Associations between sarcopenic obesity and cognitive impairment: A systematic review

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Abstract

Importance: Around 50 million people worldwide live with severe cognitive impairment and the number is predicted to triple by 2050. A previous meta-analysis reported that sarcopenia was significantly associated with cognitive impairment, but whether the coexistence of sarcopenia and obesity would have additive exacerbating effects on cognitive performance remains widely unknown.

Objective: This systematic review aims to investigate whether sarcopenic obesity, compared to having neither sarcopenia nor obesity, sarcopenia only, and obesity only, is associated with a higher risk of cognitive impairment among the middle and older aged population.

Evidence Review: An electronic search of PubMed and Embase was conducted on February 4, 2024, using keywords related to sarcopenia, obesity, and cognitive impairment. Original research articles written in English, not previously published literature reviews or systematic reviews, based on participants aged 40 years or older, assessed sarcopenia, obesity, and sarcopenic obesity, and reported cognitive impairment were included. Risk of bias was assessed based on the Newcastle-Ottawa scale and the narrative method was used to present the results.

Findings: After reviewing 468 studies, seven studies (one cohort and six cross-sectional studies) were included in this systematic review. Sample population sizes

varied from 353 to 5822. The methods of exposure and outcome measurements varied by studies. Despite the lack of consensus on diagnostic criteria, sarcopenic obesity was consistently associated with an increased risk of cognitive impairment compared to having neither or one of sarcopenia and obesity (odds ratios or a hazard ratio ranging from 1.20 to 2.55). Sarcopenia alone was positively associated with cognitive impairment but with varying statistical significance.

Conclusions and Relevance: Future prospective cohort studies are required to determine the necessary prevention and treatment strategies to reduce the burden of sarcopenic obesity as well as sarcopenia followed by cognitive impairment. Standardized definitions for sarcopenic obesity and more precise diagnostic tools for obesity are highly demanded.

Keywords: Sarcopenia, Obesity, Cognitive dysfunction

Introduction

Deterioration in cognitive function occurs as a neurodegenerative process of aging and poses a substantial public health burden as the aging of the population has become a predominant trend globally. Around 50 million people worldwide live with severe cognitive dysfunction such as dementia, and the number is predicted to increase by 152 million in less than 30 years [1]. Some risk factors known to be related to cognitive impairment include immune or inflammatory response, hormonal dysregulation, oxidative stress, and malnutrition, all of which share pathophysiology with geriatric syndromes, such as sarcopenia.

Sarcopenia is a complex skeletal muscle disease accompanied by progressive loss of skeletal muscle mass and strength with age. Along with the increasing prevalence of cognitive decline, sarcopenia has become a major public health concern as previous studies demonstrated an independent positive association between sarcopenia and cognitive impairment [2-7]. A meta-analysis on sarcopenia and cognitive dysfunction reported that sarcopenia was significantly associated with cognitive impairment independent of confounders such as age, sex, education level, depression, physical performance, and common comorbidities [3].

Changes in body composition among elderly individuals not only manifest muscle weakness but could entail obesity, particularly featured as excessive accumulation of visceral fat. Obesity has been an established risk factor for a range of chronic diseases and premature death [8]. However, unlike sarcopenia, the exact mechanisms linking obesity to cognitive dysfunction are yet to be determined, although several pathways

including sedentary behavior, inflammation, and vascular damage have been proposed [9,10].

Moreover, there has been rising concern if the coexistence of sarcopenia and obesity – sarcopenic obesity – would have additive exacerbating effects on cognitive performance [11,12]. Preliminary evidence suggests that sarcopenic obesity is associated with cognitive impairment by causing an imbalance in myokine secretion and memory impairment [13] and exacerbating the secretion of pro-inflammatory myokines [14]. However, the evidence on this relationship remained inconclusive, and no consensus was made on whether sarcopenic obesity presents a greater risk for cognitive dysfunction compared to sarcopenia or obesity alone.

In this systematic review, we aimed to (1) summarize the associations of sarcopenic obesity with cognitive impairment among middle and older aged population, and (2) investigate whether the coexistence of sarcopenia and obesity heightened the risk of cognitive impairment compared with either sarcopenia or obesity alone.

