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Research Article

Sarcopenia definitions and their association with fracture risk in older Swedish women

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Abstract

The purpose of this study was to investigate the prevalence of three sarcopenia definitions and their associations with fracture risk in older Swedish women when adjusted for fracture risk assessment (FRAX)-based risk factors; 2,883 women with a mean age of 77.8 years were included. Sarcopenia was defined based on the Sarcopenia Definitions and Outcomes Consortium (SDOC; low handgrip strength [kg] and gait speed (m/s)), revised European Working Group on Sarcopenia in Older People (EWGSOP2; low appendicular lean mass index, appendicular lean mass [ALM]/height; kg/m^2], and hand grip strength [kg]), and Asian Working Group for Sarcopenia (AWGS; low ALM (kg), and hand grip strength [kg]) definitions. Femoral neck *T*-score was obtained from dual-energy X-ray absorptiometry. All fractures, confirmed by X-ray or medical record review, were subsequently categorized as major osteoporotic fractures (MOFs) and hip fractures. Deaths were verified through regional registers. The total follow-up time was 6.4 ± 1.3 (mean ± SD) yr. Cox regression (hazard ratios [HR] and 95% CIs) analyses were performed with adjustment for age, FRAX variables, and femoral neck *T*-score. Sarcopenia prevalence was 4.5% ($n = 129$) according to SDOC, 12.5% ($n = 360$) for EWGSOP2, and 10.3% ($n = 296$) defined by AWGS. Individuals with sarcopenia defined by SDOC had a higher mortality risk than individuals without sarcopenia (HR: 3.41; 95% CI: 2.51, 4.62) after adjusting for age and FRAX variables. Sarcopenia according to EWGSOP2 and AWGS was not associated with an increased fracture risk after adjusting for age and FRAX variables. Individuals with sarcopenia defined by SDOC had a higher risk for any fractures (HR: 1.48; 95% CI: 1.10, 1.99) and MOF (HR: 1.42; 95% CI: 1.03, 1.98) compared with individuals without sarcopenia after adjusting for clinical risk factors used in FRAX. In conclusion, sarcopenia defined by SDOC, incorporating muscle function/strength, was the only sarcopenia definition associated with fracture risk in older women.

Keywords: sarcopenia, fracture, older adults

Lay Summary

This study aimed to investigate the risk of sarcopenia on fracture risk in older Swedish women. Data were utilized from 2,883 women aged 75–80 yr in the Swedish Sahlgrenska University Hospital Prospective Evaluation of Risk of Bone Fractures cohort. Sarcopenia was defined using three different definitions, including the Sarcopenia Definitions and Outcomes Consortium (SDOC), which includes grip strength and gait speed, while the revised European Working Group on Sarcopenia in Older People (EWGSOP2) and the Asian Working Group for Sarcopenia (AWGS) definitions include appendicular lean mass measured by dual-energy X-ray absorptiometry and grip strength. The results demonstrated that SDOC-defined sarcopenia was associated with a higher mortality risk, with increased risk of any fractures, and major osteoporotic fractures, whereas the EWGSOP2 and AWGS definitions were not associated with fracture risk. In summary, the study demonstrates that sarcopenia defined by SDOC, considering muscle function and strength, rather than lean mass, was the only investigated sarcopenia definition associated with fracture risk.

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Introduction

Osteoporosis is a common condition among older adults and is characterized by low areal bone mineral density (aBMD) and deterioration of bone microarchitecture, leading to increased risk of fractures.[1-3] Fractures in the aging population markedly increase the risk of hospitalization, morbidity, and mortality, posing a significant financial burden to society in addition to the negative impact on population health.[4,5]

Sarcopenia is a condition defined as an age-associated loss of skeletal muscle mass and function.[6-8] Sarcopenia is associated with several adverse health outcomes, including functional decline, immobility, falls and fractures, hospitalization, and mortality.[9-14] Clinical recognition of sarcopenia among older adults is limited due to the lack of a single universally accepted operational definition, making it difficult for clinicians to diagnose and treat this condition[10,11,15] The prevalence of sarcopenia varies widely as it is dependent upon several factors, including age, sex, ethnicity, definition, and diagnostic criteria applied.[13,16-18] In a recent study of Swedish older adults, the prevalence of sarcopenia defined by the European Working Group on Sarcopenia in Older People (EWGSOP) and revised EWGSOP (EWGSOP2) definitions ranged between 1.4% and 7.8% in those aged 70 yr and 42%–62% in those aged 85 yr.[8,16,19] Recent studies have demonstrated concerns over the predictive capacity of dual-energy X-ray absorptiometry (DXA)–determined appendicular lean mass (ALM) on several health outcomes such as falls and fractures.[20,21] Although, several definitions with various cut-points of muscle mass and/or muscle function have been previously proposed, no studies have investigated the associations between several sarcopenia definitions and fracture risk in a population of older women.[8,9,19,22]

