

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "**A retrospective analysis of surgically treated pT4b gastric cancer with pancreas head invasion at National Cancer Center in China**" (Manuscript NO.: 68720, Retrospective Study). All of these comments were valuable to revise and improve the quality of this manuscript. We have carefully studied the comments and have made the necessary corrections that we hope will meet your approval. The main corrections in the paper and our responses to the reviewer's comments are as follows.

Responses to the reviewer's comments:

Reviewer #1: This is a unique study comparing two types of surgery in pT4b locally advanced gastric cancer 1. What was the selection criteria of doing a GP or a GA. That should be more clear.

1. Response to comment: Thank you for your good comments. We have added the statement at "SURGICAL PROCEDURES" as follows: The curative-intent GP procedures were performed with en-bloc gastrectomy combined with pancreaticoduodenectomy and D2 or D2+ lymphadenectomy when the surgeon considered pancreas invasion during operation. En-bloc gastrectomy with D2 or D2+ lymphadenectomy without pancreatectomy defined as GA was performed when the surgeon considered macroscopically inflammatory reactions, but postoperative pathology confirmed pancreatic invasion.

2. What kind of surgery is GA? Please elaborate... In many places it is written as palliative gastrectomy...

2. Response to comment: Thank you for your good comments. We have added the statement at "SURGICAL PROCEDURES" as follows: En-bloc gastrectomy with D2 or D2+ lymphadenectomy without pancreatectomy defined as GA was performed when the surgeon considered macroscopically inflammatory reactions, but postoperative pathology confirmed pancreatic invasion.

3. The details of neoadjuvant treatment should be more clear... which type of chemotherapy is used and how many cycles... Why were some patients taken up directly for surgery and why some were given neoadjuvant treatment... The arms are not balanced...

3. Response to comment: Thank you for your good suggestion. We have added one paragraph at "MATERIALS AND METHODS" to explain this more clearly. As a national cancer center, we have patients from all over the country. Therefore, different patients received different treatments pre-operation. We have explained this limitation

at the “DISCUSSION”.

4. The details of adjuvant treatment should also be more clear as it can play an important role in final outcome. What was the differentiating factor in giving a patient post operative radiotherapy or post operative chemotherapy... If chemotherapy was given how many cycles? What protocol? And if radiotherapy was given what dose? Was it combined with concurrent chemotherapy... When we are discussing about overall survival of any patient the details of adjuvant treatment are very important...

4. Response to comment: Thank you for your good suggestion. We have added one paragraph titled “ADJUVANT CHEMOTHERAPY” at “MATERIALS AND METHODS” to explain this more clearly.

Reviewer #2:

Specific Comments to Authors: This article is about the efficacy of pancreaticoduodenectomy combined with gastrectomy in patients with gastric cancer invading the pancreatic head. I agree that a pancreaticoduodenectomy is an important option for R0 resection. However, I have several comments. Major 1. Among the patients who underwent palliative gastrojejunostomy, were there patients who had to have the possibility for curative resection by PD? If yes, I am interested in the comparison between patients who underwent PD and gastrojejunostomy.

1. Response to comment: Thank you for your good comments. I couldn't agree with you more on that some patients with palliative gastrojejunostomy can indeed undergo radical surgery. We have compared the overall survival of these patients. Unfortunately, patients with palliative surgery have a worse prognosis. However, the aim our study is to compare the two surgical procedures for T4b patients.

2. According to the inclusion and exclusion criteria, all GA patients seem to be R1 or more, which might have greatly affected the comparison of overall survival between GP and GA groups. It is unclear because there was no information about this factor in Table 1.

2. Response to comment: Thank you for your good comments. We have added surgical margin and revised table 1 as you suggested.

3. The way of neoadjuvant and adjuvant treatment is unclear. Did patients receive neoadjuvant for 6 months? Did patients receive adjuvant treatment for 6 months regardless of R0 or R1/2? What if in the case of recurrence?

3. Response to comment: Thank you for your good suggestion. We have added one paragraph titled “ADJUVANT CHEMOTHERAPY” at “MATERIALS AND METHODS” to explain this more clearly.

4. Most importantly, the GP or GA was not a prognostic factor in the multivariate analysis. The authors concluded that GP should be performed to prolong survival, but this conclusion is not supported by their results.

4. Response to comment: Thank you for your good comments. We have added surgical margin at table 1 as you suggested. Multivariate analysis have indicated surgical margin (HR 0.274; 95% CI 0.102–0.738; $p = 0.010$) as independent predictors of survival. The GP or GA was associated with surgical margin.

5. Discussion section should be constructed better. Minor 1. Abbreviations should be defined at their first mentioned there. 2. The approval number of IRB should be mentioned. 3. There are some misspellings in the manuscript and table. (p8 “PGA group”, Table 3 “Tumor tpye”) 4. If p values were less than 0.001, <0.001 would be better than 0.000 in the tables. 5. Chi2 in table 3 might be inappropriate. HR would be appropriate.

5. Response to comment: Thank you for your good comments. 1. We have revised as you have suggested. 2. We have added the approval number at “MATERIALS AND METHODS”. 3. We have checked and revised the whole manuscript for misspelling. 4. We have revised accordingly as you suggested. 5. We have replaced Chi2 with HR. We hope the revised manuscript meets your approval.

EDITORIAL OFFICE’S COMMENTS:

Response to comment: Thank you for your good comments. We have revised accordingly.