

Lian-Sheng Ma
Company Editor-in-Chief
Editorial Office
Baishideng Publishing Group Inc

Dear Dr. Lian-Sheng Ma

Thank you very much for your letter dated September 12, 2020, and for the careful review of our manuscript, which we have amended following the reviewers' suggestions. A copy of the revised manuscript has been uploaded to the submission system. Also, please find below an itemized point-by-point response to the reviewers' comments.

We look forward to hearing the status of this manuscript, which we hope is now acceptable for publication in World Journal of Gastrointestinal Pharmacology and Therapeutics. Please feel free to contact me if you require any additional information.

Sincerely,

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Reviewer #1:

1.Abstract: in background part, the author mentioned (We evaluated the RRE by indirect calorimetry (CI) and compared it with electrical bioimpedance (BIA) and predictive formulas, trying to identify which is the best evaluation method.) and again in the abstract repeated the same in the aim of the work, please remove it from the background.

Response: As requested, it was removed from the background part, as follows:
“The diagnosis of malnutrition in patients with independent hepatocellular carcinoma (HCC) varies from 20 to 50%, being related to important complications and direct impact on the prognosis. Determining the resting energy expenditure (REE) becomes an important parameter for this population, as it allows therapeutic adjustments to recover their nutritional status. The REE in HCC is not clearly defined, with and without cirrhosis, which implies the search and definition of the best nutritional conduct.”

2. Correct in the method section in abstract RRE? do you means REE?

Response: It was revised. The correct abbreviation is REE. It was corrected in the following sentences:

AIM: “The aim of this study is to evaluate the REE of patients with HCC with and without cirrhosis.”

Methods “Prospective observational study evaluating the REE of 118 patients, 33 with hepatocellular carcinoma and a control group of 85 patients, with cirrhosis without HCC, using IC, BIA, and predictive formulas.”

Results: “The REE determined by IC in cirrhotic patients with HCC was 1643 ± 364 and of those without HCC was 1526 ± 277 ($P=0.064$).”

3. What are the causes of cirrhosis and its impact on the REE?

Response: We added the following paragraph at the beginning of the Introduction section:

“The main causes of liver cirrhosis worldwide are due to alcoholic liver disease and HBV and/or HCV chronic infections. Over a period of 15 to 30 years, chronic liver diseases can lead to liver cirrhosis and its complications. The prognosis is highly variable and influenced by several variables, such as etiology, severity of liver disease, presence of complications and comorbidities.”

The impact of cirrhosis is already described in the following paragraphs:

“The prevalence of sarcopenia observed in patients with hepatocellular carcinoma (HCC) varies from 27.5% to 78.2% and malnutrition affects 20% to 50% of cirrhotics, both related to important complications and direct impact on the prognosis.”

“Early nutritional diagnosis is of great relevance for cirrhotics, as it reflects positively on their recovery, enables specific therapeutic interferences and prevents the appearance of complications”

4.The author mentioned that, cirrhosis depends on liver biopsy in some patients. What are the grade/stage of cirrhosis and if there is differences in REE according to stage of cirrhosis.

Response: We did not mention that cirrhosis depends on liver biopsy. As stated in the “Patients and Methods” section: “The diagnosis of cirrhosis and/or HCC was made by clinical, laboratory, imaging and/or, eventually, liver biopsy. The classification of patients with HCC was made by the staging system of the Barcelona Clinic Liver Cancer Group (BCLC).

The diagnosis of liver cirrhosis can be made by evaluating the clinical conditions of the patients, and the evaluation of patients’ functional activity is determined by Child-Pugh Score. This study does not aim to identify if there is differences in REE according to stage of cirrhosis.

Reviewer #2:

I guess the authors wanted to study the difference in energy expenditure between different methods in patients with liver disease, However, I recommend authors only aim to study one liver disease such as LC or HCC, and The results are more concise and clear.

Response: The aim of this study is to evaluate the REE of patients with cirrhosis, with and without CHC, measured by IC and to compare with those obtained by BIA and predictive formulas, in order to identify which is the best method of evaluation.

This is an attempt to show that patients with cirrhosis and associated tumor have a higher metabolic expenditure than patients without the tumor, even with cirrhosis. In both groups there are the same etiologies, with no confusion and selection bias. Consequently, this result is a guide for future clinical and nutritional therapy.

Science Editor:

The focus of the study is puzzling, for that readers may confuse whether the author focuses on the difference in energy expenditure between cirrhosis and liver cancer patients, or the difference in methodology of expenditure. The reviewer recommends the authors only aim to study one liver disease such as LC or HCC, and the results are more concise and clear.

Response: As cited before, the aim of this study is to evaluate the REE of patients with cirrhosis, with and without CHC, measured by IC and to compare with those obtained by BIA and predictive formulas, in order to identify which is the best method of evaluation.

This is an attempt to show that patients with cirrhosis and associated tumor have a higher metabolic expenditure than patients without the tumor, even with cirrhosis. In both groups there are the same etiologies, with no confusion and selection bias. Consequently, this result is a guide for future clinical and nutritional therapy.