



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 40433

**Title:** Non-invasive prediction of non-alcoholic steatohepatitis in Japanese patients with morbid obesity by artificial intelligence using rule extraction technology.

**Reviewer's code:** 00070280

**Reviewer's country:** Sri Lanka

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-02

**Date reviewed:** 2018-07-09

**Review time:** 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

This is an interesting study it can be accepted.

### INITIAL REVIEW OF THE MANUSCRIPT



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**Manuscript NO:** 40433

**Title:** Non-invasive prediction of non-alcoholic steatohepatitis in Japanese patients with morbid obesity by artificial intelligence using rule extraction technology.

**Reviewer’s code:** 00071662

**Reviewer’s country:** Turkey

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-23

**Date reviewed:** 2018-07-23

**Review time:** 4 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

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



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**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 40433

**Title:** Non-invasive prediction of non-alcoholic steatohepatitis in Japanese patients with morbid obesity by artificial intelligence using rule extraction technology.

**Reviewer’s code:** 02447091

**Reviewer’s country:** Japan

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-23

**Date reviewed:** 2018-07-26

**Review time:** 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input checked="" type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

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



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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.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 40433

**Title:** Non-invasive prediction of non-alcoholic steatohepatitis in Japanese patients with morbid obesity by artificial intelligence using rule extraction technology.

**Reviewer's code:** 02959015

**Reviewer's country:** Italy

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-23

**Date reviewed:** 2018-07-27

**Review time:** 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

To the authors 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). Major revision



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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). 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 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. 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 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 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

Minor revision 1) In the abstract the sentence in row 1 on the role of elastography should be better clarified 2) the conclusions of the abstract do not make it clear if the algorithm is useful 3) There are abbreviations (Fe) in the text and in the tables unexplained



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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 40433

**Title:** Non-invasive prediction of non-alcoholic steatohepatitis in Japanese patients with morbid obesity by artificial intelligence using rule extraction technology.

**Reviewer’s code:** 03646639

**Reviewer’s country:** Japan

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-23

**Date reviewed:** 2018-07-27

**Review time:** 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

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



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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. 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. 2) The authors should show significance levels (p values) for each comparison between NASH and non-NASH group in supplement Table2. 3) It would be helpful if the authors showed the distribution of 102 patients in 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. 1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes 3 Key words. Do the key words reflect the focus of the manuscript? appropriate 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Method is appropriate. The percutaneous liver biopsy is not safe to obtain liver tissue specimens in morbidity obese. The patients underwent liver biopsy during the bariatric surgery. 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 authors validated the non-invasive prediction algorithm for predicting NASH in Japanese morbidly obese. 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



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clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? above mentioned 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Tables and figure have good quality 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Yes 10 Units. Does the manuscript meet the requirements of use of SI units? 11 References. Does the manuscript cite appropriately 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? 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? 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? 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

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**Manuscript NO:** 40433

**Title:** Non-invasive prediction of non-alcoholic steatohepatitis in Japanese patients with morbid obesity by artificial intelligence using rule extraction technology.

**Reviewer’s code:** 01809054

**Reviewer’s country:** Brazil

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-23

**Date reviewed:** 2018-07-30

**Review time:** 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

There is a very interesting and original manuscript about non invasive methods in NAFLD morbily obese patients. It is original and have implication in clinical pratice. I suggest accept with major revision in english, improve the format of figures and explain



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more in the methods section Re-RX with J48graf. Best Regards

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