REVIEW

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Sarcopenia and its association with falls and fractures in older adults: A systematic review and meta-analysis

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Abstract

Sarcopenia is a potentially modifiable risk factor for falls and fractures in older adults, but the strength of the association between sarcopenia, falls, and fractures is unclear. This study aims to systematically assess the literature and perform a meta-analysis of the association between sarcopenia with falls and fractures among older adults. A literature search was performed using MEDLINE, EMBASE, Cochrane, and CINAHL from inception to May 2018. Inclusion criteria were the following: published in English, mean/median age ≥ 65 years, sarcopenia diagnosis (based on definitions used by the original studies' authors), falls and/or fractures outcomes, and any study population. Pooled analyses were conducted of the associations of sarcopenia with falls and fractures, expressed in odds ratios (OR) and 95% confidence intervals (CIs). Subgroup analyses were performed by study design, population, sex, sarcopenia definition, continent, and study quality. Heterogeneity was assessed using the I^2 statistics. The search identified 2771 studies. Thirty-six studies (52 838 individuals, 48.8% females, and mean age of the study populations ranging from 65.0 to 86.7 years) were included in the systematic review. Four studies reported on both falls and fractures. Ten out of 22 studies reported a significantly higher risk of falls in sarcopenic compared with non-sarcopenic individuals; 11 out of 19 studies showed a significant positive association with fractures. Thirty-three studies (45 926 individuals) were included in the meta-analysis. Sarcopenic individuals had a significant higher risk of falls (cross-sectional studies: OR 1.60; 95% CI 1.37–1.86, $P < 0.001$, $I^2 = 34\%$; prospective studies: OR 1.89; 95% CI 1.33–2.68, $P < 0.001$, $I^2 = 37\%$) and fractures (cross-sectional studies: OR 1.84; 95% CI 1.30–2.62, $P = 0.001$, $I^2 = 91\%$; prospective studies: OR 1.71; 95% CI 1.44–2.03, $P = 0.011$, $I^2 = 0\%$) compared with non-sarcopenic individuals. This was independent of study design, population, sex, sarcopenia definition, continent, and study quality. The positive association between sarcopenia with falls and fractures in older adults strengthens the need to invest in sarcopenia prevention and interventions to evaluate its effect on falls and fractures.

Keywords Sarcopenia; Falls; Fractures; Meta-analysis

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Introduction

Approximately one-third of older adults fall at least once a year[1] and a median of 4.1% of falls results in fractures.[2] Falls are associated with physical disability, functional impairment, dependency in activities of daily living, institutionalization, increased morbidity, and mortality.[3,4] A number of risk factors have been found to predispose older adults to falls. These include old age, female sex, fear of falling, impaired cognition, mobility, and gait.[5–8] One of the potentially modifiable risk factors is sarcopenia, that is, age-related low skeletal muscle mass, strength, and physical performance.[9]

Sarcopenia is prevalent between 2% and 37% in community-dwelling older adults, depending on the sarcopenia definition applied[10–12] and associated with decreased mobility, impaired standing balance, functional decline, hospitalization, and mortality.[13–15] Interventions to prevent and treat sarcopenia have been shown to be effective in increasing muscle mass, strength, and physical performance,[9,16] although it is not proven yet that this leads to a decrease of falls and fractures.

The aim of this systematic review and meta-analysis was to evaluate whether sarcopenic individuals have a higher risk of falls and fractures compared with non-sarcopenic individuals and whether this association is influenced by study design, population, sex, sarcopenia definition, continent, or study quality.

Methods

Data sources and searches

The protocol of the systematic review was registered at PROSPERO International prospective register of systematic reviews: CRD42017068485. The systematic review was conducted according to the PRISMA standards.[17] A systematic search was performed by a librarian in four electronic databases, that is, MEDLINE, EMBASE, Cochrane Central, and CINAHL from date of inception to 1 May 2018 (Online Resource S1). The search included the keywords 'sarcopenia', 'falls', 'fractures', and synonyms. The reference section of each included article was also used to identify additional related research studies.

Study selection

The studies obtained using the search strategy were assessed for eligibility independently by two authors (S. S. Y. Y. and V. K. P.) by screening titles and abstracts. Subsequently, the full-text articles of potentially relevant studies were screened independently by two reviewers (S. S. Y. Y. and V. K. P.). A third reviewer (E. M. R.) resolved any disagreements between the authors regarding the eligibility by discussion and reaching a consensus. Studies were included in the systematic review when the following inclusion criteria were met: published in English; mean or median age of ≥65 years or with subgroup analysis in those aged ≥65 years; diagnosis of sarcopenia using any definition used by the original studies' authors; and at least one of the following outcomes: falls and/or fractures. No restriction regarding study population was applied. Studies were excluded if they did not contain primary data (conference abstracts, reviews, letters to the editor, and case reports with <5 cases). Studies were excluded if no comparison group was included; that is, all individuals suffered from falls, fractures, or sarcopenia. If studies used data from the same cohort,[18,19] the studies with the largest sample size were included.[18]

Data extraction and quality assessment

The following variables were extracted independently by two reviewers (S. S. Y. Y. and V. K. P.) from the included studies: author, year of publication, total number of individuals included in the study, mean/median age of individuals, percentage of females, population, continent, prevalence of falls, study design of falls outcome, prevalence of fractures, study design of fractures outcome, applied definition(s) of sarcopenia, prevalence of sarcopenia, assessment method of muscle mass, cut-off point of muscle mass, assessment method of muscle strength, cut-off point of muscle strength, assessment method of physical performance, and cut-off point of physical performance.

Risk of bias of the included studies was assessed independently by two reviewers (S. S. Y. Y. and V. K. P.) using the Newcastle Ottawa Scale (NOS)[20,21] for case–control and cohort studies and a modified version of the NOS for cross-sectional studies. A system of points was given to the eligible categories: (i) selection of the study population, (ii) comparability, and (iii) description of the outcome (Online Resource S2). A study was given a maximum of one point in each item within the Selection and Outcome categories and a maximum of two points was given for the Comparability category. The scale scores varied depending on the study design. For case–control and cohort studies, it ranged from 0 to 9 points with ≥7 points classified as high quality.[20] For cross-sectional studies, it ranged from 0 to 7 points. Because a modified version of NOS was used and there was no cut-off available from the literature, a median of ≥4 points was considered as high quality for cross-sectional studies.[22,23]

Data synthesis and analysis

A meta-analysis was performed stratified for falls and fractures, using a random-effects model because of assumed heterogeneity between the studies. Studies were excluded from the meta-analysis if an odds ratio (OR) could not be calculated because of insufficient data or confidence intervals (CIs) were not given. When both crude and adjusted ORs were reported, adjusted ORs were used. When the studies only reported ORs stratified by sex, the overall OR was calculated from a two-by-two table including the total number of sarcopenic and non-sarcopenic individuals with falls/fractures. Sarcopenia definitions differ in their composition including muscle mass, muscle strength, and physical performance, and applying different definitions has an impact on the prevalence of sarcopenia.[11,12] Some definitions are based on low muscle mass alone: Baumgartner *et al.*,[24–28] Delmonico *et al.*,[24,27] Newman *et al.*,[25] Cheng *et al.*,[29] Scott *et al.*,[28] Sanada *et al.*,[30,31] Levine and Crimmins,[28] and Bouchard *et al.*.[28] Other definitions are based on both low muscle mass and low muscle strength/physical performance: European Working Group on Sarcopenia in Older People (EWGSOP),[24,25,28,32–52] Asian Working Group for Sarcopenia (AWGS),[18,51,53,54] Foundation for the National Institutes of Health (FNIH),[24,25,27,35,44,46,55] International Working Group on Sarcopenia (IWGS),[24,25,27,35] Society for Sarcopenia, Cachexia, and Wasting Disorders (SCWD),[24,27] and ESPEN Special Interest Group on 'cachexia-anorexia in chronic wasting diseases' and 'nutrition in geriatrics'.[24] In cases where studies applied multiple sarcopenia definitions, results based on the EWGSOP definition[52] were prioritized over the Baumgartner definition[56] and other definitions.[57–68]

