

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 69658

Title: Metabolic dysfunction is associated with steatosis but no other histologic features in nonalcoholic fatty liver disease

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02536349

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2021-07-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-27 15:07

Reviewer performed review: 2021-07-27 20:18

Review time: 5 Hours

Scientific quality	<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 Grade E: Do not publish
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 type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" 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

- Non-MAFLD group is also a heterogenous population. It includes simple steatosis, NASH, advanced fibrosis and cirrhosis. The nomenclature has not changed to MAFLD from NAFLD. There are recommendations but still has unmet needs. The issue is still under debate. This should be noted. The clinics • “Subjects with a BMI <23 kg/m² were defined as having lean NAFLD”. Could be: “Asian subjects with a BMI <23 kg/m² were defined as having lean NAFLD.” since BMI <25 is lean NAFLD for Western World. • “Analyze” can be preferred instead of “analyse” • How the sample size calculated? The sample size seems insufficient for reliable comparison according to “power analysis” as stated in limitations paragraph. Sample Size Calculator (clincalc.com)
- The graphs could be more expressive and less space occupying with segmented bars, all in one graph as coupled two bars for each criteria. The percentages may be more readable as a table. • Table 1: Please use widely accepted abbreviations in tables. Prefer “Neu” instead of “N” for Neutrophil. “N” is usually abbreviated for Nitrogen. ChE instead of CHE.. Typographic error: CLU should be GLU.... Hs-CRP as hs-CRP,... “ALP” instead of “AKP”, etc... “Glycemia” instead of “glycometabolism.” • Table 2: “Correlations between steatosis and other hepatic histologic features” can be “Correlations between degree of steatosis and severity of other hepatic histologic features” * The title focuses only on metabolic dysregulation lacks the diabete and obseity. MAFLD can be replaced.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04213276

Position: Peer Reviewer

Academic degree: MD, MSc

Professional title: Doctor

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2021-07-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-26 16:49

Reviewer performed review: 2021-07-30 20:00

Review time: 4 Days and 3 Hours

Scientific quality	<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
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [Y] Anonymous [] Onymous Conflicts-of-Interest: [] Yes [Y] No
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SPECIFIC COMMENTS TO AUTHORS

The manuscript addresses a hot topic of our time, the proposed change from NAFLD to MAFLD, and attempts to evaluate the differences that these two definitions have with regards to patients with liver steatosis. Although it is reasonable to research differences between NAFLD patients with and without MAFLD, the article does not have a sufficient sample to offer definitive conclusions, in a topic that is at the center of liver research, resulting in studies with bigger population samples.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05225141

Position: Peer Reviewer

Academic degree: DVM, PhD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2021-07-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-26 15:44

Reviewer performed review: 2021-08-01 14:14

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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 type="checkbox"/> Accept (General priority) <input checked="" 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

Nonalcoholic fatty liver disease (NAFLD) has been suggested to rename to metabolic-associated fatty liver disease. However, there are many concerns about the new nomenclature. In this study, the authors further investigate the significant associated histological features with MAFLD in patients diagnosed with NAFLD, when compared to non-MAFLD patients but with diagnosed NAFLD. Study results showed that MAFLD patients have more severe NAS and hepatic steatosis than that in non-MAFLD patients, but not other histological features and the presence of NASH, the advanced form of NAFLD. Overall, the study was well-designed and performed. The data were well analyzed, with a limitation of case numbers. However, there are some concerns about enhancing the quality of the paper. A major suggestion is that representative histological images should be added to give an overview of the pathological change, but not only with numbers in all the figures. All the words in the Figures are small, so the size should be increased. In addition, Figure 1H is suggested to be combined in one for all groups to have the same y-axis scale for easy comparison. Similar changes are suggested for Figure 2H, Figure 3H, and Figure 4H. For manuscript format, a Core Tip part is suggested except the abstract. In addition, some minor changes are needed. Minors: 1. On page 3, does NAFLD include cirrhosis and hepatocellular carcinoma (HCC)? Or NAFLD can lead to cirrhosis and HCC. 2. On page 4, 1.70 mmol/l should be 1.70 mmol/L. In addition, whether adding a space between >, <, or ≥ and number or not should be consistent across the manuscript. 3. On page 5, with an alanine aminotransferase (ALT) 'level was needed here' < 3-fold of the ULN. On page 9, a group of lean and metabolically healthy individuals are not included; 'are'



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changes to is. On page 10, that only fibrosis stage instead of other histologic features of NASH were related to; were > was.

PEER-REVIEW REPORT

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Title: Metabolic dysfunction is associated with steatosis but no other histologic features in nonalcoholic fatty liver disease

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05081737

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor, Postdoc, Postdoctoral Fellow, Research Fellow

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2021-07-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-26 15:38

Reviewer performed review: 2021-08-03 21:49

Review time: 8 Days and 6 Hours

Scientific quality	<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
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

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

Authors explored an intriguing aspect of a new topic in this field. The study is original and well designed. It adds to the current knowledge, although data derived from a small cohort of patients. My comments are listed below: - abstract: in the results section, percentage should be given. - introduction : Metabolic dysfunction should be defined accordingly to MAFLD criteria - discussion: both usefulness and effectiveness of MAFLD definition have been investigated in several recent studies. This should be added and discussed (e.g. PMIDs 33806784 and 32819754) -table 1: W/Hr (as adiposity measurement) should be given and compared between the groups. English language needs to be largely revised and polished throughout the paper.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD, MSc

Professional title: Doctor

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2021-07-26

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2021-09-06 05:07

Reviewer performed review: 2021-09-06 16:18

Review time: 11 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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

the authors have revised the paper according to the instructions of the reviewers and it was transferred to a more suitable journal in terms of academical prestige and impact.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Academic degree: MD, PhD

Professional title: Doctor, Postdoc, Postdoctoral Fellow, Research Fellow

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2021-07-26

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2021-09-06 06:26

Reviewer performed review: 2021-09-06 16:56

Review time: 10 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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Authors have well addressed my previous comments.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2021-07-26

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2021-09-06 03:38

Reviewer performed review: 2021-09-07 05:34

Review time: 1 Day and 1 Hour

Scientific quality	<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
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for revisions Still there are few grammar errors. e.g. Core Tip: Non-obese and metabolically healthy patients with fatty liver is excluded >> “are” Non-obese and metabolically healthy patients with nonalcoholic fatty liver disease (NAFLD) is excluded from the definition >> “are” the TERM "non-MAFLD" Lacks indicating the presence of fatty liver or not. The below link highlights the possible subgroups. non-MAFLD covers more clinical spectrum than authors' definition. <https://pubmed.ncbi.nlm.nih.gov/32930521/#&gid=article-figures&pid=figure-1-uid-0> The nomenclature change is still as a proposal. In manuscript it has been stated as NAFLD has totally removed to MAFLD and non-MAFLD.. So it is early to use -formerly for NAFLD Metabolic dysfunction is associated with steatosis but no other histologic features in the formerly named NAFLD could it be? Metabolic dysfunction is associated with steatosis but no other histologic features in MAFLD and non-MAFLD subgroups of NAFLD