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Sarcopenic Obesity and Cardiovascular Disease Risk and Mortality: A Systematic Review and Meta-Analysis

ABSTRACT

Background: While both sarcopenia and obesity independently elevate cardiovascular disease (CVD) risk, their combined effects, known as sarcopenic obesity (SO), remain incompletely understood. This systematic review and meta-analysis aimed to evaluate the association between SO and the risk of CVD and CVD-related mortality.

Methods: A comprehensive search of scientific databases was conducted from inception to May 2025, including observational studies assessing SO in relation to incident CVD or CVD mortality. Pooled odds ratios (ORs) with 95% CIs were calculated using random-effects models. Subgroup analyses examined variations by age, sex, geography, study design, and CVD subtypes, with *P*-values for interaction being assessed.

Results: Sixteen studies involving 578 408 participants were included. Sarcopenic obesity was significantly associated with a 95% higher CVD risk (OR = 1.95, $P < .001$, 95% CI: 1.62-2.36) and a 64% increased CVD mortality risk (OR = 1.64, $P = .007$, 95% CI: 1.15-2.34). Subgroup analyses revealed stronger associations in males and diabetic subgroups. The highest risks were observed for myocardial infarction (OR = 4.07, $P = .015$, 95% CI: 1.31-12.63) and atrial fibrillation (OR = 2.93, $P < .001$, 95% CI: 2.23-3.86). Significant interactions were detected by sex ($P = .032$) and cardiovascular outcome type ($P = .001$), but not by age, region, or study design.

Conclusion: Sarcopenic obesity is a high-risk phenotype associated with significantly elevated CVD incidence and mortality, with effect modification by sex and outcome type. These findings highlight the need for standardized diagnostic criteria and targeted interventions to mitigate cardiovascular risk in this growing population.

Keywords: Aging, cardiovascular disease, meta-analysis, mortality, sarcopenic obesity

META-ANALYSIS

INTRODUCTION

The global rise in both obesity and population aging has led to the emergence of a complex and clinically significant phenotype known as sarcopenic obesity (SO). Defined by the concurrent presence of excessive adiposity and reduced skeletal muscle mass and strength, SO represents a convergence of 2 detrimental conditions—sarcopenia and obesity—each independently associated with increased cardiometabolic and functional risk. The combination, however, appears to exert a synergistic effect, accelerating physiological decline and disease progression, particularly in older adults.[1,2]

Aging is accompanied by significant changes in body composition, including an increase in fat mass—particularly visceral and ectopic fat—and a progressive decline in lean muscle mass and muscle function. These changes not only impair physical performance but also shift metabolic homeostasis towards insulin resistance, inflammation, and oxidative stress, key mechanisms implicated in cardiovascular disease (CVD).[3] Meanwhile, obesity, especially when characterized by central fat distribution, contributes to an inflammatory milieu through adipokine dysregulation and endothelial dysfunction.[4,5] When sarcopenia and obesity coexist, these effects are amplified, creating a proatherogenic environment and raising the risk of atherosclerosis, coronary artery disease, and heart failure.[6,7]

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While sarcopenia and obesity have long been studied as separate entities in the context of cardiovascular risk, SO has only recently gained attention as a distinct syndrome. Epidemiologic studies have shown that older adults with SO have higher rates of CVD and cardiovascular mortality than those with either condition alone.[8]

A growing body of evidence from large-scale observational studies and cohort analyses suggests that SO confers a markedly elevated risk for multiple cardiometabolic disorders. Individuals with this dual burden of excess adiposity and low muscle mass exhibit significantly higher odds of developing hypertension,[9] dyslipidemia,[10] type 2 diabetes,[11] and major cardiovascular events such as myocardial infarction and heart failure,[12] compared to those with normal body composition. The link between SO and CVD is believed to arise from a convergence of adiposity-driven inflammation and muscle-related metabolic impairment. This unfavorable interaction fosters a pro-inflammatory, insulin-resistant state that accelerates vascular dysfunction and elevates cardiometabolic risk.[9,13]

As the aging population grows, SO is expected to become increasingly prevalent. Given its strong association with CVD morbidity and mortality, there is an urgent need for heightened clinical awareness and development of targeted interventions. Due to inconsistencies and heterogeneity in findings from prior research, this meta-analysis was conducted to determine whether SO is associated with an increased risk of CVD and all-cause mortality, compared to individuals without this condition.

METHODS

Study Design and Selection Criteria

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines and structured according to the PECO framework. The population included adults aged 18 years and older from any demographic background. The exposure of interest was SO, defined as the co-occurrence of sarcopenia (characterized by reduced muscle mass and/or strength) and obesity, based on diagnostic criteria specified in each individual study (Supplementary Table 1). The Comparator group comprised individuals without SO with normal body composition. The outcomes were incident CVD (such as myocardial infarction, stroke, heart failure, arrhythmias, etc.) and/or CVD mortality (if reported separately from all-cause mortality). We included observational studies (cohort, cross-sectional, and case-control designs) that investigated the association between SO and CVD or related mortality were included, and effect estimates (e.g., odds ratios [ORs], hazard ratios [HRs], or risk ratios [RRs]) with corresponding 95% CIs were reported, or sufficient data were provided to calculate them. Studies were excluded if they assessed the effects of sarcopenia or obesity alone without evaluating SO, if they focused on non-CVD outcomes (e.g., hypertension), lacked a proper definition of SO or CVD, or were case reports, case series, reviews, editorials without original data, or animal studies.

Search Strategy

A comprehensive literature search was conducted to identify relevant studies examining the association between SO and CVD. Four electronic databases—PubMed/MEDLINE, Embase, Scopus, and Web of Science—were searched from inception to May 10, 2025. The search strategy combined Medical Subject Headings (MeSH) and relevant keywords, including but not limited to: sarcopenic obesity, sarcopenia, obesity, CVD, myocardial infarction, stroke, and cardiovascular mortality (Supplementary Table 2). In addition, grey literature and reference lists of included articles and relevant reviews were manually screened to identify additional eligible studies. No geographical, time, and language restriction was applied.

Data Extraction and Quality Assessment

Two trained reviewers (Z.Z. and X.Z.) independently screened titles, abstracts, and full texts using a standardized eligibility form in an Excel spreadsheet. Disagreements were resolved by consensus. For each included study, the following data were extracted: author, year of publication, study duration, study location, design, sample size, numbero of participants in each group (normal, sarcopenia, obesity, SO), mean follow-up duration (in cohort studies), participant characteristics (sex and age), definition of SO, outcome definitions, effect measures (OR, RR, or HR), and adjustment variables.

The methodological quality of included studies was assessed using the Newcastle–Ottawa Scale (NOS) for cohort and cross-sectional studies. This tool evaluates selection, comparability, and outcome (or exposure) domains, with scores ranging from 0 to 9. Studies scoring ≥7 were considered high quality. The risk of bias was independently assessed by 2 reviewers, and discrepancies were resolved through discussion.

Statistical Analysis

The statistical analysis was performed following rigorous methodological standards to ensure robust and reproducible findings. All analyses were conducted using Stata version 18 (StataCorp, College Station, TX, USA), with statistical significance set at $P < .05$ using 2-tailed tests. Given the inclusion of studies reporting different effect measures, all estimates were harmonized by converting HRs and RRs to ORs for consistency. For studies reporting HRs, established conversion methods that account for baseline risk were applied,

HIGHLIGHTS

- The study found that individuals with sarcopenic obesity had a 95% higher cardiovascular disease (CVD) risk than those without.
- Sarcopenic obesity was linked to a 64% higher risk of CVD-related mortality.
- The association was stronger in East Asian populations compared to Western populations.
- The association was stronger in diabetic patients compared to general patients.
- The highest CVD risk was related to myocardial infarction and atrial fibrillation.

particularly when CVD incidence was non-rare. When necessary, standard errors for log-transformed ORs were derived from reported CIs using standard methods. Random-effects meta-analysis (REM) models were employed using the restricted maximum likelihood estimator as the primary analytical approach, which accounts for between-study heterogeneity. This method was preferred over fixed-effects models due to the anticipated clinical and methodological diversity across studies. The degree of heterogeneity was quantified using 3 complementary measures: Cochran's Q-test and Higgins' I^2 statistic. I^2 values of 0%-40% were interpreted as indicating low heterogeneity, 40%-75% as moderate, and >75% as substantial heterogeneity. To explore potential sources of heterogeneity, pre-specified subgroup analyses stratified by participant sex, age categories, and specific cardiovascular outcomes were conducted. These analyses helped identify whether the association between SO and CVD risk varied across clinically relevant subgroups. The robustness of these findings was assessed through comprehensive sensitivity analyses. A leave-one-out approach was employed to evaluate whether any single study disproportionately influenced the pooled estimates. Furthermore, cumulative meta-analysis was conducted to examine how the evidence base evolved chronologically with the addition of new studies. Publication bias was systematically evaluated using multiple complementary methods. Visual inspection of funnel plots provided an initial assessment of potential asymmetry. When asymmetry was detected, trim-and-fill analysis was employed to estimate the potential impact of missing studies on the effect estimates.