Methods

Search Strategy and Selection Criteria

We performed an extensive search for eligible studies using PubMed and Embase as search engines until February 4th, 2024. Search terms for each search engine are presented in **Supplementary Table 1**. The searches included combinations of the following search terms: *sarcopenia, muscle atrophy,* or *muscle loss,* and *obesity, adiposity, body fat, body composition, body mass index,* or *obesity paradox,* and *cognitive impairment, cognitive decline, cognitive defect,* or *cognitive dysfunction*. This

review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines modified for a single independent reviewer. The inclusion and exclusion criteria of studies were defined based on the PICOT elements as follows: Population (P) = Middle and older aged population with ≥40 years of age; Intervention/Exposure (I) = Sarcopenic obesity measured by any methods; Comparison (C) = Sarcopenia only, obesity only, and being in a healthy status (having neither of them); Outcome (O) = Cognitive impairment; and Time (T) = All types of observational studies including cross-sectional design. Thus, eligible studies included all types of observational studies targeting persons aged 40 years or older, assessed sarcopenia, obesity, and sarcopenic obesity using any methods, and reported cognitive impairment using any methods. We only included original research articles written in English and not previously published literature reviews or systematic reviews. The flow chart for the study selection is presented in **Figure 1**.

Data Extraction and Quality Assessment

One reviewer screened the titles and abstracts through EndNote 21 and selected full texts of articles for review. The following information was extracted from the included studies: author; year; country/area; study design; type of population; sample size; sex; age; definition of sarcopenia, obesity, sarcopenic obesity, and cognitive impairment; follow-up duration; and associations (odds ratios, relative risk, and beta coefficients) of sarcopenia, obesity, and sarcopenic obesity with cognitive impairment. The qualitative summaries are presented in **Tables 1** and **2**. Quality appraisal including study sample selection, ascertainment of exposure and outcome variables, and comparability of the

clinical studies was evaluated by the Newcastle-Ottawa Scale (NOS). The NOS scale examined possible selection bias of study samples as well as measurement errors of exposure and outcome variables used in the studies. The NOS form for cohort studies was used to assess the included cohort study. The scale was modified for the cross-sectional studies to remove control group-related items. A study with scores of 0-3 was regarded as low quality, 4-6 as moderate, and 7-9 as high quality.

Results

PubMed and Embase searches returned 277 and 191 articles each and a total of 377 articles were left after removing duplicates. The overall flow of article inclusion/exclusion is described in **Figure 1**. The reviewer (HJ) screened the titles and abstracts of the list to remove irrelevant articles and 317 articles were excluded from this step (68 with irrelevant article type, 171 with irrelevant exposure, and 78 with irrelevant outcome). The remaining 60 articles were screened by reading full-text, and 53 articles were additionally excluded due to irrelevant exposure (n=25), irrelevant outcome (n=19), inappropriate categorization of sarcopenic obesity (n=8), and inappropriate age range (n=1, included age <40 years). Seven studies remained at the end of the screening to be included in this systematic review [12,15-20].

Study Characteristics

Table 1 shows the characteristics of the original studies included. Among the included studies, one was a cohort study and the other six were cross-sectional studies. Studies were published between 2018 and 2023 and the earliest year of data collection

was 2010. Two of the seven sample populations were from the United States [12,15], three from China [16,19,20], one from Japan [18], and one from Colombia [17]. Five out of seven studies were based on the general community-dwelling populations [12,15,17-19] while one study recruited subjects who were regular participants of square dance [16], and another study was based on patients of maintenance hemodialysis (MHD) [20]. Sample population sizes varied between studies ranging from 353 to 5,822.

The definitions of exposure variables, including obesity, sarcopenia, and sarcopenic obesity, varied widely between studies. The measurement methods as well as cut-offs used to diagnose exposure status are listed in **Table 2**. Obesity was measured using body mass index (BMI) [12,15-17], body fat percentage (fat mass / weight) [12,16,19,20], waist circumference (WC) [15,16], and visceral fat area (VFA) [16]. Sarcopenia was defined based on grip strength [12,15,17,18,20], appendicular skeletal muscle index (ASMI) [16,19,20], short physical performance battery (SPPB) [16], sit-to-stand test [12,17], and muscle mass (MM) [12]. Sarcopenic obesity was defined as the coexistence of obesity and sarcopenia in all studies.

The outcome of cognitive impairment was measured using different components or combinations of cognitive function tests. Overall, the impaired cognitive function was assessed based on cognitive tests such as Alzheimer's Disease 8 (AD-8) [15], Montreal Cognitive Assessment (MoCA) [12,16,18], and Mini-Mental State Examination (MMSE) [17,19,20]. One study adopted a simplified version of MMSE [17].

All seven studies adjusted for age and sex, and six studies included education as a covariate [12,15-18,20]. In addition to this, physical activity [15,16,18,19], smoking status [15-17,19,20], and alcohol drinking [16,17,19,20] were adjusted in the majority of the studies

included. Depression [12,18,19], income [16,17], and chronic comorbidity burden [18-20] were added to the covariates in some of the studies.

