST_{DXA}$ (6 cases). Thus, although the

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

Given this problem, anthropometric equations were proposed to predict ALST (Table 5). The assumptions for proposing and validating new models considered: analysis of the accuracy of explanatory variables, statistical and biological relationships within and between variables (explanatory and response variables), structuring of the statistical methods used to formulate the equation from sample size, and inter-collinearity between response variables and homoscedasticity of results (32). Once these recommendations were met, three new anthropometric equations were generated using linear regression analyses. The new equations were able to explain the variance of the ALST with high significance ($^{*}p < 0.01$ and $^{**}p < 0.001$).

Table 5. New anthropometric predictive equations of Appendicular Lean Soft Tissue (ALST) of 60- to 79-year-old males.

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

Legend: Weight (kg); Circumference (cm); β=Constante; r²adjust= adjusted coefficient of determination; SEE= Standard Error of the Estimate (kg); VIF= Variance Inflation Factor; *=p<0.01; **=p<0.001; †= valid equation (p<0.05 *vs* DXA; r^2_{PRESS}>0.70; SEE_{PRESS}<3.5kg).

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

The practical simulation was again tested for our equations 2 and 3 using the same cut-point (ALSTI < 7.0 kg/m^2) (3) previously adopted. Equation 2 presented the same classification error of Kulkarni 1 and Kulkarni 3, in identical inverse proportion (-33 %) of misclassification. That is, there was a misdiagnosis with the result (i.e., 'false positive'). In the other hand, for equation 3 the diagnosis showed 100% agreement with the reference method ($ALST_{DXA}$).

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

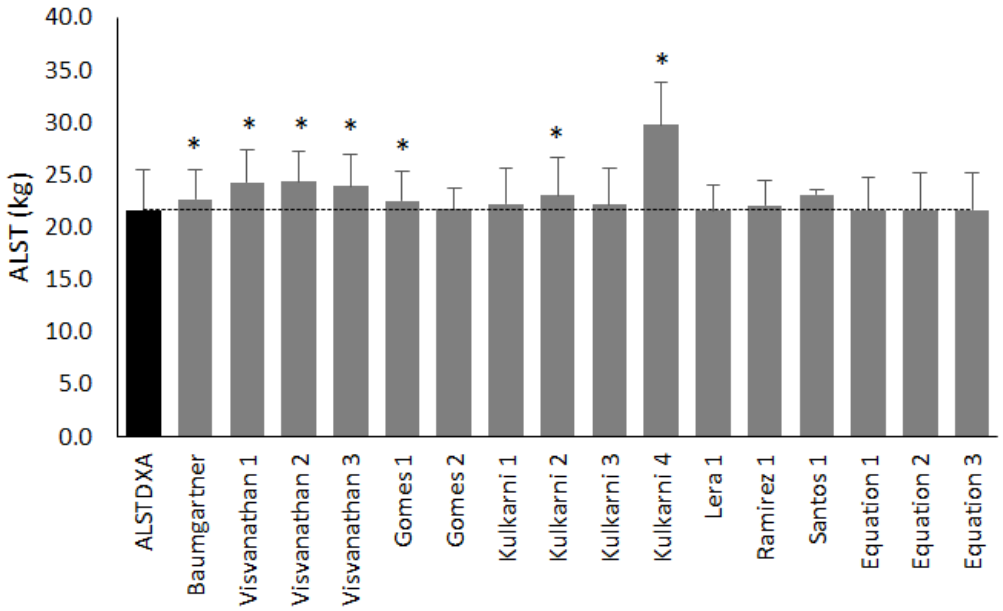

Figure 2. Mean and standard deviation of Appendicular Lean Soft Tissue DXA reference measurement ($ALST_{DXA}$) (black bar) and values estimated by anthropometric equations (gray bars).
*=different from $ALST_{DXA}$ ($p<0.05$).

DISCUSSION

Our results suggest that of the 13 equations tested to evaluate the ALST of male elderly Brazilians, only two Indian equations (Kulkarni 1 and Kulkarni 3) met the validity criteria adopted in this study, confirming the predictive potential of anthropometric equations. However, they presented biases (Bland-Altman) and failed to identify low muscle quantity, a fundamental criterion for the diagnosis of sarcopenia (3). A diagnostic simulation of the Indian equations to identify low muscle quantity resulted in the misclassification of 33 % of false-negative cases, as it considered EWGSOP cutoff points (ALSTI < 7.0 kg/m^2) (3). Thus, new explanatory equations that met the criteria (29) were developed. However, only one (equation 3) showed adequate agreement with the reference (DXA). This was demonstrated by lack of bias and non-polarization of the

means (Bland-Altman plot). The referred equation identified cases of low muscle quantity with 100% agreement with DXA (3).

Our hypothesis that populational nonspecific equations fail to predict ALST was confirmed. The use of equations generated in a population other than their origin may result in overestimation of ALST, since they are generated based on the body tissue of individuals from different nationalities (19,34). Part of these differences is explained because ALST has great variability in regard to gender and ethnicity. In terms of sex, the quantitative ALST peak in young adults occurs at 27 years for both sexes, but muscle volumes are very different among them. Men have an average of 28.6 kg of muscle tissue while women have 19.2 kg (9.4 kg difference) (36). This distinction may be accentuated over time when age-relative decrease in ALST is greater for men (0.8 kg/ decade) than women (0.4 kg/decade) (37). Regarding the ethnic factor, the difference in ALST can be up to 10 % when comparing, for example, African American and Asian populations (36). Understanding the interdependent influence of age and ethnicity on older people's muscle mass can be helpful for improving functional capacity and decreasing health risks, especially in older people of different ethnic groups (36). Therefore, the specificity of the referentials specific to each population must obey well-established criteria and diagnostic thresholds based on their young (3). Considering the various factors when predicting ALST, it can ensure the reliability and adequate diagnosis of our elderly (38).

Our developed equation 3 (Table 5) proved its validity (r^2_{adjust}, SEE, PRESS, r^2_{PRESS} and SEE_{PRESS}), allowing for an adequate diagnosis of low muscle quantity among older adults. Sophisticated imaging methods for ALST determination are not always available in clinical settings. Thus, alternative methods (e.g., anthropometric equations) may greatly reduce monitoring costs and allow for more frequent measurements and more accurate estimations of low muscle quantity. This would vastly favor interventions. The assumptions of reduced multi-collinearity and variance inflation factor (VIF) less than 10 were considered for the development of the equation (31,39). The predictive validation criteria adopted in this study to test the anthropometric equations are often adopted in studies of this nature (19,20). The PRESS internal validation method (33) confirmed the efficacy of equation 3 to predict ALST with high internal validity, high determination coefficient ($r^2_{press} = 0.83$) and low prediction error ($SEE_{PRESS} = 1.53$ kg) (Table 5). Therefore, the use of the equation developed for older Brazilian males with similar characteristics may avoid bias in the diagnosis of sarcopenia. However, it is important to

conduct validation studies in other regions of the country, as well as to define the specific ALSTI cutoff points as recommended by the EWGSOP (3).

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

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

In summary, this study sought to test the validity of equations to predict ALST among younger older Brazilians. The use of anthropometry to predict ALST was confirmed as equations from other populations met the criteria adopted for the Brazilian population. However, when applied to the diagnosis of sarcopenia, the values were biased because they were not generated from this specific population. Thus, we can conclude

that anthropometric models to predict ALST are valid alternatives for diagnosing and monitoring sarcopenia among older individuals. However, the specificity of the population affects predictive validity, with risk for a false-positive diagnosis. Therefore, the validation of nonspecific equations is still possible, but their precision for the diagnosis of sarcopenia is reduced in older Brazilian males.

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4.2 Artigo Original II - Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: a cross-sectional study

Neste tópico está apresentado o segundo artigo da tese, que contempla o segundo objetivo específico. O artigo intitulado "*Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: a cross-sectional study*" (ROSSINI-VENTURINI et al., 2022) encontra-se publicado no periódico *BMC Sports Science, Medicine and Rehabilitation* [https://doi.org/10.1186/s13102-022-00559-2], com fator de impacto de 1.934 (2022).

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Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: a cross-sectional study

ABSTRACT

Background: To verify 1) the association between classic and *specific* bioelectrical impedance vector analysis (BIVA) with body composition, hydration, and physical performance in older adults with and without sarcopenia; 2) which BIVA most accurately distinguishes sarcopenia. Methods: A sample of 94 older adults with and without sarcopenia (29 men and 65 women, 60-85 years) was evaluated. The classic and *specific* BIVA procedures, Dual energy x-ray absorptiometry (DXA), and deuterium dilution were performed. Sarcopenia was defined by muscle weakness and low skeletal muscle index, while severity was indicated by low physical performance. Results: The BIVA's potential to monitor hydration and muscle mass loss in older adults seems feasible. Classic and *specific* BIVA were able to distinguish sarcopenia in women ($p<0.001$), but not in men. When the sarcopenia criteria were individually analyzed, both classic and *specific* BIVA were able to distinguish low skeletal muscle index in women, while only classic BIVA did for men. For the criterion of slow physical performance, only the classic BIVA showed severity differences for women. The vectors of adults without sarcopenia of both sexes tended to be positioned in the left region of the ellipses, revealing a predominance of soft tissues. Conclusions: Classic BIVA has a distinct sarcopenic association with body composition, hydration, and physical performance in older adults, while *specific* BIVA was similar between groups. Both BIVAs are sensible to detect female morphological changes (skeletal muscle index) but not for functional (handgrip, 6-minute walk test) sarcopenia criteria. These procedures are promising tools for monitoring sarcopenia risks during aging.

Keywords: Bioelectrical impedance analysis; phase angle; sarcopenia; older adults; body composition.

BACKGROUND

Sarcopenia is a progressive and generalized skeletal muscle illness [1] that is related to low strength [2] and muscle quantity [1] that is related to increased adverse consequences including falls, fractures, physical disability and mortality [1, 3]. Moreover, it has a strong impact on the ability to perform activities of daily living [4] and greatly reduces the quality of life [5]. The diagnosis of sarcopenia is established by the presence of low muscle strength and muscle quantity [3], and is considered severe when low physical performance is detected [3]. Usually, during ageing, bone mineral content (BMC), lean soft tissue (LST) and total body water (TBW) decrease throughout life, while the fat mass (FM) increases and is redistributed to the abdominal region [6, 7]. Thus, analyzing and monitoring hydration and body composition (BC) changes during ageing is necessary. Since LST major component is water (about 76%) and that it is commonly reduced during ageing, TBW losses may affect muscle function [8, 9].

Several techniques are available for BC analysis, with their advantages and disadvantages [10]. Although Dual-energy X-ray absorptiometry (DXA) is a reference method for BMC, also consists in a three-compartment model [11] for BC, being recognized as a precise and accurate technique for determining FM, LST and BMC [12]. The hydration can be accurately assessed through dilution techniques using deuterium [13], as an important measure for a healthy body [9]. However, DXA and dilution techniques are expensive, need specialized technicians to analyze the exams, are difficult to use in the field setting [14, 15], and are available in a few research centers. In this way, simple methods proposed to monitor TBW and BC are desired during ageing. Bioelectrical impedance analysis (BIA) is a non-invasive, low-cost, easily applicable method, and can be an alternative to TBW and BC diagnostic tool for routine examinations in clinical and research practice [16, 17]. Nevertheless, BIA has limitations in terms of development of *specific* equations [18] that is why bioelectrical impedance vector analysis (BIVA) has been used.

BIVA is based on the analysis of impedance vectors, designed on an RXc-score graph to reference values (tolerance ellipses) or for intergroup comparisons - confidence ellipses [18]. In the classic BIVA analyses, bioelectrical values are standardized for the subject's height (R/H: resistance standardized for height; Xc/H: reactance standardized for height) to remove the effect of conductor length [19, 20]. Instead, the *specific* BIVA corrects the bioelectrical values for height and transverse areas (Rsp: resistance

standardized for height and transverse areas; Xcsp: reactance standardized for height and transverse areas), to reduce the effect of body dimensions [21, 22]. According to the classic BIVA [19], alterations of bioelectrical vectors along the major axis of tolerance ellipses show changes in TBW (fluid excess in the direction of the lower pole, dehydration towards the upper pole). In relation to *specific* BIVA [23], the major axis refers to variations in FM% (higher values towards the upper pole). The minor axis refers to the variations in body cell mass, skeletal muscle mass in particular, and ICW/ECW ratio (higher values on the left side).

Since sarcopenia represents muscle mass reduction, BIVA could be used to identify these muscle changes. However, which BIVA best defines sarcopenia, or how bioelectrical impedance vectors are associated with BC, hydration, and diagnostic criteria for sarcopenia in older adults have not been established up until now. Thus, our objectives were: 1) To evaluate the association between classic and *specific* BIVA with BC, hydration, and physical performance of older adults with and without sarcopenia; 2) To verify which BIVA (classic or *specific*) is more accurate for distinguishing sarcopenia for both sexes. We hypothesize that since the *specific* BIVA corrects the BIA values by transverse areas, it better distinguishes sarcopenia for both sexes than classic BIVA.

METHOD

Design and Study population

In this study, we adopted a cross-sectional design to evaluate physically independent community-dwelling older adults, living in a city in southeastern Brazil. The study was conducted from October 2016 to May 2017. This manuscript followed the guidelines from The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) conference list, and the completed checklist is attached.

A sample of older adults aged between 60 and 85 years old of both sexes were considered for analysis. They were recruited in special projects for seniors (Exercise Program for older adults on campus on the interior of the University of São Paulo) and health services in a great regional community from a mid-west zone of Brazil. Former research participants (Fragility project) at the university were also invited to participate in the study. The approach was made by phone and personal invitation. The inclusion criteria were: adults aged 60-85 years old, both sexes, who walked independently. The exclusion criteria were: the presence of diseases that restrict mobility or muscle strength;

presence of unstable cardiovascular condition; acute infection; back pain; prostheses, individuals with a diagnosis of cancer or uncontrolled diseases, who presented sequel of stroke, experienced a weight loss more than three kilograms (kg) in the last 3 months, had a cognitive limitation that restricts understanding and taking tests, who did not complete all the stages, or desired to withdraw from the study.