RESULTS

Study Selection and Characteristics

The PRISMA flow diagram illustrates the screening and selection process (Central Figure and Figure 1). A total of 1610 records were identified through comprehensive searches of 4 electronic databases: PubMed/MEDLINE (n=111), Scopus (n=382), Embase (n=667), and Web of Science (n=428). An additional 22 records were retrieved from other sources, including reference lists of relevant articles and grey literature. Following initial screening, 1536 records were excluded, including 526 duplicates and 1010 papers deemed clearly irrelevant based on title and abstract assessment. The full texts of the remaining 74 articles were assessed for eligibility. Of these, 58 studies were excluded for the following reasons: (I) The study focused solely on sarcopenia or obesity without examining effect of SO on CVD (n=41); (II) The publication type was case reports/series (n=5); (III) The study assessed outcomes unrelated to CVD (n=11); (IV) The article was a review, systematic reviews, letter, editorial, or other non-original research format (n=17). Ultimately, 16 studies met all the eligibility criteria and were included in the final meta-analysis (Table 1).[8,11,12,14-26] Additionally, 1 study[27] assessed just CVD-related mortality and was included in the meta-analysis related to CVD-related mortality risk.

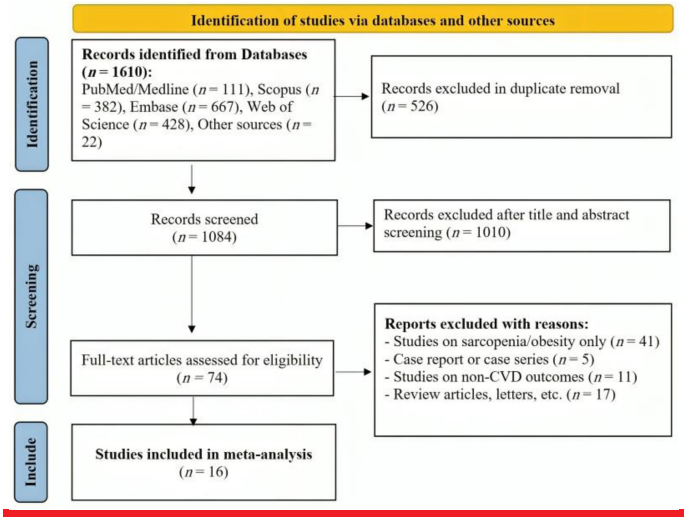

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram illustrating the study selection process for the systematic review and meta-analysis on sarcopenic obesity and cardiovascular diseases risk.

The 16 included studies (comprising 19 datasets) spanned 7 countries across East Asia (11 studies: China [6], South Korea [4], Japan [1]) and Europe/North America (5 studies: England [2], USA [1], Cyprus [1], and 1 multinational cohort from the UK Biobank). Geographically, 62.5% and 31.2% of studies were conducted in East Asia and Europe. Study designs varied: 8 prospective cohorts (50%) with follow-up periods ranging from 2.6 to 12 years, 6 cross-sectional studies (37.5%), and 2 retrospective cohorts (12.5%). The largest cohort (Farmer et al,[8] 2019; n=452 931) utilized UK Biobank data. Study populations predominantly involved general middle-aged and older adults (11 studies), though 3 studies targeted high-risk subgroups (e.g., type 2 diabetes patients), and 1 included cancer survivors. Cardiovascular outcomes were heterogeneous. Six studies assessed composite CVD endpoints, while others examined specific subtypes: heart failure/diseases, coronary artery calcification, atrial fibrillation, left ventricular dysfunction, and stroke. Five and 6 studies provided adjusted effect sizes based on sex and age, respectively. Three studies reported CVD-related mortality, with effect sizes ranging from HR=1.14 (Atkins et al,[15] 2014) to HR=2.48 (Saito et al,[27] 2022). All studies adjusted for key confounders, including age, sex, lifestyle factors (smoking, physical activity), cardiometabolic comorbidities (hypertension, diabetes) and other confounders (Supplementary Table 3). All studies were rated as high quality on the NOS, with prospective cohorts demonstrating robust methodology.

Results of Overall Meta-Analysis

As shown in Figure 2, the REM revealed that SO is significantly associated with an increased risk of CVD, with a pooled OR=1.95, $P < .001$, 95% CI: 1.62-2.36. However, substantial heterogeneity was observed across studies ($I^2=84.59\%$, $\tau^2=0.12$, Q-test $P < .001$). Moreover, the analysis of 3 studies examining the association between SO and CVD-related mortality revealed a statistically significant increased risk (OR=1.64, $P=.007$, 95% CI: 1.15-2.34; Figure 3), with moderate heterogeneity among studies ($I^2=53.65\%$,

Table 1. Mean Characteristics of Included Studies Evaluating the Association Between Sarcopenic Obesity and Cardiovascular Diseases

Studies[1]	Country	Study Design	Mean Follow-Up Period	Type CVD	Total Population	Subject Characteristics	Effect Size
Stephen & Janssen (2009)[14]	USA	PC	10 years	CVD	3366	Normal people (n = 1481); sarcopenic (n = 750); obese (n = 762); SO (n = 373)	HR, 1.06 (0.85-1.33)
Atkins et al (2014)[15]	England	PC	11.3 years	CVD	4111	Normal people (n = 1490); sarcopenic (n = 1443); obese (n = 983); SO (n = 195)	HR, 1.08 (0.77-1.52)
Kim et al (2015)[16]	South Korea	CS	NA	CVD	1458	Normal people (n = 778); sarcopenic (n = 146); obese (n = 350); SO (n = 184)	OR, 2.49 (1.53-4.06)
Kim et al (2015)[16]	South Korea	CS	NA	CVD	1862	Normal people (n = 983); sarcopenic (n = 253); obese (n = 294); SO (n = 332)	OR, 1.87 (1.02-3.41)
Fukuda et al (2018)[17]*	Japan	RC	2.6 years	CVD	716	Normal people (n = 187); sarcopenic (n = 171); obese (n = 275); SO (n = 83)	HR, 2.63 (1.1-6.28)
Farmer et al (2019)[8]	England	PC	5.1 years	CVD	452 931	Normal people (n = 296567); sarcopenic (n = 48250); obese (n = 89906); SO (n = 18208)	HR, 1.42 (1.31-1.55)
Xia et al (2020)[18]	China	CS	NA	MI	2432	Normal people (n = 662); sarcopenic (n = 576); obese (n = 1114); SO (n = 80)	OR, 4.07 (1.31-12.62)
Xia et al (2020)[18]	China	CS	NA	AF	2432	Normal people (n = 662); sarcopenic (n = 576); obese (n = 1114); SO (n = 80)	OR, 5.68 (1.34-24.12)
Yoo et al (2020)[19]	South Korea	CS	NA	LVDD	31 258	Normal people (n = 17476); sarcopenic (n = 2693); obese (n = 6875); SO (n = 4214)	OR, 1.7 (1.44-1.99)
Chung et al (2021)[20]	Cyprus	ROS	3.46 years	CAC	1282	Normal people (n = 746); sarcopenic (n = 14); obese (n = 414); SO (n = 108)	OR, 1.92 (1.16-3.18)
Lee at al (2021)[21,†]	South Korea	CS	NA	CVD	1023	Normal people (n = 611); sarcopenic (n = 106); obese (n = 277); SO (n = 29)	OR, 1.79 (0.68-4.74)
Lee at al (2021)[21]	South Korea	CS	NA	CVD	17 996	Normal people (n = 10548); sarcopenic (n = 1118); obese (n = 5800); SO (n = 530)	OR, 3.01 (2.42-3.73)
Jia et al (2024)[22,*]	England	PC	12.0 years	HF	22 496	Normal people (n = 9158); sarcopenic (n = 1254); obese (n = 11024); SO (n = 1033)	HR, 2.29 (1.92-2.73)
Jiang et al (2024)[23]	China	PC	7 years	CVD	7703	Normal people (n = 1132); sarcopenic (n = 3580); obese (n = 635); SO (n = 2356)	HR, 1.47 (1.2-1.8)
Yang et al (2024)[24]	China	CS	NA	CVD	2821	Normal people (n = 1911); sarcopenic (n = 330); obese (n = 489); SO (n = 91)	OR, 2.2 (1.16-4.19)
Yu et al (2024)[11]	China	PC	3 years	CVD	15 252	Normal people (n = 7616); sarcopenic (n = 2219); obese (n = 4568); SO (n = 849)	HR, 2.302 (1.24-4.23)
Shi et al (2025)[12]	China	PC	7 years	HF	4665	Low sarcopenic abdominal obesity (n = 2332); low sarcopenic abdominal obesity (n = 2333)	HR, 1.2 (1.01-1.4)
Yu et al (2025)[25]	China	PC	10.9 years	AF	4321	Normal people (n = 2887); sarcopenic (n = 269); obese (n = 753); SO (n = 412)	HR, 2.669 (2.11-3.38)
Shi et al (2025)[26,*]	China	PC	3 years	CVD	283	Normal people (n = 72); sarcopenic (n = 85); obese (n = 73); SO (n = 53)	HR, 3.03 (1.39-6.63)

Most studies recruited participants from the general population, except for 3 that recruited patients with type 2 diabetes (marked as *) and 1 that included cancer patients (marked as †).
AF, atrial fibrillation; CAC, coronary artery calcification; CS, cross-sectional; CVD, cardiovascular diseases; HF, heart failure; LVDD, left ventricular diastolic dysfunction; MI, myocardial infarction; PC, prospective cohort; RC, retrospective cohort; ROS, retrospective observational; SO, sarcopenic obesity.

