TCR TRANSLATIONAL CANCER RESEARCH
ADVANCES CLINICAL MEDICINE TOWARD THE GOAL OF IMPROVING PATIENTS' QUALITY OF LIFE
IMPACT FACTOR 0.986

Peer Review File

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Reviewer A

Comment 1: V-lock is not correct, V-loc is correct.
Reply 1: Thanks for the comments of reviewer, and we have revised it in the text.
Changes in the text: we have modified our text as advised (see Page 5, line123).
Comment 2: Energy devices and companies of all devices and thread should be presented.
Reply 2: Thanks for the comments of reviewer, we have added some data in the text.
Changes in the text: we have modified our text as advised (see Page 5-6, line113-130).
Comment 3: GraphPad: edition number and company?
Reply 3: Thanks for the comments of reviewer, and we have added it in the text.
Changes in the text: we have modified our text as advised (see Page 6, line154).
Comment 4: PTCD rate seems to be higher. Why did not employ ERBD? It is very strange.
Reply 4: Thanks for the comments of reviewer, ERBD is associated with an increased risk of biliary tract infection, cholangitis and postoperative biliary-enteric anastomosis leakage. In addition, ERBD is more expensive than PTCD. Therefore, PTCD is more commonly used for preoperative biliary drainage, and ERBD was selected when PTCD fails.

Changes in the text: Nothing has been changed.

Comment 5: In Fig. 3, POPF should be also analyzed.
Reply 5: Thanks for the comments of reviewer, In Fig. 3(A), We used the cumulative sum to analyze the major postoperative pancreatic fistula rate (see Page 9, line299-230).
Changes in the text: Nothing has been changed.
Comment 6: Diseases should be presented in Table 1. PDAC is the most important tumor for LPD, because PDAC should be co-resected with retroperitoneum and SMA plexus.
Reply 6: Thanks for the comments of reviewer, and we have added PDAC data in Table 1.
Changes in the text: we have modified our text as advised (see Table 1 and Page 7, line165).
Comment 7: What is high risk for POPF? This definition is not accepted in worldwide.
Reply 7: Thanks for the comments of reviewer. The definition of high risk for POPF is not accepted in worldwide but POPF represents the most frequent and life-threatening complication after pancreaticoduodenectomy. Some important articles have analyzed high risk for POPF. (van Hilst J, de Rooij T, Bosscha K, et al. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomized controlled phase 2/3 trial. Lancet

Gastroenterol Hepatol 2019; 4: 199-207) We think it is important to add high risk for POPF. Therefore, we analyzed the high risk for POPF according to the standard of this paper, and we have added a reference paper to the high risk for POPF standard.

Changes in the text: we have added a reference paper (Page 5, line105 and Reference (10)).

Comment 8: Blood loss in both groups are too high, over 500ml of BL in OPD is not qualified as specialized center in Table. 2.

Reply 8: Thanks for the comments of reviewer. The reviewers thought that blood loss in both groups are too high. We have checked the previous articles and found that the bleeding volume of OPD is mostly around 400-500ml.The reason why the bleeding was higher than 500ml was that it contained bile, tissue fluid and blood, but we could not accurately remove bile and tissue fluid, and could only objectively attribute them to BL.

Changes in the text: Nothing has been changed.

Comment 9: DGE is mainly affected by POPF. Table. 5 did not show the effect of POPF for DGE.

Reply 9: Thanks for the comments of reviewer, reviewer is an experienced expert. We analyzed the correlation between POPF (B/C) and delayed gastric emptying. POPF and DGE are closely related.

Changes in the text: We have modified our text as advised (see Page 9, line218 and Table 5).

Comment 10: Table.4 does not give new information for readers.

Reply 10: Table4 aims to illustrate that the biliary-enteric anastomosis leakage and may lead to the severe complications after LPD. The biliary-enteric anastomosis leakage and may be the most serious complication after LPD. We regard this view as instructive, and we want to keep it.

Changes in the text: Nothing has been changed.

Reviewer B

Comment 1: In the surgical technique, insert some photos and add number for each step. Mention what kind of stapler you use etc.?

Reply 1: Thanks for the comments of reviewer, and we have added some photos and data in the text.

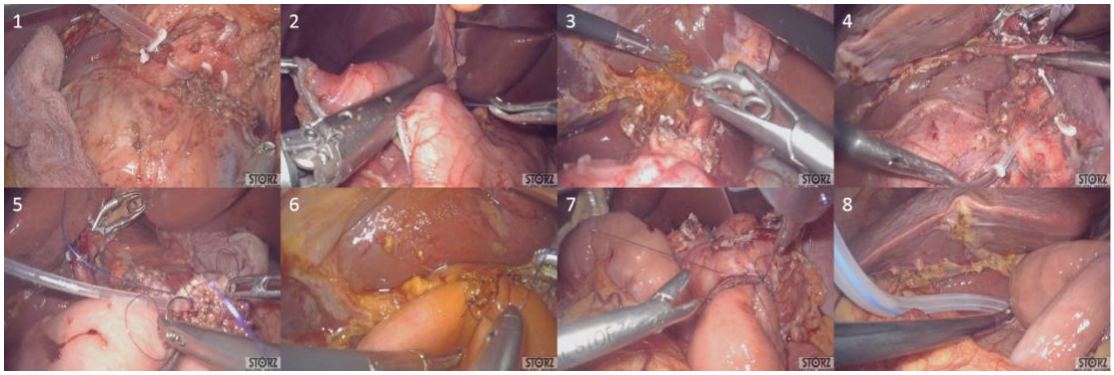


Fig1. Eight-Step Laparoscopic Operative Technique. 1: Exposure and stripping of the pancreatic head; 2: Exposure of pancreas and gastrectomy; 3: Dissection of porta

