Detailed Responses to Reviewers

Response to reviewer #1:

The manuscript is not prepared according the World Journal guidelines.

Response: We apologize for our carelessness, and we have revised the manuscript according to the World Journal guidelines.

The manuscript needs grammar, style and spelling polishing-for example the sentence can't begin with a number.

Response: We apologize for the language problems in the original manuscript and we are ashamed for our unsatisfactory English. We spent a lot of time, after we received your email, working through the paper and made some changes to improve the English expression. According to the reviewer's suggestion, we have deleted the numbers at the beginning of sentences in the results section.

The abstract chaotically presents the manuscript I suppose that the authors excluded patients taking hepatotoxic drugs (for example methotrexate…) and it should be mentioned in the material and methods section.

Response: We agree with the comment, and we have rewritten the inclusion and exclusion criteria in the revised manuscript as follows:

The inclusion criteria were as follows: (1) hepatitis B surface antigen (HBsAg) present in the serum for at least 6 months and (2) availability of the liver histologic assessment and SWE and TE results determined within 1 month. The exclusion criteria were (1) any previous anti-HBV therapy; (2) decompensate liver cirrhosis and hepatocarcinoma (HCC); (3) other chronic liver diseases, including hepatitis C virus (HCV), autoimmune liver disease (AID), alcoholic liver disease (ALD), nonalcoholic fatty liver disease (NAFLD) or drug-induced liver injury (DILI); and (4) age more than 65 years old or less than 18 years old, pregnant woman and patients with psychiatric disorders.

The technique of taking livers tissue samples should be explained in at least one sentence, if the technique of TE examination was explained thoroughly.

Response: We deeply appreciate the reviewer's suggestion. According to the reviewer's comment, we provided more details to describe the percutaneous liver biopsies as follows:

Patients were placed in a supine position. Percutaneous liver biopsies were performed using 18-gauge automated needles. During the puncture, the large blood vessels, common bile duct and gallbladder were bypassed. Liver tissue specimens were obtained from the right hepatic lobe, and then these samples were fixed in formalin and embedded in paraffin for pathological interpretation.

"Fifty-four Chinese treatment-naive CHB patients were eligible for the study" – Is it important for the study to mention that the patients were Chinese? In LSM measurement ethical differences are not expected.

Response: We agree with the comment, and ethnic group is not an independent factor in LSM measurement. We have rewritten the sentence in the revised manuscript as follows:

Fifty-four treatment-naive CHB patients were eligible for the study.

The discussion should include more results of previous published studies, and not just discussion of personal results.

Response: We agree with the comment, and we have cited and discussed previous literature in the 2-4 paragraphs of the discussion section. In a previous review, the authors discussed the diagnostic efficiency by comparing AUROCs between SWE and TE, whereas in the present manuscript, in addition to AUROCs, we focused mainly on comparing the performance of SWE and TE for diagnosing significant fibrosis by analyzing independent factors that influenced SWE and TE. Therefore, we added a discussion about factors that were correlated with the LSMs assessed with SWE in CHB patients.

Despite this limitation, this is well conducted study with clinically important conclusions.

Response: We appreciate the reviewer's positive evaluation of our work.

Response to reviewer #2:

1. Correlations between fibrotic variables (SWE and TE) and liver functional variables (ALB, PT, PLT, and ALT) should be presented.

Response: We agree with the reviewer's comment that clinical liver function variables such as ALB, PT, PLT, and ALT are critical in reflecting liver function. All liver functional variables and elastography measurements are indirect indicators of liver function and fibrosis. In recent years, ALT, AST and PLT have been used in the traditional formulas for the FIB-4 value and APRI to predict liver fibrosis. In the present study, the FIB-4 value and APRI did not show any difference with the progression of fibrosis stages, whereas SWE and TE could distinguish different liver fibrosis stages (in the third part of the results section). The correlations between SWE/TE and liver functional variables (ALB, PT, PLT, and ALT) are presented in Additional Table 2. The results revealed that TBIL is correlated with both SWE and TE, but the r value is low. The PLT count is correlated with TE but not SWE, which is in accordance with our univariate analysis (Table 1).