$\tau^2 = 0.05$). However, the test for heterogeneity was not statistically significant (Q = 4.33, $P = .11$). Visual inspection of the funnel plot indicated an asymmetric distribution of studies. This was supported by Egger's test, which provided statistical evidence of potential publication bias (intercept $P = .044$; Supplementary Figure 1).

Results of Subgroup Meta-Analyses

Five studies provided stratified data on sex (Supplementary Table 4). The subgroup analysis based on sex indicated a significant association between SO and the risk of CVD in both males (OR = 2.56, $P < .001$, 95% CI: 2.15-3.06) and females (OR = 2.35, $P < .001$, 95% CI: 1.90-2.92). In the age-based subgroup analysis (6 studies), studies were stratified into younger (<60, <65, and <70) and older (≥60, ≥65, and ≥70). Among younger participants, the pooled OR was 1.97 ($P < .001$, 95% CI: 1.49-2.60), while in older participants, the pooled OR was 1.81 ($P < .001$, 95% CI: 1.32-2.47), both indicating a significant and comparable association with increased risk (Supplementary Table 4).

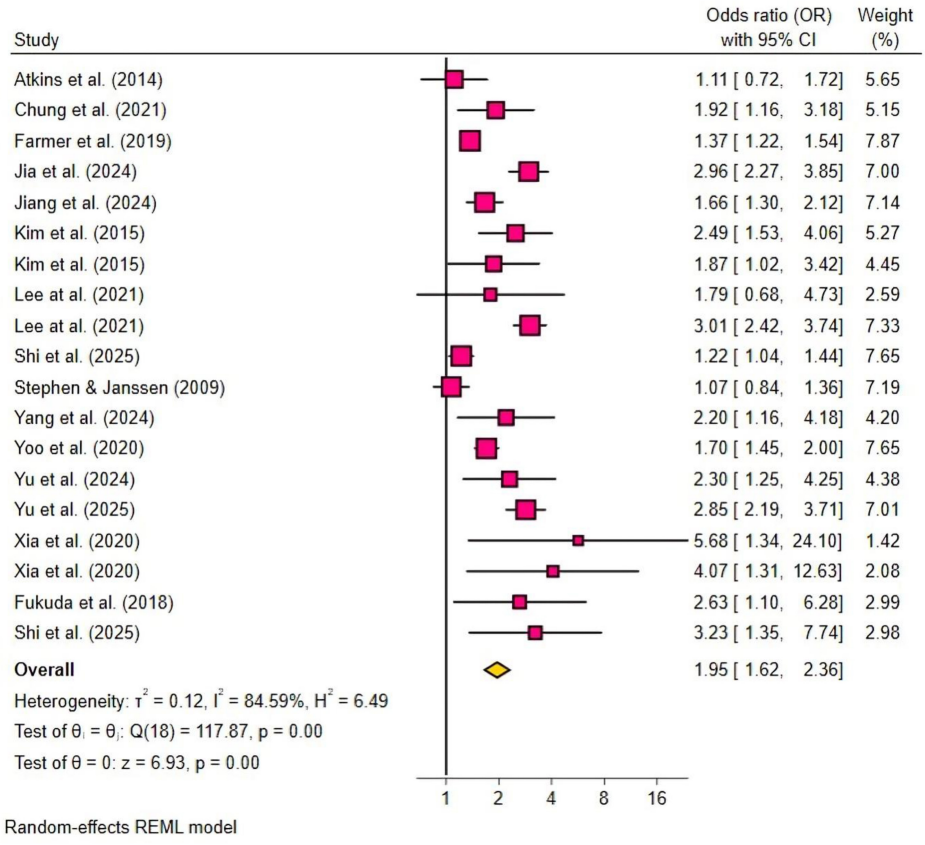

Figure 2. Forest plot of the pooled odds ratios for the association between sarcopenic obesity and overall cardiovascular diseases risk.

The subgroup analysis stratified by geographical region (Supplementary Table 4) revealed that studies performed in both categorized regions showed significant positive associations, although the effect sizes and heterogeneity patterns varied substantially. The pooled analysis of 5 studies from Europe and North America demonstrated a moderate but significant association between SO and CVD risk (OR = 1.56, $P = .023$, 95% CI: 1.06-2.28; $I^2 = 90.81\%$, $\tau^2 = 0.16$). In contrast, the East Asian subgroup showed a stronger and more consistent association (OR = 2.16, $P < .001$, 95% CI: 1.75-2.65), while still exhibiting substantial heterogeneity ($I^2 = 74.75\%$, $\tau^2 = 0.08$). The subgroup analysis by study design (Supplementary Table 4) also revealed significant positive associations in both cohort and cross-sectional studies. The analysis of prospective and retrospective cohort studies showed a significant association between SO and CVD risk (OR = 1.77, $P < .001$, 95% CI: 1.35-2.32; $I^2 = 90.13\%$, $\tau^2 = 0.15$). Cross-sectional analyses demonstrated a somewhat stronger pooled association (OR = 2.25, $P < .001$, 95% CI: 1.80-2.82) with moderate heterogeneity ($I^2 = 52.04\%$, $\tau^2 = 0.05$). With respect to population characteristics (Figure 4), analyses of the general population (OR = 1.84, $P < .001$, 95% CI: 1.50-2.26; $I^2 = 86.19\%$, $\tau^2 = 0.11$) and diabetic subgroups (OR = 2.95, $P < .001$, 95% CI: 2.32-3.76; $I^2 = 0\%$) showed significant associations

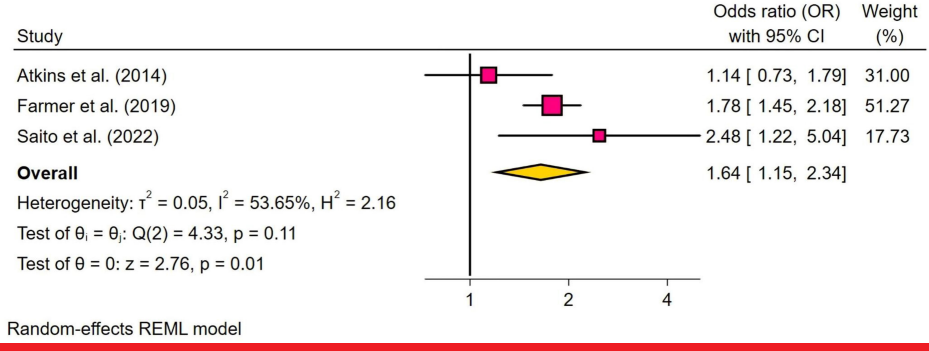

Figure 3. Forest plot of the pooled odds ratios for the association between sarcopenic obesity and cardiovascular disease–related mortality.

