Technical aspects of pancreaticoduodenectomy and their outcomes

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Abstract: Pancreatic cancer is the fourth leading cause of cancer-related death in the Unites States and is rising in incidence. For the 15–25% of patients who do not have either metastatic or locally advanced disease, surgical resection with pancreaticoduodenectomy is the standard of care and results in improved 5-year survival of 15–25%. While mortality at high-volume centers is less than 5%, morbidity remains high at approximately 30–45%. This paper reviews technical aspects of pancreaticoduodenectomy and their outcomes. Specifically, we review technique and the outcome literature on vascular reconstruction, attempts to decrease delayed gastric emptying (DGE), including pylorus-preserving versus classic pancreaticoduodenectomy and gastrojejunostomy (GJ) technique, as well as attempts to decrease the rate of pancreatic fistula, including the use of pancreatic stents, fibrin sealant, and pancreaticojejunostomy (PJ) technique. Vascular resection and reconstruction have been associated with increased morbidity and mortality. However, the literature suggests that if it allows for an R0 resection, the survival is improved with comparable complication rates. DGE, one of the most common post-pancreaticoduodenectomy complications, has not been reliably decreased with various technical modifications of the GJ. The incidence of pancreatic fistula, one of the most morbid postoperative complications, is not definitively reduced by either the use of pancreatic stents or fibrin sealant. Additional research is needed to determine methods to further decrease rates of morbidity.

Keywords: Pancreas; cancer; pancreaticoduodenectomy; Whipple; outcome

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Background

Pancreatic cancer is the ninth leading cause of cancer-related death in women and the eighth leading cause in men worldwide (1). In the United States (US), over 53,000 new cases of pancreatic cancer were diagnosed, accounting for 3.1% of all new cancer cases in 2016. In the same year, pancreatic cancer was responsible for nearly 42,000 deaths, accounting for 7% of all annual cancer deaths (2). Despite its relatively low incidence, pancreatic cancer represents the fourth leading cause of cancer-related death in the US (2). This larger proportion of cancer deaths is reflective of the aggressive nature and overall poor prognosis of pancreatic ductal adenocarcinoma (PDAC). Specifically, 5-year survival for all pancreatic cancer patients is reported between 5.8–7.7% (2,3). This is in large part due to the presence of metastatic or unresectable disease at the time of diagnosis. Only an estimated 15–25% of patients are eligible for surgical resection at initial presentation (4). While there has been a slight rise in the incidence of PDAC over the past decade, mortality rates have remained relatively stable (5,6).

When technically possible, surgical resection offers the best hope for a long-term cure. Combined with adjuvant cytotoxic therapy and possible radiotherapy, patients who undergo surgical resection for PDAC have an estimated 5-year survival of 15–25% (7-10). For PDAC in the head of the pancreas, surgical resection is via pancreaticoduodenectomy (PD). The PD is commonly referred to as the Whipple surgery after Dr. Allen Whipple, the surgeon who presented the technique in the 1930's (11). In addition to PDAC, this operation is also commonly performed for other periampullary cancers, including distal bile duct cholangiocarcinoma, adenocarcinoma of the ampulla of Vater, and duodenal adenocarcinoma. Less common indications for pancreaticoduodenectomy include neuroendocrine tumors, gastrointestinal stromal tumors, intraductal papillary mucinous neoplasms, sarcomas, and isolated metastatic lesions in the head of the pancreas. While the mortality of PD at high-volume centers is less than 1–2%, postoperative morbidity remains high, affecting approximately 30–45% of patients (10). The most frequent sources of postoperative morbidity include delayed gastric emptying (DGE), postoperative pancreatic fistula (POPF), intra-abdominal abscess, and postoperative pancreatectomy hemorrhage (12,13). This review focuses on the technical aspects of PD. Specifically, we address technical issues of PD that have been proposed to potentially decrease the postoperative morbidity associated with this technically challenging operation and/or improve long-term oncologic outcomes.

