



# Surgical management of pancreatic ductal adenocarcinoma: a narrative review

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**Background and Objective:** Pancreatic ductal adenocarcinoma (PDAC) is the third-leading cause of cancer-related death in the United States and is projected to become the second-leading cause of cancer-related death by 2030. Despite advances in systemic and radiation therapy, for patients with surgically resectable PDAC, complete surgical resection is the only potentially curative treatment option. The conduct of a safe, technically excellent pancreatectomy is essential to achieve optimal perioperative outcomes and long-term survival. In this narrative review, evidence from large, well-executed studies and clinical trials examining the technical aspects of pancreatectomy is reviewed.

**Methods:** A search was conducted in PubMed, Medline, and Cochrane Review databases to identify English-language randomized clinical trials, meta-analyses, and systematic reviews assessing surgical aspects of pancreatectomy for PDAC published between 2010 to 2023.

**Key Content and Findings:** We identified retrospective and prospective studies evaluating the technical aspects of surgery for PDAC. In this review, we evaluate data on surgical techniques of pancreatectomy for PDAC, including the role of minimally invasive techniques, extent of lymphadenectomy, reconstruction options after pancreatoduodenectomy, and the role of surgical drainage.

**Conclusions:** Surgical resection has a critical role in the treatment of operable PDAC. While pancreatic cancer surgery is an active area of research, conducting a technically excellent surgical resection maintains paramount importance for both oncological and perioperative outcomes. In this review, we summarize the latest evidence on surgical technique for operable PDAC.

**Keywords:** Pancreatic ductal adenocarcinoma (PDAC); surgical resection; surgical techniques; perioperative complications

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## Introduction

The incidence of pancreatic ductal adenocarcinoma (PDAC) has increased in recent years by 0.5–1% per year, with an estimated 64,050 new cases in 2023. The 5-year survival rate has risen to 12% from 3–4% historically, due

to improvements in systemic therapy. The cornerstone of curative treatment for PDAC is surgical resection, however only 10–15% of patients with PDAC have localized, resectable tumors (1,2). The role of adjuvant systemic therapy has been well-established in multiple randomized

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**Table 1** Search summary

Items	Specification
Date of search	02/01/2023
Databases and other sources searched	PubMed, Medline, Cochrane Review
Search terms	“Carcinoma, Pancreatic Ductal” AND “Diagnosis” OR “Surgery” OR “Complications” “Pancreatectomy” OR “Pancreatoduodenectomy” AND “Methods” OR “Standrads” OR “Trends” OR “Adverse effects” “pancreatic fistula” AND “epidemiology” OR “etiology” OR “therapy”
Timeframe	01/01/2010–01/31/2023
Inclusion and exclusion criteria	Inclusion: English-language randomized clinical trials, meta-analyses, and systematic reviews assessing surgical aspects of pancreatectomy for PDAC  Exclusion: studies assessing pancreatectomy for other indications
Selection process	ES reviewed all identified articles for inclusion and exclusion criteria. References of articles were further reviewed to identify possible sources

controlled trials (RCTs) (3,4), and the use of neoadjuvant systemic therapy and radiation is evolving and being actively investigated in multiple trials of resectable and borderline resectable PDAC (5-7).

Due to the technical complexity of pancreatectomy and the attendant high rates of postoperative morbidity, a substantial body of surgical literature has focused on the technical nuances of pancreatectomy and prevention of postoperative complications. As post-pancreatectomy complications have been associated with lower rates of adjuvant systemic therapy administration and worse prognosis, optimization of surgical technique to minimize postoperative complications is of paramount importance (8,9). While research advances in tumor biology and improvements in systemic therapy are necessary to improve long-term outcomes for all patients with PDAC, the surgical contribution to long-term survival is the conduct of a safe, technically excellent pancreatectomy while minimizing operative morbidity to facilitate receipt of systemic therapy (10,11). Herein, we review the technical aspects of pancreatectomy, including data from relevant high-quality studies. We present this article in accordance with the Narrative Review reporting checklist (available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-27/rc>).