Forest plots were used to visualize the results. Heterogeneity between the studies in effect measures were assessed using the I^2 statistic. I^2 values greater than 25% were considered to reflect low heterogeneity, 50% moderate, and 75% high heterogeneity.[69] Subgroup analyses were performed regarding study design, population, sex, sarcopenia definition, continent, and study quality. We contacted 17 authors of studies to obtain the data needed to compute ORs when the study did not report ORs stratified by sex. Ten authors responded, which allowed us to include these studies in the subgroup analysis.[27,28,32,33,40–43,49,54] Funnel plots of log OR against its standard error were plotted to visually evaluate publication bias, while Egger's regression test[70] and Begg's test[71] were used to statistically evaluate publication bias. Comprehensive Meta-Analysis (CMA version 2.0; Biostat Inc., Engle-wood, NJ) was used to produce pooled estimates and forest plots. P-values < 0.05 were considered statistically significant (two-sided).

Results

Search results

Online Resource S3 shows the flow chart of the study selection. A total of 4129 studies were retrieved through electronic database searches. After removal of duplicates, 2771 studies were identified for title and abstract screening. Review of the titles and abstracts yielded 241 relevant studies for full-text screening. Thirty-six studies met all inclusion criteria and were included in this review.[18,24–52,54,55,72–75] A total of 33 studies were included in the meta-analysis; four of them presented data for both falls and fractures, leaving 20 studies included in the meta-analysis for falls[24,26,28,32–36,40–44,48–50,72–75] and 17 studies for fractures.[18,27,29–31,34,35,38,39,42,46,47,49,51,54,55,73]

Study characteristics

Table 1 shows the study characteristics of the included studies. A total of 52 838 individuals (48.8% females) with a mean age of the study populations ranging from 65.0 to 86.7 years were included, and sample sizes ranged from 58 to 6,658 individuals. Study populations included community-dwelling individuals (22 studies),[18,24–28,34–36,40–42,44–46,48–51,72,73,75] hospitalized patients (3 studies),[43,47,54] outpatients (4 studies),[32,38,39,55] and nursing home residents (3 studies).[33,37,74] Four studies included a combined group of hospitalized patients with fractures and community-dwelling individuals without fractures.[29–31,51] Two studies reported retrospective data,[31,55] 20 studies were cross-sectional,[26,29,30,32,35,36,38,39,41–44,48–51,54,72,73,75] 13 studies were prospective,[18,25,27,28,33,34,37,40,45–47,53,74] and 1 study was a randomized controlled trial examining the effect of nutritional supplementation on bone mineral density and risk of falls.[24] Most of the studies were performed in Europe (12 studies),[26,27,33,35,40,42,47,49,55,73,74] and Asia (12 studies),[18,29–31,44,48,50,51,53,54,72,75] followed by Australia (5 studies),[28,37–39,46] South America (4 studies),[32,36,41,43] and North America (3 studies).[24,25,34] The prevalence of falls ranged from 4.2% to 63.8%, and the prevalence of fractures ranged from 3.5% to 63.6% in the studies. Follow-up periods varied from 1 to 3 years for falls and 2 to 11 years for fractures.

Table 2 shows the prevalence and applied diagnostic criteria of sarcopenia. The prevalence of sarcopenia varied from 0.3% to 73.0%, depending on the sarcopenia definition applied and the study population. Sarcopenia was diagnosed using one definition[18,26,29–34,36–43,47–50,53,54,72,73,75] or more than one definition.[24,25,27,28,35,44–46,51,55,74] Out of the 36 included studies, EWGSOP (23 studies) was the most commonly used definition,[24,25,28,32–49,51] followed by FNIH (7 studies),[24,25,27,35,45,56,55] Baumgartner definition (5 studies),[24–28] AWGS (4 studies),[18,51,53,54] and IWGS (4 studies).[24,25,27,35]

Study quality

Online Resource S4 shows the results of the NOS quality assessment of the included studies. The quality of 12 falls studies[24,26,33,35,37,41,45,48,53,72,73,75] and 14 fracture studies[18,25,27,29–31,34,35,45,49,51,54,55,73] was rated high. Ten studies for falls were rated as low quality.[28,32,34,36,40,43,44,49,50,74] Five studies for fractures were rated as low quality.[38,39,42,46,47]

Association of sarcopenia with falls

Twenty-two studies investigated the association of sarcopenia and falls, of which 10 studies (45%) reported higher risks of falls among sarcopenic individuals compared with non-sarcopenic individuals.[28,34,40,41,48,50,53,72,73,75] Non-