Result Synthesis

The simplified and synthesized results are listed in **Table 3**. All seven studies reported a significant association between sarcopenic obesity and cognitive impairment compared to the healthy group (not having both sarcopenia and obesity), despite the different measurements or definitions used. Among seven studies, five studies [12,15-18] reported an elevated risk or increased prevalence of cognitive impairment among individuals with sarcopenia alone, while three studies [12,16,19] showed an elevated risk of increased prevalence of cognitive impairment among individuals with obesity alone.

Among seven studies, two studies showed higher ORs in sarcopenia alone than in sarcopenic obesity[15,17], compared to the healthy reference. A cohort study conducted by Batsis et al. reported an increased risk of cognitive impairment from both sarcopenia only and sarcopenic obesity. However, the hazard ratios (HRs) were somewhat smaller in sarcopenic obesity (HR [95%CI] = 1.20 [1.03-1.40] in BMI-based SO and 1.39 [1.19-1.63] in WC-based SO) than in sarcopenia alone (HR [95%CI] = 1.60 [1.42-1.80] in BMI-based SO and 1.59 [1.35-1.87] in WC-based SO). O'Donovan et al. also found a similar result of a higher prevalence of cognitive impairment in both sarcopenia and sarcopenic obesity, but the OR was smaller in sarcopenic obesity compared to sarcopenia alone.

On the other hand, five studies showed an increased prevalence of cognitive impairment in sarcopenic obesity compared to sarcopenia alone or obesity alone, indicating a potential synergetic interaction effect between sarcopenia and obesity

[12,16,18-20]. Fu et al., Someya et al., Wang et al., and Zhou et al. reported higher ORs of cognitive impairment among sarcopenic obesity than among sarcopenia or obesity alone, and Tolea et al. reported the lowest score in MoCA among sarcopenic obesity, followed by sarcopenia alone and obesity alone, whatever definition used to define sarcopenia and obesity.

Quality Assessment

Table 4 presents the result of the bias assessment using the Newcastle-Ottawa scale. Five studies scored 7 or more from the total score of 9 [15-18,20], indicating they had good quality. The remaining three studies received either a 5 or 6 [12,19], indicating they had fair quality. One cohort study received a full score of 9 [15]. The other six studies lost a point due to unclear explanations of their non-response rate. Among the six studies, O'Donovan et al., Tolea et al., and Zhou et al. additionally lost a point for not including important confounding factors, such as physical activity, smoking status, or household income. Someya et al., Tolea et al., and Wang et al. lost a point due to a small sample size and low prevalence of sarcopenic obesity and/or cognitive impairment. Despite not receiving a full score, all studies were considered sufficient quality for the systematic review as they were all fair or good quality.

Discussion

In this systematic review, we explored the relationship between sarcopenic obesity and cognitive impairment, particularly by cross-tabulating the exposure as obesity only, sarcopenia only, sarcopenic obesity, and having neither of them. Despite

the lack of consensus on diagnostic criteria for sarcopenic obesity, we found that sarcopenic obesity was consistently associated with an increased risk of cognitive impairment across all the studies included. Sarcopenia in the absence of obesity was also positively associated with cognitive impairment, but the statistical significance varied by studies. Obesity in the absence of sarcopenia, on the other hand, showed an inconsistent direction of association with cognitive impairment.

Studies proposed several shared pathophysiologies explaining the observed association between sarcopenic obesity and cognitive impairment. Five studies [16-20] mentioned a possibility of shared inflammatory links between sarcopenia, obesity, and cognitive impairment. Excess body fat activates systematic inflammatory processes and triggers insulin resistance while muscle catabolism could also induce inflammation and insulin resistance [16-20]. In addition, ectopic fat infiltration especially in the skeletal muscle, entailed by obesity, could further aggravate the inflammation and enlarge the vicious circle between obesity and sarcopenia [18-20]. Chronic inflammation and insulin resistance, in turn, could deteriorate brain function and exacerbate poor cognitive efficiency and executive dysfunction, attributed to elevated serum levels of C-reactive protein and interleukin-6 [19]. Furthermore, higher insulin resistance has been found to be associated with poorer cognitive efficiency, executive dysfunction, and worse brain function [16,19,20]. Two studies [16,19] further suggested the possible interrelationship through growth hormone secretion. Both sarcopenic obesity and cognitive impairment were known to show the same hormonal deficits. Growth hormone secretion was found to be depressed in individuals with sarcopenic obesity [16,19]. Deficits in growth hormones were also likely linked to impaired cognitive function. Lastly, two studies [17,20] mentioned that

physical exercise was likely interrelated between sarcopenic obesity and brain metabolism. Both obesity and sarcopenia could result in decreased physical activity and the reverse is also possible [17,20]. Reduced amount of physical activity means decreased energy expenditure and muscle usage leading to an increased risk of sarcopenic obesity [20]. Physical activity improves cognition and brain vascular function as well, while the lack of physical exercise could result in cognitive decline.