To the sample size calculation was considered the desired maximum error (ε) and degree of confidence (Zy), previously knowing the population variability (σ^2) [24]. For this, we used the variable with the greatest variability (FM; SD=8.7 kg) expected for such a population [25]. Once the predetermined error estimate (ε≤1.8 kg) and maximum desired error (5%) the ideal n for the study [24] was defined (n=90). All participants volunteered, received an explanation about the study's objectives and signed the written consent in agreement with the Declaration of Helsinki. The study was approved by the Ethical Review Board of Hospital das Clinicas at the Medical School of University of Sao Paulo (HC-FMRP/USP).

Procedures

A multidisciplinary health team (nurses, nutritionists, pharmacists, physical education professors, physicians, and physiotherapists) performed data collection. All procedures, for each participant, were completed during one visit to the laboratories at the Hospital das Clinicas at the Medical School of University of Sao Paulo at Ribeirao Preto (HCFMRP/USP). Subjects came to the laboratory after an overnight fast (8h fast), abstaining from vigorous exercises, no caffeine and alcohol during the preceding 24h.

Cognition Assessment

The cognition was assessed using the short version of the Mini-mental state examination (MMSE), which presents a maximum score of 19 points [26]; the individuals with scored ≤12 were considered with cognitive limitations.

Anthropometry

Weight (kg) and height (cm) were measured according to standardized procedures [27]. Body mass index (BMI) was derived (kg/m^2). Upper arms, waist, and calf (cm) circumferences were measured by an anthropometric tape.

Dual-energy X-ray Absorptiometry

BC was determined by DXA (Hologic® scanner, model QDR4500W; version 11.2, Bedford, MA). Skeletal muscle mass index (SMI) was derived from Appendicular lean soft tissue (ALST) and squared height ratio (kg/m^2). The calibration and measurements were following the manufacturer's instructions and were always carried out by the same technician. The examination was performed according to standardized procedures previously informed [28, 29]. The DXA measurements included absolute and relative values (ALST and ALST%; FM and FM%; BMC and BMC%).

Bioelectrical impedance

The bioelectrical impedance measurements were performed with BIA Imp DF50 Body Composition Analysis (ImpediMed, Brisbane, Queensland, Australia) according to international standard criteria [17]. The participants were in the supine position with a leg opening of 45° compared to the median line of the body and the upper limbs and with a distance of 30° from the trunk. The skin was cleaned with alcohol, then two electrodes were placed on the right hand back and two electrodes on the neck of the corresponding foot [30]. Phase angle (degrees) was calculated as the arctangent of Xc/H * 180°/π.

Bioelectrical impedance vector analysis was carried out using the classic and *specific* BIVA methods. The classic BIVA was applied, adjusting individual vectors for height (H) in meters (R/H, Ohm/m; Xc/H Ohm/m [19] to eliminate conductor length effect. The characteristics of the sample were compared with the concentric tolerance ellipses (50%, 75% and 95% of cases) representing the variability of the reference population [31]. The *specific* BIVA was applied to compensate for the whole effect of conductor volume. The bioelectrical values were multiplied by a correction factor (A/L, in centimeters; R*A/L, Ohm/cm; Xc*A/L, Ohm/cm). Where L=1.1*H (cm) and A is estimated cross-sectional area:

A= (0.45*arm area + 0.10*waist area + 0.45*calf area) (in cm^2),

Note that segment area = $C^2/4\pi$, and C is the circumference of the arm, waist, and calf in centimeters [23, 32]

The coefficients were assigned considering the different contribution of body segments to resistance and the proportions of total body length. Italian older adults' bioelectrical values [33] were used as reference.

Sarcopenia identification

The criteria established by the EWGSOP [3] to identify sarcopenia were: decreased levels of handgrip strength and SMI. Physical performance (6-minute walk test) was tested to check the severity of sarcopenia. As described below, the cutoff points for muscle strength, muscle quality and physical performance were those suggested by EWGSOP [34]. This choice is justified considering that they were better to define sarcopenia in the Brazilian population [35].

Muscle strength

The handgrip strength was measured (kg) using a dynamometer Jamar®, model 5030 J1, and the protocol followed the American Society of Hand Therapists recommendations [36]. The participants were verbally stimulated and made three attempts with their dominant hands, with one-minute rest between attempts. The highest measure value was recorded [35, 37]. Muscle strength was considered low when handgrip strength was below 30 kg or 20 kg for men and women, respectively [38].

Muscle quantity

SMI was the criterion used for muscle mass, where ALST is divided by squared height (kg/m^2). The SMI below 7.26 kg/m^2 and 5.45 kg/m^2 was considered low for men and women, respectively [39].

Physical performance

To assess physical performance the 6-minute walk test (6MWT) was performed on a flat, non-slip surface, in a space of 30-m, with calibrated markings every three meters. Before the test, the participants were asked to walk as fast as possible for six minutes. Then, after a verbal command, they began to walk. Although time was not paused during execution, the participants could slow down or stop to rest and return to the test at will. The total walked distance was noted in meters. Sarcopenia was considered severe when 6MWT≤400m [40]. Participants with sarcopenia who had 6MWT<400m had the disease classified as severe [3]

Total Body Water

TBW was assessed by isotopic dilution of deuterium oxide. This method is based on stable isotopes and consists of ingesting a deuterium oxide dose and determining, by mass spectrometry, deuterium enrichment in a sample of body water (e.g., saliva). Due to the difference in enrichment before and after ingestion of the dose, the TBW is precisely determined [13]. Each participant had an 8-hour overnight fast. Afterwards, a fixed dose of 70 ml of 7% deuterium oxide was consumed, followed by 50 ml of water to rinse the mouth, this last process was repeated to ensure that there was no water left in the bottle. Saliva samples of each participant were collected before ingesting the deuterium oxide dose (basal) and 3 hours later. Deuterium enrichment was determined by isotopic ratio mass spectrometry (IRMS Hydra, Europa Scientific, Cheshire, United Kingdom).

Statistical Analysis

Descriptive statistics using measures of central tendency were used to describe the characteristics of the sample. To verify the normality of the data, the Shapiro–Wilk test was applied. Comparisons between men and women and between individuals with and without sarcopenia were performed using Student's t-test for independent samples for parametric data and the Mann-Whitney U test for nonparametric data. The association between body composition, hydration, physical performance, and bioelectrical variables was investigated using Pearson's correlation analysis. The Hotelling's t-squared statistic (t^2) was used to compare the impedance vectors mean between sarcopenic and non-sarcopenic groups. Statistical significance was pre-determined as $p<0.05$. SPSS 23.0 and NCSS 2020 were used for all statistical calculations.

RESULTS

Table 1 shows the characteristics of the eligible participants. From the EWGSOP [3] criteria, sarcopenia was found in four men (13.8% of the male sample) and six women (9.2% of the female sample). Sarcopenic older adults showed statistically lower calf circumference, ALST, SMI, and handgrip strength than those older adults without sarcopenia ($p<0.05$). Sarcopenic women were older and had higher R, Z, R/H, and Z/H values, while women without sarcopenia were heavier and had higher upper arm circumference, BMI, PA, Xcsp, and FM values. Table 1 also shows anthropometric, body

composition, hydration, bioelectrical and physical performance variables, which have significant differences between sexes (*$p<0.05$). Men without sarcopenia were taller, heavier, had higher values of waist circumference, BMC (kg and %), ALST (kg and %), SMI, TBW (liter and %), grip strength, and lower values of FM (kg and %) and for all bioelectrical variables (except the PA) compared to women without sarcopenia. And sarcopenic men showed higher values of ALST (kg and %), SMI, TBW%, handgrip strength, and lower R, Z, R/H, and Z/H than sarcopenic women.

Table 1 – Descriptive values of older adults, including the correlation between bioelectrical variables and difference test.

	Men					Women				
	Without sarcopenia (n=25)		With sarcopenia (n=04)			Without sarcopenia (n=59)		With sarcopenia (n=06)		
	Mean (SD)	CI-95%	Mean (SD)	CI-95%	*p*	Mean (SD)	CI-95%	Mean (SD)	CI-95%	*p*
Age (years)	71.0 (7.6)	67.8 to 74.1	76.8 (6.6)	66.2 to 87.3	0.164	69.5 (5.8)	68.0 to 71.0	75.3 (5.6)	69.4 to 81.3	0.023
Anthropometric variables										
Height (cm)	169.2 (7.6)	166.1 to 172.3	164.3 (9.8)	148.6 to 179.9	0.255	156.4 (6.0)*	154.8 to 157.9	154.3 (7.4)	146.5 to 162.0	0.418
Weight (kg)	75.1 (12.8)	69.8 to 80.4	62.3 (16.7)	35.7 to 88.8	0.085	67.8 (11.1)*	64.9 to 70.7	54.4 (10.2)	43.8 to 65.1	0.014
Upper arm crf (cm)	29.4 (3.3)	28.0 to 30.7	26.1 (4.4)	19.1 to 33.1	0.090	30.3 (3.7)	29.3 to 31.2	26.5 (3.7)	22.5 to 30.3	0.017
Waist crf (cm)	92.9 (10.6)	88.5 to 97.3	89.4 (16.9)	62.5 to 116.2	0.576	86.9 (10.0)*	84.3 to 89.5	79.6 (11.0)	68.0 to 91.2	0.096
Calf crf (cm)	36.4 (3.1)	35.1 to 37.7	31.2 (3.2)	26.2 to 36.3	0.005	35.3 (2.9)	34.5 to 36.0	31.7 (2.3)	29.2 to 34.1	0.004
BMI (kg/m^2)	26.2 (3.5)	24.7 to 27.6	22.8 (4.5)	15.7 to 30.0	0.102	27.7 (4.3)	26.6 to 28.8	22.8 (3.5)	19.1 to 26.5	0.009
Body composition variables										
FM (kg)	22.2 (6.6)	19.5 to 24.9	19.6 (10.6)	2.6 to 36.5	0.661	28.2 (6.9)*	26.4 to 30.0	22.1 (7.4)	14.4 to 29.9	0.046
FM (%)	29.2 (6.5)	26.5 to 31.0	29.7 (9.4)	14.7 to 44.7	0.900	41.2 (5.2)*	39.8 to 42.6	39.8 (6.7)	32.7 to 46.9	0.548
BMC (kg)	2.6 (0.5)	2.4 to 2.8	1.8 (0.4)	1.2 to 2.4	0.079	1.9 (0.3)*	1.8 to 2.0	1.8 (0.3)	1.4 to 2.1	0.287
BMC (%)	3.5 (0.5)	3.3 to 3.7	3.0 (0.7)	1.9 to 4.1	0.123	2.9 (0.5)*	2.8 to 3.0	3.3 (0.7)	2.6 to 4.1	0.144
ALST (kg)	21.5 (4.0)	19.9 to 23.2	16.8 (2.9)	12.1 to 21.4	0.032	15.0 (2.5)*	14.3 to 15.6	11.5 (1.4)*	10.0 to 12.9	0.001
ALST (%)	29.3 (3.5)	27.8 to 30.7	27.9 (3.8)	21.9 to 34.0	0.370	22.5 (2.4)*	21.9 to 23.2	21.6 (2.4)*	19.1 to 24.1	0.345
SMI (kg/m^2)	7.9 (1.0)	7.5 to 8.3	6.5 (0.5)	5.6 to 7.3	0.009	6.5 (1.0)*	6.2 to 6.7	5.1 (0.3)*	4.8 to 5.4	0.001
Hydration variables										
TBW (liter)	40.5 (6.1)	36.8 to 44.2	32.0 (7.5)	13.3 to 50.7	0.055	28.8 (3.4)*	27.5 to 30.1	25.3 (3.0)	17.8 to 32.7	0.165
TBW (%)	53.7 (5.8)	50.2 to 57.2	55.9 (4.2)	45.5 to 66.3	0.549	44.0 (3.7)*	42.6 to 45.5	43.5 (2.4)*	37.4 to 49.6	0.815
Bioelectrical variables										
R (ohm)	475.1 (64.6)	448.4 to 501.8	511.6 (56.1)	422.3 to 600.1	0.297	541.1 (68.9)*	523.2 to 559.1	638.0 (84.9)*	548.9 to 727.1	0.002
Xc (ohm)	48.9 (12.9)	43.5 to 54.2	51.0 (11.7)	32.4 to 69.6	0.762	56.9 (10.4)*	54.2 to 59.6	54.5 (21.8)	31.6 to 77.3	0.308
Z (ohm)	474.9 (65.9)	447.7 to 502.1	514.2 (57.0)	423.5 to 604.8	0.272	545.8 (68.5)*	527.9 to 563.6	640.5 (86.0)*	550.3 to 730.7	0.002

PA (degrees)	6.0 (1.6)	5.3 to 6.2	5.6 (0.7)	4.4 to 6.8	0.669	6.0 (1.0)	5.7 to 6.3	4.7 (1.7)	2.9 to 6.5	0.043
R/H (ohm/m)	281.1 (38.2)	265.3 to 296.8	313.1 (46.7)	238.8 to 387.3	0.141	346.0 (42.0)*	335.1 to 357.0	413.5 (49.9)*	361.1 to 465.9	0.004
Xc/H (ohm/m)	29.0 (7.7)	25.8 to 32.1	31.3 (8.4)	17.9 to 44.8	0.578	36.4 (6.7)*	34.7 to 38.2	35.3 (14.1)	20.5 to 50.1	0.248
Z/H (ohm/m)	280.9 (38.8)	264.9.1 to 296.9	314.7 (47.3)	239.5 to 389.9	0.127	349.0 (41.5)*	338.2 to 359.8	415.1 (50.6)*	362.0 to 468.2	0.004
Rsp (ohm*cm)	372.6 (43.5)	354.6 to 390.5	356.7 (109.5)	182.4 to 531.0	0.793	433.4 (71.3)*	414.8 to 452.0	422.6 (110.9)	306.2 to 539.1	0.739
Xcsp (ohm*cm)	39.1 (12.1)	34.1 to 44.1	35.7 (13.5)	14.3 to 57.2	0.612	45.7 (9.8)*	43.2 to 48.3	35.3 (15.9)	18.7 to 52.0	0.024
Zsp (ohm*cm)	374.8 (43.9)	356.6 to 392.9	358.5 (110.3)	183.1 to 534.0	0.789	435.9 (71.6)*	417.2 to 454.5	424.3 (111.4)	307.3 to 541.2	0.720
Physical performance variables										
6MWT (m)	452.4 (106.9)	408.3 to 496.5	465.9 (49.2)	387.7 to 544.1	0.150	407.0 (97.2)	381.6 to 432.3	440.9 (66.5)	371.2 to 510.7	0.202
Hand grip Strenght (kg)	37.1 (8.3)	33.7 to 40.5	28.3 (2.1)	25.0 to 31.5	0.045	24.5 (4.4)*	23.3 to 25.6	18.7 (1.2)*	17.4 to 19.9	0.001
Correlations										
r R-Xc	0.017		0.988			0.465		0.907		
r R/H-Xc/H	0.075		0.998			0.447		0.944		
r Rsp-Xcsp	0.489		0.967			0.659		0.742		

Note: crf: circumference; BMI: body mass index; R: resistance; Xc: reactance; Z: vector length; PA: phase angle; R/H: resistance standardized for height; Xc/H: reactance standardized for height; Z/H: vector length standardized for height; Rsp: resistance standardized for height and transverse areas; Xcsp: reactance standardized for height and transverse areas; Zsp: vector length standardized for height and transverse areas; 6MWT: 6-minutes walk test; ALST: Appendicular lean soft tissue; FM: fat mass; BMC: bone mineral content; TBW: total body water; SMI: Skeletal muscle mass index; r R-Xc: correlation between R and Xc; r R/H-Xc/H: correlation between R/H and Xc/H; r Rsp-Xcsp: correlation between Rsp and Xcsp; *: sex differences (p<0.05); Independent t test for parametric and ^{U}: Mann–Whitney U test for non-parametric data.