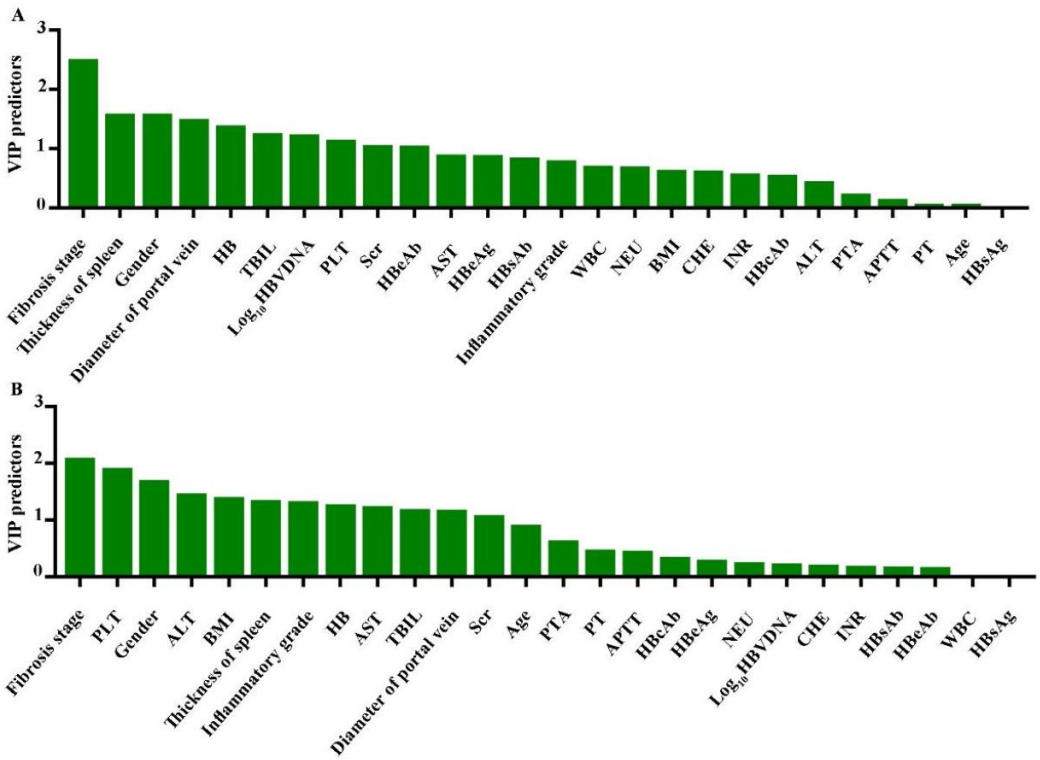
Additional Table 2. Correlations between fibrotic variables (SWE and TE) and liver functional variables (ALB, PT, PLT, and ALT).

	SWE					TE				
	ALB	PT	PLT	ALT	TBIL	ALB	PT	PLT	ALT	TBIL
Correlation	-0.307	0.021	-0.234	-0.047	0.275	-0.345	0.214	-0.372	0.261	0.475
P value	0.077	0.879	0.088	0.737	0.046	0.046	0.125	0.006	0.059	0.000

2. In Fig.2, the scale of the vertical axis among SWE and TE was different. It should be adjusted.

Response: We apologize for our carelessness. In Figure 1, the scale of the vertical axis was different for SWE and TE. The scale of the vertical axis has been adjusted in the revised Figure 1 as follows:

Figure 1. The results of orthogonal partial least squares (OPLS) discriminant analysis (DA) of SWE (A) and TE (B). The abscissa indicates various factors and is arranged from left to right according to the influence on LSMs. The ordinate shows the VIP value, which represents the power of the effect.