Vascular reconstruction in pancreaticoduodenectomy

In 2009, a consensus statement by the American Hepato-Pancreatico-Biliary Association (AHPBA), the Society for Surgery of the Alimentary Tract (SSAT), and the Society of Surgical Oncology (SSO) was published on the definition of resectable, borderline resectable, and locally advanced/unresectable PDAC. Per the consensus statement, which was also adapted by the National Comprehensive Cancer Network (NCCN), a localized and resectable PDAC should have (I) no distant metastases; (II) no radiographic evidence of super mesenteric vein (SMV) or portal vein abutment, distortion, tumor thrombus, or venous encasement; and (III) clear fat planes around the celiac axis, hepatic artery, and superior mesenteric artery (SMA). The authors also defined borderline resectable tumors as those without evidence of metastatic disease with (I) venous involvement of the SMV/portal vein with tumor abutment, encasement without encasement of nearby arteries, or short segment venous occlusion with suitable vessel proximal and distal; (II) gastroduodenal artery (GDA) encasement up to the hepatic artery without extension to the celiac axis; or (III) tumor abutment of the SMA not to exceed more than 180 degrees of the circumference (14).

The desire to surgically resect borderline PDAC derives both from the survival benefit obtained for patients who undergo surgical resection as well as from data suggesting specifically that an R0 resection, with no evidence of malignant cells at the surgical margins microscopically, has a better overall survival outcome as compared to an R1 (residual microscopic malignant cells at margins) or R2 resection (gross disease at margin) (15,16). Vascular resection and reconstruction is therefore often required in order to achieve an R0 resection when tumor involves major venous or arterial structures (17). For patients in whom vascular resection is anticipated preoperatively, patients should be discussed at a multi-disciplinary tumor board to determine eligibility for neoadjuvant chemotherapy and/or radiation. It is common practice at our institution to administer neoadjuvant chemotherapy and stereotactic body radiation therapy to patients with borderline resectable tumors to potentially (I) downsize the primary tumor to increase likelihood of complete resection and (II) potentially improve overall and recurrence-free survival (18-20). Though investigational, these practices are in line with a unified expert consensus statement from the AHPBA/SSAT/SSO which stated that neoadjuvant therapy should be considered by centers with multidisciplinary expertise in pancreatic cancer treatment (21).

Resection and reconstruction options for tumors involving the portal vein or SMV include excision of a small ellipse of vein with primary repair of the defect, resection with patch repair using either harvested vein, synthetic material such as polytetrafluoroethylene (PTFE), or cadaveric vein, and segmental resection with or without splenic vein ligation and repair with either primary anastomosis or interposition graft (autonomous vein, synthetic conduit) (17,22). Generally, primary anastomosis can be achieved for defects up to 3 cm (23). In combination with splenic vein ligation and extensive mobilization of the portal vein both proximally and distally, gaps of up to 4 cm may be eligible for primary anastomosis. If any tension is present between the two ends, interposition graft is necessary. Autologous grafting, as opposed to the use of synthetic material, is preferred if possible. Options for autologous vein harvest include the internal jugular vein, left renal vein, splenic vein, gonadal vein, as well as the greater saphenous vein. In a recent meta-analysis, synthetic grafting was associated with higher rates of acute thrombosis as compared to primary repair. Furthermore, synthetic grafting may result in a higher rate of infection, particularly in the presence of a pancreatic fistula (24). To our knowledge, no studies have compared outcomes based on the type of autologous vein utilized.

Arterial resection is performed less frequently than venous resection but usually entails resection of a portion of the hepatic artery with either primary anastomosis or interposition graft depending on the length of vessel resected and the patient's arterial anatomy. It is imperative to study and understand the arterial anatomy and identify any aberrant arterial anatomy prior to surgical resection. If a replaced right hepatic artery is resected, revascularization is often required to preserve blood supply to the bile duct, especially to allow for the new hepaticojejunostomy to heal postoperatively (17).

