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Risk factors for hypertension complicated with sarcopenia: a systematic review and meta-analysis protocol

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Abstract

Background: With the aging of society, hypertension (HTN) and sarcopenia (SAR) are common diseases among the elderly. The purpose of this study is to identify the risk factors of HTN complicated with SAR, and to provide a reference basis for primary prevention and early intervention of SAR in middle-aged and elderly patients with HTN.

Methods: This meta-analysis will include observational studies (cohort, case-control, cross-sectional) in humans in which the role of risk factors for hypertension complicated with sarcopenia was investigated. Pubmed, EMBASE, Web of Science, Cochrane Database of Systematic Reviews, CNKI, Wangfang, Vip, and Sionmed will be searched in June, 2025 using a comprehensive search strategy and manual screening of references. Two reviewers will independently identify eligible studies and extract the data from the included studies. The quality of studies will be assessed by using the Newcastle-Ottawa scale. Fixed-effects models will be used to estimate pooled measures of association (where feasible). Meta-regression analyses will be conducted to explore the potential sources of heterogeneity. The Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement will be followed for reporting. Discussion: Deepening knowledge regarding the etiology hypertension complicated with sarcopenia and potential implications of risk factors in this disease is instrumental for prevention of this often-aging disease. This review will produce summarized current evidence on this topic.
Systematic review registration: This systematic review protocol has been registered with the International Prospective Register of Systematic Reviews (PROSPERO, CRD420251074136) on 15 June 2025.

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Protocol

Abstract

Background: With the aging of society, hypertension (HTN) and sarcopenia (SAR) are common diseases among the elderly. The purpose of this study is to identify the risk factors of HTN complicated with SAR, and to provide a reference basis for primary prevention and early intervention of SAR in middle-aged and elderly patients with HTN. *Methods:* This meta-analysis will include observational studies (cohort, case-control, cross-sectional) in humans in which the role of risk factors for hypertension complicated with sarcopenia was investigated. Pubmed, EMBASE, Web of Science, Cochrane Database of Systematic Reviews, CNKI, Wangfang, Vip, and Sionmed will be searched in June, 2025 using a comprehensive search strategy and manual screening of references. Two reviewers will independently identify eligible studies and extract the data from the included studies. The quality of studies will be assessed by using the Newcastle-Ottawa scale. Fixed-effects models will be used to estimate pooled measures of association (where feasible). Meta-regression analyses will be conducted to explore the potential sources of heterogeneity. The Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement will be followed for reporting. *Discussion:* Deepening knowledge regarding the etiology hypertension complicated with sarcopenia and potential implications of risk factors in this disease is instrumental for prevention of this often-aging disease. This review will produce summarized current evidence on this topic.

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Keywords: hypertension; sarcopenia; risk factors; systematic review; meta-analysis; protocol

1. Introduction

Hypertension (HTN) is one of the most common chronic diseases among the elderly population, mainly characterized by elevated arterial pressure in the circulation. High blood pressure is one of the most important risk factors for ischaemic heart disease, stroke, other cardiovascular diseases, chronic kidney disease and dementia.[1] The findings showed that the number of people aged 30-79 with high blood pressure doubled from 1990 to 2019. Of these, about 50% was known, about 45% were treated, and only 20% had been controlled within the target range.[2] The aging process involves changes in the mechanisms that regulate neurocardiovascular functions, and blood pressure variability is a potential marker of aging.[3 4] As a result, hypertension is one of the major global public health problems. Sarcopenia (SAR) is a gradual and widespread impairment of skeletal muscle typically observed in the elderly population but can also occur earlier in life, which involves the reduction in muscle strength, muscle mass, and muscle quality. [5] [6] Same as hypertension, sarcopenia is receiving increasing attention and become a global public health problem in the ageing society.

