

9/8/2022

Dear editor,

We would like to thank you for giving us the chance to revise our manuscript. The point-by-point responses to the reviewers and editorial office are described in red below. I had contacted the editorial office to ask for a Microsoft Word version for the Conflict-of-Interest disclosure form because I could not open the PDF version, but unfortunately, I have not got a reply yet. Due to limited time, I wrote a declaration statement and uploaded it to the system.

Regards,

Sara Haj Ali

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The present manuscript summarizes current knowledge of the different aspects of malnutrition in patients with liver cirrhosis. It presents guidelines for estimation of the severity of malnutrition using clinical scores, lab parameters, and imaging techniques. I have only minor points: 1. In Figure 1, the increased protein catabolism may be included as a factor contributing to malnutrition. 2. My question: Are there lab marker or biomarkers that could better indicate malnutrition/hypermetabolism/hypercatabolism than the usual biochemical parameters? E.g. BCAA, ammonia, markers of intestinal permeability (zonulin family, intestinal fatty acid binding protein), cytokines (e.g. IL6, TNF-alpha) 3. Which is the influence of portal hypertension on malnutrition? 4. Many patients receive propranolol for prevention of variceal bleeding. Does this play a role in the nutritional status? 5. Is there an effect of steroid hormone levels? Androgens or estrogens?

1. In Figure 1, the increased protein catabolism may be included as a factor contributing to malnutrition.

As the reviewer suggested, we modified Figure 1 to include protein catabolism and other important factors mentioned in the manuscript that contribute to malnutrition.

2. My question: Are there lab marker or biomarkers that could better indicate malnutrition/hypermetabolism/hypercatabolism than the usual biochemical

parameters? E.g. BCAA, ammonia, markers of intestinal permeability (zonulin family, intestinal fatty acid binding protein), cytokins (e.g. IL6, TNF-alpha).

We added the sentence 'The use of serum biomarkers for diagnosis of malnutrition is controversial and currently, they only complement nutritional assessment' to paragraph 3 page 8.

3. Which is the influence of portal hypertension on malnutrition?

We added the paragraph 'The role of portal hypertension in malnutrition and sarcopenia is not clear. There is very limited literature about the prevalence of malnutrition and sarcopenia in non-cirrhotic portal hypertension. A study by Lattanzi et al. found that the prevalence of sarcopenia in non-cirrhotic portal hypertension was similar to that in patients with compensated cirrhosis²³. This could suggest that portal hypertension per se may play a role in the development of malnutrition and sarcopenia given the fact that those patients have less liver damage compared to cirrhotic patients. This theory could be supported by the fact that nutritional status improves after transjugular intrahepatic portosystemic shunt (TIPS) and resolution of portal hypertension' to the last paragraph in page 5.

4. Many patients receive propranolol for prevention of variceal bleeding. Does this play a role in the nutritional status?

We added the paragraph 'Beta blockers have been suggested as a possible external factor contributing to malnutrition in cirrhosis. However, a recent study found that patients who received non-selective beta blockers had actually better skeletal muscle index and improvement in sarcopenia' to paragraph 3 page 5.

5. Is there an effect of steroid hormone levels? Androgens or estrogens?

We added the sentence 'Testosterone levels are decreased in cirrhotic males and this further contributes to decreased protein synthesis and loss of muscle mass' to paragraph 1 page 5.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This is a nutritional assessment review of patients with liver cirrhosis. Please summarize each evaluation result in a table from the references in an easy-to-understand manner.

As the reviewer suggested, we created Table 1 that summarizes body composition testing modalities.

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Thank you

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review

Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Figure legends should be more detailed.

Figure legend was added to Figure 2. Figure 1 is self-explanatory.