

Peer Review File

Article information: <http://dx.doi.org/10.21037/atm-20-5194>

Reviewer Comments:

It was with great pleasure that I received the manuscript "Bioelectrical Impedance Analysis for Predicting Postoperative Complications and Survival After Liver Resection for Hepatocellular Carcinoma" for a review. The main goal of this study was to investigate whether preoperative bioelectrical impedance analysis could predict postoperative complications and survival in patients with hepatocellular carcinoma.

-- Background

1) The first paragraph (lines 78 to 94) needs a more robust review.

Response: Thank you for your feedback. Following your suggestion, we reviewed recent studies again and reinforced this part by adding more references (references 6 and 8). Reinforcement was made by citing a recently reported study which stated that the risk of postoperative ascites related to acute portal hypertension may increase postoperatively because patients undergoing hepatectomy for HCC have a high probability of underlying liver diseases such as viral infection or alcoholic liver disease (reference 8) (see Page 5, line 76-91)

References:

6. Ishizawa T, Hasegawa K, Kokudo N, et al. Risk factors and management of ascites after liver resection to treat hepatocellular carcinoma. Arch Surg. 2009;144(1):46-51.
8. van Mierlo KMC, Schaap FG, Dejong CHC, et al. Liver resection for cancer: New developments in prediction, prevention, and management of postresectional liver failure. J Hepatol. 2016;65(6):1217-31.

2) The description of BIA also needs improvements. There is a large body of evidence about the use of BIA in different clinical situations. This fact could be better described.

Response: Thank you for your suggestion. We have comprehensively reviewed the studies published in recent years. They include a paper that states that phase angle is associated with postoperative prognosis in patients with gastrointestinal or hepatobiliary cancer (reference 21), and that phase angle can play a role as a prognostic factor in patients with colorectal cancer (reference 22). The phase angle is a prognostic factor in patients with head and neck cancer. (reference 23) Based on these references, content has been added to the introduction section of the manuscript. (see page 6, lines 106-116)

References:

21. Yasui-Yamada S, Oiwa Y, Saito Y, et al. Impact of phase angle on postoperative prognosis in patients with gastrointestinal and hepatobiliary–pancreatic cancer. *Nutrition*. 2020;79-80:110891.
22. Barao K, Abe Vicente Cavagnari M, Silva Fucuta P, et al. Association between nutrition status and survival in elderly patients with colorectal cancer. *Nutr Clin Pract*. 2017;32(5):658-63.
23. Axelsson L, Silander E, Bosaeus I, et al. Bioelectrical phase angle at diagnosis as a prognostic factor for survival in advanced head and neck cancer. *European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*. 2018;275(9):2379-86.

3) It was not clear the association between BIA and Sarcopenia,

Response: Thank you for your comment. Various factors, such as the type of BIA device, can interfere, so caution is required when interpreting the results (reference 34). However, BIA is a relatively accurate test that can measure sarcopenia compared to other test methods (reference 35). Since studies have shown that sarcopenia can act as a prognostic value in patients with liver cirrhosis (reference 19), measuring the presence of sarcopenia with BIA may be a clinically important factor. The contents described above were additionally inserted into the introduction and discussion section of the manuscript. (see page 6, lines 120-123)

References:

19. Kim G, Kang SH, Kim MY, et al. Prognostic value of sarcopenia in patients with liver cirrhosis: A systematic review and meta-analysis. PLoS One. 2017;12(10):e0186990.
34. Gonzalez MC, Barbosa-Silva TG, Heymsfield SB. Bioelectrical impedance analysis in the assessment of sarcopenia. Curr Opin Clin Nutr Metab Care 2018;21(5):366-74.
35. Aleixo GFP, Shachar SS, Nyrop KA, et al. Bioelectrical impedance analysis for the assessment of sarcopenia in patients with cancer: A systematic review. Oncologist. 2020;25(2):170-82.

4) The objective of the paper has to be clearer.

