REVIEW

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Predictive validity of current sarcopenia definitions (EWGSOP2, SDOC, and AWGS2) for clinical outcomes: A scoping review

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Abstract

Over the last 3 years new definitions of sarcopenia by the Sarcopenia Definition and Outcome Consortium (2020, SDOC), European Working Group on Sarcopenia in Older People (2019, EWGSOP2) and Asian Working Group on Sarcopenia (2019, AWGS2) have been proposed. The objective of this scoping review was to explore predictive validity of these current sarcopenia definitions for clinical outcomes. We followed the PRISMA checklist for scoping reviews. Based on a systematic search performed by two independent reviewers of databases (Pubmed and Embase) articles comparing predictive validity of two or more sarcopenia definitions on prospective clinical outcomes published since January 2019 (the year these definitions were introduced) were included. Data were extracted and results collated by clinical outcomes and by sarcopenia definitions, respectively. Of 4493 articles screened, 11 studies (mean age of participants 77.6 (SD 5.7) years and 50.0% female) comprising 82 validity tests were included. Overall, validity tests on the following categories of clinical outcomes were performed: fracture (n = 40, assessed in one study), mortality (n = 18), function (n = 11), institutionalization (n = 7), falls (n = 4), and hospitalization (n = 2). Thereby, EWGSOP2 was investigated in 15 validity tests (18.3%) on all categories of clinical outcomes, whereas SDOC was investigated in four validity tests (4.9%) in one study on fractures in men only, and none of the validity tests investigated predictive validity by the AWGS2. However, we were not able to pool the data using a meta-analytic approach due to important methodological heterogeneity between the studies. We identified various definitions of clinical outcomes that were used to test predictive validity of sarcopenia definitions suggesting that an agreement on an operational definition of a clinical outcome is key to advance in the field of sarcopenia. Moreover, data on predictive validity using the sarcopenia definitions by the SDOC and AWGS2 are still scarce and lacking, respectively. In a next step, prospective studies including both women and men are needed to compare predictive validity of current sarcopenia definitions on defined key clinical outcomes.

Keywords Falls; Fracture; Mortality; Prediction; Validity; Older adults

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Introduction

Sarcopenia has become an increasingly popular field in clinical research and clinical practice.[1,2] With the inclusion of sarcopenia in the International Classification of Diseases (ICD-10) as a distinct diagnosis in 2016,[3] studies related to sarcopenia have increased even more rapidly. It is well acknowledged that sarcopenia is a common disease primarily affect-

ing older people being associated with adverse outcomes such as functional decline and mortality.[4]

Over the last 3 years new definitions of sarcopenia have been proposed by the European (EWGSOP2, 2019),[5] Asian (AWGS2, 2019),[6] and the American (SDOC, 2020)[7] Societies. Currently, there is no agreement on a unique definition of sarcopenia and a variety of diagnostic tools is being used in clinical practice and research.[8] For example, the definition of sarcopenia by the European Working Group on Sarcopenia in Older People (EWGSOP2)[5] is based on low muscle strength and low muscle mass, whereas the Sarcopenia Definitions and Outcomes Consortium (SDOC)[7] defines sarcopenia as low muscle strength and low gait speed, instead. Moreover, cut-off of sarcopenia components differ between sarcopenia definitions. Although the AWGS2[6] suggests a cut-off of 28 kg in men and 18 kg in women for low grip strength, the EWGSOP2[5] proposed a lower cut-off of 27 kg in men and 16 kg in women, respectively.

Prior studies investigated different clinical outcomes to assess predictive validity of various sarcopenia definitions. For example, Bischoff-Ferrari et al.[9] found that the sarcopenia definitions based on EWGSOP1 and based on Baumgartner et al. predicted rate of falling. Similarly, Zhang et al.[10] found that sarcopenia is associated with falls among community dwelling patients no matter if applying the EWGSOP1, AWGS, or FNIH definition of sarcopenia. Other studies investigated predictive ability of sarcopenia for the outcomes of fractures,[11] readmission,[12] and mortality.[13] However, all these studies included original data dating before 2019 and therefore did not investigate the recently published definitions of sarcopenia such as EWGSOP2 (2019), SDOC (2020), and AWGS2 (2019). Therefore, it is of interest if and to what extent the current sarcopenia definitions were tested for predictive validity on various clinical outcomes.

To contribute to advances in the broad field of sarcopenia the purpose of this paper is to provide an overview of literature by conducting a systematic search of the literature since 2019, the year when new consensus definitions of sarcopenia were published. The specific objective of this scoping review was to explore predictive validity of the current sarcopenia definitions for clinical outcomes.

Methods

The methodology for this scoping review was based on the recommendations by the PRISMA extension for scoping reviews by Tricco et al.[14] The review included the following five key phases: (1) identifying the research question, (2) identifying relevant studies, (3) study selection, (4) charting the data, and (5) collating summarizing and reporting the results.

Research question

This scoping review was guided by the question: 'What is the extent of predictive validity of the three recently proposed sarcopenia definitions (EWGSOP2, SDOC, and AWGS2) for what clinical outcomes in older adults?'