## Methods

A search was performed in PubMed, Medline, and Cochrane Review databases to identify English-language RCTs, meta-analyses, and systematic reviews of the surgical

aspects of pancreatectomy for PDAC published between 2010 to 2023. We utilized search phrases outlined in *Table 1*. The references of acquired sources were reviewed to identify potentially missed studies. Only studies assessing pancreatectomy for PDAC were included.

## Clinical staging, surgical management, and post-pancreatectomy complications

### *Work-up of PDAC*

High-quality cross-sectional imaging is required for accurate staging and surgical planning. Dual-phase computed tomography (CT) with fine collimation and overlapping slice reconstruction of the chest, abdomen, and pelvis, assesses the tumor relationship to mesenteric vasculature and extent of disease. Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) are used interchangeably or to supplement CT imaging and can evaluate small and non-hypoattenuating pancreas tumors and assess liver lesions. No clear advantage between CT and MRI has been demonstrated (12). Endoscopic ultrasound (EUS) is used to assess small lesions with equivocal imaging findings and to perform needle biopsy. In addition to biliary stenting for preoperative biliary obstruction, endoscopic retrograde cholangiopancreatography (ERCP) and intraductal brushing for cytology can be used to diagnose pancreatic head tumors (13,14).

Tumor resectability is determined by its relationship with mesenteric vasculature. Combined international guidelines consider a radiographically resectable tumor as without

distant metastasis, and with no arterial [celiac axis, superior mesenteric artery (SMA), or common hepatic artery] tumor contact, and  $\leq 180^\circ$  of venous (superior mesenteric vein or portal vein) contact without contour irregularity (15-17).

### ***Definitions of surgical resections***

Most (60–70%) PDAC arises in the pancreatic head (18). Pancreatoduodenectomy is resection of the pancreatic head/uncinate process, duodenum, and common bile duct with or without an antrectomy, and is the surgical procedure for tumors located to the right of the mesenteric vasculature. Distal pancreatectomy is resection of the pancreatic body/tail and spleen, and is indicated for tumors located to the left of the mesenteric vasculature (19-21). Radical antegrade modular pancreato-splenectomy (RAMPS) is a more contemporary variation of distal pancreatectomy, which aims to achieve increased lymph node yield and to maximize the chance for negative margins in left-sided pancreatectomies (22-24). For tumors involving a large volume of the pancreas on either side of the mesenteric vasculature or in selected cases requiring arterial reconstruction, total pancreatectomy is employed, where the entire pancreas, duodenum, bile duct, and spleen are removed.

### ***Post-pancreatectomy complications and impact on adjuvant systemic therapy***

Post-pancreatectomy complications are common (25), with major complications occurring in 36–43% of post-pancreatoduodenectomy patients, resulting in a perioperative mortality rate of 3.2–3.9% (26-28). Postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), post-pancreatectomy hemorrhage, and wound infections are the most common complications. POPF, extravasation of pancreatic fluid from the pancreatic stump or anastomosis, is a severe post-pancreatectomy complication, and much attention is dedicated to defining and preventing this serious complication (29,30).

The International Study Group of Pancreatic Surgery (ISGPS) previously defined Grade A POPF as amylase-rich abdominal fluid without physiologic derangement. As it is not clinically actionable, Grade A POPF is redefined as a biochemical leak. POPFs that require invasive procedures are Grade B, and Grade C includes patients who develop organ failure, require reoperation, or die due to

POPF (31). In a systemic review, Pedrazzoli *et al.* report an overall POPF rate of 21.3% (range, 3–40%). Other studies report prevalence of Grade B POPF 10–25% and Grade C 5% (32-34). Ke *et al.* have shown that a soft pancreas [odds ratio (OR) 5.2] and low fasting blood glucose level ( $<108$  mg/dL, OR 3.0), are associated with the development of a POPF (32). The Fistula Risk Score predicts POPF after pancreatoduodenectomy based on risk factors of small pancreas duct, soft pancreas, high-risk pathology, and excessive blood loss (35). In addition, a recent systematic review and meta-analysis found that for distal pancreatectomies, pancreas texture, body mass index (BMI), blood transfusion, intraoperative blood loss, and operative time were clinical predictor for POPF (36). Importantly, a meta-analysis reported worse disease-free [hazard ratio (HR) 1.59] and overall survival (HR 1.15) in patients with POPF (33).