Table 1. Study characteristics and falls and fractures outcomes

Author	Year	*N*	Mean age ± *SD* (years)	Female, *n* (%)	Population	Continent	Falls: Prevalence/incidence[a], *n* (%)	Falls: Study design	Fractures: Prevalence/incidence[a], *n* (%)	Fractures: Study design
Bae	2017	3901	≥65	2259 (57.9)	Community	Asia	109 (2.5)	Cross-sectional	NA	NA
Benjumea	2018	534	74.4 ± 8.2	403 (75.5)	Outpatient	South America	309 (60.4)	Cross-sectional	NA	NA
Bischoff-Ferrari	2015	445	71.0 ± 4.61	246 (55.3)	Community	North America	231 (51.9)	RCT	NA	NA
Buckinx	2018	565	82.8 ± 9.0	413 (73.1)	Nursing home	Europe	211 (37.3)	Prospective	NA	NA
Cawthon	2015	5934	73.6 ± 6.0	0	Community	North America	NA	NA	207 (3.5)	Prospective
Chalhoub	2015	6658	74.34 ± 5.0	1114 (16.7)	Community	North America	1518 (22.8)	Retrospective	1142 (17.2)	Prospective
Clynes	2015	298	76.1 ± 2.57	142 (47.7)	Community	Europe	190 (63.8)	Cross-sectional	70 (23.5)	Cross-sectional
Dietzel	2015	288	71.9 ± 7.5	142 (49.3)	Community	Europe	47 (16.0)	Cross-sectional	NA	NA
Gadelha	2018	196	68.6 ± 6.45	196 (100)	Community	South America	65 (33.2)	Cross-sectional	NA	NA
Hars	2016	913	65.0 ± 1.4	729 (79.9)	Community	Europe	NA	NA	40 (4.4)	Prospective
Henwood	2017	58	84.5 ± 8.2	41 (70.7)	Nursing home	Australia	24 (41.4)	Prospective	NA	NA
Hida	2013	2868	71.3 ± 10.4	2197 (76.6)	Hospital and outpatients	Asia	NA	NA	357 (12.4)	Cross-sectional
Hida	2016	1824	70.4 ± 9.5	1824 (100)	Hospital and outpatients	Asia	NA	NA	216 (11.8)	Retrospective
Hong	2015	3077	78.0 ± 6.6	1492 (48.5)	Hospital and community	Asia	NA	NA	757 (24.6)	Cross-sectional
Huo	2015	680	79.0 ± 7.1	455 (66.9)	Outpatient	Australia	NA	NA	242 (35.6)	Cross-sectional
Huo	2016	680	79.0 ± 9.0	418 (61.5)	Outpatient	Australia	NA	NA	293 (43.1)	Cross-sectional
Iolascon	2015	121	67.2 ± 8.47	121 (100)	Outpatient	Europe	NA	NA	77 (63.6)	Retrospective
Landi	2012	260	86.7 ± 5.4	177 (68.1)	Community	Europe	37 (14.2)	Prospective	NA	NA
Lera	2017	1006	67.6 ± 5.9	687 (68.3)	Community	South America	332 (33.0)	Cross-sectional	NA	NA
Locquet	2018	288	74.7 ± 5.7	170 (59.0)	Community	Europe	NA	NA	134 (46.5)	Cross-sectional
Martinez	2015	110	71.0 ± 8.2	46 (41.8)	Hospital	South America	28 (25.5)	Cross-sectional	NA	NA
Matsumoto	2017	162	74.2 ± 7.1	103 (63.6)	Community	Asia	50 (30.9)	Prospective	NA	NA
Menant	2017	419	81.2 ± 4.5	207 (49.4)	Community	Australia	194 (46.3)	Prospective	NA	NA
Meng	2015	771	73.0 ± 5.7	359 (46.6)	Community	Asia	173 (22.4)	Cross-sectional	NA	NA
Schaap	2018	496	75.2 ± 6.4	250 (50.4)	Community	Europe	130 (26.6)	Prospective	60 (12.1)	Prospective
Scott	2017	861	76.6 ± 5.5	0	Community	Australia	371 (30.0)	Prospective	152 (17.7)	Prospective
Sjöblom	2013	590	67.9 ± 1.9	590 (100)	Community	Europe	119 (21.7)	Cross-sectional	85 (14.9)	Cross-sectional
Steihaug	2018	201[b]	79.4 ± 8.2	151 (75.1)	Hospital	Europe	NA	NA	14 (7.0) 15 (7.9)	Cross-sectional Prospective
Tanimoto	2014	1110	73.4 ± 6.0	738 (66.5)	Community	Asia	220 (19.8)	Cross-sectional	NA	NA
Trajanoska	2018	5911	69.2 ± 9.1	3361 (56.8)	Community	Europe	1097 (18.6)	Cross-sectional	939 (15.9)	Cross-sectional
Van Puyenbroeck	2012	276	83.4	193 (69.9)	Nursing home	Europe	69 (25.0)	Prospective	NA	NA
Woo	2014	2848	73.17 (SE 0.14)	1675 (58.8)	Community	Asia	120 (4.2)	Cross-sectional	NA	NA
Yamada	2013	1882	74.9 ± 5.5	1314 (69.8)	Community	Asia	470 (25.0)	Cross-sectional	NA	NA
Yoo	2016	1970	66.3 ± 9.1	1221 (62)	Hospital and community	Asia	NA	NA	359 (18.2)	Case–control
Yoshimura	2018	637	74 ± 13	366 (57.5)	Hospital	Asia	NA	NA	131 (20.6)	Cross-sectional
Yu	2014	4000	72.5 ± 5.2	2000 (50)	Community	Asia	NA	NA	565 (14.1)	Prospective

N, sample size; NA, not applicable; RCT, randomised controlled trial; SD, standard deviation.
[a]Prevalence is reported for cross-sectional study design; incidence is reported for prospective study design.
[b]*n* = 191 for complete follow-up.

Table 2. Prevalence and diagnostic criteria of sarcopenia of the included studies

Author	Year	N	Sarcopenia		Diagnostic criteria					
			Definition	Prevalence, n (%)	Muscle mass		Muscle strength		Physical performance	
					Measure	Cut-off	Measure	Cut-off	Measure	Cut-off
Bae	2017	3827	Cho et al.	1619 (42.3)	DXA	ASM (as % body weight): M: <30.3%; F: <23.8%	NA	NA	NA	NA
Benjumea	2018	534	EWGSOP	380 (71.2)	Lee equation	ASM/ht^2: M: ≤6.37 kg/m^2; F: ≤8.90 kg/m^2	HGS	M: <30 kg; F: <20 kg	4-m GS	≤0.8 m/s
Bischoff-Ferrari	2015	443	Baumgartner	49 (11.0)	DXA	ALM/ht^2: M: ≤7.26 kg/m^2; F: ≤5.45 kg/m^2	NA	NA	NA	NA
		443	Delmonico 1	75 (16.9)	DXA	ALM/ht^2: M: ≤7.25 kg/m^2; F: ≤5.67 kg/m^2	NA	NA	NA	NA
		443	Delmonico 2	95 (21.4)	DXA	Observed ALM—predicted ALM: <20th percentile of the sex-specific distribution	NA	NA	NA	NA
		445	EWGSOP	31 (7.0)	DXA	ALM/ht^2: M: ≤7.26 kg/m^2; F: ≤5.54 kg/m^2	HGS	M: <30 kg; F: <20 kg	15-ft GS	<0.8 m/s
		440	IWGS	22 (4.9)	DXA	ALM/ht^2: M: ≤7.23 kg/m^2; F: ≤5.67 kg/m^2	NA	NA	15-ft GS	<1.0 m/s
		445	SCWD	12 (2.7)	DXA	ALM/ht^2: M: ≤6.81 kg/m^2; F: ≤5.18 kg/m^2	NA	NA	15-ft GS	<1.0 m/s
		445	Muscaritoli	104 (23.6)	DXA	SM/body mass: M: ≤37%; F: ≤28%	NA	NA	15-ft GS	<0.8 m/s
		443	FNIH 1	52 (11.7)	DXA	ALM_{BMI}: M: <0.789; F: <0.512	NA	NA	NA	NA
		445	FNIH 2	14 (3.1)	DXA	ALM_{BMI}: M: <0.789; F: <0.512	HGS	M: <26 kg; F: <16 kg	NA	NA
Buckinx	2018	247	EWGSOP	166 (67.2)	BIA	Not specified	HGS	Not specified	SPPB	≤8 points
Cawthon	2015	5934	Baumgartner	1301 (21.9)	DXA	ALM/ht^2: M: ≤7.23 kg/m^2	NA	NA	NA	NA
		5934	EWGSOP	257 (4.3)	DXA	ALM/ht^2: M: ≤7.23 kg/m^2	HGS	M: <30 kg	6-m GS	≤0.8 m/s
		5934	IWGS	277 (4.7)	DXA	ALM/ht^2: M: ≤7.23 kg/m^2	NA	NA	6-m GS	<1.0 m/s

(*Continues*)

Table 2 (continued)