Data sources and search strategy

We conducted a systematic search in Pubmed and Embase using a protocol based on the extended version of the PRISMA statement on scoping reviews for conducting, and reporting scoping reviews. No language restrictions were applied in the search strategy. We identified additional articles by manual searching of cited references of relevant articles. The detailed search strategy is shown in the supporting information (*Figure* S1).

Eligibility criteria

We included original and published studies that compared predictive validity of two or more internationally recognized definitions of sarcopenia (diagnostic tool) regarding a clinical outcome. We included articles that were published from 1 January 2019 until 11 May 2022. We chose the time restriction in 2019, because guidelines by the updated EWGSOP2 and the AWGS2 were published in 2019, and the SDOC in 2020, respectively. We excluded articles that only included patients with a specific disease (e.g., only cancer patients), or aged $<$18 years. Articles investigating only sarcopenic obesity or osteosarcopenia were not included because definitions differ from sarcopenia definitions. Articles that only compared screening tools of sarcopenia (e.g., SARC-F) were excluded. Similarly, cross-sectional studies that reported associations of sarcopenia definitions on baseline characteristics were excluded. Non-English articles, letters, reviews, and editorials were also excluded.

Screening

Titles and abstracts were screened by two independent reviewers (A.K.S. and G.B.) who then performed a full-text screening based on the eligibility criteria. Cohen's kappa was 0.99 for inclusion of the studies indicating high inter-rater agreement to select studies. Discrepancies were resolved through discussion and eventually if no agreement could be achieved resolved by a third reviewer (G.F.).

Data summary and synthesis

Data were extracted using a standardized predefined data extraction tool. We extracted study characteristics (study

design, study size, setting, country, and year of publication) and patient characteristics (age, gender, inclusion and exclusion criteria), descriptive data on the sarcopenia definition (name of tool, methods to assess sarcopenia components (e.g., grip strength, gait speed, and prevalence of sarcopenia). For each validity test we extracted data on the definition and prevalence of the clinical outcome that was used to test predictive validity. Moreover, we extracted the corresponding estimates (e.g., hazard ratio (95% confidence interval) of the regression models and the covariates used for adjustment of the models that were reported for each definition and clinical outcome, respectively. If there were multiple estimates (unadjusted/adjusted) for the same sarcopenia definition and clinical outcome reported, we extracted data on the adjusted model that was highlighted to be the main model of interest by the authors.

The data were compiled in a spreadsheet for validation and coding.

Results

Overall, 4493 records were identified through the systematic search strategy (*Figure* 1). Thereof, 4366 were excluded based on screening the abstract, leaving 115 studies for full-text screening. In all, 11 records comprising 82 validity tests were included in this scoping review.

Study characteristics

Table 1 describes characteristics of included reports (*n* = 11). Mean age of participants was 77.6 (SD 5.7) years and 50% were female. Except for one study including hospitalized patients (Bianchi et al.[16]), the other studies were conducted among community-dwelling participants. The studies were conducted in various countries (Australia, Belgium, Brazil, China, Italy, Korea, Sweden, and United

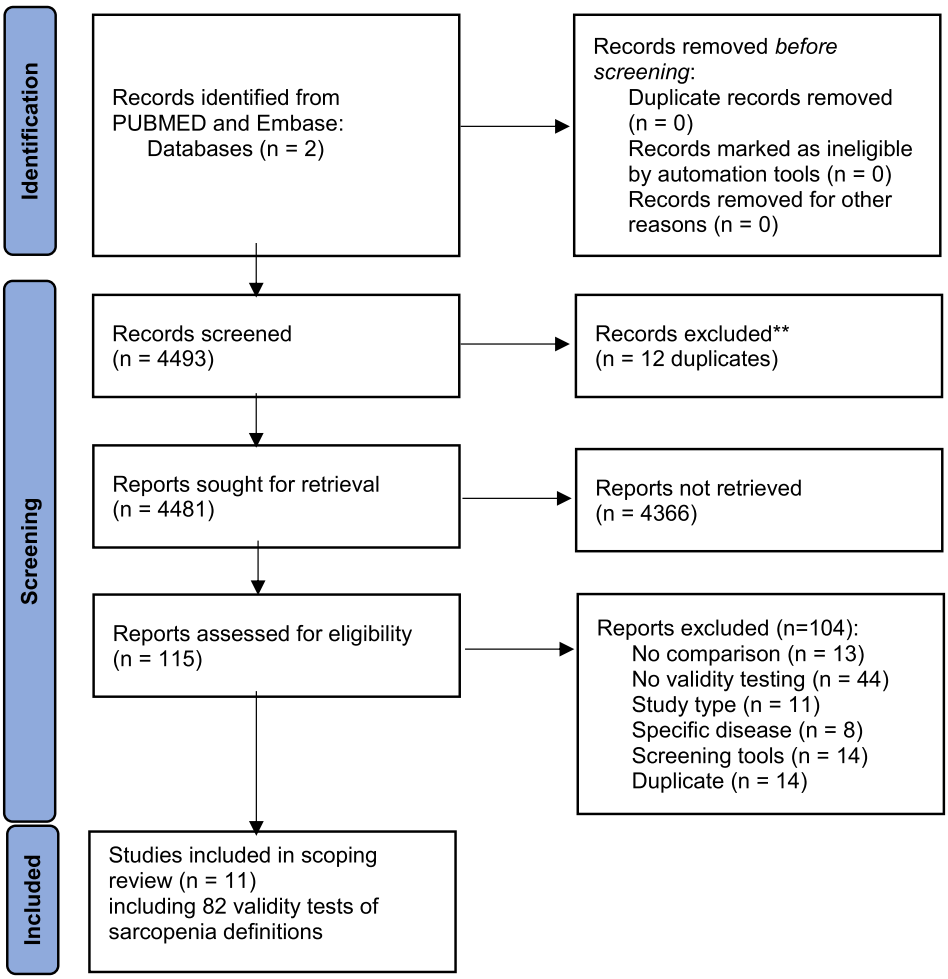

Figure 1 Flow chart.