With the aging of society, HTN and SAR are common diseases among the elderly population. Previous studies had revealed a substantial correlation between sarcopenia and hypertension among older people,[7] with sarcopenic obesity amplifying this risk.[8] Lately, although there have been more frequent reports suggesting a potential “cross-talk” between the two previously mentioned conditions. Insulin resistance, oxidative stress, imbalance of catabolism and anabolism, and chronic inflammation are the underlying mechanisms that explain the association between hypertension and sarcopenia.[9] RASS can rewind insulin resistance in sarcopenia by ACE axis to regulate ROS and IGF-R, which in turn affects protein turnover, apoptosis and collagen metabolism of muscle.[10 11] Same as the muscle mcrovascular perfusion of sympathetic nervous system, RASS can be affected by exercise and resistance exercise. Key metabolic benefits of exercise and resistance exercise include increased glucose uptake, enhanced fat oxidation, and the release of exercise-induced

molecules called myokines, such as IGF-1, IL-6, Irisin, and FGF21, which mediate interorgan communication and improve overall metabolic function.[12-14]

There was previous cross-sectional study had explored the risk factors for hypertension and sarcopenia.[15] However, due to study design, sample size, etc., we were unable to obtain uniform and credible results. The purpose of this study is to understand the prevalence of hypertension complicated with sarcopenia in middle-aged and elderly population, to explore the correlation between the two diseases, to identify the risk factors of HTN and SAR, and to provide a reference basis for primary prevention and early intervention.

2.Methods

The protocol has been developed in accordance with the preferred reporting items for systematic review and meta-analysis protocols 2015 (PRISMA-P, *Supplement file 1*).[16 17] However, as at issue in this review is the topic of disease etiology (rather than intervention effects), the PICO format will be replaced by PECO (population, exposure, control, outcome), as detailed in the MOOSE (the Meta-analysis of Observational Studies in Epidemiology) guidelines.[18]

Inclusion and exclusion criteria

Studies will be selected according to the following criteria: (1) Study design. Original observational research studies that address the association between HTN and SAR will be included in this review. This includes cohort studies, case-control studies, and cross-sectional studies. Case reports, position papers, and reviews will be excluded from the current review. (2) Population. The population of interest will be unrestricted in terms of age, sex, ethnicity, socioeconomic status, occupation, or history of other diseases. (3) Exposure. Age (year), sex (male of female), alcohol history (yes or no), smoking (yes or no), Obesity (BMI, kg/m2), Diabetes (yes or no), Osteoporosis(yes or no), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg), Grip strength (kg), Calf circumference (cm), Skeletal muscle mass(kg), Insulin-like growth factor IGF-1 (g/L), IL-6 (ug/L), Creatine kinase(U/L) , 25-hydroxyvitamin D (μg/L). (4) Outcomes. The outcome

of interest will be the presence of HTN complicated with or without SAR, based on clinically confirmed diagnosis (i.e., hospital, or doctors' records). (5)Setting and language. There will be no restriction by study setting. English- and Chinese-language publications will be considered for full-text analysis in this systematic review, and eligible articles in other languages will be translated using Google Translate.

Information sources

An electronic literature search will be conducted in the following databases: Pubmed, EMBASE, Web of Science, Cochrane Database of Systematic Reviews, CNKI, Wangfang, Vip, and Sionmed. The start date for the literature search will not be limited in order to maximize the number of publications considered. The electronic literature search will be complemented by hand searching the list of references in the identified publications or relevant reviews. NICE Evidence and TRIP database will be searched for gray literature using subject keywords. Ongoing studies (which have not resulted in publications on the topic at issue) will not be considered in the review.

Databases search strategy

Using medical subject headings (MeSH), EMTREEs and title/abstract related to the field of the study, the research team has developed a draft version of literature search strategies with the help of Chan Wang, an expert librarian at the Institute of Medical Information, Chinese Academy of Medical Sciences and Peking Union Medical College (*supplement file 2*). This draft of the MEDLINE search strategy will be finalized and adapted to the other databases using the proper syntax, subject headings, and controlled vocabulary considering maximized sensitivity of the search. In order to maximize the yield of the search strategy, no language restrictions in the search strategy will be used. The PROSPERO will be searched for recently completed systematic reviews on the topic. The references of relevant studies will be verified for relevant publications.

Included study records

Data management, selection, and data collection process. Data will be collected using EndNote

software and a pre-designed data collection form. The reliability of data selection process will be pilot tested in 10% of randomly included articles, and Cohen's kappa will be calculated to assess the inter-reviewer (WLP and LST) agreement on study eligibility. Two independent reviewers (WLP and LST) will screen all retrieved titles and abstracts using the eligibility criteria. In the case of incomplete information provided by the title and abstract, the full text will be used to determine the study's eligibility to be included for the study. In the case of multiple reports of the same study, the most recent article will be included in the review. Disagreements between the two reviewers will be resolved by discussion and resolved through consensus-seeking. If an agreement cannot be achieved, the opinion of a third reviewer (NGQ) will be sought.