Author	Year	N	Sarcopenia		Diagnostic criteria					
			Definition	Prevalence, n (%)	Muscle mass		Muscle strength		Physical performance	
					Measure	Cut-off	Measure	Cut-off	Measure	Cut-off
		5934	FNIH 1	88 (1.5)	DXA	ALM_{BMI}: M: <0.789	NA	NA	6-m GS	≤0.8 m/s
		5934	FNIH 2	18 (0.3)	DXA	ALM_{BMI}: M: <0.789	HGS	M: <26 kg	6-m GS	≤0.8 m/s
		5934	Newman	1186 (20.0)	DXA	Residual of actual ALM minus predicted ALM: ≤−0.204 kg/m^2	NA	NA	NA	NA
Chalhoub	2015	6658	EWGSOP	371 (5.6)	DXA	ALM adjusted for height and fat mass: 20th percentile of the distribution of residuals	HGS	M: <30 kg; F: <20 kg	6-m GS	<0.8 m/s
Clynes	2015	298	IWGS	25 (8.4)	DXA	ALM/ht^2: M: ≤7.23 kg/m^2; F: ≤5.67 kg/m^2	NA	NA	3-m GS	<1.0 m/s
		298	EWGSOP	10 (3.4)	DXA	SMI: M: ≤7.26 kg/m^2; F: ≤5.5 kg/m^2	HGS	M: <30 kg; F: <20 kg	3-m GS	≤0.8 m/s
		298	FNIH	6 (2.0)	DXA	ALM_{BMI}: M: <0.789; F: <0.512	HGS	M: <26 kg; F: <16 kg	NA	NA
Dietzel	2015	288	Baumgartner	34 (11.8)	DXA	ASM/ht^2: M: <7.26 kg/m^2; F: <5.5 kg/m^2	NA	NA	NA	NA
Gadelha	2018	196	EWGSOP	36 (18.4)	DXA	SMM (as % body mass): not specified	Isokinetic muscle torque	Not specified	TUG	Not specified
Hars	2016	913	Baumgartner	102 (11.2)	DXA	ALM/ht^2: M: <7.26 kg/m^2; F: <5.45 kg/m^2	NA	NA	NA	NA
		913	Delmonico 1	157 (17.2)	DXA	ALM/ht^2: M: <7.25 kg/m^2; F: <5.67 kg/m^2	NA	NA	NA	NA
		913	Delmonico 2	184 (20.2)	DXA	Observed ALM minus predicted ALM: <20th percentile of the sex-specific distribution	NA	NA	NA	NA
		913	IWGS	156 (17.1)	DXA	ALM/ht^2: M: ≤7.23 kg/m^2; F: ≤5.67 kg/m^2	NA	NA	NA	NA

(*Continues*)

Table 2 (continued)

Author	Year	N	Sarcopenia: Definition	Sarcopenia: Prevalence, n (%)	Muscle mass: Measure	Muscle mass: Cut-off	Muscle strength: Measure	Muscle strength: Cut-off	Physical performance: Measure	Physical performance: Cut-off
		913	SCWD	42 (4.6)	DXA	ALM/ht^2: M: ≤6.81 kg/m^2; F: ≤5.18 kg/m^2	NA	NA	NA	NA
		913	FNIH	32 (3.5)	DXA	ALM$_{BMI}$: M: <0.789; F: <0.512	NA	NA	NA	NA
Henwood	2017	58	EWGSOP	23 (40.2)	BIA	SMM/ht^2: M: <8.87 kg/m^2; F: <6.42 kg/m^2	HGS	M: <30 kg; F: <20 kg	2.4-m GS	<0.8 m/s
Hida	2013	2868	Sanada	1019 (35.5)	DXA	ALM/ht^2: M: <6.87 kg/m^2; F: <5.46 kg/m^2	NA	NA	NA	NA
Hida	2016	1824	Sanada	493 (27.0)	DXA	ALM/ht^2: F: <5.46 kg/m^2	NA	NA	NA	NA
Hong	2015	3077	Cheng	966 (31.4)	DXA	SMI: M: <7.01 kg/m^2; F: <5.42 kg/m^2	NA	NA	NA	NA
Huo	2015	680	EWGSOP	345 (50.7)	DXA	ALM/ht^2: M: <7.26 kg/m^2; F: <5.5 kg/m^2	HGS	M: <30 kg; F: <20 kg	GS	<0.8 m/s
Huo	2016	680	EWGSOP	380 (55.9)	DXA	ALM/ht^2: M: <7.26 kg/m^2; F: <5.5 kg/m^2	HGS	M: <30 kg; F: <20 kg	GS	<0.8 m/s
Iolascon	2015	121	FNIH 1 FNIH 2	10 (8.3) 13 (10.7)	DXA DXA	ALM$_{BMI}$: F: <0.512 ALM$_{BMI}$: F: <0.512	HGS HGS	F: ≥16 F: <16	4-m GS 4-m GS	≤0.8 m/s ≤0.8 m/s
Landi	2012	260	EWGSOP	66 (25.4)	MAMC	M: <21.1 cm; F: <19.2 cm	HGS	M: <30 kg; F: <20 kg	4-m GS	<0.8 m/s
Lera	2017	1006	EWGSOP	192 (19.1)	DXA	ASM/ht^2: M: <7.19 kg/m^2; F: <5.77 kg/m^2	HGS	M: ≤27 kg; F: ≤15 kg	3-m GS	<0.8 m/s
Locquet	2018	288	EWGSOP	43 (14.9)	DXA	AMM/ht^2: M: <7.26 kg/m^2; F: <5.50 kg/m^2	HGS	M: <30 kg; F: <20 kg	SPPB	<8 points
Martinez	2015	110	EWGSOP	24 (21.8)	Lee equation	SMM/ht^2: M: ≤8.90 kg/m^2; F: ≤6.37 kg/m^2	HGS	M: <30 kg; F: <20 kg	6-m GS	≤0.8 m/s
Matsumoto	2017	162	AWGS	9 (5.6)	BIA	M: <7.0 kg/m^2; F: <5.7 kg/m^2	HGS	M: <26 kg; F: <18 kg	5-m GS	≤0.8 m/s
Menant	2017	410	EWGSOP	88 (21.5)	DXA	ASM/ht^2: M: <7.2 kg/m^2; F: <5.5 kg/m^2	HGS	M: <30 kg; F: <20 kg	6-m GS	≤0.8 m/s
		419	Baumgartner	97 (23.2)	DXA	ASM/ht^2: M: <7.26 kg/m^2; F: <5.45 kg/m^2	NA	NA	NA	NA
		419	Scott	139 (33.2)	DXA	Bottom tertile of the residuals from the regression of ALM (g) on height (m) and fat	NA	NA	NA	NA

(*Continues*)

Table 2 (continued)

