

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 72131

Title: Comments on validation of conventional non-invasive fibrosis scoring systems in patients with metabolic associated fatty liver disease

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02939909

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Hungary

Author's Country/Territory: China

Manuscript submission date: 2021-10-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-07 18:58

Reviewer performed review: 2021-10-17 11:44

Review time: 9 Days and 16 Hours

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 Grade E: Do not publish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



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Peer-reviewer statements	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

I agree with the comments of Xian Li 1. Multivariate analysis should be preformed to recognize the independent variables in the prediction of advanced fibrosis. 2. Authors should state if the contionuous variables fit normal distriburtion and if normal distribution tests have been preformed 3. Thresholds sould be further evaluated in external validation cohort and in prospective cohort.

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Manuscript NO: 72131

Title: Comments on validation of conventional non-invasive fibrosis scoring systems in patients with metabolic associated fatty liver disease

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03834342

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: France

Author's Country/Territory: China

Manuscript submission date: 2021-10-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-25 09:34

Reviewer performed review: 2021-11-02 08:27

Review time: 7 Days and 22 Hours

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

Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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SPECIFIC COMMENTS TO AUTHORS

Comments and suggestions for Authors In the present letter to the Editor, Li et al., raised important questions regarding the paper published by Wu et al., entitled “Validation of conventional non-invasive fibrosis scoring systems in patients with metabolic associated fatty liver disease (Wu et al., World J Gastroenterol. 2021;27(34):5753-5763. doi:10.3748/wjg.v27.i34.5753). The study by Wu et al., as well as the letter by Li et al., have clinical relevance as both deal with development of scoring systems for the prediction of advanced fibrosis in patients with metabolic associated fatty liver disease (MAFLD). - In their first comment, Li et al. suggest that Wu et al. should have used the multivariate analyses instead of the univariate analysis to assess the diagnostic the performance of: aspartate aminotransferase to platelet ratio index (APRI), fibrosis-4 index (FIB-4), body mass index, aspartate aminotransferase/alanine aminotransferase ratio diabetes score (BARD) and nonalcoholic fatty liver disease fibrosis score (NFS), in the prediction of advanced fibrosis in patients with MAFLD. I agree with the authors since applying the standard approach of the univariate tests on individual response variables may fail to account for the covariance/correlation in the data. By contrast, the multivariate statistical techniques have advantages such as allowing confounding factors to be considered, by adjusting for these factors, which might more adequately capture the multi-dimensional pathophysiological pattern of advanced fibrosis and therefore provide increased sensitivity to the scoring systems in patients. - The authors raised another interesting suggestion regarding the calibration of the prediction scores, which is another key aspect of performance that is often overlooked. Indeed, the calibration is the accuracy of risk estimates, relating to the

agreement between the estimated and the distribution of realized outcomes (Van Calster B et al. J Clin Epidemiol. 2016;74:167–176; doi:10.1016/j.jclinepi.2015.12.005). In addition, discrimination and calibration are especially important when the aim is to support decision-making. Thus, I agree with Li et al. about the advice they gave to the authors (Wu et al.) of the initial study. - The third comment is with regard to PPV and NPV which describe the performance of a prediction models and are crucial to evaluating the practical utility of a testing procedure. As mentioned by the authors, PPV and NPV cannot be compared directly among different samples except when subjects are selected from a population with known prevalence of the disease. Finally, I really found these comments, opinions and advices very interesting especially for coming studies in the area. However, there are few things that should be addressed by the authors before proceeding further. Minor comments 1) There is now evidence from a prospective cohort that common genetic variants can capture additional prognostic insights not conveyed by validated clinical/biochemical parameters. Thus, in their comments, Li et al. should encourage the integration of genetics (perhaps epigenetics also) with clinical fibrosis scores as it may refine individual risk and improve risk stratification and prediction of severe liver disease (De Vincentis et al. Clinical Gastroenterology and Hepatology 2021; DOI:<https://doi.org/10.1016/j.cgh.2021.05.056>). 2) I am surprised that the authors did not reference the paper they are supposed to comment: (Wu et al., World J Gastroenterol. 2021;27(34):5753-5763. doi:10.3748/wjg.v27.i34.5753). 3) The English language: There are many punctuation errors, grammar mistakes, and unclear sentences that make the paper hard to understand sometimes.