Reviewer's report

Title: Independent association of HbA1c and nonalcoholic fatty liver disease in an elderly Chinese population

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Reviewer: Xin Gao

Reviewer's report:

This study provides solid evidence demonstrating an independent association between HbA1c levels and the occurrence of non-alcoholic fatty liver disease in an elderly community population including 1142 subjects. The finding are interesting, and suggest a central role of liver steatosis in the pathogenesis of glucose metabolic disorders in non-diabetic subjects. The conclusion can be consolidated by considering the points below.

1# Materials and Methods: Page 5, Line 77. HbA1c levels reflected average blood glucose exposure over the preceding 2-3 months, and could be affected remarkably by several conditions in a short time, e.g. glucose-lowering treatment, renal anemia, hemolytic anemia, et al. So subjects who have accepted glucose-lowering treatment or had anemia should be carefully excluded from the study in order to ensure that HbA1c stably and accurately reflect the state of glucose metabolism.

Page 5, Line 89. Please describe the measurement of waist circumference in detail.

2# Results: Page 8 Line 124. A great gender difference in the prevalence of NAFLD was reported in participants younger than 50 years according to the study by Bae JC et al. I encourage the authors to compare the prevalence of NAFLD between male and female participants in their elderly Chinese population.

Page 10 Line 173. How were parameters for multiple logistic regression analysis selected? Collinearity diagnostics should be performed and multivariate analyses modified accordingly.

3# Discussion: Paragraph 2. The most likely explanation for the association between HbA1c and NAFLD is not discussed. Hepatic steatosis played an important role in the pathogenesis of insulin resistance. The accumulation of excessive fat in liver could cause severe hepatic insulin resistance and increase the hepatic glucose production and export to the peripheral circulation, which is also characterized by an elevation of serum HbA1c. Studies by Yki-Järvinen H et al., D'Adamo E et al., and Bian H et al. and references within these articles shed light on the association. Therefore, insulin resistance is the most likely explanation for the increased HbA1c in NAFLD patients. Highlights from this study show that even in non-diabetic participants, serum HbA1c elevation within
the normal range is closely associated with non-alcoholic fatty liver disease, so a discussion should focus on the contribution of liver steatosis to the pathogenesis of abnormal glucose metabolism.

4# Discussion: Line 191. I understand the author’s rationale to explain the association between HbA1c and NAFLD from the perspective of erythrocyte stability and oxidative stress. Recent studies by Yu C et al. revealed the diagnostic value of hemoglobin for non-alcoholic fatty liver disease, and the HbA1c level could be affected by the lifespan of erythrocytes as well as serum hemoglobin concentration. If the blood samples are available for the patients, serum hemoglobin levels could be measured and included in the multivariate regression analysis to adjust for the effects of serum hemoglobin on the association between HbA1c and NAFLD. I recommend that the author should shorten his speculation in the discussion.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.