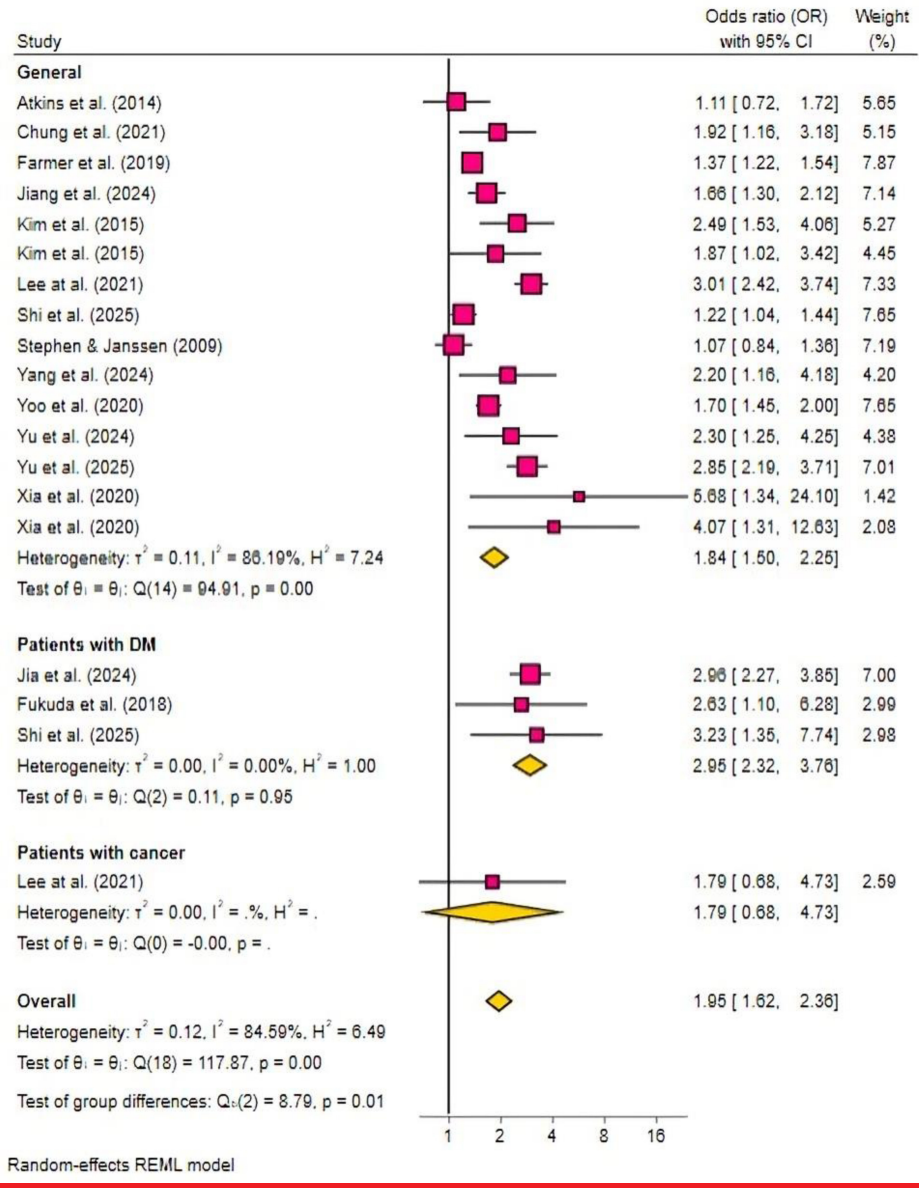

Figure 4. Subgroup analysis of the association between sarcopenic obesity and cardiovascular diseases risk stratified by population characteristics.

between SO and CVD, while the single cancer survivor study showed a non-significant association (OR = 1.79, *P* = .24, 95% CI: 0.68-4.73).

The subgroup analysis on different specific cardiovascular outcomes showed that the association between SO and CVD risk varies by outcome type (Supplementary Table 4). Four datasets examining general heart disease showed a modest but significant pooled association (OR = 1.21, *P* = .003, 95% CI: 1.11-1.70). Three studies examining heart failure demonstrated a pooled OR of 1.69 (*P* = .065, 95% CI: 0.97-2.94), which did not reach statistical significance. The strongest associations were observed for myocardial infarction (OR = 4.07, *P* = .015, 95% CI: 1.31-12.63; 1 study) and atrial fibrillation (OR = 2.93, *P* < .001, 95% CI: 2.23-3.65; 2 studies). More details are available in Supplementary Table 4.

To further investigate potential sources of heterogeneity and examine the robustness of the primary findings, *P*-values were calculated for interaction. Subgroup analyses revealed that the association between SO and CVD risk differed significantly by sex (*P*-interaction = .032) and by specific cardiovascular outcome type (*P*-interaction = .001). In contrast, the effect sizes did not differ significantly across age groups (*P*-interaction = .683), geographic regions (*P*-interaction = .143), or study designs (*P*-interaction = .181) (Supplementary Table 4). These results confirm that the strength of the association is modified by sex and the specific cardiovascular endpoint being assessed.

Sensitivity and Cumulative Analysis

In sensitivity analysis (Figure 5A), the pooled OR remained statistically significant (all *P* < .001) regardless of which

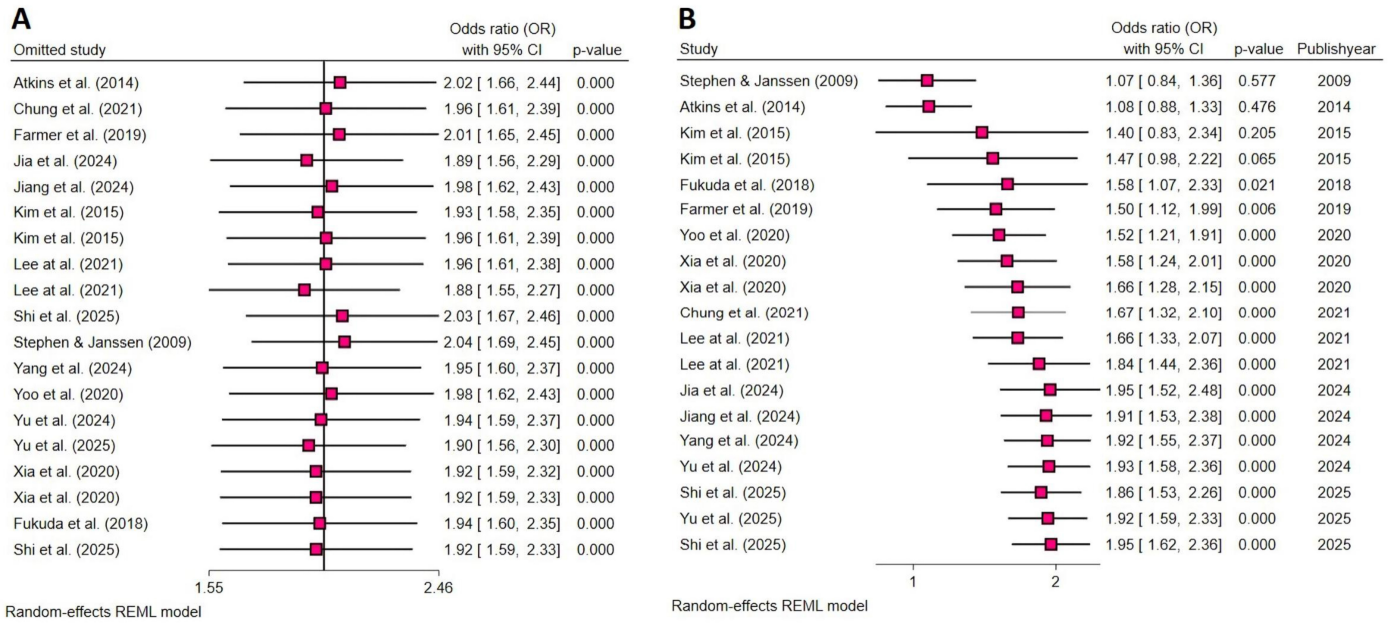

Figure 5. Sensitivity and cumulative meta-analysis. (A) Leave-one-out sensitivity analysis showing robustness of the pooled cardiovascular disease risk estimate. (B) Cumulative meta-analysis demonstrating the temporal strengthening of evidence linking sarcopenic obesity to cardiovascular disease risk as studies were added chronologically.

single study was omitted, ranging from 1.88 [1.55-2.27] to 2.04 [1.69-2.45]. Moreover, the cumulative meta-analysis revealed a progressive strengthening of evidence linking SO to CVD risk over time (Figure 5B).

DISCUSSION

Our meta-analysis demonstrates a significant association between SO and increased risk of CVDs. Individuals with SO had nearly twice the odds of developing CVD compared to non-sarcopenic, non-obese counterparts. Moreover, the analysis of CVD-related mortality indicated a 64% increase in risk among individuals with SO, further emphasizing the adverse prognostic implications of this phenotype. Subgroup analyses provided additional insight into population-specific patterns. The association between SO and CVD remained statistically significant across sex, with pooled effect sizes slightly higher in males than females (Supplementary Table 4); importantly, the *P*-value for interaction indicated a significant difference between sexes ($P = .032$). Age-stratified analyses showed a comparable risk elevation in both younger and older adults, with no significant interaction by age ($P = .683$; Supplementary Table 4). Studies conducted in East Asian populations yielded stronger and more consistent associations compared to those from Western populations, though this difference was not statistically significant (*P*-interaction = .143). Similarly, both cohort and cross-sectional studies demonstrated significant positive associations, but without evidence of a significant difference by study design ($P = .181$). Similarly, SO was more strongly associated with CVD in diabetic individuals than in the general population, suggesting heightened vulnerability in this subgroup. Notably, the association between SO and CVD risk varied significantly across cardiovascular outcomes (*P*-interaction = .001): the strongest effects were observed for myocardial infarction and atrial fibrillation, while associations with stroke and heart failure were weaker or non-significant (Supplementary Table 4). These findings confirm that the strength of the association is modified by sex and by the specific cardiovascular endpoint being assessed. The robustness of these findings was supported by sensitivity analyses, which showed that the overall effect estimates remained stable across all leave-one-out iterations. Cumulative meta-analysis further revealed a temporal strengthening of the association between SO and CVD risk, indicating consistency and growing evidence across studies over time.

