Author’s response to reviews

Title: Evaluation of Risk Factors for Perforated Peptic Ulcer

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Author’s response to reviews:

Dear Editor

Subject: Submission of revised paper “Evaluation of Risk Factors for Perforated Peptic Ulcer”, ID: BMGE-D-17-00333

We thank referees for careful reading our manuscript and for giving useful comments. We feel the comments will significantly improve our paper. In response to the Referees' comments, we have revised the manuscript. Our responses are given in a point by point manner below. We hope the revised version is now suitable for publication.

Sincerely,

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Our responses to the referees' reports are as follows:
RESPONSE TO EDITOR

We wish to express our strong appreciation to the EDITOR for insightful comments on our paper. We feel the comments have helped us significantly improve the paper.

Comment 1: Thanks so much for the chance to review this again. While the article itself is interesting, but in the era of widespread PPI use, especially in the West, I am not sure how generalizable this is. This is a single center study in one ethnic group.

Response: We thank the EDITOR for this pertinent comment.

We understand that this is a single center study in one ethnic group, thus generalization is difficult. We think this is a limitation of our study and added as our limitation part.

In accordance with the EDITOR’s comment, the following sentence has been inserted and changed the following text from (P 10, line 185).

There are some limitations in our study. Our study is a research at a single institution and targets only one ethnic group. Thus, generalization of our outcome into different ethnicity might be difficult and these could be a selection bias.

RESPONSE TO REVIEWER 3:

We thank you for your comments, which have helped us to substantially improve the manuscript.

Comment 1: To my Comment 8 [In table 1 and table 2, I found out that some variables are significant in Multivariate analysis but not significant in univariate analysis. This phenomenon might be caused by following four reasons; (1) the effect of unbalanced sample size; (2) the influence of missing data; (3) an extremely large within-group variation, relative to between-group variation; and (4) the presence of interaction. Please describe authors' view on this statistical phenomenon in authors' paper], Authors replied as follows "Moreover, the phenomenon which some variables are significant in multivariate analyses but not significant in univariate analysis is mainly coming from confounding factors." I would like to ask why authors thought that this result came from confounding factors. How can authors explain that this statistical consequence did not come from any of (1) the effect of unbalanced sample size; (2) the
influence of missing data; (3) an extremely large within-group variation, relative to between-group variation.

Response: Thanks you for the insightful comment.

I agree with the Reviewer’s comment above, the following sentence has been inserted and changed the following text from (P 11, line 194).

Moreover, the phenomenon which some variables are significant in multivariate analyses but not significant in univariate analysis is mainly coming from confounding factors. In addition, the effect of unbalanced sample size, the influence of missing data and an extremely large within-group variation, relative to between-group variation are other variables, contributing to the discrepancy.

Comment 2: To my Comment 11 [Authors described "increase in platelet count was statistically significant in PPU, and could be used as a prediction factor. Platelets are the component of blood, necessary to arrest bleeding, thus thrombocytopenia is the known cause of bleeding. In our PPU study, however, platelet counts were significantly increased. We presumed that peritonitis caused inflammation and perforation stimulated coagulation; therefore, platelet counts were increased especially in the PPU patients." Do you think this is the logical explanation? You said that thrombocytopenia is the known cause of bleeding AND said stimulated coagulation is the cause of thrombocytopenia. Would you please show logically missed explanation to make me understand?], Authors replied as follows ""We presumed that peritonitis caused inflammation and perforation stimulated platelet aggregation; therefore, platelet counts were increased especially in the PPU patients." I would like to ask authors to re-consider this phenomenon as the result of "reactive thrombocytosis".

I will wait for your reply.

Response: Reactive thrombocytosis is the word I wanted to use for describing the phenomenon. Thank you very much for your recommendation. In accordance with the Reviewer’s comment above, the following sentence has been inserted and changed the following text from (P 10, line 183).
We presumed that peritonitis caused inflammation and perforation stimulated platelet aggregation; reactive thrombocytosis is a phenomenon seen in the PPU patients. therefore, platelet counts were increased especially in the PPU patients.

RESPONSE TO REVIEWERs:
We wish to express our strong appreciation to the Reviewer for insightful comments on our paper. We feel the comments have helped us significantly improve the paper.

Comment from Reviewer 1): After revisions the paper is well written and organized.
Comment from Reviewer 3): The article is well developed. I need no revisions.
Comment from Reviewer 4): Thanks so much for the chance to review this again.

Response: We thank the Reviewer for this insightful comment.