

Dear Editor

We are very glad to hear from you about reviewing our manuscript entitled "**Frequency of Hepatic Steatosis and Its Association with the Pneumonia Severity Score on Chest CT in Adult COVID-19 Patients**" We thank the reviewers for their contributions to our paper. We have revised the manuscript according to the reviewers' suggestions using red font, and our responses to the comments are given in this letter.

This paper, improved with valuable comments and contributions from the reviewers, describes an important clinical and radiological situation related to COVID-19. Several previous studies have investigated the presence of hepatic steatosis in patients with COVID-19 based on laboratory data. However, our data suggest that the inclusion of hepatic steatosis measurement as part of routine CT evaluation can provide useful prognostic information in patients with COVID-19 at no additional cost. In addition, we think that it will contribute to the literature since it is the first study investigating the relationship between pneumonia severity and liver attenuation. It will be an important reference for future studies.

Reviewer #1:

The paper deals with an interesting and up to date question and is of importance for the readership of the WJG. The overall quality of the paper is good and I have only some minor questions:

Comment 1:

The timeframe in which the patients were recruited is only 1 month according to the method section. Even for a high volume center 1216 CT's of the chest for suspected COVID 19 disease seems extremely high. Please explain.

Response 1:

The city where the study was conducted (Sanliurfa / Turkey) has a population of over two million. Our hospital is the city's largest hospital and a referral hospital for COVID-19. The number of patients admitted to the emergency department in 1 month is 17,632. In addition, the patients included in the study belonged to the period when the disease was most intense. Therefore, the number of cases and CT scans were too high.

Comment 2:

Was permission gained from the patient for usage of the CT scans in figure 1?

Response 2:

Informed consent forms were obtained from all patients before the CT scan. Permission was also obtained from the patient in Figure.

Reviewer #2:

Comment 1:

Title.

Does the title reflect the main subject/hypothesis of the manuscript?

Comment

The title partially reflects the study. The authors should make clear that they selected moderate COVID-19 patients.

Response

We have added severe COVID-19 patients to the study. Therefore, our study includes not only moderates but also all COVID-19 patients.

2 Abstract.

Does the abstract summarize and reflect the work described in the manuscript? Yes.

3 Key words.

Do the key words reflect the focus of the manuscript? Yes.

4 Background.

Does the manuscript adequately describe the background, present status and significance of the study? Yes.

5 Methods.

Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Yes.

6 Results.

Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes.

7 Discussion.

Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically?

Are the findings and their applicability/relevance to the literature stated in a clear and definite manner?

Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Moderate.

Comment

Authors should make clear the possible implication involving the age difference, possible implication of COVID-19 in the aggravating Hepatic Steatosis. They did not evaluate important variables such as comorbidities (obesity, diabetes, smoking,...) that could impact both hepatic steatosis and COVID-19, therefore are crucial for this manuscript.

Response

We have included comorbidities (hypertension, obesity, diabetes, smoking, ...) in the study.

We have done a logistic regression analysis for age.

8 Illustrations and tables.

Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Yes.

9 Biostatistics.

Does the manuscript meet the requirements of biostatistics? Yes.

10 Units.

Does the manuscript meet the requirements of use of SI units? Yes.

11 References.

Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes.

12 Quality of manuscript organization and presentation.

Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Yes. the language and grammar is appropriate.

13 Research methods and reporting.

Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? Yes

14 Ethics statements.

For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes

Specific Comments To Authors:

First, what are the original findings of this manuscript? What are the new hypotheses that this study proposed? What are the new phenomena that were found through experiments in this study? What are the hypotheses that were confirmed through experiments in this study?

The manuscript identifies and correlate the frequency of hepatic steatosis, Pneumonia Severity Score in adults with moderate COVID-19 in Turkey.

Second, what are the quality and importance of this manuscript? What are the new findings of this study? What are the new concepts that this study proposes? What are the new methods that this study proposed? Do the conclusions appropriately summarize the data that this study provided? What are the unique insights that this study presented? What are the key problems in this field that this study has solved? The study identifies the presence of hepatic steatosis in COVID-19 patients in comparison with non-COVID-19 patients. This further confirms previous investigations with similar findings but performed in a different country, and add important and relevant information.

Third, what are the limitations of the study and its findings? What are the future directions of the topic described in this manuscript? What are the questions/issues that remain to be solved? What are the questions that this study prompts for the authors to do next? How might this publication impact basic science and/or clinical practice?

Comment

The limitations of the study hinder the application of the investigation. Hepatic Steatosis is highly associated with different diseases that are also associated with COVID-19, such as obesity and type 2 Diabetes mellitus. Other important information is when was the tested performed in relation to the infection/hospital admission. I suggest that the table with data from patients be complemented with the clinical information (comorbidities) and the information on when was the tests performed.

Response:

We have included comorbidities (hypertension, obesity, diabetes, smoking, ...) in the study. We have done a multivariate analysis for age. We have added a table relevant to this state.

Reviewer #3:

SPECIFIC COMMENTS TO AUTHORS

Brief summary This is a consecutive series of 1216 patients who was admitted to ER between September 2020 and October 2020. Among them, 252 (54.4%) patients with COVID-19 and pneumonia or 211 patients (45.6%) without COVID-19 were included for liver steatosis evaluation. The frequency of hepatic steatosis detected by CT in the COVID-19 positive group was significantly higher than the control group (42.9 vs. 19.4%, $p < 0.001$). They concluded that hepatic steatosis is associated with severe COVID-19 disease, can be considered as a new parameter in the risk analysis of infected patients.

Comments 1:

Among 1216 patients, only 463 were included. Readers will be appreciated to understand the reasons of exclusion in a list.

Response 1:

We have specified the inclusion and exclusion criteria using the flow chart (Figure 1).

Comment 2.

Do not understand why severe cases were excluded. These cases should be included and be examined as a confounding factor in multivariate analysis. In addition, those CoVID-19 RT-PCR positive patients without pneumonia should be included as a mild case group. How many CT or chest X ray were done in COVID-19 RT PCR negative subjects? Pneumonia may

occur in the course of a disease. How the COVID-19 RT-PCR were done was not well described. How many RT-PCR for each case were done in both groups?

Response 2

As recommended, we scanned the CT scans of severe COVID-19 patients and those with positive RT-PCR tests without pneumonia. We have included those who had CTs underwent with the appropriate protocol. The CTs of negative subjects during the disease process was evaluated and we have added this situation to the method section. We have defined both groups more clearly in the method section. We have shown the groups using the flow chart.

Comment 3. No information on alcohol beverage, body weight, body height, diabetes and hypertension. These are important messages for a hepatic steatosis study.

Response 3

We have included comorbidities (hypertension, obesity, diabetes, smoking, alcohol beverage and BMI) in the study. We have shown the comorbidities in Tables

Comment 5. The study design compared COVID-19 positive and negative group. No comparison was made between COVID-19 positive cases with or without pneumonia. Therefore, the conclusion hepatic steatosis occurred in severe COVID-19 group may be not appropriated.

Response 5

We have revised the conclusion.

Comment 6. In general, older patients may associated with higher prevalence of liver steatosis. The COV-19 positive cases were 9 years older than COVID-19 negative cases. We will need a multivariate or age adjusted analysis.

Response 6

We have done a multivariate analysis for age. We have adjusted for age and comorbidities.

We have given an odds ratio value.