

Peer Review File

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Reviewer A:

Thanks for designating me as a peer reviewer. Emergent PD for hemorrhage is not a very uncommon procedure and is a condition that hepatobiliary surgeons encounter from time to time, so there is no novelty. In addition, the authors should discuss the use of artificial vessels in gastrointestinal surgery with bacterial infection. Since klebsiella has been detected, there should be a full discussion whether autologous renal vein, external jugular vein or iliac vein should have been used rather than PTFE. Also, to make a minor point, once the text abbreviates acute pancreaticoduodenectomy as EPD, the abbreviation should then be used.

Comment 1: Emergent PD for hemorrhage is not a very uncommon procedure and is a condition that hepatobiliary surgeons encounter from time to time, so there is no novelty.

Reply 1: Thank you for your valuable feedback, which helps us clarify the focus of our research. Our study highlights a particularly challenging and life-threatening scenario: massive hemorrhage caused by pancreatic cancer invading the duodenum. In such cases, simple hemostatic interventions such as vessel ligation, endoscopic treatment, or interventional embolization often lead to recurrent bleeding if the tumor is not resected. Therefore, a radical pancreaticoduodenectomy is essential. We reviewed similar cases in the literature and summarized them in the discussion, while also emphasizing the need for larger-scale studies to better understand the outcomes in such scenarios. It is crucial to highlight that even when the tumor has invaded the portal vein, an emergency pancreaticoduodenectomy with portal vein resection and reconstruction can still be performed, offering a survival benefit. Although the patient in our case had a prognosis of only 10 months, this approach provided a chance of survival compared to imminent death from acute hemorrhage. We also conducted a literature search on PubMed and did not find any reported cases of emergency pancreaticoduodenectomy with portal vein reconstruction using synthetic grafts for duodenal ulcer bleeding caused by pancreatic cancer.

Changes in the text: Currently, there are three methods for treating duodenal cancer ulcer bleeding: EH, TAE, and EPD. EH is generally preferred but has limitations, especially in cases where pancreatic tumors invade the duodenum, causing lumen stenosis or occlusion (13). TAE is feasible and effective for bleeding that cannot be controlled by EH but serves as only a temporary measure (14). EPD can achieve both hemostasis and tumor resection in cases of pancreaticoduodenal injury, perforation, and bleeding caused by tumor invasion. We have collected relevant case reports from PubMed and compiled them in Table 1. Comparison of the success rates across EH, TAE, and EPD revealed rates of 22.22%, 57.14%, and 87.50%, respectively. Given the limited clinical sample size, statistical validation is not feasible, and only large-scale cohort studies or randomized clinical trials can definitively establish EPD as the most effective approach. A literature search on PubMed did not identify any reported cases of emergency pancreaticoduodenectomy with portal vein reconstruction using synthetic grafts

for duodenal ulcer bleeding secondary to pancreatic cancer. These findings suggest that, in certain cases, EPD may be considered the preferred strategy for bleeding control.

References:

13. Ghaphery AD, Gupta R, Currie RA. Carcinoma of the head of the pancreas with aortoduodenal fistula. *Am J Surg* (1966) 111:580–583. doi: 10.1016/0002-9610(66)90289-3

14. Tomita H, Osada S, Matsuo M, Shimokawa K. Pancreatic cancer presenting with hematemesis from directly invading the duodenum: report of an unusual manifestation and review. *Am Surg* (2006) 72:363–366.

Comment 2: In addition, the authors should discuss the use of artificial vessels in gastrointestinal surgery with bacterial infection. Since klebsiella has been detected, there should be a full discussion whether autologous renal vein, external jugular vein or iliac vein should have been used rather than PTFE.

Reply 2: Thank you for raising this critical point. We agree that bacterial contamination, particularly with pathogens like Klebsiella, presents a significant risk when using synthetic grafts such as PTFE. In cases of active infection, graft selection is especially important, and autologous veins like the renal, external jugular, or iliac veins may indeed offer advantages due to their superior biocompatibility and lower risk of infection. However, in this case, one of the reasons for choosing PTFE was that, following preoperative anti-infection treatment, the patient's temperature, white blood cell count, and procalcitonin levels had significantly decreased, and the drainage fluid had cleared. The decision to use a PTFE graft was ultimately driven by several factors, including the urgency of the surgery, the need for a readily available and appropriately sized conduit, and the challenges of harvesting autologous veins in an emergency setting. We have now expanded the discussion to address this issue in greater detail and included relevant recent literature.