With an increase in the age of the population and the prevalence of sarcopenia and osteoporosis, the incidence and rate of fractures are markedly increasing.[23] In particular, the incidence of hip fractures in Swedish women is the highest among the world, but whether the presence of sarcopenia exacerbates the risk of fractures has been insufficiently investigated.[24] Previous studies have yielded inconsistent results, with some, but not others, have found associations between sarcopenia according to the Asian Working Group for Sarcopenia (AWGS), EWGSOP, and fracture.[25] Furthermore, there is a notable scarcity of studies examining the relationships between fractures at various sites and multiple definitions of sarcopenia within a single cohort.[26] Recent evidence suggests that the clinical characteristics and poor health outcomes among individuals with sarcopenia make it a critical indicator of higher fracture risk.[9,27,28] It is therefore necessary to determine if the assessments of sarcopenia components should be included as part of the fracture prevention tools for an early diagnosis, treatment, and to reduce the risk of subsequent consequences associated from this condition such as hospitalization and mortality.

This study aimed to investigate the prevalence of sarcopenia and to determine the associations of various sarcopenia definitions with fracture risk in a population of Swedish older women, including adjustment for fracture risk assessment (FRAX)-based risk variables.

Materials and methods

Study design and participants

Data from the Sahlgrenska University Hospital Prospective Evaluation of Risk of Bone Fractures (SUPERB) study, a prospective population-based study of 3,028 older women residing in the greater Gothenburg area, Sweden, were utilized for this analysis. Participants aged between 75 and 80 yr were recruited from the Swedish national population register. Participants were excluded from this study if they were unable to walk with or without supportive walking aids, understand Swedish, and have at least one hip that could be evaluated for aBMD determined by the DXA. The total follow-up time was 6.4 ± 1.3 (mean $\pm$ SD) yr. This study was approved by the regional Ethics Review Board in Gothenburg, and all study participants provided written informed consent.

Questionnaires

Participants completed self-administered questionnaires, including questions on physical activity.

Ten-year probabilities of major osteoporotic and hip fractures were calculated by the FRAX tool (https:frax.shef.ac.uk/FRAX/) using self-reported information on clinical risk factors (CRFs) based on medical history, prior fractures (after the age of 50 yr, excluding face and skull fractures), current smoking, parental history of hip fracture, oral glucocorticoids in doses of at least 5 mg per day of prednisolone or equivalent for $\geq$3 months, diabetes, rheumatoid arthritis, and high alcohol consumption (three standard measures of alcohol per day or more). The FRAX scores were calculated with and without aBMD of the femoral neck along with all CRF's except for secondary osteoporosis, which does not contribute to the calculations of fracture risk when aBMD is included.[4]

Incident fractures

Incident fractures were verified by radiographs, with radiology reports retrieved from the regional digital X-ray archive. Research nurses reviewed all radiology reports examined from the baseline visit (March 2013–May 2016). Radiographs without any record of radiology reports, or with uncertainty in the diagnosis of fractures, underwent a formal review by an orthopedic surgeon. The follow-up time consisted of time from the baseline exam to the first fracture (per category) and was censored for the end of the study (July 31, 2021) and death. Fractures were categorized into hip fractures and major osteoporotic fractures (MOFs) for any fractures which occurred at the vertebrae, hip, proximal humerus, or the proximal femur.[29] Fractures of the skull, fingers, and toes were excluded from any fractures.

Anthropometry

Weight (kg) was measured to the nearest 0.1 kg with heavy items of clothing removed using an electronic scale and body height (m) was measured with a standardized wall-mounted calibrated stadiometer with footwear removed to the nearest 0.01m for two consecutive times. If the two height measurements differed by ≥ 5 mm, a third measurement was performed. An average of the two height measurements, or the two most similar measurements if three were taken, was used. The BMI was calculated as weight/height (kg/m^2).

Physical function

Hand grip strength was measured using a hydraulic dynamometer (Saehan dynamometer, model SH5001, Saehan Corporation, Masan, Korea), as previously described.[30] In summary, participants gripped the dynamometer with maximal force in a seated position. Participants repeated this measurement twice in both arms with a 30-s rest between trials, and the mean force of the dominant hand from the two trials was

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used to calculate average hand grip strength. Gait speed was performed twice and was measured over a 10-m distance. To prevent the effects of acceleration and deceleration, only the middle 6-m distance was utilized to calculate the average gait speed (m/s). Participants also completed a chair stand test where they were instructed to stand up straight from a seated position and sit down as many times as possible within 30-s with their arms across their chest. A slow chair stands time (>15 s for 5 rises) was calculated using the number of stands per second over 30-s and then by selecting those who needed >15 s to do 5 chair stands.

