Operational definitions of sarcopenia and their associations with five-year changes in falls risk in community-dwelling middle-aged and older adults

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Abstract

Purpose: To verify associations between sarcopenia and falls risk, and to determine changes in sarcopenia prevalence over five years in middle-aged and older men and women according to different anthropometric and performance-based operational definitions.

Methods: N = 681 volunteers (48% female; mean $\pm$ SD age 61.4 ± 7.0 years) participated in baseline and follow-up assessments (mean 5.1 ± 0.5 years later). Appendicular lean mass (ALM) was assessed by dual-energy X-ray absorptiometry (DXA), hand-grip (HGS) and lower-limb (LLS) strength were assessed by dynamometry, and falls risk was determined using the Physiological Profile Assessment. Anthropometric definitions (ALM/height squared [ALM-H], ALM/weight $\times$ 100 [ALM-W] and a residuals method [ALM-R]) and performance-based definitions (HGS, LLS, upper- and lower-limb muscle quality [UMQ and LMQ]) of sarcopenia were examined. The lowest 20% of the sex-specific distribution for each definition at baseline was classified as sarcopenia.

Results: Sarcopenia prevalence increased after five years for all operational definitions except ALM-H (men: -4.0%; women: -5.5%). Men classified with sarcopenia according to anthropometric definitions, and women classified with sarcopenia according to performance-based definitions, had significant increases in falls risk over five years (all $P < 0.05$) compared to individuals without sarcopenia. Significant sex interactions were observed for ALM-R, LLS and LMQ (all $P < 0.05$) definitions.

Conclusions: Sarcopenia prevalence generally increases at a higher rate when assessed using performance-based definitions. Sarcopenia is associated with increases in falls risk over five years in community-dwelling middle-aged and older adults, but sex-specific differences may exist according to different anthropometric or performance-based definitions.

Keywords: Sarcopenia, Falls, Muscle Mass, Muscle Strength

Mini Abstract: Sarcopenia may be diagnosed in the clinic using operational definitions based on low muscle mass or function. This prospective, population-based study revealed that sex-specific associations may exist between operational definitions of sarcopenia and falls in community-dwelling middle-aged and older adults.

Introduction

Although the definition of sarcopenia currently encompasses age-related declines in both skeletal muscle mass and function [1], the two parameters are not synonymous; mass declines may explain as little as five per cent of the variation in change in muscle strength during ageing [2,3]. Clearly, age-related declines in muscle function are not attributable to mass declines alone, but also neurologic and skeletal muscle property changes [4]. The discordance between skeletal muscle mass and function has led some investigators to suggest that the two declines should be considered independently [5].

Nevertheless, the bilateral concept of sarcopenia persists despite the fact that most existing operational definitions generally include assessments of muscle mass alone [6]. The earliest and most commonly utilised anthropometric operational definition was provided by Baumgartner and colleagues [7]. This definition classified sarcopenia as values of appendicular lean mass (ALM; kg) relative to height (m^2) greater than two standard deviations below that of the sex-specific mean of a young adult reference group. Subsequent definitions have been proposed which normalise skeletal muscle mass to body weight [8] and body fat mass [9].

The disparities between anthropometric operational definitions results in substantial divergence in prevalence estimates for sarcopenia [10]. There is also a paucity of data from prospective studies investigating how the prevalence of sarcopenia changes over time in middle-aged and older adults. Moreover, as described above, skeletal muscle atrophy is not the only factor that explains age-related changes in muscle strength, and therefore anthropometric operational definitions may not be valid predictors of functional declines. Indeed, a recent cross-sectional study of Australian women in low-level aged care reported that two anthropometric definitions are not associated with poor performance in the timed up-and-go test or walking speed [11]. It is therefore possible that performance-based sarcopenia

definitions may be preferable for identifying middle-aged and older adults whose functional deficits and subsequent risk of falling may substantially increase in the near future.

The aim of this analysis of a large prospective cohort of community-dwelling middle-aged and older adults was to verify associations between sarcopenia and falls risk, and to determine changes in sarcopenia prevalence over five years in middle-aged and older men and women according to different anthropometric and performance-based operational definitions.