Multimodal therapy including surgical resection, systemic chemotherapy, and possibly radiation therapy is the optimal management of localized, resectable PDAC (37). However, overall efficacy is dependent upon treatment adherence. As post-pancreatectomy complications are common, adjuvant therapy is delayed or not administered to 25–50% of patients (3,38), and serious post-pancreatectomy complications double the likelihood of not receiving adjuvant therapy.

Tzeng *et al.* compared recommended systemic therapy completion rates in patients who received neoadjuvant therapy-first or underwent upfront surgical resection (39). No significant difference in major postoperative complications were found between the two groups. Completion of all recommended systemic therapy was higher in the neoadjuvant-first cohort, 83% *vs.* 58%. In another study, Merkow *et al.* found that serious complications increased the likelihood of not receiving adjuvant therapy (OR 2.20) (40). Importantly, patients who completed systemic therapy had a longer median overall survival. Interestingly, median overall survival between cohorts were not statistically significant, suggesting that treatment order does not matter, so long as all systemic therapy is completed (41). To prevent delays in adjuvant therapy from post-pancreatectomy complications, clinical practice has adopted neoadjuvant therapy even for patients with resectable tumors, with a six-fold increase in use of neoadjuvant therapy from 2004 to 2016 (42). As post-pancreatectomy complications can delay or preclude administration of adjuvant systemic therapy (39,40), a

substantial body of surgical literature is dedicated to the technical aspect of pancreatectomy to mitigate these complications.

## Technical aspects in pancreatic resection

### *Preoperative biliary drainage*

Obstructive jaundice is common in patients with pancreatic head PDAC due to obstruction of the common bile duct. Preoperative biliary drainage is recommended for jaundiced patients who will receive neoadjuvant systemic therapy, are malnourished with very high bilirubin levels, require prolonged preoperative medical optimization, or with a replaced right hepatic artery (15,43). For patients with resectable PDAC who undergo upfront surgical resection, an RCT demonstrated that preoperative biliary drainage increases postoperative complications and adds drainage-related complications (44). Saffo *et al.* reported high drainage-related complications (30%) and need for reintervention (34%) in patients with resectable PDAC who underwent biliary stenting prior to neoadjuvant systemic therapy (45). Meta-analyses have concluded that preoperative biliary drainage should not be routinely utilized solely for preoperative biliary decompression (46,47).

### *Role of staging laparoscopy*

While diagnostic studies including CT, magnetic resonance imaging (MRI), and endoscopy have significantly improved staging accuracy (48), staging laparoscopy is an important staging method to identify radiographically-occult metastatic disease (49-51) and to assess vascular involvement by the tumor, which may be more advanced than detected on imaging studies (52,53). The approach to diagnostic laparoscopy is variable across available literature. An important consideration is that metastases or vascular involvement may be missed even on laparoscopy unless the lesser sac is entered and the duodenum is mobilized (53,54). A 2019 meta-analysis reported metastatic disease in 14–38% of patients initially staged as resectable by imaging and in 36% of patients with locally advanced tumors (55). A Cochrane review reported avoiding unnecessary laparotomy in 21% of patients based on laparoscopic findings (56). Furthermore, Fong *et al.* assessed the efficacy of staging laparoscopy between two timeframes to account for advances in diagnostic imaging and increased utilization of neoadjuvant chemotherapy. Findings on laparoscopy

avoided non-therapeutic laparotomy in 44% (64/144) of patients in the first period (2001–2008) and 24% (45/187) of patients in the second period (2009–2014) (57). By avoiding non-therapeutic laparotomies, patients found to have advanced PDAC received systemic therapy without further delays, with a median of 3 days to receiving chemotherapy after laparoscopy *vs.* 11 days after nontherapeutic laparotomy (58). National Comprehensive Cancer Network guidelines recommend diagnostic laparoscopy for patients with borderline resectable tumors, elevated serum carbohydrate antigen (CA) 19-9 levels, large tumors, or regional lymphadenopathy (15).