Data items. The data will be extracted independently by two reviewers (WLP and LST) from the full text of the included studies. The extracted information will include authors, country, year of publication, aim of the study, study design, sample size, study participants' characteristics (age, sex), study population, exposure description, the technique used to quantify the exposure, type and number of controls, and the number of SAR, as well as the main results. In the case of insufficient data, we will contact authors via email for additional information. If the missing data cannot be rectified by author contact, we will use narrative approaches to describe the major findings.

Outcomes and prioritization

As stated in the outcomes section, the presence of HTN complicated with SAR will be the study outcome.

Risk of bias and level of evidence

Two reviewers (WLP and LST) will independently assess the risk of bias of the eligible studies using the Newcastle-Ottawa scale (NOS) (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).[19] This 8-item scale allows to assess the quality of the articles based on the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort

studies, respectively. Disagreement will be resolved by consultation with a third reviewer. We will also evaluate the level of evidence of all studies according to the Oxford Level of Evidence.[20]

3. Data synthesis

Statistical analyses will be performed with Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) and STATA 12.0 (StataCorp LP, College Station, Texas). Odds ratio (OR) with 95% confidence interval (Cl) will be used to compare binary variables. The standardized mean difference(SMD) and 95% CI will be calculated for continuous outcomes. For all meta-analyses, the Cochrane Q *P* value and I^2 statistic will be applied to check heterogeneity. When *P* value < 0.05 or I^2 > 50%, there was a significant heterogeneity, a random-effect model will be used to merge the results. Otherwise, a fixed-effectmodel will be used. Subgroup analyses and meta-regression will be conducted. A *P* value less than 0.05 is considered statistically significant. We will perform egger's test to assess publication bias (only for outcomes including ten or more studies).

Meta-biases

The potential publication bias will be assessed by funnel plots.[21] Tests for funnel plot asymmetry will be conducted if the number of studies included in the meta-analysis is more than 10 (http://handbook.cochrane.org. Accessed 2017).

Confidence in cumulative evidence

The Oxford Level of Evidence (http://www.cebm.net/index.aspx?o=5653". Accessed 2017) and The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [22] [23] will be used to evaluate the level of evidence of all studies.

Differences between the protocol and the review

Any deviations from the protocol due to unanticipated issues will be reported in the final review. [24]

4. Discussion

This study will assess the role of risk factors in HTN complicated with SAR. Specifically, we will

identify, assess, and synthesize the available evidence from published observational studies on the role played by risk factors in the population.

Caution will have to be taken when interpreting the results of this systematic review. We are aware that observational studies are subject to a high risk of bias due to potential outcome confounding. In addition, if the heterogeneity of the studies is high, this may preclude obtaining a meaningful pooled estimate of the association of interest (or introduce challenges in interpreting a pooled estimate of the association).

Despite the above limitations, we expect that the systematic review proposed here will be of high scientific and pragmatic value. The study aims to facilitate achieving a comprehensive and up-to-date understanding of the association between risk factors and HTN complicated with SAR. To our knowledge, our meta-analysis will be the first to synthesize the available evidence on this association. Findings from this study could help pave the way for the development of new methods of prevention of HTN complicated with SAR.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Contributions

All authors have made significant contributions to this systematic review protocol. As a first author, ZJF has developed this review protocol and conducted the preliminary literature review. He designed the search strategy with an expert librarian at Institute of Medical Information, Chinese Academy of Medical Sciences and Peking Union Medical College. WLP and LST will extract the data. NGQ and PW as the corresponding author will coordinate all aspects of the study. They have collaborated in the protocol development and writing the protocol and will be involved in the data collection and data analysis and interpretation of the results. All the authors revised the manuscript and approved the final version.

References

1. Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. Nat Rev Cardiol 2021;18(11):785-802 doi: 10.1038/s41569-021-00559-8.
2. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021;398(10304):957-80 doi: 10.1016/s0140-6736(21)01330-1.
3. Baker SE, Limberg JK, Dillon GA, Curry TB, Joyner MJ, Nicholson WT. Aging Alters the Relative Contributions of the Sympathetic and Parasympathetic Nervous System to Blood Pressure Control in Women. Hypertension 2018;72(5):1236-42 doi: 10.1161/hypertensionaha.118.11550.
4. Bencivenga L, De Souto Barreto P, Rolland Y, et al. Blood pressure variability: A potential marker of aging. Ageing Res Rev. 2022;80:101677 doi: 10.1016/j.arr.2022.101677.
5. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48(1):16-31 doi: 10.1093/ageing/afy169.
6. Chen LK, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 Consensus

Update on Sarcopenia Diagnosis and Treatment. J. Am. Med. Dir. Assoc. 2020;21(3):300-07.e2 doi: 10.1016/j.jamda.2019.12.012.

