**Author's response to reviews**

**Title:** Factors associated with peritoneal metastasis in non-serosa-invasive gastric cancer: a retrospective study of a prospectively-collected database

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Respond to the reviewer's comments (MS: 3839975926627486 - Factors associated with peritoneal metastasis in non-serosa-invasive gastric cancer: a retrospective study of a prospectively-collected database)

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript. Those comments are all valuable and very helpful for revising and improving our paper. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

Reviewer 1 (Douglas Curran-Everett)

1. Abstract. Results, page 3. Of what value are paired correlations between age, Borrmann type, etc and peritoneal dissemination when those factors may be interrelated? Why not simply present results from the Cox regression so you can comment on the impact of one factor after taking into account the other factors?

Reply:

Many thanks for your good suggestion. In this study, we want to investigate the factors associated with peritoneal dissemination in patients with non-serosa-invasive gastric cancer. As known to all, free cancer cells (FCC) in the peritoneal cavity is the direct cause for peritoneal metastasis in gastric cancer. First of all, we assessed the correlation between clinicopathological factors such as age, Borrmann type, etc and peritoneal dissemination using univariate analysis. Considering interrelationship maybe exist among the
clinicopathological factors each other, multivariate analysis by logistic regression was used to further assess the correlation between clinicopathological factors and peritoneal dissemination. This could eliminate the bias from the interference among clinicopathological factors. In the following survival analysis, Cox regression was used to estimate the prognostic factors, so we can comment on the impact of one factor after taking into account the other factors.

2. Throughout the paper. Percentages can be rounded to the nearest integer. Is 0.1% all that important?

Reply:

Thank you for your constructive question. In this revised manuscript, percentages was rounded to the nearest intiger shown in red color.

3. Abstract. Results, page 3, 4 lines from bottom. INF, Borrmann type, and TNM node stage were correlated with what?

Reply:

Many thanks for your good suggestion. In abstract results, INF, Borrmann type, and TNM node stage were correlated with peritoneal dissemination by multivariate analysis. This was added in red color.

4. Methods, page 7, line 5. Why report mean follow-up for a skewed distribution? Mean follow-up is not meaningful. Median and range are sufficient.

Reply:

Many thanks for your constructive question. In the revised manuscript, mean follow-up period was deleted.

5. Figure Legends. The Figure Legends are mislabeled. My copy of the manuscript had duplicate copies of Figures 4-6.

Reply:

We are very sorry for our negligence of the mislabeled. In the revised manuscript, we merged the figure 1A, B and C into one picture named figure 1. The survival curves in relation to INF, Borrmann type and TNM node stage were redrewed and named figures 2-4. The figure legends has been relabeled in the revised manuscript.

6. P values, throughout the manuscript. P values greater than 0.01 can be rounded to 2 decimal places. Anything more is artificial precision.

Reply:

Thank you for your good suggestion. In the revised manuscript, P values greater than 0.01 has been rounded to 2 decimal places as shown in red color, including
the tables.

7. Tables 2 and 4. Why include the actual coefficients, SE, and Wald values? The hazard ratios, P values, and conf intervals are sufficient.

Reply:

Thank you for your good question. In the revised manuscript, In tables 2 and 4, coefficients, SE, and Wald were deleted.

8. Table 3. A SD is reported better as 59.6 (SD 9.9). The +/- is superfluous since a SD is a single positive number.

Reply:

Many thanks for your good suggestion. In table 1 and 3, A SD has been reported as the style as you advised.

Reviewer 2 (Richard Szydlo)

1. In the Results section "Univariate and multivariate analyses of peritoneal metastasis" hazard ratios are quoted for various factors (table 2). Table 1 shows univariate analyses of categorical data. The multivariate extension of univariate analyses is logistic regression which generates odd ratios and not hazard ratios. Reference groups should be included in the multivariate table as well as numbers of patients in each group.

Reply:

Many thanks for your good suggestion. In the revised manuscript, odd ratios took the place of hazard ratios, and reference groups as well as numbers of patients in each group were included in table 2 in red color.

2. The survival analysis. Only 70 patients were included in this analysis? Why was the analysis restricted to over 10 yrs follow-up.? From the survival curves in the figures it would appear that there are many more than 70 patients included. Table 4 shows results of the multivariate analysis, but shows that variables were added as a continuous variable instead of categorical. No reference groups are presented and we have no idea how many patients were included. Showing isolated univariate analysis is not appropriate if there are additional factors that have a strong influence on outcome.

Reply:

Many thanks for your constructive question. In this study, all the 685 patients were included into the cox regression model simultaneously. The previous reviewer (Gabriel Glockzin) suggested that the number of patients with 10-year follow-up should be indicated. So we added it in the text. In the revised manuscript, we removed this sentence. We reanalyzed the prognosis by cox
regression model using categorical variable. The reference groups as well as numbers of patients in each group were added in table 4 in red color. The survival curves in relation to INF, Borrmann type and TNM node stage were redrewed in the revised manuscript.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper. We appreciate for the reviewer’s positive comments and elaborative revision concerning our manuscript and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

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