Author	Year	N	Sarcopenia		Diagnostic criteria					
			Definition	Prevalence, n (%)	Muscle mass		Muscle strength		Physical performance	
					Measure	Cut-off	Measure	Cut-off	Measure	Cut-off
						mass (g): M: <326.4; F: <2217.8				
		419	Levine & Crimmins	57 (13.6)	DXA	ALM (as % body mass): M: <25.72%; F: <19.43%	NA	NA	NA	NA
Menant	2017	419	Bouchard	306 (73.0)	DXA	ASM/ht^2: M: <8.51 kg/m^2; F: <6.29 kg/m^2	NA	NA	NA	NA
		314	HGS-based	127 (40.4)	NA	NA	HGS	M: <30 kg; F: <20 kg	NA	NA
		419	KES-based	84 (20.0)	NA	NA	KES	M: <23.64 kg; F: <15.24 kg	NA	NA
Meng	2015	771	EWGSOP 1	44 (5.7)	DXA	ALM/ht^2: M: <6.39 kg/m^2; F: <4.84 kg/m^2	HGS	M: <30 kg; F: <20 kg	5-m GS	<0.8 m/s
			EWGSOP 2	75 (9.7)	DXA	ALM (as % body mass): M: <27.1%; F: <22.3%	HGS	M: <30 kg; F: <20 kg	5-m GS	<0.8 m/s
Schaap	2018	496	EWGSOP	158 (31.9)	DXA	ASM/ht^2: M: ≤7.26 kg/m^2; F: ≤ 5.45 kg/m^2	HGS	M: <30 kg; F: <20 kg	GS (walk 3 m, a turn of 180° and walk the 3 m)	≤0.8 m/s
			FNIH 1	39 (7.9)	DEXA	M: <19.75 kg; F: <15.02 kg	HGS	M: <26 kg; F: <16 kg	NA	NA
			FNIH 2	31 (6.3)	DEXA	M: <19.75 kg; F: <15.02 kg	HGS	M: <26 kg; F: <16 kg	GS (walk 3 m, a turn of 180° and walk the 3 m)	≤0.8 m/s
Scott	2017	1486	EWGSOP	237 (15.9)	DXA	ALM/ht^2: M: <7.25 kg/m^2	HGS	M: <30 kg	6-m GS	≤0.8 m/s
		1486	FNIH	119 (8.0)	DXA	ALM_{BMI}: M: <0.789	HGS	M: <26 kg	NA	NA
Steihaug	2018	201	EWGSOP	77 (38.3)	Heymsfield formula using anthropometry to estimate ALM (Kim et al. formula)	ALM/ht^2: M: ≤7.25 kg/m^2; F: ≤5.67 kg/m^2	HGS	M: ≤30 kg; F: ≤20 kg	Questionnaire (new mobility score)	<5 points
Sjöblom	2013	590	NG	69 (11.7)	DXA	Relative SMI: F: <6.3 kg/m^2	HGS	F: <22.3 kPA	10-m GS	F: >7 s
Tanimoto	2014	1110	EWGSOP	160 (14.4)	BIA	AMM/ht^2: M: <7.0 kg/m^2; F: <5.8 kg/m^2	HGS	Lowest HGS quartile	5-m GS	Slowest GS quartile

(Continues)

Table 2 (continued)

Author	Year	N	Sarcopenia		Diagnostic criteria					
			Definition	Prevalence, n (%)	Muscle mass		Muscle strength		Physical performance	
					Measure	Cut-off	Measure	Cut-off	Measure	Cut-off
Trajanoska	2018	5911	EWGSOP	260 (4.4)	DXA	ALM/ht^2: M: $\leq$7.25 kg/m^2; F: $\leq$5.67 kg/m^2	HGS	M: $\leq$29 kg (if BMI $\leq$ 24); $\leq$30 kg (if BMI $\leq$ 24.1–28); $\leq$32 kg (if BMI $>$ 28); F: $\leq$17 kg (if BMI $\leq$ 23); $\leq$17.3 kg (if BMI $\leq$ 23.1–26), $\leq$18 kg (BMI $\leq$ 26.1–29), $\leq$21 kg (if BMI $>$ 29)	5.79-m GS	M: $<$0.65 m/s (if height $\leq$ 173 cm) or $<$0.76 m/s (if height $>$ 173 cm); F: $<$0.65 m/s (if height $\leq$ 159 cm) or $<$0.76 m/s (if height $>$ 159 cm)
Van Puyenbroeck	2012	276	NG	67 (24.3)	BIA	SM/ht^2: M: 8.058 kg/m^2; F: 6.154 kg/m^2	NA	NA	NA	NA
		276	NG	225 (81.5)	BIA	SM/weight × 100: M: $<$33.94; F: $<$24.76	NA	NA	NA	NA
		276	NG	178 (64.5)	BIA	SM: M: $<$25.99 kg; F: $<$16.15 kg	NA	NA	NA	NA
Woo	2014	2848	Kim	1404 (49.3)	DXA	ASM/weight: M: $<$29.9%; F: $<$25.1%	NA	NA	NA	NA
Yamada	2013	1882	EWGSOP	414 (22.0)	BIA	Appendicular SMM/ht^2: M: $<$6.75 kg/m^2; F: $<$5.07 kg/m^2	HGS	M: $<$30 kg; F: $<$20 kg	10-m GS	$<$0.8 m/s
Yoo	2016	1970	AWGS	352 (17.8)	DXA	SMM/ht^2: M: $<$7.0 kg/m^2; F: $<$5.4 kg/m^2	NA	NA	NA	NA
		1970	EWGSOP	439 (22.3)	DXA	SMM/ht^2: M: $<$7.26 kg/m^2; F: $<$5.5 kg/m^2	NA	NA	NA	NA
Yoshimura	2018	637	AWGS	343 (53.0)	BIA	SM/ht^2: M: $<$7.0 kg/m^2; F: $<$5.7 kg/m^2	HGS	M: $<$26 kg; F: $<$18 kg	NA	NA
Yu	2014	4000	AWGS	293 (7.3)	DXA	ASM/ht^2: M: $<$7.0 kg/m^2; F: $<$5.4 kg/m^2	HGS	M: $<$26 kg; F: $<$18 kg	6-m GS	$<$0.8 m/s

ALM, appendicular lean mass; AMM, appendicular muscle mass; ASM, appendicular skeletal muscle mass; AWGS, Asia Working Group for Sarcopenia; BIA, bioelectrical impedance analysis; BMI, body mass index; DXA, dual energy X-ray absorptiometry; EWGSOP, European Working Group on Sarcopenia in Older People; F, females; FNIH, Foundation for the National Institutes of Health; GS, gait speed; HGS, handgrip strength; ht, height; IWGS, International Working Group on Sarcopenia; KES, knee extension strength; M, males; MAMC, mid-arm muscle circumference; *N*, sample size; NA, not applicable; NG, not given; SCWD, Society for Sarcopenia, Cachexia, and Wasting Disorders; SM, skeletal muscle; SMM, skeletal muscle mass; SMI, skeletal muscle index; SPPB, short physical performance battery; TUG, Timed Up & Go.

significant associations between sarcopenia and falls were found in the remaining 12 studies.[24,26,32,33,35–37,43–45,49,74]

Among the 20 studies included in the meta-analysis, a pooled OR of 1.60 for cross-sectional studies (95% CI 1.37–1.86, $P < 0.001$, $I^2 = 34\%$) and a pooled OR of 1.89 for prospective studies (95% CI 1.33–2.68, $P < 0.001$, $I^2 = 37\%$) indicated a significantly higher risk of falls for sarcopenic compared with non-sarcopenic individuals (*Figure 1*A). The results of the subgroup analyses are presented in *Figure 1*A–F. The significant association between sarcopenia and falls was independent of study design (*Figure 1*A), study population (*Figure 1*B), and sex (*Figure 1*C). When stratified by sarcopenia definition, sarcopenia diagnosed by use of EWGSOP (OR 1.62, 95% CI 1.38–1.90, $P < 0.001$), Baumgartner (OR 1.50, 95% CI 1.07–2.12, $P = 0.020$), and IWGS (OR 2.02, 95% CI 1.09–3.74, $P = 0.025$) definitions was significantly associated with falls, but the association was insignificant for the FNIH definition (two studies) (OR 0.67, 95% CI 0.26–1.77, $P = 0.422$) (*Figure 1*D). The significant association between sarcopenia and falls was independent of continent (*Figure 1*E) and study quality (*Figure 1*F).

