REVIEW

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Global epidemiological features and impact of osteosarcopenia: A comprehensive meta-analysis and systematic review

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Abstract

Osteosarcopenia is defined as the concurrent occurrence of osteopenia/osteoporosis and sarcopenia. The aim of the current study was to perform a systematic review with meta-analysis to determine the global prevalence, risk factors and clinical outcomes of osteosarcopenia. This review was registered in PROSPERO (CRD42022351229). PubMed, Cochrane, Medline and Embase were searched from inception to February 2023 to retrieve eligible observational population-based studies. Pooled osteosarcopenia prevalence was calculated with 95% confidence interval (CI), and subgroup analyses were performed. The risk factor of osteosarcopenia and its association with clinical outcomes were expressed as odds ratio (OR) and hazard ratio (HR), respectively. Heterogeneity was estimated using the I^2 test. Study quality was assessed using validated instruments matched to study designs. The search identified 55 158 studies, and 66 studies (64 404 participants, mean age from 46.6 to 93 years) were analysed in the final analysis, including 48 cross-sectional studies, 17 cohort studies and 1 case–control study. Overall, the pooled prevalence of osteosarcopenia was 18.5% (95% CI: 16.7–20.3, I^2 = 98.7%), including 15.3% (95% CI: 13.2–17.4, I^2 = 97.6%) in men and 19.4% (95% CI: 16.9–21.9, I^2 = 98.5%) in women. The prevalence of osteosarcopenia diagnosed using sarcopenia plus osteopenia/osteoporosis was 20.7% (95% CI: 17.1–24.4, I^2 = 98.55%), and the prevalence of using sarcopenia plus osteoporosis was 16.1% (95% CI: 13.3–18.9, I^2 = 98.0%). The global osteosarcopenia prevalence varied in different regions with 22.9% in Oceania, 21.6% in Asia, 20.8% in South America, 15.7% in North America and 10.9% in Europe. A statistically significant difference was found in the subgroups of the study population between the hospital (24.7%) and community (12.9%) (P = 0.001). Frailty (OR = 4.72, 95% CI: 2.71–8.23, I^2 = 61.1%), malnutrition (OR = 2.35, 95% CI: 1.62–3.40, I^2 = 50.0%), female sex (OR = 5.07, 95% CI: 2.96–8.69, I^2 = 73.0%) and higher age (OR = 1.10, 95% CI: 1.06–1.15, I^2==86.0%) were significantly associated with a higher risk for osteosarcopenia. Meta-analysis of cohort studies showed that osteosarcopenia significantly increased the risk of fall (HR = 1.54, 95% CI: 1.20–1.97; I^2 = 1.0%, three studies), fracture (HR = 2.13, 95% CI: 1.61–2.81; I^2 = 67.8%, seven studies) and mortality (HR = 1.75, 95% CI: 1.34–2.28; I^2 = 0.0%, five studies). Despite the heterogeneity arising from varied definitions and criteria, our findings highlight a significant global prevalence of osteosarcopenia and its negative impact on clinical health. Standardizing diagnostic criteria for osteosarcopenia would be advantageous in the future, and early detection and management should be emphasized in this patient population.

Keywords Fracture; Frailty; Mortality; Osteosarcopenia; Osteoporosis; Prevalence; Sarcopenia

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Introduction

Sarcopenia and osteoporosis/osteopenia are common geriatric diseases. Patients who have osteoporosis or osteopenia have lower bone mineral density (BMD) and are more likely to fracture.[1] Patients who suffer from sarcopenia experience a decrease of muscle strength, mass and power, which increases their risk of falling, hospitalization, disability and even death.[2] Studies have demonstrated that these illnesses share common risk factors[3,4] and often coexist and develop alongside one another.[4,5] Therefore, Duque et al. proposed a new concept of osteosarcopenia to define having both osteoporosis/osteopenia and sarcopenia.[4]

A growing body of pathophysiological and epidemiological evidence suggests that the muscular and skeletal systems of the elderly are mechanically interconnected at the macroscopic level during the process of decline, and at the microscopic level, muscle and skeletal tissues also secrete myokines and osteokines that interact with each other,[4,6,7] leading to a synergistic effect of loss of both[3,8,9] Therefore, due to macroscopic and microscopic crosstalk in muscle and bone tissue,[10] patients with osteosarcopenia tend to have poor activities of daily living and quality of life, which is substantially associated with a spectrum of negative outcomes.[11–13] Studies have shown that those who have osteosarcopenia are significantly more likely than non-osteosarcopenic groups to experience falls, fractures and even death.[11,14]

The prevalence of osteosarcopenia in hospitalized and community-dwelling older persons has been reported in various cross-sectional studies.[15–18] In a 2018 meta-analysis, a global prevalence of 5–37% was estimated for osteosarcopenia,[19] but without a breakdown by sub-regions, countries and geographical settings, which would have been helpful for interventional measures in particular settings and for identifying the areas where more research is required. Moreover, no single study has synthesized data concerning potential risk factors for osteosarcopenia which may be helpful for physicians to early screen those at higher risk and prevent negative outcomes.

With a global population of two billion older adults by 2050, the patients with osteosarcopenia will continue to increase in the future, gradually becoming a new public issue in the world and posing a serious global health burden.[3,5,10] To our knowledge, there has been no study that has systematically and comprehensively synthesized data from all available studies to estimate the prevalence, risk factors and outcomes of osteosarcopenia. Hence, we performed a systematic review and meta-analysis to better characterize osteosarcopenia to provide a theoretical foundation for lowering the incidence of osteosarcopenia and improving adverse clinical outcomes.

