

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Sarcopenia in Systemic Sclerosis: Prevalence and Impact - A Systematic Review and Meta-analysis
AUTHORS	Tu, Xiangping; Lin, Taiping; Ju, Yuan; Shu, Xiaoyu; Jiang, Tingting; Ge, Ning; Yue, Jirong

VERSION 1 – REVIEW

REVIEWER	Rezus , Elena Grigore T Popa University of Medicine and Pharmacy Iasi
REVIEW RETURNED	03-Oct-2023

GENERAL COMMENTS	<p>Sarcopenia in Systemic Sclerosis: Prevalence and Impact - A Systematic Review and Meta-analysis</p> <p>Systemic sclerosis is a debilitating immune-mediated disease, affecting a great number of organ systems. This translates as a low quality of life and a high mortality. As is the case with all autoimmune connective tissue disorders, treatment must be implemented early in the course of the disease in order to limit pathology related damage and lower morbidity. This can only be attained by predicting disease complications. As such, being aware of the prevalence of the aforementioned complications is the first step in achieving this and benefitting from the window of opportunity. Therefore, the manuscript is a valuable step in this direction regarding sarcopenia in systemic sclerosis, and has a major impact in bringing awareness to the clinician to this particular aspect. By taking into account this possible evolution of the disease and the clinical aspects associated with it, the physician may be one step ahead by taking special consideration through a thorough anamnesis, clinical examination and further investigations concerning this aspect, both at baseline and at all the subsequent follow-ups. This systematic review and meta-analysis highlights the need for further studies regarding sarcopenia in these patients and is a stepping stone in this direction.</p> <p>The manuscript is well-structured, has a high level of written clarity, it is concise and logical, while the notions are thoroughly explained. It presents in a detailed manner the well conducted research and proves a high discernment and careful analysis of the relevant studies. While presenting the methods used, all the major relevant variables and notions were succinctly and accurately conferred. The use of tables, graphics and figures further increases the level of understanding and facilitates the review. The manuscript is well referenced. Furthermore, it offers all the necessary information and transparently provides the strengths and weaknesses of this systematic review and meta-analysis.</p>
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	After analyzing the manuscript, it can be considered for publication.
REVIEWER	Chen, Yaolong Lanzhou University, Evidence-Based Medicine Centre, School of Basic Medical Sciences
REVIEW RETURNED	28-Oct-2023
GENERAL COMMENTS	<p>This systematic review provides an estimation of sarcopenia prevalence and its impact on clinical characteristics in patients with systemic sclerosis, which is commendable. However, there are still areas for improvement:</p> <p>Page 2, Abstract: The expression forms of confidence intervals appear to be inconsistent and need to be standardized. Furthermore, it is essential to ensure consistency in the main-text to improve clarity.</p> <p>Page 2, Conclusions: The first sentence is inappropriate in the conclusion, please delete it.</p> <p>Page 6, Inclusion and exclusion criteria: Please provide precise definitions of low muscle mass and low muscle strength, supported by relevant references. Additionally, the second item of the exclusion criteria needs to be removed as the type of literature included in the inclusion criteria has already been established to be observational studies.</p> <p>Page 6, Outcomes: It would be helpful to have information on how these factors are determined and reasons for choosing specific factors over others.</p> <p>Page 8, Statistical Analysis: The statement, "If I2 > 50%, a random-effects model was employed," is incorrect as the selection of the random-effects model is not solely based on the size of I2. Please delete the sentence and replace it with an accurate one such as, "Considering the variation in the definition of outcomes, diagnostic criteria, and population characteristics among the included studies, this study employed a random-effects model."</p> <p>Page 8, Statistical Analysis: Provide the reasons for grouping in subgroup analysis to improve the transparency of the study's methodology.</p> <p>Page 9, Patient and public involvement: Please revise this section in line with the BMJ Open requirements.</p> <p>Page 10, Impact of sarcopenia on the clinical characteristics of SSc patients: All MD values should be written in specific units. For example, duration should be written as MD, 2.97 years (95% CI - 0.13 to 6.08).</p>

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Elena Rezus, Grigore T Popa University of Medicine and Pharmacy Iasi

Comments to the Author:

Sarcopenia in Systemic Sclerosis: Prevalence and Impact - A Systematic Review and Meta-analysis

Systemic sclerosis is a debilitating immune-mediated disease, affecting a great number of organ systems. This translates as a low quality of life and a high mortality. As is the case with all autoimmune connective tissue disorders, treatment must be implemented early in the course of the disease in order to limit pathology related damage and lower morbidity. This can only be attained by predicting disease complications. As such, being aware of the prevalence of the aforementioned complications is the first step in achieving this and benefitting from the window of opportunity. Therefore, the manuscript is a valuable step in this direction regarding sarcopenia in systemic sclerosis, and has a major impact in bringing awareness to the clinician to this particular aspect. By taking into account this possible evolution of the disease and the clinical aspects associated with it, the physician may be one step ahead by taking special consideration through a thorough anamnesis, clinical examination and further investigations concerning this aspect, both at baseline and at all the subsequent follow-ups. This systematic review and meta-analysis highlights the need for further studies regarding sarcopenia in these patients and is a stepping stone in this direction. The manuscript is well-structured, has a high level of written clarity, it is concise and logical, while the notions are thoroughly explained. It presents in a detailed manner the well conducted research and proves a high discernment and careful analysis of the relevant studies. While presenting the methods used, all the major relevant variables and notions were succinctly and accurately conferred. The use of tables, graphics and figures further increases the level of understanding and facilitates the review. The manuscript is well referenced. Furthermore, it offers all the necessary information and transparently provides the strengths and weaknesses of this systematic review and meta-analysis. After analyzing the manuscript, it can be considered for publication.