Dual-energy X-ray absorptiometry

Whole-body DXA scans measured body composition parameters, including body fat percentage and lean mass, using Hologic Discovery A (S/N 86491, Waltham, MA, United States) for $n = 2995$ participants, and owing to machine failure, $n = 33$ scans were performed using another Hologic Discovery A device. The ALM was calculated as the sum of lean mass in the upper and lower limbs. The DXA scans were also used to measure aBMD at the non-dominant total hip, femoral neck, lumbar spine, and whole body. The coefficient of variation for aBMD was 0.7% at the femoral neck and 1.3% at the lumbar spine at our center.

Sarcopenia definitions

Three of the most commonly and recently developed sarcopenia definitions were utilized to compare differences in the prevalence of sarcopenia in this group of older women and to determine the associations with fracture risk. Sarcopenia was defined using the Sarcopenia Definitions and Outcomes Consortium (SDOC),[22] revised European Working Group on Sarcopenia in Older People (EWGSOP2)[8] definitions, and the revised AWGS definition.[31] The SDOC definition utilizes low hand grip strength (<20 kg) and low gait speed (<0.8 m/s).[22] The EWGSOP2 definition utilizes low appendicular lean mass index (ALMI) (<5.5 kg/m^2 for women) and low hand grip strength (<16 kg for women) or slow chair stands time (>15 s for 5 rises).[8] The AWGS definition utilizes low ALMI (<5.4 kg/m^2) and low hand grip strength (<18 kg) or low gait speed (0.8 m/s).[31] Information for ≥1 variables used in these sarcopenia definitions was unavailable for 145 women, resulting in $n = 2{,}883$ women in the present study.

Statistical analysis

All data analyses were performed using SPSS Statistics 25 (IBM, NY, United States). Participant characteristics were reported as mean and SDs for continuous variables, or as percentages for categorical variables. Independent samples *t*-tests or X^2 tests were performed to compare the means between individuals with and without sarcopenia. Cox regression analysis was performed to investigate the associations between three frequently used sarcopenia definitions (SDOC, EWGSOP2, and AWGS), mortality risk, and fracture risk (any fractures, MOFs, and hip fractures).[8,19,22,31] The Cox assumption of proportional hazards was tested using graphical methods, and the observed relative hazards remained constant over time.

Statistical imputation was performed for the missing CRFs variables (198 [6.7%] women had missing data on 1 CRF) using the MICE-package in R-Studio (Multivariate imputation by Chained Equations) by using a single imputation with 10 iterations. In addition to the fracture outcomes, all the other CRFs were included in the imputation. Similar frequencies of CRFs were observed before and after imputation (Supplemental Table S1 and Table 1).

Incidence per 1000 person-yr was calculated as the number of events divided by the total follow-up time (until fracture, death, or censored) per 1000 yr. Adjustment for CRFs included age, BMI, other FRAX variables, and femoral neck *T*-score. In addition, to assess the implications of death as a competing risk, the Fine and Gray sub-distributed hazard for fracture was compared between individuals with/without sarcopenia using the stcrreg command in Stata 17.0.[32]

For all analyses, $P < .05$ or 95% CIs not including the null point was considered to be statistically significant.

Results

In total, 2883 older women with the mean age of 77.8 yr were included in this study. Prevalence of sarcopenia varied based on the sarcopenia definitions with the highest among older women when sarcopenia was defined by the EWGSOP2 definition (12.5%), followed by AWGS (10.3%), with the lowest prevalence by the SDOC definition (4.5%) (Table 1). A higher proportion of individuals based on the SDOC definition had a low hand grip strength compared to when defined by EWGSOP2 and AWGS definitions (Supplemental Table S2).

Women with sarcopenia defined by SDOC definition had the highest proportion of incident fractures, including any fractures, MOFs, and hip fractures (37.2%, 30.2%, and 9.3%, respectively; Table 2). In addition, sarcopenia defined by SDOC definition was the only definition that was associated with all the fracture outcomes, although the association with hip fracture only reached significance in the unadjusted model (Table 2). For those with SDOC-defined sarcopenia, the risk of any fractures was increased by 48% and the risk of MOFs was increased by 42% in fully adjusted models. By contrast, sarcopenia defined by the AGWS definition was not associated with any fractures, MOF, or mortality (all $P > .05$; Table 2), while an increased risk for hip fracture was observed, but only in an unadjusted model. Sarcopenia defined by the EWGSOP2 definition was also not associated with the risk of fracture (Table 2). Intriguingly, it was associated with a 24% lower risk of MOFs compared to individuals without sarcopenia after adjusting for CRFs and aBMD (Table 2).