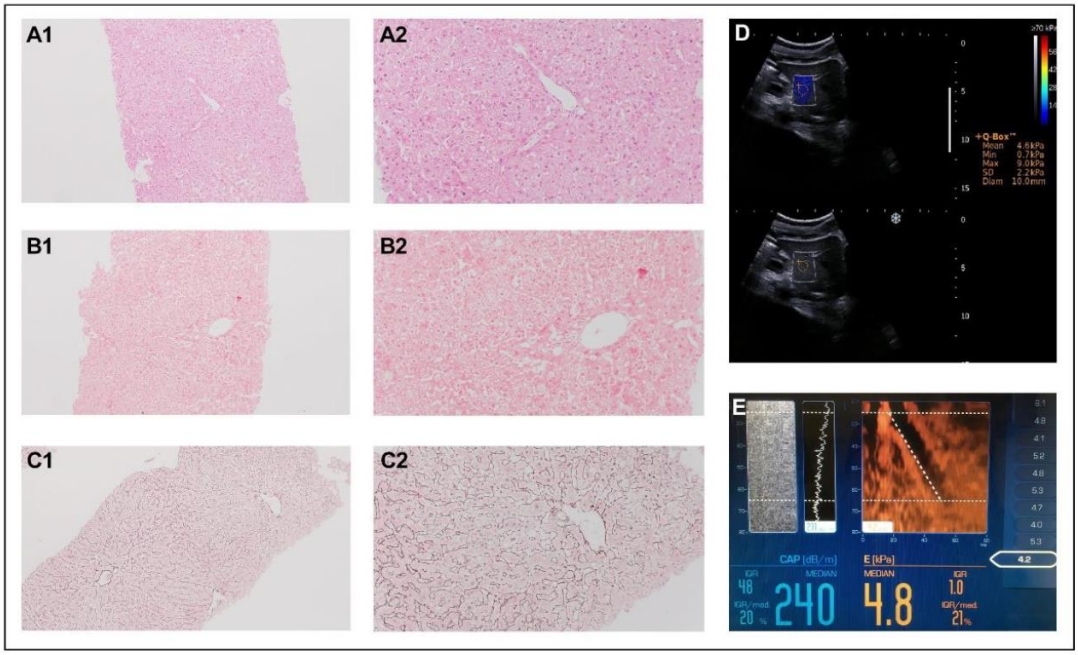


3. Pathological samples and image samples from SWE and TE should be presented, such as F0, F1, F2, F3, and F4.

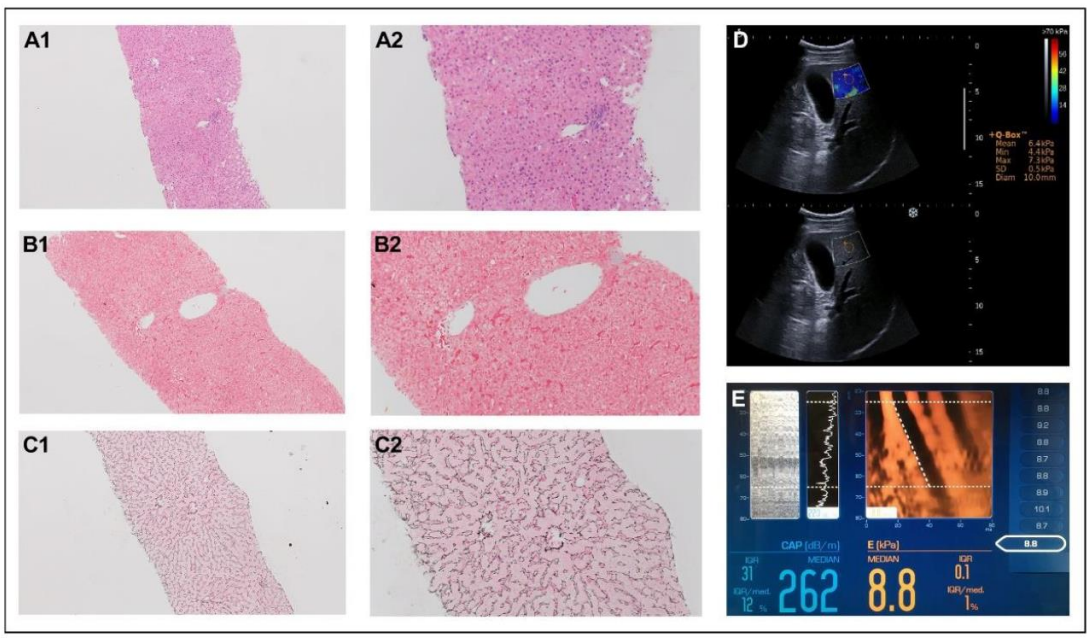
Response: We appreciate the reviewer's comment. We agree that pathological SWE/TE images should be added. Therefore, we have added additional Figures 1-6 in the revised manuscript showing F0-F5 CHB patients as follows:

Additional Figure 1. Pathological images of liver sections and the corresponding shear wave elastography (SWE) and transient elastography (TE) images for an F0 patient. A. Liver section stained with hematoxylin and eosin (HE); B. Liver section with Masson staining; C. Liver section with reticular staining; A1, B1, C1 (100X); A2, B2, C2 (200X). D. SWE image. The mean LSM was 4.6 kPa. E. TE

image. The mean LSM was 4.8 kPa.