7. Bai T, Fang F, Li F, Ren Y, Hu J, Cao J. Sarcopenia is associated with hypertension in older adults: a systematic review and meta-analysis. BMC Geriatr. 2020;20(1):279 doi: 10.1186/s12877-020-01672-y.
8. Quan YW, Wang C, Wang LF, Li G. Geriatric sarcopenia is associated with hypertension: A systematic review and meta-analysis. J. Clin. Hypertens. 2023;25(9):808-16 doi: 10.1111/jch.14714.
9. Toba A, Ishikawa J. Sarcopenia as a risk factor for hypertension. Hypertens. Res. 2024;47(12):3363-66 doi: 10.1038/s41440-024-01898-y.
10. Ekiz T, Kara M, Ata AM, et al. Rewinding sarcopenia: a narrative review on the renin-angiotensin system. Aging Clin. Exp. Res. 2021;33(9):2379-92 doi: 10.1007/s40520-020-01761-3.
11. Bueno V, Frasca D. Mini-review: Angiotensin- converting enzyme 1 (ACE1) and the impact for diseases such as Alzheimer's disease, sarcopenia, cancer, and COVID-19. Front Aging 2023;4:1117502 doi: 10.3389/fragi.2023.1117502.
12. Lopes KG, Bottino DA, Farinatti P, et al. Strength training with blood flow restriction - a novel therapeutic approach for older adults with sarcopenia? A case report. Clin. Interv. Aging 2019;14:1461-69 doi: 10.2147/cia.S206522.
13. Trovato E, Di Felice V, Barone R. Extracellular Vesicles: Delivery Vehicles of Myokines. Front. Physiol. 2019;10:522 doi: 10.3389/fphys.2019.00522.
14. Shero JA, Lindholm ME, Sandri M, Stanford KI. Skeletal Muscle as a Mediator of Interorgan Crosstalk During Exercise: Implications for Aging and Obesity. Circul. Res. 2025;136(11):1407-32 doi: 10.1161/circresaha.124.325614.
15. Xing E, Wan C. Prevalence of and factors associated with sarcopenia among elderly individuals

with hypertension. J. Int. Med. Res. 2022;50(7):3000605221110490 doi: 10.1177/03000605221110490.

16. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. Bmj 2015;350:g7647 doi: 10.1136/bmj.g7647.
17. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4(1):1 doi: 10.1186/2046-4053-4-1.
18. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. Jama 2000;283(15):2008-12 doi: 10.1001/jama.283.15.2008.
19. Costa Pereira JPD, Rebouças AS, Prado CM, et al. Phase angle as a marker of muscle quality: A systematic review and meta-analysis. Clin. Nutr. 2024;43(12):308-26 doi: 10.1016/j.clnu.2024.11.008.
20. Söder B, Yakob M, Meurman JH, Andersson LC, Klinge B, Söder P. Periodontal disease may associate with breast cancer. Breast Cancer Res. Treat. 2011;127(2):497-502 doi: 10.1007/s10549-010-1221-4.
21. Sutton AJ, Duval SJ, Tweedie RL, Abrams KR, Jones DR. Empirical assessment of effect of publication bias on meta-analyses. Bmj 2000;320(7249):1574-7 doi: 10.1136/bmj.320.7249.1574.
22. Guyatt GH, Oxman AD, Kunz R, Vist GE, Falck-Ytter Y, Schünemann HJ. What is "quality of evidence" and why is it important to clinicians? Bmj 2008;336(7651):995-8 doi: 10.1136/bmj.39490.551019.BE.
23. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J. Clin. Epidemiol. 2011;64(4):383-94 doi:

10.1016/j.jclinepi.2010.04.026.

24. Silagy CA, Middleton P, Hopewell S. Publishing protocols of systematic reviews: comparing what was done to what was planned. Jama 2002;287(21):2831-4 doi: 10.1001/jama.287.21.2831.

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