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Table 1 Characteristics of included studies (n = 11)

Author, year of publication	Country	Number of participants	Mean age	Female	Study participants	Assessments used to diagnose sarcopenia	Definitions of sarcopenia	Prevalence of sarcopenia by definition	Clinical outcome(s) investigated
Bacchettini, 2020[15]	Brazil	1291	N.r.	63%	Community, aged 60+	Grip strength, calf circumference, gait speed	EWGSOP1 EWGSOP2	8.8% 3.4%	Mortality
Bianchi, 2020[16]	Italy	610	80.2	55.8%	Hospitalized, aged 65+	Grip strength, BIA	EWGSOP2 FNIH	22.8% 23.9%	Mortality
Costanzo, 2020[17]	Italy	535	77	53.6%	Community, aged 65+ Exclusion criteria: no BIA measurement, disabled, died within 3 years	Grip strength or chair rise, BIA	EWGSOP1 EWGSOP2	6.2% 3.2%	Mortality, function (disability)
Franzon, 2019[18]	Sweden	287	87	0%	Community, men, birth cohort	Grip strength, DXA, gait speed	EWGSOP1 EWGSOP2	21% 20%	Function (independent ageing)
Harvey, 2021[19]	United States, Sweden, China	10 411	73.5[a]	0%	Community, men aged 65+ from three cohorts in the United States, Sweden, China	Grip strength, or chair rise, DXA, gait speed	Baumgartner Delmonico FNIH1 IWGS EWGSOP1 EWGSOP2 SDOC Morley AWGS FNIH2	21%[a] 21% 17% 4% 4% 5.5% 1.7% 2% 2% 0.9%	Fractures (overall fractures, osteoporotic fractures, major osteoporotic fractures, and hip fractures)
Jang, 2020[20]	Korea	1408	74.1	N.r.	Community, aged 65+	Grip strength, BIA, gait speed	EWGSOP1 EWGSOP2	35.2% 26.3%	Mortality and Institutionalization
Locquet, 2019[21]	Belgium	534	73.5	60.5%	Community, aged 65+	Grip strength, DXA, gait speed and SPPB	EWGSOP1 IWGS Morley AWGS1 FNIH1	13.6% 18.4% 8.6% 6.6% 5.6%	Function (physical disability), Institutionalization, mortality
Sim, 2019 (falls)[22]	Australia	903	79.9	100%	Community, aged 70+, measures of grip strength, ALM, TUG available	Grip strength, DXA, TUG	EWGSOP1 FNIH1	9.4% 24.1%	Falls (falls-related hospitalization)

(*Continues*)

Table 1 (continued)

Author, year of publication	Country	Number of participants	Mean age	Female	Study participants	Assessments used to diagnose sarcopenia	Definitions of sarcopenia	Prevalence of sarcopenia by definition	Clinical outcome(s) investigated
Sim, 2019 (mortality)[23]	Australia	903	79.9	100%	Community, aged 70+, measures of grip strength, ALM, TUG available	Grip strength, DXA, TUG	EWGSOP1 FNIH1	24.1% 9.4%	Mortality
Sobestiansky, 2019[24]	Sweden	287	86.6	0%	Community, men aged 85–89	Grip strength, DXA, gait speed	EWGSOP1 EWGSOP2 FNIH1	21% 20% 8%	Mortality
Wallengren, 2021[25]	Sweden	884	70.5[b]	56%[b]	Community, two birth cohorts (70 years, and 85 years)	Grip strength, DXA, gait speed	EWGSOP1 EWGSOP2	3.1% 2.8%	Mortality, function (ADL dependence)
Yang, 2019[26]	China	384	71.5	58.3%	Community, aged 60+ Exclusion criteria: pacemaker, unable to walk, unable to talk, severe mental illness, severe renal failure, severe heart failure, chronic visible oedema	Grip strength, BIA, gait speed	EWGSOP1 EWGSOP2	27.3% 26.8%	Falls, hospitalization

Abbreviations: n.r., not reported; EWGSOP, European Working Group on Sarcopenia in Older People; SDOC, Sarcopenia Definitions and Outcomes Consortium, FNIH, Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia project; IWGS, International Working Group on Sarcopenia Definition; AWGS, Asian Working Group on Sarcopenia; BIA, bioelectrical impedance analysis; DXA, dual energy X-ray absorptiometry; TUG, timed get up and go test; SPPB; short physical performance battery; ALM, appendicular lean muscle mass; ADL, activities of daily living.