Methods

Study design and participants

The Tasmanian Older Adult Cohort (TASOAC) study was a prospective, population-based study primarily aimed at identifying factors associated with the development and progression of osteoarthritis and osteoporosis in community-dwelling older adults. Ethics approval was provided by the Southern Tasmanian Health and Medical Human Research Ethics Committee. Written informed consent was obtained from all participants.

The cohort consisted of 1100 males and females aged 50 to 79 years, selected from electoral rolls in southern Tasmania (population 229,000) using stratified simple random sampling by sex without replacement (response rate 57%). Institutionalised adults were excluded from participating in the study and participants were also excluded due to contraindication for magnetic resonance imaging (MRI), as MRI tests were required to examine osteoarthritis progression.

Enrolled participants attended a clinic at the Menzies Research Institute in Hobart, Tasmania between March 2002 and September 2004. Participants were invited to attend a follow-up clinic five to six years after the baseline visit. The assessments described below were completed at both time-points.

Anthropometrics

Height was measured to the nearest 0.1 cm (with shoes, socks, and headwear removed) using a Leicester stadiometer (Invicta, Leicester, UK). Weight was measured to the nearest 0.1 kg (with shoes, socks, and bulky clothing removed) using electronic scales (Heine, Dover, USA) that were calibrated at the beginning of each clinic. Body mass index (BMI; kg/m^2) was calculated from these measurements.

Participants underwent a whole body scan by dual-energy X-ray absorptiometry (DXA; Hologic Delphi, Hologic, Waltham, USA) from which soft tissue composition was determined. Total body fat mass, body fat percentage, and ALM (the sum of lean mass in the upper and lower limbs) were calculated. The same densitometer was used throughout the study and quality control was performed using a spine phantom prior to testing. Although precision of soft tissue measurements was not monitored, the longitudinal coefficient of variation for bone mineral density using the spine phantom was 0.39% in this study [12]. A separate study has reported that the coefficients of variation for total body lean and fat mass using the Hologic Delphi densitometer are 0.5% and 1.5%, respectively [13].

Muscle performance

Lower-limb strength (LLS) was measured to the nearest kilogram in both legs simultaneously, using a dynamometer (TTM Muscular Meter, Tokyo, Japan). This test examines isometric strength, predominantly of the quadriceps and hip extensors, and has been described in detail previously [14]. Two trials were recorded, and the mean score was taken as the criterion value for LLS. Intra-class correlation coefficients (ICC's) demonstrated high reproducibility between trials 1 and 2 at baseline (ICC: 0.95, 95% CI 0.94 to 0.96) in the present study.

We also examined lower-limb muscle quality (LMQ; an estimate of specific force), which has been shown to decrease with age, and is commonly used in studies of aging muscle [15]. LMQ was calculated as the magnitude of leg strength from the LLS test divided by the combined lean mass of the legs from the DXA scans using the following formula:

$$LMQ \text{ (kg/kg)} = LLS \text{ (kg)} / [\text{left leg lean mass (kg)} + \text{right leg lean mass (kg)}].$$

Hand grip strength (HGS) was measured using a pneumatic bulb dynamometer (North CoastTM Bulb Dynamometer; Adult 0-30 psi, model no. 70154). Participants were required to

grip the bulb with the right hand and squeeze as hard as possible. The protocol was repeated for the left hand, and two trials were recorded for each hand. The mean score (psi) for each hand was recorded. Intra-class correlation coefficients (ICC's) also demonstrated high reproducibility for hand grip strength of the right hand for trials 1 and 2 at baseline (ICC: 0.96, 95% CI 0.92 to 0.97). HGS was calculated as the mean score for the left and right hands, and upper-limb muscle quality (UMQ) was calculated as the mean HGS divided by the combined lean mass of the left and right arms: $UMQ (psi/kg) = HGS (psi) / [left arm lean mass (kg) + right arm lean mass (kg)]$. Lower-limb and hand grip dynamometers were calibrated prior to testing using known weights.

