Dear editor,

Thank you very much for your letter on August 23, 2016, with regard to our manuscript (Manuscript NO: 28905). We greatly appreciate the comments and really have learned a lot from the reviewers' comment. Appropriate changes are made and highlighted in the revised manuscript. We made the following point-by-point responses to address the editors' and the reviewers' comments.

Major concerns

Q1: It would be helpful if the authors could show aspartate aminotransferase (AST) level and platelet count in Table 2 and investigated.

A1: Because the FIB-4 and APRI were calculated based on serum AST level and platelet count, it's very reasonable to give the data of AST and platelet count in the Table 2. From the results, we could find that the serum AST levels were significantly higher in NASH patients than those in controls and NAFL patients, but the platelet count showed no significant difference among these groups.

Q2: It would also be helpful to determine a diagnostic value of AST to platelet ratio index (APRI) and compare the diagnostic accuracy of different markers include miR-34a, ALT, CK18 and APRI with receiver operating characteristic curve analysis in the detection of NASH.

A2: It is surely a good point that needs to be elaborate on. The APRI was calculated as AST [× upper limit of normal] / PLT [10^9/L] × 100. The AUROC of miR-34a, ALT, CK18 (M30), CK18 (M65), FIB-4, and APRI for NASH was 0.811, 0.677, 0.697, 0.718, 0.676, and 0.727 in patients with NAFLD, respectively. The diagnostic value of miR-16, FIB-4, and APRI for significant fibrosis was 0.716, 0.835, and 0.853, respectively. Still, the AUROC of miR-34a for NAFLD was the highest. Compared with miR-34a, FIB-4 had the same sensitivity (0.704) but lower specificity (0.687) for the diagnosis of NASH, and APRI showed the same specificity (0.875) but lower sensitivity (0.556). For the diagnosis of significant fibrosis, miR-16 displayed a relatively lower AUROC than that of FIB-4 (0.835) and APRI (0.853). These results were listed in Figure 4 and elaborated on in the revised manuscript.

Q3: There seems to be a discrepancy between the data presented in table 3 and the result section (Page 13 line 12 and Page 14 line 1). This point needs checking.

A3: Thanks very much for your reminder. We have checked the results and analyzed our original data again to make sure that the results were correct. The correlation between hepatic steatosis and miR-122, -192, and -34a were 0.302, 0.323, and 0.470, respectively ($P<0.05$) and the correlation between inflammatory activity and miR-122, -192, and -34a were 0.445, 0.447, and 0.517, respectively ($P<0.01$). We have corrected the data in the Table 3.

Minor concern

Q: The authors concluded that circulating mi-R34 had a strong correlation with hepatic steatosis and inflammatory activity in Page 20 line 13, although the correlation coefficient is no more than 0.6. I suggest that circulating mi-R34 had a moderate correlation.

A: Thanks for the good advice. In order to make this manuscript more rigorous, we have corrected our expression as "Circulating miR-34a had a moderate correlation with hepatic steatosis and inflammatory activity.".

We believe that the comments by the respected reviewers and editor will surely improve our revised presentation, and we feel that these changes are more clear and persuasive. We hope the reviewers agree with our answers and the new version of this manuscript meets the standard of the prestigious journal of World Journal of Gastroenterology. Thank you very much for your kindly consideration.

With best regards.

Yours Sincerely,

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