

Dear editor and reviewers:

Thank you for your letter and your comments. Please allowed me to express my sincere gratitude for your valuable and helpful comments in peer reviews which help improve the quality and have important guiding significance to our researches entitled “ *Clinical value of extended lymphadenectomy in radical surgery of pancreatic head carcinoma at different T stages*”. We have studied those comments carefully and have made revision which marked by using BLUE colored in the paper. Revised portion can be found in the paper. The main corrections in the paper and the responds to the comments are as follows:

**Reviewer #1:** The manuscript entitled "Clinical value of extended lymphadectomy in radical surgery of pancreatic head carcinoma as different T stages" by Shao-cheng Lyu describes a study that aims at evaluating the effects of extended lymphadenectomy on long-term prognosis of patients at different T stage. Their results suggests that extended lymphadenectomy may promote prognosis in PHC patients at T3 stage. The study was performed with adequade methods and obtained interesting results. It has to be emphasized that the study has important limitations, including the fact that the avarage age of extended lymphadenectomy group was younger than standard lymphadectomy group, and this might have been a crucial bias for the results obtained. However, the results still have clnical significance. The manuscript language should undergo a thorough revision. The manuscript file is not formatted according the requirements of the manuscript guidelines of this journal and it should be adjusted as well.

**Reply:** Thank you for your pertinent suggestions. The statistic difference of average age between extended lymphadenectomy(ELD) group and standard lymphadenectomy(SLD) group mentioned in your review was noticed during our research. Considering the close correlation between age and surgical tolerance in patients, we tend to perform ELD in relatively young patients

which may attribute to this difference in age and it do cause a bias which may have a negative effect on our result and conclusion as you pointed out. Thus, we agree with your comments that our study has a selection bias and add this limitation in the last paragraph in discussion to address this problem. However, this selection bias truly observed in our study may be inevitable since it is a single-center retrospective study, urging the necessity to carry out a multi-center prospective study to further verify our result in the future. Besides, the statistic difference in age between ELD and SLD in our research may have little effect on our result and conclusion because age was not identified as an risk factor for postoperative prognosis in patients that received ELD and SLD, according to randomized controlled studies and our previous studies. Therefore we think that our result and conclusion is still of clinical value. As for the language and file, we have already revise the manuscript according to the guideline of magazine. Thanks again for your suggestion, we believe the quality of our research will improve under your comments!

**Reviewer #2: Confined Major points**

**1. Patient selection: The study period was Jan 2011 to Dec 2021; therefore, some patients were followed up less than 6 months. To perform accurate survival analyses, all (survived) patients should complete the index period of follow-up (in this study, 3 years).**

**Reply 1:** Thank you very much for your comments. In our research we retrospectively analysed the patients who were diagnosed as pancreatic head carcinoma and received surgical treatment in our hospital from Jan 2011 to Dec 2021. As you mentioned in peer review, all survival patients should complete the 3-year followed-up period which is ideal for survival analysis, requiring an earlier study period and early follow-up period in our research. However, this will inevitably cause an exclusion of recent qualified patients. Thus we adopt Kaplan-Meier methods to calculate the survival outcomes and

eliminate the negative effect of patients with short follow-up period on overall survival outcome and survival analysis. Besides, since the 1-year survival rate of pancreatic head carcinoma is about 50%, patients with pancreatic head carcinoma should be followed up at least 1 year. In our researches, 28 patients were followed up less than 1 years, having little effect on the overall survival outcome. To make this point clear, we revised the "statistic analysis" in method part to clearly illustrate the methods we applied in our research.

**2. Inclusion and exclusion criteria: How many patients had adjacent arterial (celiac, common hepatic, and superior mesenteric artery) invasions? How many patients underwent surgery without en bloc resection? And how many patients were lost to follow-up? A flow diagram of the patient recruitment may be helpful for the queries.**

**Reply 2:** In terms of the inclusion and exclusion criteria, the description of included and excluded patients was unclear in our manuscript as you mentioned. We adopt the flow diagram in our revised manuscript to illustrate the recruitment procedure according to your advice. Thanks again for your comments!

