Dear Dr. Dou,

No.: 47004 in World Journal of Clinical Cases

Title: Performance of Common Imaging Techniques vs. Serum Biomarkers to Assess Fibrosis in Patients with Chronic Hepatitis B: A Systematic Review and Meta-analysis

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Response to Editor

Dear Dr. Dou,

Firstly, thank you for your kindest comments on our manuscript. The following are our responses to your comments accordingly:

1. Please provide language certificate letter by professional English language editing companies.

We have resubmitted the "Non-Native Speakers of English Editing Certificate" *via* the F6Publishing system.

2. Please provide the decomposable figure of Figures, whose parts are movable and editable. So you can put the original pictures in PPT and submit it in the system.

We have uploaded the PPT with decomposable figure of Figure 2 and Figure 3. Figure 1 is a flow chart. If you still asked to separate it, we will revise the Figure 1 again, thank you.

3. Your manuscript should be prepared with word-processing software, using 12 pt Book Antiqua font and 1.5 line spacing with ample margins.

We have 1.5 spaced the text throughout the revised manuscript and changed the font to Book Antiqua 12 pt.

Response to reviewer #1 (Reviewer's code: 00070577)

Dear reviewer，

Thank you for your kindest comments on our manuscript. Thank you for choosing "accept" for our article. We also carefully polish language with the help of native speakers. Thank you.

Response to reviewer #2 (Dr. Tai)

Dear Dr. Tai，

Thank you for your kindest comments on our manuscript. We really appreciate your patient help with not only scientific critiques but also our some corrections. We carefully studied your comments word by word as soon as getting your comments back, and made revisions on the previous manuscript accordingly.

1. The reason for select HBV series in this study is unclear in the introduction. Please make a brief description on inflammation and fibrosis mechanisms of HBV, as compare with other etiologies.

Thank you very much for your comments. Primarily, chronic hepatitis B virus causes a global health problem. Approximately 2 billion people worldwide have been infected with HBV, and most of patients are just infected by single HBV, especially in Asia Pacific and sub-Saharan region resulting in 600,000 to one million deaths annually. Therefore, we select single HBV series in this study. We have made a brief description in the beginning of introduction section due to the article space limitation.

2. The investigators made an extensive literature search but deceived to report

significant fibrosis only. Why severe fibrosis and cirrhosis were not reported should be discussed.

Thank you for your comments. Severe fibrosis and cirrhosis should be reported and discussed because of their clinic significances. However, according to chinese clinical practice guidelines, the stage of significant fibrosis (F ≥ 2) is one of the criteria for starting antiviral treatment. If liver fibrosis was assessed accurately at the early period of disease, it would take significant clinical effect. It could be of great help for a doctor to determine patients' suitability and the optimal time for antiviral therapy to achieve the best curative effects as well as to prevent excessive medication. From the perspective of preventive medicine, we may be more concerned about significant fibrosis. In addition, significant fibrosis is more often discussed in original literatures. Of course, considering your advices we will also study severe fibrosis and cirrhosis in future research.

3. Inflammation is the most important factor for the poor performance of non-invasive diagnosis of liver fibrosis in chronic HBV infection. The authors neither mention ALT level during the studies selection process in the methodology section, nor consideration ALT level in the result section.

Thank you very much for your suggestion. It is important for inflammation and ALT level to assess the performance of non-invasive diagnosis of liver fibrosis. But In the serum biomarkers (APRI, FIB-4, etc.), ALT is a part of noninvasive markers considering the possible impact of ALT on inflammation and significant fibrosis. So in some researches, ALT levels were mentioned only in the basic description of the result section, not analyzed in subgroup, especially assessing fibrosis by serum biomarkers. These also limited our study. We have rewritten the limitation of discussion for more rigorous (in line 81-82 of discussion section). The change made is marked in highlight in the revised manuscript. Thank you again for your comment.

4. According to the results, ARFI seems to be the 2nd best modality for predicting mod. Fibrosis. However, in the conclusion only LSM was recommended. This need to be clarified.

Thank you very much for your comments. We have revised in conclusion (in line 5-7 of conclusion section "ARFI could be a better choice, than FibroScan, for assessment of liver

fibrosis in HBV-mono infected patients with obesity or ascites.”). The change made is marked in highlight in the revised manuscript. I hope we can learn more knowledge from you. Thank you again for your advices.

Response to reviewer #3 (Reviewer’s code: 02527808)

Dear reviewer，

Firstly, thank you for your kindest comments on our manuscript. We really appreciate your patient help with not only scientific critiques but also our some minor corrections including study selection. We carefully studied your comments word by word as soon as getting your comments back, and made major revisions on the previous manuscript accordingly.

The following are our responses to your comments accordingly:

1. The article is interesting and important in the field of noninvasive diagnosis of liver fibrosis but some items were missed for example the role of diffusion MRI imaging in the diagnosis of liver fibrosis as many articles discuss this role in children and adults.

Thank you for your comments. Diffusion MRI imaging (DWI) also is another sensitive MRI technique. Many studies have reported that DWI can be used for assessing the presence of moderate and advanced liver fibrosis.

However, most researchers focused on fibrosis in all chronic liver diseases/HCV or compared the diagnostic effects of other diseases, such as esophageal varices, within the domain of imaging techniques. According to our selection criteria, the number of articles about diffusion MRI imaging is inadequate. Therefore, we regretfully give up this indicator. Reasons for exclusion of example studies are listed in the following table.

Study	Excluded reason
Razek AA 2011	data for HBV-infected patients couldn't be independently extracted
Kanematsu M 2012	it is review without original data
Razek AA 2015	predicted esophageal varices in cirrhotic patients and only five HBV patients
Huang C 2014	compared serum miR-29 to blood white blood cell and platelet counts
Tarek Besheer 2019	the objects were 208 patients with only CHC.
Sandrasegaran 2009	only 8 patients with HBV
Soylu 2010	data for HBV-infected patients couldn't be independently extracted

We believe that with the development of medicine, there will be more researches with HBV patients and our team will compare more methods to assess fibrosis. Thank you again for your comment.