There have been some reports in the literature of higher morbidity as well as mortality associated with vascular reconstruction during PD (25,26). For example, Castleberry *et al.* retrospectively analyzed 3,582 patients undergoing PD from the National Surgical Quality Improvement Program (NISQIP) database and found that the 281 patients who underwent vascular resection had significantly greater risk-adjusted 30-day postoperative mortality (5.7% *vs.* 2.9% in patients without vascular resection) and morbidity (39.9% of patients with postoperative complications *vs.* 33.3%) (both P<0.03) (25). On the other hand, multiple single-institutional studies have demonstrated success with obtaining an R0 resection with vascular resection with comparable morbidity and mortality outcomes to standard PD (17). Sgroi *et al.* recently published their experience comparing the outcome of 60 PD with vascular resections (49 venous, 11 arterial) to 87 standard PD (24). All 147 patients in the study had either T3N0 or T3N1 PDAC, and the two groups differed only in that the vascular group received significantly more neoadjuvant chemotherapy. The two groups did not differ significantly with regards to postoperative morbidity, the length of hospital stay, or 1- and 3-year survival. However, patients in the PD-only group had significantly better 5-year survival (24). The data suggested that the 18.9 months mean survival of these patients who were borderline resectable and underwent vascular resection far exceeds the median survival of 10–12 months for patients with locally advanced PDAC who undergo chemoradiation alone (23). Taken together, when technically possible, it appears that vascular resection by experienced surgeons in high-volume centers may improve overall survival with minimal additional perioperative morbidity.

DGE

DGE is one of the most common postoperative morbidities following PD, with a wide range of incidences reported in the literature, from as low as 5% to as high as 61% (27-29). This variance is due, in part, to varying definitions of DGE. The International Study Group of Pancreatic Surgery (ISGPS) therefore established a standardized definition of DGE in 2007 to attempt to bring consistency to diagnosing DGE and reporting its incidence. Grade A, or mild, DGE is defined as a nasogastric tube (NGT) required between postoperative days (POD) 4–7 or reinsertion of the NGT after removal by POD3 and inability to tolerate a solid diet by POD7 (with tolerating a solid diet defined as taking in greater than 1,000 kcal and not requiring intravenous fluids). Grade B, or moderate, DGE is defined as requiring NGT from POD8-14 or reinsertion of the NGT after POD7 and inability to tolerate a solid diet by POD14. Grade C, or severe, DGE is defined by an NGT that cannot be discontinued or is reinserted after POD14 and inability to tolerate solid diet by POD21 (30). Several factors have been suggested to increase the risk for DGE, including male gender, preoperative diabetes mellitus, smoking history, pancreatic fistulas, and abdominal infection (27,29). Given the high prevalence and morbidity associated with DGE, several surgical techniques have been proposed with the goal of decreasing the rate of DGE.

Pylorus preserving versus classic pancreaticoduodenectomy

In a "classic" PD, the distal portion of the stomach, including the pylorus, is taken en bloc with the head of the pancreas, bile duct, duodenum, and gallbladder (11). The pylorus-preserving pancreaticoduodenectomy, whereby the stomach and pylorus are left in situ, was first described by Dr. Watson in 1944 and was later popularized by Drs. Traverso and Longmire. This was initially performed under the hypothesis that preserving the pylorus could reduce postoperative reflux, dumping, diarrhea, and its accompanying weight loss. A 2016 Cochrane review analyzed composite data from a total of eight randomized controlled trials (RCTs) published between the years 1998 and 2015 (31). Postoperative mortality and overall survival did not differ between the 257 patients who underwent classic PD versus the 255 patients who underwent pylorus-preserving PD. The proportion of R0 resections was similar between groups, leading the authors to conclude one procedure was not superior over the other in terms of curative and oncologic benefit. In regards to postoperative morbidity, there was no difference between groups in the rates of pancreatic fistula, biliary leak, postoperative bleeding, wound infection, reoperation, or length of hospital stay (31).

Patients who underwent classic PD, however, had significantly less DGE (23.5%) than those who underwent pylorus-preserving PD (31.4%; OR 3.03, 95% CI,1.05–8.7, P=0.04). Notably, however, this observed difference lost statistical significance when only trials with the same definition of DGE were included, highlighting the importance of a standardized definition. Additional differences between the classic and pylorus-preserving PD included significantly reduced operating time [mean difference (MD): −45.22 minutes], intraoperative blood loss (MD: −0.32 L), and packed red blood cell transfusion (MD: −0.47 units) with the pylorus-preserving technique (31).