[a]Results are only displayed for the US cohort (data for cohort from Sweden, and Hong Kong cohorts in accordance to paper by Harvey et al.).

[b]Results are only displayed for one birth cohort (the 70-year); cohort (data for the second birth cohort (85-year) are displayed in the article by Wallengren et al.).

Name of sarcopenia definition	Low muscle strength (grip strength)		Low muscle mass (appendicular skeletal muscle mass/height^2 ratio)		Low muscle performance (gait speed)
	Women	Men	Women	Men	Women and men
Baumgartner			≤5.45 kg/m^2	≤7.26 kg/m^2	
Delmonico			≤5.67 kg/m^2	≤7.25 kg/m^2	
FNIH1			<0.512 kg/kg/m$^{2\,a)}$	<0.789 kg/kg/m$^{2\,a)}$	
AWGS2	<18kg	<28kg	<5.4 kg/m$^{2\,b)}$	<7.0 kg/m$^{2\,b)}$	
EWGSOP2	<16 kg **OR** chair rise test >15sec	<27 kg	<5.5 kg/m^2	<7.0 kg/m^2	
FNIH2	<16 kg	<26 kg	<0.512 kg/kg/m$^{2\,a)}$	<0.789 kg/kg/m$^{2\,a)}$	
IWGS			≤5.67 kg/m^2	≤7.23 kg/m^2	≤1.0 m/sec
Morley			≤5.18 kg/m^2	≤6.81 kg/m^2	<1.0m/sec
AWGS1	<18kg ( )$^{c)}$ <26kg		<5.4 kg/m^2	<7.0 kg/m^2	( )$^{c)}$ <0.8m/sec
EWGSOP1	<20 kg	<30 kg	<5.5 kg/m^2 ( )$^{d)}$	<7.26 kg/m^2	( )$^{d)}$ <0.8m/sec **OR** SPPB ≤8 points
SDOC	<20 kg	<35.5 kg			<0.8m/sec

Figure 2 Summary of criteria and corresponding cut-off values for sarcopenia definitions. Abbreviations: EWGSOP, European Working Group on Sarcopenia in Older People; SDOC, Sarcopenia Definitions and Outcomes Consortium, FNIH, Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia project; IWGS, International Working Group on Sarcopenia Definition; AWGS, Asian Working Group on Sarcopenia; ASM, appendicular skeletal muscle mass; ALM, appendicular lean mass; BMI, body mass index; SPPB, short physical performance battery. (A) Cut-off for appendicular skeletal muscle mass/BMI ratio. (B) Cut-off for DXA. (C) Low muscle strength and/or low muscle performance. (D) Low muscle mass and/or low muscle performance.

States). Study duration ranged between 12 and 130 months. Overall, data of 18 437 participants are described in this scoping review.

Overall, we identified the following 13 unique clinical outcomes that were used to test predictive validity of sarcopenia definitions: Falls-related hospitalization, incident falls, incident fractures, osteoporotic fractures, major osteoporotic fractures, hip fractures, independent ageing, physical disability, disability, activities of daily living (ADL) dependence, incident hospitalization, institutionalization, and mortality (*Table* 1). To summarize data we categorized clinical outcomes that were used to test predictive validity into the following six categories of clinical outcomes: (1) falls (falls-related hospitalization and incident falls); (2) fractures (incident fractures, osteoporotic fractures, major osteoporotic fractures, and hip fractures); 3) function (independent ageing,

physical disability, disability, and ADL dependence); (4) hospitalization (incident hospitalization); (5) institutionalization; and (6) mortality (*Table* 1). Most studies (n = 7) compared sarcopenia definitions on one outcome (e.g., mortality), while some publications (n = 4) performed validity tests for several clinical outcomes.

The following definitions of sarcopenia (n = 10) were tested for predictive validity in these studies: AWGS1, Baumgartner, Delmonico, EWGSOP1, EWGSOP2, FNIH, FNIH2, IWGS, Morley, and SDOC. A summary figure displaying criteria and cut-offs for definitions of sarcopenia are displayed in *Figure* 2.

Overall, mean prevalence of sarcopenia was 13.1% ranging between 0.9% and 35.2% depending on the study and the definition of sarcopenia that was applied. Measurement methods to assess components of sarcopenia (muscle strength, muscle mass, and physical performance) varied between studies.

Characteristics of validity tests

Among the 82 validity tests the following proportions of sarcopenia definitions were applied: EWGSOP1 (19, 23.2%), EWGSOP2 (15, 18.3%), FNIH2 (11, 13.4%), AWGS1 (7, 8.5%), IWGS (7, 8.5%), Morley (7, 8.5%), Baumgartner (4, 4.9%), Delmonico (4, 4.9%), FNIH1 (4, 4.9%), and SDOC (4, 4.9%). None of the validity tests investigated the definition by AWGS2.