The present meta-analysis is the first to comprehensively evaluate the association between SO and both CVD and CVD-related mortality. It revealed significantly increased odds of CVD and CVD-specific mortality. These results are in line with previous literature, though broader in scope, integrating various populations and cardiovascular endpoints. Among studies directly evaluating SO, Tian et al[28] (2015) reported a 24% increased risk of all-cause mortality in SO individuals (HR = 1.24, $P < .001$, 95% CI: 1.12-1.37), with a stronger effect in men (HR = 1.23, $P = .0017$, 95% CI: 1.08-1.41) than women (HR = 1.16, $P = .13$, 95% CI: 0.96-1.41). Similarly, Atkins et al[15] (2014) found SO was associated with increased CVD mortality (HR = 1.72, $P < .001$, 95% CI: 1.35-2.18) in older men. Zhang et al[29] (2019) also confirmed elevated mortality risk in SO populations (HR = 1.21, $P < .001$, 95% CI: 1.10-1.32), particularly in hospitalized patients (HR = 1.65, $P < .001$, 95% CI: 1.17-2.33). Regarding sarcopenia alone, Xu et al[30] (2022) synthesized 56 cohort studies and found sarcopenia doubled mortality risk (HR = 2.00, $P < .001$, 95% CI: 1.71-2.34), independent of population or definition. Zuo et al[31] demonstrated a

pooled sarcopenia prevalence of 35% in CVD patients versus 13% in the general population, with the highest prevalence in CAD (43%) and heart failure (32%). Zhang et al[32] estimated a similar 34% prevalence in HF patients, rising to 55% in hospitalized settings. These findings support the high CVD burden in sarcopenic patients, consistent with the present meta-analysis. In studies evaluating obesity alone, Flegal et al[33] showed that class II/III obesity increased all-cause mortality (HR = 1.18, $P < .001$, 95% CI: 1.12-1.25). Du et al[34] performed a meta-analysis of 16 studies and found significant associations between sarcopenia and metabolic syndrome components—body mass index (BMI), glucose, blood pressure, lipids, and insulin resistance—with stronger effects in males. These metabolic dysfunctions support a shared pathophysiological link between sarcopenia and CVD. Together, these studies support the current findings and indicate that SO is more detrimental than sarcopenia or obesity alone. The present meta-analysis further expands the evidence by including subgroup analyses (e.g., sex, region, age, outcome type), providing a nuanced understanding of SO's impact on cardiovascular health.

Sarcopenic obesity contributes significantly to cardiovascular risk through a convergence of metabolic, inflammatory, and hormonal dysfunctions. Visceral adiposity promotes a chronic low-grade inflammatory state characterized by elevated levels of tumor necrosis factor-alpha, interleukin-6 (IL-6), and C-reactive protein, which accelerate endothelial dysfunction and atherogenesis.[7,35] Simultaneously, sarcopenia reduces skeletal muscle insulin sensitivity and impairs glucose disposal, compounding systemic insulin resistance. These interdependent processes result in increased arterial stiffness, vascular remodeling, and higher susceptibility to hypertension, atherosclerosis, and myocardial infarction.[36] Notably, SO is more than the additive effects of obesity and sarcopenia; it represents a synergistic phenotype with a distinct inflammatory and metabolic signature.[1,2] Additionally, SO is associated with mitochondrial dysfunction, oxidative stress, and lipid accumulation within muscle fibers (myosteatosis), leading to reduced energy capacity, impaired muscle regeneration, and enhanced proteolysis.[37] This muscle deterioration further limits physical activity and metabolic rate, exacerbating fat gain and cardiometabolic burden. Hormonal alterations common in aging, such as reduced levels of testosterone, estrogen, growth hormone, and insulin-like growth factor 1 (IGF-1), impair muscle protein synthesis and promote visceral fat deposition, reinforcing the SO phenotype.[38] Reduced secretion of protective myokines (e.g., irisin, IL-15) diminishes skeletal muscle's anti-inflammatory and cardioprotective roles.[39] Collectively, these pathophysiological changes establish a high-risk cardiovascular environment, highlighting the need for SO to be incorporated into clinical cardiovascular risk stratification and targeted prevention strategies.[8,40]

This meta-analysis is one of the most comprehensive to date evaluating the association between SO and CVD, and it offers several important strengths. First, it includes a large pooled sample derived from 16 studies (19 datasets), spanning more than 7 countries across East Asia, Europe, and North America, which enhances both the statistical power and the generalizability of the findings. The geographic diversity of included studies allowed for meaningful cross-regional comparisons, highlighting potential population-specific risk patterns. Second, the analysis incorporated multiple high-quality prospective cohort studies, some with long-term follow-up, along with well-conducted cross-sectional and retrospective cohorts. The majority of included studies utilized objective and validated tools to define SO—such as dual-energy X-ray absorptiometry or bioelectrical impedance analysis—and reported standardized cardiovascular outcomes including myocardial infarction, heart failure, atrial fibrillation, and multimorbidity. Third, the extensive subgroup analyses conducted in this review—by sex, age, geographic region, study design, population characteristics, and specific cardiovascular outcomes—allowed for exploration of effect modifiers and revealed important variations in risk profiles. Fourth, sensitivity analyses and cumulative meta-analysis confirmed the robustness and temporal consistency of these findings, demonstrating that the overall results were not driven by any single study.

Despite its strengths, this meta-analysis has several limitations that warrant careful consideration. First, substantial heterogeneity was observed across the included studies ($I^2 = 84.6\%$), which may reflect differences in study design, sample characteristics, measurement tools, and outcome definitions. Although subgroup and sensitivity analyses were conducted to explore potential sources of heterogeneity, residual variation remains and may limit the precision of pooled effect estimates. Second, the diagnostic criteria for SO varied considerably among studies. Definitions of sarcopenia differed based on muscle mass index, grip strength, or gait speed, and obesity was assessed using different indices such as BMI, fat mass percentage, or visceral fat area. This inconsistency may have led to misclassification and variability in identifying affected individuals across studies. As a result, sensitivity or subgroup analyses could not be conducted based on specific definitions (e.g., BMI-based vs. other measures). Future studies should adopt standardized diagnostic criteria for SO to enable such subgroup analyses and improve comparability across research. Third, while the inclusion of both cohort and cross-sectional studies allowed for a broader synthesis, the reliance on non-longitudinal designs in a substantial portion of the dataset (6 cross-sectional, 2 retrospective) limits causal inference. Even among prospective cohorts, residual confounding remains a concern, as unmeasured or inconsistently reported variables (e.g., nutritional status, hormonal factors, inflammatory biomarkers, or physical performance metrics) were not uniformly accounted for. Fourth, although most studies adjusted for common cardiovascular risk factors such as age, sex, hypertension, and diabetes, there was variation in the covariates included in multivariable models, potentially affecting comparability and effect size estimation. Fifth, only a small number of studies (n = 3) reported CVD-related mortality as a distinct outcome, limiting the precision and generalizability of the pooled estimate for mortality risk. Sixth, few studies clearly differentiated between visceral

and subcutaneous fat or used advanced imaging to characterize body composition in more physiologically meaningful ways. Additionally, none of the included studies incorporated biomolecular markers or omics-based profiling (e.g., metabolomics, proteomics) to explore mechanistic pathways linking SO and CVD. Finally, this assessment suggests the presence of publication bias, as indicated by the funnel plot asymmetry and a significant Egger's test. Therefore, the overall estimate may be influenced by the absence of unpublished studies with null results, which may have been missed despite the comprehensive search of databases and grey literature. Collectively, these limitations highlight the methodological challenges inherent in synthesizing SO-related outcomes and emphasize the need for standardized definitions, improved reporting, and more mechanistic investigation in future research.

In conclusion, this meta-analysis provides robust evidence that SO is significantly associated with increased risk of CVDs and CVD-related mortality. The strength and consistency of this association across diverse populations, study designs, and cardiovascular outcomes underscore the clinical importance of recognizing SO as a distinct and high-risk phenotype. Compared to sarcopenia or obesity alone, SO confers a substantially higher cardiovascular burden, likely due to the synergistic interplay between metabolic dysfunction, inflammation, and physical decline. Given the growing prevalence of SO in aging populations worldwide, early identification, risk stratification, and tailored interventions are urgently needed. Future studies should prioritize the use of standardized definitions, longitudinal designs, and mechanistic investigations to further elucidate the pathophysiological links between SO and cardiovascular health.

Data availability statement: All data supporting the findings of this study are included within the manuscript and its supplementary materials. Additional datasets, if required, are available from the corresponding author upon reasonable request.

