PROTOCOL

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Comparative efficacy of exercise, nutrition, and combined exercise and nutritional interventions in older adults with sarcopenic obesity: a protocol for systematic review and network meta-analysis

Youwen Gong^{1*}, Yongqiang Yang¹, Xueqing Zhang² and Li Tong^{2*}

Abstract

Background Sarcopenic obesity (SO) in older adults is associated with certain adverse outcomes, including falls, fractures, and disability, all of which affect patient quality of life, represent an economic burden, and potentially enhance the risk of death. Although a number studies have examined the effects of exercise, nutrition, and combined exercise and nutritional interventions on older adults with SO, the optimal therapeutic approach has yet to be sufficiently established. In this systematic review and network meta-analysis (NMA) protocol for SO in older adults, we aim to compare the combined effects of exercise and nutrition with those of exercise or nutritional interventions alone on the body composition and physical performance of older adults with SO.

Methods The PubMed, Web of Science, Embase, OVID, CINAHL, CNKI, Wanfang Data, and VIP databases will be used to systematically search for randomized controlled trials published from the time of database inception to December 2024. Outcomes will include body composition and physical performance, and data will be extracted independently by two researchers. In cases of disagreement, a consensus will be reached by consulting a third researcher. The Cochrane risk-of-bias tool will be used to assess randomized controlled trials, and data analysis will be performed using Stata 15.0 and R software, based on homogeneity, sensitivity, transitivity, consistency, and publication bias tests.

Discussion By comprehensively assessing the relative efficacies of exercise, nutrition, and combined interventions in older adults with SO, we aim in this systematic review and NMA to fill an important gap in the existing literature. These findings will provide a reference for healthcare providers and policymakers and facilitate the development of evidence-based guidelines that will contribute to optimizing SO management and gaining more favorable outcomes for this vulnerable population.

Systematic review registration CRD42024504706.

Keywords Sarcopenic obesity, Exercise intervention, Nutritional intervention, Muscle mass decline, Bayesian network meta-analysis

*Correspondence: Youwen Gong 1755144149@qq.com Li Tong 1751209835@qq.com



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Background

The findings of recent studies have revealed that with advancing age, fat mass gradually increases, with adipose tissue tending to accumulate in the abdominal regions. Contrastingly, there is a corresponding decline in muscle mass. As a consequence, advanced aging is often accompanied by the development of obesity and sarcopenia [1]. Obesity is characterized by increases in body and visceral fat, which can lead to impaired health and physical conditions [2], whereas sarcopenia refers to the progressive decline in muscle mass, strength, or muscle physiological function associated with aging [3]. Sarcopenic obesity (SO) is a geriatric condition characterized by a combination of the loss of muscle mass, insufficient muscle strength, lower physical function, and obesity [4]. A previous systematic review and meta-analysis of the prevalence of SO in older adults revealed a prevalence of 11% globally and 23% among older adults aged 75 years and above [5], and a further meta-analysis of the association between SO and the risk of all-cause mortality has indicated that patients with SO have a 24% higher risk of mortality than those without SO, which was particularly significant among men [6]. Older adults with SO are at a higher risk of diverse unfavorable outcomes, including a heightened risk of falls, fractures, metabolic disorders, cognitive impairment, and depression [7], which collectively influence the quality of life, represent a substantial economic burden [8], and increase the risk of death [9].