Association of sarcopenia with fractures

Nineteen studies investigated the association of sarcopenia and fractures. Higher risks of fractures were reported in 11 studies (58%) among sarcopenic individuals compared with non-sarcopenic individuals.[18,27,29–31,34,39,46,49,51,73] Non-significant associations between sarcopenia and fractures were found in eight studies.[25,35,38,42,45,47,54,55]

Among the 17 studies included in the meta-analysis, a significantly higher risk of fractures was found for sarcopenic compared with non-sarcopenic individuals (cross-sectional studies: pooled OR 1.84, 95% CI 1.30–2.62, $P = 0.001$, $I^2 = 91\%$; prospective studies: pooled OR 1.71, 95% CI 1.44–2.03, $P = 0.011$, $I^2 = 0\%$) (*Figure 2*A). The association between sarcopenia and fractures remained significant when excluding one particular study with large CIs,[51] and heterogeneity decreased from 91% to 10%. The results of the subgroup analysis are presented in *Figure 2*A–F. The significant association between sarcopenia and fractures was independent of study design (*Figure 2*A), study population (*Figure 2*B), and sex (*Figure 2*C). Sarcopenia diagnosed by use of EWGSOP (OR 1.93, 95% CI 1.19–3.13, $P = 0.008$) and Sanada *et al*. (OR 1.66, 95% CI 1.26–2.18, $P < 0.001$) definitions was associated with fractures, while the association between sarcopenia and fractures was not significant for sarcopenia diagnosed with AWGS (3 studies), FNIH (3 studies), and IWGS (2 studies) definitions (*Figure 2*D). The significant association between sarcopenia and fractures was independent of continent (*Figure 2*E) and study quality (*Figure 2*F).

Publication bias

Asymmetry was observed by visual inspection of funnel plots (Online Resource S5). However, Egger's regression test ($P = 0.463$ for falls and $P = 0.928$ for fractures) and Begg's test ($P = 0.627$ for falls and $P = 0.232$ for fractures) indicated no statistically significant publication bias among the studies in this meta-analysis.

Discussion

This systematic review and meta-analysis highlights the positive association between sarcopenia, falls, and fractures; this was independent of study design, population, sex, sarcopenia definition, continent, and study quality.

This is the first meta-analysis examining the association between sarcopenia, falls, and fractures among older adults including various definitions of sarcopenia. A meta-analysis[76] published in 2004 showed a positive association between muscle strength and falls; since then, the literature has expanded substantially. A previous systematic review assessing various health outcomes of sarcopenia showed positive associations but was based on the EWGSOP definition only.[14] A recently published meta-analysis (9 studies)[77] has found a significant association between sarcopenia and fractures with a smaller pooled effect size (risk ratio 1.34) compared with the subgroup analysis for community-dwelling older adults (OR: 1.73, 95% CI: 1.50–2.00) in our meta-analysis. The previous study included only prospective studies in community-dwelling older adults aged 60 years, which contrasts our review addressing both prospective studies and cross-sectional studies in adults aged 65 years and older.

Evidence was found for both cross-sectional and prospective studies, implying the existence of different directions of causal pathways, that is, sarcopenia as a cause for falls and fractures, and falls and fractures as a cause for sarcopenia. Falls and fractures can result in loss of mobility, fear of falling, and hospital admissions.[78] Physical inactivity associated with these consequences accelerates loss of muscle mass and muscle strength.[79] This may explain the results from cross-sectional studies in which sarcopenic individuals had higher risk of retrospective falls and fractures compared with non-sarcopenic individuals. On the other hand, impaired standing balance is a strong risk factor for falls.[80] The ability to maintain balance requires interaction of motor (muscle), nervous, and sensory systems.[81] Muscle strength and muscle mass have been shown to be positively associated with the ability to maintain standing balance in older adults,[15,82] which may explain the positive associations between sarcopenia and falls/fractures in the prospective studies.

Figure 1 Forest plots of odds ratio for falls in sarcopenic individuals vs. non-sarcopenic individuals, stratified by (*A*) study design; (*B*) study population; (*C*) sex; (*D*) sarcopenia definition; (*E*) continent; and (*F*) study quality. AWGS, Asia Working Group for Sarcopenia; CI, confidence interval; EWGSOP, European Working Group on Sarcopenia in Older People; FNIH, Foundation for the National Institutes of Health; IWGS, International Working Group on Sarcopenia; OR, odds ratio.