Methods

We conducted and reported this systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[20] The full review protocol is available in the PROSPERO database, registration number: CRD42022351229. The quality of evidence was rated using the Newcastle-Ottawa Scale (NOS)[21] and the Agency for Healthcare Research and Quality (AHRQ).[22]

Databases and search strategies

We systematically searched the PubMed, Cochrane Library, Embase and Medline databases from inception to February 2023. Medical subject headings (MESH) terms, free terms, and suitable Boolean logical characters were used to construct the search formula, main search terms were related to osteosarcopenia (e.g., 'Osteo-sarcopeni*', 'Sarco-osteopeni*'), sarcopenia (e.g., 'Sarcopenia', 'Sarcopenic') and osteoporosis (e.g., 'Osteoporosis', 'Osteopenia', 'Bone Loss*', 'Metabolic Bone Disease', 'Low Bone Density'). Also, to ensure the accuracy of the search process, the search strategy was adjusted to fit each database. The references of the included articles, grey literature and the connected paper (www.connectedpapers.com) were screened to identify potential studies missed by the initial literature search. Subsequently, we repeated the search in January 2023 to update the data. The search strategy for each database is included in the Supplementary Search Strategy. Endnote X9–a was used to remove duplicates.

Inclusion and exclusion criteria

Observational population-based studies, either cross-sectional or cohort in design, that reported the prevalence of osteosarcopenia or focused on the related factors or clinical outcomes of the patients with osteosarcopenia were included. The following studies were excluded: (1) articles such as reviews, conferences, letters, cases and experimental studies for which valid data could not be extracted; (2) non-English literature; (3) pregnant women and patients younger than 18 years of age; (4) duplicate publications.

Data extraction

Data extraction was performed independently by two investigators (C. S. P. and X. X.) using a standardized data extraction form. First, the titles and abstracts of the articles were read to make a preliminary determination for inclusion in this review. Then, the final inclusion in the systematic review was further determined by reading the full text. Similar publications based on the same data source were carefully compared, and the one with the most comprehensive results or the most recent data was included.

The data extracted are as follows: (1) study characteristics (first author, publication year, country and study design); (2) participant details (sample size, mean age, sex ratio, country and region of population origin); (3) osteosarcopenia definition (diagnosis standards or scales of osteoporosis/osteopenia and sarcopenia); (4) related factors and clinical outcome (frailty, fracture, and mortality); (5) time of follow-up. Data on potential risk factors and clinical outcomes were recorded between groups of patients with osteosarcopenia and without osteosarcopenia.

Quality assessment

The quality of included articles was assessed by two independent authors (C. S. P. and X. X.), using scales based on the Newcastle-Ottawa Scale (NOS) and the Agency for Healthcare Research and Quality (AHRQ).

The NOS scale primarily evaluates cohort studies for representativeness, selection, comparability and outcome/exposure. The scale scores ranged from 0 to 9 points. Studies with a score of $\leq$3 indicated low quality study, score $\geq$7 indicated a high quality study, others were considered moderate quality.[21]

The 11-item AHRQ scale was used to assess the risk of bias in cross-sectional studies. Each question chose 'Yes' got a score of 1; 'No' and 'Unclear' were assigned a score of 0. Studies with a total score of 8–11 were considered high quality, 4–7 were medium quality, and 0–3 were low quality.[22]

Any disagreements in review, data extraction and quality assessment were resolved through discussions with a senior investigator (G. H. P).

Statistical analysis

The primary outcome of interest was the prevalence of osteosarcopenia. For cross-sectional and cohort studies, prevalence was extracted. Random effects models were used to calculate pooled prevalence rate with corresponding 95% confidence interval (CI), dependent on heterogeneity. Then, a series of subgroup analyses was performed to explore variations in the pooled prevalence among the following subgroups: (1) type of study, (2) whether the population was of advanced age ($\geq$80 years), (3) gender (male or female), (4) origin of the population, (5) different definitions of osteosarcopenia ('osteoporosis+sarcopenia', 'osteopenia+sarcopenia' or 'osteoporosis/osteopenia+sarcopenia'), (6) diagnostic criteria for osteoporosis/osteopenia (WHO or JOS or Other), (7) diagnostic criteria for sarcopenia (EWGSOP or AWGS or Other).

Secondary outcomes were related factors and clinical outcomes. We only included related factors or clinical outcomes that had been reported in at least three investigations in our meta-analysis. We transformed the number of incidences in the exposed and non-exposed groups was extracted to calculate effect sizes not given in the article. We also performed subgroup analyses for related factors and clinical outcomes reported in at least three studies according to pre-defined subgroups in prevalence analysis. For the clinical outcome, we in addition designed a subgroup of whether the follow-up time was long enough for the clinical outcome (with a 5-year cut-off). In addition, we also pooled the related factors extracted from the cross-section (effect size OR) and the clinical outcomes extracted from the cohort study (effect size HR) separately. Because all data were binary data, we transformed OR and HR into ln (OR) and ln (HR) for statistical analysis.

Heterogeneity was assessed using the I^2 statistic and Q test. $I^2 > 50\%$ was considered statistically significant heterogeneity. $P < 0.05$ is the threshold for statistical significance. For outcomes with high heterogeneity, we pooled using a random effects model If $I^2 > 50\%$, $P < 0.05$,[11] otherwise using the fixed-effects model. To explore the sources of heterogeneity in the results, we performed meta-regression for each subgroup. Publication bias of the results was assessed using funnel plots and performing Begg's tests. Finally, we performed sensitivity analysis of the results to identify the stability of the results.

All analyses were conducted using Stata (version 16.0) and R (version 4.3.1).

Results

Search results

A total of 5158 bibliographic records were initially identified through searches of PubMed, Cochrane, Embase and Medline. After removing 2018 duplicates and 1212 irrelevant records in titles and abstracts. Subsequently, two authors independently read the titles and abstracts to exclude 1778 citations, leaving 150 articles. After reading the full text of the remaining literature, a total of 61 papers fulfilled the