The Physiological Profile Assessment (PPA; Prince of Wales Medical Research Institute, Sydney, Australia), a validated predictor of falls in older adults, assessed participant falls risk at baseline and follow-up [16]. The PPA examines five physiological domains (vision, reaction time, proprioception, knee extension strength and balance) and provides a standardized falls risk score. Falls risk scores less than 0 indicate a low risk of falls, between 0 and 1 indicate a mild risk, between 1 and 2 indicate a moderate risk, and greater than 2 indicate a high risk.

Operational definitions of sarcopenia

We investigated three anthropometric and four performance-based operational definitions of sarcopenia. In the absence of reference data for anthropometric and performance variables from local populations of young adults, participants in the lowest 20% of the sex-specific distribution for each anthropometric and performance-based definition were classified as having sarcopenia [17]. Anthropometric definitions of sarcopenia included the lowest 20% of the sex-specific distribution for ALM/height² (ALM-H) [7], ALM/weight x 100 (ALM-W) [8], and for the residuals of the linear regression of ALM on height and total

body fat (ALM-R) [9]. Performance-based definitions of sarcopenia included the lowest 20% of the sex-specific distribution for HGS, LLS, UMQ and LMQ [18]. We also determined sarcopenia prevalence according to ALM-H at baseline using previously established cut-points for sarcopenia by this definition obtained from the US Rosetta Study and Health ABC Study. These cut-points were 7.26kg/m² (men) and 5.50 kg/m² (women) [7], and 7.23kg/m² (men) and 5.67 kg/m² (women), respectively [9].

Statistical analyses

We initially compared differences in baseline age, gender proportions, ALM, LLS and falls risk scores between participants lost to follow-up and included participants, using independent samples t-tests and Chi-square tests. For included participants with data at baseline and follow-up, we examined sex differences in baseline descriptive characteristics, including anthropometric and muscle performance variables, using independent samples t-tests. Sex-stratified linear regression analyses examined differences in follow-up values of falls risk score between participants classified with sarcopenia and those without sarcopenia, according to each operational definition. Regression analyses also examined differences in five-year change in falls risk, with adjustment for the baseline value for falls risk. In post-hoc analyses, two-way ([operational definition: sarcopenic; non-sarcopenic] X [sex: male; female]) ANOVAs examined whether associations of anthropometric and performance-based definitions with falls risk differed according to sex, and knee extension strength score at baseline was added to the regression model to determine whether significant associations with change in falls risk were mediated by muscle strength at baseline. For all statistical analyses, a *P* value of less than 0.05 (2-tailed) or a 95% confidence interval not including the null point was considered statistically significant. All statistical tests were performed using SPSS Statistics Version 19 (IBM, New York, USA).

Results

1098 participants attended baseline data collection clinics and 330 (30%) participants were lost to follow-up five years later. Of 768 participants who attended a follow-up data collection clinic (mean 5.1 ± 0.5 years after baseline) 87 did not complete all anthropometric or muscle function assessments, thus 681 participants were included in the analyses.

Participants lost to follow-up were significantly older than those who completed follow-up (64.9 ± 8.0 vs 61.9 ± 7.0 years; $P < 0.001$) and a greater proportion were female (42 vs 34%; $P = 0.008$). Participants lost to follow-up also had significantly lower values for ALM (23.6 ± 5.3 vs 24.9 ± 5.3 kg; $P < 0.001$) and LLS (83.1 ± 46.6 vs 97.9 ± 49.6 kg; $P < 0.001$), and significantly higher falls risk scores (0.36 ± 0.89 vs 0.08 ± 0.82 ; $P < 0.001$).

Table 1 presents baseline characteristics of included participants. 48% of the cohort was female, and the mean age of participants was 61.4 ± 7.0 years, with no age differences between males and females. Men were significantly taller and heavier than women, but there were no differences in mean BMI. Women had significantly higher mean body fat percentages and men had significantly higher ALM. Men had significantly higher mean scores for HGS and LLS, and significantly lower falls risk scores, compared with women.

