ANSWERING REVIEWERS

February 14, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7223-review.doc).

Title: Should peri-gastrectomy gastric acidity be our focus among gastric cancer patients?

Author: Lei Huang, A-Man Xu, Tuan-Jie Li, Wen-Xiu Han, Jing Xu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 7223

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
(1) Reply to Reviewer #02537595:

a) *English editing is required.*

We thank the reviewer for the suggestion. The manuscript has been edited by a company.

b) *Abstract-Result: (1) '~higher RDQ (TG vs PG~' -> TG vs. DG, (2) '~GERD-Q scores (TG vs PG~' -> TG vs. DG*

We thank the reviewer for the thoughtful suggestions. Corrections have been made accordingly.

c) *RESULTS-3.2: (1) '~higher RDQ (TG vs PG~' -> TG vs. DG, (2) '~GERD-Q scores (TG vs PG~' -> TG vs. DG*

We thank the reviewer for the thoughtful suggestions, and corrections have been made as guided.

d) *RESULTS-3.4: the order of several values (A vs. B) should be changed like B vs. A*

We thank the reviewer for the constructive suggestion, and have made the changes accordingly.

e) *Regarding RDQ and GERD-Q, it is important to compare pre- and post-gastrectomy scores instead of one spot score. I recommend the authors would make Table 3 by using the score change (pre- and 6 months post-) instead of 6 months score.*

We thank the reviewer for the thoughtful and constructive suggestion. As pointed out by the reviewer, it's much better to analyze the score change rather than one spot score when RDQ and GERD-Q scores are concerned, and we've re-made Table 3 as suggested. Accordingly, the relevant contents in the text have been changed (RESULTS-3.3 and DISCUSSION).

(2) Reply to Reviewer #02528467:

Although the not a very hot topic it deserves attention and therefor I think can be published in WJG .

Sincerest thanks for the reviewer's positive, supportive, thoughtful and constructive comment.

(3) Reply to Reviewer #01426893:

a) *Please explain the objective to collect gastrointestinal juice for the first 5 consecutive post-operative days.*

The reviewer has raised a good question. The objectives are: 1) to investigate from what day on the post-operative gastrointestinal juice pH will reach a stable level, and a level similar to that a long period (6 months) post-gastrectomy, 2) to observe the detailed trend of perioperative gastrointestinal juice pH, and 3) to monitor whether a specific patient's pH on a specific postoperative day without acid suppression reaches below 4, which is a risk factor of stress ulcer, and relevant actions will be taken accordingly then. Besides, perioperative gastrointestinal juice samples are easily obtained through the gastric tube.

b) *Please explain if gastrointestinal juice could be collected after total gastrectomy with a method similar to the cases after proximal gastrectomy or distal gastrectomy in apite of no space to pool gastrointestinal juice. Please address if any modifications were needed in the current procedure.*

We thank the reviewer for the thoughtful question. As pointed out by the reviewer, there may be no space to pool gastrointestinal juice after the whole stomach is removed. However, we believe that the gastrointestinal juice samples could still be collected, and actually we do have obtained them. Possible explanations are: 1) patients lie on bed most of the time in a day post-gastrectomy, and fluid could easily enter the tube, 2) the suction disc attached to the tube is accompanied with negative pressure, facilitating the absorption, 3) the bowel function does not recover completely in a short time post-gastrectomy, and even reverse peristalsis may exist, leading to ineffective transmission of fluid secreted to the distal intestine, and 4) there are side holes on the gastric tube wall, which facilitate entrance of the fluid. What's more, patients lie on different sides in a day during sample collection, and we collected the juice every 24 hours.

As pointed out by the reviewer, there may be modifications needed. However, we cannot think out of any better procedure to be performed on a patient undergoing gastrectomy during the perioperative days, with the patient's consent and under the guidance of Helsinki Declaration. We are looking forward to learning from the reviewer about what other possible methods could be taken.

c) *A change in gastric emptying from vagus nerve blocking might also contribute to GERD symptoms after gastrectomy. Are there any data to suggest this factor in this study? Irrespective of data availability, please discuss the following point, i.e., a potential change in gastric emptying after the operation.*

We thank the reviewer for the thoughtful and constructive suggestion. As pointed out by the reviewer, bowel function may be influenced by blocking vagus nerve, leading to a delay in gastric emptying, which might contribute to GERD symptoms. For the sake of safety and complete clearance of tumor cells, however, we believe it's better to remove the nerve near the malignant lesion, in case of nerve invasion. Besides, it's difficult to preserve the nerve in some cases. As mentioned in our manuscript, we cut both vagus trunks during total and proximal gastrectomy, and cut the gastric brunch of the nerve in distal gastrectomy. We have not got any specific data indicating GERD symptoms due to the change in gastric emptying caused by vagus nerve blocking. As instructed by the reviewer, we have added discussion of potential change in gastric emptying after gatrectomy in the DICUSSION part of our manuscript accordingly.

d) *Since GERD might also be associated with hiatus hernia, please address any findings of hernia before/after the operation.*

We thank the reviewer for the thoughtful comment and suggestion. As pointed out by the reviewer, hiatus hernia also contributes to GERD. As mentioned in our text, 'patients having other gastroenterological diseases were excluded from our study', and there were not any findings of hernia indicated by X-ray and gastroscopy before operation among the patients included in the final analysis. During the postoperative follow-up, again, no finding of hernia was observed suggested by X-ray, which might be partly explained by the fact that most Chinese patients were accompanied with relatively low body mass index. Besides, our delicate operation and a relatively short follow-up period might also contribute to the 0 findings. We have addressed this issue in our text as suggested (METHODS AND METERIALS-*Patients and specimens* and RESULTS-3.2).

e) *Please describe the presence/absence of esophagitis before the operation and 6 months after the operation, if any data are available.*

We thank the reviewer for the thoughtful and constructive suggestion. As mentioned in our text, 'Before operation, patients were certified to be free from successive diseases associated with reflux by endoscopy', and patients with esophagitis possibly caused by reflux were excluded in our study. After surgery, for patients receiving total gastrectomy, no one would be willing to undergo another gastroscopy, mainly because they believe that their whole stomach had been removed, and that it's useless for a novel 'gastric examination'; while for those undergoing proximal or distal gastrectomy, informed consent for a new test was only available from a very limited number of patients, which was not applicable in the statistical analysis, for most of them were unwilling to endure the pain of undergoing gastroscopy, which was invasive, again.

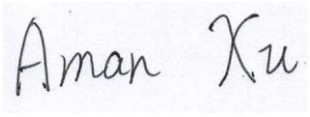
f) *Please describe any limitations of this study.*

We thank the reviewer for the reminder, and have added the limitations of our study in the DISCUSSION part of our text.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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