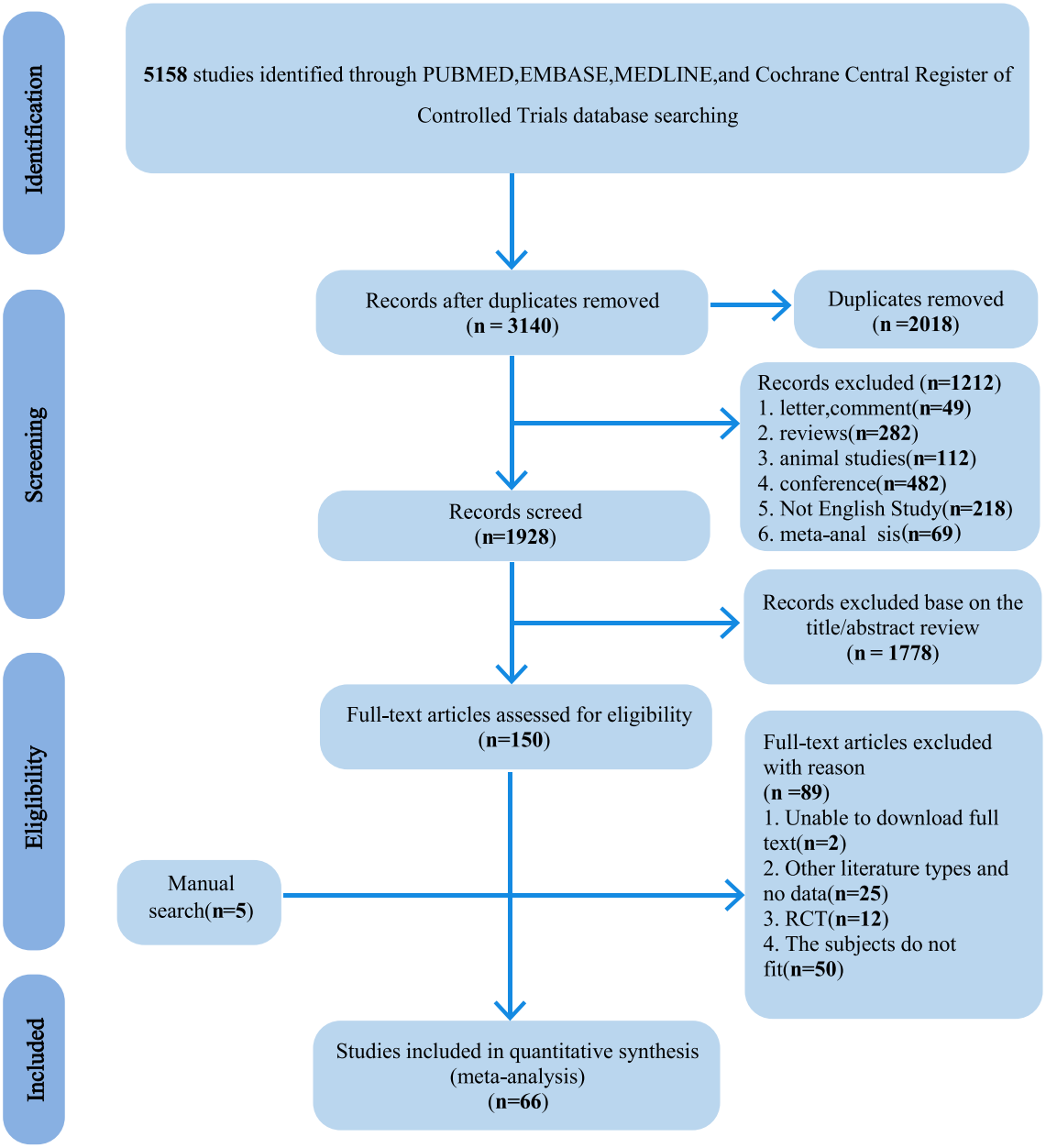

Figure 1 The flow diagram of studies selection.

inclusion criteria for this systematic review. Moreover, five additional papers were obtained by manually searching.[23–27] Finally, 66 articles fulfilled the selection criteria and were included in the meta-analysis (Figure 1).

Study summary and patient characteristics

A total of 66 studies involving 64 404 subjects fulfilled the selection criteria and were included in this systematic review. The characteristics of the included articles are given in Supporting Information S1. Generally, 48 were cross-sectional studies, 17 were cohort studies (11 prospective and 6 retrospective studies), and 1 was a case–control study. In addition, 56 (84.84%) of the included articles were published in the past 5 years (2018 and onwards). Most of the studies used 'Sarcopenia plus Osteoporosis' (n = 29, 43.93%) or 'Sarcopenia plus Osteopenia/Osteoporosis' (n = 21, 31.81%) for detecting osteosarcopenia. The study populations were mainly located in Asia (n = 28 550), Americas (n = 21 878), and Europe (n = 9497). And 37 019 (57.48%) were investigated in community-dwelling, and others were visited

in hospitals (n = 27 385, 42.52%). The mean age ranges from 46.6 to 93.

Sixty-three of the 66 studies reported the prevalence of osteosarcopenia. For related factors of osteosarcopenia, six studies[15,25,28–31] reported an association between frailty and osteosarcopenia, six[16,29,32–35] reported age, while four[16,30,34,35] reported gender and four[16,30,35,36] reported malnutrition. In terms of outcome, seven[12,37–42] reported data on fractures, three[37,39,41] on falls, and five[14,24,37,40,43] on mortality. Additional information on the included studies can be found in Supporting Information S1.

Quality assessment

Of the 66 papers assessed by the scales based on the NOS or AHRQ, 55 (83.33%) were of high quality, and others were of moderate quality, no studies were considered low quality. The number of high-quality literature of cross-sectional studies was 41 (85.41%) and of cohort studies was 14 (82.35%), and the rests were moderate quality. The case–control studies were of moderate quality (For more quality information, see Supporting Information S2: Table S1; Table S2).

Prevalence of osteosarcopenia

Based on 63 369 subjects from 63 articles, an overall osteosarcopenia prevalence of 18.5% (95% CI: 16.7–20.3%; $P < 0.001$; $I^2 = 98.7\%$) was estimated in adults worldwide from the meta-analysis based on a random effects model.

