

### Reviewer 1

The article is of scientific interest and aims to expand the understanding of the diagnosis of in autoimmune hepatitis-primary biliary cholangitis overlap syndrome. At the same time, a significant role in the article is assigned to risk factors for the course of the disease, both in the direction of improvement and aggravation of the patient's status. Referring to their previous works, the authors reinforce this position (at least three links to their articles and articles of co-authors are given). This manuscript is part of the work that was carried out earlier. Tables, graphs and figures are sufficient and informative. It is easy to understand the data reflected in the latter. Statistical methods and units of measurement are used correctly. In conclusion, it is desirable to add more data on two-dimensional shear-wave elastography in monitoring disease course, despite the fact that the authors pointed this out in the shortcomings of their work. **Many scales of assessment of morphological changes of the liver in the studied autoimmune conditions have also been used, which will create difficulties for a layman in this field when familiarizing himself with the work??** In general, after finalizing the comments, the manuscript can be considered for approval. And also the wish to the authors, to submit the accompanying documents in English, for the correct understanding of their content by the reviewers.

### Reviewer 2

- 1. Dear authors! I read with pleasure and interest your manuscript entitled "Usefulness of two-dimensional shear-wave elastography in monitoring disease course in autoimmune hepatitis-primary biliary cholangitis overlap syndrome". The manuscript is based on the results of a single-centre prospective study. It contains novelty and may be interesting for the readers. However, I have a few minor comments. please, consider revision of the manuscript title. "Usefulness" seems to be not fully appropriate (may be, "**clinical utility**"?), as it may depend on the demand and other factors.**

RE: Thanking the reviewer for this valuable suggestion, we revised the title to "Clinical utility of two-dimensional shear-wave elastography in monitoring disease course in autoimmune hepatitis-primary biliary cholangitis overlap syndrome"

- 2. Please, ensure study type (retrospective study) is correct (abstract, page 3, line 7). It is in conflict with the information on page 8, lines 2-3 (patients were ... consecutively collected).**

RE: Thanking the reviewer for pointing out this confusion. This is a retrospective study. Our hospital is the center of complex liver disease in the Southwest China. Autoimmune liver disease is a disease that we focus on. Patients with autoimmune liver disease could acquire more regularly follow-up than other etiologies. The data of AIH-PBC is collected prospectively and analyzed retrospectively. Therefore, this is a retrospective study. "Consecutively" maybe be not suitable, and we delete it in the revised manuscript.

- 3. Study population. Please, add the references for alcoholic hepatitis, NAFLD diagnostic criteria used for exclusion of these conditions.**

RE: We are grateful for this meaningful suggestion and add the reference of alcoholic hepatitis, NAFLD diagnostic criteria in the revised manuscript. (11 Standard Definitions and Common Data Elements for Clinical Trials in Patients With Alcoholic Hepatitis: Recommendation From the NIAAA Alcoholic Hepatitis Consortia. Gastroenterology 2016; 150(4): 785-790; 12 Characteristics and diagnosis of NAFLD/NASH. J Gastroenterol Hepatol 2013; 28 Suppl 4: 64-70)

- 4. Please, clarify, whether other toxic liver injuries (including potential DILI), beside alcohol, were excluded? If yes, add comments and references.**

RE: Thanking the reviewer for this meritorious suggestion. Drug-induced liver injury (DILI) is one of the most potential differential diagnosis for AIH-PBC. Therefore, we added DILI to the exclusion criteria and the reference for DILI diagnosis were added. (Drug-induced Liver Injury Study G, Chinese Society of H, Chinese Medical A. CSH guidelines for the diagnosis and treatment of drug-induced liver injury. Hepatol Int 2017; 11(3): 221-241)

**5. Please, check, whether treatment provided for the condition of interest before the enrolment is mentioned in the inclusion/exclusion criteria?**

RE: Some patients maybe acquire non-standard treatment before the liver biopsy.

**6. Diagnostic standards for AIH seem incomplete, please, explain.**

RE: Diagnosis criteria of PBC-AIH were checked carefully and were complete. The diagnosis of AIH-PBC was revised as follows: AIH-PBC overlap syndrome was strictly diagnosed according to the Paris criteria. The presence of at least two of the three accepted criteria was required for the diagnosis of AIH and PBC. The AIH criteria were as follows: (1) alanine aminotransferase (ALT) levels at least five times higher than the upper limit of normal (ULN); (2) serum immunoglobulin G (IgG) levels at least two times higher than the ULN or a positive test for anti-smooth muscle antibodies; and (3) a liver biopsy showing moderate or severe periportal or periseptal piecemeal lymphocytic necrosis. PBC criteria were as follows: (1) alkaline phosphatase (ALP) levels at least two times higher than the ULN or  $\gamma$ -glutamyltranspeptidase (GGT) levels at least five times higher than the ULN; (2) a positive test for anti-mitochondrial antibodies; and (3) a liver biopsy specimen showing florid bile duct lesions. Among them, moderate interfacial inflammation of the liver was necessary for AIH-PBC overlap syndrome diagnosis.

