



PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 67327

Title: Liver function tests and metabolic-associated fatty liver disease: Changes in upper normal limits, does it really matter?

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05304884

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: United Kingdom

Manuscript submission date: 2021-04-21

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-13 06:38

Reviewer performed review: 2021-05-14 21:34

Review time: 1 Day 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 checked="" 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 Grade E: Do not publish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

In this study “Liver function tests and nonalcoholic fatty liver disease (NAFLD): Changes in Upper Normal Limit, Dose it really matter? ”, Liver Stiffness Measurement (LSM) and liver biopsy were used to distinguish the severity of NAFLD and NASH, and combined with liver function (especially ALT) to explore whether the LFT classification can be used to judge the prediction and prognosis of NAFLD and NASH. Actually, the ALT value of NAFLD and NASH patients can range from normal to 200~300 U/L, rarely more than 10 times higher than the normal value. However, when NASH progresses to cirrhosis, the values of ALT and AST may return to normal values, but the disease is worsening. Use ALT and AST values as the only basis for disease tracking is not clinically feasible. In response to this research, a few comments are as follows: 1. Other indicators may be more suitable for this study, such as nonalcoholic fatty liver disease fibrosis score (NFS) and Fibrosis-4 (FIB-4). $NFS = (-1.675) + 0.037 \times \text{age (years)} + 0.094 \times \text{BMI (kg/m}^2) + 1.13 \times \text{impaired fasting glucose (IFG) / diabetes (yes = 1, no = 0)} + 0.99 \times \text{AST/ALT ratio} - 0.013 \times \text{platelet count (} \times 10^9 \text{/L)} - 0.66 \times \text{albumin (g/dL)}$; $FIB-4 = \text{age} \times \text{AST (IU/L)} / \text{platelet count (} \times 10^9 \text{/L)} \times \sqrt{\text{ALT (IU/L)}}$. In NFS, advanced fibrosis can be reliably excluded (negative predictive value [NPV], 93%) using the low cutoff score (< -1.455) and diagnosed with high accuracy (positive predictive value [PPV], 90%) using the high cutoff score (> 0.676) [1]. In FIB-4 scoring, advanced fibrosis can be reliably excluded (NPV, 90%) using the low cutoff score (< 1.45), and a FIB-4 of >3.25 is 97% specificity, with a PPV of 65% for advanced fibrosis [2]. 1. Angulo P, Hui JM, Marchesini G, et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology*. 2007;45:846-54. 2. Sterling RK,



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Lissen E, Clumeck N, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology*. 2006;43:1317-25.

2. According to the level of LSM and liver biopsy, authors can try to find the cutoff value of NFS or FIB-4, which can be used to predict the severity of NAFLD or NASH.

3. Previous papers mentioned that gender and age are the major factors associating the NAFLD and NASH, authors may be can try to subgroup participants.



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Reviewer's code: 04216189

Position: Peer Reviewer

Academic degree: MD, MSc

Professional title: Research Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: United Kingdom

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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
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SPECIFIC COMMENTS TO AUTHORS

Congrats to the authors for this nice study.