The distribution of CRF prevalence did not differ between those with and without sarcopenia, with the exception for women with SDOC in whom rheumatoid arthritis and smoking were more common (Table 1). Frequencies of CRFs according to sarcopenia definition was similar in complete cases (without imputations; Supplemental Table S1).

During follow-up, the mortality risk among individuals with sarcopenia defined by the SDOC definition was the highest (38.0%), followed by the EWGSOP2 definition (16.1%) with the lowest by the AWGS definition (15.5%). After adjusting for CRFs and femoral neck *T*-score, individuals with sarcopenia defined by SDOC had 3.4 times greater mortality risk compared to individuals without sarcopenia (Table 2).

An analysis considering the competing risk of mortality according to Fine and Gray demonstrated that, when sarcopenia was defined by the SDOC definition, it was associated

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Table 1. Descriptive characteristics based on sarcopenia definitions.

	SDOC		*P*-value	EWGSOP2		*P*-value	AWGS		*P*-value	Total ($n = 2,883$)
	No ($n = 2,754$)	Yes ($n = 129$)		No ($n = 2,523$)	Yes ($n = 360$)		No ($n = 2,587$)	Yes ($n = 296$)		
Age (yr)	77.78 ± 1.6	78.5 ± 1.5	**.023**	77.8 ± 1.7	77.9 ± 1.7	.303	77.8 ± 1.6	77.9 ± 1.6	.908	77.8 ± 1.6
BMI (kg/m^2)	26.08 ± 4.3	29.2 ± 5.5	**.000**	26.78 ± 4.3	22.3 ± 2.5	**.000**	26.74 ± 4.3	21.7 ± 2.3	**.000**	26.2 ± 4.4
Femoral neck *T*-score	-1.63 ± 0.88	-1.74 ± 1.08	**.003**	-1.59 ± 0.88	-1.99 ± 0.83	**.000**	-1.60 ± 0.89	-1.95 ± 0.81	**.000**	-1.64 ± 0.89
FRAX MOF										
With aBMD	22.9 ± 11.7	25.9 ± 13.1	**.014**	22.6 ± 11.5	26.1 ± 13.6	**.000**	22.8 ± 11.6	25.7 ± 13.3	**.001**	23.1 ± 11.8
Without BMD	33.6 ± 13.2	33.6 ± 13.2	.956	32.9 ± 12.9	38.5 ± 14.2	**.016**	32.9 ± 12.9	39.6 ± 14.2	**.016**	33.6 ± 13.2
FRAX Hip										
With aBMD	11.0 ± 11.0	13.0 ± 12.0	.066	10.6 ± 10.6	14.2 ± 13.2	**.000**	10.7 ± 10.7	14.1 ± 13.2	**.000**	11.1 ± 11.1
Without aBMD	20.5 ± 13.7	19.8 ± 13.3	.578	19.6 ± 13.14	26.3 ± 15.5	**.000**	19.6 ± 13.1	27.8 ± 15.6	**.000**	20.5 ± 13.6
Parental hip fracture (%)	486 (17.6%)	24 (18.6%)	.781	447 (17.7%)	63 (17.5%)	.920	453 (17.5%)	57 (19.3%)	.456	510 (17.7%)
Oral glucocorticoid use[a] (%)	89 (3.2%)	4 (3.1%)	.614	79 (3.1%)	14 (3.9%)	.447	82 (3.2%)	11 (3.7%)	.614	93 (3.2%)
Rheumatoid arthritis (%)	86 (3.1%)	9 (7.0%)	**.017**	78 (3.1%)	17 (4.7%)	.105	82 (3.2%)	13 (4.4%)	.264	95 (3.3%)
Secondary osteoporosis[b] (%)	703 (25.5%)	37 (28.7%)	.240	646 (25.6%)	94 (26.1%)	.837	665 (25.7%)	75 (25.3%)	.891	740 (25.7%)
Alcohol use (%)	15 (0.5%)	0 (0.0%)	.494	14 (0.6%)	1 (0.3%)	.494	14 (0.5%)	1 (0.3%)	.645	15 (0.5%)
Current smoking (%)	138 (5.0%)	9 (6.8%)	**.001**	116 (4.6%)	31 (8.6%)	**.001**	117 (4.5%)	30 (10.1%)	**.000**	147 (5.1%)
Previous self-reported fracture[c] (%)	1011 (36.7%)	62 (48.1%)	.260	933 (37.0%)	140 (38.9%)	.260	956 (37.0%)	117 (39.5%)	.386	1073 (37.2%)
Gait speed (m/s)	1.29 ± 0.21	0.66 ± 0.12	**.000**	1.27 ± 0.25	1.24 ± 0.25	.789	1.26 ± 0.25	1.28 ± 0.24	.592	1.26 ± 0.25
Grip strength (kg)	15.0 ± 5.4	9.9 ± 4.7	**.001**	15.3 ± 5.5	11.2 ± 4.1	**.000**	15.2 ± 5.52	11.3 ± 3.8	**.000**	14.8 ± 5.5
Chairs stand test (s)	11.0 ± 4.0	3.4 ± 4.1	**.001**	10.8 ± 4.3	9.8 ± 4.1	.789	10.7 ± 4.3	10.4 ± 4.1	.420	10.6 ± 4.3
Appendicular lean mass (kg/m^2)	6.26 ± 0.82	6.62 ± 1.12	**.000**	6.43 ± 0.78	5.18 ± 0.27	**.000**	6.4 ± 0.78	5.1 ± 0.2	**.000**	6.27 ± 0.84