### *Minimally invasive vs. open pancreatectomy*

Minimally invasive surgery (MIS) is an accepted approach and has become a mainstay of oncologic resections for some gastrointestinal tumors (59). While MIS distal pancreatectomy is commonly practiced, MIS pancreatoduodenectomy has been less widely implemented due to increased technical complexity.

### **Pancreatoduodenectomy**

Four RCTs have compared open and laparoscopic pancreatoduodenectomy. The laparoscopic approach requires longer operating time (60-62). The LEOPARD-2 RCT reported similar postoperative recovery (63-66) and complication rates including POPE, DGE, and postoperative hemorrhage between the open and laparoscopic groups (63,67,68), however the LEOPARD-2 trial was terminated early due to higher postoperative mortality rates in the laparoscopic group (60,62,63,69). Oncologic outcomes are comparable, with similar margin-negative (R0) resection rates and higher lymph node harvest using the laparoscopic approach. Long-term survival differences between the two approaches are not frequently reported. Retrospective studies report improved survival for the laparoscopic approach, although this may be attributed to a higher percentage of patients with early-stage disease and smaller tumor size undergoing laparoscopic pancreatoduodenectomy (66,70). No RCT has reported on robotic-assisted pancreatoduodenectomy. Multiple meta-analyses have reported comparable complication rates, mortality, and oncologic outcomes at an exchange for longer operative times and increased associated costs (71-73).

### **Distal pancreatectomy**

Retrospective series have reported comparable morbidity

rates and 90-day mortality rates between MIS and open distal pancreatectomy (74-79). Sulpice *et al.* reported reduced morbidity rate with laparoscopic *vs.* open distal pancreatectomy (6.6% *vs.* 10.4%) (75). Two RCTs, LEOPARD and LAPOP (80,81), reported reduced operative blood loss and shorter hospitalization in the MIS groups (80,81). In the LEOPARD trial, lower rates of DGE and improved quality of life was reported in the MIS group (80). The LAPOP trial failed to detect a difference in postoperative complications, including DGE (81). In a meta-analysis of these RCTs, the MIS group had shorter lengths of stay, reduced blood loss, and lower rates of DGE (82). Additional RCTs are ongoing to evaluate postoperative morbidity and mortality, oncological outcomes, recurrence, and survival (83).

### *Lymph node dissection*

#### **Pancreatoduodenectomy**

Lymph node metastasis is an important prognostic marker of survival and predictor of recurrence in PDAC. Extended lymphadenectomy was first described by Fortner *et al.* in 1973 and continues to be debated (84). Early retrospective studies demonstrated improved survival in extended resections (85,86).

The first RCT to compare standard and extended lymphadenectomy reported a trend for improved survival for node-positive patients who underwent extended lymphadenectomy on an ad-hoc analysis (87), however, multiple subsequent RCTs (88-93), meta-analyses (94-98), and a Cochrane review analysis (99) failed to identify a survival advantage for extended lymphadenectomy.

While no difference in overall survival has been reported between standard and extended lymphadenectomy for pancreatic head cancers, extended lymphadenectomy is associated with prolonged operative time and increased lymph node yield, as expected with a wider anatomical resection. A meta-analysis of five RCTs reported increased postoperative morbidity after extended lymphadenectomy (95). Complications including increased blood loss and transfusion requirements (89,91,93), increased rates of bile leak, pancreatic leak, lymphatic fistula formation, DGE, and diarrhea (96,98) have been reported in extended lymphadenectomy.

A 2014 ISGPS consensus statement recommends standard lymphadenectomy for pancreatic head PDAC, defined as removal of stations no. 5, 6, 8a, 12b1, 12b2, 12c, 13a, 13b, 14a, 14b, 17a, and 17b based on the failure of multiple studies to demonstrate a survival advantage for

extended lymphadenectomy (100).

