Name of journal: World Journal of Hepatology

Manuscript NO: 72023

Title: Gravity assistance enables liver stiffness measurements to detect liver fibrosis under congestive circumstances

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05383840

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer’s Country/Territory: Poland

Author’s Country/Territory: Japan

Manuscript submission date: 2021-09-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-30 06:19

Reviewer performed review: 2021-10-04 15:59

Review time: 4 Days and 9 Hours

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<th>[ ] Grade B: Very good</th>
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| Re-review          | [Y] Yes | [ ] No |
SPECIFIC COMMENTS TO AUTHORS

Dear Authors, The presented manuscript titled “Gravity assistance enables liver stiffness measurement to detect liver fibrosis under congestive circumstance” is an interesting approach to the problem of liver elastography in patients with congestive heart diseases. At this point I have a list of concerns, that I hope You will be able to address: 1) In the Patients section you declare, that 2D-SWE was performed in 298 cases of patients (cohort #1). Then you state that 41 cases of cohort #2 were performed with virtual touch quantification method. In the Shear Wave Elastography Measurements you declare, that 2 devices were used for this group: pSWE with ACUSON S2000 and 2dSWE by Aplio 500. If my understanding is correct, those two cohorts were diagnosed with different devices and different methods. What was the reason for that? As it is already proven there is a significant difference between the vendors and elastography methods in results as well as error ratios. How did you address this problem? 2) What was the number and experience of ultrasonographers performing the elastography examinations? Did you calculate their compliance? What was the examination protocol? 3) What was the percentage of non-diagnostic measurements? What measurement quality parameters have been used and with what cut-offs? 4) In Patients section you declare, that fatty liver disease was diagnosed by US on the basis of liver hyperechogenicity and presence of at least two additional findings. Did you obtain the quantitative information in the form of the liver/kidney b-mode ratio? How were the vascular blurring and deep-attenuation of echo-beam evaluated? Did you in any way evaluate the liver fat (for example attenuation, sound speed, fat fraction etc.)? 5) What were the inclusion and exclusion criteria for this work, as they are not clearly stated? 6) In Table 1 you present the Hepatocellular
carcinoma group of patients. It is proven, that liver focal changes can increase the measurement values in their vicinity. How this problem was addressed? Additionally diffused HCC can be non-detectable in ultrasound - were there any cases included in this work? What methods of verification did you apply? 7) Did you exclude any underlying liver diseases in the cohort #2 patients? There is no characterization of the cohort #2 in your work, Table 1 presents only cohort #1 – could you please provide full information on this group? 8) What was the time period between the SWE and cardiac surgery? As it is proven that invasive procedures can elevate the liver stiffness due to congestion - how this problem was addressed? 9) Why there was no correlation to golden standard, the liver biopsy? 10) As this work is claimed to be a retrospective one - is it a standard procedure to evaluate liver stiffness in your center in left decubitus position? If that is the issue, for what reason and according to what guidelines? Due to inability to clearly evaluate the methodology of your work I am unable to recommend its publication.
Name of journal: World Journal of Hepatology
Manuscript NO: 72023
Title: Gravity assistance enables liver stiffness measurements to detect liver fibrosis under congestive circumstances
Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed
Peer-review model: Single blind
Reviewer’s code: 05872770
Position: Peer Reviewer
Academic degree: MPhil
Professional title: Teacher
Reviewer’s Country/Territory: Pakistan
Author’s Country/Territory: Japan
Manuscript submission date: 2021-09-30
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-10-03 12:15
Reviewer performed review: 2021-10-06 10:03
Review time: 2 Days and 21 Hours

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SPECIFIC COMMENTS TO AUTHORS

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Name of journal: World Journal of Hepatology

Manuscript NO: 72023

Title: Gravity assistance enables liver stiffness measurements to detect liver fibrosis under congestive circumstances

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 00003629

Position: Editorial Board

Academic degree: MD

Professional title: Emeritus Professor

Reviewer’s Country/Territory: Greece

Author’s Country/Territory: Japan

Manuscript submission date: 2021-09-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-30 09:29