Data presented as mean ± SD for continuous variables or *n* (%) for categorical variables. Bold indicates significance at $P < .05$. Abbreviations: EWGSOP2, revised European Working Group on Sarcopenia in Older People definition; SDOC, Sarcopenia Definitions and Outcomes Consortium; AWGS, Asian Working Group for Sarcopenia; FRAX, fracture risk assessment; MOF, major osteoporotic fracture; aBMD, areal bone mineral density. [a]Daily oral treatment with glucocorticoids with at least 5 mg for three months or more. [b]Secondary osteoporosis—diabetes (type 1 and type 2), menopause before 45 yr of age, inflammatory bowel disease, and chronic kidney disease. [c]After 50 yr of age, fractures of the skull and face are excluded.

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Table 2. Associations between sarcopenia definitions, mortality risk and fracture risk.

	SDOC		EWGSOP2		AWGS	
	No (*n* = 2,754)	Yes (*n* = 129)	No (*n* = 2,523)	Yes (*n* = 360)	No (*n* = 2,587)	Yes (*n* = 296)
Mortality						
n (%)	313 (11.4%)	49 (38.0%)	304 (12.0%)	58 (16.1%)	316 (12.2%)	46 (15.5%)
Rate per 1,000 person-yr	17.7	63.4	18.9	24.7	19.1	23.8
HR (95% CI):						
Model 1	REF	**3.46 (2.56, 4.68)**	REF	1.25 (0.95, 1.66)	REF	1.20 (0.88, 1.63)
Model 2	REF	**3.41 (2.51, 4.62)**	REF	1.22 (0.92, 1.62)	REF	1.16 (0.85, 1.58)
Any fractures						
n (%)	733 (26.6%)	48 (37.2%)	681 (27.0%)	100 (27.8%)	699 (27.0%)	82 (27.7%)
Rate per 1,000 person-yr	47.6	79.5	48.8	49.2	48.8	49.3
HR (95% CI):						
Model 1	REF	**1.63 (1.21, 2.18)**	REF	1.01 (0.81, 1.24)	REF	1.01 (0.80, 1.27)
Model 2	REF	**1.51 (1.13, 2.03)**	REF	0.97 (0.78, 1.19)	REF	0.97 (0.77, 1.22)
Model 3	REF	**1.48 (1.10, 1.99)**	REF	0.82 (0.66, 1.02)	REF	0.85 (0.67, 1.07)
MOFs						
n (%)	604 (21.9%)	39 (30.2%)	564 (22.4%)	79 (21.9%)	575 (22.2%)	68 (23.0%)
Rate per 1,000 person-yr	38.1	62.3	39.2	37.5	38.9	39.7
HR (95% CI):						
Model 1	REF	**1.57 (1.14, 2.18)**	REF	0.94 (0.75, 1.20)	REF	1.01 (0.79, 1.30)
Model 2	REF	**1.46 (1.05, 2.03)**	REF	0.91 (0.72, 1.15)	REF	0.98 (0.76, 1.26)
Model 3	REF	**1.42 (1.03, 1.98)**	REF	**0.76 (0.60, 0.97)**	REF	0.84 (0.65, 1.09)
Hip fractures						
n (%)	144 (5.2%)	12 (9.3%)	128 (5.1%)	28 (7.8%)	131 (5.1%)	25 (8.4%)
Rate per 1,000 person-yr	8.7	14.8	8.1	12.3	8.1	13.4
HR (95% CI):						
Model 1	REF	**1.91 (1.05, 3.44)**	REF	1.48 (0.98, 2.22)	REF	**1.62 (1.05, 2.48)**
Model 2	REF	1.76 (0.98, 3.19)	REF	1.39 (0.92, 2.10)	REF	1.50 (0.97, 2.31)
Model 3	REF	1.51 (0.83, 2.76)	REF	1.03 (0.68, 1.57)	REF	1.16 (0.75, 1.80)