#### **Distal pancreatectomy/splenectomy**

Lymphadenectomy for pancreatic body/tail PDAC has not been studied as extensively as pancreatic head tumors. To date, no RCT has been performed to evaluate the extent of lymphadenectomy during distal pancreatectomy. In 1997, Nakao *et al.* reported outcomes of 30 patients who underwent distal pancreatectomy for PDAC and reported highest involvement of lymph nodes surrounding the splenic artery, celiac trunk, and aorta (101). A 2014 ISGPS consensus statement recommends resection of nodal basins along the splenic artery, splenic hilum, and inferior border of the pancreas (100), in addition to station 9 nodes around the celiac axis for pancreas body tumors (100). Nodal metastasis to the common hepatic and SMA node stations have been reported in patients with pancreas body tumors (102-104). Patients with such distant metastasis also tend to have disease in the standard nodal stations (104). To date, no survival difference has been reported for extended lymphadenectomy (105). RAMPS is a promising technique, offering an N1 lymphadenectomy that includes the celiac lymph nodes and the nodes along the anterior and left side of the SMA (22,23). Given the lack of RCTs, performing a standard lymphadenectomy is recommended.

#### ***Classic Whipple vs. pylorus-preserving pancreatoduodenectomy (PPPD)***

In 1980, Traverso *et al.* introduced the PPPD, a modified version of the classic Whipple procedure, which spares the stomach and the first portion of the duodenum, thus preserving pyloric function. The goal of this modified procedure was to reduce post-gastrectomy symptoms, such as dumping syndrome, diarrhea, and dyspepsia (106). Prospective studies comparing perioperative and long-term outcomes after classic Whipple *vs.* PPPD, have been inconclusive. With respect to intraoperative measures, operative time, blood loss, morbidity and mortality, several studies have shown comparable outcomes following both procedures (107-110), while one large retrospective study reported a longer operative time, longer hospital stay, and increased transfusion requirements after classic Whipple procedure (111). In an RCT, Kawai *et al.* reported lower DGE rates in the classic Whipple group (4.5% *vs.* 17.2%) (112), while another more recent trial demonstrated comparable results between groups (109). When assessing long-term outcome and nutritional status, most recent data report equivalence

between the two approaches (109,112). Finally, several studies have demonstrated similar survival and oncologic outcomes after both procedures (108,110,111,113). Possible advantages of the PPPD are shorter operative times, hospital stays, and reduced blood transfusion requirements, although PPPD has been associated with an increased incidence of DGE. Currently, the choice of procedure is determined by surgeon experience, and the scientific evidence thus far does not significantly favor one procedure over the other.

### ***Roux-en-Y vs. Billroth II gastrojejunostomy***

Machado first described the Roux-en-Y anastomosis instead of the Billroth II gastrojejunostomy reconstruction in 1976 as a method to reduce POPF, hypothesizing that isolating the pancreatobiliary and alimentary limbs would reduce complications by isolating the gastrojejunostomy anastomosis from the pancreatic enzymes (114). However, the superiority of Roux-en-Y reconstruction has not been established, and morbidity rates reported in RCTs are inconsistent. Ke and Tani found no difference in rates of POPF (115,116). DGE rates also appear comparable (117) and one study by Shimoda *et al.* reported lower rates of Grade B and C DGE in patients who underwent Billroth II gastrojejunostomy reconstruction compared to Roux-en-Y (118). The evidence remains inconsistent in meta-analyses. While Yang *et al.* reported a decreased rate of DGE in those who underwent Billroth II anastomosis (119), Ma *et al.* failed to replicate these results (120). The same meta-analysis of 1,072 patients by Ma, reported no difference in abscess formation, infection, and bleeding while another meta-analysis by Xiao reported a higher rate of Grade B and C DGE in the Roux-en-Y group (14.8% *vs.* 8%), which is comparable to the results reported by Shimoda *et al.* The same study found no difference for POPF, bile leak, or abscess formation (118,120,121). Given the inconsistent evidence, there is no clearly superior method of gastroenteric reconstruction.