The inconsistency of associations between sarcopenia and cognitive impairment might partly be attributed to different covariates adjusted in the model. Specifically, whether or not adjusting for chronic disease comorbidities would be a critical factor that can contribute to the inconsistency. According to the aforementioned possible pathophysiologies between sarcopenic obesity and cognitive impairment, chronic inflammation and insulin resistance could act as a mediator connecting sarcopenia and cognitive impairment. Three studies [18-20] that reported a positive but insignificant association between sarcopenia and cognitive impairment had a similarity in that they included chronic disease comorbidities, such as hypertension, diabetes, and dyslipidemia, as covariates in the model. Thus, it is possible that the impact of sarcopenia on cognitive impairment could be attenuated by conditioning on the pathway linking sarcopenia, chronic inflammation and insulin resistance, and cognitive decline.

The inconsistent associations between obesity and cognitive impairment could partly be explained by the limitation of proxy measures used to examine body fat accumulation, and the inability to take mid-life obesity into account. Unlike sarcopenia, obesity was both positively and inversely associated with cognitive impairment in the included studies. While some found obesity related to a decline in cognitive function,

others reported improved cognitive performance in obese older adults. However, one thing observed consistently was that the associations between BMI (either $\geq$ 25 kg/m^2 or $\geq$ 30 kg/m^2 cutoff points) and cognitive impairment were statistically insignificant. All but one [20] study included BMI as their diagnostic tool to classify obesity and three studies [12,15,16] used multiple diagnostic tools for comparison. Fu et al. reported that sarcopenic obesity was associated with higher odds of MCI when using visceral fat area (VFA), WC, and body fat percentage (BF%) but not when using BMI. Tolea et al. proposed that obesity determined by BF% was a more sensitive marker for cognitive impairment than obesity defined by BMI, since BMI is unable to distinguish body fat mass from body lean or muscle mass. In the study, when BMI $\geq$ 30 kg/m^2 was used to define obesity, no effect of obesity independent of sarcopenia was detected. However, when BF% was used, obesity was significantly associated with a lower score on animal naming tests. Despite the limited ability to diagnose obesity, BMI is often measured or collected in studies for convenience. However, using secondary or multiple methods to measure body fat is recommended whenever possible. The variability in the results may also be partially attributed to the different times at which obesity was measured in the participants' lives. Previous studies have indicated that obesity in mid-life is associated with an increased risk of dementia and a decline in executive function compared to maintaining a normal weight [21,22]. Conversely, other research suggests that obesity later in life may be linked to a decreased risk of dementia and enhanced cognitive function [21,23]. The studies included in this review assessed obesity cross-sectionally among older adults and did not account for whether participants had been obese during mid-life.

To our knowledge, this is the first study that summarized and assessed the associations of sarcopenic obesity compared to obesity only, sarcopenia only, or having neither of them, with cognitive impairment. However, our study had several limitations. First, there was a lack of consensus on the diagnostic criteria used to classify sarcopenia, obesity, and sarcopenic obesity. Inconsistent diagnostic standards impeded the comparability of findings of different studies. Using multiple methods and combinations is recommended to complement for limitations of each single measurement method. Second, among 7 included articles, only one study conducted a cohort study and 6 studies used a cross-sectional method. Thus, temporality could not be fully taken into account and the internal validity was limited. Third, this review was limited to studies that used four mutually exclusive categories to combine sarcopenia and obesity. Studies employing different categorizations for these conditions may have been excluded. Lastly, the studies included in this review utilized varying methods for measuring outcomes and different cutoff points for diagnosing cognitive impairment. Most studies set their thresholds at levels corresponding to mild cognitive impairment. Therefore, the results might not be applicable to, or could exaggerate the risk in severe cases of cognitive impairment.

Conclusion

In summary, sarcopenic obesity was associated with a higher risk of cognitive impairment compared to having neither condition. Furthermore, the risk was greater in cases of sarcopenic obesity than in cases of either sarcopenia or obesity alone, indicating a possible synergistic effect when both conditions are present simultaneously.

However, the effect size and statistical significance varied between studies, possibly due to the discordant definitions used for sarcopenia, obesity, and cognitive impairment. Future studies using standardized definitions for sarcopenic obesity and cognitive impairment are highly required. Overall, developing effective prevention and treatment strategies for sarcopenic obesity and subsequent cognitive impairment may be crucial to reducing their combined public health burden.