At baseline, no participant was diagnosed with sarcopenia according to ALM-H using previously established cut-points for sarcopenia derived from US populations [7,9]. Using the lowest 20% of the sex-specific distribution there was low agreement between anthropometric and performance definitions; there were 254 participants with sarcopenia according to either ALM-H or HGS, but only 39 (5%) participants had sarcopenia according to both definitions.

Figure 1 demonstrates the change in sarcopenia prevalence at follow-up using baseline cut-points (lowest 20% of the sex-specific distribution) for each anthropometric and performance-based definition. The prevalence of sarcopenia in both men and women after five years, defined by ALM-H, was lower than at baseline. Prevalence of sarcopenia

increased for all other definitions, with greater increases observed for performance-based compared with anthropometric definitions, and for women compared with men. Across all definitions, the overall proportion of participants who were sarcopenic at baseline but non-sarcopenic at follow-up ranged from 5 to 9%.

Table 2 describes differences in five-year falls risk scores between participants classified with or without sarcopenia according to each operational definitions. Higher falls risk at follow-up was observed in men and women classified as having sarcopenia according to ALM-W, HGS and LLS. Men with sarcopenia according to ALM-H and ALM-R, and women with sarcopenia according to UMQ and LMQ, had significantly higher falls risk scores at follow-up compared with normal older adults. Anthropometric definitions (ALM-H, ALM-W and ALM-R) predicted a significant greater increase in falls risk over five years in men with sarcopenia compared with normal men, but similar associations were not observed in women; ALM-R predicted a significant greater decrease in falls risk for women with sarcopenia compared with normal women. There were no associations between performance-based definitions and the five-year changes in falls risk in men, but women classified as having sarcopenia according to HGS, LLS, UMQ and LMQ demonstrated significant greater increases in falls risk scores over five years, compared with non-sarcopenic women.

Two-way ANOVAs demonstrated significant sex interactions for associations of ALM-R, LLS and LMQ with follow-up falls risk score and change in falls risk score. Post-hoc regression analyses demonstrated that adjustment for baseline knee extension strength attenuated the associations of ALM-H ($\beta = 0.07$; $P = 0.160$) & ALM-R ($\beta = 0.07$; $P = 0.143$) in men, and of UMQ ($\beta = 0.07$; $P = 0.146$) in women, with change in falls risk score such that they were no longer significant. All other previously described associations remained significant after adjustment for baseline knee extension strength (data not shown).

Discussion

This analysis of a prospective population-based study of community-dwelling middle-aged and older adults demonstrates that sex-specific associations exist between anthropometric and performance-based definitions of sarcopenia and five-year changes in falls risk. The tool used to assess falls risk in this study is a valid predictor of incident falls [19-21] which has previously predicted the risk of multiple incident falls in community-dwelling older adults with 75% accuracy [21]. Our findings indicate that while anthropometric definitions of sarcopenia may be appropriate for assessing risk of future falls in men, performance-based definitions may be preferable for women. Interactions were observed for the ALM-R, LLS and LMQ definitions, demonstrating that associations with five-year falls risk differ significantly according to sex. Furthermore, the significant associations observed were generally not explained by muscle strength, suggesting that operational definitions are predictive of changes in other physiological components that contribute to falls in middle-aged and older adults.

Prospective population-based studies which have previously examined associations of low absolute muscle mass (as opposed to operational definitions of sarcopenia) have suggested that muscle mass is not independently predictive of functional decline in older adults. Several studies have reported that muscle weakness, but not mass, is associated with increased risks of falls [22] and mortality [23,24]. However, a recent twelve-year analysis of the Longitudinal Aging Study Amsterdam, including 477 adults aged 65 years and older, revealed that lower muscle mass is associated with an increased mortality risk in men, but not women [25]. This finding may be reflective of our own results suggesting that men categorised as having sarcopenia according to anthropometric definitions, have greater increases in falls risk over five years than those without sarcopenia.