Data presented as hazard ratios (HRs) and 95% CIs. **Bold** indicates significance at $P < .05$. Abbreviations: EWGSOP2, revised European Working Group on Sarcopenia in Older People definition; SDOC, Sarcopenia Definitions and Outcomes Consortium; AWGS, Asian Working Group for Sarcopenia; FRAX, fracture risk assessment; MOF, major osteoporotic fracture. Model 1: Adjusted for age. Model 2: Adjusted for age and FRAX variables. Model 3: Adjusted for age, FRAX variables and femoral neck *T*-score.

with any fractures and MOF in the models adjusted for CRFs and femoral neck *T*-score ($P < .05$), although the association with hip fracture was only significant in models adjusted for age and CRFs (Table 3). EWGSOP2 and AWGS sarcopenia definitions were not associated with fracture risk in Fine and Gray models, adjusted for age and CRFs (Table 3).

Discussion

In this population of older adults, sarcopenia defined by SDOC was the only definition associated with fractures and mortality risk, but at low population prevalence. In addition, both the EWGSOP2 and AWGS sarcopenia definitions failed to be associated with fractures and mortality in this population of older women. These results indicate that fracture prediction methods in older women may be improved by assessing the physical performance and/or muscle strength, but that such assessment will only affect a small proportion of those investigated.

Prevalence of sarcopenia varied largely according to individual definitions, again highlighting the difficulties with the operationalization of sarcopenia definitions in clinical practice and impeding the diagnosis and treatment of this condition among older adults. Sarcopenia definitions have differential associations with adverse health outcomes, including fractures.[33-35] In the current study, sarcopenia defined by SDOC was consistently associated any fractures and MOFs. Likewise, in a study of 10,411 men aged ≥65 yr, the SDOC definition was associated with fracture outcomes.[9] Similarly, a study, including 1,3 421 community-dwelling men and 4,282 women aged ≥65 yr, demonstrated that both components of SDOC definitions, including low hand grip strength and gait speed, were associated with a higher risk of adverse health outcomes, including hip fractures.[36] By contrast, in the current study, SDOC definition was not significantly associated with the hip fractures in models adjusted for CRFs and femoral neck *T*-score, but the lack of significant association was likely due to low statistical power for that specific analysis. In addition, in the current study, the SDOC definition was significantly associated with an increased risk of any fractures and MOFs. Sarcopenia is therefore an important risk factor for fractures in this population of older women even when

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Table 3. Associations between sarcopenia definitions and fracture risk considering the competing risk of death.

	SDOC		EWGSOP2		AWGS	
	No (n = 2,754)	Yes (n = 129)	No (n = 2,523)	Yes (n = 360)	No (n = 2,587)	Yes (n = 296)
Any fractures						
SHR (95% CI):						
Model 1	REF	**1.63 (1.21, 2.18)**	REF	1.00 (0.81, 1.24)	REF	1.01 (0.80, 1.27)
Model 2	REF	**1.54 (1.14, 2.08)**	REF	0.95 (0.76, 1.19)	REF	0.95 (0.74, 1.22)
Model 3	REF	**1.40 (1.04, 1.89)**	REF	0.88 (0.70, 1.10)	REF	0.91 (0.72, 1.17)
MOFs						
SHR (95% CI):						
Model 1	REF	**1.57 (1.14, 2.18)**	REF	0.94 (0.75, 1.19)	REF	1.01 (0.79, 1.30)
Model 2	REF	**1.48 (1.06, 2.06)**	REF	0.90 (0.70, 1.15)	REF	0.97 (0.74, 1.27)
Model 3	REF	**1.32 (0.95, 1.84)**	REF	0.83 (0.64, 1.06)	REF	0.93 (0.71, 1.22)
Hip fractures						
SHR (95% CI):						
Model 1	REF	**1.91 (1.06, 3.44)**	REF	1.48 (0.98, 2.22)	REF	**1.62 (1.05, 2.48)**
Model 2	REF	**2.06 (1.13, 3.76)**	REF	1.16 (0.74, 1.80)	REF	1.23 (0.77, 1.97)
Model 3	REF	1.56 (0.85, 2.86)	REF	1.02 (0.65, 1.59)	REF	1.16 (0.73, 1.86)

