



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 83741

**Title:** Novel multi-parametric diagnosis of non-alcoholic fatty liver disease using ultrasonography, body mass index, and Fib-4 index

**Provenance and peer review:** Unsolicited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05038583

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2023-02-08

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-02-26 14:17

**Reviewer performed review:** 2023-02-26 15:25

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

General comments The authors described a novel NASH pentagon for discrimination between NASH and NAFLD. This study is clinically relevant, given the increasing global burden of NASH and NAFLD. This study is well conducted and written; however, generalizability and clinical utility may be limited. Strength This study is well written and designed methodology. This study showed a very high AUROC for the NASH pentagon. Weakness Single center study in a Japanese population, so generalizability is limited. A small number of patients Many North American Centers use Fibroscan, so interpreting the result may be difficult. The area of the NASH pentagon was calculated with Aplio i800, which is unavailable for many centers. Specific comments In the abstract, please rewrite the background, as this sounded more like methodology. Please combine these sentences into one sentence: Patients with a history of alcohol intake of ethanol  $\geq 20$  g/day were excluded. Patients who had hepatitis B, hepatitis C, or autoimmune liver disease were also excluded. In addition, patients with concurrent drug-induced liver injury or cholangitis were excluded. ATI value, BMI, and Fib-4 index had a lower AUROC. I wonder if removing these parameters can increase the accuracy



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of prediction. In other words, is it worth adding these parameters to make the model more complicated? The FIB-4 index has lower accuracy in patients with an age>65. The average age of the large pentagon group was 60.8 yo. Is there any possibility that this explains the low AUROS for the FIB-4 index compared to the previously published value? Previous studies based on fibroscan suggested the utility of the FAST score and AGILE 3+ score, which is easy to use in clinical settings. FAST score ([https://www.thelancet.com/journals/langas/article/PIIS2468-1253\(19\)30383-8/fulltext](https://www.thelancet.com/journals/langas/article/PIIS2468-1253(19)30383-8/fulltext)) AGILE 3+ Score ([https://www.cghjournal.org/article/S1542-3565\(22\)00646-2/fulltext](https://www.cghjournal.org/article/S1542-3565(22)00646-2/fulltext))



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**Reviewer's code:** 04623150

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Doctor, Research Fellow

**Reviewer's Country/Territory:** Hungary

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2023-02-08

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-02-24 10:32

**Reviewer performed review:** 2023-03-05 10:05

**Review time:** 8 Days and 23 Hours

<b>Scientific quality</b>	<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
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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 reviewed the manuscript titled "Novel multi-parametric diagnosis of non-alcoholic fatty liver disease using ultrasonography". In this study, the authors propose a non-invasive method to diagnose NASH, this method contains specialized US measurements (SWS, DS, ATI value) and also blood parameters (Fib-4) and BMI. This NASH pentagon has a high diagnostic accuracy, however only a small sample size with limited number of patients with liver biopsies were available and more studies are needed. The use of the CONSORT statement however is not appropriate in the study, I suggest using the STARD statement (<https://www.equator-network.org/reporting-guidelines/stard/>). Based on these points a revision is needed in my opinion.

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Since not only US methods were included in the new diagnostic method, it should be mentioned for more clarity.

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Was this a true, non-invasive study? Some patients needed liver biopsies, which is the gold standard and needed for the diagnosis of NASH. I would leave that out.

3 Key Words.



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Do the key words reflect the focus of the manuscript? Seems appropriate. I would include diagnosis. 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? There is enough background in the Introduction. I suggest providing reference for the paragraph about Fib-4. 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? This part should be structured by the STARD statement. In the diagnosis of NASH section, I wonder why only this low number of patients received a liver biopsy, even if NASH was suspected in them? 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? The results should be reported as in the guidelines. 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? I found this section to be a little repetitive, some things were already mentioned in the methods section. The authors should discuss their results in contrast to the existing literature and not mentioning the methods again and make this section unnecessary long. Could other parameters not be included in this study? E.g. co-morbidities as diabetes mellitus, dyslipidaemia could be included in the model for more precision. 8 Illustrations and tables. Are the figures, diagrams, and tables sufficient, good quality and appropriately illustrative, with labeling of figures using arrows, asterisks, etc, and are the legends adequate and accurately reflective of the images/illustrations shown? In Fig 2, the top number (n=107) should be 126 as in the legends. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Seems to be appropriate. The method about generating the pentagons could be more



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detailed. 10 Units. Does the manuscript meet the requirements of use of SI units? Yes.  
11 References. Does the manuscript appropriately cite 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? In the Introduction, should include a reference about Fib-4. 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? The style and grammar is generally acceptable. 13 Research methods and reporting. STARD guidelines should be used (CONSORT is for RCTs). 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.