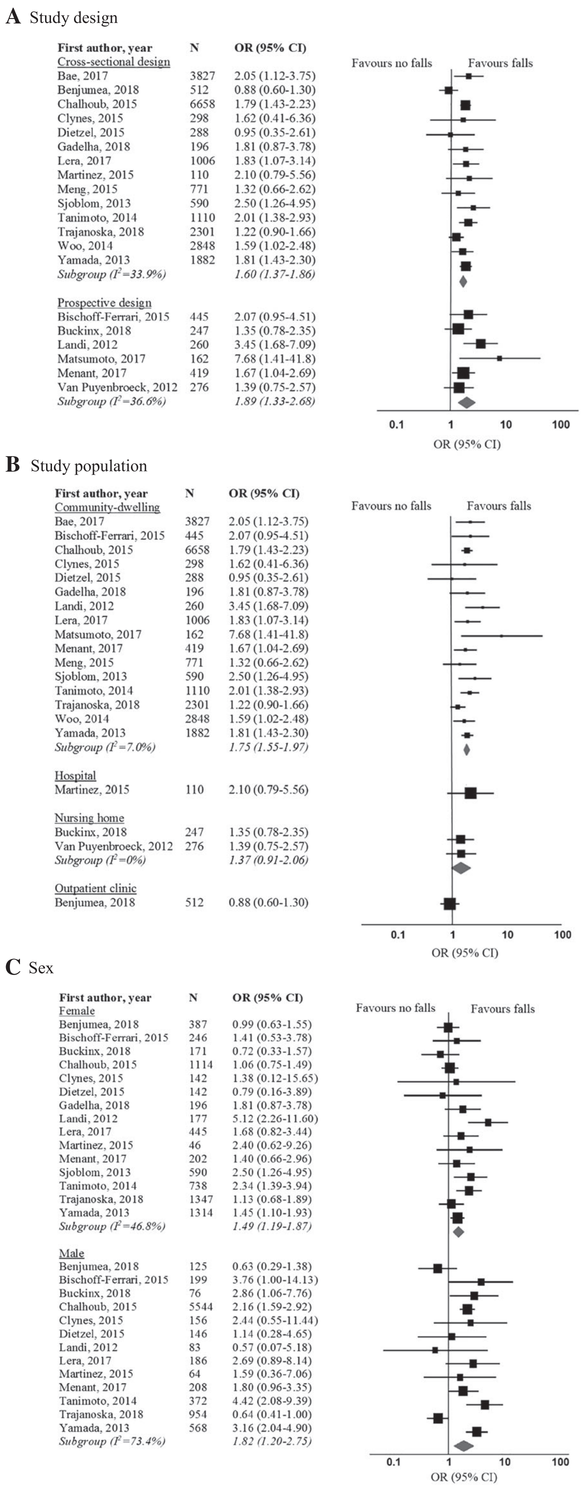


Figure 1 Continued

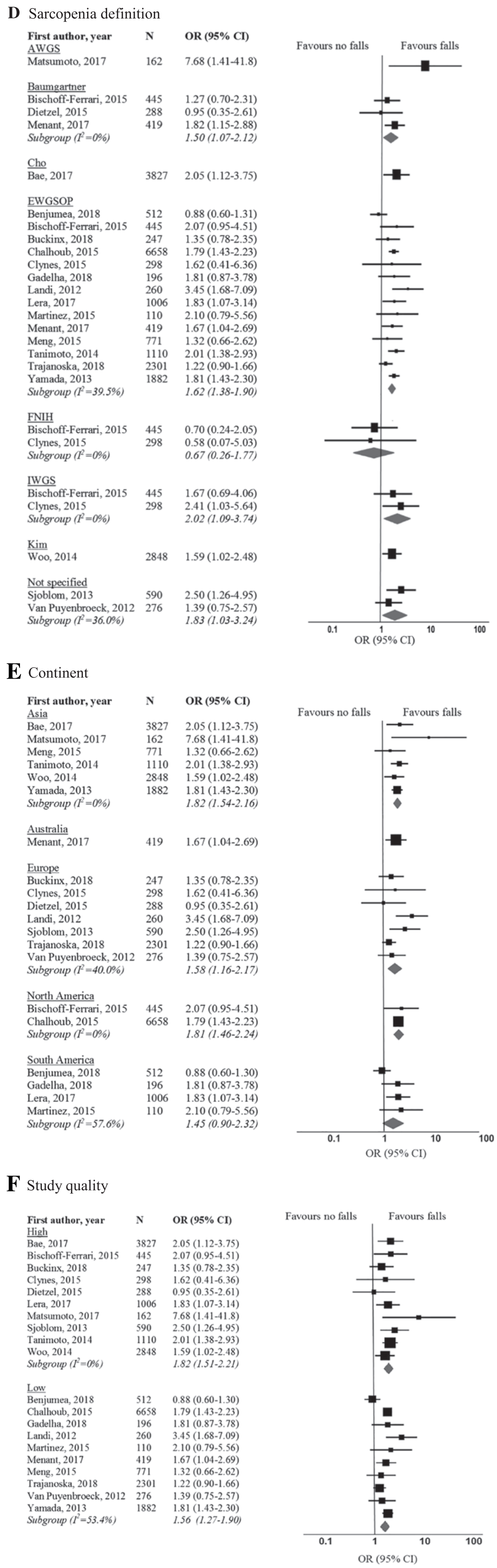


Figure 2 Forest plots of odds ratio for fractures in sarcopenic individuals vs. non-sarcopenic individuals, stratified by (*A*) study design; (*B*) study population; (*C*) sex; (*D*) sarcopenia definition; (*E*) continent; and (*F*) study quality. AWGS, Asia Working Group for Sarcopenia; CI, confidence interval; EWGSOP, European Working Group on Sarcopenia in Older People; FNIH, Foundation for the National Institutes of Health; IWGS, International Working Group on Sarcopenia; OR, odds ratio.

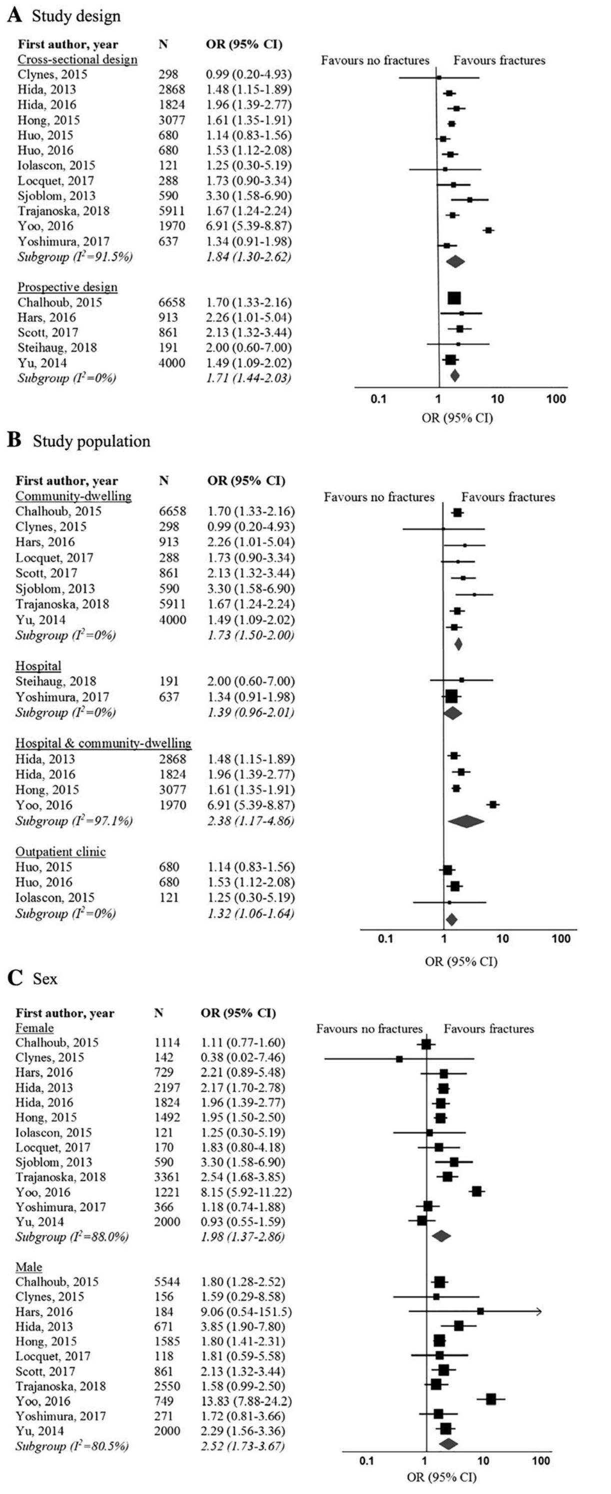
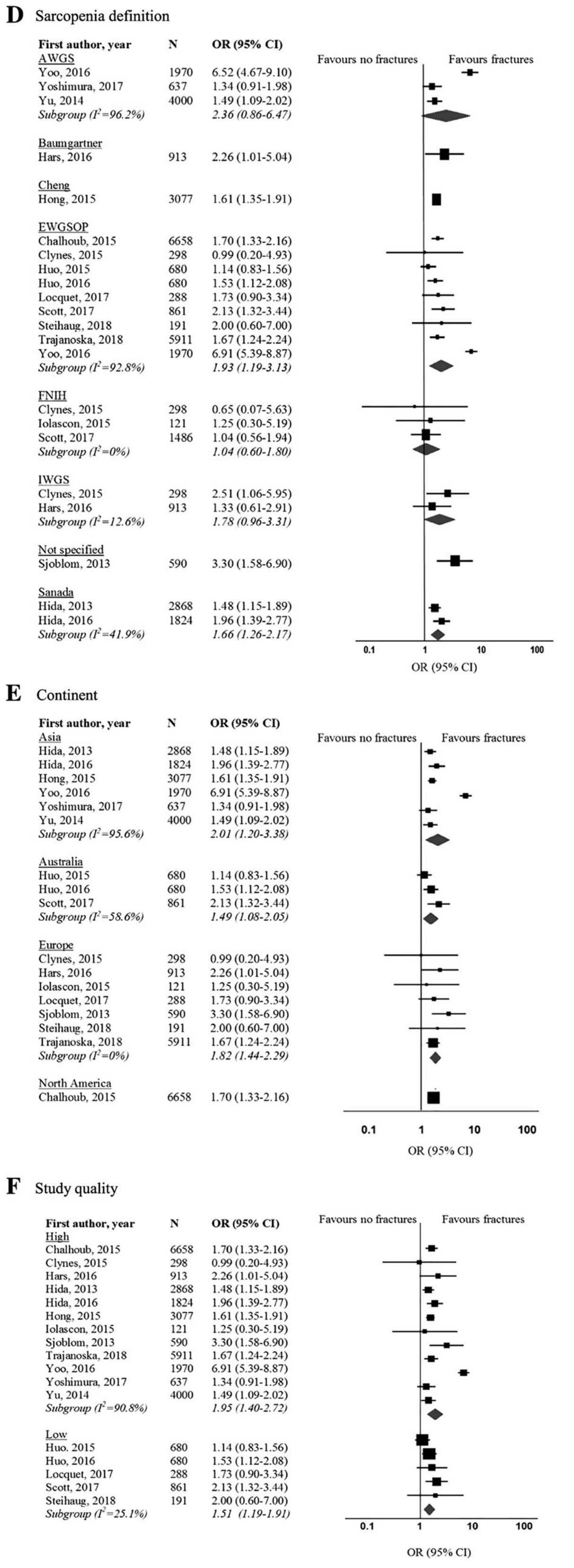