Risk factors for SO include age, disease, malnutrition, and lack of exercise [10, 11], all of which influence the occurrence and progression of SO in older adults [12], and, accordingly, recent studies on SO interventions have tended to focus primarily on exercise, nutrition, and pharmacological interventions [13]. Although pharmacological interventions have generally been proved to have limited efficacy [14], certain drugs (e.g., hormone replacement or anti-inflammatory medications) may address certain aspects of SO, such as inflammation or insulin sensitivity. However, these interventions tend to have limited effects on the accumulation of muscle mass or the redistribution of fat [15]. Contrastingly, exercise and nutritional interventions are considered effective non-pharmacological strategies for SO [16], and several studies have assessed the combined effects diet and exercise on improving muscle strength, body composition, and quality of life in older adults with SO [17]. Exercise has garnered particular attention as a non-pharmacological intervention for the treatment and management of SO in older adults [18], with research indicating that physical activity and functional exercise can contribute to retarding or even reversing the decline in muscle strength associated with aging, thereby effectively delaying the progression of SO [19]. The mechanisms underlying the preventive and therapeutic effects of exercise on SO may include enhancing insulin sensitivity [20], reducing inflammatory responses, restoring normal mitochondrial function, and reducing muscle fat infiltration [21], among others [15]. A number of studies have also investigated the efficacy of different exercise training methods for the treatment and management of SO [22], including resistance training, traditional Chinese exercises, and mixed training. Exercise can contribute to enhancing muscle strength and gait speed, improve insulin sensitivity, increase energy expenditure, and augment the supply of blood to the muscles in older adults with SO. However, exercise does not appear to have any substantial effects with respect to promoting muscle cell growth or increasing muscle mass.

With regard to diet, malnutrition can accelerate muscle loss, leading to SO, and it has been established that nutritional supplements, such as vitamin D, proteins, and amino acids, can contribute to promoting increases in muscle mass and enhance muscle function [23, 24]. For example, providing supplementary essential amino acids, proteins, or n-3 polyunsaturated fats during or after exercise has been shown to promote significant improvements in the strength and protein synthesis of muscles in older adults and delay the onset of SO [25]. Contrastingly, however, a further meta-analysis found no substantial evidence to indicate that nutritional intervention could improve grip strength [26].

Notably, however, whereas previous systematic reviews and meta-analyses have sought to assess the effects of exercise or nutrition alone on SO outcomes, by and large, they have not adequately assessed the comparative efficacies of exercise, nutrition, and combined interventions [27, 28]. Individual studies have often focused on specific interventions, thereby limiting the scope for evaluating the effects of intervention type or combinations that may yield more favorable outcomes for SO management. Indeed, despite the widely acknowledged efficacy of appropriate exercise schedules and dietary interventions in the management of SO, to the best of our knowledge, there has to date been only a single meta-analysis that has evaluated the impact of exercise and nutritional interventions in adults with SO [26]. However, the finding of this study failed to reveal the optimal therapeutic effects of exercise, nutrition, or a combination of exercise and nutrition in adults with SO, which accordingly highlights the need to adopt a Bayesian network metaanalysis (NMA) approach to address these challenges. We believe that adopting a Bayesian NMA approach will enable us to incorporate uncertainty into comparative efficacy estimates, thereby making it particularly useful for clinical decision-making. In this context, we intend using surfaces under the cumulative ranking (SUCRA)

values to rank each intervention, clearly indicating the most promising approaches for SO management. Moreover, by exploiting the attributes of a network structure, this analysis will enable us to clarify the hierarchy of interventions, and address inconsistencies and heterogeneity among different studies, which is essential given the limited direct evidence available for the comparison of certain interventions.

In summary, by performing this systematic review and NMA, we aim to fill an important gap in the literature, based on a comprehensive assessment of the relative efficacies of exercise, nutrition, and combined interventions in the treatment older adults with SO. We anticipate that the findings emerging from this study will provide a valuable reference for healthcare providers and policymakers and contribute to the development of evidence-based guidelines that will facilitate the optimization of SO management and hence lead to more favorable outcomes for this vulnerable population.

Objectives

The purpose of this systematic review and Bayesian NMA is to report studies on the efficacy of exercise, nutrition, and combined exercise and nutritional interventions on body composition and physical performance outcomes in older adults diagnosed with SO and to identify which type of intervention is more beneficial to older adults. This study will provide medical staff with a reference for exercise and nutritional interventions.

Methods

In this systematic review protocol, which is guided by the PRISMA-P [29], a Bayesian NMA will be performed to compare the efficacies of exercise, nutrition, and combined interventions. The study has been registered with PROSPERO (CRD42024504706).

Eligibility criteria

Types of studies

This review will focus on randomized controlled trials (RCTs) reported in English and Chinese. The exclusion criteria include posters, comments, letters, conference papers, literature reviews, study protocols, and studies with incomplete data.