Antecolic versus retrocolic gastrojejunostomy (GJ)

The GJ can be constructed in either a retrocolic manner or in an antecolic manner. A systematic review published by Bell *et al.* assessed nine studies with a total of 878 patients undergoing pyloric-preserving PD and concluded that the rate of DGE was lower with an antecolic reconstruction (RR 0.31, P=0.010) (32). Additionally, length of stay (MD: −4 days) and days to beginning a solid diet (MD: −5 days) were significantly shorter for patients who underwent antecolic GJ reconstruction (32). There were no significant differences in the rates of pancreatic fistula, intra-abdominal collection, bile leak, or mortality (32). A Cochrane review on the same topic included 576 patients across six RCTs conducted between the years 2006 and 2014 and found no statistically significant difference in the rate of DGE, mortality, POPF, hemorrhage, intra-abdominal abscess, bile leak, reoperation rate, duration of operation, length of hospital stay, or time to NGT removal (33).

End-to-side versus side-to-side GJ

The GJ can be conducted via an end-to-side or a side-to-side manner. In one of the few published trials evaluating the differences in technique, Nakamura *et al.* published their institutional results with performing side-to-side GJ in subtotal stomach-preserving PD with the aim of reducing DGE. Between 2007 and 2010, the authors performed 80 consecutive PD's with end-to-side GJ anastomoses and subsequently performed 80 consecutive PD's with a side-to-side GJ anastomosis between 2010 and 2012 (27). In all cases, the stomach was divided 2–3 cm proximal to the pylorus, the PJ and HJ were constructed end-to-side, the GJ was antecolic, the GJ anastomotic aperture was approximately 5 cm, and all patients followed the same postoperative pathway. In the side-to-side anastomosis, a Gambee stitch was used to anastomose the greater curvature of the stomach 5–10 cm proximal to the closed gastric stump to the jejunal loop. The authors found a significant benefit to the side-to-side technique. Specifically, the authors found a reduction in DGE from 21.3% of end-to-side GJ patients to 2.5% in side-to-side GJ patients (P=0.0002) (27). Further studies are needed to reproduce and confirm these findings.

Pancreatic fistula

POPF is another common and potentially serious complication after PD. It can occur in approximately 10–20% of patients (34). A pancreatic fistula, also often called a "leak", occurs when pancreatic enzymatic fluid leaks from the pancreatic-enteric anastomosis. In 2005, the ISGPS published a consensus definition of pancreatic fistula for standardization in the literature (34). The authors defined a pancreatic fistula as drain output on POD3 or beyond with an amylase content that is more than three times the upper limit of normal serum amylase. Pancreatic fistulas were further subdivided into three grades. In 2016, the ISPGS updated the definition of POPF (35). Grade A, or "transient," pancreatic fistula, was redefined as a "biochemical leak". This biochemical leak was renamed, as it has no clinical importance in the postoperative course following PD. A biochemical leak requires little change in clinical management, except perhaps removing surgical drains more slowly. These patients are given a regular diet, and they do not require parenteral nutrition, antibiotics, or somatostatin analogs. Grade B pancreatic fistulas require a change in management, such as keeping the patient nothing by mouth (NPO) with parenteral nutrition. A peripancreatic collection is often present on imaging. Such patients often require antibiotics and/or somatostatin analogs, and they may be discharged with an operative drain still in place. Finally, a grade C pancreatic fistula requires a major change in clinical management, managed with NPO status, parenteral nutrition, antibiotics, somatostatin analogs, and often additional percutaneous drain. Grade C pancreatic fistulas cause a major delay in hospital discharge (34). Grade B and C fistulas are most likely to lead to additional morbidity and even mortality. Risk factors for the development of a POPF include older age, obesity, cardiovascular disease, diabetes mellitus, soft pancreatic texture, and a small pancreatic duct diameter (<3 mm) (36).

Pancreatic stent

The use of a pancreatic stent in an effort to reduce fistula and complications after pancreaticojejunostomy (PJ) was first described by Manabe *et al.* in 1986 (37). In the authors' original description, a vinyl chloride tube was inserted into the pancreatic duct and tied, with the PJ then sewed from the seromuscular layer of the jejunum to the pancreas parenchyma surrounding the stent. The tube was then removed 2 to 3 weeks postoperatively (37). This technique has been adapted to the current internal PJ stent, consisting of a plastic catheter (usually a pediatric feeding tube) placed into the pancreatic duct and across the anastomosis into the jejunum to direct the drainage of pancreatic fluid into the jejunum (38). This is theorized to protect the anastomosis from the enzymatic action of pancreatic secretions and to provide directed flow of the pancreatic juices through the anastomosis. An external stent similarly consists of a plastic catheter placed into the pancreatic duct, but as opposed to an internal stent, it drains pancreatic fluid externally to divert and protect the PJ anastomosis.

