Editorial Commentary

A new perspective on post-operative pancreatic fistulas: the impact of post-pancreatectomy acute pancreatitis

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Pancreatoduodenectomy (PD) is frequently utilized to treat both malignant and benign disease of the pancreatic head, duodenum, and periampullary region. While surgical techniques and operative technology have improved over the years, PD remains associated with significant post-operative morbidity, affecting upwards of 50% patients (1,2). Notably, post-operative pancreatic fistula (POPF) remains a significant complication, with clinically relevant fistulas occurring in 10–20% of cases (3,4). Significant emphasis has been placed on accurately classifying POPF to optimize mitigation strategies and identify potential causes (5). In this regard, multiple technical aspects of PD have been extensively evaluated for association with POPF, including utilization of pancreatic duct stent placement, various pancreaticojejunostomy anastomotic techniques, and intra-peritoneal drainage (6,7). However, despite these efforts, POPF rates remain high and continue to be a significant issue following PD.

Post-pancreatectomy acute pancreatitis (PPAP) is a common occurrence after PD that has recently garnered more attention for its association with other postoperative complications. The International Study Group for Pancreatic Surgery (ISGPS) has formalized a definition for PPAP according to radiologic and laboratory findings following pancreatic surgery (8). PPAP is defined as an acute inflammatory condition of the pancreatic remnant that begins within the first three postoperative days after partial pancreatectomy and is characterized by (I) sustained postoperative serum hyperamylasemia greater than the institutional upper limit of normal for at least 48 hours, (II) clinically relevant features, and (III) radiologic alterations consistent with PPAP. Risk factors for PPAP have been extensively investigated and include soft pancreatic texture, receipt of neoadjuvant treatment, gender, and pancreatic ductal diameter (9,10).

In a recent issue of *Annals of Surgery*, Chen and colleagues investigated the risk and clinical significance of POPF after PPAP among patients undergoing PD (11). In their retrospective study of 817 patients who underwent open or minimally invasive PD, they observed that POPF occurred in 159 (19.5%) patients. Of these, 73 (45.9%) cases of POPF occurred following PPAP, as defined by ISGPS criteria. When compared to non-POPF cases, PPAP-associated POPF was associated with higher body mass index (BMI), higher rate of non-dilated main pancreatic duct, soft pancreatic texture, and non-PDAC pathology. When compared to non-PPAP-associated POPF, PPAP-associated POPF was associated with a trend towards younger age, female gender, lower rate of preoperative biliary drainage, and softer pancreatic texture. Compared to all patients, PPAP-associated POPF was associated with higher common Fistula Risk Score (FRS). On subsequent multivariable logistic regression, factors associated with development of PPAP-associated POPF included greater

intraoperative blood loss, small pancreatic duct size, and soft pancreatic texture. In contrast, non-PPAP-associated POPF was linked to different risk factors, including age. Importantly, there were no significant differences in postoperative outcomes between PPAP-associated POPF and non-PPAP-associated POPF. However, the authors observed that PPAP-associated POPF presented with unique radiologic features.

These findings by Chen and colleagues contribute to the growing body of evidence linking PPAP to the development of POPF (10,12-14). Retrospective studies by Bellotti *et al.* (55.0% *vs.* 11.6%, P<0.001) and Wu *et al.* (33.3% *vs.* 12.5%, P<0.001) have similarly reported a strong association between PPAP and POPF compared to patients without PPAP (10,12). Across multiple studies, further analysis of factors associated with PPAP-related POPF identified similar risk factors as those described by Chen and colleagues, including smaller duct size and softer pancreatic texture (10,12,14). Ultimately, these findings by Chen and colleagues corroborate previously recognized risk factors and challenge the conventional dogma that POPF solely results from breakdown or leakage of the pancreatic stump or anastomosis. Their finding of temporal development of PPOF following PPAP, alongside unique risk factors for PPAP-associated PPOF, suggests that PPOF following PPAP should be recognized as a potential complication secondary to PPAP. This prompts the consideration of additional PPOF subtypes and underscores the necessity for innovative prevention strategies. While surgeons have focused on refining surgical techniques to reduce POPF, additional efforts and attention may also need to be directed towards minimizing PPAP in post-PD patients.

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References

1. Sukharamwala P, Thoens J, Szuchmacher M, et al. Advanced age is a risk factor for post-operative complications and mortality after a pancreaticoduodenectomy: a meta-analysis and systematic review. HPB (Oxford) 2012;14:649-57.
2. Kokkinakis S, Kritsotakis EI, Maliotis N, et al. Complications of modern pancreaticoduodenectomy: A systematic review and meta-analysis. Hepatobiliary Pancreat Dis Int 2022;21:527-37.
3. McMillan MT, Soi S, Asbun HJ, et al. Risk-adjusted Outcomes of Clinically Relevant Pancreatic Fistula Following Pancreatoduodenectomy: A Model for Performance Evaluation. Ann Surg 2016;264:344-52.
4. Schuh F, Mihaljevic AL, Probst P, et al. A Simple Classification of Pancreatic Duct Size and Texture Predicts Postoperative Pancreatic Fistula: A classification of the International Study Group of Pancreatic Surgery. Ann Surg 2023;277:e597-608.
5. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery 2017;161:584-91.
6. Kawaida H, Kono H, Hosomura N, et al. Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery. World J Gastroenterol 2019;25:3722-37.
7. Van Buren G 2nd, Bloomston M, Hughes SJ, et al. A randomized prospective multicenter trial of

pancreaticoduodenectomy with and without routine intraperitoneal drainage. Ann Surg 2014;259:605-12.
8. Marchegiani G, Barreto SG, Bannone E, et al. Postpancreatectomy Acute Pancreatitis (PPAP): Definition and Grading From the International Study Group for Pancreatic Surgery (ISGPS). Ann Surg 2022;275:663-72.
9. Bannone E, Andrianello S, Marchegiani G, et al. Postoperative Acute Pancreatitis Following Pancreaticoduodenectomy: A Determinant of Fistula Potentially Driven by the Intraoperative Fluid Management. Ann Surg 2018;268:815-22.
10. Wu S, Wu H, Xu G, et al. Risk Factors and Clinical Impacts of Post-Pancreatectomy Acute Pancreatitis After Pancreaticoduodenectomy: A Single-Center Retrospective Analysis of 298 Patients Based on the ISGPS Definition and Grading System. Front Surg 2022;9:916486.
11. Chen H, Wang W, Fu N, et al. Characterization of Pancreatic Fistula after Post-pancreatectomy Acute Pancreatitis. Ann Surg 2024. [Epub ahead of print]. doi: 10.1097/SLA.0000000000006277.
12. Bellotti R, Pably D, Morell-Hofert D, et al. Post-pancreatectomy acute pancreatitis after pancreatoduodenectomy: Analysis of a clinically-relevant complication in a single-center retrospective study. Pancreatology 2024;24:137-45.
13. Chen H, Wang C, Shen Z, et al. Postpancreatectomy Acute Pancreatitis After Pancreaticoduodenectomy: A Distinct Clinical Entity. Ann Surg 2023;278:e278-83.
14. Radulova-Mauersberger O, Oehme F, Missel L, et al. Analysis of predictors for postoperative complications after pancreatectomy--what is new after establishing the definition of postpancreatectomy acute pancreatitis (PPAP)? Langenbecks Arch Surg 2023;408:79.

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