

Manuscript Title	Longitudinal Assessment of Liver Stiffness by Transient Elastography for Chronic Hepatitis C Patients
Study Type	Retrospective Cohort Study
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S. No.	Reviewer / Section	Comments	Response
Peer Review Comments			
1	Reviewer #1:	<p>Scientific Quality: Grade B (Very good)</p> <p>Language Quality: Grade A (Priority publishing)</p> <p>Conclusion: Accept (General priority)</p> <p>Specific Comments to Authors: It is an interesting manuscript about “Longitudinal Assessment of Liver Stiffness by Transient Elastography for Chronic Hepatitis C patients”. My concern is determined in the following points.</p> <p>Cirrhosis regression is not only about fibrosis regression but also reversal of vascular and parenchymal abnormalities.</p> <p>The best evidence and definition of regression of cirrhosis will be based on the assessment of long-term clinical outcomes.</p> <p>Further longer time (a few years) follow-up of this cohort with histological, hemodynamic, elastographic, and clinical data,</p>	<p>-Thank you so much for taking your time and review our manuscript and sharing your comments. We appreciate that</p> <p>-We have made the following changes in the manuscript based on your valuable comments:</p> <p>We concur with the reviewer that cirrhosis encompasses a multitude of changes in liver architecture, commonly scored using the METAVIR criteria, and the development of portal hypertension, which can be precisely quantified using the hepatic venous pressure gradient measurement.</p> <p>The individuals in our study are at-risk for liver fibrosis and cirrhosis from chronic hepatitis C infection and the majority of clinicians, both at the time of data collection (2014- 2018), as well as today, prefer to avoid subjecting patients to a liver biopsy with hepatic venous pressure gradient measurements</p>

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		<p>stratified by stage of liver disease, will provide invaluable data toward regression of HCV cirrhosis. Above mentioned should be referred to.</p>	<p>in favor of transient elastography as the initial screen for liver fibrosis. Our study took advantage of real-world clinician ordering practices, which means that physicians who prescribed HCV treatment after an initial Fibroscan repeated the Fibroscan after treatment was completed, presumably with the expectation of an improvement in liver stiffness.</p> <p>We wanted to determine the magnitude of this change over time and compare this change over time directly between treated and untreated patients. Surprisingly, we did not find that DAA treatment itself led to lower stiffness scores after treatment, but instead, patients who were prescribed DAA had higher baseline readings.</p> <p>We fully acknowledge that we do not have data in our cohort regarding hepatic decompensations and a prolonged period of follow-up. However, we think it is important to describe that in a racially and ethnically diverse population with CHC, clinicians who order TE on a short-term basis after treatment may find that stiffness scores do not meaningfully change.</p> <p>We offer multiple potential explanations for why the stiffness measurements did not improve in our study. Although</p>

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			<p>this is beyond the scope of the current paper, the allusion to false positive findings on TE also implies that cirrhosis “regression” may be an artifactual construct if patients in our study did not actually have advanced fibrosis/cirrhosis as suggested by the initial Fibroscan.</p> <p>Hence, we have advocated for repeat TE measurements in the patient population suspected to have advanced liver disease based on TE alone, especially if it will alter clinical management.</p>
2.	Science editor:	<p>Language Quality: Grade B (Minor language polishing)</p> <p>Scientific Quality: Grade C (Good)</p> <p>The manuscript elaborated longitudinal assessment of liver stiffness by transient elastography for Chronic Hepatitis C Patients. The manuscript is well written and can be helpful for the readers to ameliorate the diagnostic and therapeutic approach for this scenario. The author's manuscript lacks a conclusion. The form is broken, please modify it. DAA treatment was not associated with a differential change in liver stiffness over time in patients with CHC compared to untreated patients. Is there any other method to measure</p>	<p>Thank you so much for taking your time and review our manuscript and sharing your comments. We appreciate that</p> <p>The goal of the study was to specifically concentrate on Fibroscan measurements as the modality of choice among clinical gastroenterologists and hepatologists interested in gauging the severity of fibrosis in patients with chronic hepatitis C infection.</p> <p>We have revised the conclusion to emphasize the need for judicious interpretation of transient elastography results that suggest advanced fibrosis/cirrhosis and to consider repeat confirmatory Fibroscan in this patient population (as per Baveno VI consensus</p>

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		liver stiffness?	<p>guidelines).</p> <p>We did not examine biomarker-based and serological tests (such as APRI, FIB4, or the proprietary FibroTest/FibroSure) which can be used for non-invasive assessment of liver stiffness.</p> <p>A comparison of performance characteristics of other non-invasive testing for liver stiffness, as compared with liver biopsy and transient elastography, is the focus of a different body of work.</p>
3.	Company editor-in-chief:	<p>I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted.</p> <p>I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.</p> <p>Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.</p> <p>Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and</p>	<p>Thank you so much for taking your time to review our manuscript and consideration for conditional acceptance. We appreciate that</p> <p>The figures are computer-generated images, so proving the image in an editable format would be challenging. However, we have included the images in PowerPoint.</p> <p>We have modified the tables as of three line format</p>

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		column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content	