

## **Response to reviewers**

Reviewer #1:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** Dear colleagues! I read with interest your minireview "Sarcopenia in the chronic viral hepatitis: from concept to clinical relevance", that covers an important topic of clinical hepatology that evades the attention of practitioners. The matters you brought up are really, actual. I have only a few minor comments.

- 1. The paper is not organized according to general rules. Normally, the order of sections is as follows: Introduction, aim, methods, results, discussion, conclusions). I feel that the manuscript benefit if the search criteria are placed next after the aim.**

We thank you for your helpful comments. This minireview was performed according to the following aims: "firstly, we contextualized our review in relation to the connections between the liver and nutrient metabolism. Secondly, we briefly reviewed the origin of the sarcopenia concept alongside the progress in understanding viral hepatitis biology and its related clinical manifestations. Finally, we performed a review to identify and summarise the available literature on the prevalence and clinical implications of sarcopenia in patients with chronic viral hepatitis." We rewrote the aims and added them to the manuscript.

Regarding your last comment, we totally agree with you. In this way, following your suggestion, we rewrote the further objective in the "Prevalence and clinical implications associated with sarcopenia in patients with chronic viral hepatitis" section. Then, we added the search criteria after the aim.

- 2. Please, avoid "skeletal muscle abnormalities" in the aim, as this condition is not certain (may include myodystrophias, but they are not covered in the paper). Is it better to use "skeletal muscles weight", or "lean body weight" instead?**

We agree with you. We rewrote the aims, and the terms "skeletal muscle abnormalities" were deleted from the text and used in the text, the terms recommended by previous studies as follows: "Cruz-Jentoft *et al.*, Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16-31. DOI: 10.1093/ageing/afy169." Then we modified to "skeletal muscle loss".

- 3. In search criteria, the search criteria, the use of "body composition" in combination with HBV and HCV could yield additional number of papers. Eligibility criteria are not sufficiently described, please, add the information about extraction of the information from the abstracts, in case they were informative and data of previously published reviews. The study design and flow chart would be appreciated.**

We agree with you, and we added in detail all steps followed to perform our review in the section "Prevalence and clinical implications associated with sarcopenia in patients with chronic viral hepatitis". Concerning the search criteria: "body composition", which was described in the manuscript as "bioelectrical impedance analysis", we removed this descriptor and did a new search strictly following each step as described in the manuscript, including the study design and flow chart.

- 4. The data of 17 papers are provided in the results. It seems that some outcomes, like osteoporosis/fractures are not related to the condition of interest (viral hepatitis B or C), or associations are not sufficiently reflected.**

We apologize for not making it clear, but osteoporosis/fractures were included in adverse clinical outcomes. These clinical implications were addressed in the discussion of the manuscript.

- 5. Is it possible to reflect the outcomes of antiviral treatment also?**

Although the literature is still scarce concerning this subject, previous investigations have been demonstrating an increase in skeletal muscle mass in parallel with the recovery of liver function in patients with a sustained virologic response after treatment with direct-acting antiviral agents (DAA). We tried to be moderate in exposing the data and added in the manuscript that future longitudinal and multicentre studies may contribute to reduce this gap in knowledge.

**6. Discussion section is lacking. It seems that the text on page 6-12 may be used to organize this section.**

We agree with you and have included the discussion section.

**7. Please, avoid the use of references in the Conclusion, as this part of the manuscript should be based on the results of your search and your analysis of the information. I hope that my comments help you to improve your manuscript.**

We apologize for that, and we amended the conclusion section.

## **Response to the reviewers**

Reviewer #2:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** 1. Nice review. 2. Please change 'in this study' to 'in this review' at the final paragraph of the introduction section. 3.

Thank you very much for your kind comments. We agree with you and have included “in this review” to the final paragraph of the introduction section.

Please explain why "phase angle" is a necessary descriptor in searching articles for sarcopenia and chronic viral hepatitis.

Although low phase angle has been associated with sarcopenia, it is not a necessary descriptor for our review. Then, we removed “phase angle” from the search criteria and did a new search strictly following each step as described in the manuscript, including the study design and flow chart. We added in detail all steps followed to perform our review in the section “Prevalence and clinical implications associated with sarcopenia in patients with chronic viral hepatitis”.