**3. Classification of portal vein invasion and surgical procedure (Line 128-139): Are the Chaoyang classifications available in the literature? If so, please add the citations. If not available, additional simple figures may help readers for better understanding.**

**Reply 3:** Chaoyang classification is a classification of portal vein invasion that put forward by our department and had been published before. It is a classification basing on the site and length of portal vein system invasion and recommended the optimal surgical procedure to restore the continuity of portal vein system. In our manuscript we failed to illustrate the specific classification and the corresponding surgical procedure which can cause difficulty in understanding. To address this problem, we added the citation of our published research at the relevant part in our revised manuscript according to

your comment.

**4. Figure 1 and 2: For readers who are not familiar with Japanese classification, it may be useful to show some schema with extent of lymph node dissection locating the designated lymph node stations.**

**Reply 4:** Figure 1 and 2 was the picture taken intraoperatively that illustrate the extent of lymph node dissection in extended lymphadenectomy (ELD) group and standard lymphadenectomy (SLD) group, which may be abstract and difficult for readers to understand. Therefore we adopted the schema of lymph node station from “International Study Group on Pancreatic Surgery. Definition of a standard lymphadenectomy in surgery for pancreatic ductal adenocarcinoma: a consensus statement by the International Study Group on Pancreatic Surgery (ISGPS) ” and make appropriate adaptation before it is used in our research to visualize the extent of lymph node dissection, which are Fig 2-A, B. Please allow me to express my gratitude for your comment again !

**5. The possible impact of perioperative chemotherapy: Recently, the efficacy of neoadjuvant chemotherapy and the advance of systemic chemotherapy using molecular targeting agents have been shown to improve survivals of patients with PHC. Discussion may include these updates as well as the importance of surgical resection with appropriate extent of lymph node dissection.**

**Reply 5:** With the rapid progression in medical science, the treatment of pancreatic head carcinoma(PHC) is gradually transforming to a comprehensive treatment pattern centered on surgeries, including preoperative neoadjuvant chemotherapy and postoperative systematic chemotherapy which are gradually gaining its popularity. Currently neoadjuvant chemotherapy are widely used in patients with pancreatic carcinoma and become the first-line treatment for borderline resectable pancreatic carcinoma according to NCCN guidelines. Molecular targeting agents has also been used in clinical practice. Considering the current

comprehensive treatment pattern centered on surgeries is the mainstream of treatment, we can not agree more to add relative content about perioperative chemotherapy in our discussion. In our manuscript we add these contents to discussion according to your comments and revise the limitation part, discussing potential guiding effect of extended lymphadenectomy and retrieved lymph node counts on postoperative chemotherapy. Your comment is of great value to our research, thanks again!

**Minor points:**

**1. Line 189-190: What is "sualci margin"?**

**Reply 1:** "Excision margin" was mistakenly written as "sualci margin" in our manuscript and this mistake has already been corrected.

**2. Discussion can be shortened (particularly, 1st and 2nd paragraph), more focused on the observed findings with point-to-point review of the literature.**

**Reply 2:** We've revised the discussion part and shorten it according to your comment.

**Reviewer #3:**

**1. line 211: "( P>0.05)" is unnecessary. Authors are advised to indicate significance level only for meaningful results to avoid confusion among readers.**

**Reply 1:** Thank you for you comment! After reviewing our research, the "P>0.05" is unnecessary for our result and conclusion, therefore we deleted it from our manuscript in the revision. We also review other significance level in our research according to your comment and confirmed that the rest are necessary for our research.

**2. It is recommended that the last paragraph of the discussion section go to the conclusion section.**

**Reply 2:** The last paragraph of discussion draw a conclusion of our research.

We included it in the conclusion part according to your comment. Thanks again for your valuable and helpful comments !

**Revision reviewer:**

**The authors have made a tremendous effort and dedicated their time to revise this manuscript to be more valuable to readers. They have responded very well to the queries and I believe this manuscript is now recommendable to all GI surgeons.**

**Reply:** Thanks for your comments.