In different articles, the prevalence of osteosarcopenia ranged from 1.50% to 64.30%. The stratified prevalence of osteosarcopenia by age, sex, sampling size, definition of osteosarcopenia, region and other factors were also estimated. Worldwide, the prevalence of osteosarcopenia increased with advanced age, ranging from 17.8% (95% CI: 15.9–19.7) in people under 80 years to 24.8% (95% CI: 17.0–32.7) in those aged 80 years and upper. In addition, the prevalence of osteosarcopenia did differ between males (15.3%, 95% CI: 13.2–17.4) and females (19.4%, 95% CI: 16.9–21.9), and was higher in hospitals (24.7%, 95% CI: 21.0–28.3) than in communities (12.9%, 95% CI: 10.7–15.0). The prevalence of osteosarcopenia was significantly higher in retrospective cohort study (30.0%, 95% CI: 20.4–39.6) than in prospective cohort study (10.7%, 95% CI: 7.6–13.9). Studies with a bigger sample size (≥5000) have a lower prevalence (5.4%, 95% CI: 1.5–9.4) than the smaller ones (19.9%, 95% CI: 17.7–22.2). Geographically, osteosarcopenia was most prevalent in

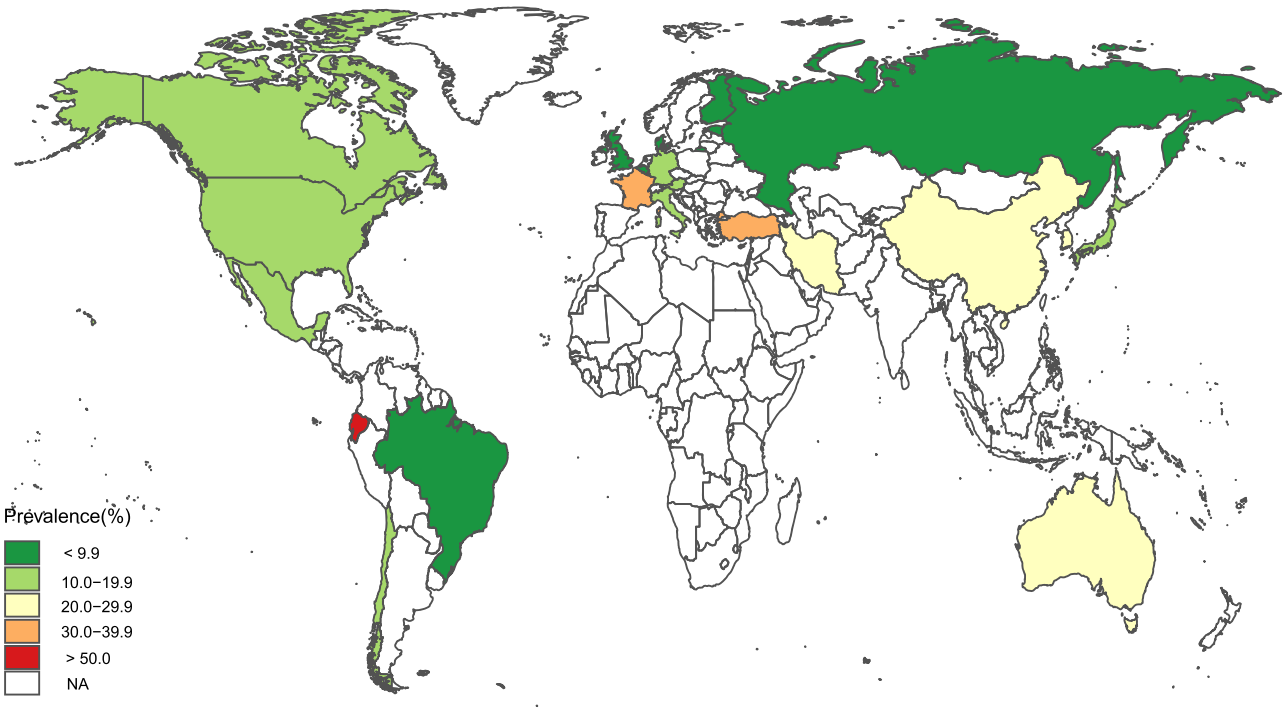

Figure 2 Geographical differences in the global prevalence of osteosarcopenia.

Oceania (22.9%, 95% CI: 13.2–32.6) and least prevalent in Europe (10.9%, 95% CI: 8.2–13.6) (Figure 2). Osteosarcopenia prevalence also varied by study year, its definition, and research quality (Table 1). Finally, meta-regressions performed on subgroups showed statistically significant differences in different sample size (P = 0.041) and study population (P = 0.001) (Table 2).

Related factors of osteosarcopenia

We pooled four related factors (age, female, frailty and malnutrition) of osteosarcopenia (Figure 3). Female individuals seem to have an increased risk of developing osteosarcopenia compared to males (OR = 5.07, 95% CI: 2.96–8.69; I^2 = 73.0%, six studies). Regarding comprehensive geriatric assessment, frailty (OR = 4.72, 95% CI: 2.71–8.23; I^2 = 61.1%, four studies) and malnutrition (OR = 2.35, 95% CI: 1.62–3.40; I^2 = 50.0%, four studies) were associated with a higher risk of osteosarcopenia. In addition, the results show that age contributes to the development of osteosarcopenia in patients (OR = 1.10, 95% CI: 1.06–1.15; I^2 = 86.0%, six studies).

The results of the analysis of the frailty subgroup showed that patients with osteosarcopenia from community sources were more strongly correlated with frailty (OR = 5.54, 95% CI: 2.52–12.20; I^2 = 17.8%) compared with patients with osteosarcopenia from hospital sources (OR = 4.30, 95% CI: 1.95–9.47; I^2 = 75.6%). Also, the association between osteosarcopenia patients and frailty varied across regional sources, definitions, and diagnostic criteria (See Supporting Information S3: Table S1). Our meta-regressions for each subgroup of the frailty did not appear significant (See Supporting Information S4: Table S1). Finally, we performed subgroup analyses and meta-regressions for age, female and malnutrition. The results are shown in Supporting Information S4: Table S2, Table S3, Table S4 and Supporting Information S5: Table S1.