Newman et al. [9] compared ALM-H and ALM-R definitions of sarcopenia and reported that for older adults in the Health ABC study, both classifications were associated with impaired lower-limb function in men, but only ALM-R was associated with lower-limb function in women. This finding is generally supportive of our own results, but we did not observe ALM-R to be a better predictor of increased falls risk in women; in fact, those classified as having sarcopenia by the ALM-R definition demonstrated significant declines in falls risk over five years. In a previous study of older women residing in low-level aged care, hip strength, but not ALM-H and ALM-W, was correlated with physical function [11]. Similarly, we observed that women with sarcopenia defined by HGS, LLS, UMQ and LMQ had significantly greater increases in falls risk compared with normal women, while no differences were observed for the anthropometric definitions. In addition, it is notable that the increased falls risk associated with sarcopenia according to UMQ and LMQ was of a similar or smaller magnitude to that of sarcopenia according to HGS and LLS. A cross-sectional study of older men has reported similar findings [18], and this suggests that DXA-derived muscle quality measures may not provide additional value beyond that of absolute measures of muscle strength in predicting physical function declines.

The secondary aim of this study was to examine changes in the prevalence of sarcopenia over five years. The wide range of prevalence estimates for sarcopenia at follow-up (15 to 46%) according to all definitions has been noted previously [10]. Prevalence of sarcopenia generally increased from baseline to follow-up, and greater increases were generally observed in women compared to men and for performance-based definitions compared to anthropometric definitions. This finding is probably attributable to the fact that muscle strength declines at a faster rate than muscle mass in older adults [26]. Significantly, the prevalence of sarcopenia according to the ALM-H definition actually decreased over five years. We believe this observation may be explained by age-related height loss. ALM-H is

closely related to the BMI (but substitutes body weight with ALM) and it has previously been demonstrated that age-related height loss causes artifactual increases in BMI of up to 1.4kg/m^2 and 2.6kg/m^2 in men and women by the age of 80 years [27]. It is likely that a similar artifactual increase in ALM-H was observed in the present study due to reductions in height during the follow-up period and this would potentially account for the decrease in the proportion of participants categorised as having sarcopenia. This finding may indicate that changes in sarcopenia prevalence are best determined by anthropometric operational definitions of sarcopenia which adjust for body mass, such as the ALM-W and ALM-R definitions, or by performance-based definitions.

No participant in this Australian cohort of middle-aged and older adults was classified as having sarcopenia at baseline according to previously established ALM-H cut-points recommended by the European Working Group on Sarcopenia in Older People (EWGSOP) [28] and derived from US older adult populations [7,9]. Similarly, only four out of 57 Finnish community-dwelling women with low muscle strength or gait speed had low muscle mass using a previously established US cut-point for ALM-H [29]. Taken together, these findings indicate that cut-points for low muscle mass established from US populations may not be appropriate for diagnosing sarcopenia in international populations.

It is unclear why sarcopenia associations with five-year functional decline vary according to sex. Low muscle mass in women may be less strongly associated with poor muscle function than in men; women classified as having sarcopenia had higher LMQ values compared with normal women according to ALM-H at baseline in post-hoc analyses (5.2 ± 2.1 vs 4.3 ± 1.8 kg/kg, respectively; $P = 0.004$). Although investigation of possible contributors to the observed sex-specific relationships was not an aim of this study, it is also likely that disparities in prevalence of chronic disorders, sex hormone concentrations and

lifestyle behaviours (such as physical activity and nutrient intakes), play a role in the sex-specific associations between operational definitions of sarcopenia and falls risk.

The findings from this study are subject to limitations including a low response rate (57%) and substantial loss to follow-up (38%). Although a post-hoc analysis revealed that the cut-points obtained for sarcopenia did not vary substantially when all participants at baseline were included (data not shown), these findings may apply only to relatively healthy middle-aged and older Australian adults, and may not be appropriate for diagnosis of sarcopenia in clinical settings elsewhere.

The EWGSOP recommend assessment of muscle mass *and* function, including gait speed, HGS and ALM, in the clinical diagnosis of sarcopenia [28], although this notably overlaps with operational definitions for frailty [30]. Gait speed was not assessed in this study, but we observed poor agreement between low muscle mass (ALM-H) and strength (HGS) in this cohort, reflecting substantial discordance between age-related muscle mass and strength declines [5], and supporting previous research indicating that low numbers of community-dwelling adults may be classified as sarcopenic using the EWGSOP definition [29,31]. Nevertheless, the results of this study support the combined assessment of skeletal muscle mass, strength and performance in the clinical diagnosis of sarcopenia, given that associations with five-year falls risk may differ between men and women.