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Figure 1. Study selection for the systematic review of sarcopenic obesity and cognitive impairment association

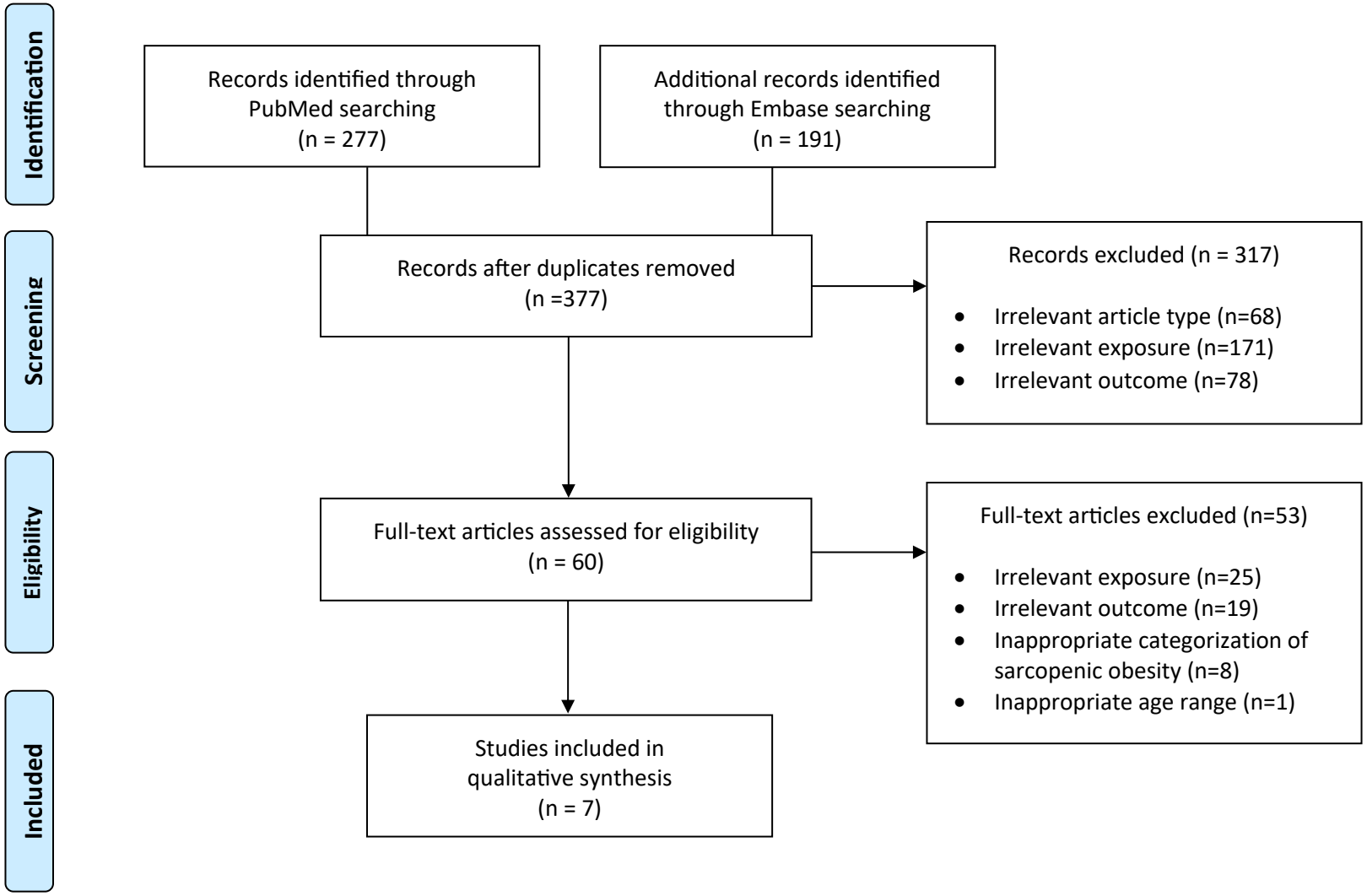

Table 1. Baseline characteristics of studies included in the systematic review of sarcopenic obesity and cognitive impairment association