The highest correlation values for classic (R/H-Xc/H) and *specific* (Rsp-Xcsp) bioelectric variables were observed in sarcopenic groups, both in men and women. Complete correlation analysis between body composition, hydration, physical performance and bioelectrical variables, considering sexes and sarcopenic status (Table 2 and 3).

Table 2 – Correlation between body composition, hydration, physical performance and bioelectrical variables in men without/with sarcopenia.

Men without sarcopenia	BIA			Classic BIVA			Specific BIVA			PA
	R	Xc	Z	R/H	Xc/H	Z/H	Rsp	Xcsp	Zsp	
FM (kg)	-0.459*	0.074	-0.431*	-0.490*	0.055	-0.463*	0.745**	0.490*	0.747**	0.255
FM%	-0.298	0.094	-0.287	-0.208	0.133	-0.199	0.576**	0.372	0.576**	0.184
BMC (kg)	-0.473*	-0.202	-0.460*	-0.640**	-0.279	-0.628**	0.290	0.138	0.290	0.049
BMC%	-0.032	-0.317	-0.055	-0.056	-0.319	-0.080	-0.447*	-0.389	-0.450*	-0.259
ALST (kg)	-0.321	0.041	-0.310	-0.554**	-0.072	-0.543**	0.384	0.332	0.390	0.230
ALST%	0.306	0.031	0.273	0.198	-0.017	0.167	-0.474*	-0.217	-0.471*	-0.055
SMI (kg/m^2)	-0.565**	0.105	-0.564**	-0.680**	0.048	-0.681**	0.317	0.469*	0.327	0.409*
TBW (l)	-0.693**	-0.218	-0.647*	-0.849**	-0.357	-0.813**	0.323	0.340	0.327	0.304
TBW%	0.072	-0.170	0.028	0.164	-0.109	0.122	-0.922**	-0.579*	-0.920**	-0,190
6MWT (min)	-0.060	0.430*	-0.121	-0.209	0.351	-0.270	0.141	0.477*	0.154	0.472*
Hand grip Strenght (kg)	-0.012	0.283	-0.021	-0.191	0.190	-0.199	-0.131	0.217	-0.122	0.304
Men with sarcopenia	BIA			Classic BIVA			Specific BIVA			PA
	R	Xc	Z	R/H	Xc/H	Z/H	Rsp	Xcsp	Zsp	
FM (kg)	0.410	0.273	0.407	0.027	0.068	0.027	0.924	0.796	0.923	0.199
FM%	0.548	0.417	0.545	0.186	0.224	0.186	0.960*	0.864	0.959*	0,347
BMC (kg)	-0.195	-0.226	-0.196	-0.406	-0.349	-0.405	0.318	0.240	0.317	-0.253
BMC%	-0.494	-0.367	-0.492	-0.232	-0.236	-0.232	-0.717	-0.620	-0.716	-0.308
ALST (kg)	-0.229	-0.362	-0.232	-0.588	-0.549	-0.588	0.522	0.300	0.519	-0.429
ALST%	-0.675	-0.559	-0.673	-0.338	-0.377	-0.339	-0.990*	-0.935	-0.990*	-0.495
SMI (kg/m^2)	0.128	0.018	0.125	-0.240	-0.183	-0.240	0.762	0.627	0.761	-0.046
TBW (l)	-0.361	-0.528	-0.365	-0.674	-0.670	-0.675	0.629	0.293	0.626	-0.596
TBW%	-0.462	-0.290	-0.458	-0.109	-0.116	-0.109	-0.999*	-0.912	-0.999*	-0.209
6MWT (min)	-0.364	-0.384	-0.365	-0.534	-0.484	-0.533	0.147	0.058	0.146	-0.404
Hand grip Strenght (kg)	-0.813	-0.893	-0.815	-0.960*	-0.959*	-0.960*	-0.208	-0.447	-0.211	-0.924

Note: crf: circumference; BMI: body mass index; R: resistance; Xc: reactance; Z: vector length; PA: phase angle; R/H: resistance standardized for height; Xc/H: reactance standardized for height; Z/H: vector length standardized for height; Rsp: resistance standardized for height and transverse areas; Xcsp: reactance standardized for height and transverse areas; Zsp: vector length standardized for height and transverse areas; ALST: Appendicular lean soft tissue; FM: fat mass; BMC: bone mineral content; TBW: total body water; SMI: Skeletal muscle mass index; %: relative values (ratio) to body weight; 6MWT: 6-min walk test; r R-Xc: correlation between R and Xc; r R/H-Xc/H: correlation between R/H and Xc/H; r Rsp-Xcsp: correlation between Rsp and Xcsp;

* $p< 0.05$; ** $p<0.001$.

Table 3 – Correlation between body composition, hydration, physical performance and bioelectrical variables in women without/with sarcopenia.

Women without sarcopenia	BIA			Classic BIVA			Specific BIVA			PA
	R	Xc	Z	R/H	Xc/H	Z/H	Rsp	Xcsp	Zsp	
FM (kg)	-0.257*	-0.176	-0.272*	-0.339**	-0.221	-0.358**	0.638**	0.452**	0.638**	0.007
FM%	-0.097	-0.096	-0.102	-0.104	-0.099	-0.109	0.399**	0.249	0.398**	-0.049
BMC (kg)	-0.175	-0.067	-0.184	-0.314*	-0.156	-0.327*	0.242	0.230	0.243	0.064
BMC%	0.112	0.030	0.120	0.086	0.008	0.094	-0.531**	-0.397**	-0.532**	-0.049
ALST (kg)	-0.312*	-0.068	-0.324*	-0.425**	-0.134	-0.442**	0.500**	0.474**	0.502**	0.176
ALST%	0.009	0.134	0.001	-0.009	0.133	-0.001	-0.313*	-0.112	-0.312*	0.157
SMI (kg/m^2)	-0.474**	-0.125	-0.496**	-0.452**	-0.095	-0.477**	0.457**	0.495**	0.460**	0.244
TBW (l)	-0.063	-0.098	-0.107	-0.201	-0.188	-0.251	0.579**	0.381*	0.579**	-0.038
TBW%	0.035	0.203	0.021	0.098	0.237	0.085	-0.388*	-0.118	-0.386*	0.254
6MWT (min)	0.202	0.330*	0.195	0.138	0.279*	0.132	-0.249	-0.027	-0.247	0.202
Hand grip Strenght (kg)	-0.017	-0.048	-0.031	-0.129	-0.126	-0.145	0.188	0.137	0.188	-0.037
Women with sarcopenia	BIA			Classic BIVA			Specific BIVA			PA
	R	Xc	Z	R/H	Xc/H	Z/H	Rsp	Xcsp	Zsp	
FM (kg)	-0.261	-0.554	-0.267	-0.429	-0.608	-0.433	0.627	-0.035	0.623	-0.634
FM%	-0.347	-0.557	-0.352	-0.400	-0.569	-0.404	0.618	-0.020	0.614	-0.598
BMC (kg)	0.102	-0.137	0.099	-0.194	-0.240	-0.196	-0.045	-0.199	-0.046	-0.260
BMC%	0.190	0.331	0.194	0.184	0.329	0.188	-0.565	-0.131	-0.562	0.334
ALST (kg)	0.343	-0.054	0.337	0.011	-0.182	0.006	0.540	0.207	0.538	-0.213
ALST%	0.504	0.688	0.508	0.611	0.713	0.614	-0.430	0.215	-0.426	0.715
SMI (kg/m^2)	-0.078	-0.462	-0.086	-0.207	-0.513	-0.214	0.542	-0.044	0.538	-0.573
TBW (l)	-0.158	-0.359	-0.160	-0.389	-0.438	-0.389	0.334	-0.089	0.331	-0.464
TBW%	0.276	0.469	0.278	0.497	0.543	0.498	-0.218	0.208	-0.215	0.568
6MWT (min)	0.393	0.433	0.394	0.325	0.398	0.326	-0.477	-0.008	-0.475	0.417
Hand grip Strenght (kg)	-0.107	0.244	-0.100	0.006	0.290	0.012	-0.560	-0.100	-0.558	0.370

Note: crf: circumference; BMI: body mass index; R: resistance; Xc: reactance; Z: vector length; PA: phase angle; R/H: resistance standardized for height; Xc/H: reactance standardized for height; Z/H: vector length standardized for height; Rsp: resistance standardized for height and transverse areas; Xcsp: reactance standardized for height and transverse areas; Zsp: vector length standardized for height and transverse areas; ALST: Appendicular lean soft tissue; FM: fat mass; BMC: bone mineral content; TBW: total body water; SMI: Skeletal muscle mass index; 6MWT: 6-min walk test; r R-Xc: correlation between R and Xc; r R/H-Xc/H: correlation between R/H and Xc/H; r Rsp-Xcsp: correlation between Rsp and Xcsp;
* $p<0.05$; ** $p<0.001$.

Table 2 emerge that specific vector length (Zsp) is significantly associated with %FM in non-sarcopenic and sarcopenic individuals, thus suggesting that specific BIVA could be helpful to assess sarcopenic obesity diagnosis.

Figure 1 graphically shows the greatest correlations found (Table 2 and 3) between bioelectrical impedance variables (Classic and *Specific* BIVA) and hydration (TBW,

TBW%), physical performance (Handgrip strength) and body composition (SMI, ALST, FM) variables of older adults with and without sarcopenia. The classic BIVA of men without sarcopenia showed inverse significantly high correlation between R/H (r=-0,849) and TBW, as seen in Figure 1a. For sarcopenic men, Handgrip strength showed a negative and significant very high correlation with R/H (r=-0.960), (Figure 1b).

In the *specific* BIVA, the sarcopenic men showed significantly quasi-perfect correlation (r=-0,922) between Rsp and TBW% (Figure 1c). Likely, in men without sarcopenia, the TBW% also showed a higher association (r=0.922) with BIVA parameters (Rsp; Figure 1c).

For the women parameters, Classic BIVA of women without sarcopenia shown the highest correlation (r=-0,477) occurred between Z/H and SMI (Figure 1e). Again, the sarcopenic women, showed a non-significant, but positive and high correlation between ALST% and Xc/H (r=0.713), as seen in Figure 1f.

In the *specific* BIVA, the women without sarcopenia presented moderated (r=0.638) and positively significant correlation between Zsp and FM. Similarly, in sarcopenic women, the FM also indicated positive, but non-significant moderate correlation (r=0.623) with *specific* bioelectrical variables (Zsp, Figure 1g). Furthermore, Table 2 and 3 emerge that Zsp was significantly associated with FM% for men and women without and with sarcopenia, like Figure 1d, h.

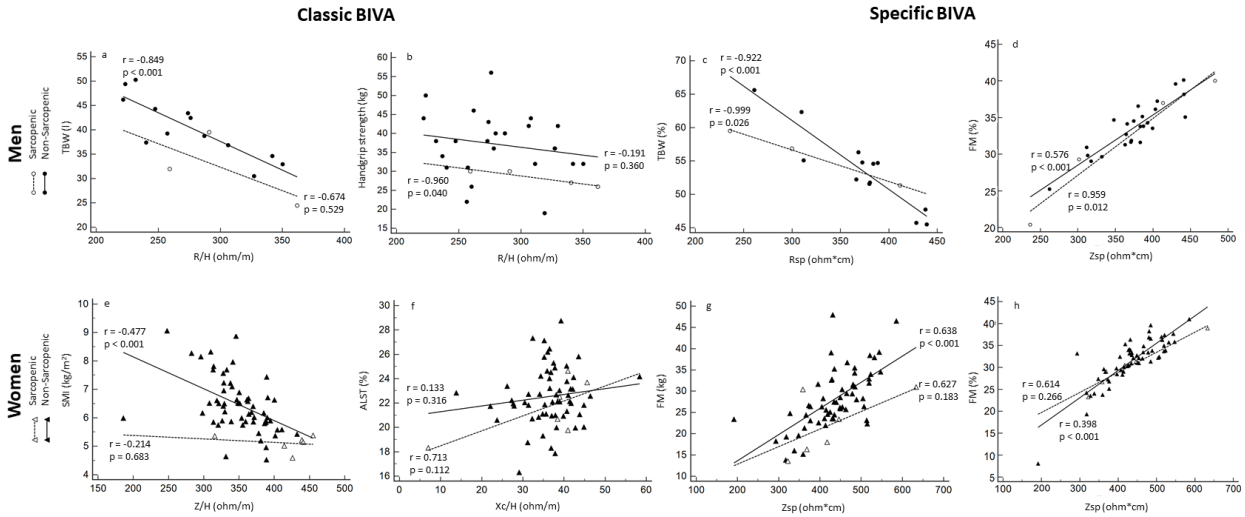

Figure 1. Bivariate correlations between classic and *specific* BIVA with body composition and handgrip for both sexes.