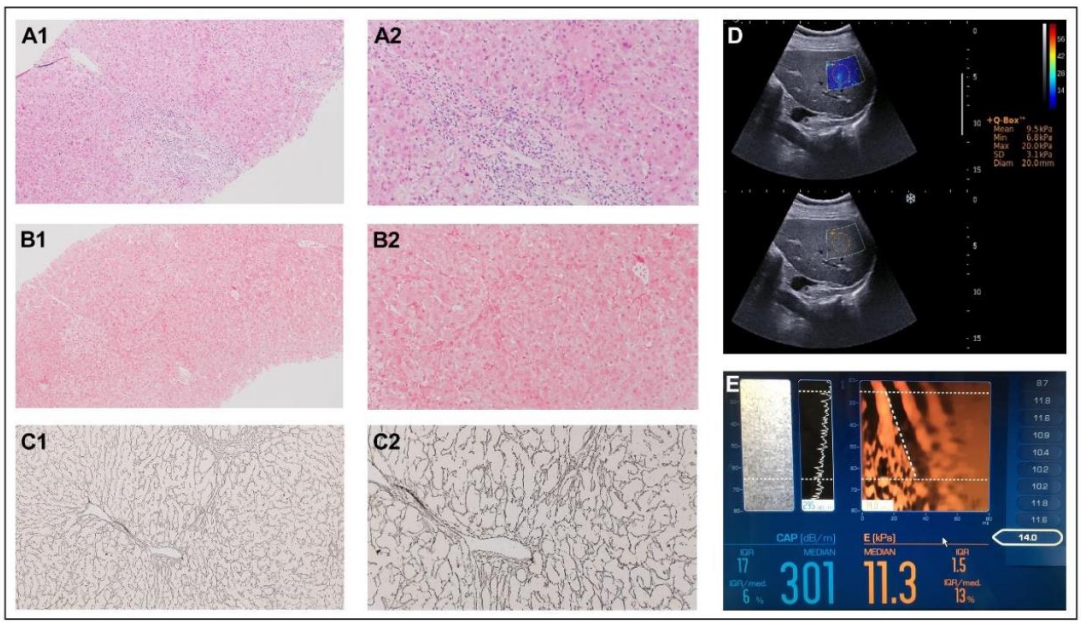


Additional Figure 2. Pathological images of liver sections and the corresponding shear wave elastography (SWE) and transient elastography (TE) images for an F1 patient. A. Liver section stained with hematoxylin and eosin (HE); B. Liver section with Masson staining; C. Liver section with reticular staining; A1, B1, C1 (100X); A2, B2, C2 (200X). D. SWE image. The mean LSM was 6.4 kPa. E. TE image. The mean LSM was 8.8 kPa.