Participants

Participants will include older adults aged 60 years and above diagnosed with SO, with diagnosis being based on a two-step approach [30]. Initially, skeletal muscle function is assessed by measuring muscle strength, typically using grip strength or knee extensor strength tests (adjusted for body weight when necessary) or chair stand tests such as the five-repetition sit-to-stand test or the 30-s chair stand test. Reference values for muscle function are established on the basis of age, sex, and race. If reduced skeletal muscle function is observed, the body composition can be evaluated using either dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA). Where feasible, skeletal muscle composition should be assessed using computed tomography (CT). The exclusion criteria are sarcopenia and obesity alone and osteosarcopenia or osteosarcopenic obesity.

Interventions

The participants will perform exercise alone, receive dietary supplementation alone, or be subjected to a combined exercise and nutritional intervention, whereas participants in the control group will receive no intervention and maintain their usual diet and physical activity. The exclusion criteria include the lack of a programmed physical exercise for at least 6 weeks, lack of body composition assessment with a validated instrument, and lack of a control group.

Outcomes

Types of outcome measures are as follows: Body composition and physical performance.

The primary outcomes will be interpreted in accordance with the following:

- Body composition should be evaluated using DXA or BIA, and when feasible, skeletal muscle composition should be assessed using CT.
- Physical function tests include gait speed, walking tests, get-up-and-go tests, and a simple physical performance battery (SPPB). Although gait speed is safe and readily measured, potential clinical confounders (e.g., knee osteoarthritis) may influence the test results. The SPPB, which includes standing, gait speed, and chair-up tests, is also widely used in clinical settings.

Secondary outcomes are as follows: Quality of life (e.g., SF-36 scores, Euro-Qol-5)

Search strategy

Systematic searches for published RCTs will be conducted by two researchers using the PubMed, Web of Science, Embase, OVID, CINAHL, CNKI, Wanfang Data, and VIP databases, covering studies published from the inception of the respective databases to December 2024. Appendix 1 illustrates the search strategy used for Pub-Med. Eligible studies will be also selected from the reference lists of retrieved articles.



Fig. 1 A flow diagram showing the study selection process

Study selection

To ensure that all relevant studies are included, the study selection process will follow a systematic and transparent approach, as shown in Fig. 1. The search results from the databases will initially be imported into EndNote software (version X9) for citation management. Duplicate records will be identified and removed using the de-duplication function of EndNote, followed by a manual review to ensure the accurate elimination of duplicates. Having removed duplicates, two researchers will independently screen the titles and abstracts of all the remaining articles based on the predefined inclusion and exclusion criteria. In cases of disagreement, a consensus will be reached by consulting a third researcher.

Data extraction

Two researchers will independently extract and enter data using a predesigned standardized form in Excel (Microsoft, 2010). The content of data extraction mainly includes the following: (1) basic information of the included studies, including research title, first author, published journal, and date of publication; (2) baseline characteristics of research, including age, sex, and sample size; (3) intervention details, including the type of exercise, nutrition, combined exercise and nutritional interventions, duration, frequency, and follow-up time after the intervention; and (4) outcomes, including body composition, physical performance, and quality of life.

Risk-of-bias assessment

Two reviewers will independently evaluate the risk of bias in the included studies using the Cochrane Collaborative risk-of-bias tool (RoB 2) for RCTs [31]. The assessment tools will include the following five aspects: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. Each aspect will be assigned to one of three grades: "low risk," "some concern," or "high risk."

Statistical analysis

Network meta-analysis

Data analysis will be performed using Stata 15.0 and R software [32], and network diagrams will be used to distinguish between direct comparisons (studies comparing two interventions directly) and indirect comparisons (inferences drawn regarding the relative efficacies of interventions that are not directly compared using a

common comparator). If the difference is not statistically significant (P>0.05), a consistency model will be used for analysis; otherwise, an inconsistency model will be applied. The results of the analysis will be ranked using cumulative probability ranking. Using this method, we will generate SUCRA values for each intervention, with higher values representing a more effective treatment, and these values will be plotted using Stata software to visually display the relative efficacies of each intervention. In addition to network diagrams and SUCRA plots, forest plots will be employed to illustrate the results of pairwise comparisons. All statistical tests will be two-sided, with the level of significance set at α =0.05.