Note: TBW: total body water; SMI: skeletal muscle index; ALST: appendicular lean soft tissue; FM: fat mass; R/H: resistance standardized for height; Rsp: resistance standardized for height and transverse areas; Z/H: vector length standardized for height; Xc/H: reactance standardized for height; Zsp: vector length standardized for height and transverse areas;

The BIVA accuracy for distinguishing sarcopenia is shown in Figure 2, as classic and *specific* BIVA of older adults by sexes and sarcopenia status.

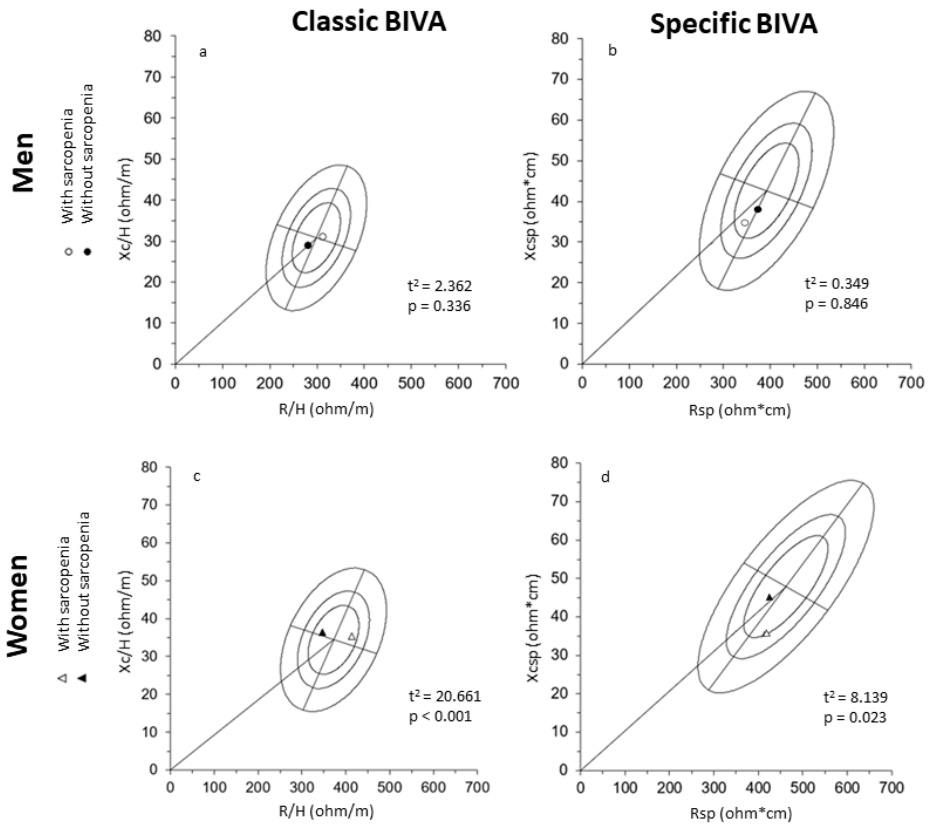

Figure 2. Classic and *specific* mean vectors of older adults with and without sarcopenia.

Note: Filled circles: men without sarcopenia; Hollow circles: men with sarcopenia; Filled triangles: women without sarcopenia; Hollow triangles: women with sarcopenia; a: men classic BIVA; b) men *specific* BIVA; c) women classic BIVA; d) men *specific* BIVA. R/H: resistance standardized for height; Xc/H: reactance standardized for height; Rsp: resistance standardized for height and transverse areas; Xcsp: reactance standardized for height and transverse areas; t^2: Hotelling's t-squared statistic.

The classic BIVA vectors of men groups with and without sarcopenia were not statistically different (T^2=2.362; p=0.336; Figure 2a). But women are (T^2=20.661; p<0.001; Figure 2c), demonstrating the ability of classic BIVA to discriminate sarcopenia in women due to higher values of R/H, Z/H, and the lower PA of women with sarcopenia As noted, the Classic BIVA mean vectors of sarcopenia groups for both sexes were located within the 50% tolerance ellipses (central circle), like the healthy reference population, indicating relatively normal tissue impedance properties. Furthermore, the mean vector for men without and with sarcopenia fell into the third and second quadrant, while for women, the mean vectors fell into the first and second quadrant, respectively. As expected, the classic mean vectors of men and women without sarcopenia (filled

figures) were positioned in the left side of tolerance ellipses, suggesting higher values of body cell mass (Figure 2a, c). In addition, the vector of men without sarcopenia was in the lower pole, demonstrating more TBW, while for men with sarcopenia (hollow circle), the vector mean was situated in the higher pole, representing less TBW (Figure 2a). For women, both sarcopenia groups are at the upper pole, demonstrating no differences in their TBW. Thus, in terms of vector length, the classic BIVA (Z/H) is indicative of TBW).

In *specific* BIVA (like the classic BIVA), the mean vectors of the men sarcopenia groups (Figure 2b) were not significantly different (T^2=0.349; p=0.846), but women are (T^2=8.139, p=0.023, Figure 2d). For the men's sarcopenia groups mean vectors fell into the third quadrant and were found inside the 50% tolerance ellipses. Their proximity in the graphic ellipses (filled or hollow figures) already suggested no differences between sarcopenia groups, confirmed by the p values (p>.05). Women, in turn (Figure 2d), showed mean of vectors of sarcopenia groups significantly distinguished (p=0.023). The mean vectors of women groups without and with sarcopenia were located both within the 50% tolerance ellipses, into the third and fourth quadrants, respectively (Figure 2d).The cases without sarcopenia (filled figures) towards the left side of tolerance ellipses, indicating higher values of body cell mass, skeletal muscle mass in particular, and ICW/ECW ratio, while the cases with sarcopenia fell on the right side, indicating lower values of body cell mass, skeletal muscle mass and ICW/ECW ratio. Furthermore, the vector of men without sarcopenia was towards the upper pole, demonstrating higher values of %FM, while for men with sarcopenia (hollow circle), the vector mean was situated towards the lower pole, representing lower %FM (Figure 2b). For women, the behavior was the same (Figure 2d). So, in terms of vector length, the *specific* BIVA is indicative of %FM, variations in body cell mass, skeletal muscle mass and ICW/ECW.

Figure 3 represents the classic and *specific* BIVA for older adults separately grouped according to the sarcopenia criteria (muscle strength [hand grip], muscle quantity [SMI] and physical performance [6MWT]). The mean vectors of groups with low (men=7; women=17) and normal muscle strength (men=22; women=48) were classified according to their handgrip strength (cutoff: 30 and 20 kg for men and women, respectively) [38]. For Handgrip strength both classic and *specific* BIVA were not significantly different between groups (p>0.05; Figure 3a, b, g, h). The mean vectors of groups with low (men=10; women=12) and normal (men=19; women=53) muscle quantity of SMI (cutoff 7.26 kg/m^2 and 5.45 kg/m^2 for men and women, respectively) [39] were significantly different between groups in the classic BIVA; and for women in

the specific BIVA (Figure 3c, i, j). As expected, the classic and specific mean of men and women with low muscle quantity (hollow circle) were positioned in the right region (Figure 3c, i, j), indicating a smaller amount of body cell mass.

Groups with slow (men=21; women=8) and normal (men=38; women=27) physical performance were clustered using 6MWT (cutoff<400 m). The mean vectors of groups were not statistically different for classic and *specific* BIVA ($p<0.05$) for both sexes in most comparisons (Figure 3e, f, l), except for women in the classic BIVA (Figure 3k).

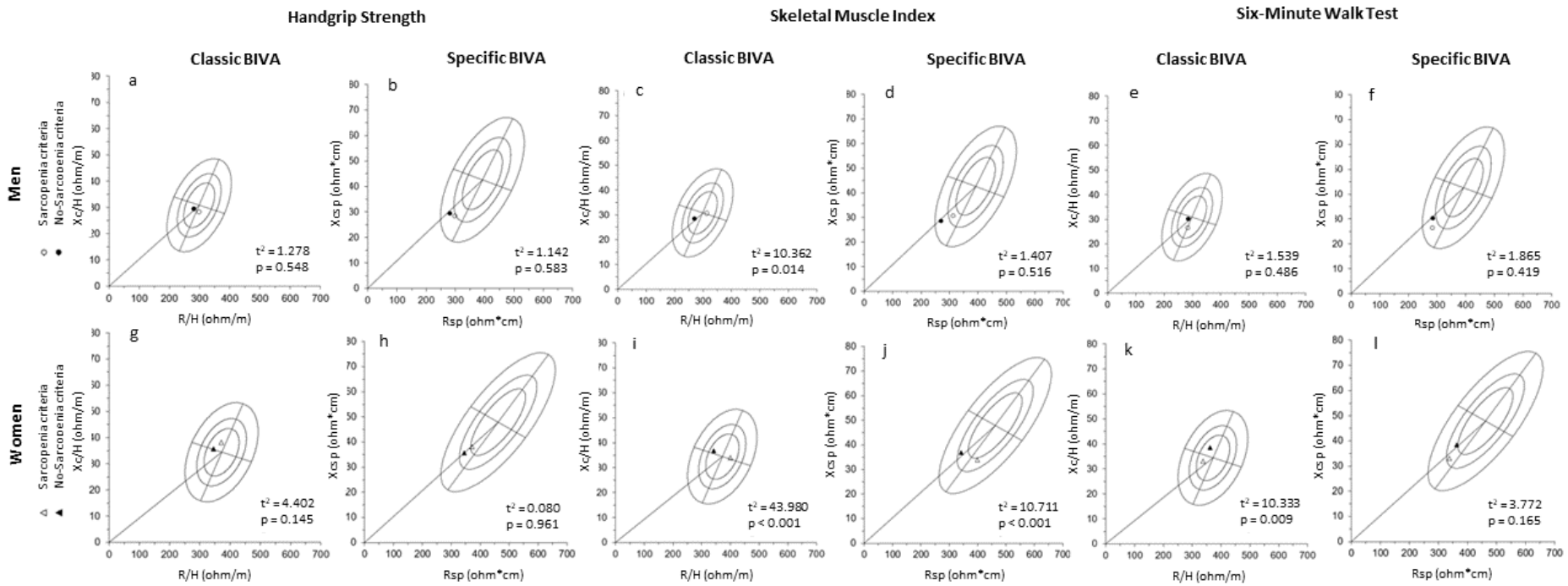

Figure 3. Classic and *specific* BIVA of older adults with low/normal values of the sarcopenia criteria

Note: Filled circles: men with values above the cutoff point; Hollow circles: men with values below the cutoff point; Filled triangles: women with values above the cutoff point; Hollow triangles: women with values below the cutoff point. a: men with normal-low strength and classic BIVA; b: men with normal-low strength and *specific* BIVA; c: men with normal-low muscle quantity and classic BIVA; d: men with normal-low muscle quantity and *specific* BIVA; e: men with normal-low physical performance and classic BIVA; f: men with normal-low physical performance and *specific* BIVA; g: women with normal-low strength and classic BIVA; h: women with normal-low strength and *specific* BIVA; i: women with normal-low muscle quantity and classic BIVA; j: women with normal-low muscle quantity and *specific* BIVA; k: women with normal-low physical performance and classic BIVA; l: women with normal-low physical performance and *specific* BIVA; R/H: resistance standardized for height; Xc/H: reactance standardized for height; Rsp: resistance standardized for height and transverse areas; Xcsp: reactance standardized for height and transverse areas; t^2: Hotelling's t-squared statistic.

DISCUSSION

Our findings suggest that classic BIVA presented a distinct association between BC, hydration, physical performance and sarcopenia in older adults' men and women. Data showed that classic BIVA variables were highly associated with two variables: handgrip strength and TBW for men with and without sarcopenia, respectively, whereas it was associated with ALST% and SMI for women with and without sarcopenia, respectively. In *specific* BIVA, the same variable presented the highest correlation coefficients for older adults with and without sarcopenia, for men were TBW%, and for women FM, and FM% for both. In addition, we found that classic and *specific* BIVA were able to distinguish sarcopenia in women, but not in men (Figure 2). When the sarcopenia criteria were used individually, both classic and *specific* BIVA were able to distinguish muscle reduction (SMI) in women, but only classic BIVA was able to do so for men. For the physical performance criterion, the classic BIVA showed differences only for women (Figure 3k).

In the classic BIVA, adjustments are made for height to reduce the effect of conductor length [23]. Classic BIVA can be used to detect body fluids and hydration changes and has been proved to be a valid technique for TBW assessment [23, 41, 42], as our results for men without sarcopenia. We found relationships between classic BIVA and hand grip strength in adults with sarcopenia. This association can be explained because the dielectric properties of cell membranes are related to the area and integrity of cell membranes. Integrity of cell membranes is a determinant of membrane potential and, together with area, thereby probably a determinant of cell function [43]. Furthermore, is known that vector migration in the RXc-score graph is associated with an increase in handgrip strength [44]. The *specific* BIVA indicated concordance with the same variable of non-sarcopenic and sarcopenic for men (TBW%) and women (FM), suggesting greater sensitivity of the *specific* BIVA to identify body components. This occurs because the bioelectrical values are also corrected by the cross-sectional areas and this can reduce the effect of body dimensions [45] increasing the sensitivity of bioelectrical values to identify tissues' properties and body composition [46]. Moreover, significant correlation between specific vector and FM% suggests that specific BIVA could be helpful to evaluate sarcopenic obesity diagnosis [47]. Similar associations were also evident in other studies and population groups both at the whole body [22, 45, 46] and segmental level [23].