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Author Contributions: Concept – Z.Z., X.Z.; Design – Z.Z., X.Z.; Supervision – Z.Z., X.Z.; Resource – Z.Z., X.Z.; Materials – Z.Z., X.Z.; Data Collection and/or Processing – Z.Z., X.Z.; Analysis and/or Interpretation – Z.Z., X.Z.; Literature Search – Z.Z., X.Z.; Writing – Z.Z., X.Z.; Critical Reviews – Z.Z., X.Z.

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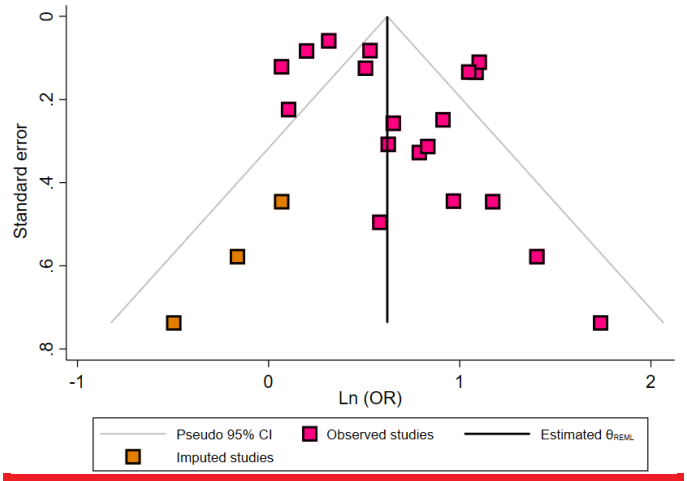

Supplementary Figure 1. Funnel plot assessing publication bias for studies included in the meta-analysis. Visual inspection revealed no significant asymmetry, suggesting evidence of publication bias.

Supplementary Table 1. Sarcopenic obesity definition in individual studies

Study	Sarcopenic obesity definition
Stephen & Janssen (2009)[12]	**Obesity:** Classified using sex-specific tertiles of waist circumference (WC). Subjects in the highest WC tertile were considered "obese." **Sarcopenia:** Classified using sex-specific tertiles of skeletal muscle mass (estimated via bioelectrical impedance analysis, BIA). Subjects in the lowest muscle mass tertile were considered "sarcopenic." **Sarcopenic-Obesity:** Subjects in the highest WC tertile (obese) and lowest muscle mass tertile (sarcopenic) were classified as "sarcopenic-obese."
Atkins et al. (2014)[13]	**Obesity:** Waist circumference (WC) > 102 cm. **Sarcopenia:** Lowest two-fifths of the midarm muscle circumference (MAMC) distribution (≤ 25.9 cm). ***Sarcopenic-Obesity:*** Participants with WC > 102 cm (obese) and MAMC ≤ 25.9 cm (sarcopenic).
Kim et al. (2015)[14]	**Obesity** • **Measurement**: Body mass index (BMI). • **Obesity Cutoff**: BMI ≥ 25 kg/m² (Asian-specific cutoff for obesity). **Sarcopenia:** • **Measurement**: Appendicular skeletal muscle mass (ASM; kg) was measured using **dual-energy X-ray absorptiometry (DXA)**. • **Sarcopenia Cutoff**: o Participants with **ASM/body weight (ASM/Wt) < 1 standard deviation (SD) below the mean** of a sex-specific healthy reference group (aged 20–39 years). o **Cutoff Values**: • **Men**: ASM/Wt < 31.30%. • **Women**: ASM/Wt < 24.76%. **Sarcopenic-Obesity:** BMI ≥ 25 kg/m² and ASM/Wt < 31.30% (men) or < 24.76% (women).
Kim et al. (2015)[14]	**Obesity** • **Measurement**: Body mass index (BMI). • **Obesity Cutoff**: BMI ≥ 25 kg/m² (Asian-specific cutoff for obesity). **Sarcopenia:** • **Measurement**: Appendicular skeletal muscle mass (ASM; kg) was measured using **dual-energy X-ray absorptiometry (DXA)**. • **Sarcopenia Cutoff**: o Participants with **ASM/body weight (ASM/Wt) < 1 standard deviation (SD) below the mean** of a sex-specific healthy reference group (aged 20–39 years). o **Cutoff Values**: • **Men**: ASM/Wt < 31.30%. • **Women**: ASM/Wt < 24.76%. **Sarcopenic-Obesity:** BMI ≥ 25 kg/m² and ASM/Wt < 31.30% (men) or < 24.76% (women).

Supplementary Table 1. Sarcopenic obesity definition in individual studies (Continued)

Study	Sarcopenic obesity definition
Fukuda et al. (2018)[15]	**Obesity** **Android-to-Gynoid Fat Ratio (A/G ratio):** Higher than the sex-specific median: Men: >0.80; Women: >0.62 **Android Fat Mass:** Higher than the sex-specific median: Men: >2.16 kg; Women: >1.95 kg **Percentage of Body Fat (%BF):** Higher than the sex-specific median: Men: >31.8%; Women: >38.8% **Body Mass Index (BMI):** BMI ≥25 kg/m^2 (standard threshold for obesity in Japan). **Sarcopenia:** Sarcopenia was defined as SMI less than 7.0kg/m2 (in men) or 5.4kg/m2 (in women) according to the criteria for Asians. **Sarcopenic-Obesity:** Coexistence of low SMI and obesity.
Farmer et al. (2019)[6]	The study used multiple definitions of sarcopenic obesity by combining different measures of adiposity and muscle quality. Here are the specific definitions employed: **Primary Definition:** • **Adiposity**: Measured by **Body Mass Index (BMI)** with obesity defined as **BMI > 30 kg/m^2**. • **Muscle Quality**: Measured by **Handgrip Strength (HGS)** with sarcopenia defined as: o **<30 kg for men** o **<20 kg for women**. **Secondary Definitions:** 1. **Alternative Adiposity Measures:** o **Waist-Hip Ratio (WHR)**: • Obesity cutoffs: **≥0.95 for men** and **≥0.80 for women**. o **Fat Mass Percentage**: • No standard cutoff for obesity was used; instead, quintiles were compared. 2. **Alternative Muscle Quality Measures:** • **Skeletal Muscle Mass Index (SMMI)**: o Calculated from bioelectrical impedance using the Janssen equation. o Sarcopenia defined as the **bottom 40% of the distribution**. **Sarcopenic obesity**: Both obese and sarcopenic.
Xia et al. (2020)[16]	The study defines sarcopenic overweight/obesity based on two criteria: 1. **Sarcopenia**: Defined using the Asian Working Group for Sarcopenia (AWGS) criteria, where sarcopenia is identified by a low appendicular skeletal muscle mass (ASM) adjusted for height (ASM/height^2). The cutoff points are: o **Men**: ASM/height^2 < 7.0 kg/m^2 o **Women**: ASM/height^2 < 5.4 kg/m^2 2. **Overweight/Obesity**: Defined according to BMI thresholds for Chinese adults: o **Overweight**: BMI ≥ 24 kg/m^2 o **Obesity**: BMI ≥ 28 kg/m^2 **Sarcopenic overweight/obese**: BMI ≥ 24 kg/m^2 with sarcopenia.
Xia et al. (2020)[16]	The study defines sarcopenic overweight/obesity based on two criteria: 3. **Sarcopenia**: Defined using the Asian Working Group for Sarcopenia (AWGS) criteria, where sarcopenia is identified by a low appendicular skeletal muscle mass (ASM) adjusted for height (ASM/height^2). The cutoff points are: o **Men**: ASM/height^2 < 7.0 kg/m^2 o **Women**: ASM/height^2 < 5.4 kg/m^2 4. **Overweight/Obesity**: Defined according to BMI thresholds for Chinese adults: o **Overweight**: BMI ≥ 24 kg/m^2 o **Obesity**: BMI ≥ 28 kg/m^2 **Sarcopenic overweight/obese**: BMI ≥ 24 kg/m^2 with sarcopenia.
Yoo et al. (2020)[17]	The study defines **sarcopenic obesity** based on two criteria: 1. **Sarcopenia**: Defined as having a **skeletal muscle mass index (SMI)** below 1 standard deviation (SD) of the sex-specific mean for a young reference group (aged 18–40 years). The cutoff points are: o **Men**: SMI < 30.0% o **Women**: SMI < 26.8% 2. **Obesity**: Defined using **three methods** (applied separately in analyses): • **BMI**: BMI ≥ 25 kg/m^2 (Asian-specific cutoff for obesity). o Men: FM% ≥ 25% o Women: FM% ≥ 35%. • **Body Fat Percentage (FM%)**: Above the 60th percentile of the study population: o Men: WC ≥ 90 cm o Women: WC ≥ 85 cm (reflecting visceral obesity). • **Waist Circumference (WC)**: **Sarcopenic Obesity**: Both sarcopenic and obese.

