

Dear Editors and Reviewers:

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript entitled "Recurrence and survival after surgery for pancreatic cancer with or without acute pancreatitis. (Manuscript NO: 50682) again. We are very sorry for our negligence in the main text. The three special comments from the editor have been modified respectively. The second revision was marked with red color. The changes were listed as follows:

1. Article highlights was added with red color.
2. The grant application form(s) or certificate of funding agency was uploaded.
3. Figures were removed in the text and decomposable figure of figures was submitted as "Manuscript No. 50682-Figures.ppt" on the system.
4. Figures numbered was corrected with red color in the RESULTS.

All the first revisions were highlighted with yellow. The changes in the first revision were listed as follows:

1. Considering the Reviewer's suggestion, we have summarized the common etiology of acute pancreatitis in the first paragraph of Introduction which was highlighted with yellow. Some new contents highlighted with yellow were added in the Discussion. Decomposable figure of figures were added.
2. The abstract has been modified according to the word count requirement.

3. The key words were added according to the count requirement.

4. The reference numbers were deleted the space.

5. At the end of the first paragraph in the Results, the etiology and complications were added.

6. PubMed citation numbers and DOI citation to the reference list were added. All authors were listed in the reference. Duplicate reference has been removed.

7. Abbreviations were deleted in the title of the figure/table. And all the abbreviations of each figure/table were explained under each piece of figure/table legends.

8. The wrong data in the table have been corrected. The modified data were highlighted with yellow.

9. All vacant columns have been completed according to the editor.

we appreciate editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are highlighted in the updated version of the manuscript. The wrong data in the table have been corrected. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: in the study it's need to determine the etiology of acute pancreatitis in the patients with pancreatic ductal adenocarcinoma.

Response: It is really true as reviewer suggested that we need to determine the etiology of acute pancreatitis. So we reviewed the patients' etiology data and added them to table1. 5 of 21 AP were caused by ERCP operation. 9 of 21 AP were due to alcoholic factor. The etiology of remain 8 cases was unknown.

2. Response to comment: in the Introduction should be necessary more order in the definitions of each acute pancreatitis etiology

Response: Considering the Reviewer's suggestion, we have summarized the common etiology of acute pancreatitis in the Introduction. There are a large number of etiological factors involved in the development of acute pancreatitis (AP). Excluding common etiologies, such as alcohol and gallstones, it is well known that the onset of acute pancreatitis (AP) may be due to cancer progression itself or to complications of the diagnostic and therapeutic interventional procedures used in pancreatic ductal adenocarcinoma (PDAC) treatment, such as endoscopic retrograde cholangiopancreatography (ERCP), surgery and chemotherapy. In our study, according to the patients' data, the etiology of acute pancreatitis included ERCP, alcohol consumption, and unknown.

3. Response to comment: define the interval time between the AP attack and

the surgery for PDAC

Response: We appreciate editor so much for his/her constructive suggestions that we need to define the interval time between the AP attack and the surgery for PDAC. we reviewed the patients' data. The interval time started with clinical suspicious diagnosis. Due to the necessary preoperative treatment, the average interval time between the AP attack and the surgery for PDAC was 41.4 days. The average interval time of No-AP group was 10.8 days for preoperative preparation. The corresponding data have been added in the table1.

4. Response to comment: In the Discussion can be useful the clear definition of the role of acute pancreatitis on the evolution and on the therapeutic results of surgical treatment of PDAC: the etiological relationship, the effect of AP on the immediate results, on recurrence rate, on long-term survival of pancreatic ductal adenocarcinoma

Response: Considering the reviewer's suggestion, we added corresponding contents in the Discussion. First of all, AP was negatively associated with survival time and early recurrence. Secondly, the exact mechanism of PDAC evolution affected by AP is poorly understood and needs to further study. At last, AP improved the grade B/C pancreatic fistula occurrence rate. Although there was no difference of statistics due to the small sample, the incidence of pancreatic fistula was significantly higher in AP group. Besides, our previous study suggested that AP was an independent risk factor for pancreatic fistula

after pancreaticoduodenectomy.

Reviewer #2:

1. Response to comment: To emphasize the particular importance of the findings, it may be helpful, to give some notes, mentioned in the concluding "limitation paragraph" in Discussion, as an emphasize already in Introduction.

Response: We appreciate editor very much for his/her constructive suggestions. We agree with the comments by the editor. Although the sample size of our present study was small. The relatively low incidence of moderate or severe AP of PDAC and the low radical resection rate, makes that even an relatively small simple size would be particularly indicative. The corresponding explanation has been added in the concluding "limitation paragraph" in Discussion. Special thanks to you for your good comments.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

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

Yours

sincerely,

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