

Author's Responses to the Comments

We are very grateful to the valuable comments of the reviewer and now responding to the comments as follows:

Interesting topic, well-written manuscript. Few comments/suggestions that could ameliorating the description of results and giving some important additional information to apply these data into clinical practice:

Comment: 1-In the abstract authors should specify the threshold of fibrosis scored according to METAVIR that corresponded to: significant fibrosis (F2), severe fibrosis (F3), cirrhosis (F4).

Response: The threshold of fibrosis scored according to METAVIR has been specified. The sentence now reads as follows:

The optimal cut-off values associated with significant fibrosis ($F \geq 2$), severe fibrosis ($F \geq 3$), and cirrhosis (F4) were 9.7 kPa, 13.2 kPa, and 16.3 kPa, respectively.

Comment: 2-The cut-offs of 2D-SWE finally chosen in accordance with ROC-curve analysis were not “predictive” of fibrosis, but “associated” with it. In my opinion it is better association than prediction in this context.

Response: The term “predict” has been changed to “associate”. The sentence now reads as follows:

The optimal cut-off values associated with significant fibrosis ($F \geq 2$), severe fibrosis

($F \geq 3$), and cirrhosis (F4) were 9.7 kPa, 13.2 kPa, and 16.3 kPa, respectively.

Comment: 3-At a certain point authors compare the cut-offs of 2D-SWE used in HCV and HBV patients with those deriving from their analysis. Please, specify, in the result section, which cut-offs found by other authors for viral hepatitis you refer to. It would be better including also the references of the papers you took out this information (those quoted in the discussion?).

Response: We have added a sentence to specify the cut-offs by other authors for viral hepatitis in the result section. The sentence reads as follows:

The corresponding optimal cut-off values in patients with chronic hepatitis B (CHB) were 7.2 kPa, 9.1 kPa, and 11.7 kPa, and the corresponding values for patients with chronic hepatitis C (CHC) were 7.1 kPa, 8.7 kPa, and 10.4 kPa^[8,22].

Comment: 4-Finally authors did not find a perfect agreement between the non-invasive and the invasive technique. They clearly stated it in the conclusion of the discussion and I totally agree. In my opinion, they should add this comment also in the abstract.

Response: We have added sentences about the imperfect agreement between the non-invasive and the invasive technique in the abstract. The sentences read as follows:

RESULTS

The overall concordance rate of the liver stiffness measurements obtained using 2D-SWE *versus* fibrosis stages was 53.5%.

CONCLUSION

Low overall concordance rate was observed in the liver stiffness measurements obtained using 2D-SWE *versus* fibrosis stages.

Comment: 5-It was quite hard understanding the utility of the multivariable analysis performed at the end of the analysis. It is expected that the value of 2D-SWE is associated with a high degree of fibrosis measured by the Metavir score and the albumin level as marker of an advanced liver disease. I really think that it could be more useful analysing which variables present at baseline influenced the lack of agreement between the 2D-SWE and Metavir score (obesity? Transaminase level? Age?...etc.). In particular, I suggest to pay attention to F2 stage of fibrosis since it refers to a degree of fibrosis whom starting the treatment is mandatory for. Or to F4 since patients with cirrhosis need new studies and new scheduled visits to manage the risk related with an advanced liver disease. This could allow clinician to better understanding if it exists a subgroup of patients whose fibrosis staging can be detected non-invasively and has the potential of changing their clinical practice.

Response: We have deleted Table 6 about the multivariable analysis of the factors associated with the liver stiffness measurement. We have analyzed which variables present at baseline influenced the lack of agreement between the 2D-SWE and F2/F4.

The results were as follows:

According to the multivariate logistic regression analysis, the disagreement between LSMs obtained using 2D-SWE and cirrhosis was independently associated with the following factors: an age of greater than 46 years (OR: 7.5, 95% CI: 1.7-33.3, $P=0.008$), abnormal ALP levels (OR: 14.0, 95% CI: 1.5-129.1, $P=0.02$) and abnormal serum albumin levels (OR: 11.6, 95% CI: 3.2-42.0, $P<0.001$). No factors were significantly associated with the disagreement between LSMs obtained using 2D-SWE and significant fibrosis.

Comment: 6-Since the analysis was finally conducted on 114 patients I suggest to rewrite Table 1 which includes 117 patients. Table 1 and 2 do not coincide on the total number of patients involved in the analysis.

Response: 117 patients included 114 patients and three patients with failed liver stiffness measurements obtained using 2D-SWE. We have rewritten Table 1 including demographic data, blood test and histologic results of 114 patients and have rewritten the sentence about Table 1 in the results. The sentence reads as follows:

The characteristics of 114 patients are summarized in Table 1.

Comment: 7-Were all patients not under treatment at time of biopsy and 2D-SWE test? Please, specify it in the methodology section. How many patients included were diagnosed of suffering from an autoimmune liver disease without biopsy? In my practice the diagnosis of an autoimmune disorder of the liver often require liver biopsy. If it was the same for their series, authors should discuss that probably their

study opens possibilities for a non-invasive assessment of fibrosis progression in patients suffering from an autoimmune liver disease more than diagnosing the stage of fibrosis at baseline.

Response: We have specified the treatment of patients and the diagnosis of AILD in methodology section as follows:

The diagnoses of AIH, PBC and PSC in all patients were confirmed by histological evidence ^[13-18]. All patients were not under immunosuppressive treatment at time of the LB and 2D-SWE examinations.

The comments of the reviewer were very valuable. We added a sentence as follows at the end of the discussion.

Our study opens possibilities for a non-invasive assessment of fibrosis progression in patients suffering from ALID.