Pairwise meta-analysis

Review Manager 5.4 software will be used to pool data from studies comparing the efficacies of interventions in older adults with SO, with both dichotomous and continuous outcomes being analyzed to evaluate the effects of these interventions. Odds ratios with 95% confidence intervals (CIs) will be calculated for dichotomous outcomes, the former of which will be used to summarize the relative effects of the interventions among studies. For continuous outcomes, mean differences with 95% CIs will be calculated, and if the included studies report outcomes using different scales, standardized mean differences will be used to ensure comparability. Heterogeneity among the studies will be assessed using the I^2 statistic, and if the value of I^2 is 40% or less, a fixed-effects model will be used for data synthesis, assuming that the effect sizes of the included studies are sufficiently similar. Conversely, in cases in which the I^2 value exceeds 40%, indicating a moderate-to-high heterogeneity, a randomeffects model will be employed to account for betweenstudy variability.

Multi-arm trials

Multi-arm trials, which compare more than two interventions within the same study, will be managed as follows.

- Data decomposition: Each arm comparison will be treated as a distinct comparison, although shared control groups will be split to avoid double-counting, thereby ensuring that each comparison remains independent.
- (2) Variance adjustment: Adjustments will be made to account for correlations between comparisons within the same study, thereby avoiding an inflation of sample sizes and enhancing the accuracy of estimates.

Assessment of model fit

The fit of the statistical models will be evaluated using selected key measures. The deviance information criterion (DIC) is used to compare models in Bayesian analyses, with lower DIC values indicating a better fit, whereas residual deviance examines the fit of the model to the observed data, with smaller residuals reflecting a better fit. By comparing the direct and indirect evidence of a particular comparison, node-splitting analysis is applied in NMA to assess local inconsistencies, with statistical tests being conducted to assess the inconsistencies between the direct and indirect estimates. The test calculates a P-value, which, if greater than 0.05, indicates no statistically significant difference between the direct and indirect evidence, and hence consistency, whereas a values of less than 0.05, implying a significant difference between direct and indirect evidence, is taken to be indicative of an inconsistency for that specific comparison. If a global inconsistency is identified, further steps include revising the assumptions and methodology of the NMA. An inconsistency model will be applied to account for these discrepancies. Subgroup or sensitivity analyses will be conducted to assess heterogeneity or remove influential studies. In the case of Bayesian models, posterior predictive checks will be applied to evaluate whether the predictions made by the model are consistent with the observed data. Collectively, these additional analyses will contribute to enhancing the methodological rigor of the review, thereby ensuring that the findings are reliable and applicable in clinical practice for managing SO in older adults.

Transitivity assumption

To ensure that the interventions being compared are similar for all relevant effect modifiers among studies, we will evaluate the transitivity assumption, which is essential for validating indirect comparisons made in NMAs [33]. Specifically, we assume that the participants included in the studies are comparable in terms of key characteristics such as age, sex, baseline SO status, and comorbidities. Moreover, it is assumed that the settings of the interventions (exercise, nutrition, or combined exercise and nutrition) among trials will be similar in terms of intervention duration, intensity, and type. The fulfillment of the transitivity assumption enables us to generalize the findings and make valid indirect comparisons among the interventions. To assess the plausibility of the transitivity assumption, we will examine the distribution of these effect modifiers among studies.

Publication bias

If at least 10 studies are included in the analysis, funnel plots will be visually inspected, in addition to which, we will use Egger's regression test and Begg's rank correlation test to statistically evaluate the symmetry of the funnel plot. A *P*-value of less than 0.10 from either test will be interpreted as evidence of a publication bias.

Sensitivity and subgroup analyses

To assess the robustness of our findings, we will conduct sensitivity analyses to examine the impact of the methodological and statistical assumptions on our results. We will reanalyze the data by excluding studies with a high risk of bias, which will contribute to determining whether studies with a higher risk of bias have a significant influence on the overall effect estimates. The results of these analyses will be presented in the supplementary material along with the results of the main analyses to provide transparency regarding the effects of these factors on the comparative efficacy conclusions.

