

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Hepatology*

**Manuscript NO:** 74061

**Title:** Relationship between the phase angle, steatosis and liver fibrosis in HIV/HCV  
coinfectd patients

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 04122997

**Position:** Peer Reviewer

**Academic degree:** MSc, PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Malaysia

**Author's Country/Territory:** Brazil

**Manuscript submission date:** 2021-12-12

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-12-13 06:11

**Reviewer performed review:** 2021-12-22 01:17

**Review time:** 8 Days and 19 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [ ] Yes [Y] No

The English used is understandable but has some errors in spelling throughout the manuscript which requires cross-checking (For example in the abstract: the word 'conveniencev' should be spelled as 'convenience'; in methods: the word 'stabilishe' should be spelled as 'stabilished' etc.)

**Answer:** All the grammar was extensively reviewed by an expert.

The method and statistical test used is generally appropriate and would require further description and elaboration

**Answer:** Methods and statistical analysis were adjusted and better described.

#### **SPECIFIC COMMENTS TO AUTHORS**

Introduction: This study aimed to assess the relationship between phase angle (PA), steatosis and liver fibrosis in HIV/HCV coinfecting patients. A total of 43 HIV/HCV coinfecting patients from a tertiary reference center in Brazil was evaluated. The authors found that there was no significant correlation between fibrosis grade with PA and lean mass as well as CAP (controlled attenuation power) with PA. However, significant inverse correlation was found between CAP and lean mass. On the other hand, a significant positive correlation was found between PA and lean mass whereas a significant negative correlation was observed between PA and fat mass. There was no correlation between PA and CAP. When evaluated by gender, no correlation was observed between PA with lean mass, fat mass and CAP. The authors concluded that PA determines muscle functionality in patients coinfecting with HIV/HCV, and CAP value reinforces the association with lean muscle mass, suggesting patients who need early nutritional intervention. Merits: This study has some merits. The title of the paper reflects its content. The keyword use reflects the focus of the manuscript. The English used is understandable but has some errors in spelling throughout the manuscript which requires cross-checking (For example in the abstract: the word 'conveniencev' should be spelled as 'convenience'; in methods: the

word 'stabilishe' should be spelled as 'established' etc.). The method and statistical test used is generally appropriate and would require further description and elaboration. In addition, this study provides a better understanding on the relationship between PA with steatosis and liver fibrosis in patients co-infected with HIV/HCV.

**Answer:** All the grammar was extensively reviewed by an expert. Methods and statistical analysis were adjusted and better described.

Specific comments:

1. Abstract a. Lean muscle and fat mass stated in result was not reflected in the study aim statement.

**Answer:** Ok, this is now inserted in the abstract

b. There is no clear description in the methods section pertaining the way to assess muscle functionality. Expand the write up in the method section.

**Answer:** Ok, this is now inserted in the methods

c. HCV-suggest providing in expanded form of the abbreviation during the first use (i.e., Hepatitis C virus).

**Answer:** Ok, adjusted

d. CAP-suggest providing in expanded form of the abbreviation during the first use (i.e., controlled attenuation parameter).

**Answer:** Ok, adjusted

e. Method: state what statistical test was employed.

**Answer:** Ok, this is now inserted in the abstract

f. Results: suggest stating the r-value (to better indicate the direction and strength of the association) and p-value for all correlation findings.

**Answer:** Ok, this is now inserted in the abstract

2. Introduction a. It would be good if the authors could add few lines to explain physiology of advanced HIV/AIDS in relation to development of malnutrition.

**Answer:** Ok, this information is now included in the introduction

b. The authors stated that the nutritional assessment method in patients with liver disease has limitations due to difficulties with reproducibility and the lack of gold standard method. Further elaboration and examples are needed to strengthen the problem statement. Suggest providing few examples on the current nutritional assessment methods available for patients with liver disease (e.g., anthropometric measurements? Biochemical measurements? Subjective global assessment?).