Changes in the text: Portal vein reconstruction is common in pancreaticoduodenectomy with vascular resection, typically achieved through lateral venorrhaphy, primary end-to-end anastomosis, or the interposition of autologous or synthetic grafts (15,16). Autologous grafts, such as the saphenous vein, offer superior biocompatibility and minimal immunogenicity but are often limited by availability and donor site morbidity (17,18). Additionally, autologous replacement may not be feasible due to prior harvesting or the patient's compromised health. Over time, the quality of autologous blood vessels can be difficult to guarantee, and the incidence of postoperative complications is higher (19). Synthetic alternatives, particularly polytetrafluoroethylene (PTFE), provide consistent quality and reduced operative time. Wang et al. (2021) highlight their benefits, including light weight and facilitation of tissue integration (20). However, artificial grafts carry inherent risks, such as thrombosis and infection (21). A comprehensive review on the history, progress, and future challenges of artificial blood vessels emphasizes emerging polymers and fabrication techniques, focusing on innovations designed to improve biocompatibility and mitigate complications (22). These advancements underscore the need for continued development in biomaterial science to refine vascular reconstruction strategies.

References:

15. Ouyang G, Zhong X, Cai Z, Liu J, Zheng S, Hong D, Yin X, Yu J, Bai X, Liu Y, Liu J, Huang X, Xiong Y, Xu J, Cai Y, Jiang Z, Chen R, Peng B. The short- and long-term outcomes of

laparoscopic pancreaticoduodenectomy combining with different type of mesentericoportal vein resection and reconstruction for pancreatic head adenocarcinoma: a Chinese multicenter retrospective cohort study. *Surg Endosc.* 2023 Jun;37(6):4381-4395. doi: 10.1007/s00464-023-09901-2IF: 2.4 Q2 .

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18. Cai Y, Gao P, Li Y, Wang X, Peng B. Laparoscopic pancreaticoduodenectomy with major venous resection and reconstruction: anterior superior mesenteric artery first approach. *Surg Endosc.* 2018 Oct;32(10):4209-4215. doi: 10.1007/s00464-018-6167-3.

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20. Wang D, Xu Y, Li Q, Turng LS. Artificial small-diameter blood vessels: materials, fabrication, surface modification, mechanical properties, and bioactive functionalities. *J Mater Chem B.* 2020 Mar 4;8(9):1801-1822. doi: 10.1039/c9tb01849b.

21. Eftimie MA, Lungu V, Tudoroiu M, Vatachki G, Batca S, David L; -. Emergency Pancreatico-Duodenectomy with Superior Mesenteric and Portal Vein Resection and Reconstruction Using a Gore-Tex Vascular Graft. *Chirurgia (Bucur).* 2017 Jan-Feb;112(1):50-57. doi: 10.21614/chirurgia.112.1.50.

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Comment 3: Also, to make a minor point, once the text abbreviates acute pancreaticoduodenectomy as EPD, the abbreviation should then be used.

Reply 3: Thank you for pointing this out. We will ensure consistency in the use of abbreviations throughout the manuscript. Specifically, once "emergency pancreaticoduodenectomy" is abbreviated as "EPD," we will use this abbreviation consistently in all subsequent references.

Reviewer B:

Comment 1: The study investigates the association between the location of the main pancreatic duct and the development of postoperative pancreatic fistula (POPF) following pancreaticoduodenectomy (PD). The study enrolled 871 patients who underwent PD between January 2018 and December 2021, analyzing independent risk factors for POPF through logistic regression. The study introduces a novel pancreaticojejunostomy technique based on the anatomical location of the main pancreatic duct. The findings suggest that patients with a

central pancreatic duct have a significantly lower incidence of POPF compared to those with an eccentric pancreatic duct. Additionally, the novel technique demonstrated a reduced incidence of POPF and other complications, supporting its potential for clinical application.

Reply 1: Thank you very much for your valuable feedback on our study. Your comments are of great value to us in further improving our paper.

Comment 2: While the study is well-conducted, several aspects require further clarification and elaboration:

Distinction between Anterior and Posterior Duct Locations:

The manuscript should clarify whether there are differences in POPF incidence and complications based on whether the main pancreatic duct is located near the anterior or posterior wall of the pancreas. This distinction is crucial for understanding the implications of the duct's location on surgical outcomes.