In a 2006 prospective randomized trial on the use of pancreatic stents, Winter *et al.* described a technique whereby the largest plastic pediatric feeding tube that could easily pass into the pancreatic duct (ranging from 3.5 to 8 French) is cut to a length of 6 cm, positioned with 3 cm in the pancreatic duct and 3 cm in the jejunal lumen, and secured in place with one absorbable suture (38). In this study, patients were first characterized as having a hard or a soft pancreas and were then randomized to stent versus no stent. The authors found that in both pancreatic texture groups, internal pancreatic duct stenting did not decrease the frequency or the severity of POPFs (38).

In a Cochrane review of eight RCTs with a total of 1,018 patients, the impact of pancreatic stenting on the incidence of pancreatic fistula was uncertain due to the relatively low quality of the evidence (39). The authors similarly were unable to find any difference in the rate of in-hospital mortality, need for reoperation, rates of DGE, intra-abdominal abscess, or wound infection when comparing those patients who underwent PD with a PJ stent to those who underwent PD without a PJ stent. In a subgroup analysis comparing internal versus external stenting, the results were similarly uncertain with regards to the impact on rates of pancreatic fistula, DGE, reoperation, and intra-abdominal abscess. The only significant difference reported was a shorter hospital stay for patients who received stents (MD −3.68 days) compared to patients who did not receive a stent (39). Given that stenting may decrease hospital length of stay, our institution commonly utilizes internal stenting across the PJ anastomosis, particularly in patients at high-risk for the development of a pancreatic fistula (small pancreatic duct, soft gland).

Fibrin sealant

Fibrin sealant is a tissue adhesive product derived from either human or animal plasma. It consists of fibrinogen and thrombin and therefore promotes blood clotting and cross-linking of fibrin, leading to its use as a hemostat and sealant (40). Given these properties, it has been applied to the PJ anastomosis or to the pancreatic stump closure in distal pancreatectomies in an effort to decrease rates of POPF. A Cochrane review of nine trials and 1,095 patients over the years 1994–2013 (albeit including distal pancreatectomies in addition to PDs) showed no difference in the rates of POPF, postoperative mortality, morbidity, reoperation rate, or length of hospital stay between patients who did and did not have fibrin sealant used (41). Three trials specifically compared the incidence of pancreatic fistulas when fibrin sealant was applied to the PJ anastomosis as reinforcement following PD and found no difference as compared to patients who underwent PD and PJ anastomosis without fibrin sealant application (41).

PJ versus pancreaticogastrostomy (PG)

An additional technique developed in an effort to reduce rates of POPF is making the pancreatic-enteric anastomosis via a PG rather than a PJ. Proposed potential mechanisms by which a PG anastomosis could reduce rates of pancreatic fistula include prevention of pancreatic enzymatic activity upon contact with the acidic environment of the stomach and improved healing of the anastomosis via the abundant gastric blood supply (42). The data to date on this technique have been mixed but do not clearly support one technique as superior in terms of reducing the incidence of pancreatic fistula. For instance, an RCT published by Yeo *et al*. in 1995 and a German trial from 2012 found similar rates of POPF in patients who underwent PJ versus patients who underwent a GJ (43,44). A meta-analysis by Menahem *et al.* collated data from seven RCTs and 1,121 patients and found that the incidence of pancreatic fistula was significantly lower in PG anastomosis (11.2% versus 18.7% in PJ), but only four of the RCTs included in this analysis used the ISGPS definitions (45). In general, the heterogeneity in defining the incidence of a pancreatic fistula (as well as DGE, as discussed above) has made it difficult to definitively show the superiority of one technique versus the other. This highlights the importance of using standardized definitions in the literature to allow for comparison and pooled data as well as the need for additional RCTs using such defined outcomes to better determine the impact of interventions aimed at reducing the morbidity associated with PD.