(*Continued*)

Supplementary Table 1. Sarcopenic obesity definition in individual studies (Continued)

Study	Sarcopenic obesity definition
Chung et al. (2021)[18]	In this study, **sarcopenic obesity (SO)** was defined based on the following criteria: 1. **Sarcopenia**: o **Men**: ASM% < 29.0 o **Women**: ASM% < 22.9 • Measured using **appendicular skeletal muscle mass (ASM)** via bioelectrical impedance analysis (BIA). • Sarcopenia was defined as an ASM% **more than two standard deviations below the sex-specific mean** for healthy young adults: 2. **Obesity**: o Defined as a **body mass index (BMI) ≥ 25 kg/m²**, based on World Health Organization recommendations for the Asian-Pacific population. 3. **Sarcopenic Obesity (SO)**: o The coexistence of **both sarcopenia (ASM% < 29.0 in men or < 22.9 in women) and obesity (BMI ≥ 25)** in the same individual.
Lee at al. (2021)[19]	In this study, sarcopenic obesity (SO) was defined based on the following criteria: 1. Sarcopenia: • These cutoffs align with the Asian Working Group for Sarcopenia (AWGS) consensus. o Men: HGS < 26 kg o Women: HGS < 18 kg • Measured using handgrip strength (HGS) via a digital dynamometer. • Defined as: 2. Obesity: • Defined as body mass index (BMI) ≥ 25 kg/m², following WHO guidelines for the Asian-Pacific population. Sarcopenic Obesity (SO): -The coexistence of sarcopenia (low HGS) and obesity (high BMI).
Lee at al. (2021)[19]	In this study, sarcopenic obesity (SO) was defined based on the following criteria: 1. Sarcopenia: • These cutoffs align with the Asian Working Group for Sarcopenia (AWGS) consensus. o Men: HGS < 26 kg o Women: HGS < 18 kg • Measured using handgrip strength (HGS) via a digital dynamometer. • Defined as: 2. Obesity: • Defined as body mass index (BMI) ≥ 25 kg/m², following WHO guidelines for the Asian-Pacific population. Sarcopenic Obesity (SO): -The coexistence of sarcopenia (low HGS) and obesity (high BMI).
Jia et al. (2024)[20]	In this study, sarcopenic obesity (SO) was defined using the following criteria: 1. Sarcopenia: • Based on the European Working Group on Sarcopenia in Older People 2019 (EWGSOP2) criteria for "probable sarcopenia." o Men: HGS < 27 kg o Women: HGS < 16 kg • Measured by handgrip strength (HGS) using a Jamar dynamometer. • Defined as: 2. Obesity: • Defined as body mass index (BMI) ≥ 30 kg/m², following standard WHO thresholds. Sarcopenic Obesity (SO): • The coexistence of sarcopenia (low HGS) and obesity (high BMI).
Jiang et al. (2024)[21]	In this study, sarcopenic obesity is defined as the co-occurrence of sarcopenia and obesity, where: 1. Sarcopenia is diagnosed based on the AWGS 2019 criteria, requiring: o Low muscle mass (measured via DXA or BIA, adjusted for height), combined with o Low muscle strength (assessed by handgrip strength) or o Low physical performance (evaluated via SPPB, 6-m walk, or five-time chair stand test). 2. Obesity is defined using two criteria: o General obesity: BMI ≥ 28.0 kg/m² (Chinese criteria). o Abdominal obesity: Waist circumference ≥ 85 cm (men) or ≥ 80 cm (women). **Sarcopenic obesity**: Both obese and sarcopenic.

(*Continued*)

Supplementary Table 1. Sarcopenic obesity definition in individual studies (Continued)

Study	Sarcopenic obesity definition
Yang et al. (2024)[22]	In this study, **sarcopenic obesity (SO)** is defined as the co-occurrence of **sarcopenia** and **obesity**, where: 1. **Sarcopenia** is diagnosed based on the **Asian Working Group for Sarcopenia (AWGS) criteria**, requiring: o **Men**: <1.05 m/s o **Women**: <1.01 m/s • **OR low gait speed**: o **Men**: <28.5 kg o **Women**: <18.6 kg • **Low handgrip strength (HGS)**: • **Low muscle function**: Either: o **Men**: ASMI <7.05 kg/m^2 o **Women**: ASMI <5.85 kg/m^2 • **Low muscle mass**: Measured via bioelectrical impedance analysis (BIA), with cutoff values for the appendicular skeletal muscle mass index (ASMI) set at: 2. **Obesity** is defined as: o **Men**: ≥32.6% body fat o **Women**: ≥41.0% body fat • **High body fat percentage**: ≥80th percentile of the study population: **Sarcopenic obesity**: Sarcopenia (low muscle mass + low muscle function) + Obesity (high body fat).
Yu et al. (2024)[9]	In this study, **sarcopenic obesity (SO)** is defined as the co-occurrence of **possible sarcopenia** and **obesity**, based on the following criteria: 1. **Possible Sarcopenia** (simplified screening definition from AWGS 2019): o **Men**: <28 kg o **Women**: <18 kg • **Low muscle strength**: Measured by handgrip strength: 2. **Obesity**: o **General obesity**: Body mass index (BMI) ≥25 kg/m^2 (Asian cutoff). o **Abdominal obesity** (used in sensitivity analysis): Waist circumference (WC) ≥85 cm (men) or ≥80 cm (women). **Sarcopenic obesity**: Low grip strength (possible sarcopenia) + High BMI (obesity).
Shi et al. (2025)[10]	In this study, **sarcopenic obesity (SO)** is defined using a novel index called the **Sarcopenic Abdominal Obesity (SAO) Index**, which combines measures of sarcopenia and abdominal obesity. Participants were stratified into high SAO Index (>91.19, the median value) and low SAO Index (≤91.19) groups for analysis.
Yu et al. (2025)[23]	In this study, **sarcopenic obesity (SO)** is defined using the **ESPEN/EASO (European Society for Clinical Nutrition and Metabolism/European Association for the Study of Obesity) consensus criteria** for Asian populations. The diagnosis involves a three-step process combining **sarcopenia** and **obesity**: 1. **Sarcopenia Definition** Sarcopenia is identified by **low muscle mass** and **low muscle strength**, based on the following criteria: • **Low skeletal muscle mass (SMM) to body weight (BW) ratio**: o Men: <38.2% o Women: <32.2% • **Low appendicular lean mass (ALM) to BW ratio**: o Men: <32.5% o Women: <25.7% • **Low handgrip strength (HGS)**:Men: <28 kg Women: <18 kg2. **Obesity Definition** Obesity is defined by **high fat mass (FM) to BW ratio**: o Men: >29% o Women: >41% • **Sarcopenic Obesity (SO) Diagnosis** Participants are classified as having SO if they meet **both sarcopenia and obesity criteria** (i.e., low muscle mass/strength + high fat mass).

(*Continued*)

Supplementary Table 1. Sarcopenic obesity definition in individual studies (Continued)	
Study	**Sarcopenic obesity definition**
Shi et al. (2025)[24]	In this study, **sarcopenic obesity (SO)** is defined using the following criteria based on **body composition and skeletal muscle mass** assessed via **cardiac MRI**: 1. **Obesity Definition** • **Body Mass Index (BMI)**: o Obesity is defined as **BMI ≥ 25 kg/m²** (adjusted for Asian populations, where lower BMI thresholds are used compared to Western standards). 2. **Sarcopenia Definition** • **Thoracic Skeletal Muscle Index (SMI)**: o Sarcopenia is defined as **SMI < 42.75 cm²/m²**, where SMI is calculated as: SMI=Total bilateral axial thoracic skeletal muscle area (cm^2)Body surface area (BSA, m^2)SMI=Body surface area (BSA, m^2)Total bilateral axial thoracic skeletal muscle area (cm^2) o The thoracic skeletal muscle area includes pectoralis major/minor, serratus anterior, periscapular, paraspinal, and trapezius muscles measured at the carina level via MRI. **Sarcopenic Obesity (SO) Diagnosis** • Patients are classified as having **SO** if they meet **both criteria**: o **BMI ≥ 25 kg/m²** (obesity) o **SMI < 42.75 cm²/m²** (sarcopenia).