Reply 2: Thank you for your valuable feedback. In pancreaticoduodenectomy (PD), the location of the main pancreatic duct—whether anterior or posterior—can significantly impact the complexity of the surgery and the risk of postoperative complications. Anterior duct positioning generally facilitates easier exposure and manipulation, potentially reducing surgical difficulty and enhancing the stability of pancreatic anastomosis, which may lead to a lower incidence of pancreatic fistula. In contrast, a posteriorly located duct complicates the surgical approach, often involving deeper tissue layers and additional anatomical structures, which can increase procedural complexity and the risk of complications. Studies suggest that an anterior duct is associated with fewer postoperative issues, while a posterior duct may elevate the risk of pancreatic fistula and other complications such as pancreatitis and gastric emptying difficulties.

References:

Zhou B, Gao Z, Tian Y, Yan S. A modified Blumgart method using a homemade crochet needle facilitates pancreaticojejunostomy in laparoscopic pancreaticoduodenectomy: a retrospective cohort study. *BMC Surg.* 2024 Jan 13;24(1):22. doi: 10.1186/s12893-023-02308-9.

Comment 3: Detailed Explanation of Pancreaticojejunostomy Techniques:

The descriptions of the 1 mode and 1² mode pancreaticojejunostomy techniques are not sufficiently detailed. Providing illustrations or step-by-step diagrams would greatly enhance comprehension. Additionally, a more explicit explanation of the differences between these techniques, including the rationale for their use based on the duct's location, is needed.

Clarification on "Pancreatic head cannot be separated":

The phrase "Pancreatic head cannot be separated" needs clarification. In the context of PD, the pancreatic head is typically separated. If this term refers to a specific technical challenge or anatomical variation, it should be clearly explained.

Reply 3: Thank you for your insightful comment. The phrase "pancreatic head cannot be separated" refers to situations where separation of the pancreatic head is particularly challenging. This difficulty may arise in specific contexts, such as when there has been a history of pancreatitis or when the pancreatic head is involved with tumors that invade the superior mesenteric vein.

Comment 4: Details on 1² Mode for Posterior Duct Location:

The manuscript should provide a clearer explanation of the 1² mode pancreaticojejunostomy, particularly when the main pancreatic duct is located near the posterior wall. Details on the reinforcement of the posterior wall and the additional steps involved are necessary.

Suturing Technique for Anterior Duct Location:

The manuscript should address whether the suturing technique changes when the main pancreatic duct is located near the anterior wall of the pancreas. If different approaches are used for anterior versus posterior duct locations, these should be described in detail.

Reply 4: Thank you for your question. In pancreaticojejunostomy, reinforcing the posterior wall sutures is critical to ensure the stability of the anastomosis and reduce the risk of postoperative complications, such as pancreatic fistula. This can be achieved by employing a double-layer suturing technique, where the inner mucosal layer and outer serosal layer are sutured separately using fine absorbable and thicker sutures, respectively, to enhance the seal and strength of the anastomosis. Additional reinforcement may involve placing extra sutures specifically on the posterior wall or using biological or synthetic materials, such as patches, to provide added support. Techniques such as "inside-out" suturing or "running" suturing can further increase stability. Ensuring smooth and even surfaces of the pancreas and jejunum before suturing, along with maintaining adequate blood supply to the anastomosis area, is also crucial for promoting effective healing and minimizing complications.

References:

Liu GH, Tan XY, Li JX, Zhong GH, Zhai JW, Li MY. A modified Blumgart anastomosis with a simple and practicable procedure after laparoscopic pancreaticoduodenectomy: our center's experience. BMC Surg. 2023 Nov 16;23(1):349. doi: 10.1186/s12893-023-02221-1.

Comment 5: Consistency in Terminology:

Ensure consistent use of terms such as "central pancreatic duct" and "eccentric pancreatic duct" throughout the manuscript to avoid confusion.

Reply 5: Thank you very much for your valuable feedback, Professor.

Comment 6: Addressing Potential Biases:

Discuss potential biases introduced by variations in surgical techniques among different surgeons, even within the same institution. This will provide a more comprehensive understanding of the study's limitations.

Reply 6: Thank you for your suggestions. We will include an analysis of factors related to different primary surgeons in the revised manuscript.

Comment 7: Future Research Directions:

Expand on future research directions, including specific recommendations for prospective, multi-center trials and mechanistic studies to understand the impact of the pancreatic duct's anatomical location on POPF development.

Reply 7: Thank you for your suggestions. We will consider conducting a multicenter study in the future to further address these factors.

Comment 8: Clinical Recommendations:

The authors should emphasize the need for further validation through larger, randomized controlled trials before recommending widespread clinical adoption of the new pancreaticojejunostomy technique.

These revisions will enhance the clarity, comprehensiveness, and impact of the manuscript, making it more informative and useful for the surgical and medical communities.

Reply 8: Thank you for your valuable suggestions. Your input will greatly enhance the quality of my manuscript.