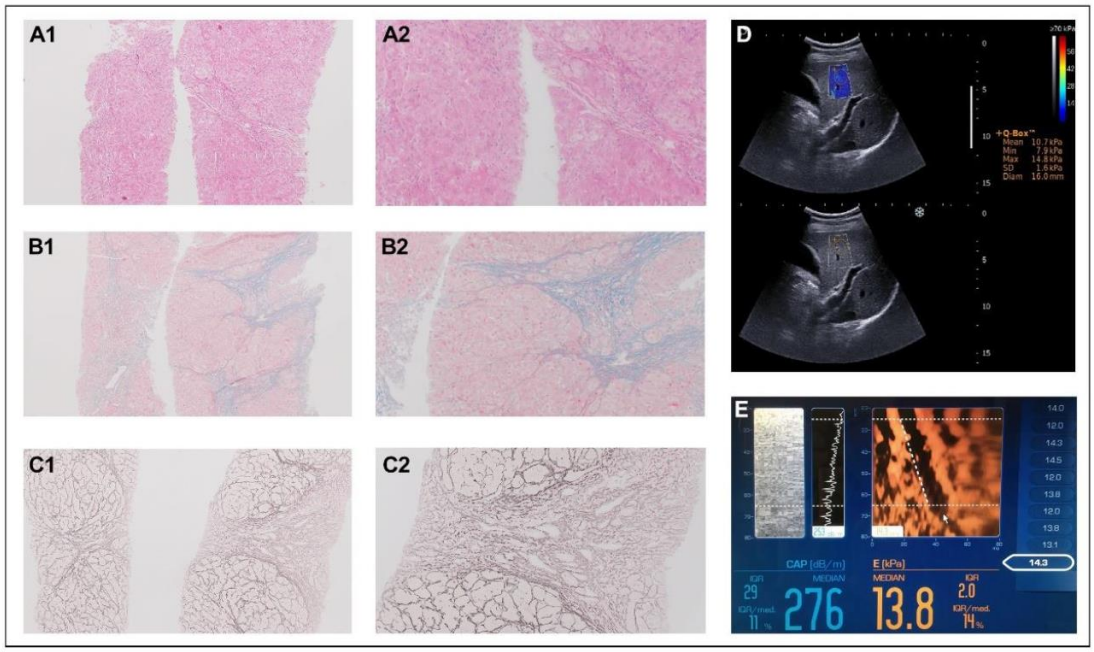


Additional Figure 3. Pathological images of liver sections and the corresponding

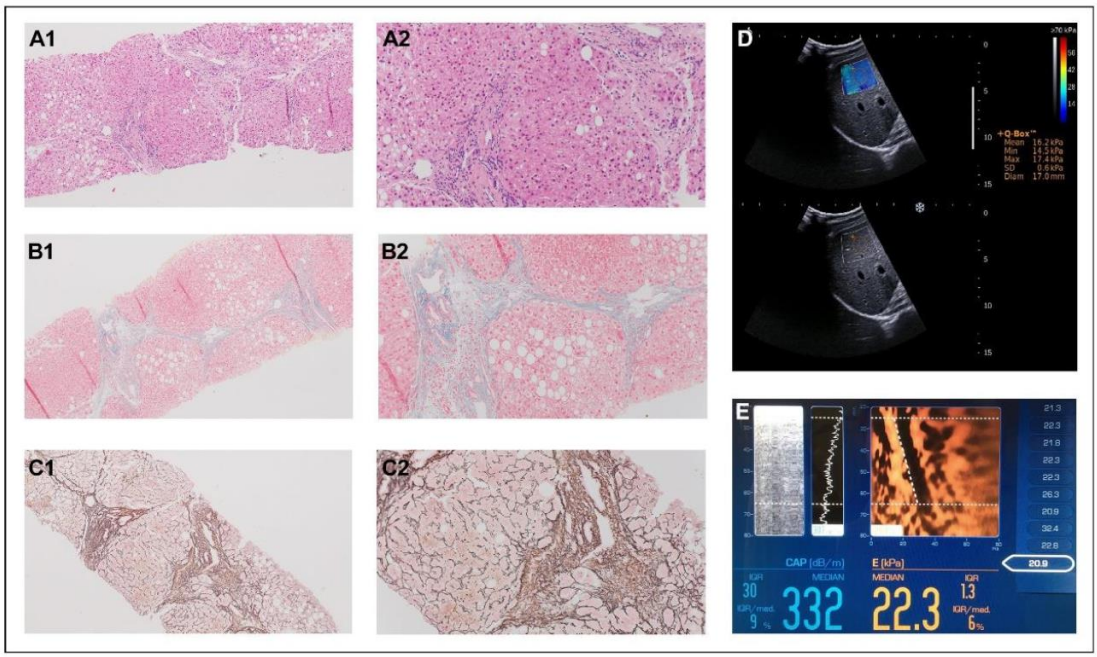
shear wave elastography (SWE) and transient elastography (TE) images for an F2 patient. A. Liver section stained with hematoxylin and eosin (HE); B. Liver section with Masson staining; C. Liver section with reticular staining; A1, B1, C1 (100X); A2, B2, C2 (200X). D. SWE image. The mean LSM was 9.5 kPa. E. TE image. The mean LSM was 11.3 kPa.



Additional Figure 4. Pathological images of liver sections and the corresponding shear wave elastography (SWE) and transient elastography (TE) images for an F3 patient. A. Liver section stained with hematoxylin and eosin (HE); B. Liver section with Masson staining; C. Liver section with reticular staining; A1, B1, C1 (100X); A2, B2, C2 (200X). D. SWE image. The mean LSM was 10.7 kPa. E. TE image. The mean LSM was 13.8 kPa.