Specific BIVA has been considered adequate as it has been validated against DXA, showing high sensitivity and specificity in the evaluation of %FM [22, 47].

In this study, it was observed that the PA was lower in sarcopenic women, a result that was not replicated among men probably because of the low statistical power of the relatively small sample. In a study with 207 older adults found that sarcopenic individuals had a PA lower than patients without sarcopenia ($p<0.05$) for both sexes [47]. The PA depends on several biological factors, including the integrity and functionality of the cell membrane, intracellular composition and the ratio of extracellular to intracellular water [48]. A high amount of extracellular water reduces the PA, while a higher proportion of intracellular water is reflected by a higher PA [48].

The classic and specific BIVA were sensitive to distinguish sarcopenia in older women (Figure 2c, d). Although the technique does not imply any direct evaluation of sarcopenia, individuals whose vectors lay to the left of the major axis were characterized by higher body cell mass (without sarcopenia) than those whose vectors were to the right (with sarcopenia). To the best of our knowledge, only one previous research found that both classic and *specific* BIVA were able to identify sarcopenia in older adults [47]. However, they classified sarcopenia using only SMI values (7.26 kg/m^2 for men and 5.45 kg/m^2 for women) [39]. In our study, we used three criteria (Handgrip Strength, SMI and 6MWT) [3]. The inclusion of strength and physical performance criteria is important since muscle strength is better than mass in predicting adverse outcomes [2, 49, 50]. Our results indicated that both classic and specific BIVA were not able to distinguish sarcopenia for men. Part of this result can be explained by the different criteria used, and the typical differences in body composition [33], strength levels [51] and hydration [9] between the sexes, as we shown in Table 1, which should directly impact on recent indicators for the classification of sarcopenia (handgrip and SMI). This result should be interpreted with caution given that this study was developed with a specific population of older adults and with small size of the male sarcopenic group. Furthermore, as this issue has been little explored by the scientific literature, there are few comparative results that enable to obtain a more consistent and conclusive information on the use of BIVA as a sarcopenia marker.

Our results (Figure 3a, b, g, h) showed that BIVA has not enough sensitivity to distinguish strength levels differences from the cutoff points established [38]. On other side, for muscle quantity criterion (SMI), both classic and specific BIVA were able to distinguish sarcopenia in women, and only classic BIVA for men (Figure 3c, i, j). For the

physical performance criterion (6MWT), the classic BIVA showed differences only for women (Figure 3k). These differences are a well-known expression of the sexual dimorphism of body composition [33]. Women have a cross-sectional muscle area between 25 to 45% smaller than men, lesser amounts of type I fibers, which also gives them less muscle strength than men [51]. From these results, we can infer that as the BIVA indicates variations in tissue hydration and body cell mass, its use to identify sarcopenia is justified in terms of body components of a morphological character. On the other hand, changes in strength (handgrip) seem to depend more on the integrity of the nervous system than on muscle reduction [52]. Thus, this may explain why handgrip and 6MWT were not sensitive to BIVA. Therefore, both BIVAs cannot infer functionality in older adults.

The current investigation has several strengths. As far as we know, this is the first study investigating the association between classic and *specific* BIVA with BC, hydration, and physical performance through DXA and dilution techniques to identify sarcopenia in older adults. From our study, correlation values between classic and *specific* bioelectric variables were generated. Thus, our correlation values can be used in BIVA calculations as reference values for older adults Brazilians with and without sarcopenia. We used the current EWGSOP criterion to identify sarcopenia (by strength as the first criterion), in an actualized way [3]. In addition, for the first time, each criterion was tested individually. Despite the promising results obtained in this study, some limitations are present and should be considered. We used reference values from the Italian population since BIVA values of Brazilian older adults were not yet available. Another point to consider is the sample size and the cross-sectional design of the study which limit the extrapolation of our finds. In addition, the greater participation of women than men can impact the findings. Another limitation is the low number of older adults with sarcopenia (10.6%). However, this value is similar to the worldwide prevalence (10%) [53].

Monitoring the BC and hydration is a relevant topic during ageing mainly because age-related changes in fat, skeletal muscle mass and strength losses are associated with various adverse health outcomes, including a higher risk for disability, morbidity and early mortality [54, 55]. These findings are certainly of interest in clinical practice since many countries around the world are experiencing a change in the age distribution of their populations, with worrying economic impacts [56]. In this sense, BIVA shows to be a promising and inexpensive resource for regular and reliable health monitoring in older adults. Then, the risk diagnosis can be made earlier.

CONCLUSION

Our findings demonstrated that the classic BIVA could be used to analyze absolute hydration (TBW) for men without sarcopenia. Equally, classic BIVA monitors variations in muscle index (SMI) and limbs relative muscle mass (ALST%) for women without and with sarcopenia, respectively. Regardless of sarcopenia status, the highest correlation coefficients between *specific* BIVA were observed in the sex-dependent variables of the older adults (TBW% for men and FM for women). Furthermore, the *specific* BIVA could be helpful to assess sarcopenic obesity diagnosis. Both classic and *specific* BIVA were able to distinguish sarcopenia in women.

Both classic and *specific* BIVA were sensitive to individually detect morphological changes, but not the functional criteria of sarcopenia. It is possible to state that BIVA procedures are promising tools to monitor body changes in ageing at the risk of sarcopenia. In the current context of prioritizing functional criteria in the diagnosis of sarcopenia, BIVA shows potential as a confirmatory alternative, economically viable and good sex-dependent morphological sensitivity.

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4.3 Artigo Original III – Multicompartimental body composition analysis in older adults: a cross sectional study.

Este tópico encontra-se o terceiro artigo, que compreende o terceiro objetivo específico da presente tese. Este estudo transversal aceito pelo períodico BMC Geriatrics tem como título "*Multicompartimental body composition analysis in older adults: a cross sectional study*". A BMC Geriatrics é um periódico internacional que publica pesquisas científicas focadas em todos os aspectos da saúde e no processo do envelhecimento. O período possui fator de impacto de 3.97 (2022).

Referência: ROSSINI-VENTURINI, A. C. et al. Multicompartimental body composition analysis in older adults: a cross sectional study. BMC Geriatrics, 2022.

Multicompartmental body composition analysis in older adults: a cross sectional study

ABSTRACT

Background: During aging, changes occur in the proportions of muscle, fat, and bone. Body composition (BC) alterations have a great impact on health, quality of life, and functional capacity. Several equations to predict BC using anthropometric measurements have been developed from a bi-compartmental (2-C) approach that determines only fat mass (FM) and fat-free mass (FFM). However, these models have several limitations, when considering constant density, progressive bone demineralization, and changes in the hydration of the FFM, as typical changes during senescence. Thus, the main purpose of this study was to propose and validate a new multi-compartmental anthropometric model to predict fat, bone, and musculature components in older adults of both sexes.

Methods: This cross-sectional study included 100 older adults of both sexes. To determine the dependent variables (fat mass [FM], bone mineral content [BMC], and appendicular lean soft tissue [ALST]) whole total and regional DXA body scans were performed. Twenty-nine anthropometric measures and sex were appointed as independent variables. Models were developed through multivariate linear regression. Finally, the predicted residual error sum of squares (PRESS) statistic was used to measure the effectiveness of the predicted value for each dependent variable.

Results: An equation was developed to simultaneously predict FM, BMC, and ALST from only four variables: weight, half-arm span (HAS), triceps skinfold (TriSK), and sex. This model showed high coefficients of determination and low estimation errors (FM: R^2_{adj}: 0.83 and SEE: 3.16; BMC: R^2_{adj}: 0.61 and SEE: 0.30; ALST: R^2_{adj}: 0.85 and SEE: 1.65).

Conclusion: The equations provide a reliable, practical, and low-cost instrument to monitor changes in body components during the aging process. The internal cross-validation method PRESS presented sufficient reliability in the model as an inexpensive alternative for clinical field use.

Keywords: aging; DXA; equation; fat mass; bone mineral content; ALST.

BACKGROUND

Muscle, fat, and bone are three main components of interest in the body composition (BC) field (1). The aging process involves proportional changes in these components (1) due to decreased levels of anabolic steroids and sex hormones (2). These alterations in the older adults' BC have a great impact on their health and quality of life (3). Skeletal muscle mass (SMM) has various essential physiological functions in humans and its maintenance is important to keep the body healthy, especially during aging. Thus, the reduction of SMM impairs muscle strength, and functional capacity, increasing the chances of morbidity and mortality (4). As a large proportion of SMM (≅74%) is found in the extremities, the appendicular lean soft tissue (ALST) is a representative measure of the SMM (5). In addition, ALST is used to identify sarcopenia (6). In turn, the bone mineral content (BMC) presents important variations throughout the older' life. Peak BMC occurs in the third decade of life and declines over the years (7). This reduction is similar in men and women before 50 years of age, but after this, the differences become very distinct among women because of menopause (8). This skeletal reduction restrains bone strength and can cause osteopenia and osteoporosis. Osteoporosis increases the risk of fractures and is considered the main consequence of the disease (9). Meanwhile, fat mass (FM) presents an increase during aging (10). From 70 years old, the FM increases (7.5%) in a similar way for both sexes (11), becoming one of the main risk factors for chronic diseases (12), colon cancer (13), physical function (14) and mortality (15). In this sense, changes in ALST, BMC, and FM during senescence have a great impact on their health (16), quality of life, and physical functional (17). To monitor this BC variability, simple and low-cost methods are required (18).

Several equations to predict BC using anthropometric measurements have been developed to determine FM and fat-free mass (FFM). However, these models have limitations regarding the estimation of adult older's body density (BD) and BC (19). The traditional bi-compartmental (2-C) model assumes that there is a linear relationship between subcutaneous fat, total fat, and BD. However, the correlation between total and subcutaneous body fat decreases with age (20). Perhaps it is due to; 1) the redistribution of FM from the extremities to the visceral area, and 2) due to fat infiltration in the SMM. Thus, there is an overestimation of the BD, and consequently, the FM is underestimated (21). Another worrying limitation is to assume a constant density of 0.9007 g/cm^3 and 1.100 g/cm^3 for the FM (22) and FFM (23), respectively. However, the natural aging

process causes progressive bone demineralization (24) and changes in the hydration of the FFM, causing a decrease in its density (25) which also affects the FM estimate (24). Furthermore, these 2-C equations do not evaluate other components, such as ALST and BMC, fundamental components in older adults.

From methodological advances it is necessary to analyze BC in a more precise and detailed way (26). Among imaging analysis methods, dual-energy X-ray absorptiometry (DXA) is widely used because its offers advantages such as low cost, speed of measurement, noninvasive, efficiency in the simultaneous determination of several components in a single scan (27), and their radiation exposure are considered small and safe for repeated measures (<1 mrem for whole-body scans) (28). Furthermore, DXA is considered a 3-C model (29), once it can accurately measure FM, BMC, and ALST (30). However, BC assessment with sophisticated equipment such as DXA is restricted to specific professionals, requiring a specialized structure. Then, why anthropometric measurements are simple and with a low cost associated (31), their use has been presented as valid alternatives for estimating BC in a multicompartmental approach in children and adolescents of both sexes (32, 33). So, the objective of this study was to propose and validate a multi-compartmental anthropometric model for the prediction of fat, bone, and musculature components in older adults of both sexes. Our hypothesis is that body composition can be estimated through anthropometric measurements.

METHODS

Design and Study population

In this study, we adopted a cross-sectional design to develop and validate a multicomponent anthropometric model to simultaneously estimate LST, BMC, and FM. The study was conducted from October 2016 to May 2017. The study sample was derived from physically independent community-dwelling older adults in a city in southeastern Brazil. The inclusion criteria were: adults aged 60-85 years, of both sexes, who walk independently. The exclusion criteria were: the presence of diseases that restrict mobility or muscle strength; absence of unstable cardiovascular condition; acute infection; tumor; back pain; prostheses, individuals with a diagnosis of cancer or uncontrolled diseases, who presented sequel of stroke, experienced a weight loss more than three kilograms (kg)

in the last 3 months, had a cognitive limitation that restricts understanding and taking tests, who did not complete all the stages or desired to withdraw from the study.

The study was approved by the Ethical Review Board of Hospital das Clinicas at the Medical School of the University of Sao Paulo (HC-FMRP/USP), following the ethical guidelines outlined in the 1975 Helsinki Declaration. Written informed consent was obtained from all individuals included in the study, after a brief explanation of the study objectives and evaluations. This manuscript followed the guidelines from The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) conference list, and the completed checklist is attached.

The sample size calculation was considered the desired maximum error (ε) and degree of confidence (Zy), previously knowing the population variability (σ^2) (34). For this, we used the variable with the greatest variability (FM; SD=8.7 kg) expected for such a population (35). Once the predetermined error estimate ($\varepsilon \leq 1.8$ kg) and maximum desired error (5%) the ideal n for the study (34) was defined (n=90).

Study protocol

A multidisciplinary health-trained team (nurses, nutritionists, pharmacists, physical education professors, physicians, and physiotherapists) performed data collection. All procedures, for each participant, were completed during one visit to the laboratories at the Hospital das Clinicas at the Medical School of the University of Sao Paulo at Ribeirao Preto (HCFMRP/USP). Participants came to the laboratory after an overnight fast (8h fast), abstaining from vigorous exercises, and no caffeine and alcohol during the preceding 24h. Before the measurements, the subjects were asked to empty their bladders. A total-body DXA scan was executed according to the manufacturer's guidelines. The anthropometric measures were taken according to the literature guidelines (36), whose procedures are summarized below.

The dependent variables

Whole and regional body composition were determined by DXA (Hologic® scanner, model QDR4500W; version 11.2, Bedford, MA). The DXA measurements included absolute values of appendicular lean soft tissue (ALST, kg), bone mineral content (BMC, kg), and fat mass (FM, kg), considered dependent variables. As the BMC represents the gray portion of bone, the bone adjustment was performed by multiplying the BMC by 1.0436 (37). The ALST was obtained through the sum of the lean soft tissue

(LST) of the lower and upper limbs on both sides (38). The DXA measurements were electronically transferred to an external HD and organized into a general data sheet without manual typing.