**Answer:** Ok, this information is now included in the introduction

c. Include data/information pertaining to the prevalence of malnutrition in patients living with HIV to indicate the seriousness.

**Answer:** Ok, this information is now included in the introduction

d. Some statement would require citations. Example " In patients coinfectd with HIV and chronic hepatitis C virus (HCV) (HIV/HCV), not only the natural history of the disease, but the clinical treatment and previous clinical conditions significantly compromise the body homeostasis"

**Answer:** Ok, reference inserted

3. Methods: a. Methods section need to be reorganised based on subheadings to improve clarity (Study design; subject selection criteria; sample size; diagnosis of HIV/HCV; staging of liver fibrosis; anthropometric measurement; BIA measurement; statistical test).

**Answer:** OK, subheadings were added to Methods section

b. Suggest to follow STROBE statement/checklist for clear reporting.

**Answer:** OK, STROBE statement was followed and this was informed in the text

c. It is unclear on the study design that was employed in this study. The study design stated in the abstract was retrospective observational study design whereas in the methods and discussion section, prospective observational study design was stated instead. Suggest author to relook on the statement.

**Answer:** We agree that this is a retrospective study. Adjusted in text.

d. Please provide sample size required and how it was calculated (which formula was used).

**Answer:** The study was by convenience, and because of this, there is no need to calculate the number of patients.

e. The author stated that PA was classified according to the cut-off point of 5.4°, based on the reference parameters of the study by Fernandes et al (Page 7). However, this piece of information was missing in the result section.

**Answer:** It was included in the text.

f. Pearson's chi square test statement that was mentioned in Page 7 (Pearson's chi-square was used to assess the association between CAP and BIA,...) was not reported in the result section.

**Answer:** All the correlations are described appropriately in the text.

g. Suggest providing the model/type/brand of stadiometer that was used

**Answer:** Ok, this information is now added in the text

h. To state whether the BIA (Biodynamics,model 450) used was a single- or multi-frequency device

**Answer:** Ok, this information is now added in the text

i. Please state at which frequency phase angle was measured

**Answer:** Ok, this information is now added in the text

j. State individually what are the BIA parameters being evaluated besides phase angle. Was phase angle the only parameter derived from BIA? How about lean mass and fat mass? Are they measured using BIA as well or by anthropometric measures?

**Answer:** Ok, this information is now added in the text

k. Provide more elaboration/description on what does F2, F3 and F4 indicates for staging of liver fibrosis

**Answer:** It was included in the methods.

l. Include scoring/cut-offs for CAP which indicates the severity/degree of steatosis for reader to get a better understanding on how steatosis was being categorized.

**Answer:** It was included in the methods.

m. Elaborate more on the parameters evaluated using student t-test

**Answer:** All the parameters are now described appropriately in the text.

n. The result for Pearson correlation (continuous variables) was depicted in Table 2 but was not stated in the statistical test section under methods. Only Spearman correlation test statement was being reported.

**Answer:** All the correlations are described appropriately in the text.

4. Results a. Descriptive results in Table 1 were not completely described in text. (For example: lean muscle mass, fat mass, CAP score, BMI). Please expand the write up.

**Answer:** It was included in the text.

b. It is unclear how patients were divided into two groups fibrosis grades of F0-2 and F3-4 for t-test. What is the basis of this group division?

**Answer:** A sentence was included in the Methods section informing that groups were separated according the presence of advanced fibrosis. This is currently used to avoid the stratification due to a small number of patients

c. Suggest including flow diagram of patient recruitment.

**Answer:** We think there is no need to include a flow diagram explaining the recruitment process, because the number of excluded patients was low, but this is now explained in the text, reporting the number and the reason for exclusion

d. Provide measurement unit for phase angle (°).

**Answer:** Ok, adjusted

e. Provide measurement unit for lean mass (%).

**Answer:** Ok, adjusted

f. To present the result of student t-test in table format as well.

**Answer:** We did included a new table and expanded the results, which are also fully described in the text.

g. Include both r-value and p-value for all correlation findings in text.