Response: Thank you for pointing this out. Following your suggestion, we clarified various factors, such as phase angle, presence of sarcopenia, and edema index, which can be measured through BIA and content that we tried to confirm as end-points in this study, such as survival and prognosis, in the last paragraph of the introduction. (see page 7, lines 125-128)

-- Methods

1) The inclusion/exclusion criteria were not clear.

Response: Thank you for your feedback. Following your suggestion, we modified the patient section to clarify the inclusion and exclusion criteria in the following sentences: “We prospectively enrolled the patients who underwent hepatectomy for HCC at our hospital from July 2016 to June 2018. The inclusion criteria were patients over 19 years of age scheduled to undergo liver resection for hepatocellular carcinoma. The exclusion criteria were as follows: 1) patients who had previously undergone implantable electronic devices; 2) patients who had previously undergone liver transplantation; and 3) patients who refused BIA.” (see page 7, lines 134-138)

2) Is BIA a gold-standard tool to assess patients with liver cirrhosis?

Response: As mentioned by the reviewer, cirrhotic patients have various interfering factors, such as that the results may be different from those of normal populations; it may be an important point to think about whether it is appropriate to perform BIA in cirrhotic patients. As mentioned above, caution is required when interpreting BIA due to various disturbing factors (reference 34). There is a previous study that shows that BIA is useful for monitoring refractory ascites in LC patients and is associated with prognosis (reference 33). Based on these studies, it is worth considering that BIA is clinically used in patients with liver cirrhosis; particularly, the advantage that it is a very simple test should be considered. The above is additionally described in the Discussion section of the manuscript. (see page 15, lines 313-320)

References:

33. Ontanilla-Clavijo G, Ampuero J, Borreguero S, et al. Usefulness of bioelectrical impedance analysis for monitoring patients with refractory ascites. *Rev Esp Enferm Dig.* 2019;111(3):223-7.
34. Gonzalez MC, Barbosa-Silva TG, Heymsfield SB. Bioelectrical impedance analysis in the

assessment of sarcopenia. Curr Opin Clin Nutr Metab Care 2018;21(5):366-74.

3) Statistical Analyses:3.1) Previous studies are mentioned on line 157, although there is no reference about them.

3.2) Previous studies are also mentioned on line 158, but there is only 1 reference. Is that correct?

Response: We apologize for this mistake. We reviewed several previously published papers, but only one paper was used as the basis for sample size estimation, and the phrase 'previous studies' was revised to 'previous study'. Once again, we request for your patience for our mistakes. (see page 9, line 177)

-- Discussion

1) On average this section also needs improvements. I strongly suggest including more studies which performed BIA in liver patients.

Response: Thank you for your suggestion. We reviewed recently published studies, and content about the study that the phase angle is related to postoperative prognosis in patients with hepatobiliary cancer (reference 21). BIA was useful for monitoring patients with refractory ascites (reference 33). was added to the discussion section. (see page 14, line 308-313)

References:

21. Yasui-Yamada S, Oiwa Y, Saito Y, et al. Impact of phase angle on postoperative prognosis in patients with gastrointestinal and hepatobiliary–pancreatic cancer. Nutrition. 2020;79-80:110891.

33. Ontanilla-Clavijo G, Ampuero J, Borreguero S, et al. Usefulness of bioelectrical impedance analysis for monitoring patients with refractory ascites. Rev Esp Enferm Dig. 2019;111(3):223-

7.

2) It was still not clear the role of sarcopenia.

Response: Thank you for your comment. There are various precautions in the interpretation of BIA; however, since BIA is a relatively accurate test to determine the presence of sarcopenia and is particularly simple, it deserves a positive consideration for the presence of sarcopenia and clinical application. We thought about the role of sarcopenia once again; accordingly, we have added content as a new paragraph in the Discussion section. (see page 15, lines 314-320)

-- References

1) It would be really interesting to see more recent studies.

Response: Thank you for your feedback. All the references as supporting articles mentioned above have been added to the manuscript (see page 17, line 375-453). I would like to thank you again for your careful review.