Figure 3 visually displays the distribution of 82 validity tests according to the clinical outcome investigated and categorized between the three most recent sarcopenia definitions (AWGS2, EWGSOP2, and SDOC) and former sarcopenia definitions (including AWGS1, Baumgartner, Delmonico, EWGSOP1, FNIH1, FNIH2, and Morley). Among the 82 validity tests, the majority of validity tests (n = 40, 48.8%) evaluated the association of sarcopenia definitions on the outcome of fractures including data of 10 411 participants. Eighteen validity tests (22.0%) investigated the association of sarcopenia definitions on the outcome mortality including 5044 participants. Eleven validity tests (13.40%) investigated predictive validity of sarcopenia definitions on a function outcome including 1706 participants. Seven validity tests (8.5%) were performed on institutionalization including 1942 participants, and four validity tests (4.9%) reported associations of sarcopenia definition on the outcome of falls including data of 1287 participants. Finally, two validity tests (2.4%) were performed on hospitalization including 384 participants.

Estimates of validity tests

Detailed estimates (hazard ratio, 95% confidence intervals) of all validity listed by clinical outcomes are displayed in *Table* 2. Estimates that reached statistical significance are highlighted in bold. We identified one large cohort[19] including 10 411 men in three countries (United States, Sweden, and China) that reported results of totally 40 validity tests of different sarcopenia definitions on different types of fractures (*Table* 2). Thereby, the SDOC definition showed the strongest association to all four types of fractures (overall fractures,

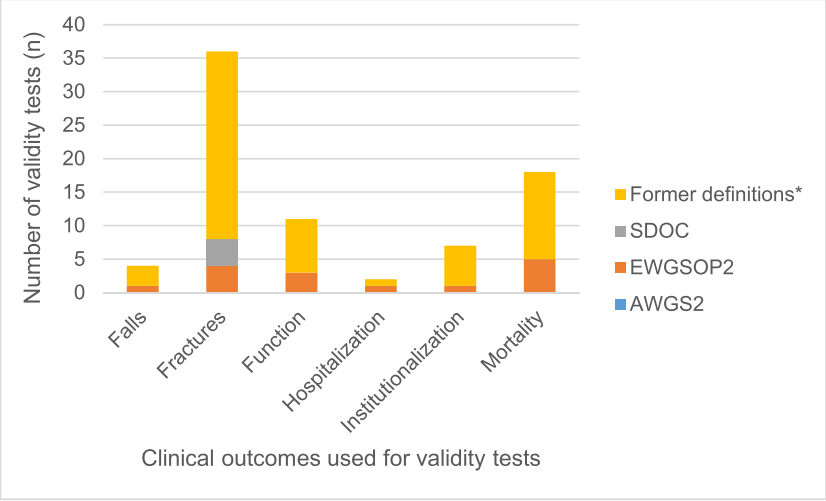

Figure 3 Clinical outcomes used to test predictive validity of sarcopenia definitions by SDOC, EWGSOP2, AWGS2 and former sarcopenia definitions (n = 82 validity tests). *Former definitions include the following sarcopenia definitions: AWGS1, Baumgartner, Delmonico, EWGSOP1, FNIH1, FNIH2, IWGS, and Morley. Abbreviations: EWGSOP, European Working Group on Sarcopenia in Older People; SDOC, Sarcopenia Definitions and Outcomes Consortium; AWGS, Asian Working Group on Sarcopenia.

Table 2 Results of validity tests of sarcopenia definitions (n = 82), listed by categories of clinical outcomes

Author, year	Clinical outcome	Study duration (months)[e]	Prevalence of clinical outcome, overall (%)	Result of validity tests		Included variables for adjustment in validity tests as reported by the authors
				Name of sarcopenia definition	HR (95% CI)	
Falls						
Sim, 2019	Falls-related hospitalization	60	34.8%	EWGSOP1	1.18 (0.8–1.75)	Age
				FNIH2	0.93 (0.51–1.70)	
Yang, 2019	Incident falls	12	25.5%	EWGSOP1	1.52 (0.99–2.34)	Age, gender, coronary heart disease, cognitive impairment, history of falls
				EWGSOP2	**1.86 (1.22–2.83)**	
Fractures						
Harvey, 2021	Incident fractures	130[a,b]	19%	Baumgartner	1.04 (0.94, 1.15)	Age, follow up time, prior falls, femoral neck BMD
				Delmonico	1.06 (0.96, 1.18)	
				FNIH1	1.06 (0.94, 1.20)	
				FNIH2	1.06 (0.71, 1.59)	
				IWGS	1.15 (0.95, 1.39)	
				EWGSOP1	**1.29 (1.06, 1.58)**	
				EWGSOP2	**1.31 (1.08, 1.58)**	
				SDOC	**1.52 (1.15, 1.96)**	
				Morley	1.20 (0.93, 1.55)	
				AWGS1	**1.47 (1.15, 1.88)**	
Harvey, 2021	Osteoporotic fractures	130[a,b]	15%	Baumgartner	1.02 (0.91, 1.15)	Age, follow up time, prior falls, femoral neck BMD
				Delmonico	1.04 (0.93, 1.17)	
				FNIH1	1.04 (0.90, 1.19)	
				FNIH2	1.05 (0.66, 1.66)	
				IWGS	1.13 (0.91, 1.39)	
				EWGSOP1	**1.36 (1.09, 1.69)**	
				EWGSOP2	**1.35 (1.10, 1.65)**	
				SDOC	**1.60 (1.21, 2.12)**	
				Morley	1.12 (0.84, 1.48)	
				AWGS1	**1.52 (1.17, 1.98)**	
Harvey, 2021	Major osteoporotic fractures	130[a,b]	7%	Baumgartner	1.05 (0.92, 1.20)	Age, follow up time, prior falls, femoral neck BMD
				Delmonico	1.06 (0.93, 1.22)	
				FNIH1	1.04 (0.89, 1.21)	
				FNIH2	0.95 (0.55, 1.64)	
				IWGS	1.24 (0.98, 1.56)	
				EWGSOP1	**1.34 (1.04, 1.73)**	
				EWGSOP2	**1.39 (1.11, 1.75)**	
				SDOC	**1.43 (1.03, 1.99)**	
				Morley	1.24 (0.91, 1.69)	
				AWGS1	**1.54 (1.15, 2.07)**	
Harvey, 2021	Hip fractures	130[a,b]	3%	Baumgartner	1.01 (0.82, 1.23)	Age, follow up time, prior falls, femoral neck BMD
				Delmonico	1.03 (0.85, 1.26)	

