

Reviewer 1

Comment; This manuscript has very original idea to diagnose the patients who are under risk of NASH. Many patients could refuse liver biopsy or sometimes it is not possible so we need noninvasive methods to confirm NASH as a first step before liver biopsy

Response; Thank you for your comments.

Reviewer 2

Comment 1; The authors investigated the diagnostic accuracy of the non-invasive prediction algorithm for predicting NASH in Japanese morbidly obese patients. They found that predictive accuracy, the positive predictive value, negative predictive value, sensitivity and specificity were 88.9%, 35.7%, 86.2%, and 41.7%, respectively. They stated that the new algorithm achieved prediction accuracy of approximately 80%. They concluded that Japanese algorithm of Morbid Obesity for NASH Prediction may be useful for predicting NASH in Japanese in the clinical setting. This is a well written paper that presents interesting data.

Response; Thank you for your comments.

Comment 2; I have the following concerns. 1) Plasma CRP levels are not predictive of the diagnosis of NASH in obese patients (Am J Gastroenterol. 2006;101:1824). It would be helpful to give the mechanism to identify CRP as a predictive marker. The authors should discuss about this point in the Discussion section.

Response; Thank you for your comments. We cited this article as reference and discussed in discussion section. Anty et al. reported plasma CRP levels are not predictive of the diagnosis of NASH in obese patients. On the other hand, high sensitivity-CRP is reported as useful marker for prediction of NASH. The level of CRP were affected by many factors. The cohort used in this study was relatively homogenous. All patients were candidate for bariatric surgery and blood sample were collected by relatively same condition before surgery. As the result, our cohort may be protected by miscellaneous factors that influence to CRP level. We described this in discussion section and mentioned that further confirmation will be needed.

2) The authors should show significance levels (p values) for each comparison between NASH and non-NASH group in supplement Table2.

Response; We showed significance levels for each comparison to supplement Table 2.

3) It would be helpful if the authors showed the distribution of 102 patients in the derivation cohort.

Response; Thank you for comments. We added the distribution of the derivation cohort.

4) The authors use clinical samples in this study. It would be helpful if the Declaration of Helsinki was included in the manuscript.

Response; Thank you for comments. We added it.

Reviewer 3

Comment; Uehara D et al attempted to predict non-alcoholic steatohepatitis (NASH) in Japanese patients with morbid obesity by artificial intelligence using rule extraction technology in this manuscript and showed a considerable improvement in predictability (predictive accuracy rate) of NASH. English writing is fair (no grammatical error) and this work is worth enough for possible publication in WJG. Major comments. None. Minor comments. None.

Response; Thank you for your comments.

Reviewer 4

Comment; The authors, given the difficulty of defining the diagnosis of NASH with non-invasive tools, propose an algorithm with the help of artificial intelligence, they define it as Japanese algorithm of morbid obesity (JOMO).

Patients and methods 1) The authors must clearly define which histological criteria they use for the diagnosis of NASH, if in their criteria of diagnosis there is a score they should better define the classes of histological score (grading and staging).

Response; Thank you for comments. Precise methods for liver biopsies and sampling have been described in previous study [ref 7]. When we submitted this manuscript to another journal, we have described precisely. However, a reviewer of another journal pointed it as duplication. So, we simply cited our previous study in this manuscript. We added the description of liver histology following your suggestion. The staging and grading of NASH followed Brunt's classification and the NASH activity score was described in previous study. We cited it.

2) NAFLD scoring system consists of grading and staging. It is not clear from the study if the authors use the algorithm only for the evaluation of inflammation and necrosis or even of fibrosis. The presence of the two scores: HARI, grading index and the BARD index of fibrosis, would suggest that the authors would like to evaluate both, but this is not clear. It is necessary to better define the aim of the study and to do this a better definition of the diagnosis of NASH is necessary as it is written in point 1. If the authors evaluate only the diagnosis of NASH, without fibrosis, they should eliminate the BARD score

Response; Thank you for comments. The methods of histological diagnosis are added to

method section following your point 1. We also evaluated the fibrosis in the study.

3) The authors, if they can, should define whether there is a relationship between histological scores according to the NAS score or the SIF score and the classes : R2, R4, R5.

Response; Thank you for comments. We also think it is useful evaluation. Because of small number of each group, we did not evaluate it in this study. It is future project for us.

4) I suggest to calculate the AUROC and the difference between the curves, and if there are differences, which clarify the usefulness of the algorithm, insert them into the text

Response; Thank you for your suggestion. We calculated AUROC and added to the text. ROC curve was added as Figure 4.

5) Some results of the algorithm are clinically poorly understandable. R5 indicates the presence of NASH but one of its parameters CRP is not very specific, especially in obese patients who have many co morbidities. These aspects need to be discussed and must still indicate the limits of the results and how this is a preliminary study and that there is a need for further confirmation

Response; Thank you for your comments. We cited the article as reference and discussed in discussion section. Anty et al. reported plasma CRP levels are not predictive of the diagnosis of NASH in obese patients. On the other hand, high sensitivity-CRP is reported as useful marker for prediction of NASH. The level of CRP were affected by many factors. The cohort used in this study was relatively homogenous. All patients were candidate for bariatric surgery and blood sample were collected by relatively same condition before surgery. As the result, our cohort may be protected by miscellaneous factors that influence to CRP level. We described this in discussion section and mentioned that further confirmation will be needed.

6) Since, as is correctly reported by the authors, obesity is more frequent in Western countries, in the discussion the authors should make some reflections on the effects of a higher prevalence of the disease in the estimation of the reliability of the score, in other words the effects of a higher prevalence in Bayesian statistics

Response; Thank you for comments. We added the description concerning the high prevalence of NASH and its influence to this algorithm.

Minor revision

1) In the abstract the sentence in row 1 on the role of elastography should be better clarified

Response; We changed the abstract following the suggestion from editorial office.

2) the conclusions of the abstract do not make it clear if the algorithm is useful

Response; Thank you for your comments. We added it.

3) There are abbreviations (Fe) in the text and in the tables unexplained

Response; We explained it.

Reviewer 5

Comment; There is a very interesting and original manuscript about noninvasive methods in NAFLD morbidly obese patients. It is original and have implication in clinical practice. I suggest accept with major revision in English, improve the format of figures and explain more in the methods section Re-RX with J48graft. Best Regards.

Response; Thank you for your comments. The manuscript was re-checked by native English speaker. We added the explanation of the Re-RX with J48graft in methods.

Reviewer 6

Comment; This is an interesting study it can be accepted.

Response; Thank you for your comments.