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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 86696

Title: Diagnostic role of transient elastography in patients with autoimmune liver diseases: A systematic review and meta-analysis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00503448
Position: Peer Reviewer
Academic degree: MD

Professional title: Associate Professor, Research Assistant Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2023-07-02

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-08-08 06:14

Reviewer performed review: 2023-08-18 14:12

Review time: 10 Days and 7 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this systematic review and meta-analysis, the Authors aimed to compare the diagnostic accuracy of imaging techniques with serum biomarkers of fibrosis in autoimmune liver disease (AILD). Overall, 60 articles were selected according to inclusion/exclusion criteria, and the numbers of AIH, PBC and PSC patients were 1594, 3126 and 501, respectively. They found that liver stiffness by transient elastography exerted better diagnostic accuracy for staging liver fibrosis in AILD patients compared to other serum biomarkers, particularly in PBC patients. The appropriate cutoff values for staging in advanced fibrosis and cirrhosis ranged from 9.6 to 10.7 kPa and 14.4 to 16.9 kPa, respectively, for patients with PBC. The study is of interest with potential clinical impact, however several points deserve further detail and should be addressed. -a very important pint in the inclusion criteria is the characteristics of enrolled patients. Were they studied at diagnosis or after starting treatment? This is a very important issue because the LS value might be affected by inflammatory infiltrate that when is significant in liver parenchima may produce higher stiffness values. -liver fibrosis assessment: this point also deserve a comment and should be discussed since METAVIR

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is originally developed for chronic viral diseases and not for autoimmune liver diseases. The authors should discuss whether in your opinion the METAVIR criteria could be considered as reliable histological assessment for AILD. -AIH selected studies: among the 22 selected AIH studies, there are differences in AIH diagnostic criteria that were used since the diagnostic scoring systems (1999 original revised AIH score vs 2008 Simplified score) and this could be introduce unintentional bias in enrolled population. Therefore, in my opinion, the authors should recall the two different diagnostic scoring systems and their differences as well described in a comprehensive review (Diagnosis and therapy of autoimmune hepatitis. Mini Rev Med Chem. 2009 Jun;9(7):847-60. doi: 10.2174/138955709788452676.) that highlighted that the two scoring systems are not interchangeable, and each may be useful in certain clinical situations. In particular, the original scoring system has greater value in diagnosing patients with few or atypical features of AIH, especially in patients with cryptogenic or autoantibody-negative chronic hepatitis, while the simplified scoring system is more useful to exclude the diagnosis in patients with etiologically distinctive disease who have concurrent immune manifestations. Importantly, for the diagnostic purpose, the diagnostic accuracy of the simplified AIH score has been validated in real-life, clinical practice, as previously reported (Validation of simplified diagnostic criteria for autoimmune hepatitis in Italian patients. Hepatology. 2009 May;49(5):1782-3;).

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Manuscript NO: 86696

Title: Diagnostic role of transient elastography in patients with autoimmune liver diseases: A systematic review and meta-analysis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00032933
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Attending Doctor, Chief Doctor, Professor
Reviewer's Country/Territory: Taiwan
Author's Country/Territory: China

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Summary A total of 1594 AIH, 3126 PBC and 501 PSC patients in 60 articles were reviewed in this study. The AUROCs of transient elastography (TE) in the diagnosis of significant fibrosis, advanced fibrosis and cirrhosis were 0.84, 0.88 and 0.90, respectively in AIH patients, while 0.93, 0.93 and 0.91, respectively in PBC patients. The AUROC of cirrhosis for PSC patients was 0.95. Other noninvasive indices had AUROCs less than 0.80. They concluded that liver stiffness by TE exerted good diagnostic accuracy for staging liver fibrosis in AILD patients. Comments 1. In the supplementary Table 2, please arrange these references according to the reference No in Table 1. 2. In 3.1 Characteristics of the included studies and patients, please give the references for those reports included AIH and PBC, or PSC and PBC. 3. In Table 2, the modalities and cut-off values are confusing in related to SF, AF and cirrhosis. 4. In Figures, the markers, authors, titles, and CI are too small to be seen. 5. In supplementary Table 4, the first 3 lines were not data of ARFI. 6. In the discussion section, the first paragraph is unnecessary. Please start with “TE had excellent accuracy,”. 7. Both fibrosis and inflammation may have significant impact on liver stiffness.