The independent variables

The participant's body mass and height were measured with a digital scale (Filizola® (model Personal, *Campo Grande*, MS) and a hall fixed stadiometer (Sanny® Professional – ES2020), respectively. The skinfolds (n=09; subscapular, triceps, biceps, media axillary, pectoral, suprailiac, vertical abdominal, media thigh and calf) were measured with Lange caliper with precision in mm, on the right side of the body in the regions. The circumferences (n=08; chest, arm, forearm, waist, abdominal, hip, medial thigh and calf) were realized using inelastic and inextensible tape (Sanny®). The girths (n=08; bi-acromial, bi-iliac, bi-trochanteric, bi-malleolar, biepicondylar humerus, bi-styloid, biepicondylar femur and transverse thoracic) were measured with Pachymeter (Sanny®). In addition, knee height and half-arm span (HAS) were measured using a Sanny® segmometer. All anthropometric measurements were performed by the same trained evaluator. All these procedures followed conventional standardization (39). The anthropometric measurements of our laboratory remain within the limits of reliability (33).

Statistical analysis

The basic analysis involved descriptive statistics using measures of central tendency to describe the characteristics of the sample. To verify the data normality, the Shapiro–Wilk test was applied. Comparisons between sex were performed using Student's t-test for independent samples. For the Multicompartmental anthropometric equation development, we adopted previous procedures (32, 33), briefly described below.

Through the determination of 30 independent variables plus the sex for the prediction of the 3 dependent variables, the multivariate regression model ($nYm = nX(r + 1)(r + 1)\beta m + n\varepsilon m$) by diagonal mutual analysis, parameter estimation, and the least squares errors method was used (40) by R Statistical Software (version 4.1.2, R Foundation for Statistical Computing, Vienna, Austria). The criteria for selection and reduction of independent variables followed the following steps: a) factor analysis and model adequacy (Kaiser-Meyer-Olkin) and Sphericity test (Bartlett) were performed to verify the suitability of the sample; b) univariate linear regression to determine all

common independent variables for each dependent variable (ALST, BMC, and FM), with significantly less than 5%; c) multivariate linear regression to estimate the parameters and Pillai approximation method for showing possible variables exclusions; d) testing of the remaining model (enter - univariate method), with estimated values of VIF (<10.0) and multicollinearity (L<1000) maximum permitted; e) adjustments by Pillai approach to testing the F values; f) as the variable sex is a categorical variable, it could not enter in the factor analysis. However, it will be added to the multivariate model due to its theoretical relevance and assumption of improving the model; g) then multivariate β parameters were determined, with the proposition of equations and residual distribution for each dependent variable; h) Akaike information criterion (AIC) statistic to ensure greater quality and simplicity of the statistical model. The details of the statistical procedures have been previously described in adolescents of both sexes (32, 33).

Finally, the predicted residual error sum of squares (PRESS) statistic was used to measure the effectiveness of the predicted equations for each dependent variable. The procedure may be understood as design efficiency in estimating the actual parameters by a virtual simulation that is, from the exclusion of an observation, equations are proposed with the remaining sample and replicated through cross-validation for each participant that was excluded. For validation, we follow the following steps: a) the correlation coefficients were estimated between predicted and measured values and b) cross-validation by PRESS method, coefficients of determination (Q^2_{PRESS}), and error (S_{PRESS}) for each dependent variable (ALST, BMC, and FM) (40).

RESULTS

Table 1 shows the anthropometric and body composition measures of the eligible participants. The means of all variables are within the confidence interval (95% CI), within the range limits for normal trends of distribution. Men were statistically taller, heavier, larger, and longer in most comparisons with women. Also had higher values of ALST, BMC, and residual mass. On other hand, women presented higher skinfolds, fat mass, and circumferences of hip and thigh values (p<0.05).

Table 1 – Descriptive values of anthropometric and body composition variables in older adults, difference test by sex.

	Men (n=31)					Women (n=69)					
	Mean (SD)	95% CI		Variance	Min - Max	Mean (SD)	95% CI		Variance	Min - Max	*p*
		IL	UL				IL	UL			
Age (years)	72 (7.6)	69.2	74.8	57.8	60.0 – 88.0	69.8 (5.9)	68.4	71.3	35.4	60.0 – 85.0	0.133
Anthropometric variables											
Height (cm)	168.0 (8.0)	165.0	170.9	64.0	150.5 – 188.0	156.2 (6.0)	154.8	157.6	35.4	145.0 – 174.0	<0.001
Weight (kg)	71.7 (13.3)	66.9	76.6	177.8	42.0 – 108.0	65.8 (11.4)	63.0	68.5	130.9	39.0 - 102.0	0.022
Knee height (cm)	53.6 (2.6)	52.6	54.5	7.0	49.1 - 61.8	49.6 (2.1)	49.1	50.1	4.5	45.0 - 54.4	<0.001
Half-arm span (cm)	87.4 (4.7)	85.6	89.1	21.8	78.7 – 101.0	80.9 (3.7)	79.9	81.8	13.9	69.1 - 89.5	<0.001
Skinfold											
Subscapular skinfold (mm)	23.2 (8.5)	20.0	26.3	72.3	6.0 – 37.0	28.3 (8.8)	26.2	30.4	77.0	8.0 – 47.0	0.007
Triceps skinfold (mm)	15.1 (5.8)	13.0	17.3	34.0	4.0 – 26.0	25.8 (6.9)	24.2	27.5	48.0	9.0 – 46.0	<0.001
Biceps skinfold (mm)	8.1 (3.5)	6.8	9.4	12.2	3.0 – 15.0	15.2 (5.3)	13.9	16.5	28.6	5.0 – 34.0	<0.001
Media axillary skinfold (mm)	18.5 (7.6)	15.8	21.3	57.4	4.0 – 30.0	23.7 (6.8)	22.1	25.4	46.5	5.0 – 41.0	0.001
Pectoral skinfold (mm)	16.9 (5.4)	15.0	18.9	28.9	4.0 – 26.0	14.7 (6.4)	13.2	16.2	40.5	4.0 – 40.0	0.094
Suprailiac skinfold (mm)	19.7 (9.8)	16.1	23.3	95.5	5.0 – 39.0	29.3 (7.9)	27.4	31.2	63.0	8.0 – 50.0	<0.001
Vertical abdominal skinfold (mm)	25.9 (8.3)	22.8	28.9	68.5	5.0 – 39.0	33.6 (8.6)	31.6	35.7	74.5	6.0 – 55.0	<0.001
Media Thigh skinfold (mm)	18.1 (7.5)	15.4	20.9	56.0	5.0 – 40.0	32.2 (11)	29.6	34.8	120.1	9.0 – 65.0	<0.001
Calf skinfold (mm)	11.9 (6.4)	9.5	14.3	41.4	2.0 – 34.0	23.8 (7.4)	22.0	25.6	55.2	6.0 – 45.0	<0.001
Circumference											
Chest circumference (cm)	97.8 (9.2)	94.4	101.1	84.5	82.0 - 116.5	92.9 (7.6)	91.1	94.8	58.2	72.0 - 115.5	0.007
Arm circumference (cm)	28.8 (3.5)	27.6	30.1	12.0	20.0 – 36.0	29.9 (3.8)	29.0	30.8	14.1	22.0 - 40.8	0.178
Forearm circumference (cm)	26.0 (2.0)	25.2	26.7	3.8	20.0 – 30.0	23.8 (2.3)	23.3	24.4	5.1	19.0 – 30.0	<0.001
Waist circumference (cm)	92.2 (11.1)	88.1	96.2	122.8	68.5 – 115.0	86.2 (10.0)	83.8	88.6	100.6	65.0 – 113.0	0.009
Abdominal circumference (cm)	96.1 (10.9)	92.1	100.1	118.5	68.0 - 115.5	95.4 (10.9)	92.8	98.0	119.7	70.0 – 120.0	0.766
Hip circumference (cm)	96.8 (6.6)	94.4	99.2	43.1	80.0 - 111.5	100.6 (9.0)	98.5	102.8	81.7	81.5 – 128.0	0.038

Medial thigh circumference (cm)	47.1 (5.6)	45.1	49.2	31.7	32.0 – 57.0	52.8 (6.3)	51.3	54.3	40.3	37.5 – 69.0	<0.001
Calf circumference (cm)	35.6 (3.5)	34.3	36.9	12.1	26.5 - 42.5	34.9 (3.0)	34.2	35.6	8.7	25.2 – 42.0	0.268
Girth											
Bi-acromial breadth (cm)	39.9 (2.7)	38.9	40.9	7.1	33.6 - 44.1	37 (2.0)	36.6	37.5	4.1	32.9 – 45.0	<0.001
Bi-iliac breadth (cm)	31.3 (2.6)	30.3	32.3	6.9	28.1 - 39.8	30.8 (2.1)	30.2	31.3	4.3	26.2 – 37.0	0.268
Bi-trochanteric breadth (cm)	33.8 (1.7)	33.2	34.5	2.9	31.4 - 39.7	33.3 (2.3)	32.8	33.9	5.2	28.7 - 39.9	0.289
Bi-malleolar breadth (cm)	7.0 (0.5)	6.8	7.2	0.3	6.0 - 8.2	6.3 (0.4)	6.2	6.4	0.1	5.4 - 7.4	<0.001
Biepicondylar humerus breadth (cm)	6.7 (0.5)	6.5	6.9	0.2	5.7 - 7.7	5.8 (0.5)	5.7	5.9	0.2	4.8 - 6.8	<0.001
Bi-styloid breadth (cm)	5.7 (0.4)	5.6	5.9	0.2	5.2 - 6.8	5.1 (0.4)	4.9	5.2	0.1	4.4 - 6.4	<0.001
Biepicondylar femur breadth (cm)	9.7 (0.7)	9.5	9.9	0.4	7.9 - 11.6	9.4 (0.8)	9.2	9.6	0.6	8.0 - 12.4	0.062
Transverse thoracic breadth (cm)	30.8 (2.6)	29.9	31.8	6.6	24.9 - 36.7	27.7 (1.8)	27.3	28.2	3.3	22.3 - 31.4	<0.001
Body composition											
ALST (kg)	20.7 (4.1)	19.2	22.2	16.5	12.6 – 32.5	14.6 (2.6)	14.0	15.2	6.5	9.2 – 22.5	<0.001
Fat mass (kg)	21.7 (6.9)	19.2	24.2	47.4	7.7 - 33.6	27.9 (7.2)	26.1	29.6	51.7	13.6 - 47.9	<0.001
Bone mineral content	2.6 (0.6)	2.3	2.8	0.3	1.4 – 3.8	2.0 (0.3)	1.9	2.1	0.1	1.4 - 3.1	<0.001
Residual mass	22.8 (3.9)	21.4	24.2	15.1	15.8 – 36.2	18.5 (2.8)	17.8	19.2	8.1	12.7 – 27.7	<0.001

CI: confidence interval; SD: standard deviation; UL: upper limit; IL: inferior limit; Min-Max: minimum-maximum; ALST: appendicular lean soft tissue.

The Kaiser-Meyer-Olkin test showed the sample adequacy and resulted in a value of 0.885, classified as meritorious (41) and the Barlett sphericity test yielded a X^2 of 3368.04 ($p < 0.001$), indicating homogeneous variance between groups. From the univariate regression (stepwise), the number of remaining variables to ALST (n=08), FM (n=05), and BMC (n=06) showed high r^2_{adj} (0.68 to 0.88) for the independent common variables for the three dependents variables (Table 2). In bold, variables with statistically significant coefficients ($p<0.05$), common in at least two of the dependent variables are shown.

Table 2. Univariate regression for selecting common independent variables at least twice (bold).

Appendicular lean soft tissue			**Fat mass**			**Bone mineral content**		
Variables	**Coefficient**	***p***	**Variables**	**Coefficient**	***p***	**Variables**	**Coefficient**	***p***
Pectoral skinfold (mm)	0.13018	<0.001	Media axillary skinfold (mm)	0.16083	0.012	Bi-styloid breadth (cm)	0.210010	0.020
Weight (kg)	0.13214	<0.001	**Pectoral skinfold (mm)**	-0.24240	<0.001	Waist circumference (cm)	-0.030637	0.001
Knee height (cm)	0.23779	0.009	**Media thigh skinfold (mm)**	0.12626	0.008	**Triceps skinfold (mm)**	-0.020330	0.001
Bi-acromial breadth (cm)	0.30532	0.001	**Weight (kg)**	0.35620	<0.001	**Weight (kg)**	0.038668	<0.001
Biepicondylar humerus breadth (cm)	1.22979	<0.001	**Half-arm span (cm)**	-0.29770	0.002	**Half-arm span (cm)**	0.032912	0.005
Calf circumference (cm)	0.26318	0.001				Medial thigh circumference (cm)	-0.028782	0.001
Media thigh skinfold (mm)	-0.07881	<0.001						
Triceps skinfold (mm)	-0.09662	0.003						
R^2= 0.88			R^2= 0.85			R^2= 0.68		

R^2: coefficient of determination variables with statistically significant coefficients ($p<0.05$), common in at least two of the dependent variables are shown in bold.

Next, a multivariate linear regression model was developed, simultaneously for the three dependent variables from variables selected in the univariate models. The categorical sex variable has not been previously tested in the models; however, it was added to the multivariate procedure due to its theoretical relevance, as demonstrated by their significant differences in Table 1. The coefficients, variance inflation factor (VIF), Pillai's trace, and precision and cross-validation results are shown in Table 3. The equations presented below in Table 3, should be also presented as:

$ALST_{[kg]}$ = (0,19336 x $weight_{[kg]}$) + (0,20139 x half-arm $span_{[cm]}$) + (- 0,04796 x triceps $skinfold_{[mm]}$) + (- 3,16675 x $sex_{[women=1;\ men=0]}$) - 10,21376.

$FM_{[kg]}$ = (0,50239 x $weight_{[kg]}$) + (- 0,40498 x half-arm $span_{[cm]}$) + (0,17292 x triceps $skinfold_{[mm]}$) + (4,73524 x $sex_{[women=1;\ men=0]}$) + 17,85412).