(*Continues*)

Table 2 (continued)

Author, year	Clinical outcome	Study duration (months)[e]	Prevalence of clinical outcome, overall (%)	Result of validity tests		Included variables for adjustment in validity tests as reported by the authors
				Name of sarcopenia definition	HR (95% CI)	
				FNIH1	0.84 (0.65, 1.08)	
				FNIH2	0.85 (0.37, 1.95)	
				IWGS	1.39 (1.00, 1.93)	
				EWGSOP1	1.18 (0.80, 1.75)	
				EWGSOP2	**1.55 (1.02, 2.36)**	
				SDOC	**2.36 (1.57, 3.56)**	
				Morley	1.18 (0.75, 1.87)	
				AWGS	**1.60 (1.03, 2.49)**	
Functional outcome						
Franzon, 2019	Independent ageing	60	69%	EWGSOP1	OR (95% CI): 1.04 (0.40–2.74)	Age, smoking status, Charlson comorbidity index, total fat mass
				EWGSOP2	OR (95% CI): 1.14 (0.43–3.06)	
Locquet, 2019	Physical disability	35	16.4%	EWGSOP1	OR (95% CI): 1.70 (0.87–3.35)	Age, sex, BMI, number of comorbidities, number of drugs, cognitive status, nutritional status
				IWGS	OR (95% CI): 1.18 (0.64–2.18)	
				Morley	OR (95% CI): 1.55 (0.69–3.45)	
				AWGS1	OR (95% CI): 2.98 (0.98–7.07)	
				FNIH2	OR (95% CI): 1.74 (0.72–4.22)	
Costanzo, 2020	Disability	36	15.9%	EWGSOP1	RR: 2.16 (0.99–4.29)	Age, sex, SAFE score
				EWGSOP2	RR: 2.57 (0.4–9.06)	
Wallengren, 2021	ADL dependence[c]	50[b]	4.4%	EWGSOP1	**OR (95% CI): 2.2 (1.2–3.9)**	Cohort, sex
				EWGSOP2	**OR (95% CI): 2.2 (1.2–4.0)**	
Hospitalization						
Yang, 2019	Incident hospitalization	12	13.3%	EWGSOP1	1.51 (0.81–2.77)	Age, gender, coronary heart disease, cognitive impairment, history of falls
				EWGSOP2	1.56 (0.87–2.82)	
Institutionalization						
Jang, 2020	Mortality and institutionalization	30[b]	10.4%	EWGSOP1	**2.19 (1.50–3.22)**	Age, gender, baseline disability, multimorbidity
				EWGSOP2	1.14 (0.58–2.23)	
Locquet, 2019	Institutionalization	36	2.0%	EWGSOP1	0.39 (0.05–3.15)	Age, sex, BMI, number of comorbidities, number of drugs, cognitive status, nutritional status
				IWGS	1.31 (0.29–6.00)	
				Morley	0.78 (0.10–5.98)	
				AWGS1	0.78 (0.10–5.98)	
				FNIH2	1.19 (0.20–7.04)	
Mortality						
Bacchettini, 2020		30[b]	6.8%	EWGSOP1	1.18 (0.53–2.65)	

(*Continues*)

Table 2 (continued)

Author, year	Clinical outcome	Study duration (months)[e]	Prevalence of clinical outcome, overall (%)	Result of validity tests		Included variables for adjustment in validity tests as reported by the authors
				Name of sarcopenia definition	HR (95% CI)	
						Age, sex, marital status, smoking, physical activity at leisure, BMI, comorbidities, depressive symptoms
				EWGSOP2	1.36 (0.52–3.57)	
Bianchi, 2020		36	33.8%	EWGSOP2	**1.84 (1.33–2.57)**	Age, gender, short portable mental status questionnaire, severe activities of daily living, Charlson comorbidity index
				FNIH2	1.26 (0.89–1.79)	
Costanzo, 2020		36	10.5%	EWGSOP1	1.29 (0.41–4.03)	Age, sex, BMI, marital status, education, comorbidities
				EWGSOP2	2.95 (0.86–10.16)	
Locquet, 2019		36	6.0%	EWGSOP1	**2.93 (1.17–7.35)**	Age, sex, BMI, number of comorbidities, number of drugs, cognitive status, nutritional status
				IWGS	**2.94 (1.19–7.25)**	
				Morley	**2.79 (1.11–5.07)**	
				AWGS1	**4.43 (1.64–11.96)**	
				FNIH2	2.35 (0.63–8.78)	
Sim, 2019		60	10.5%	EWGSOP1	**1.88 (1.24–2.85)**	Age
				FNIH2	1.08 (0.56–2.08)	
Sobestiansky, 2019		36	21%	EWGSOP1	**1.95 (1.12–3.4)**	Age, Charlson comorbidity index, education, smoking, MMSE
				EWGSOP2	1.70 (0.94–3.05)	
				FNIH2	1.65 (0.73–7.72)	
Wallengren, 2021		50	9.3%	EWGSOP1	**2.3 (1.0–4.9)**	Cohort, sex
				EWGSOP2	**2.4 (1.1–5.2)**	