In conclusion, sarcopenia prevalence generally increases at a higher rate when assessed using performance-based definitions. Sarcopenia is associated with increases in falls risk over five years in community-dwelling middle-aged and older adults, but sex-specific differences may exist according to different anthropometric or performance-based definitions. These findings may indicate that current operational definitions of sarcopenia should be sex-based, with differential weightings for muscle mass and performance in middle-aged and older men and women.

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Author Roles

Study design: GJ. Study conduct: GJ, DD and DS. Data collection: DS and DD. Data analysis: DS and KS. Data interpretation: DS, AH and KS. Drafting manuscript: DS. Revising manuscript content: DS, KS, DD, PE and AH. Approving final version of manuscript: DS, AH, KS, DD, PE and GJ. DS takes responsibility for the integrity of the data analysis.

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Figure Legends

Figure 1. Five-year gender-specific change in prevalence of sarcopenia according to different anthropometric and performance-based definitions.

Table 1. Characteristics of TASOAC participants (N = 681) at baseline.

	Male (N = 352)	Female (N = 329)	P-value
Age (y)	61.7 ± 7.1	61.0 ± 6.8	0.141
Height (cm)	173.9 ± 6.1	161.3 ± 6.2	<0.001
Weight (kg)	83.6 ± 12.6	71.0 ± 12.6	<0.001
BMI (kg/m ²)	27.6 ± 3.8	27.3 ± 4.6	0.294
Total body fat (%)	27.5 ± 4.9	39.2 ± 5.0	<0.001
ALM (kg)	29.0 ± 3.2	20.4 ± 2.9	<0.001
HGS (psi)	14.4 ± 2.6	10.3 ± 1.8	<0.001
LLS (kg)	131.4 ± 42.2	61.5 ± 25.9	<0.001
Falls risk score	-0.04 ± 0.81	0.19 ± 0.88	<0.001

± standard deviation.

Abbreviations: BMI; body mass index, ALM; appendicular lean mass, HGS; hand grip strength, LLS; lower-limb strength

Table 2. Standardised regression coefficients expressing the differences in five-year falls risk scores for sarcopenic compared to non-sarcopenic older adults according to anthropometric and performance-based definitions of sarcopenia.

	Anthropometric definitions			Performance-based definitions			
	ALM-H	ALM-W	ALM-R	HGS	LLS	UMQ	LMQ
Falls risk score (follow-up)	Standardised β -coefficient (<i>P</i> -value)						
Male	0.16 (0.003)	0.13 (0.012)	0.15 (0.005)	0.17 (0.001)	0.11 (0.032)	0.10 (0.066)	0.10 (0.062)
Female	0.02 (0.718)	0.13 (0.021)	-0.09 (0.115)	0.24 (< 0.001)	0.26 (< 0.001)	0.20 (< 0.001)	0.27 (< 0.001)
<i>P</i> -value for interaction	0.082	0.963	0.002	0.186	0.032	0.145	0.014
Falls risk score (change)*							
Male	0.10 (0.032)	0.09 (0.037)	0.09 (0.048)	0.06 (0.181)	0.05 (0.308)	0.05 (0.277)	0.07 (0.126)
Female	0.03 (0.592)	0.08 (0.098)	-0.13 (0.007)	0.15 (0.001)	0.21 (< 0.001)	0.10 (0.031)	0.21 (< 0.001)
<i>P</i> -value for interaction	0.300	0.883	0.001	0.098	0.006	0.374	0.013

Participants in the lowest 20% of the distribution were defined as sarcopenic for each definition.

*Adjusted for baseline falls risk score

Abbreviations: ALM; appendicular lean mass, ALM-H; ALM/height², ALM-W; ALM/weight x 100, ALM-R; residuals of linear regression of ALM with height and fat mass, HGS; hand grip strength, LLS; lower-limb strength, UMQ; upper-limb muscle quality, LMQ; lower-limb muscle quality