Author, Year	Study design	Study period	Country	Study population	Sample size	Age	Race	Female (%)	Sarcopenia only (%)	Obesity only (%)	SO (%)	Neither sarcopenia nor obesity (%)	Cognitive impairment (%)
Batsis, 2021	Cohort	2010-2017 (8-year follow-up)	United States	The National Health and Aging Trends Study (NHATS): Community-based older adults	5,822	Range: 65-85+	White (71.4%), Black (20.5%)	55.7	39.4	14.4	12.9	33.3	21.2
Fu, 2023	Cross-sectional	2020-2021	China	Middle and older aged regular square dance member	2,451	Mean (SD): 62.1 (6.1)	Chinese	89.9	5.5	44.8	7.4	42.3	13.7
O'Donovan, 2022	Cross-sectional	2015	Colombia	The National Survey of Health, Wellbeing and Aging in Colombia: Community-dwelling adults living in urban and rural areas	5,760	Mean (SD): 71 (8)	Colombian	59.6	51.8	8.1	15.2	24.9	16.86
Someya, 2022	Cross-sectional	2015-2018	Japan	The Bunkyo Health Study: residents in Bunkyo-ku, Tokyo	1,615	Range: 68-77	Japanese	57.6	14.6	21.2	4.7	59.4	18.1
Tolea, 2018	Cross-sectional	2012-2015	United States	Community dwelling adults residing in the local catchment area	353	Mean: 69	White (68.3%), Black (24.7%)	65.4	42.0	32.0	14.3	11.7	NA
Wang, 2019	Cross-sectional	2014	China	Elderly Chinese community-dwelling volunteers	948	Mean (SD): 68.8 (6.5)	Chinese	50.8	29.2	14.1	6.0	50.7	13.4
Zhou, 2023	Cross-sectional	2020	China	MHD patients enrolled in multicenter cross-sectional study in GuiZhou province	2,743	Range: 44-66	Chinese	41.6	15.6	30.9	21.6	31.9	23.3

Abbreviations: MHD, Maintenance hemodialysis; SO, Sarcopenic Obesity.

Table 2. Definitions of sarcopenia, obesity, sarcopenic obesity, and cognitive impairment with covariates used in each included study

Author, Year	Sarcopenia definition	Obesity definition	Sarcopenic obesity definition	Cognitive impairment measurement	Covariates
Batsis, 2021	**Grip strength <35.5 kg** in men and **<20 kg** in women	Self-reported **BMI ≥30 kg/m^2** or directly measured **WC ≥88cm** for women or **≥102cm** for men	Low grip strength with BMI-defined obesity or low grip strength with WC-defined obesity	Classified as having cognitive impairment from any of the listed cognitive tests: 1) AD-8 ≥2; 2) Memory (10-word recall); 3) Orientation (date check and naming president/vice-president); 4) Executive function (clock-drawing test)	Age, race, smoking status, education, physical activity, health conditions
Fu, 2023	**AWGS 2019 criteria:** Low muscle mass (**ASMI <7 kg/m^2** for men and **<5.7 kg/m^2**), grip strength **(<28 kg** in men and **<18 kg** in women), and physical performance (**SPPB score ≤9**)	Directly measured **BMI ≥28 kg/m^2** or **BF% ≥35%** for women and **≥25%** for men or **VFA >100 cm^2** or **WC >80 cm** in women and **>90 cm** in men	AWGS+VFA or AWGS+WC or AWGS+BF% or AWGS+BMI	1) Self-reported memory decline & 2) Lower score (<1.5 SD below normative means) in any cognitive tests (TMT-B, ALVT, DSST, and VFT) & 3) Intact daily functioning & 4) Absence of dementia (CDR ≤0.5)	Age, sex, marital status, education, employment, family income, smoking status, drinking status, living arrangement, physical activity
O'Donovan, 2022	**EWGSOP2 criteria**: Low **grip strength** (**<27 kg** in men and **<16 kg** in women) or a **slow chair stands** (**>15** s in men and women)	Directly measured **BMI ≥30 kg/m^2**	BMI ≥30 kg/m^2 and EWGSOP2 based sarcopenia	Shorter version of the MMSE score ≤12: 6 questions including date and day test, repeat and remember three words, order the reverse of 1-3-5-7-9, fold paper in half and put it on their lap, reiterate three words, copy a drawing	Age, sex, education, income, civil status, cigarette smoking, alcohol drinking
Someya, 2022	**AWGS criteria**: **Grip strength <28 kg** in men and **<18 kg** in women	Directly measured **BMI ≥25 kg/m^2**	BMI ≥25 kg/m^2 and AWGS based sarcopenia	MoCA (≤22 for MCI) and MMSE (≤23 for dementia)	Age, sex, year of education, depression, physical activity, hypertension, diabetes, and dyslipidemia