Outcomes of osteosarcopenia

We pooled outcomes of osteosarcopenia, including fractures, falls, and mortality. The results showed that patients with osteosarcopenia had a higher risk of falls (HR = 1.54, 95% CI: 1.20–1.97; I^2 = 1.0%, three studies) and of fracture (HR = 2.13, 95% CI: 1.61–2.81; I^2 = 67.8%, seven studies) compared with those without. Compared with non-osteosarcopenia participants, mortality was higher in osteosarcopenia patients (HR = 1.75, 95% CI: 1.34–2.28; I^2 = 0.0%, five studies) (Figure 4).

Some significant results show that patients diagnosed using the 'osteopenia plus sarcopenia' definition had a higher risk of fracture (HR = 3.03, 95% CI: 1.84–4.99; I^2 = 62.1%) compared with those diagnosed using other definitions. Osteosarcopenia patients aged 65 years and upper have a higher risk of getting fractures (HR = 2.25, 95% CI: 1.59–3.17; I^2 = 66.9%). The risk of fracture in osteosarcopenia patients was more significant in the prospective cohort study (HR = 2.36, 95% CI: 1.63–3.43; I^2 = 73.6%) compared with the retrospective cohort study (HR = 1.61, 95% CI: 1.23–2.10; I^2 = 0.0%). Additionally, the risk of fractures, mortality and falls in patients with osteosarcopenia varied across different diagnostic criteria, study design, follow-up and sample size. (see Supporting Information S3: Table S5, Table S6, Table S7). Finally, our meta-regressions for all clinical outcomes were insignificant (see Supporting Information S4: Table S1).

Sensitivity analysis and bias test

We performed a sensitivity analysis on the results derived from the meta-analysis to determine the stability of the results. The sensitivity analysis results showed no significant change in the pooled results after removing one study at a time, and the results were relatively stable (see Supporting Information S5). In addition, the funnel plot was fairly symmetrical. No significant publication bias was found between the results of Begg's test (see Supporting Information S6: Table S1).

Discussion

The prevalence of osteosarcopenia among older adults has been estimated to be 18.5% in the current systematic review and meta-analysis. It was found that frailty, female, malnutrition and age could all be risk factors for osteosarcopenia. Compared with those without osteosarcopenia, individuals with the condition were more likely to experience adverse outcomes, such as fractures, falls and mortality.

In this systematic review, we found that osteosarcopenia has an overall pooled prevalence of 18.5% (CI: 16.7–20.3%) among a population of 63 369 older patients, which is similar to or even higher than the global prevalence of osteoporosis (21.7%) and sarcopenia (10%).[44,45] Because osteosarcopenia is a condition that describes the coexistence of osteoporosis/osteopenia and sarcopenia, its prevalence should be lower than that of either osteoporosis/osteopenia or sarcopenia as a single disease. This may be related to the interaction of muscle and bone, which are macroscopically interconnected and microscopically influenced through genetic and pathophysiological mechanism.[9,46] Our subgroup analysis revealed that estimated prevalence of osteosarcopenia varies widely due to heterogeneous populations, geographical region, age, sex, designs, diagnostic criteria and settings. This is comparable with findings from a prior meta-analysis of 17

Table 1 Subgroup analysis of prevalence in patients with osteosarcopenia

Category	Number of study	Number of participants	Prevalence [95% CI]*	I^2 (%)	*P*
Overall	63	63 369	18.5% [16.7–20.3]	98.7	<0.001
Study year					
2012–2014	2	2227	7.4% [6.3–8.4]	-	-
2015–2017	8	19 662	18.1% [12.3–23.9]	99.3	<0.001
2018–2020	30	18 231	21.7% [18.4–25.0]	98.4	<0.001
2021–2023	23	23 249	16.7% [13.3–20.2]	98.8	<0.001
Gender					
Male	-	22 986	15.3% [13.2–17.4]	97.6	<0.001
Female	-	33 683	19.4% [16.9–21.9]	98.5	<0.001
Mix	-	6700	17.9% [13.5–22.2]	97.4	<0.001
Study design					
Prospective cohort study	11	25 319	10.7% [7.6–13.9]	98.6	<0.001
Retrospective cohort study	6	1117	30.0% [20.4–39.6]	91.5	<0.001
Cross-sectional study	46	36 933	19.4% [17.0–21.9]	98.8	<0.001
Sample size					
≥5000	4	29 475	5.4% [1.5–9.4]	99.7	<0.001
<5000	59	33 894	19.9% [17.7–22.2]	97.8	<0.001
Definition of osteosarcopenia					
Sarcopenia plus osteoporosis	26	26 011	16.1% [13.3–18.9]	98.5	<0.001
Sarcopenia plus osteopenia	16	18 394	19.7% [16.0–23.3]	98.8	<0.001
Sarcopenia plus osteopenia/osteoporosis	21	18 964	20.7% [17.1–24.4]	98.0	<0.001
Assessment of sarcopenia					
EWGSOP	28	44 078	17.2% [14.6–19.8]	99.0	<0.001
AWGS	16	13 800	17.2% [13.1–21.4]	98.6	<0.001
JSH	3	1022	12.5% [4.3–20.7]	92.2	<0.001
SMI	6	1683	20.0% [12.0–28.0]	95.6	<0.001
FHIN	1	427	27.4% [23.2–31.9]	-	-
Other	9	2359	29.0% [19.8–38.1]	96.4	<0.001
Assessment of osteopenia/osteoporosis					
WHO	54	60 297	18.8% [16.9–20.8]	98.8	<0.001
JOS	4	1398	11.7% [7.4–16.0]	83.2	<0.001
Other	5	1674	20.8% [12.9–28.7]	94.7	<0.001
Different participants					
Hospital patients	34	26 350	24.7% [21.0–28.3]	98.9	<0.001
Community-dwelling patients	29	37 019	12.9% [10.7–15.0]	98.4	<0.001
Age, years					
≥65 years	51	35 744	19.1% [16.8–21.3]	98.4	
<65 years	12	27 625	17.1% [12.7–21.5]	99.3	<0.001
Advanced age					
≥80 years	7	1774	24.8% [17.0–32.7]	93.4	<0.001
<80 years	56	61 595	17.8% [15.9–19.7]	98.8	<0.001
Country or territory					
Asia	31	27 515	21.6% [18.3–25.0]	98.9	
China	4	3665	19.8% [6.5–33.0]	98.9	<0.001
Iran	2	2789	21.8% [20.2–23.3]	-	-
Japan	14	4022	19.3% [14.9–23.7]	94.9	
Singapore	2	693	6.0% [4.2–7.8]	-	-
South Korea	7	15 746	24.2% [17.3–31.1]	99.5	
Turkey	2	600	36.1% [32.4–39.8]	-	-
Europe	13	9497	10.9% [8.2–13.6]	95.6	<0.001
Austria	1	141	14.2% [8.9–21.1]	-	-
Belgium	1	126	9.5% [5.0–16.0]	-	-
Britain	1	405	3.0% [1.5–5.1]	-	-
Denmark	1	529	1.5% [0.7–3.0]	-	-
Estonia	1	227	7.0% [4.1–11.2]	-	-
France	1	101	32.7% [23.7–44.7]	-	-
Finland	1	5911	3.3% [2.9–3.8]	-	-
Germany	3	747	11.7% [4.3–19.1]	-	-
Russia	1	387	6.5% [4.2–9.4]	-	-
Italy	1	801	11.2% [9.1–13.6]	-	-
Romania	1	122	50.8 [41.6–60.0]	-	-
North America	9	20 183	15.7% [11.0–20.4]	99.1	<0.001
America	5	18 193	14.5% [8.2–20.8]	99.3	<0.001
Canada	2	738	14.3% [11.8–16.7]	-	-
Mexico	2	1252	12.2% [10.4–14.0]	-	-
Oceania	6	4479	22.9% [13.2–32.6]	98.8	<0.001
Australia	6	4479	22.9% [13.2–32.6]	98.8	<0.001