Supplementary Table 2. Search strategy for systematic review on sarcopenic obesity and risk of cardiovascular disease

Database	Descriptors	Number of studies reached
PubMed/Medline	("Sarcopenic Obesity"[MeSH] OR "sarcopenic obesity"[tiab] OR ("sarcopenia"[MeSH Terms] AND "obesity"[MeSH Terms]) OR ("sarcopenia"[tiab] AND "obesity"[tiab])) AND ("cardiovascular diseases"[MeSH] OR "cardiovascular disease"[tiab] OR "CVD"[tiab] OR "heart disease"[tiab] OR "coronary artery disease"[tiab] OR "myocardial infarction"[tiab] OR "stroke"[tiab]) AND ("Mortality"[MeSH] OR "mortality"[tiab] OR "death"[tiab] OR "fatal outcome"[tiab])	**111**
Scopus	(TITLE-ABS-KEY("sarcopenic obesity") OR (TITLE-ABS-KEY("sarcopenia") AND TITLE-ABS-KEY("obesity"))) AND (TITLE-ABS-KEY("cardiovascular disease") OR TITLE-ABS-KEY("CVD") OR TITLE-ABS-KEY("heart disease") OR TITLE-ABS-KEY("coronary artery disease") OR TITLE-ABS-KEY("myocardial infarction") OR TITLE-ABS-KEY("stroke")) AND (TITLE-ABS-KEY("mortality") OR TITLE-ABS-KEY("death") OR TITLE-ABS-KEY("fatal outcome"))	**382**
Embase	('sarcopenic obesity'/exp OR 'sarcopenic obesity':ti,ab OR ('sarcopenia'/exp AND 'obesity'/exp) OR ('sarcopenia':ti,ab AND 'obesity':ti,ab)) AND ('cardiovascular disease'/exp OR 'cardiovascular disease':ti,ab OR 'CVD':ti,ab OR 'heart disease':ti,ab OR 'coronary artery disease':ti,ab OR 'myocardial infarction':ti,ab OR 'stroke':ti,ab) AND ('mortality'/exp OR 'mortality':ti,ab OR 'death':ti,ab OR 'fatal outcome':ti,ab)	**667**
Web of Sciences	TS=("sarcopenic obesity" OR ("sarcopenia" AND "obesity")) AND TS=("cardiovascular disease" OR "cardiovascular diseases" OR "CVD" OR "heart disease" OR "coronary artery disease" OR "myocardial infarction" OR "stroke") AND TS=("mortality" OR "death" OR "fatal outcome")	**428**

Supplementary Table 3. Adjusted confounders in studies examining sarcopenic obesity and risk of cardiovascular disease

Studies	Effect size	Adjusted confounders
Stephen & Janssen (2009)	HR, 1.06 (0.85-1.33)	The final model (Model 3) was adjusted for age, sex, race, income, smoking, alcohol use, cognitive function, physical activity, diabetes, hypertension, HDL-cholesterol, total cholesterol, and triglycerides.
Atkins et al. (2014)	HR, 1.08 (0.77-1.52)	The final model was adjusted for age, smoking, alcohol, occupational social class, physical activity
Kim et al. (2015)	OR, 2.49 (1.53-4.06)	The final model was adjusted for total calorie intake, protein intake, resistance exercise, flexibility exercise, regular walking, equivalent income, and alcohol use disorder identification test score category.
Kim et al. (2015)	OR, 1.87 (1.02-3.41)	The final model was adjusted for total calorie intake, protein intake, resistance exercise, flexibility exercise, regular walking, equivalent income, and alcohol use disorder identification test score category.
Fukuda et al. (2018)	HR, 2.63 (1.1-6.28)	The multivariate models included high-density lipoprotein cholesterol, HbA1c, estimated glomerular filtration ratio, the use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers, the use of dipeptidyl peptidase 4 inhibitors, and history of CVD as covariates
Farmer et al. (2019)	HR, 1.42 (1.31-1.55)	The model was adjusted for age (linear term), sex, smoking status, ethnic group,deprivation, diabetes mellitus status, alcohol consumption,and moderate physical activity at baseline
Xia et al. (2020)	OR, 5.68 (1.34-24.12)	The final model (Model 3) was adjusted for: Demographic & lifestyle factors (Age, gender, alcohol drinking, cigarette smoking, and menopause (in women); Cardiometabolic factors: BMI, waist circumference (WC), fasting blood glucose (FBG), systolic blood pressure (SBP), triglycerides (TG), total cholesterol (TC), and HDL cholesterol (HDL-c); Inflammatory & liver markers: White blood cell count (WBC), alanine aminotransferase (ALT), and aspartate aminotransferase (AST).
Xia et al. (2020)	OR, 4.07 (1.31-12.62)	The final model (Model 3) was adjusted for: Demographic & lifestyle factors (Age, gender, alcohol drinking, cigarette smoking, and menopause (in women); Cardiometabolic factors: BMI, waist circumference (WC), fasting blood glucose (FBG), systolic blood pressure (SBP), triglycerides (TG), total cholesterol (TC), and HDL cholesterol (HDL-c); Inflammatory & liver markers: White blood cell count (WBC), alanine aminotransferase (ALT), and aspartate aminotransferase (AST).
Yoo et al. (2020)	OR, 1.7 (1.44-1.99)	The final model was adjusted for age, sex, smoking status, alcohol consumption, regular exercise, and LAVI
Chung et al. (2021)	OR, 1.92 (1.16-3.18)	The model was adjusted for age, sex, hypertension, diabetes, dyslipidemia, and creatinine
Lee at al. (2021)	OR, 1.79 (0.68-4.74)	The model was adjusted for sex, educational level, income level, physical activity, alcohol use, dietary intakes of protein, vitamin A, vitamin C, and calcium, time since cancer diagnosis (for cancer survivors) and current cancer therapy (for cancer survivors)
Lee at al. (2021)	OR, 3.01 (2.42-3.73)	The model was adjusted for sex, educational level, income level, physical activity, alcohol use, dietary intakes of protein, vitamin A, vitamin C, and calcium, time since cancer diagnosis (for cancer survivors) and current cancer therapy (for cancer survivors)
Jia et al. (2024)	HR, 2.29 (1.92-2.73)	The final model (Model 2) was adjusted for age, sex, ethnicity, educational level, Townsend deprivation index, smoking status, alcohol intake frequency, regular exercise, healthy diet, sedentary time, sleep duration, diabetes duration, antihyperglycemic agents use, and family histories of cardiovascular disease and diabetes.
Jiang et al. (2024)	HR, 1.47 (1.2-1.8)	adjusted for age, sex, place of residence, education level, smoking and alcoholconsumption status, hypertension, dyslipidemia, diabetes, kidney disease, anti-hypertension drug, anti-dyslipidemia and anti-diabetes medicines.
Yang et al. (2024)	OR, 2.2 (1.16-4.19)	The model was adjusting for age and sex
Yu et al. (2024)	HR, 2.302 (1.24-4.23)	The final model (Model 4) was adjusted for age, male sex, urban residence, education level, marital status, smoking, alcohol drinking, regular exercise, hypertension, hypercholesterolemia, kidney disease, antihypertensive medications, diabetes medications, lipid-lowering therapy, systolic blood pressure (SBP), and diastolic blood pressure (DBP).
Shi et al. (2025)	HR, 1.2 (1.01-1.4)	The final model (Model 3) was adjusted for age group, sex, smoking status, drinking status, hypertension, dyslipidemia, and diabetes.
Yu et al. (2025)	HR, 2.669 (2.11-3.38)	Adjusted for age, sex, smoking, alcohol consumption, regular exercise, medical and medication histories, body mass index, blood pressure, heartbeat, plasma lipid profile data,eGFR.
Shi et al. (2025)	HR, 3.03 (1.39-6.63)	The final model (Model 3) was adjusted for age, sex, NT-proBNP, hypoproteinemia, anemia, diabetes mellitus duration, use of β-blockers, insulin, ARNI, SGLT-2 inhibitors, left ventricular ejection fraction (LVEF), and global longitudinal strain (GLS).

Supplementary Table 4. Results of subgroup analyses of the association between sarcopenic obesity (SO) and cardiovascular disease (CVD) risk

Variables	Odds ratio	Heterogeneity I^2 (%)	*P*-value	*P*-interaction
Sex				0.032
Men	2.56 (2.15–3.06)	0.0	< 0.001	
Women	2.35 (1.90–2.92)	0.0	< 0.001	
Both	1.75 (1.39–2.20)	87.3	< 0.001	
Age				0.683
Younger age	1.97 (1.49–2.60)	73.5	< 0.001	
Older age	1.81 (1.32–2.47)	65.8	< 0.001	
Geographical region				0.143
Europe and North America	1.56 (1.06–2.28)	90.8	0.023	
East Asia	2.16 (1.75–2.65)	74.7	< 0.001	
Study design				0.181
Cohort	1.77 (1.35–2.32)	90.1	< 0.001	
Cross-sectional	2.25 (1.80–2.82)	52	< 0.001	
Cardiovascular outcome				0.001
Atrial fibrillation	2.93 (2.23–3.86)	0	< 0.001	
Heart diseases	1.37 (1.11–1.70)	50.8	0.003	
Heart failure	1.69 (0.97–2.94)	92.8	0.065	
Left ventricular diastolic dysfunction	1.70 (1.45-2.0)	0.0	< 0.001	
Myocardial infarction	4.07 (1.31–12.63)	0.0	0.015	
Stroke	1.39 (0.86–2.24)	76.6	0.180	
Coronary artery calcification	1.92 (1.16–3.18)	0.0	0.011	