Conclusions

Pancreaticoduodenectomy is the only potentially curative treatment for pancreatic cancer, and its mortality has drastically decreased in high-volume centers. Morbidity remains high, despite several proposed variations in technique. While vascular reconstructions are technically feasible, studies on outcomes from techniques designed to decrease complications such as DGE and pancreatic fistula have largely been mixed without clear evidence of benefit. Additional research is needed to determine methods to further decrease rates of morbidity.

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Footnote

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References

1. Jemal A, Bray F, Center MM, et al. Global cancer statistics. CA Cancer J Clin 2011;61:69-90.
2. Howlader N NA, Krapcho M, Garshell J, et al. editors. Previous Version: SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Available online: http://seer.cancer.gov/csr/1975_2013/
3. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62:10-29.
4. Jang JY, Kang MJ, Heo JS, et al. A prospective randomized controlled study comparing outcomes of standard resection and extended resection, including dissection of the nerve plexus and various lymph nodes, in patients with pancreatic head cancer. Ann Surg 2014;259:656-64.
5. Kohler BA, Sherman RL, Howlader N, et al. Annual Report to the Nation on the Status of Cancer, 1975-2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State. J Natl Cancer Inst 2015;107:djv048.
6. Malvezzi M, Bertuccio P, Levi F, et al. European cancer mortality predictions for the year 2014. Ann Oncol 2014;25:1650-6.
7. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg 2015;220:530-6.
8. Oettle H, Neuhaus P, Hochhaus A, et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. JAMA 2013;310:1473-81.
9. Alexakis N, Halloran C, Raraty M, et al. Current standards of surgery for pancreatic cancer. Br J Surg 2004;91:1410-27.
10. He J, Ahuja N, Makary MA, et al. 2564 resected periampullary adenocarcinomas at a single institution: trends over three decades. HPB (Oxford) 2014;16:83-90.
11. Whipple AO, Parsons WB, Mullins CR. Treatment of Carcinoma of the Ampulla of Vater. Ann Surg 1935;102:763-79.
12. Buchler MW, Wagner M, Schmied BM, et al. Changes in morbidity after pancreatic resection: toward the end of completion pancreatectomy. Arch Surg 2003;138:1310-4; discussion 5.
13. Gouma DJ, van Geenen RC, van Gulik TM, et al. Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. Ann Surg 2000;232:786-95.
14. Callery MP, Chang KJ, Fishman EK, et al. Pretreatment assessment of resectable and borderline resectable pancreatic cancer: expert consensus statement. Ann Surg Oncol 2009;16:1727-33.
15. Neoptolemos JP, Stocken DD, Dunn JA, et al. Influence of resection margins on survival for patients with pancreatic cancer treated by adjuvant chemoradiation and/or chemotherapy in the ESPAC-1 randomized controlled trial. Ann Surg 2001;234:758-68.