(*Continues*)

Table 1 (continued)

Category	Number of study	Number of participants	Prevalence [95% CI]*	I^2 (%)	*P*
South America	4	1695	20.8% [10.6–31.0]	96.7	<0.001
Brazil	2	484	8.7% [6.2–11.3]	-	-
Chile	1	1119	16.4% [14.3–18.7]	-	-
Ecuador	1	92	56.5% [45.8–66.8]	-	-
High quality					
Yes	53	59 801	19.9% [17.9–21.9]	98.8	<0.001
No	10	3568	11.2% [7.1–15.2]	96.4	<0.001

Abbreviations: AWGS, Asian Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia; FNIH, Foundation for the National Institutes of Health; JOS, Japan Osteoporosis Society; JSH, Japan Society of Hepatology; SMI, skeletal muscle index; WHO, World Health Organization.
*All 95% CIs confidence intervals were significant ($P < 0.05$).

Table 2 Meta-regression of prevalence in patients with osteosarcopenia

Variable	β (95% CI)	SE	*P*
Study year: 2018–2023 vs. other	0.042 (−0.059, 0.143)	0.051	0.411
Study design: cross-sectional study vs. cohort study	0.019 (−0.065, 0.104)	0.042	0.649
Whether elderly: ≥65 years vs. <65	0.014 (−0.082, 0.109)	0.048	0.778
Whether advanced age: ≥80 years vs. <80	0.063 (−0.057, 0.183)	0.060	0.297
Sample size: <5000 vs. ≥5000 patients	0.152 (0.006, 0.297)	0.073	**0.041**
Region: Asia vs. elsewhere	0.053 (−0.021, 0.126)	0.037	0.156
Study population: community-dwelling participants vs. hospital participants	−0.116 (−0.185, −0.048)	0.034	**0.001**
Definition of osteosarcopenia: osteopenia/osteoporosis and sarcopenia vs. other	0.028 (−0.051, 0.107)	0.039	0.481
Assessment of sarcopenia: EWGSOP vs. other	−0.029 (−0.104, 0.045)	0.037	0.430
Assessment of osteopenia/osteoporosis: WHO vs. other	0.023 (−0.085, 0.130)	0.054	0.677
High quality: yes vs. no	0.085 (−0.014, 0.185)	0.050	0.092

Note: The use of emphasis (bold text) in Table 2 means $P < 0.05$.
Abbreviations: aOR, adjusted odds ratio; AWGS, Asian Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia; JOS, Japan Osteoporosis Society; OR, odds ratio; WHO, World Health Organization.

studies, where the prevalence of osteosarcopenia ranged from 5% to 40%.[47]

In a subgroup analysis of osteosarcopenia prevalence, older people (>80 years) had a substantially greater prevalence (24.8%) than younger people (17.8%). According to a review of the literature, muscular mass, strength and bone mineral density all decline with age in older persons. Thus, it is not difficult to discover that as we get older, lost bone and muscle accumulate year after year, finally leading to a high prevalence of osteosarcopenia in the advanced age group.[3,5] In terms of regional differences, osteosarcopenia was more common in Oceania (22.9%), Africa (21.6%) and South America (20.8%) than it was in Europe (10.7%). We note that most research conducted in Europe provided us with the fewest subjects with the small sample sizes. Additionally, compared with community individuals (12.9%), hospital patients (24.7%) had nearly double the prevalence of osteosarcopenia. We hypothesized that patients who were hospitalized were more vulnerable than those from the community, which would explain why sarcopenia rates were higher according to the International Working Group on Sarcopenia (IWGS),[48,49] which may account for the difference[50] Currently, the definition of osteosarcopenia is ambiguous because studies have combined osteoporosis or osteopenia with sarcopenia while measuring sarcopenia using different definitions,[45] which may have contributed to the variable prevalence of osteosarcopenia. More research is required to clarify the definition of osteosarcopenia in order to create a reliable scale for evaluating osteosarcopenia.