Data presented as Fine and Gray sub-distribution hazard ratios (SHRs) and 95% CIs. **Bold** indicates significance at $P < .05$. Abbreviations: EWGSOP2, revised European Working Group on Sarcopenia in Older People definition; SDOC, Sarcopenia Definitions and Outcomes Consortium; AWGS, Asian Working Group for Sarcopenia; FRAX, fracture risk assessment; MOF, major osteoporotic fracture. Model 1: Adjusted for age. Model 2: Adjusted for age and FRAX variables. Model 3: Adjusted for age, FRAX variables and femoral neck T-score.

considering the risk of death. As a result, the cost-effective and feasible nature of assessing muscle strength and/or physical function along with its association with fractures indicates the importance of incorporating these measures into sarcopenia definitions and part of the fracture prediction tools.[37,38] The low prevalence of SDOC-defined sarcopenia in the SUPERB cohort is in agreement with low prevalence numbers seen in other similar cohorts of older adults.[14]

Importantly, the SDOC definition in the current study population identified individuals with severe functional limitations, as reflected by significantly lower gait speeds compared to sarcopenic groups defined by the EWGSOP2 and AWGS definitions. This therefore suggests that sarcopenia defined by the SDOC definition may capture individuals with a poor physical function attributable to factors beyond age-related muscle wasting, potentially implicating muscle quality, including muscle fat infiltration, which may potentially explain the increased risk of fractures in the current study.[39]

Sarcopenia definitions, including DXA-determined ALM, are not associated with fractures in older adults.[9,40] In the current study, both EWGSOP2 and AWGS sarcopenia definitions were not associated with increased fracture risk. A recent study, including 10,411 men aged ≥65 yr, demonstrated that the EWGSOP2 severe sarcopenia definition, including poor muscle strength, muscle mass, and physical performance, was associated with a higher risk of MOFs after adjusting for CRFs, including age, follow-up time, and falls or FRAX MOF probability with aBMD or femoral neck T-score.[9] This contrasts with the current study findings in which the EWGSOP2 sarcopenia definition had a 24% lower risk of MOFs, but it was not associated with hip or any fractures after adjusting for CRFs and femoral neck T-score. It is possible that DXA-determined ALM diminishes the associations between sarcopenia definitions and fractures, although the findings for MOFs in the current study are unclear.[9,41] However, these associations were likely affected by competing risk of death, supported by the lack of association between sarcopenia defined by EWGSOP2 and fracture outcomes in the Fine and Gray analysis. In addition, it is possible that measures of muscle strength/function are closely associated with biomechanical factors that contribute to falls and fractures such as balance, coordination, and flexibility.[42,43] The DXA-determined muscle mass may be less directly associated with these factors and may be a better proxy measure of overall muscle mass and body composition. Measures of physical performance and/or muscle strength may therefore be more robust predictors of fractures compared with sarcopenia definitions, which also include DXA-determined ALM as measures of muscle mass in this population of older women.[21]

Sarcopenia is associated with a higher risk for mortality, but it varies depending on the definition of sarcopenia used.[44-46] However, in a recent systematic review and meta-analysis, including 42,108 individuals aged ≥18 yr, irrespective of the definition of sarcopenia used, it was associated with a higher mortality risk.[33] Contrary to the findings of the abovementioned study, sarcopenia defined by SDOC was the only definition associated with a higher mortality risk in this population of Swedish older women. Muscle strength and/muscle performance therefore appear to be an important marker of mortality risk.[47] In addition, it was evident that the association was considerably stronger for mortality than for fracture risk when all CRFs were considered in this population of older women even when sarcopenia was defined by the SDOC definition. Similarly, in a study, including 13 ,421 community-dwelling men and 4,828 community-dwelling women, both low handgrip strength and gait speed based on the SDOC definition were associated with a higher likelihood of mortality.[36] This finding may be reflective of the current study results, suggesting that sarcopenia definitions, including handgrip strength and gait speed, but not necessarily DXA-determined lean mass, are important determinants of mortality risk among older adults..[36] Although, ALM is not associated with mortality or fracture risk, it may be associated with other adverse health outcomes such as falls.[41] In addition, assessing muscle mass using other modalities, such as through creatine dilution, peripheral QCT, or high-resolution QCT, may be more robustly associated with mortality and fracture risk among older adults.[41,48] Further studies are

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therefore warranted to assess the value of such indices and to understand the importance of muscle mass as a sarcopenia component and its effects on negative health implications in this population of older women.