Note: Estimates that reach statistical significance are highlighted in bold.
Abbreviations: EWGSOP, European Working Group on Sarcopenia in Older People; SDOC, Sarcopenia Definitions and Outcomes Consortium, FNIH, Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia project; IWGS, International Working Group on Sarcopenia Definition; AWGS, Asian Working Group on Sarcopenia; HR, hazard ratio; CI, confidence interval, MMSE, Mini-mental status examination; BMI, body mass index; BMD, bone mineral density; SAFE, Survey of Activities and Fear of Falling in the Elderly.
[a]Results are only displayed for the US cohort (data for cohort from Sweden, and Hong Kong cohorts in accordance to paper by Harvey et al.).
[b]Mean follow-up time reported.
[c]Defined as Barthel index $<$100 points.
[d]Defined as: MMSE $\geq$ 25points, absence of diagnosis of dementia, community-dwelling, independency in personal care and ability to walk outdoors alone.
[e]The term 'study duration' refers to the time point when the clinical outcome was assessed (months after baseline).
[f]Hazard ratio (95% confidence interval) is reported unless otherwise indicated.

major osteoporotic fractures, osteoporotic fractures, and hip fractures). For example, this study reported a hazard ratio for sarcopenia on incident fractures of 1.31 (95% CI, 1.08, 1.58) based on the definition by the European Working Group on Sarcopenia 2019 (EWGSOP2) compared with 1.52 (95% CI, 1.15, 1.96) based on the definition by the Sarcopenia Definitions and Outcomes Consortium 2020 (SDOC). Similarly, hazard ratio for hip fractures was 1.55 (95% CI, 1.02, 2.36) based on EWGSOP2 versus 2.36 (95% CI, 1.57, 3.56) based on SDOC.

However, we were not able to pool the data using a meta-analytic approach due to important methodological heterogeneity between the studies. First, as shown in *Table* 2, studies were conducted in different patient populations, some of them only including men. Second, the methodological approach on how to assess components of sarcopenia varied between studies. For example, some studies used Dual Energy X-ray Absorptiometry (DXA), and some used bioelectrical impedance analysis (BIA) to assess the sarcopenia component of muscle mass (*Table* 2). Third, definitions of outcomes differed within the category of outcomes (*Table* S1). For example, the clinical outcome of fractures in our studies included validity test on overall fractures, osteoporotic fractures, major osteoporotic fractures, and hip fractures not permitting pooling of results. Similarly, the outcome of function included overall disability, physical disability, independent ageing, and dependence in activities of daily living. Moreover, most of the studies addressed solely one clinical outcome of interest (*Table* S1). As a result, we did not have enough studies to permit pooling of data per clinical outcome.

Discussion

This scoping review identified 13 different clinical outcomes that were used to test predictive validity of two or more sarcopenia definitions in the last 3 years. The majority of validity tests from one large cohort in men investigated sarcopenia definitions on four types of fractures. Overall, the sarcopenia definitions by EWGSOP2 was investigated in a number of predictive validity tests, whereas a minor number of validity tests was performed for SDOC, and none for the AWGS2.

To our knowledge, this is the first scoping review summarizing studies that investigated predictive validity of two or more sarcopenia definitions since publication of the EWGSOP2 criteria in 2019. In specific, we identified the clinical outcomes of falls, fractures, function, hospitalization, institutionalization, and mortality were used to test predictive validity of sarcopenia definitions. In contrast, previous meta-analyses summarized results on one outcome only, and did not include current sarcopenia definitions such as EWGSOP2, AWGS2, and SDOC. For example, Huang et al. found in his meta-analysis that sarcopenia based on different former definitions (EWGSOP1, AWGS1, and IWGS) increased the risk of hip fractures showing a pooled hazard ratio of 1.42 (95% CI 1.18–1.71).[11]

In our scoping review, the two specific outcomes related to muscle performance and function - fractures and falls - were used to investigate predictive validity of sarcopenia definitions. Thereby, we identified a major proportion of validity tests assessed predictive validity on fractures, but only a few number of validity tests were performed on falls. Of note, the validity tests on fractures were all performed in the same study, including only men in three cohorts from the United States, Hong-Kong and Sweden. From a pathophysicological perspective, it is plausible that sarcopenia is associated with impaired gait and balance resulting in increased rate of falls, which in turn results in increased rates of fractures. Accordingly, prior studies investigated predictive validity of sarcopenia definitions proposed before 2019 on the disease-specific outcome of falls. For example, Bischoff-Ferrari et al. found that the definitions by Baumgartner and EWGSOP1 best predicted rate of falls over 3 years (RR = 1.54; 95% CI 1.09–2.18) among 445 community-dwelling seniors (mean age 71 years).[9]