Figure 2 Continued



Most of the studies included in this systematic review and meta-analysis were conducted among community-dwelling individuals. Three included studies examined the association between sarcopenia and falls among nursing home residents[33,37,74] and one study among hospitalized patients,[43] but no associations were found. In these specific populations, sarcopenia as a risk for falls may be overshadowed by other high prevalent risk factors such as the number of diseases, urinary incontinence, polypharmacy, and antidepressant use.[83]

Sarcopenia is mainly prevalent in older adults compared with younger ages, where disease pathology is likely to be different. Muscle mass loss is multifactorial. Lifestyle behaviours such as physical inactivity and poor diet are important contributors to the loss of muscle mass and strength at any age, and also, genetic contributions have been described.[84] With the aging process, other contributing factors include state of chronic inflammation,[85] functional and structural decline of the neuromuscular systems, lower muscle turnover and repair capacity due to decreased muscle protein synthesis, and altered endocrine function.[86–90]

Our study showed that the positive association between sarcopenia with falls and fractures was independent of most of the applied sarcopenia definitions. However, using the EWGSOP and IWGS definitions, which include low physical performance and/or grip strength in addition to low muscle mass in their diagnostic algorithm,[24] higher risks of falls and fractures among sarcopenic individuals compared with non-sarcopenic individuals were shown. This indicates that low muscle function has an additional role in the association with falls and fractures compared with muscle mass alone. Cross-sectional analysis among 3493 non-institutionalized older adults found that low muscle mass and low muscle function are independent risk factors for losing physical independence in later life. However, individuals with both low muscle mass and low muscle function presented the highest risk for losing physical independence.[91] In addition, a prospective study suggested that muscle strength rather than muscle mass at baseline was associated with increased falls risk score and fracture incidence at 10 years follow-up in community-dwelling older adults.[92]

This highlights the importance of muscle strength or physical performance in the sarcopenia definition, in line with current definitions.[58,59,61,62,68,93] However, literatures also showed the value of including muscle mass in sarcopenia definitions. Muscle mass but not muscle strength or physical performance was associated with bone mineral density[94] and insulin resistance.[95] This reflects the complex role of muscle as not only a strength generator but also an important organ performing protein storage, glucose regulation, hormone production, and other cellular mechanisms.[96] A discussion on the use of a single diagnostic criterion or a combination of diagnostic criteria for sarcopenia should take into account which criterion has the strongest predictive value on clinical outcomes.

High heterogeneity was found for the association between sarcopenia and fractures. This heterogeneity can largely be attributed to one specific study, which included a combination of 359 hospitalized patients with fracture and 1614 community-dwelling older individuals as control group in the same study population.[51] In that study, the hospitalized patients were older than the control group. Because the prevalence of sarcopenia is higher with age,[97] the association between sarcopenia and fractures may be overestimated, which is further underpinned by a high crude OR of the association between sarcopenia and fractures. Note that the association between sarcopenia and fractures remained significant after excluding aforementioned study from the meta-analysis.

Clinical implications

The robust outcome from our meta-analysis that sarcopenic individuals have a significantly higher risk of falls and fractures compared with non-sarcopenic individuals stresses the urgency for timely diagnosis and treatment of sarcopenia as a modifiable risk factor for falls and fractures. Interventions aimed at slowing down the decline of muscle mass and muscle strength and at treating sarcopenia should be considered. Current evidence suggests that progressive resistance training improves risk factors for falls and fractures such as muscle function, balance, and functional mobility.[16] However, it is unclear if the effect of progressive resistance training translates directly into a reduction in incidence of falls and fractures.[98] Further randomized controlled trials examining the effect of progressive resistance training on falls and fractures outcomes are warranted.

Strengths and limitations

In the absence of an international consensus definition of sarcopenia, we included studies with different diagnostic criteria of sarcopenia. In cases of missing data, we contacted authors of studies to obtain the data needed to compute ORs.

A limitation of the present review was that results of the included studies were expressed as crude as well as adjusted ORs with varying adjustments. The inconsistency in reporting effect size might have either overestimated or underestimated the overall association of interest. In addition, most of the studies included in the systematic review and meta-analysis were conducted among community-dwelling individuals and a limited number of institutionalized individuals. Subgroup analysis by continent was conducted instead of ethnicity because data stratified by ethnicity was not available.

Conclusions

This systematic review and meta-analysis highlights the positive association between sarcopenia, falls, and fractures. These findings are independent of study design, population, sex, sarcopenia definition, continent, and study quality. This strengthens the need to invest in studies evaluating sarcopenia prevention and intervention programmes on its effect on falls and fractures.

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The authors certify that they comply with the ethical guidelines for authorship and publishing of the *Journal of Cachexia, Sarcopenia and Muscle*.[99]

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Online Resource S1: Search strategy.
Online Resource S2: Newcastle-Ottawa Scale quality assessment explanation.
Online Resource S3: Flow chart of study selection.
Online Resource S4: Results of the Newcastle-Ottawa Scale quality assessment for (a) falls and (b) fractures.
Online Resource S5: Funnel plots showing the association between sarcopenia with (a) falls and (b) fractures.

Conflict of interest

S.S.Y.Y., E.M.R., V.K.P., M.C.T., W.K.L., C.G.M.M., and A.B.M. declare that they have no conflict of interest.

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Ethical approval

Ethical approval not required.

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