hepatis; 4: Resection of the uncinate process; 5: Reconstruction of the pancreaticojejunostomy; 6: Reconstruction of hepaticojejunostomy; 7: Reconstruction of gastrojejunostomy; 8: Placement of the drainage system and closure of the incision.

Changes in the text: we have modified our text as advised (see Page 5-6, line110-130, Page 19, line481-485(Figure Legends) and added Fig 1).

Comment 2: In the material and methods clarify the experience of the surgical team in laparoscopic surgery, e/o laparoscopic pancreatic surgery as this may impact the learning curve and the surgical outcomes.

Reply 2: Thanks for the comments of reviewer. We have added some data in the text.

Changes in the text: we have modified our text as advised (see Page4, line80-82).

Comment 3: In the discussion please be concise, do you see any advantage in performing robotic Whipple in terms of efficiency? Please also mention the rule of the robotic Whipple (as references Marino MV, Podda M, Gomez Ruiz M, Fernandez CC, Guarrasi D, Gomez Fleitas M. Robotic-assisted versus open pancreaticoduodenectomy: the results of a case-matched comparison. J Robot Surg. 2020 Jun;14(3):493-502. doi: 10.1007/s11701-019-01018-w. Epub 2019 Aug 31. PMID: 31473878.)

Reply 3: Thanks to reviewers for their comments and references. We have added this article and some comments about LPD/RPD in the discussion. In our article, we have introduced two articles about RPD (reviewers 12, 17). As we have seen, both RPD and LPD have less blood loss and fewer complications compared to OPD. LPD and RPD have similar learning curves and operative time. The author personally think that RPD is better than LPD in gastrointestinal reconstruction, but worse than LPD in surgical field of vision.

Changes in the text: we have modified our text as advised (see Page10, line260-264) and added an article (reviewers 18).

Reviewer C

This article is interesting and essentially important for readers of Translational Cancer research, and I have no serious criticisms.

Reviewer D

Comment 1: What was the indication for OPD or LPD?

Reply 1: Thanks for the comments of reviewer. We re-described the indications for LPD or OPD. The inclusion criteria were: benign and malignant pancreatic tumors located at the head of the pancreas, tumors located at the lower part of the common bile duct and ampulla tumors; had not received gastrointestinal surgery; and no tumor

invasion the coeliac trunk, common hepatic artery, and superior mesenteric artery. LPD and OPD had the same inclusion criteria. The exclusion criteria were: those who could not tolerate general anesthesia, and arterial invasion and distant metastases were considered contraindications for the operation. In the early stage, simple cases were selected for LPD, and after 60 cases, LPD and OPD had the same inclusion criteria, such as vascular reconstruction of the SMV.

Changes in the text: We have modified our text as advised (see Page4, line85-94)

Comment 2: There was statistical differences between OPD and LPD in terms with biliary drainage. Why?
Following three categorizations with chi-square need to be performed between two groups: No/ ERBD/ PTBD
Reply 2: Thanks for the comments of reviewer. Patient admission is random, and may be suitable for LPD surgery patients with more obstructive jaundice, but before the operation, percutaneous transhepatic cholangial drainage was performed on patients with serum bilirubin exceeding 200 mmol/ml. Therefore, we applied the preoperative biliary drainage to eliminates influence with jaundice on patients after OPD/LPD. We performed the chi-square test based on the Reviewer's suggestion. In general, there was no significant difference between LPD and OPD patients in Preoperative biliary drainage.

Changes in the text: We have modified our text as advised (see Page7, line163-165 and Table1)

Comment 3: Please check estimated blood loss between two group.

Reply 3: Thanks for the comments of reviewer. We have checked the previous articles and found that the bleeding volume of OPD is mostly around 400-500ml.The reason why the bleeding was higher than 500ml was that it contained bile, tissue fluid and blood, but we could not accurately remove bile and tissue fluid, and could only objectively attribute them to BL.
Changes in the text: Nothing has been changed. (The estimated blood loss in Table2).
Comment 4: How many surgeons were involved in this surgery? Different surgeons' performances make it difficult to analyze learning curve as usual.

Reply 4: Thanks for the comments of reviewer. We mentioned in the article that "All the operations were completed by a separate team". (see Page4, line80-82)
Changes in the text: Nothing has been changed.
Comment 5: Please check the texture of the pancreas between two groups.