We further found that a substantial proportion of validity tests were performed to test predictive validity of sarcopenia definitions on general health outcomes (mortality and functional outcome) and on outcomes related to health-care use (hospitalization and institutionalization). It is beyond dispute that all these outcomes are considered adverse outcomes. Nevertheless, it is a subject of debate if the choice of a sarcopenia definition should be based on results of predictive validity on global health outcomes only, or if rather disease-specific outcomes (such as falls and fractures) should be primarily considered. Major part of the confusion what sarcopenia definition should be agreed on may originate from the lack of clarity what clinical outcome should be used to investigate predictive validity of sarcopenia definitions. This is in contrast to other medical diagnoses, for which clear outcomes have been defined for validation of diagnostic tools. For example, the outcome of hip fracture is used as a standard outcome to test predictive validity of diagnostic tools to estimate fracture risk in the field of osteoporosis.[27]

We also found that predictive validity varied between sarcopenia definitions. Thereby, the SDOC definition showed the strongest association to all four types of fractures (overall fractures, major osteoporotic fractures, osteoporotic fractures, and hip fractures). The differences between sarcopenia definitions may be explained by the fact, that the definitions are based on different criteria, and use different cut-off definitions for these criteria. For example, while the sarcopenia definitions by the SDOC is defined as the combination of low grip strength and low gait speed, the definition by the EWGSOP2 is based on low grip strength (using other cut-off

points than the SDOC), and low muscle mass, instead. This example reflects the ongoing debate, what clinical surrogates do most reliably and validly reflect the gold standard of sarcopenia diagnosis.

Limitations

There are several limitations to our study. First, methodological approaches of measuring sarcopenia, clinical outcomes and testing associations varied between studies, thus not permitting pooling of results. Nevertheless, we were able to add important findings to literature using the approach of a scoping review. Second, while we used predefined selection criteria, it is possible that we missed an article. However, we limited selection bias by using a predefined search strategy, and by screening the articles for selection by two independent reviewers. Third, based on our predefined research question we did not include studies that investigated predictive validity of one sarcopenia definition only. The focus of our scoping review was rather to summarize studies addressing the question of comparing predictive validity of different sarcopenia definitions. Forth, there are other factors that may have an impact on the results of validity tests other than the sarcopenia definitions and clinical outcomes. The study size, setting of the participants, the definitions of outcomes may influence the results of validity tests. Finally, the conclusions of our scoping review is limited by the data of the original studies. For example, predictive validity of the clinical outcome of fractures was investigated in men only, not permitting extrapolation to women.

Implications

Our results highlight that various definitions of clinical outcomes are used to investigate predictive validity of sarcopenia definitions suggesting that this heterogeneity is hampering advances in the field of sarcopenia. Future studies should therefore focus on comparison of sarcopenia definitions on key clinical outcomes. From a pathophysicological point of view, clinical outcomes that are most closely related to sarcopenia such as falls and fractures may be preferred for assessing predictive validity. This is also in accordance with latest data from experts in the field considering falls as most import outcome.[28] Thereby, agreement on detailed operational definition of clinical outcomes (e.g., falls-related hospitalization, or overall self-reported falls, overall fractures, or osteoporotic fractures) is key to enable meta-analytical comparison of predictive validity of sarcopenia definitions in the future.

Our data further suggest that predictive validity tests using the most recently published definition (SDOC) show promising results, however, are limited in terms of number of validity tests and only refer to data in men. Data on predictive validity of the AWGS2 definition is even lacking. Thus, further prospective studies are needed to investigate and compare predictive validity of the currently proposed definitions by the EWGSOP2, SDOC, and AWGS2 including women, as well.

Our scoping review does not answer the question, which sarcopenia definition is the most valid definition to apply as a gold-standard in clinical practice and clinical research. However, our results clearly demonstrate that predictive validity of sarcopenia definitions vary between definitions and clinical outcomes suggesting that data on the diagnosis of sarcopenia need to be interpreted and compared with caution.

Conclusion

In conclusion, our scoping review identified various heterogeneous definitions of clinical outcomes used to test predictive validity of sarcopenia definitions suggesting that it is key to agree on an operational definition of a clinical outcome. Moreover, we found that the EWGSOP2 definition was investigated in a substantial number of validity tests, whereas the SDOC and the AWGS2 were tested in a minority and none of the validity tests, respectively. As a next step, further prospective cohort studies are needed to evaluate predictive validity of sarcopenia definitions using most recent definitions among women and men on key clinical outcomes eventually promoting advances in the field of sarcopenia.

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The authors of this manuscript certify that they comply with the ethical guidelines for authorship and publishing in the *Journal of Cachexia, Sarcopenia and Muscle*.[29]

Conflict of interest

All authors declare that they have no conflict of interest.

Online supplementary material

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

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