Dear Editors:

Thank you for your valuable comments on the manuscript entitled “Value of red blood cell distribution width in the prediction of diastolic dysfunction in cirrhotic cardiomyopathy” (NO:80848). We have carefully read and made corresponding revisions according to the Editors’ comments and reviewers’ opinions. The revisions to the original manuscript have been marked in red. We hope that the revised manuscript is now acceptable for publication on the Journal. The responses to the comments are listed point-to-point as follows.

Sincerely yours,

Yong-zhe Guo

1.Title: There is not enough support to consider RDW as diagnostic for diastolic dysfunction in cirrhotic cardiomyopathy.
Response:
**Thank you for your comment. We thought it would be better to change the diagnosis to prediction, we have revised the manuscript.**

2.Abstract, Background: the first sentence is confusing and needs to be re-write, please pay attention to correct spelling in English language**.**
**Thank you for your comment. We have revised this sentence.**

3.Introduction:
a.Line 1: You should be able to separate subclinical and clinical manifestations of cardiac dysfunction; LV hypertrophy is not characteristic for CCM; what is the definition of CCM?
Response:
**Thank you for your comment. We have replaced “subclinical” with “unnoticeable” and deleted LV hypertrophy in Part 1. CCM is thus redefined to avoid ambiguity.**
b.Line 7: There are well defined diagnostic criteria for cirrhotic cardiomyopathy, for both, systolic and diastolic dysfunction. Which criteria did you used?
**Thank you for your comment. According to the 2019 CCC guidelines, CCM can be divided into systolic and diastolic dysfunction. This study focused on the latter. Specific evaluation indicators of TTE were marked with red lines in Part 2.2.**
c.Line 12: NT- proBNP and other Indicators have only supportive role in the diagnosis of CCM, and are not diagnostic perse; these needs to be specify in your manuscript. Is there any data on optimal cut-off for NT-pro BNP in cirrhotic patients?
**Thank you for your comment. NT-proBNP is not the focus of the current study so its optimal cut-off value was not included. We have modified the description of NT-proBNP in Part 1.**

4.Aim of the study: why did you not also evaluated the correlation with the systolic dysfunction, in fact reduced EF or/and GLS?
**Thank you for your comment. Diastolic dysfunction appears early and can be detected at the baseline and cumulative evidence suggests that most patients with cirrhosis display a certain degree of diastolic dysfunction. The specific reason for this is marked in red in the first paragraph of Part 5. This study attempts to find indicators that can predict CCM early. Therefore, we focused on CCM diastolic dysfunction.**

5.Methods

a.Line 6: Do you have also data on the liver-stiffness measurements, or invasive measurements of portal hypertension? You should provide more detail definition of cirrhosis.

**Thank you for your comment. Because "liver-stiffness measurements" and "invasive measurements of portal hypertension" are not research objects, this study does not include the data. We have added the details of the diagnosis of cirrhosis in Part 2.1.**

b.Line 9: How about the patients after TIPS Implantation? Due to hemodynamic changes it is expected to have an impact on the diastolic function.

**Thank you for your comment. TIPS implantation is mainly applied for esophageal variceal bleeding and refractory ascites in decompensated cirrhosis, and its application is low in patients with early cirrhosis. In this study, we tried to find early indicators of CCM, so we did not include TIPS data for comparison.**

c.Line 11: You should list all the exclusion criteria used! What was the definition of the arterial hypertension, did you exclude also patients who take antihypertensive medication and have normal RR at the time of the evaluation?

**Thank you for your comment. "Arterial hypertension" should be changed to "pulmonary arterial hypertension". We have corrected the error. The study did not exclude patients with antihypertensive medications. Table 1 and Table 2 show the distribution of hypertension and the use of antihypertensive drugs in each group, respectively. We also included patients with atrial fibrillation in Table 1.**

d.Line 21: E/e` more or equal 15 is correct (E/e` ≥15)

**Thank you for your comment. We have corrected this mistake.**

6.Results

a.Basic characteristic on echocardiographic parameters are missing

**Thank you for your comment. There is no evidence that the four indicators in the diagnosis of diastolic dysfunction from echocardiography are correlated with the severity of heart failure. Besides, echocardiographic parameters are not the focus of this study, so we did not include them in the article.**

b.Line 1: Study design needs to be specify in section "Methods". Why did you used a control group consisting of CP A cirrhotic patients without CCM? Please explain this in section methods.

**Thank you for your comment. As suggested, we have explained the reason for setting up the control group in the last paragraph of Part 2.1.**

c.You need to report the absolute value of patients with diastolic dysfunction in each group; it would be also appropriate to report the systolic dysfunction, and overall prevalence of CCM, respectively

**Thank you for your comment. Cardiology experts in our team believe that different from systolic function, the absolute value of the four criteria for the diagnosis of diastolic dysfunction cannot be correlated with the severity of heart failure, which is still represented by NT-proBNP currently. The relationship between NT-proBNP and RDW has been reflected in Figure 3. The overall prevalence of CCM and the incidence of systolic and diastolic dysfunction are redescribed in the first paragraph of Part 5.**

7.Regarding the section "A strong correlation between RDW and different Child-Pugh levels"

a.Line 5: How and why did you used the multivariate logistic regression to compare two groups?

**Thank you for your comment. Table 2 shows that RDW values of different Child-Pugh levels are significantly different in the comparison, indicating significant differences in the univariate analysis, so RDW values of each group were included in multivariate regression analysis of Table 3.**

8.Table 3: Please provide more information on how did you performed the multiple regression analysis, which method type did you used? It would be better to present the univariate and multivariate analysis in the same table.

**Thank you for your comment. Multiple regression analysis was used in Table 3 and the relevant parameters were described as follows:**

**Model Fitting Information Chi-Square=761.327, P＜0.001, indicating that the final model was more significant. Cox and Snell： Pseudo R-Square=0.779, indicating a good fitting degree.**

**Statistically significant indicators in Table 1 and Table 2 were included in the multivariate regression analysis in Table 3, so univariate regression analysis was not set up separately.**

9.Discussion

a.Line 2: Refers to old diagnostic criteria; for the diastolic dysfunction, you used the new diagnostic criteria

**Thank you for your comment. Actually, the new diagnostic criteria do not deny the characteristics of diastolic dysfunction delineated in the old criteria, so it is appropriate to refer to the related studies. This sentence, "CCM..... features a blunted contractile response to stress and altered diastolic relaxation", describes the characteristics of CCM.**

b.Line 5: I don't agree that systolic dysfunction in cirrhotic patients can be detected only with stress testing. GLS as a novel parameter can identify subclinical dysfunction also in resting situations.

**Thank you for your comment. GLS are not routinely monitored by echocardiography in many Chinese hospitals, and EF is still used as a common indicator to evaluate systolic function in clinic practice. In the absence of external stimulation, EF generally has no obvious abnormalities in the early stage of CCM.**

10.Conclusion: Increased RDW may be associated with cardiac dysfunction but is not diagnostic for diastolic dysfunction in CCM, this should be clarify.

**Thank you for your comment. We have clarified the relationship between RDW and diastolic dysfunction and revised the sentence.**