Reviewer #1

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.

Response

We thank the reviewer for the insightful comments here and below. As suggested by the reviewer, we have changed the title.

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.

Response

We thank the reviewer for the kind comment. We think this study is non-invasive study.Because the liver biopsy was done for the diagnosis of NASH, and was not for this study.

3 Key Words.

Do the key words reflect the focus of the manuscript?

Seems appropriate. I would include diagnosis.

Response

As suggested by the reviewer, we have added one key word: “Diagnosis”.

4 Background.

Does the manuscript adequately describe the background, present status and significance of the study?

There is enough background in the Introducation. I suggest providing refrence for the paragraph about Fib-4.

Response

As suggested by the reviewer, we have added one reference to the Introduction (page 5, line 29).

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.
Response

We thank the reviewer for the comment.

We reviewed the Methods section according to STARD 2015 (STARD No. 5-18).

No. 5-9: These points were described in the METHODS (Patients).

No. 10a, 10b: Yes.

No. 11: This point was described in the Methods (Patients).

No. 12a, 12b: We are very sorry, but these points were not thoroughly examined in the present study.

No. 13a, 13b: Yes.

No. 14: These points were described in the Methods (Statistical analysis).

No. 16, 17: We are very sorry, but these points were not thoroughly examined in the present study.

No. 18: We collected every possible patient for an observation period (between September 2021 and August 2022).

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?
Response

We explained the need for liver biopsy to all patients who were suspected of having NASH. However, only a small proportion of these patients agreed to liver biopsy. We have reflected on this point and wish to address it in future studies.

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.
Response

We described the results of this study exactly. But we cannot understand whether it is 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 authros should discuss their results in contrast to the existing literature and not mentioning the methods again and make this section unneccessary long.
Response

We made an effort to make the contents of the Discussion section easy to understand.

As you indicate, some points in the Discussion section were already mentioned in the "METHODS" section. However, we judged that reiterating those points were necessary for clarity.

Could other parameters not be included in this study?
E.g. co-moribidities as diabetes mellitus, dyslipidaemia could be included in the model for more precision.
Response

Unfortunately, in this study, metabolic disorders were not examined.

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.
Response

As suggested by the reviewer, we have corrected the number at the top of Figure 2 to “(n=126)”.

9 Biostatistics.
Does the manuscript meet the requirements of biostatistics?
Seems to be appropriate.
The method about generating the pentagons could be more detailed.
Response

We thank the reviewer for the kind comment.

10 Units.

Does the manuscript meet the requirements of use of SI units?

Yes.

Response

We thank the reviewer for the kind comment.

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.

Response

As suggested by the reviewer, we have added one reference to the Introduction (page 5, line 29).

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.

Response

We thank the reviewer for the kind comment.

13 Research methods and reporting.

STARD guidelines should be used (CONSORT is for RCTs).

Response

We thank the reviewer for the comment.

We have addressed this problem in our earlier response to your fifth comment of ("5 Methods").

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.

Response

We thank the reviewer for the kind comment.

Reviewer #2

1. In the abstract, please rewrite the background, as this sounded more like methodology.

Response

Thank you for your insightful comments here and below. We have changed the background in the abstract according to your instruction (page 3, line 3-6).

2. Please combine these sentences into one sentence: Patients with a history of alcohol intake of ethanol ≥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.

Response

As suggested by the reviewer, we have combined those three sentences into one sentence (page 6, line 8-10)

3. ATI value, BMI, and Fib-4 index had a lower AUROC. I wonder if removing these parameters can increase the accuracy of prediction. In other words, is it worth adding these parameters to make the model more complicated?

Response

ATI is a method for assessment of hepatic steatosis and is important in a diagnosis of NASH. However, ATI is a very new technique, and there are few reports comparing it with other parameters. We understand that additional data regarding ATI are needed and an appropriate cutoff value must be established. It is for these reasons that we chose ATI level as one of the pentagon items.

The BMI seems to be an item for which there is a difference in implication between Western populations and Asians. In addition, it is considered that weight tends to decrease when NASH progresses (we described this in the Discussion section of the present manuscript). The BMI seems to be an item for which there is a difference in implication between Western populations and Asians. In addition, it is considered that weight tends to decrease when NASH progresses (we described this in the Discussion section of the present manuscript). When these point is considered, we think that it has become difficult to diagnosis the area of pentagon according to suggestion of the reviewer. However, we adopted BMI as a component of the NASH pentagon because its calculation is extremely simple.

We adopted the Fib-4 index as a component of the NASH pentagon as a clinical

parameter since it does not require special equipment for measurement.

4. 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?

Response

As you suggest, there is indeed a possibility that age influenced the AUROC for the FIB-4 index. However, we were not able to analyze it according to age group because the present study had an insufficient number of patients to do so.

5. Previous studies based on fibroscan suggested the utility of the FAST score and AGILE 3+ score, which is easy to use in clinical settings.

Response

Unfortunately, we could not examine the FAST score and AGILE3+ score because our institution does not have fibroscan. We would like to address this in future studies.