Reviewer performed review: 2021-10-19 03:22

Review time: 18 Days and 17 Hours

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SPECIFIC COMMENTS TO AUTHORS

In the article entitled: "Gravity assistance enables liver stiffness measurement to detect liver fibrosis under congestive circumstance", the authors Suda T et al. describe in detail the changes in liver stiffness (LS) observed on the supine or left lateral decubitus position in a large number of patients and normal subjects. The issue dealt, has important practical clinical and pathophysiological significance, because it shows that measurements of LS, especially those at the right liver lobe, are affected by the pressure exerted on the IVC by the weight of the liver and the deformation of the hepatic veins, depending on the posture of the examinee. The reported findings, may help solve the difficult problem of the ultrasonographic separation of the venous stasis element on LS from the actual hepatic fibrosis of interest in cases of cardiac liver. However, the data provided in the present study are not sufficient to substantiate the final solution. Further studies are needed to prove, whether increased LSM in patients with objectively verified parameters of central venous congestion becomes lower and to what degree, when the position of measurement changes from the supine to left lateral decubitus. The article makes an initial probe of the subject and it does it quite successfully. The article is well written but it is a difficult reading. The Table and the Figures are informative. The English language, however, needs much polishing. I think the article is interesting and provides an innovative and practical idea. It may be published in the WJG after some modifications, as indicated in my comments below. Major Comments: 1. (Page 6, Line 9): In the RESULTS section of the Abstract, data and their respective level of significance are missing. It is imperative to be added. 2. (Page 6, Line 26): The effect of gravity is expected to be less pronounced at the upright or even at the sitting position. Have the
authors measure liver stiffness at these positions? 3. (Page 7, Lines 16-18): This sentence must be modified. Liver congestion may be less prominent at the left lateral decubitus position because the inferior vena cava is released from liver pressure. However, liver congestion is not expected to be completely eliminated. Of course, the resulting LSM will be closer to real liver fibrosis, but still may carry some residual elements of the venous congestion. 4. (Page 11, Lines 24 & 26): Please give also the equivalent in kPa values. 5. (Page 12, Lines 11): Authors should clarify whether they refer to inter- or intra-observer CV, at the same examination or at different sessions. 6. (Page 13, RESULTS): One would expect to see first a Table with the overall view of the 2D-SWE measurements of the 3 groups in the supine and the left lateral decubitus position. In addition, besides giving only p-values, authors should provide the medians (IQR) (or means ± SD) of the respective parameters, as well. 7. (Page 13, Lines 21): Please give the critical value of “stiffness” in m/sec and kPa. 8. (Page 13, Lines 24-25): The cardiothoracic ratio is not a good indicator of congestive heart failure (CHF) (see: Future Cardiol 2015;11:171, J Royal Soc Med 2015;108:317). Authors should have had selected a parameter with higher sensitivity for CHF, as for eg. the cardiac ejection fraction, the centripedal or bidirectional blood flow in the hepatic veins, or something similar. 9. (Page 14, Lines 6-8): Do you have any measurements of the IVC diameter in the sitting or the upright position? If yes, please mention its changes in the Discussion section. 10. (Page 15, Lines 26): Figure 5 could be omitted. 11. (Page 18, Lines 12): Authors should add a comment on the possible shortcomings of their study. Minor Comments: 1. (Page 1, Line 8): circumstances. 2. (Page 5, Line 8): ...is prolonged... 3. (Page 5, Line 12): Regular measurements... 4. (Page 5, Line 24): 2D-shear wave elastography (2D-SWE) 5. (Page 6, Line ): Please refer always to "2D-SWE". 6. (Page 7, Line 13): …there are… 7. (Page 9, Lines 24 & 27): The words "hypothetically" and "hypothetical" can be omitted. 8. (Page 13, Lines 19): …was lower... 9. (Page 15, Lines 20):...at higher...