Identification of high-risk patients and potentially modifiable risk factors for osteosarcopenia is of interest in preventing development of osteosarcopenia. Our systematic review suggested that females have 5 times odds of developing osteosarcopenia, as compared with males. This might be brought on by menopause-related hormone changes that are unique to women, such as a decline in prostaglandin estradiol and a naturally lower reserve base of muscle and bone in women compared with men. Evidence from human and animal studies had shown that oestrogen based hormone replacement therapy in postmenopausal women is able to both maintain and enhance bone and muscle mass.[51] Furthermore, among the pooled risk factors, frailty was strongly correlated with osteosarcopenia. According to several recent studies,[31,52–54] an accumulation of fat is more significantly and positively correlated with frailty during aging, leading to the development of fat infiltration in muscle and bone.[46] Adipose tissue will secrete adipokines and be lipotoxic to sur-

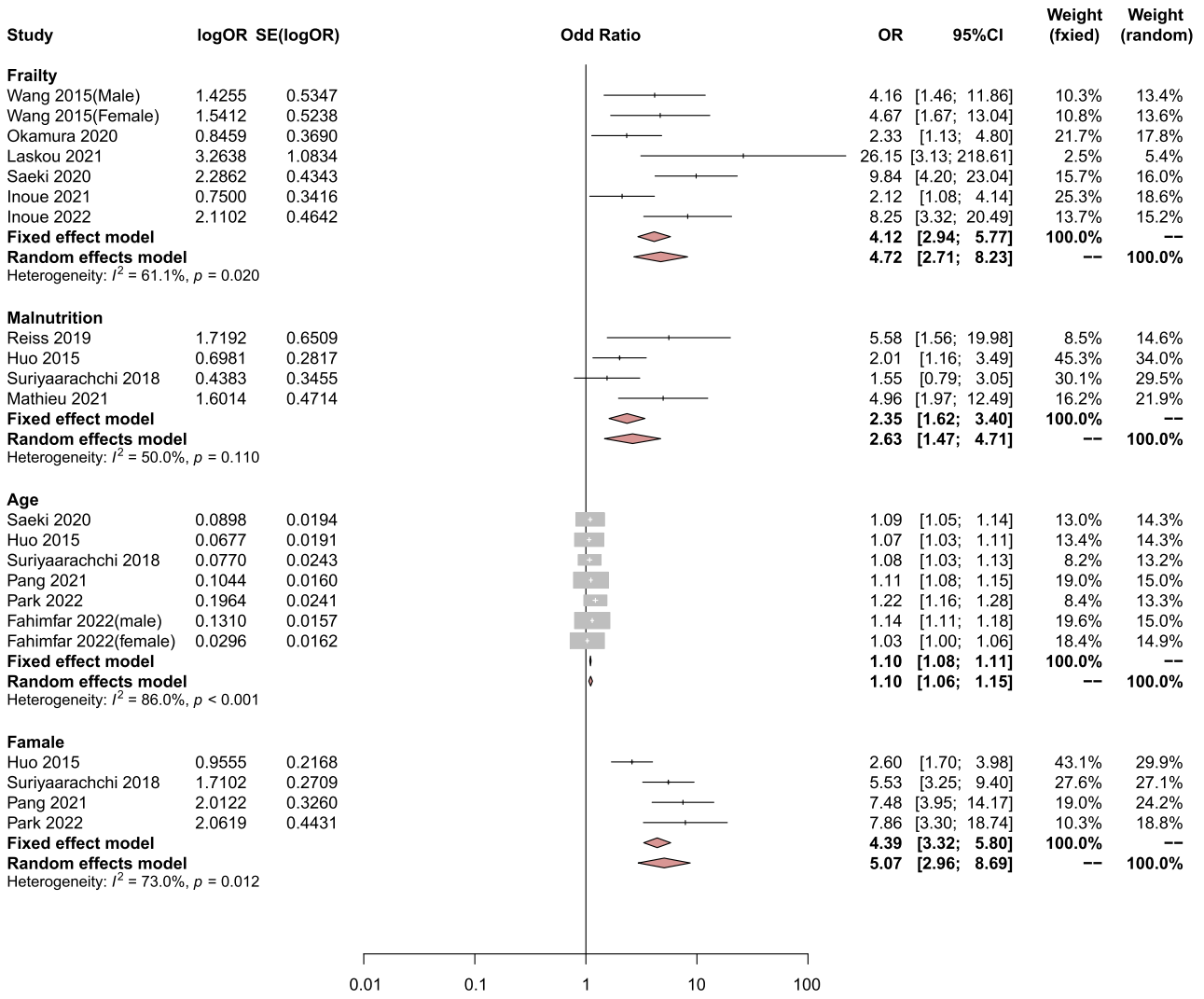

Figure 3 Meta-analysis of the related factors in patients with osteosarcopenia.

rounding musculoskeletal tissues, resulting in apoptosis of myocytes and osteocytes.[10,46] This could explain the correlation between osteosarcopenia patients and frailty. It is also worth paying attention to the fact that, according to our findings, frailty is more strongly associated with patients with osteosarcopenia than those with osteoporosis/osteopenia or sarcopenia alone (Figure S1). In addition, we discovered that malnutrition is another important risk factor for osteosarcopenia. Malnutrition induces an overall loss of body mass and have been recognized as a common physiological contributor for both osteoporosis and sarcopenia.[2,55,56] For instance, previous studies demonstrated that low vitamin D levels were commonly detected in osteosarcopenic patients and linked to low BMD.[16,57] It is also well established that MSK system's capacity to use and synthesize protein decreased with age,[58] making dietary protein intake crucial for preserving bone and muscle mass.[59] RCTs have shown the effect of augmentations in muscle and bone mass after protein supplementation in combination with resistance exercise interventions.[60,61]

A meta-analysis of patient clinical outcomes revealed that osteosarcopenia substantially increased the chance of fracture (HR = 2.13), falls (HR = 1.54) and mortality (HR = 1.75). Furthermore, patients with osteosarcopenia had a higher risk of fracture than those with either sarcopenia or osteoporosis/osteopenia (Figure S2). As shown by research studies, the loss of skeletal muscle weakens bones, thereby decreasing BMD and raising the risk of fracture.[62,63] Bone decline, in turn, further exacerbates skeletal muscle deterioration, resulting in an increased risk of falls.[15,16] A vicious circle is thus formed between muscle and skeletal tissues.[3,4,9,10] According to previous literature, individuals with either osteo-

