

Naples, January 25th 2021

Lian-Sheng Ma  
Company Chief Editor  
*World Journal of Clinical Oncology*

Re: 62034 "Prognostic role of sarcopenia in metastatic colorectal cancer patients during first line chemotherapy: a retrospective study",

Dear Dr. Ma,

Thank you for the comments of Reviewers 1 and 2 who appraised our article. We found their comments and suggestions very apt and to the point, and would like to thank them for their input that has enabled us to improve our article. Enclosed is a point-by-point reply to the reviewers' comments and a revised version of the manuscript in which the revisions are highlighted.

We would be pleased to address any further questions or comments that you may have.

Looking forward to hearing from you.

Yours sincerely,

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**Manuscript N. 62034** “Prognostic role of sarcopenia in metastatic colorectal cancer patients during first line chemotherapy: a retrospective study”, by Chiara Maddalena et al.

## **Responses to the reviewers' comments**

### **Reviewer #1:**

*1. The definition of sarcopenia is only based on SMI in this study. It is different from the current guideline for defining sarcopenia (for European or Asian population), please clarify it.*

In 2018, the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) published an updated definition that uses low muscle strength as the primary parameter for recognizing sarcopenia. According to the EWGSOP2 guidelines, sarcopenia is suspected in case of low muscle strength, and diagnosis is confirmed by the presence of low muscle quantity or quality. Sarcopenia is considered severe if it is associated with low muscle performance. We were unable to evaluate either strength or muscle performance because of the retrospective nature of our analysis. The method we used to evaluate the sarcopenia (the muscle area at the level of the third lumbar vertebra at CT scans) largely correlates with the functional state of the muscle tissue of the entire body, as previously demonstrated by Shen and Mourtzakis. We now clarify this in our Introduction.

*2. There were 14 patients with sarcopenia at the baseline, the authors also reported that 7 patients became sarcopenic. Why this study did not analyze these 7 patients with sarcopenia?*

The clinical characteristics and survival of the 7 patients who were not sarcopenic at baseline evaluation and became sarcopenic at the first disease reassessment are now reported in the Results section.

*3. Although this study focused on mCRC, the authors reported that 23 patients had II or III stage disease according to the pTNM classification and they subsequently developed metastases; 33 patients received the diagnosis at metastatic stage. This implied that 56 so-called “mCRC” patients with different time points of metastasis which will lead to different clinical outcomes, please clarify it.*

In all 56 patients, sarcopenia was evaluated at the first diagnosis of metastatic disease, whereas survival was calculated from the time of metastatic disease diagnosis until death or the last visit. Of the 56 patients, 23 developed methachronous metastases while 33 received the diagnosis at a metastatic stage. In the Results section, we now report the prevalence of sarcopenia in these two subgroups.

*4. The contents of the “Discussion” section should be concise. For example, the relevant descriptions of the study conducted by Prado et al. are too much. Please avoid describing the detail contents and just focus on discussing the key points*

We have shortened the text related to the Prado study. However, we think that the detailed description of the studies is important to point out the wide heterogeneity of the populations and treatments included in published trials.

5. In Table 1, the *p* values for the “Toxicity during the first 4 chemotherapy cycles” should not be “1”, please provide the true *p* values.

P-values for comparison between groups with respect to categorical variables (e.g. toxicity) were obtained using the exact Fisher test that may report a *p* value equal to 1, even if the two proportions are not equal.

**Reviewer #2:**

*Although the result of the study was negative, that's fine, as that answers the question asked, within the scope of the limited sample size (a factor that the authors state). Statistical analyses and interpretations seem adequate and the paper is also adequately written. As such, it is acceptable, and represents a contribution to the field.*

**Science editor:** 1 Scientific quality: The manuscript describes a retrospective study of the prognostic role of sarcopenia in metastatic colorectal cancer patients during first line chemotherapy. The topic is within the scope of the WJCO. (1) Classification: Grade B; (2) Summary of the Peer-Review Report: *Although the result of the study was negative, that's fine, as that answers the question asked, within the scope of the limited sample size. Statistical analyses and interpretations seem adequate and the paper is also adequately written.*; and (3) Format: There is 1 table and 4 figures. A total of 49 references are cited, including 15 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade A. No language editing certificate was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, and the Institutional Review Board Approval Form. The written informed consent was not provided. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJCO. 6 Recommendation: Conditional acceptance.

We thank the Science Editor for the positive comments, and for considering our paper acceptable, pending the reply to the reviewers. Regarding a language editing certificate, the Author's Editor who edited the paper for language is a longstanding member of the European Association of Science Editors, which doesn't issue certificates. Over the years she has edited a large number of scientific-medical articles.

5. Issues raised:

- (1) *The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;*

All the figures are in power point format. However, Kaplan-Meier curves are not "editable" because they have been produced by the statistical analysis program that creates the files in pdf format.

- (2) *The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.*

Thank you. We now provide “Article Highlights” section.