Author’s response to reviews

Title: What is the impact of metabolic syndrome and its components on reflux esophagitis? A cross-sectional study

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Dear Editor:

I appreciated receiving your reply of “What is the impact of metabolic syndrome and its components on reflux esophagitis? A cross-sectional study” (BMGE-D-18-00399R1) on December 11, 2018. We have made modification on the original manuscript based on the reviewers’ comments and request and proof-read the manuscript to minimize typographical, grammatical, and bibliographical errors. Here below is our description on revision.

Comment 1. First, being the major outcome or the sole dependent variable, reflux esophagitis was diagnosed in the majority (59.6%) of participants who underwent routine health check, which is extra-ordinarily high. Second, the vast majority of reflux esophagitis was diagnosed as Los Angeles Classification Grade A, which is well known to have poor interobservers' agreement and may lead to the questionable prevalence rate. Third, non-erosive reflux disease is believed to be more common than reflux esophagitis in Asian. Thus, the observation is likely due to overdiagnosis or misclassification. Overall, the possible misclassification may be a major thread to the validity of the study. Therefore it is recommended to evaluate the inter-observer agreement of the diagnosis of reflux esophagitis.

Reply: Thank you for your comments. We agree with you and acknowledge that the possible overdiagnosis may greatly affect the validity of our study. There are also other reasons may
explain the unusually high prevalence of reflux esophagitis, as follows: (1) Due to the upper gastrointestinal endoscopy was optional, relative invasive and high price, those who already had gastrointestinal symptoms tended to receive it. The above reason may lead to a higher prevalence rate of reflux esophagitis in our study than in the general population. However, this hypothesis was not confirmed due to lack of asking gastrointestinal symptoms in the initial questionnaire. (2) Poor interobservers' agreement was hard to avoid due to the upper gastrointestinal endoscopies were not done by the same performer in our health examination center. We have reflected this comment by revising the text (Discussion section, p.18-19, lines 301-313). We also added reference 36 as supporting evidence.

Comment 2. The methods to define H. pylori infection and hiatal hernia should be described. In fact, the most epidemiological data from Asian countries including Taiwan showed a negative association between H. pylori and RE.

Reply: Thank you for your kind reminder. We have accordingly revised the text (Methods section, p.9-10, lines 144-150, and Discussion section, p.19, lines 320-321).

Comment 3. The definition of alcohol consumption and smoking should also be described.

Reply: Thank you for your suggestion. There are only self-reports of smoking (yes or no), alcohol consumption (yes or no), and betel nut chewing (yes or no) were investigated. We did not investigate the type or quantity of smoking, alcohol and betel nut consumption in the questionnaire. We revised the text (Methods section, p.7, lines 114-116) to reflect this comment.

Comment 4. In table 3 of the revised manuscript, elevated TG is significantly associated with RE after adjusting age and sex, whereas elevated TG was not associated with RE in the results and abstract. Would it be possible to explain the discrepancy between them?

Reply: Thank you for your advice. We revised the text (Abstract section, p.4, lines 49-52, and Discussion section, p.14, line 230, and p.16-17, lines 271-273) to reflect this comment.

Comment 5. On page 18, line 13 'Second, the individuals with RE were not evenly distributed among the groups with LA grade A, B, and C. Because our study is a cross-sectional study rather than a randomized controlled trial, bias may occur in the treatment of study population.' I do not think that the distribution of RE severity has anything to do with either a cross-sectional study or randomized control trial.

Reply: Thank you for your suggestion. We agree with you and the following sentence “Second, the individuals with RE were not evenly distributed among the groups with LA grade A, B and C. Because our study is a cross-sectional study rather than a randomized controlled trial, bias may occur in the recruitment of study population.” has been deleted in the Discussion section.
A revised manuscript with the correction sections red marked was attached as the supplemental material and for editing purpose. All the lines and pages indicated above are in the revised manuscript. We acknowledge the reviewer’s comments and suggestions very much, which are valuable in improving the quality of our manuscript. Should you have any questions, please contact us without hesitate.

Sincerely yours,

I-Ching Lin