**7. Did you have patients with positive ANA and/or anti-LKM (or other antibodies) but negative ASMA? In case laboratory examination was performed, please, add the description of the equipment used, and reagents manufacturers. For laboratory parameters, that depend on the manufacturer, age and sex of the patient (like ALP, GGT, ALT, AST, etc), the use of relative values is more appropriate (times of ULN), please, consider revision of the information in the tables 1 and 4 (at least) and check for correctness of the use of statistics throughout the work.**

RE: We added the numbers of patients with positive ANA, anti-LKM (or other antibodies) or ASMA in Table 1. In addition, we added the reference value of laboratory parameters in Table 1 and Table 4

**8. It seems incorrect to compare patients with biochemical response and without it by serum bilirubin, ALP and GGT, as this was a criterion for selection.**

RE: We thanks the reviewer for pointing out this confusion, the describe of AIH-PBC overlapping response should include the response of AIH features and PBC features. The complete biochemical remission of AIH was defined with normal serum aminotransferases and IgG levels. The biochemical response of PBC was defined with decrease 40% or normally ALP in the first year (1 Corpechot C, Chazouilleres O, Poupon R. Early primary biliary cirrhosis: biochemical response to treatment and prediction of long-term outcome. J Hepatol 2011; 55(6): 1361-1367). In this study, the complete biochemical remission of AIH-PBC was defined with normal serum aminotransferases, ALP and IgG.

**9. To ensure, that change between baseline characteristics and at the control point is really significant, it seems reasonable to use Wilcoxon matched pairs test within each group.**

RE: We used Wilcoxon matched pairs test to compare the LS in baseline and each follow-up time within each group. In complete biochemical remission subgroup, LS values in every follow-up time were lower than the baseline point (all P values <0.01), In no biochemical remission, LS values in

follow-up times was not significantly lower than the baseline point. We added the Wilcoxon matched pairs test in statistics section and the results were added to results section in the revised manuscript.

- 10. Please, note, that the fibrosis stage is normally marked with F (F0-F4), followed by the name of the grading system (for example, METAVIR). The use of "S" is normally associated with the stage of steatosis. The same, but less widespread is for the necroinflammatory activity, which is normally marked with "A". To avoid confusion among the readers, please, consider revision throughout the text.**

RE: There are several score systems for staging liver fibrosis and necroinflammatory activity, such as Scheuer, METAVIR, Ishak, and Knodell score system. Each score system has its own advantage and disadvantage. The Scheuer score system is good at recognizing interface hepatitis. Therefore, Scheuer score system is appropriate for autoimmune liver disease. In order to avoid misunderstanding about "S". We used fibrosis stage 0 (S0), fibrosis stage 1 (S1), fibrosis stage 2 (S2), fibrosis stage 3 (S3) and fibrosis stage 4 (S4) to replace S0, S1, S2, S3 and S4 in the tables and results. Moreover, we used significant fibrosis ( $\geq$  S2), severe fibrosis ( $\geq$  S3) and cirrhosis (S4) to replace  $\geq$  S2,  $\geq$  S3 and S4 in the tables and results.

- 11. Please, explain the need for FIB-4 and APRI indexes for the fibrosis assessment in your study. These markers are useful, but are derivatives by nature. In case of histology-proven liver fibrosis stage available, the use of these instruments may be excessive.**

RE: we deleted FIB-4 and APRI indexes in the revised manuscript

- 12. Please, consider revision of the references' format according to the Journal requirements.**

RE: We revised the references' format according to the Journal requirements ("Vancouver" style.).

- 13. Figure 1 - there are two S3 groups - please, revise.**

RE: Thanking the reviewer for pointing out this mistake, and we revised Figure 1 in the revised manuscript.

- 14. Minor language polishing is required.**

RE: We revised the manuscript language by AJE service.

Reviewer 3

- 1. Background should be added in abstract.**

RE: We added background in abstract section. Background: Autoimmune hepatitis - primary biliary cholangitis (AIH-PBC) overlap syndrome has a worse prognosis than AIH or PBC alone. Therefore, accurately diagnosing liver fibrosis and dynamically monitoring disease progression are essential for it.

- 2. Mention the full word before abbreviations for the first time.**

RE: We carefully checked the full manuscript and mentioned the full word before abbreviations for the first time.

- 3. Major language revision is needed.**

RE: We revised the manuscript language by AJE service.

- 4. Place settings for this study are missing.**

RE: We added the place setting in methods section.

- 5. Time of study should be mentioned in the beginning of the methods paragraph.**

RE: The patients between September, 2016 and April 2021 were consecutively enrolled.

- 6. Discussion section needs more organization.**

RE: We carefully revised the discussion section.

(1) Science editor:

**I would like to commend the authors for the well designed study. please adress the points emphasized by the reviewers**

**Language Quality: Grade B (Minor language polishing)**

**Scientific Quality: Grade A (Excellent)**

RE: We revised the manuscript language by AJE service.

**I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.**

RE: Figures (in which all components are movable and editable) were putted into a single PowerPoint file. Tables were revised by the requirement of journal.