

PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 69318

Title: Non-alcoholic steatohepatitis in liver transplant recipients diagnosed by serum cytokeratin 18 and transient elastography: A prospective study

Reviewer's code: 05122735

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Chief Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Canada

Manuscript submission date: 2021-07-01

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-03 12:46

Reviewer performed review: 2021-07-06 02:57

Review time: 2 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" 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 Grade E: Do not publish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 type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" 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

SPECIFIC COMMENTS TO AUTHORS

Dr Alshaima Alhinai et al. have performed the current study to evaluate incidence and predictors of NAFLD and NASH by employing noninvasive testing in liver transplant recipients, namely controlled attenuation parameter (CAP) and the serum biomarker cytokeratin 18 (CK-18). They reported that 63.0%, and 48.5% of patients developed NAFLD and NASH during a median follow-up of 16.8 months (interquartile range 15.6-18.0). On multivariable analysis, after adjusting for sex and alanine aminotransferase, body mass index was an independent predictor of development of NAFLD (aHR 1.21, 95% CI: 1.04-1.41; $p=0.01$) and NASH (aHR 1.26, 95% CI 1.06-1.49; $p<0.01$). CAP had a 76.5% accuracy to diagnose NAFLD, while the accuracy of CAP plus CK-18 to diagnose NASH was 82.4%.. The results were interesting; however, some important concerns are needed to be further clarified. 1. What's the difference between NAFLD (nonalcoholic fatty liver diseases, line 3) and NAFL (nonalcoholic fatty liver, line 7) in the Introduction section? 2. What's the leading reason for liver transplantation? Does NASH rank higher than liver tumor or cirrhosis on the list for transplantation? Pls listed the reason for transplantation in the current study. 3. When was liver biopsy performed? 4. Why age was not adjusted or included in the final model? As we know, the prevalence of both NAFLD and NASH increased as the age grew older. 5. The author described that TE with CAP measurement and plasma to measure CK-18 were also acquired at each study visit, which meant that CAP and CK-18 were repeatedly assessed at month 3, 6, 9, 12 and 18 during the follow up. Further, the author explained that the median time between liver biopsies and non-invasive diagnostic testing was 38.6 ± 30 days (in Result section). Does the author mean liver biopsy were also repeated performed? If so, which one was used as outcome and why the author performed many times of liver biopsy? Similar, because CAP and CK-18 were repeatedly assessed, which



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one was used as the exposure, or the average of them was treated as the exposure? 6. Since only 25 out of 40 performed liver biopsy, how to assess NAFLD and NASH in the remain patients? The ROC was performed in 25 patients? 7. It seemed that it was a re-identified retrospective cohort study. If so, pls mentioned it in the manuscript. 8. Did the author try to compare the sensitivity and specificity of CK-18 plus CAP to alanine aminotransferase plus liver image? 9. Table 1, as the author described in the material section, LT due to chronic hepatitis C were excluded. However, 8 of 40 were patients with HCV. Another question was the title was non-alcoholic fatty liver, 1 patient with alcoholic fatty liver was included. 10. Table 2, Since only 25 out of 40 performed liver biopsy, the comparison was only possible in 25 patients. Pls clearly explained it.

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Name of journal: *World Journal of Hepatology*

Manuscript NO: 69318

Title: Non-alcoholic steatohepatitis in liver transplant recipients diagnosed by serum cytokeratin 18 and transient elastography: A prospective study

Reviewer's code: 02441106

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Romania

Author's Country/Territory: Canada

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Reviewer chosen by: AI Technique

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Reviewer performed review: 2021-07-12 17:50

Review time: 10 Days and 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 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
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a good paper, useful for practice! Some comments: -please add to keywords NAFLD -use type 2 diabetes mellitus instead of diabetes patients. -why did you take 270 dB/m as cut off for CAP. You can try to use the cut off of 290 dB/m as presented in a recent paper by Eddowes (Gastroenterology 2019). -please give more explanation for the low accuracy of TE (57.8%) for fibrosis assessment!

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 69318

Title: Non-alcoholic steatohepatitis in liver transplant recipients diagnosed by serum cytokeratin 18 and transient elastography: A prospective study

Reviewer's code: 05038583

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: Canada

Manuscript submission date: 2021-07-01

Reviewer chosen by: Jing-Jie Wang (Online Science Editor)

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Reviewer performed review: 2021-10-18 14:47

Review time: 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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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

SPECIFIC COMMENTS TO AUTHORS



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Dear authors, Thank you for let me review this manuscript. As a disclosure, I do not believe I performed your initial peer-review, but I have read the peer-review report and revised manuscripts. The authors have addressed comments by other peer-reviewers appropriately. I have a few additional comments. 1. CK-18 is not a routine test we order when taking care of liver transplant recipients. Therefore, it may be challenging to apply this result to clinical practice. 2. The main concern for LFT elevation after a liver transplant is rejection which will require a liver biopsy. It will be hard to attribute LFT elevation to NASH without doing a liver biopsy. 3. These results may be helpful for a longer duration. It is also valuable to monitor CAP scores to see if they are having a re-occurrence of steatosis. 4. I do not see a table for some reason, so I could not assess this aspect of the manuscript.