Reply 5: Thanks for the comments of reviewer. We analyzed the texture of the pancreas between LPD and OPD using the chi-square test. Chi-square test showed no significant difference in texture of the pancreas between the two groups.

Changes in the text: We have modified our text as advised (see Page8, line188 and Table2)

Comment 6: Please list the pathological diagnosis between two groups.

Reply 6: Thanks for the comments of reviewer. We analyzed the pathological diagnosis between LPD and OPD using the chi-square test. Chi-square test showed no significant difference in pathological diagnosis between the two groups.

Changes in the text: We have modified our text as advised (see Page8, line188 and Table2)

Comment 7: What is the meaning of "Intestinal exhaust time"?

Reply 7: Thanks for the comments of reviewer. We replaced "Intestinal exhaust time" with "Anal exhaust time" in the article.

Changes in the text: We have modified our text as advised (see Page2, line38, Page8, line203 and Table3)

Comment 8: Please check statistical analysis in Table 4. Correlation between categorical variables need to be evaluated by Chi-square, not linear regression.

Reply 8: Thanks for the comments of reviewer. We analyzed the correlation between Clavien-Dindo Classification ≥3 and severe postoperative complications by chi-square test. We found that biliary-enteric anastomosis leakage and intraperitoneal infection were closely associated with serious postoperative complications.

Changes in the text: We have modified our text as advised (see Page8, line204-208, Page11-12, line299-302 and Table4).

Comment 9: It would be better to evaluate the factor predicting DGE patients (21+34). There are some questions regarding clinical implication of Table 3.

Reply 9: Thanks for the comments of reviewer. More patients were observed in the LPD group than in the OPD group, but more DGE patients were seen in the LPD group. This is illogical. To explain this phenomenon, we also extracted and compared the relevant clinical data of the 34 patients with delayed gastric emptying in the LPD group. In order to find out the actual cause of DGE in 34 patients with LPD, the 21 case patients with OPD may interfere with the analysis. In Table5, we additionally analyzed the correlation between POPF (B/C) and delayed gastric emptying. POPF and DGE are closely related.
Changes in the text: We have modified our text as advised (see Page 9, line212-213,218 and Table 5).

Comment 10: Please check length of hospital stay?

Reply 10: Thanks for the comments of reviewer. Before the operation, PTCD/ERBD was performed on patients with serum bilirubin exceeding 200 umol/L. The length of time required for biliary drainage depends on the patient for many factors. There are many confounders in the length of hospital stay. It would be better to evaluate the postoperative hospital stay (in Table3).

Changes in the text: Nothing has been changed.

Comment 11: It is recommended that learning curve issue should be dealt in separate

another paper. Too many analysis, too busy to follow.

Reply 11: Thanks for the comments of reviewer. Cumulative Sum analysis of the complication rate and learning curve are the most important questions in the paper, and we sincerely hope to keep them.

Changes in the text: Nothing has been changed.

Comment 12: IRB approval needs to be commented.

Reply 12: Thanks for the comments of reviewer. We have added Ethics Policies/Statements.

Institutional review board: This study had been approved by the institutional review board of Chongqing Xinqiao Hospital (Approval Number -AF/SC-08/1.0; Approval Date - 2018.10.16).

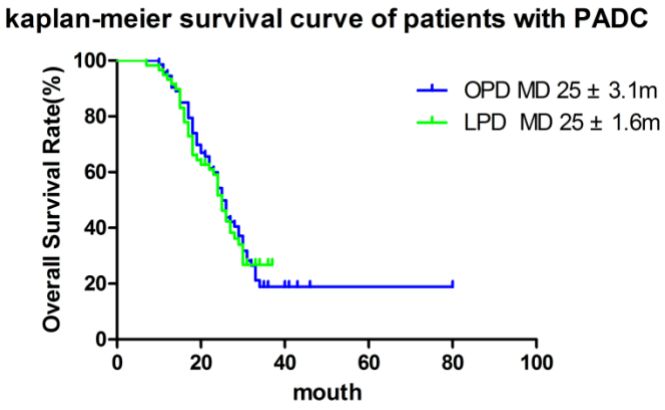
(This paper is based on retrospective study on - Three dimension laparoscopic pancreaticoduodenectomy versus open pancreaticoduodenectomy: A randomized clinical trial; Approval Number: AF/SC-08/1.0; Approval Date: 2018.03.20)

Informed consent: Each patient had signed the informed consent with regard to the operation and use of data on their status before and after the operation.

Changes in the text: We have modified our text as advised (see Page13-14, line352-360)

Comment 13: Subgroup analysis in pancreatic cancer with survival can be analyzed?

Reply 13: Thanks for the comments of reviewer. We analyzed the overall survival of LPD and OPD. We excluded 18 cases in the survival analysis [lost to follow-up (14 cases), 30-day postoperative deaths (4 cases)]. There were no significant difference in overall survival rate between LPD (25 ±1.6 months) and OPD (25 ±3.1 months)(p=0.991). (Fig. 2).



Changes in the text: We have modified our text as advised (see Page9, line223-226 and Page 19, line486(Figure Legends) and added Fig 2).