Tolea, 2018	**SPSM criteria**: **Grip strength** (≤2nd quintiles), **chair stands** (≤2nd quintiles), **BIA measured MM** (≤2nd quintiles)	Directly measured **BMI ≥30 kg/m²** or **top two quintiles of BF%**	1) lowest 2 quintiles of SPSM and BMI ≥30 kg/m² 2) lowest 2 quintiles of SPSM and highest 2 quintiles of BF% 3) lowest 2 quintiles of MM + grip strength and BMI ≥30 kg/m² 4) lowest 2 quintiles of MM + grip strength and highest 2 quintiles of BF%	MoCA <26 + additional point added for 12 years or less of formal education	Age, race, depressive symptomatology
Wang, 2019	**AWGS criteria**: **ASMI <7 kg/m²** in men and **<5.7 kg/m²** in women	**AWGS criteria**: **BF% ≥31.61%** for men and **≥40.68%** for women	High BF% and low ASMI following AWGS criteria	30-item MMSE (18-23 for MCI and 0-17 for severe cognitive impairment)	Age, gender, smoking status, alcohol drinking status, physical activity, chronic comorbidity burden, nutritional condition, depressive status
Zhou, 2023	**AWGS criteria**: Low **grip strength** (**<26 kg** in men and **<18 kg** in women) plus low muscle mass (**ASMI <7 kg/m²** in men and **<5.7 kg/m²** in women)	**AWGS criteria**: **BF% >35%** in women and **>30%** in men	High BF% and low grip strength plus muscle mass following AWGS criteria	Chinese version of MMSE <27	Age, sex, education, smoking status, drinking status, dialysis vintage, and history of chronic CVD diseases

Abbreviations: AD-8, Alzheimer's Disease 8; ALVT, auditory verbal learning test; AWGS, Asian Working Group for Sarcopenia; ASMI, appendicular skeletal muscle mass index; BF, body fat; BIA, bioelectrical impedance analysis; BMI, body mass index; CDR, clinical dementia rating; DSST, digit symbol substitution test; EWGSOP2, European Working Group on Sarcopenia in Older People 2; MCI, mild cognitive impairment; MM, muscle mass; MMSE, mini-mental state examination; MoCA, Montreal Cognitive Assessment; SPPB, short physical performance battery; SPSM, short portable sarcopenia measure; TMT-B, trail-making test B; VFA, visceral fat area; WC, waist circumference.

Table 3. Simplified, synthesized results for the association between sarcopenic obesity and cognitive impairment

Author, Year	Effect measure	Sarcopenia definition	Obesity definition	Neither Sarcopenia nor Obesity	Sarcopenia only	Obesity only	Sarcopenic obesity
Batsis, 2021	HR (95% CI)	Grip strength	BMI	1.00 (ref)	**1.60 (1.42-1.80)**	0.98 (0.82-1.16)	**1.20 (1.03-1.40)**
			WC	1.00 (ref)	**1.59 (1.35-1.87)**	0.99 (0.84-1.17)	**1.39 (1.19-1.63)**
Fu, 2023	OR (95% CI)	ASMI + grip strength + SPPB	VFA	1.00 (ref)	1.57 (0.93-2.63)	**1.35 (1.02-1.78)**	**1.75 (1.14-2.68)**
			WC	1.00 (ref)	1.34 (0.76-2.37)	**1.37 (1.03-1.82)**	**1.96 (1.29-2.99)**
			BF%	1.00 (ref)	1.13 (0.63-2.02)	1.27 (0.96-1.68)	**1.94 (1.29-2.93)**
			BMI	1.00 (ref)	**1.50 (1.06-2.14)**	1.43 (0.97-2.10)	1.45 (0.67-3.12)
O'Donovan, 2022	OR (95% CI)	Grip strength + chair stands	BMI	1.00 (ref)	**1.84 (1.25-2.71)**	1.01 (0.58-1.74)	**1.62 (1.07-2.48)**
Someya, 2022	OR (95% CI)	Grip strength	BMI	1.00 (ref)	1.33 (0.92-1.93)	0.95 (0.66-1.35)	**2.11 (1.23-3.62)**
Tolea, 2018	$\beta \pm$ SE (*p*-value)	Grip strength + chair stands + muscle mass	BMI	0.00 (ref)	**-1.88 ± 0.79 (0.02)**	-1.10 ± 0.81 (0.18)	**-2.85 ± 1.38 (0.04)**
		Muscle mass + grip strength	BMI	0.00 (ref)	**-1.87 ± 0.89 (0.04)**	-1.02 ± 1.02 (0.32)	**-2.63 ± 1.16 (0.02)**
		Grip strength + chair stands + muscle mass	BF%	0.00 (ref)	**-1.80 ± 0.83 (0.03)**	**-1.61 ± 0.79 (0.04)**	**-3.14 ± 1.00 (0.002)**
		Muscle mass + grip strength	BF%,	0.00 (ref)	**-1.88 ± 0.89 (0.03)**	-1.61 ± 0.98 (0.10)	**-3.63 ± 1.01 (<0.001)**
Wang, 2019	OR (95% CI)	ASMI	BF%	1.00 (ref)	1.36 (0.83-2.22)	**2.14 (1.23-3.73)**	**2.55 (1.20-5.44)**
Zhou, 2023	OR (95% CI)	ASMI + grip strength	BF%	1.00 (ref)	1.20 (0.86-1.69)	1.15 (0.87-1.53)	**1.54 (1.13-2.08)**

Statistically significant results (α=0.05) were bolded in the table.
Abbreviations: ASMI, appendicular skeletal muscle mass index; BF, body fat; BMI, body mass index; CI, confidence interval; HR, hazard ratio; OR, odds ratio; VFA, visceral fat area; WC, waist circumference.