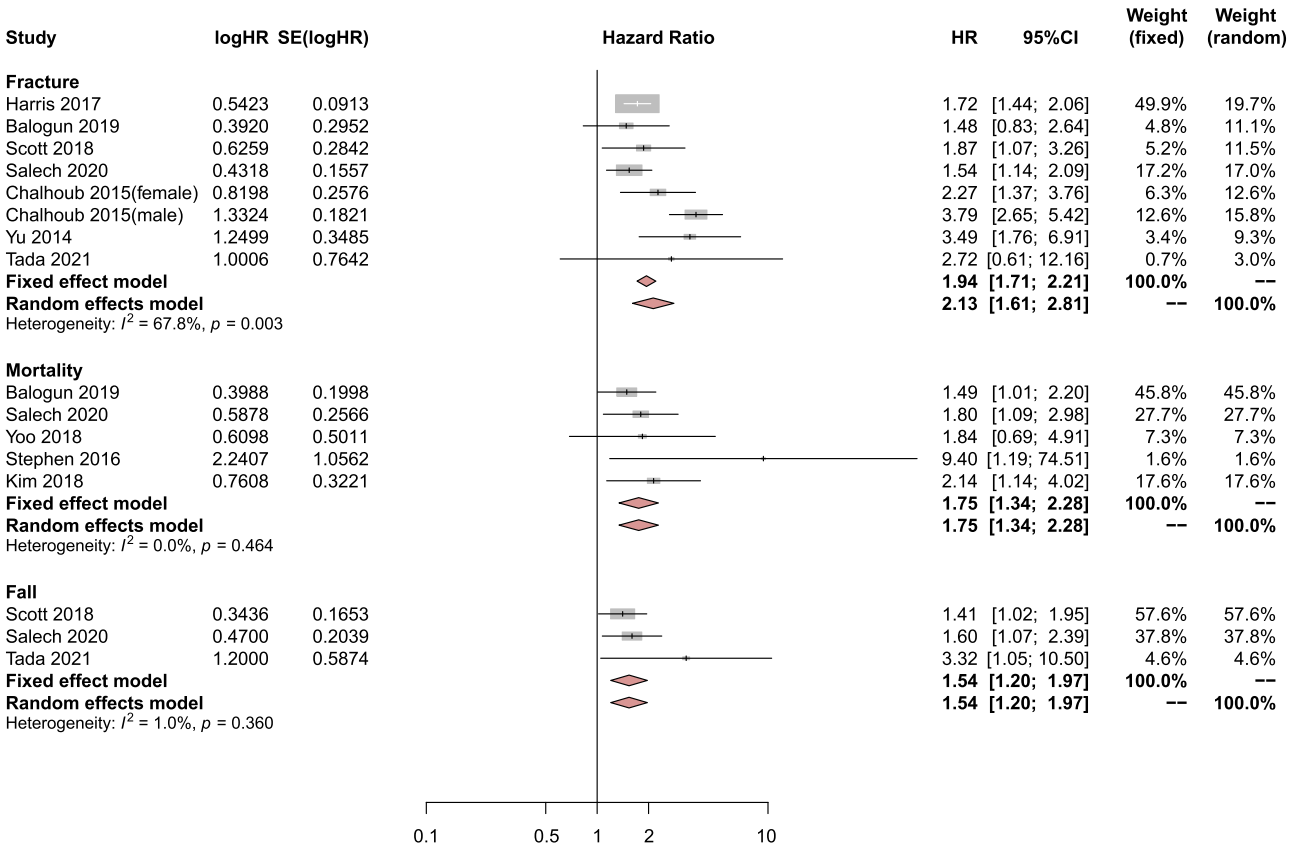

Figure 4 Meta-analysis of the outcomes in patients with osteosarcopenia.

porosis or sarcopenia had a higher risk of mortality.[64,65] Therefore, it is reasonable that the co-existence of the two aforementioned conditions could significantly increase the risk of mortality. Our results are in agreement with those by Yoo et al.,[14] who found that individuals with osteosarcopenia (15.1%) had a considerably greater risk of 1 year death from hip fractures than those with sarcopenia (10.3%) or osteoporosis alone (5.1%).

To the best of our knowledge, this systematic review is the first to thoroughly synthesize all aspects of osteosarcopenia (prevalence, risk factors and prognosis) with detailed, clinically relevant subgroup and sensitivity analyses. The strengths of our meta-analysis include systematic literature search across several multiple databases that led to the identification of 66 studies with more than 62 000 patients. Our study successfully provides an up-to-date and accurate estimation of osteosarcopenia prevalence reported in the recent studies among older patients to serve a basis for future interventions. To aid in early identification of vulnerable patients and osteosarcopenia prevention, we also summarize the risk factors along with the consequences of osteosarcopenia.

As with most studies, the design of this review was not without some limitations. Firstly, there was significant heterogeneity (I^2 = 98.7%) between the included studies, mainly in terms of diagnostic methods, measurement approaches, sample sizes and participants' characteristics. Therefore, we performed the subgroup analysis, meta-regression and sensitivity analysis to overcome this limitation. Additionally, the pooling of unadjusted data, which is used to assess the risk factors linked with osteosarcopenia, is unable to take into account the many confounding factors across studies, which may partly restrict the conclusions drawn from this research. Thirdly, the lack of data from Africa somewhat restricts the generalizability of the article, despite the fact that this review includes studies from several other continents (Europe, North America, Asia, Oceania and South America). Finally, this review may have been biased because we only considered literature that was published in English-language publications.

Conclusions

In conclusion, our meta-analysis revealed that osteosarcopenia is a clinically significant condition that has been demonstrated to be prevalent among a substantial

proportion of patients and is linked to an increased risk of fractures, falls and death. Due to the negative impact of osteosarcopenia upon health outcomes, it is crucial to screen and evaluate osteosarcopenia at an early stage, and effective diagnostic criteria for osteosarcopenia would be beneficial in the future. Prospective well-designed studies and intervention programs are urgently needed to optimize management strategies aiming to mitigate its impact upon individuals' lives and reduce social healthcare burdens.

Conflict of interest

All authors have no conflicts of interest to disclose.

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Data availability statement

The authors declare that the data collected was gathered from publicly available databases and is available upon request.

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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