Response: Thank you very much for the strong support to our work.

Reviewer: 2

Prof. Yaolong Chen, Lanzhou University

Comments to the Author:

This systematic review provides an estimation of sarcopenia prevalence and its impact on clinical characteristics in patients with systemic sclerosis, which is commendable. However, there are still areas for improvement:

1. Page 2, Abstract: The expression forms of confidence intervals appear to be inconsistent and need to be standardized. Furthermore, it is essential to ensure consistency in the main-text to improve clarity.

Response: Thank you for your constructive comment. We have revised the expression forms of the confidence intervals and ensured that they are consistent throughout the article.

2. Page 2, Conclusions: The first sentence is inappropriate in the conclusion, please delete it.

Response: Thank you very much for your advice. We have deleted the first sentence.

3. Page 6, Inclusion and exclusion criteria: Please provide precise definitions of low muscle mass and low muscle strength, supported by relevant references. Additionally, the second item of the exclusion criteria needs to be removed as the type of literature included in the inclusion criteria has already been established to be observational studies.

Response: Thank you for raising this important point. We have removed the second item of the exclusion criteria and made the following edits in the manuscript (Pg. 6, Lines 11-14): "LMM was evaluated by dividing appendicular skeletal muscle mass (in kilograms) by height in meters squared, LMS by hand grip strength, LPP by gait speed or short physical performance battery, and diagnostic cutoffs varied depending on the criterion[9,17,18,20];"

4. Page 6, Outcomes: It would be helpful to have information on how these factors are determined

and reasons for choosing specific factors over others.

Response: Thank you very much for this important comment. We have made the following edits in the manuscript (Pg. 7, Lines 3-5): “These features are frequently the focus of clinical studies in patients with SSc, and it is of significant interest to understand how sarcopenia impacts them.”

5. Page 8, Statistical Analysis: The statement, “If $I^2 > 50\%$, a random-effects model was employed,” is incorrect as the selection of the random-effects model is not solely based on the size of I^2 . Please delete the sentence and replace it with an accurate one such as, “Considering the variation in the definition of outcomes, diagnostic criteria, and population characteristics among the included studies, this study employed a random-effects model.”

Response: Thank you very much for this valuable comment. We have changed the statement “If $I^2 > 50\%$, a random-effects model was employed,” to “Considering the variation in the definition of sarcopenia, diagnostic criteria, and population characteristics among the included studies, this study employed a random-effects model.” (Pg. 8, Lines 17-19)

6. Page 8, Statistical Analysis: Provide the reasons for grouping in subgroup analysis to improve the transparency of the study's methodology.

Response: Thank you very much for this valuable comment. We have made the following edits in the manuscript (Pg. 9 Lines 1-8): “The reasons for grouping in subgroup analysis are as follows. Firstly, variability in the definition of sarcopenia will result in varied prevalence estimates for patients with SSc. Unsurprisingly, increasing the number of necessary criteria in a sarcopenia definition will eventually diminish sarcopenia prevalence. Additionally, the disease subtype is an important factor that affects the prevalence of sarcopenia. Patients with dcSSc are more prone to develop sarcopenia.[14] Moreover, age is an essential factor that influences the onset and course of sarcopenia, with the prevalence of sarcopenia increasing with age.”

7. Page 9, Patient and public involvement: Please revise this section in line with the BMJ Open requirements.

Response: Thanks for the suggestion. We have made the following edits in the manuscript (Pg. 9 Lines 15-16): “Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.”

8. Page 10, Impact of sarcopenia on the clinical characteristics of SSc patients: All MD values should be written in specific units. For example, duration should be written as MD, 2.97 years (95% CI -0.13 to 6.08).

Response: Thank you for raising this important point. We have added specific units to MD or SMD values in the article.

We hope that we have adequately addressed all comments raised by the reviewers. We look forward to your response.

Sincerely yours,

Jirong Yue, on behalf of the authors.

VERSION 2 – REVIEW

REVIEWER	Chen, Yaolong Lanzhou University, Evidence-Based Medicine Centre, School of Basic Medical Sciences
REVIEW RETURNED	28-Jan-2024
GENERAL COMMENTS	I have thoroughly reviewed the revised version of the manuscript and acknowledge that the author has effectively addressed all previously suggested comments. I think the overall quality of the

	<p>current manuscript is commendable and warrants consideration for publication.</p> <p>However, there are minor points that require attention. Firstly, it is advisable to remove units when reporting SMD results. Furthermore, in Table 1, it is recommended to incorporate a column specifying the countries where the research was conducted. These relatively small adjustments will further enhance the clarity and completeness of the manuscript.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Prof. Yaolong Chen, Lanzhou University

Comments to the Author:

I have thoroughly reviewed the revised version of the manuscript and acknowledge that the author has effectively addressed all previously suggested comments. I think the overall quality of the current manuscript is commendable and warrants consideration for publication.

However, there are minor points that require attention. Firstly, it is advisable to remove units when reporting SMD results. Furthermore, in Table 1, it is recommended to incorporate a column specifying the countries where the research was conducted. These relatively small adjustments will further enhance the clarity and completeness of the manuscript.

Response: Thank you very much for your advice. We have removed units of SMD results. Additionally, we have incorporated a column to specify the countries where the studies were conducted in Table 1.

We hope that we have adequately addressed all comments raised by the reviewers. We look forward to your response.

Sincerely yours,

Jirong Yue, on behalf of the authors.