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Autoimmune liver disease is characterized by persistent liver inflammation. This report suggests that the AUROC of TE in AILD is as good as those in hepatitis C, and better than hepatitis B. Was there any published data that may support this point? 8. Are there any differences in the cut-off values between AIH and PBC? In addition, how about the differences in cut-off values between AILD and other diseases?

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Manuscript NO: 86696

Title: Diagnostic role of transient elastography in patients with autoimmune liver diseases: A systematic review and meta-analysis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00030389
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Director
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors compared the diagnostic accuracy of imaging techniques with serum biomarkers of fibrosis in autoimmune liver disease by meta-analysis. The results are interesting, and I have a few comments. Major comments #1. P16, lines 14-17. "TE had excellent accuracy, with summary AUROC values of 0.84, 0.88 and 0.90 for SF, AF and cirrhosis, respectively, in AIH patients and 0.93, 0.93 and 0.91, respectively, in PBC patients." This description is inconsistent with the description from P7, line 22 to P8, line 2, "If the summary AUROC value was above 0.90, the method was considered to have excellent accuracy, while less than 0.80 was considered to have poor accuracy [18]." #2. P16, line 22 to P17, line 3. "Moreover, our results showed that TE had a higher specificity and relatively low sensitivity in the diagnosis of AILDs, implying that TE was a better noninvasive method for ruling in than for ruling out." This description is not correct. In AF of PBC, the sensitivity (0.91) is higher than the specificity (0.82) when the cutoff values are 9.6-10.7. Minor comments #1. Table 1. The number of study had better correspond to the reference number of study in supplementary table 2. #2. Table 3, 4 and 5. There should be lines between AIH, PBC and PSC as in Table 2.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 86696

Title: Diagnostic role of transient elastography in patients with autoimmune liver diseases: A systematic review and meta-analysis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00032933
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Attending Doctor, Chief Doctor, Professor
Reviewer's Country/Territory: Taiwan
Author's Country/Territory: China

Manuscript submission date: 2023-07-02

Reviewer chosen by: Cong Lin

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Reviewer performed review: 2023-09-11 16:14

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [ ] Anonymous [Y] Onymous

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

SPECIFIC COMMENTS TO AUTHORS

The PI addressed most of the questions. In question 7 of 2nd reviewer, I agree that most of the reports suggest that elastography showed similar accuracy between hepatitis B and C. However, many of them included a small number of patients with chronic hepatitis B. In a meta analysis from Friedrich-Rust M et al. JVH 2012, the AUROC of HBV was lower in HBV than other etiologies. Similar findings can be seen from Hsu TH et al. JMU2019 which also included AIH. The reason for poor performance could be due to unstable inflammation of HBV. 1. Friedrich-Rust M, Nierhoff J, Lupsor M, Sporea I, Fierbinteanu-Braticevici C, Strobel D, Takahashi H, Yoneda M, Suda T, Zeuzem S, Herrmann E. Performance of Acoustic Radiation Force Impulse imaging for the staging of liver fibrosis: a pooled meta-analysis. J Viral Hepat. 2012 Feb;19(2):e212-9. doi: 10.1111/j.1365-2893.2011.01537.x. Epub 2011 Oct 30. PMID: 22239521. 2. Hsu TH, Tsui PH, Yu WT, Huang SF, Tai J, Wan YL, Tai DI. Cutoff Values of Acoustic Radiation Force Impulse Two-Location Measurements in Different Etiologies of Liver Fibrosis. J Med Ultrasound. 2019 May 17;27(3):130-134. doi: 10.4103/JMU.JMU_7_19. PMID: 31867175; PMCID: PMC6905267.