$BMC_{[kg]}$ = (0,01912 x $weight_{[kg]}$) + (0,02944 x half-arm $span_{[cm]}$) + (- 0,01267 x triceps $skinfold_{[mm]}$) + (0,13021 x $sex_{[women=1;\ men=0]}$) -1,21230).

Table 3. Coefficients, precision, and validation of a multicomponent anthropometric model to estimate body composition in older adults.

	Appendicular lean soft tissue	Fat mass	Bone mineral content	VIF	F	*p* (Pillai's trace)
Coefficients						
Intercept	-10.21376	17.85412	-1.21230			
Weight	0.19336	0.50239	0.01912	2.045	676.33	< 0.001
Half-arm span	0.20139	-0.40498	0.02944	2.049	9.53	< 0.001
Triceps skinfold	-0.04796	0.17292	-0.01267	2.544	4.17	0.008
Sex	-3.16675	4.73524	-0.13021	2.407	11.33	< 0.001
Precision						
R^2	0.85	0.83	0.62			
$R^2_{adjusted}$	0.85	0.83	0.61			
SEE (kg)	1.65	3.16	0.30			
Cross-validation						
PRESS	287.00	1066.84	9.75			
Q^2_{PRESS}	0.84	0.81	0.58			
SEE_{PRESS} (kg)	0.18	0.34	0.03			

R^2: coefficient of determination; $R^2_{adjusted}$: adjusted coefficient of determination; SEE: standard error to estimate; PRESS: sum of squares of residuals; Q^2_{PRESS}: press coefficient of determination; SEE_{PRESS}: press standard error of estimate; VIF: variance inflation factor;
Sex: male = 0; female = 1.
Measurement protocol:
Weight was measured with the subject should stand still over the center of the platform with the body weight distributed between both feet, when the subject could use light indoor clothing, excluding shoes, long trousers, and sweaters.
Half-arm span was measured with the subject standing and the feet together and with their back (for women) or chest (for men) against the wall. The arms were outstretched laterally and maximally at the level of the shoulders in contact with the wall, and with the hands flat and fingers outstretched. The tip of the middle (longest) finger (excluding the fingernail) of the right hand was kept in contact with the block, while the zero ends of the tape were set at the tip of the middle (longest) finger (excluding the fingernail) of the left hand.
The triceps skinfold was measured in the midline of the posterior aspect of the arm, over the triceps muscle, at the point midway between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna. The level of measurement was determined by the distance between the lateral projection of the acromial process and the inferior border of the olecranon process of the ulna, determined with a tape measure. The subject was measured standing and the skinfold was

measured with the arm hanging loosely. The triceps skinfold was picked up with the left thumb and index finger, and the tips of the calibers were applied to the skinfold at the marked level, approximately 1 cm proximal to the marked level.

Higher precision and cross-validation values of PRESS, $Q^2_{PRESS,}$ and low SEE_{PRESS} were found for each dependent variable (Table 3). These results showed that the models are valid to simultaneously predict ALST, FM, and BMC, with accordance close to "1" (Q^2_{PRESS}) and error close to "0" (S_{PRESS}).

The model standardized residuals are normally distributed (p=0.099) according to Figure 1.

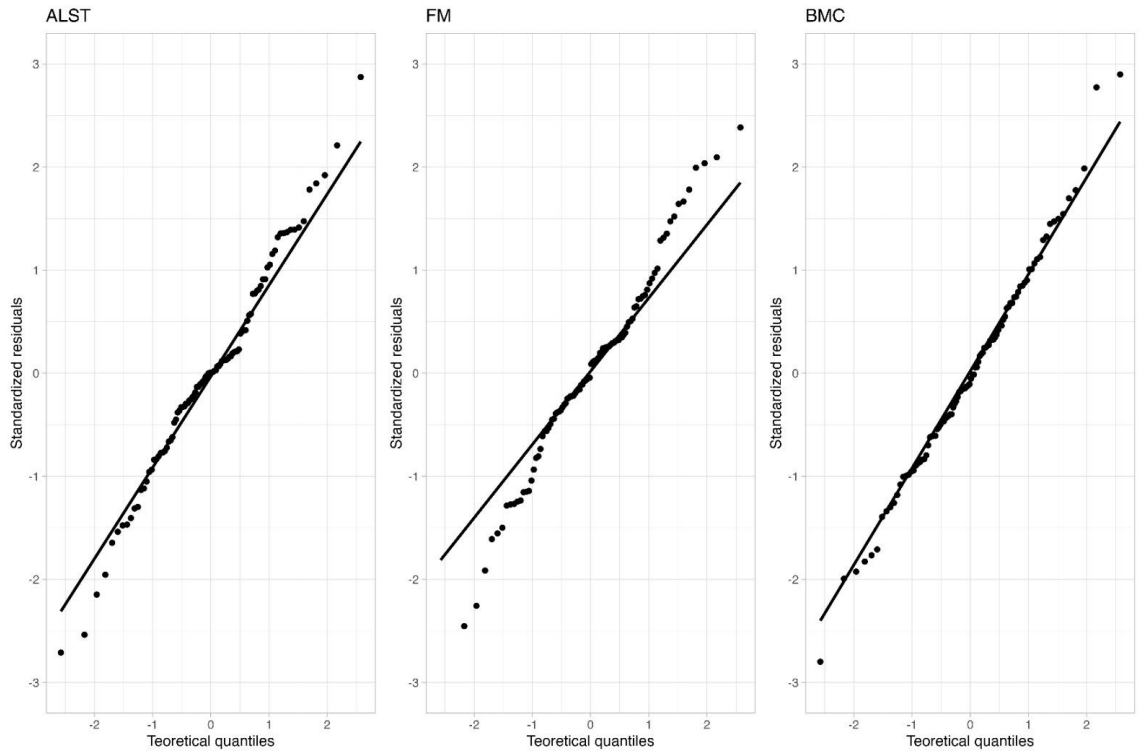

Figure 1 - Model standardized residuals
ALST: appendicular lean soft tissue; FM: fat mass; BMC: bone mineral content.

DISCUSSION

To the best of our knowledge, this is the first study that proposes a valid anthropometric model to simultaneously estimate FM, ALST, and BMC in older adults from a multicompartmental approach. DXA was used as a reference method due to its advantages in estimating all components by a single scan (42). Our proposed model with three anthropometric variables plus sex showed high prediction coefficients and low errors to simultaneously predict ALST, FM, and BMC. Since BC is affected by sex (43), and changes in BC due to aging occur differently between men and women (44), the inclusion of the variable sex was made arbitrarily in the models generated in this study. Therefore,

the current prediction equations are useful for estimating and monitoring ALST, FM, and BMC in older adults of both sexes.

Current anthropometric models to estimate BC in older adults have several limitations, causing errors in the estimation of BC. Furthermore, they have been developed using a bi-compartmental model (2-C) that determines FM and FFM (45, 46, 47), and this model is based on there is a linear relationship between subcutaneous fat, total fat, and BD. However, this is not true, because during the aging process there is age-related adipose tissue redistribution that is, an accumulation of visceral and abdominal fat occurs (48). Additionally, these equations do not evaluate ALST and BMC which are components that change during aging. The Lean equations (49) to estimate % body fat showed a coefficient of determination (r^2) of 0.77 and 0.70 and a standard error of estimate (SEE) of 4.1% and 4.7% for older adults men and women, respectively. However, our results for FM determination showed a higher coefficient of determination ($r^2 = 0.83$) and lower errors (SEE = 3,16 kg).

Progressive and metabolically unfavorable changes in BC have long been observed with aging (50). In a prospective study that investigated age-dependent changes over two decades, the main results found were an increase in BM, BMI, and FM until the age of approximately 70 and 75 years, after these parameters start to decrease (51). Regarding the changes in the SMM, the studies have shown a greater reduction in men than in women, with a more accentuated decline between 70 and 79 years old in both sexes (35, 50). However, the pattern and rate of age-related changes in BC may vary by sex, ethnicity, physical activity level, and caloric intake (52).

DXA is the most popular technique for measuring BC (53) and it has been shown to be a reliable method of FFM during aging (54). Furthermore, DXA may be considered the current reference technique for assessing SMM and BC in research and clinical practice (53). A high correlation ($r = 0.97$) between DXA-measured ALST and SMM measured by magnetic resonance imaging (MRI) was reported for both men and women (18–92 years) (5). In the same way, DXA-derived LST was found to be significantly correlated with MRI-measured SMM ($r = 0.94$; $p \leq 0.001$) in older women (55). In comparisons between DXA-measured FM and MRI-measured adipose tissue the associations were also high and significant ($r = 0.99$; $p \leq 0.001$) for older women (55). The principle of DXA depends on the property of X-rays to be attenuated in proportion to the composition and depth of the material the beam is crossed. The DXA scanner emits two different energy beams (40 and 70 keV). From the number of photons that are transmitted concerning the number detected

the quantity of BMC and soft tissue (fat and FFM) can be determined (53). Therefore, DXA can be used as a reference method to propose equations using anthropometry for clinical and professional practice (56). The anthropometric measurements are performed in both the geriatric nutritional assessment and epidemiological studies because they are painless, safe, non-invasive, simple, and low-cost procedures, which permit the estimation of the body components and also the calculation of nutritional indicators using predictive equations (21). The main anthropometric measurements used in older adults for this purpose are weight, height, calf and waist circumferences, as well as the triceps, biceps, subscapular and suprailiac skinfolds (21).

The current investigation has several strengths. As far as we know, this is the first study that proposes equations to estimate the main components of BC from the same anthropometric variables for older adults. This implies a reduction in the prediction error and facilitates its use in epidemiological studies. Another positive point is that we included the variable sex in the generated models, facilitating the application in large groups of both sexes. Despite all the research efforts in this study, there were still some limitations: for example, DXA is not a gold standard for older adults' body composition. However, the current state-of-the-art method for body composition measurement in the four compartments model (4-C models) at the molecular level, as it includes the evaluation of the main FFM components, thus reducing the effect of biological variability. Nonetheless, it requires sophisticated and highly specialized technical equipment; it implies the propagation of measurement errors, difficult to apply in certain population groups, and is time-consuming. Furthermore, it has high costs, making it difficult to use on large samples (57). Nevertheless, DXA represents a reference method for the assessment of human BC in the research field (42, 58) and it is widely considered the gold standard for BC assessment in clinical practice because of its advantages (56). Another point to consider is that overnight fast impacts the hydration status and this can influence body composition measurement (59). Moreover, reference values of BC assessed by DXA on adults over 60 years old are available from the National Health and Nutrition Examination Survey 1999–2004 and other studies on the local population (60). Although it is a program designed to assess the health of adults and children in the United States, these reference values should be helpful in the evaluation of a variety of adult abnormalities involving fat, LST, and bone.

As hypothesized, using a multivariate regression model, simple anthropometric measures can be used to simultaneously estimate body components (ALST, FM, and BMC) in older adults of both sexes. As a practical simulation, an older adult male "A" with

measurements of weight (66.3 kg), HAS (80.5 cm), TrSk (16 mm), and sex (0), when applied to our model, would have the estimated values of 18.1 kg, 21.3 kg and 2.2 kg for ALST, FM, and BMC, respectively. Their true measured values (DXA) were 18.2 kg, 20.8 kg, and 2.2 kg. If the equation is applied to an older adult woman "B" with values of weight (58.6 kg), HAS (81.5 cm), TriSK (26 mm), and sex (1) the estimated values for ALST, FM, and BMC would be: 13.1 kg, 23.5 kg and 1.9 kg, correspondingly. As noted, the values are close to the measured DXA values for ALST (13.2 kg), FM (23.4 kg), and BMC (2.0 kg). These values can be compared with the reference values National Health and Nutrition Examination Survey (NHANES) (60) and be useful for many applications in clinical and field practice. For example, using the criteria proposed by the FNIH (cutoffs < 19.75 for men and < 15.02 for women) we can classify both older adults with sarcopenia (61). Since older adult "A" presented predicted ALST values of 18.1 kg and older adult B of 13.1 kg. These findings are highly relevant as they allow permanent following/monitoring of excessive accumulation of FM, and declines in BMC and ALST, as risks to older adults throughout the life course (62, 63). Thus, keeping the balance rate of fat, muscle and bone is essential to preserving metabolic homeostasis, and health status and positively contributes to successful aging (56). For this reason, the assessment of BC in older adults is critical and could be an additional preventive strategy for age-related diseases (56), which may result in sarcopenia (6, 4, 64), osteoporosis (65) sarcopenic obesity (43) osteosarcopenic obesity (2) and osteosarcopenia (66). This should impair muscle strength, and functional capacity, as well as greater morbidity and mortality in older adults (67). Therefore, the current prediction equations could increase the available options for the estimation of body composition in older adults. To ensure dissemination and accessibility, an assessment of the main body components based on our predictive models can be found in an excel file (Additional file 1) at the following link (http://posgraduacao.eerp.usp.br/files/Model_BodyComposition_OlderAdults.xlsx).
Lastly, future studies should evaluate the efficiency of these equations applied in longitudinal and intervention studies.

CONCLUSION

Our findings demonstrated that the anthropometric prediction equations developed in this study provide a reliable, practical, and low-cost instrument to assess the components that most change during the aging process. These results suggest that the

equations can be valid alternatives and reliable information about BC in older adults since the internal validation method PRESS presented high internal validity, high coefficients of determination, and low prediction errors.

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5. CONSIDERAÇÕES FINAIS

Nesta tese verificou-se que os modelos convencionais (antropometria e BIA), embora válidos, não foram capazes de identificar os componentes corporais de maior interesse no monitoramento e riscos à saúde, em idosos. No que se refere ao cuidado com o idoso, a análise multivariada da CC em idosos permite a proposição de um modelo antropométrico com abordagem multicompartimental capaz de predizer simultaneamente os principais indicadores dos agravos degenerativos na CC durante a senescência. Como anteriormente mencionado, é importante considerar a especificidade populacional ao selecionar equações para predizer o TMMA. O uso de equações generalizadas, ou seja, não específica para uma determinada população, sugere diagnóstico falso positivo/negativo de sarcopenia. Isso implica na ausência de cuidados do idoso e resulta no agravo da doença, impactando em sua qualidade de vida. A análise de bioimpedância, ainda que mediante técnica mais específica (BIVA), não é capaz de identificar os indicadores dos agravos corporais (músculo, osso e gordura) para idosos de ambos os sexos. No entanto, a BIVA demonstra potencial para o diagnóstico de sarcopenia em mulheres, mas não em homens. Portanto, indica uma possibilidade promissora para monitorar o risco de sarcopenia no envelhecimento. Muito embora sejam necessários avanços no aprimoramento dessa abordagem.

