

Dear Editors,

Thank you very much for your letter and advice.

We have revised the manuscript, and would like to re-submit the enclosed manuscript entitled "**Determining the usefulness of a nomogram for predicting prolonged postoperative ileus in gastric cancer patients who underwent gastrectomy**" for your consideration.

We have addressed the comments raised by the reviewers. The point by point responses to the reviewers' comments are listed below this letter.

We deeply appreciate your consideration of our manuscript

I look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Corresponding author, **Lin Chen**

Prof. and Chairman of General Surgery Dept.

China PLA General Hospital

28#Fu-Xing Rd, 100853 Beijing, China

E-mail: linchenbj@163.com

We would like to express our sincere thanks to the reviewers, the editor and the editorial staff for the constructive and positive comments. We have conducted a point-by-point responses to these comments.

-----

Reviewer 1

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Comments To Authors: I would like to mention the following comments:

1- Introduction: A previous history about application of Nomogram is missing.

**Response** : We appreciate this comment about the manuscript. We have supplemented previous study of nomogram in the introduction (Page 5, Line 221-23), including the previous nomogram used in gastric cancer (Reference 16).

2- Method: A special part for explanation about nomogram is needed.

**Response**: We are very appreciated with these important suggestions. We have supplemented the explanation about nomogram in Methods (Page 8, Line 19-22 and Page 9, Line 1-2).

3- Results: Some explanations about Nomogram is better to move to method section.

**Response** : We are very appreciated with these important suggestions. Explanations about nomogram in Results have been moved to Methods.

4- Method: Is it not clear if the sampling method is random or not.

**Response** : We are very appreciated with these important suggestions. The computer resampling used a strategy of simple random sampling with replacement. We have added these information in Method (Page 9, Line 3-5)

5-Discussion: It might be better to rewrite the discussion section with the following paragraphs: Main findings (without percentages and references), similar studies, different

studies, limitations, conclusion. Good Luck

**Response** :We have rewritten the discussion following the important suggestions from the

reviewer. Thank you for your suggestion. A logical and concise discussion has been shown in the revised manuscript including main findings (Paragraph 1), similar studies and different studies different angles (Paragraph 2 for incidence and age, Paragraph 3 for laparoscopic approach and opioid analgesic, Paragraph 4 advantage of nomogram), strength and limitations (Paragraph 5), conclusion (Paragraph 6).

-----

Reviewer 2

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

This is a retrospectively analysis about PPOI in propsectively collected patients who underwent gastrectomy for gastric cancer. The authros stressed on the usefulness of nomogram of PPPI in patients in gastric cancer. which can be used in the real clinics. Because the authors analyzed the data using the detail statiscial methods, the results stated in this manuscrit are proper. In spite of these merits, there are several issues to be concerned.

(1) As stated in the discussion section, the number of included paitients is not enough.

**Response** :We understand the concern that reviewer put forward about the number of the included patients. This study was retrospectively analyzed, one reason for the small number of cases was that all data in this study were from a prospectively collected registry database. Because of the diagnosis of PPOI was made at specific time and not a routine in clinical practice, data were difficult to obtain retrospectively from medical records. In order to make up this limitation, we sought to validate this model by bootstrap for 500 repetitions. The AUC and calibration curve of the bootstrap repetitions demonstrated good performance of the prediction model.

(2) The surgical methods used in this study are not well described. For example, patients who underwent total gastrectomy tend to have a higher frequency of PPOI. Therefore, more analysis based on the degree of gastrectomy (distal vs. total) and reconstruction

method (B-1 vs B-2 vs REY) should be included. In addition, the degree of LN dissection (such as D1, D2, and D2+alpha) should be included in the analysis.

**Response** : We are very appreciated with these important suggestions. We have added the information of the degree of gastrectomy (total gastrectomy vs proximal gastrectomy vs distal gastrectomy) and lymph node dissection (D1+ vs D2) for analysis in the revised manuscript (Table 1 and 2). However, the reconstruction methods are to some extent depended on the degree of gastrectomy and have many unified classification (B-1, B-2, REY, gastroesophagostomy, esophagojejunostomy, and so on). We think it is not suitable for further analysis.

(3) The use of gender and sex is mixedly used.

**Response** : We are very appreciated with these important comments. We have changed gender to sex in the revised manuscript.

-----  
Reviewer 3

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

This is an interesting paper, which deserves publication, more in a surgical journal than in a gastroenterology journal.

I have few major points :

-this is a retrospective study, and a nomogram inevitably describes the "story" of the surgical intervention, and it is not necessarily predictive of the future. The Authors should confirm the validity of the nomogram in a prospective study.

**Response** : We understand the concern that reviewer put forward. This study was retrospectively analyzed and prospective multicenter studies about PPOI are ongoing and results are expected. In order to make up this limitation the design (retrospective), we sought to validate this model by bootstrap for 500 repetitions. The AUC and calibration

curve of the bootstrap repetitions demonstrated good performance of the prediction model.

-I do not understand if all patients had total gastrectomy, or not. From their valid experience, it is evident that the more advanced the disease, and therefore more extended the operation, higher the possibility of PPOI.

**Response :** We understand the concern that reviewer put forward and we are very appreciated with these important suggestions. We have added the information of the degree of gastrectomy (total gastrectomy vs proximal gastrectomy vs distal gastrectomy) and lymph node dissection (D1+ vs D2) for analysis in the revised manuscript (Table 1 and 2).

Minor points:

-In page 4 there is a mistake, the Authors stated that PPOI rate was higher in younger patients. This is not the case in their results.

**Response :** We are very appreciated with these important comments. We made some slips (of the pen) in previous report and have revised it as following: The risk of PPOI among patients aged  $\leq 60$  years was **lower** than those aged  $>60$  years (OR=0.43, 95% CI 0.19–0.95, P=0.033).

-The introduction is too long and it should be shorten considerably -Similarly the discussion is too long and it should be shorten considerably. In the conclusions it should be underlined the importance of a proper, less traumatic operative technique to prevent prolonged PPOI, and the importance to reduce post-operative pain medications.

**Response :** We are very appreciated with these important comments. We have rewritten the introduction (from 450 to 363 words) and discussion (from 1556 to 1037 words) following the important suggestions from the reviewer. We have highlighted the importance of less traumatic operative technique and avoidance of postoperative pain medications for gastric cancer patients in the conclusion (Page 15, Line 19-20).

-----  
Reviewer 4

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

In this manuscript the authors propose a nomogram for predicting prolonged postoperative ileus in gastric cancer patients who underwent gastrectomy. The study was conducted with methodological rigor. The results obtained may be confirmed by other publications on the subject.

**Response** : We would like to express our sincere thanks to the reviewer for the constructive and positive comments.