Subgroup analyses will be performed based on the following variables:

- 1. Patient characteristics (gender, age)
- 2. Study-specific factors
 - (1) SO status
 - (2) Sample size
 - (3) Study duration
 - (4) Risk of bias (all studies vs. low-bias studies)

Quality of evidence

The quality of evidence for each outcome in this NMA will be assessed using the Confidence in Network Meta-Analysis (CINeMA) framework, which is specifically designed to evaluate confidence in the evidence from NMAs. This framework includes within- and among-study risk of bias, inconsistency, indirectness, imprecision, and risk of publication bias, with each outcome being rated on a scale of high, moderate, low, or very low confidence based on these domains. The CINeMA tool can be systematically applied to provide a transparent and consistent evaluation of the strength of the evidence supporting each intervention [34].

Discussion

Sarcopenic obesity is characterized by cognitive impairment and high rates of morbidity among older adults, endangering the health of these individuals and imposing heavy burdens at both individual and societal levels. Recent studies on SO interventions have focused primarily on exercise, nutrition, and pharmacological interventions, and although pharmacological interventions have generally been found to have limited efficacy, addressing the complex interplay between pharmaceutical practices and patient health, targeted solutions, and recommendations for policymakers and stakeholders are essential. A more comprehensive focus on patient rights could also contribute to addressing issues relating to equitable access to non-pharmaceutical and pharmaceutical treatment options, particularly in cases in which pharmacological interventions may play an ancillary role. Furthermore, an analysis of the role of business strategies, such as drug pricing or market exclusivity practices in limiting access to newer treatments for SO, would provide a more comprehensive view of the available interventions. Policymakers and stakeholders can make meaningful changes by adopting these strategies, ultimately improving healthcare accessibility, patient trust, and the sustainability of the healthcare system.

Given the contributory effects of age, disease, malnutrition, and lack of exercise in the occurrence and development of SO in older adults, comprehensive interventions have emerged as key approaches in the prevention and management of SO in this population. Previous studies have established the positive impact of exercise and nutritional interventions in older adults with SO. Nutritional supplements, such as proteins and amino acids, can contribute to enhancing muscle mass and strength, increase the weight of malnourished older adults, and reduce mortality, whereas exercise can promote increases in muscle protein and glycogen reserves, accelerate blood circulation and the metabolism in skeletal muscles, and reduce the percentages of body fat and fat mass. At present, however, there is relatively little information available regarding the effects of exercise, nutrition, and a combination exercise and nutritional interventions on SO in older adults. By performing this study, we hope to provide a referential basis for future clinical trials and studies that seek to assess the treatment and management of SO and thereby ultimately contribute to reductions in the prevalence of this disease among the elderly population.

Abbreviations

- BIA Bioelectrical impedance analysis
- CT Computed tomography
- DXA Dual-energy X-ray absorptiometry
- NMA Network meta-analysis
- RCT Randomized controlled trial
- SO Sarcopenic obesity
- SPPB Simple physical performance battery
- SUCRA Surfaces under the cumulative ranking

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s13643-025-02825-z.

Supplementary Material 1.

Patient consent for publication

Not applicable.

Patient and public involvement

Neither patients nor the public were involved in the design, conduct, or reporting of this study.

Provenance and peer review

Not commissioned, externally peer reviewed.

Authors' contributions

YWG, designed this systematic review and meta-analysis, YWG and XQZ drafted the original manuscript, and YQY and LT critically appraised the protocol and revised the manuscript. All authors have reviewed and approved the manuscript.

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Declarations

Ethics approval and consent to participate

Ethical approval is not deemed necessary for this NMA. The outcomes will be disseminated through peer-reviewed publications.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Neurosurgery, Changde Hospital, Xiangya School of Medicine, Central South University (The First People's Hospital of Changde City), 818 Ren Min Road, Changde, Hunan Province, China. ²Department of Nursing, Changde Hospital, Xiangya School of Medicine, Central South University (The First People's Hospital of Changde City), 818 Ren Min Road, Changde, Hunan Province, China.

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