16. Verbeke CS, Menon KV. Redefining resection margin status in pancreatic cancer. HPB (Oxford) 2009;11:282-9.
17. Younan G, Tsai S, Evans DB, et al. Techniques of Vascular Resection and Reconstruction in Pancreatic Cancer. Surg Clin North Am 2016;96:1351-70.
18. Christians KK, Heimler JW, George B, et al. Survival of patients with resectable pancreatic cancer who received neoadjuvant therapy. Surgery 2016;159:893-900.
19. Ferrone CR, Marchegiani G, Hong TS, et al. Radiological and surgical implications of neoadjuvant treatment with FOLFIRINOX for locally advanced and borderline resectable pancreatic cancer. Ann Surg 2015;261:12-7.
20. Katz MH, Pisters PW, Evans DB, et al. Borderline resectable pancreatic cancer: the importance of this emerging stage of disease. J Am Coll Surg 2008;206:833-46; discussion 46-8.
21. Abrams RA, Lowy AM, O'Reilly EM, et al. Combined modality treatment of resectable and borderline resectable pancreas cancer: expert consensus statement. Ann Surg Oncol 2009;16:1751-6.
22. Christians KK, Lal A, Pappas S, et al. Portal vein resection. Surg Clin North Am 2010;90:309-22.
23. Tseng JF, Tamm EP, Lee JE, et al. Venous resection in pancreatic cancer surgery. Best Pract Res Clin Gastroenterol 2006;20:349-64.
24. Sgroi MD, Narayan RR, Lane JS, et al. Vascular reconstruction plays an important role in the treatment of pancreatic adenocarcinoma. J Vasc Surg 2015;61:475-80.
25. Castleberry AW, White RR, De La Fuente SG, et al. The impact of vascular resection on early postoperative outcomes after pancreaticoduodenectomy: an analysis of the American College of Surgeons National Surgical Quality Improvement Program database. Ann Surg Oncol 2012;19:4068-77.
26. Gong Y, Zhang L, He T, et al. Pancreaticoduodenectomy combined with vascular resection and reconstruction for patients with locally advanced pancreatic cancer: a multicenter, retrospective analysis. PLoS One 2013;8:e70340.
27. Nakamura T, Ambo Y, Noji T, et al. Reduction of the Incidence of Delayed Gastric Emptying in Side-to-Side Gastrojejunostomy in Subtotal Stomach-Preserving Pancreaticoduodenectomy. J Gastrointest Surg 2015;19:1425-32.
28. Kim DK, Hindenburg AA, Sharma SK, et al. Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy? Ann Surg Oncol 2005;12:222-7.
29. Eisenberg JD, Rosato EL, Lavu H, et al. Delayed Gastric Emptying After Pancreaticoduodenectomy: an Analysis of Risk Factors and Cost. J Gastrointest Surg 2015;19:1572-80.
30. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2007;142:761-8.
31. Diener MK, Fitzmaurice C, Schwarzer G, et al. Pylorus-preserving pancreaticoduodenectomy (pp Whipple) versus pancreaticoduodenectomy (classic Whipple) for surgical treatment of periampullary and pancreatic carcinoma. Cochrane Database Syst Rev 2014:CD006053.
32. Bell R, Pandanaboyana S, Shah N, et al. Meta-analysis of antecolic versus retrocolic gastric reconstruction after a pylorus-preserving pancreatoduodenectomy. HPB (Oxford) 2015;17:202-8.
33. Huttner FJ, Klotz R, Ulrich A, et al. Antecolic versus retrocolic reconstruction after partial pancreaticoduodenectomy. Cochrane Database Syst Rev 2016;9:CD011862.
34. Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138:8-13.
35. 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.
36. Ramacciato G, Mercantini P, Petrucciani N, et al. Risk factors of pancreatic fistula after pancreaticoduodenectomy: a collective review. Am Surg 2011;77:257-69.
37. Manabe T, Suzuki T, Tobe T. A secured technique for pancreatojejunal anastomosis in pancreaticoduodenectomy. Surg Gynecol Obstet 1986;163:378-80.
38. Winter JM, Cameron JL, Campbell KA, et al. Does pancreatic duct stenting decrease the rate of pancreatic fistula following pancreaticoduodenectomy? Results of a prospective randomized trial. J Gastrointest Surg 2006;10:1280-90; discussion 90.
39. Dong Z, Xu J, Wang Z, et al. Stents for the prevention of pancreatic fistula following pancreaticoduodenectomy. Cochrane Database Syst Rev 2016:CD008914.
40. Spotnitz WD. Fibrin sealant: past, present, and future: a brief review. World J Surg 2010;34:632-4.
41. Cheng Y, Ye M, Xiong X, et al. Fibrin sealants for the prevention of postoperative pancreatic fistula following pancreatic surgery. Cochrane Database Syst Rev 2016;2:CD009621.
42. Shrikhande SV, Sivasanker M, Vollmer CM, et al.

Pancreatic anastomosis after pancreatoduodenectomy: A position statement by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2017;161:1221-34.
43. Yeo CJ, Cameron JL, Maher MM, et al. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. Ann Surg 1995;222:580-8; discussion 8-92.
44. Wellner UF, Sick O, Olschewski M, et al. Randomized controlled single-center trial comparing pancreatogastrostomy versus pancreaticojejunostomy after partial pancreatoduodenectomy. J Gastrointest Surg 2012;16:1686-95.
45. Menahem B, Guittet L, Mulliri A, et al. Pancreaticogastrostomy is superior to pancreaticojejunostomy for prevention of pancreatic fistula after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. Ann Surg 2015;261:882-7.

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