Diante do exposto, o modelo indicado no Artigo Original III consegue responder de forma confiável, satisfatória e válida a proposição de um modelo capaz de predizer os principais indicadores responsáveis pelos agravos durante o envelhecimento. Nesse sentido, essa tese apresenta uma estratégia simples que envolve medidas corporais facilmente obtidas. Além disso, o link com planilhas automatizadas (APÊNDICE A) oferece auxílio no acompanhamento dos idosos, para facilitar o usuário com os cálculos matemáticos do(s) modelo(s).

Em conclusão, essa tese contribui com o processo de envelhecimento, e ressalta a relevância em considerar a especificidade populacional na seleção de equações para predizer o TMMA, a fim de evitar erros no diagnóstico de sarcopenia através do componente muscular. A falha da BIVA na identificação e monitoramento dos indicadores de sarcopenia para ambos os sexos requer uma alternativa simples, de baixo custo e viável capaz de predizer concomitantemente indicadores de sarcopenia, obesidade e osteoporose. Futuras pesquisas poderão validar o modelo proposto em estudos longitudinais com e sem intervenção nutricional e exercício. Portanto, o uso do modelo aqui proposto representa uma simples estratégia, capaz de monitorar, identificar e prever precocemente os agravos da sarcopenia, obesidade e osteoporose durante o envelhecimento.

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[1] As referências estão elaboradas de acordo com ABNT NBR 6023 (ASSOCIAÇÃO BRASILEIRA DE NORMAS TÉCNICAS, 2018).

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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 0230/2019, de 15/10/2019

Prezado Senhor,

Comunicamos que o projeto de pesquisa abaixo especificado foi analisado e considerado **aprovado** pelo Comitê de Ética em Pesquisa da Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo (CEP-EERP/USP) em sua 264ª Reunião Ordinária, realizada em 09 de outubro de 2019.

Protocolo CAAE: 18416619.3.0000.5393

Projeto: Estimativa da composição corporal por análise multivariada em idosos

Pesquisadores: Ana Claudia Rossini Venturini (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 – COMPROVATIVO DE FINANCIAMENTO

7882043363248820

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

PROJETO:
870282/1997-2 -

COORDENADOR:
Regina Szylit
CPF: 05640645806

ORIENTADOR:
Dalmo Roberto Lopes Machado
CPF: 02715901810

Eu, **Ana Claudia Rossini Venturini**, CPF número **36311364808**, 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: 142078/2019-0
Modalidade - Categoria: Doutorado - GD -
Vigência: De 01/06/2019 a 31/05/2022
Valor mensal da bolsa: R$ 2.200,00

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

DATA:
07 de Junho de 2019

ACEITE:

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

BENEFICIÁRIO:

Ana Claudia Rossini Venturini
CPF: 36311364808

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 07/06/2019, originário do número IP 200.130.33.73(200.130.33.73) e número de controle 7691118176911181:1759796828-2171124862.

ANEXO C – AUTORIZAÇÃO DO USO DO DIREITO AUTORAL DO ARTIGO I

Nutr hosp 2929 authorization Externa Caixa de entrada ×

N **nutricion@grupoaran.com** seg., 14 de nov. 13:10 (há 9 dias)
para mim

inglês › português Traduzir mensagem Desativar para: inglês ×

Dear Venturini, MD,

There is no problem you use your article entitled "Population specificity impacts prediction of appendicular lean tissues for diagnosed sarcopenia: a cross-sectional study" (Reference 2929) that was published in 2020

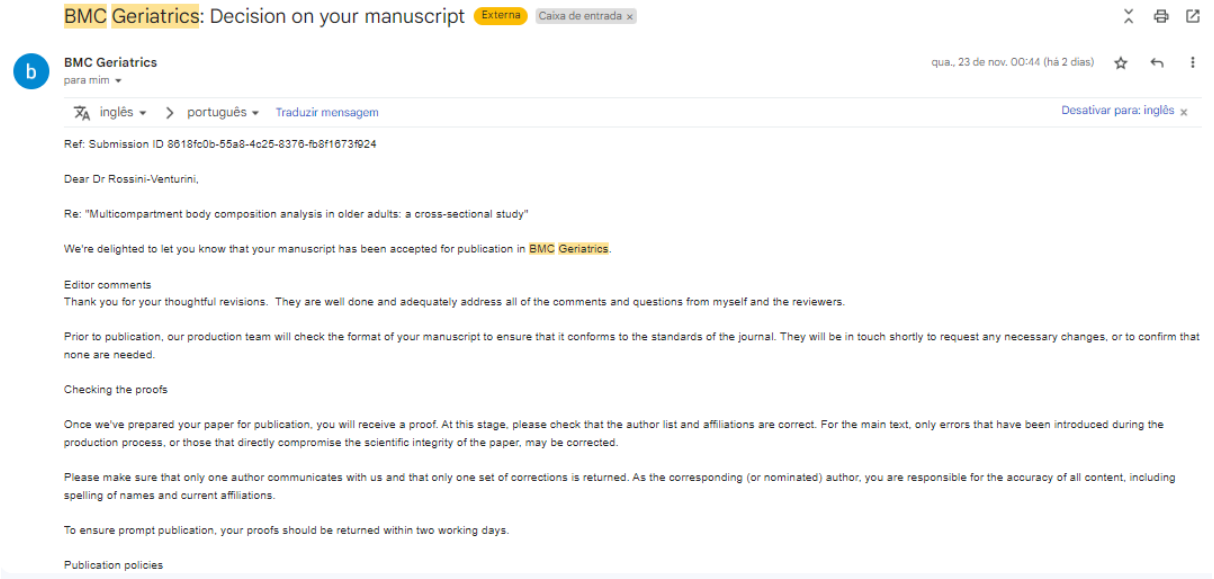
Please, cite in your thesis where the article has been published (Nutr hosp 2020;37(4):776-85). I attach the file.

The use must not be commercial anyway.

Sincerely,

Rosa Palacios
Responsable de Revistas Científicas
ARÁN Congresos Editorial Comunicación Formación
Castelló, 128, 1.º
28006 Madrid (España)
Tel. + 34 91 745 17 29
+ 34 91 782 00 30
www.grupoaran.com

ANEXO D – ACEITE ARTIGO III



BMC Geriatrics: Decision on your manuscript Externa Caixa de entrada ×

BMC Geriatrics
para mim

qua., 23 de nov. 00:44 (há 2 dias)

inglês › português Traduzir mensagem Desativar para: inglês ×

Ref: Submission ID 8618fc0b-55a8-4c25-8376-fb8f1673f924

Dear Dr Rossini-Venturini,

Re: "Multicompartment body composition analysis in older adults: a cross-sectional study"

We're delighted to let you know that your manuscript has been accepted for publication in BMC Geriatrics.

Editor comments
Thank you for your thoughtful revisions. They are well done and adequately address all of the comments and questions from myself and the reviewers.

Prior to publication, our production team will check the format of your manuscript to ensure that it conforms to the standards of the journal. They will be in touch shortly to request any necessary changes, or to confirm that none are needed.

Checking the proofs

Once we've prepared your paper for publication, you will receive a proof. At this stage, please check that the author list and affiliations are correct. For the main text, only errors that have been introduced during the production process, or those that directly compromise the scientific integrity of the paper, may be corrected.

Please make sure that only one author communicates with us and that only one set of corrections is returned. As the corresponding (or nominated) author, you are responsible for the accuracy of all content, including spelling of names and current affiliations.

To ensure prompt publication, your proofs should be returned within two working days.

Publication policies

APÊNDICE

APÊNDICE A – PLANILHAS AUTOMATIZADAS

Prediction of Appendicular Lean Soft Tissue, Fat Mass and Bone Mineral Content in Older Adults

The objective of this tool is to predict appendicular lean soft tissue (ALST) fat mass (FM) and bone mineral content (BMC) in older adults of both sexes. Muscle, fat, and bone are three main components that most change during the aging process. Muscle and BMC decrease, while FM increases. These changes during senescence have a great impact on their health, quality of life and functional capacity. The GEPEATE research group has developed a valid anthropometric model to simultaneously estimate ALST, FM, and BMC in the older adults from a multicompartmental approach. These values can be compared with the reference values and be useful for many applications in clinical and field practice.

To predict ALST, FM and BMC the following variables are required: weight (kg), half arm span (cm), triceps skinfold (mm) and sex (male = 0; female = 1). Precision of the measurements is important, because any errors can change accuracy of measurements. The details of the study protocol can be found here .

Insert →

Weight$_{(kg)}$	
Half arm span$_{(cm)}$	
Triceps skinfold$_{(mm)}$	
Sex$_{(0=male;\ 1=female)}$	

Component	Estimate (kg)	$R^2_{adjusted}$	SEE (kg)
ALST		0.85	1.65
FM		0.83	3.16
BMC		0.61	0.30

Authors:

Ana Claudia Rossini-Venturini[12*], Lucas Veras[34]; Pedro Pugliesi Abdalla[12], André Pereira dos Santos[12], Márcio Fernando Tasinafo Junior[25], Leonardo Santos Lopes da Silva[25], Thiago Cândido Alves[2], Eduardo Ferrioli[5], Jorge Mota[23], Dalmo Roberto Lopes Machado[125].

Afilliation:

[1]University of São Paulo, College of Nursing at Ribeirão Preto, Ribeirão Preto, Brazil.
[2]Study and Research Group in Anthropometry, Exercise and Sport (GEPEATE), São Paulo, Brazil;
[3]The Research Centre in Physical Activity, Health and Leisure (CIAFEL) - University of Porto. Porto, Portugal;
[4]Laboratory for Integrative and Translational Research in Population Health (ITR), University of Porto, Porto, Portugal
[5]University of São Paulo, School of Physical Education and Sport of Ribeirão Preto, Ribeirão Preto, Brazil.
[6]University of São Paulo, Faculty of Medicine of Ribeirão Preto, Ribeirão Preto, Brazil;

APÊNDICES B – PROTOCOLO DE MEDIDAS

Measurements Protocols

To simultaneously predict ALST, FM and BMC is need to measure and record the following variables: a) weight (kg), b) half arm span (cm), c) triceps skinfold (mm) and d) sex (male = 0; female = 1).

a) Our subject's body mass was measured with a digital scale (Filizola® (modelo *Personal*, Campo Grande, MS) and followed the following guidelines:

- The subject should stand still over the center of the platform with the body weight distributed between both feet;
- The subject could use light indoor clothing, excluding shoes, long trousers and sweater.
- The body mass must be recorded to nearest 0.1 kg.

b) Our subject's half arm span was measured using a tape at least 2 m long, a flat surface (wall).

- The subjects should stand with the feet together and with their back (for women) or chest (for men) against the wall.
- The arms were outstretched laterally and maximally at the level of the shoulders in contact with the wall, and with the hands flat and fingers outstretched;
- The tip of the middle (longest) finger (excluding he fingernail) of the right hand was kept in contact with the block, while the zero end of the tape was set at the tip of the middle (longest) finger (excluding the fingernail) of the left hand;

  Two measures were taken, the largest being recorded, with a precision of 0.1 cm.

c) Our subject's triceps skinfold was measured with Lange caliper with precision in mm, on the right side of the body.

- The triceps skinfold was measured in the midline of the posterior aspect of the arm, over the triceps muscle, at the point midway between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna;

- The level of measurement was determined by distance between the lateral projection of the acromial process and the inferior border of the olecranon process of the ulna, determined with a tape measure;
- The subject was measured standing and the skinfold was measured with the arm hanging loosely;
- The triceps skinfold was picked up with the left thumb and index finger, and the tips of the calibers were applied to the skinfold at the marked level, approximately 1 cm proximal to the marked level.

d) In relation to the sex variable, the number 0 was used for male and the number 1 for female.

All these procedures followed conventional standardization (LOHMAN; ROCHE; MARTORELL, 1988).

REFERENCES

LOHMAN, T.G.; ROCHE, A.F.; MARTORELL, R. **Anthropometric Standardization Reference Manual**. Champaign, Illinois:: Human Kinetics, 1988.

APÊNDICE C – CONTRIBUIÇÕES DOS AUTORES EM CADA ARTIGO

Estudo Original I - Population specificity affects prediction of appendicular lean tissues for diagnosed sarcopenia: A cross-sectional study.

Conceituação, rascunho original, coordenação e aquisição dos dados (ACRV, PPA e DRLM), recrutamento dos pacientes e coleta de dados (APS e TCA), análise estatística e revisão dos métodos (ASC e JAPSM), resultados e versão final do manuscrito (JAGM e FGB). Todos os autores contribuíram significativamente, leram e aprovaram o manuscrito final.

Estudo Original II – Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: A cross-sectional study.

Conceituação, metódos e rascunho original (ACRV e PPA), Conceituação e supervisão (PGF), análise dos dados e escrita (APS, MFTJ, TCA, EBGG e TLP), Supervisão, revisão da escrita e edição (KP, EF, JM, MRBV), Conceituação, supervisão, revisão da redação e edição (DRLM). Todos os autores contribuíram significativamente, leram e aprovaram o manuscrito final.

Estudo Original III – Multicompartment body composition analysis in older adults: A cross-sectional study.

Conceituação, metódos e rascunho original (ACRV, PPA e DRLM), análise estatística e métodos (LV), análise dos dados e escrita (PPA, APS, MFTJ, LSLS, TCA), supervisão, revisão da redação e edição (EF, JLGS, VRP, JM, DRLM). Todos os autores contribuíram significativamente, leram e aprovaram o manuscrito final.