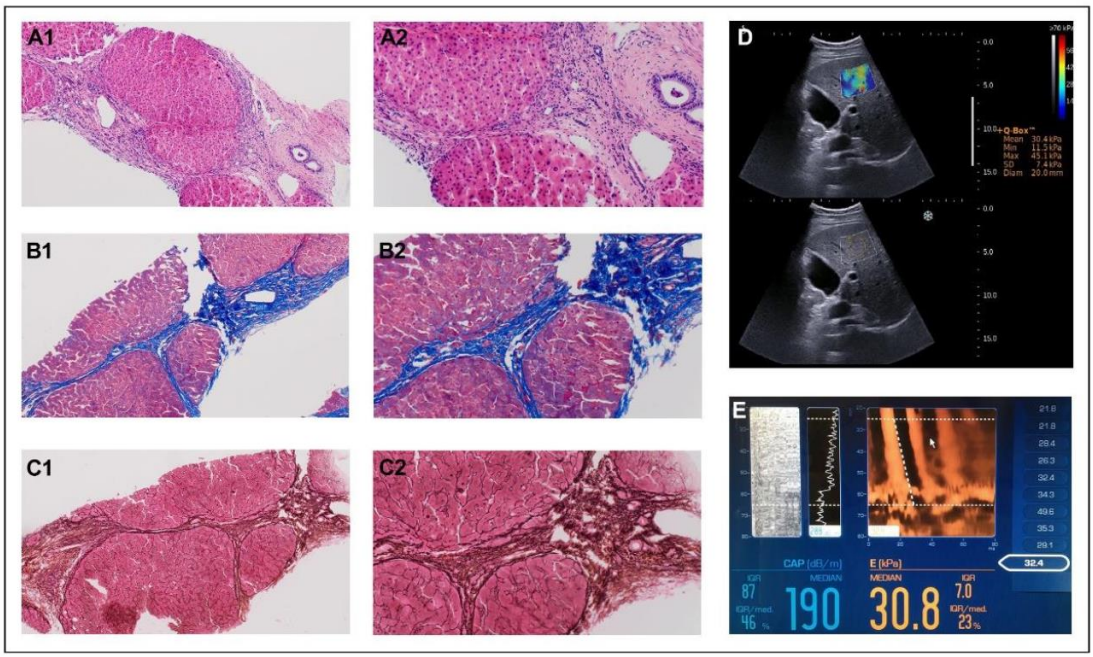


Additional Figure 5. Pathological images of liver sections and the corresponding shear wave elastography (SWE) and transient elastography (TE) images for an F4 patient. A. Liver section stained with hematoxylin and eosin (HE); B. Liver section with Masson staining; C. Liver section with reticular staining; A1, B1, C1 (100X); A2, B2, C2 (200X). D. SWE image. The mean LSM was 16.2 kPa. E. TE image. The mean LSM was 22.3 kPa.



Additional Figure 6. Pathological images of liver sections and the corresponding

shear wave elastography (SWE) and transient elastography (TE) images for an F5 patient. A. Liver section stained with hematoxylin and eosin (HE); B. Liver section with Masson staining; C. Liver section with reticular staining; A1, B1, C1 (100X); A2, B2, C2 (200X). D. SWE image. The mean LSM was 30.4 kPa. E. TE image. The mean LSM was 30.8 kPa.



Detailed Responses to the comments of re-review:

Response to reviewer #1(02544416): I have no further comments. The authors corrected the manuscript according the suggestions.

Response: We deeply appreciate the reviewer's positive evaluation of our work.

Response to reviewer #2(00053659): 1. Yao et al. seemed to revise their manuscript nicely. Although the additional figs are very good for the readers as a reference, however, they concluded that the clinical value of the SWE could be better than the TE to predict fibrosis.

Response: Yes. We added much more additional figures to revealed the accurate classification of the liver fibrosis. And the liver biopsy is the cornerstone of evaluation. According the results of the study, we could conclude that SWE can provide comparable diagnostic accuracy without being affected by various factors. 2. This is most likely inappropriate because additional Table 2 reveals their embellishment. The degree of fibrosis should be correlated with liver function. Response: Additional Table 2 showed that TBIL is correlated with both SWE and TE. It revealed that the they are more susceptible to bilirubin which is consistent with result 2. LSMs could be affected by the liver fibrosis stage as well as the TBIL level. This result could be explained by previous study that indicated that the liver stiffness values were significantly correlated with TBIL. Other liver parameters including ALT/AST in the study shown normal or less than 2ULN. What is the most important, the degree of fibrosis is evaluated by liver pathology but not serum biochemical indexes. 3. All clinical indicator to prove liver function in the TE was superior to that in the SWE. This is strongly supported that the clinical value of TE should be better than that of SWE. Response: There is only one cohort in the study including 54 patients. TE and SWE were compared on the same patient. Therefore, there's no way this group is better than the other because there is only one group. 4. Therefore, the pathological classification of the liver fibrosis could be inappropriate or misleading. Response: All liver tissue specimens were blindly and independently reviewed by two hepatopathologists. When discrepancies occurred, the final decision was made by a third, experienced hepatopathologist, who was also responsible for reassessment of

10% of samples chosen at random. In addition, the additional figures are the powerful evidence of the accuracy pathological classification.