This study is subject to limitations, including the relatively low number of hip fractures in this population of older women. In addition, all study participants resided in the greater Gothenburg area in Sweden and this study exclusively included women. As such, the results may not be generalized to men and other populations, including individuals with different ethnic backgrounds or age groups. Although the 10-m course used in this study is 1 of the most widely used assessments for gait speed, the use of this course instead of the 4-m course to assess gait speed (as recommended for SDOC) may have influenced the prevalence of sarcopenia in this study.[49] Although an adjustment for the statistical analysis for BMI, CRFs, and aBMD, other potentially important comorbidities were not accounted for, which may have affected the results. It is essential to note that the absence of adjustment for these unaccounted comorbidities could introduce biases that may influence both the magnitude and direction of the observed associations. Therefore, it is crucial to interpret the results with caution, acknowledging the potential for residual confounding effects, particularly related to unaccounted comorbidities, and recognizing the need for further research to refine and validate these findings. The current study utilized 30-s chair stand test rather than the standard 5 times chair stand test which are part of the EWGSOP2 and AWGS definitions, which may have influenced the prevalence of sarcopenia in this cohort. Due to the low statistical power, we could not compare the overlap between different sarcopenia definitions in this cohort. Hence, we used the analysis from the available larger cohorts, for example, the Rotterdam study,[50] with data on sarcopenia and fractures, to compare the fracture risk between different definitions to better understand the underlying mechanisms could be warranted. Furthermore, the low prevalence of SDOC found in this cohort suggests that incorporating the definition in existing fracture prediction tools will not have a substantial impact on fracture risk in most older women, since a very small proportion is expected to have their fracture risk reclassified if SDOCs were to be added. Moreover, applying cut-points developed in Asian populations (AWGS) to the current study cohort may introduce uncertainties and it is important to interpret the results with caution, as the muscle mass and strength profiles of our population may differ from those in the Asian population for which AWGS was originally designed.

In conclusion, the SDOC definition was the only investigated sarcopenia definition associated with fracture risk. Further studies are required to determine if sarcopenia components should be an integral part of fracture prediction tools to reduce the overall burden of adverse health outcomes in this population of older women.

Author contributions

Anoohya Gandham (Conceptualization, Methodology, Project administration, Visualization, Writing—original draft), Giulia Gregori (Data curation, Investigation, Methodology, Validation, Writing—review & editing), Lisa Johansson (Data curation, Investigation, Methodology, Writing—review & editing), Helena Johansson (Data curation, Investigation, Methodology, Supervision, Writing—review & editing), Nicholas C. Harvey (Conceptualization, Investigation, Methodology, Writing—review & editing), Liesbeth Vandenput (Conceptualization, Investigation, Methodology, Visualization, Writing—review & editing), Eugene McCloskey (Conceptualization, Investigation, Methodology, Visualization, Writing—review & editing), John A. Kanis (Conceptualization, Investigation, Methodology, Visualization, Writing—review & editing), Henrik Litsne (Data curation, Investigation, Methodology, Writing—review & editing), Kristian Axelsson (Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Visualization, Writing—review & editing), and Mattias Lorentzon (Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing—review & editing)

Supplementary material

Supplementary material is available at *Journal of Bone and Mineral Research* online.

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Conflicts of interest

M.L. has received lecture fees from Amgen, Astellas, Lilly, Meda, Renapharma, UCB Pharma, and he received consulting fees from Amgen, Radius Health, UCB Pharma, Parexel International, Renapharma and Consilient Health. J.A.K. has received grant support from UCBN. N.C.H. has received consultancy, lecture fees, and honoraria from Alliance for Better Bone Health, Amgen, MSD, Eli Lilly, Servier, Shire, UCB, Kyowa Kirin, Consilient Healthcare, Radius Health, and Internis Pharma. E.M. has received research funding, consultancy, lecture fees, and/or honoraria from Amgen, AstraZeneca, Consilient Healthcare, Fresenius Kabi, GSK, Hologic, Internis, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, Servier, Synexus, UCB, Unilever, and Warner Chilcott. K.A. has received lecture fees from Lilly, Meda/Mylan, and Amgen. Dr L.J. has received lecture fees from UCB. All other authors have no conflicts of interests.

Data availability

Data cannot be made publicly available for ethical and legal reasons. Such information is subject to legal restrictions according to national legislation. Specifically, in Sweden, confidentiality regarding personal information in studies is regulated in the Public Access to Information and Secrecy Act (SFS 2009:400). The data underlying the results of this study might be made available upon request after an assessment of confidentiality. There is thus a possibility to apply to get access to certain public documents that an authority holds. In this case, the University of Gothenburg is the specific authority that is responsible for the integrity of the documents with research data. Questions regarding such issues can be directed to the head of the Institute of Medicine, Sahlgrenska

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