Table 4. The Newcastle-Ottawa Scale (NOS) for assessing the quality of cohort & cross-sectional studies

Cohort study

	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration of outcome not presenting at start of study	Comparability of cohorts based on design/analysis	Assessment of outcome	Followed-up long enough	Adequacy of follow-up of cohorts	Overall score
Batsis, 2021	1	1	1	1	2	1	1	1	9

Cross-sectional study

	Selection				Comparability	Outcome		Total
	Representativeness of the cases	Sample size	Non-response rate	Ascertainment of the exposure	Comparability of outcome groups based on design/analysis, confounding factors	Assessment of outcome	Statistical test	Overall score
Fu, 2023	1	1	0	2	1	2	1	8
O'Donovan, 2022	1	1	0	2	0	2	1	7
Someya, 2022	1	0	0	2	1	2	1	7
Tolea, 2018	1	0	0	2	0	2	1	6
Wang, 2019	1	0	0	1	1	2	1	6
Zhou, 2023	1	1	0	2	0	2	1	7

Supplementary Table 1. Search terms for sarcopenic obesity and cognitive dysfunction for PubMed and Embase (Last update on February 4th, 2024)

PubMed (N=277)	Embase (N=191)
(Sarcopenia OR Sarcopenic OR Muscle atrophy OR Muscular atrophy OR Muscle loss) AND (Obesity OR Overweight OR Adiposity OR Body weight OR Body fat distribution OR Body composition OR Body mass index OR Quetelet Index OR Quetelet's Index OR BMI Paradox OR Obesity Paradox OR Body Mass Index Paradox OR BMI OR Obese) AND (Cognitive dysfunction OR Cognitive impairment OR Cognitive disorder OR Cognitive defect OR Cognitive decline OR Mental deterioration)	('sarcopenia':ti,ab OR 'sarcopenic':ti,ab OR (muscle NEAR/2 (atrophy OR loss)) OR ((muscular NEAR/2 (atrophy OR loss)):ti,ab)) AND ('obesity':ti,ab OR 'body composition':ti,ab OR 'body mass':ti,ab OR 'body mass index':ti,ab OR 'bmi':ti,ab OR 'body weight':ti,ab OR 'body fat':ti,ab OR 'adiposity':ti,ab OR 'overweight':ti,ab OR 'body fatness':ti,ab OR 'fat mass':ti,ab) AND ('cognitive defect':ti,ab OR ((cognitive NEAR/2 (dysfunction OR impairment OR disorder OR decline OR defect)):ti,ab)) NOT ([animals]/lim NOT [humans]/lim) NOT (('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'case report'/de OR 'in vitro study'/de OR 'nonhuman'/de OR 'review'/it OR 'systematic review'/de) AND 'meta analysis'/de OR 'network meta-analysis'/de)

Modified PRISMA checklist. Items marked 'optional' only need to be included if they apply to your review. Items that you do not need to include are in grey.

Section and Topic	Item #	Checklist item	Page # where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	4-5, Suppl Table 1, Figure 1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	4-5, Suppl Table 1, Figure 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved (one), and if applicable, details of automation tools used in the process.	5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report (n=1), any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study (n=1), and if applicable, details of automation tools used in the process.	5-6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Figure 1
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing	5

		summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). (optional)	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results. (optional)	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. (optional; could be appendix)	NA
Study characteristics	17	Cite each included study and present its characteristics.	6-8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	9
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	8-9, Table 1, Table 2
Results of syntheses	20a	For synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	8-9
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	NA
	20c	Present results of all investigations of possible causes of heterogeneity among study results. (optional)	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	NA
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	9-10

	23b	Discuss any limitations of the evidence included in the review.	11-13
	23c	Discuss any limitations of the review processes used.	13
	23d	Discuss implications of the results for practice, policy, and future research.	13-14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	NA
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	NA
Competing interests	26	Declare any competing interests of review authors.	NA
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NA

PRISMA checklist for the abstract

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	1
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	1
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	1
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	1
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	1
Synthesis of results	6	Specify the methods used to present and synthesise results. (optional)	
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	1
Synthesis of results	8	Present results for outcome, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval.	1-2

		If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	2
Interpretation	10	Provide a general interpretation of the results and important implications.	2
OTHER			
Funding	11	Specify the primary source of funding for the review.	NA
Registration	12	Provide the register name and registration number.	NA

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
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