**Answer:** The values were included.

h. Table 1: suggest removing height and weight as it provides redundant information with BMI.

**Answer:** We removed these values of table 1.

i. Any statistical test conducted for BMI or only descriptive analysis was performed?

**Answer:** Only descriptive analysis was performed.

j. Suggest to provide a description in text on how severe the degree of steatosis based on the mean CAP score of  $241.1 \pm 55.7$  (Table 1).

**Answer:** A sentence was included in the discussion explaining about the finding of the mean CAP.

k. Table 2: Suggest to revise the correlation coefficient symbol used to represent Spearman test (rho or rs), to distinguish from Pearson correlation test.

**Answer:** It was corrected.



1. Table 3: include measurement unit for phase angle, lean mass and fatty mass; include in table footnote whether Spearman or Pearson correlation was performed.

**Answer:** Ok, adjusted

5. Discussion a. Strengths-It is unclear what are the two important tools that are not operator-dependent being used in this study. How does it serve as a strength to this study?. Suggest author to revise the sentence for better readability.

**Answer:** Ok, adjusted

b. To provide reference for the sentence: One of the main clinical complications of advanced liver disease is protein-calorie malnutrition, which has a prevalence ranging from 10% to 100%, regardless of the stage and etiology of the disease (Page 10).

**Answer:** Ok, this information is now added in the text

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**Reviewer's code:** 05821532



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**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Doctor, Senior Scientist

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Brazil

**Manuscript submission date:** 2021-12-12

**Reviewer chosen by:** Fei-Yan Lin (Online Science Editor)

**Reviewer accepted review:** 2022-03-04 02:45

**Reviewer performed review:** 2022-03-12 10:58

**Review time:** 8 Days and 8 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

1. Too many grammar, spelling and syntax errors were found

**Answer:** The grammar was completely reviewed

2. Description is confusing: it is retrospective or prospective observational study? I think it is retrospective

**Answer:** We agree that this is a retrospective study. Adjusted in text

3. bioelectrical impedance analysis and TE are low sensitive and specific

**Answer:** Nowadays, BIA is the nutritional assessment method with the best performance in patients with chronic liver diseases since it reflects muscle volume and functionality without the influence of confounding factors. The sensitivity and specificity of the PA, presents on average (depending on the evaluated population), 68.9% and 70% respectively (Fernandes SA, Bassani L, Nunes FF, Aydos ME, Alves AV, Marroni CA. Nutritional assessment in patients with cirrhosis. *Arq Gastroenterol* 2012; 49: 19-27 [PMID: 22481682 DOI: 10.1590/S0004-28032012000100005]). In the study by Osuna-Padilha et al (Osuna-Padilla IA, Salazar Arenas MA, Rodríguez Moguel NC, Aguilar Vargas A, Montano Rivas JA, Ávila-Ríos S Phase angle as predictor of malnutrition in people living with HIV/ AIDS. *Nutr Clin Pract*. 2021;1-7. <https://doi.org/10.1002/ncp.10744>), we can observe similar sensitivity and specificity of PA as a prognostic factor in patients with HIV. In the same way, hepatic elastography is considered the non-invasive method with better performance to evaluate liver fibrosis (Transient hepatic elastography has the best performance to evaluate liver fibrosis in non-alcoholic fatty liver disease (NAFLD). Tovo CV, et al. *Ann Hepatol*. 2019 May-Jun;18(3):445-449.)

4. outcome is not compelling

**Answer:** This study evaluated a small number of patients. On the other hand, this is an original study, and to the best of our knowledge is the first study in Brazil to evaluate this population of patient, being important for early intervention in the clinical/nutritional treatment of patients co-infected with the HIV/HCV virus that guarantee a better quality of life and prognosis.

We sincerely thank you for your time and insightful comments on our manuscript and we have modified it to address all concerns. We believe that all comments have elevated the quality of our manuscript significantly and we hope you will be satisfied with our amendments.

Yours sincerely,



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