### ***Pancreatojejunostomy (PJ) vs. pancreatogastrostomy (PG)***

Following pancreatoduodenectomy, an anastomosis must be made to restore drainage of the pancreas remnant into the digestive tract. The technique used for this anastomosis is of particular importance, given that POPF is one of the most common and severe complications after pancreatoduodenectomy. Two techniques are commonly

used, PJ and PG, with PJ being the more common of these procedures (122). Multiple RCTs have been conducted to compare the techniques, however, results are inconclusive. Several RCTs have demonstrated similar incidence of POPF after both procedures (123-125), while at least two RCTs have reported higher incidence of clinically significant POPF after PJ (126,127). A recent meta-analysis of 10 RCTs showed lower incidence of POPF and intra-abdominal collections (OR =0.73, P=0.02; OR =0.59, P=0.02) at the cost of a higher incidence of postoperative hemorrhage after PG (OR =1.52; P=0.02), and a similar incidence of DGE in both groups (128). Overall, there is no compelling evidence to favor one technique for pancreatic reconstruction over the other after pancreatoduodenectomy. Thus, the choice of technique is largely determined by surgeon preference and experience.

### ***Surgical tissue adhesive to reduce pancreatic fistula***

The use of intraoperative surgical tissue adhesives, or fibrin sealants, during pancreatectomy is controversial. Multiple RCTs evaluating the effectiveness of fibrin sealants on distal pancreatectomy remnant stump showed no reduction in POPF (129-131). To further assess these interventions, Carter *et al.* analyzed the addition of a falciform patch and fibrin glue to currently used methods, finding no significant difference between groups (132). Two large RCTs evaluated the effect of fibrin sealants on POPF in patients undergoing pancreatoduodenectomy and reported no difference in POPF rates (133,134). Currently there is no evidence to support the use of fibrin sealants.

### ***Stapled vs. hand-sewn closure of the main pancreas duct for distal pancreatectomy***

The two most common methods of dividing the pancreas for distal pancreatectomy are sharp division with a scalpel and oversewing the divided main pancreas duct and the use of stapling devices to simultaneously divide and close the pancreas stump. In the DISPACT RCT, comparing stapler and hand-sewn closure, rates of POPF (32% *vs.* 28%, respectively) and mortality (0% *vs.* 0.6%, respectively) were similar, as were operating times (135). A separate RCT assessing the utility of mesh reinforcement of the staple line closed early, finding a lower clinically significant POPF rate in the group with mesh reinforcement (1.9% *vs.* 24%) (136). However, two recent RCTs compared reinforced and standard stapler transection and found no difference in POPF rates (137,138).

### *Role of drains in pancreatic resection*

The utilization of surgical drains is common after pancreatectomy, as the theoretical purpose of drainage is to mitigate the clinical consequences of POPF. Whether the use of drains reduces postoperative complications is still controversial. In a recent worldwide survey of experienced hepatopancreatobiliary surgeons, routine intraperitoneal drainage was reported by 59.2% of surgeons, while 26.9% use drains selectively, and 13.9% never leave drains. Of those who place drains, 45.4% reported that they remove drains early (postoperative day  $\leq 3$ ) based upon drain fluid amylase values (139). An RCT assessing the role of surgical drainage was terminated early due to increased mortality rates in the patients randomized to no surgical drain (140). A meta-analysis determined that drain fluid amylase level on the first postoperative day is highly predictive of POPF (141). In an RCT, patients with low drain fluid amylase levels on day 1 were randomized to early drain removal (postoperative day 3) or standard removal (postoperative day 5 or beyond). Compared with late drain removal, early drain removal may reduce the rate of POPF (1.8% *vs.* 26.3%), intra-abdominal infection rate, morbidity (38.5% *vs.* 61.4%), and hospital costs and length of stay for patients with low risk of POPF (142). Data on the universal use of drains are not conclusive, suggesting the decision to leave an intraperitoneal drain should be tailored to each patient's individual risk of developing POPF (143).

### *Vascular reconstruction*

Venous and arterial vascular resection and reconstruction during pancreatectomy is guided by the anatomical location and extent of the tumor. In general, the length of the vascular reconstruction has a negative prognostic value as it reflects the extent of the disease. Venous resections  $>2-3$  cm is highly correlated with a poorer prognosis (144-146). The ISGPS classifies venous reconstruction into four types: Type I: partial venous excision with direct closure; Type II: partial venous excision using a patch; Type III: segmental resection with primary venovenous anastomosis; and Type IV: segmental resection with an interposition venous conduit and at least two anastomoses (147). The conduits may include an autologous venous or peritoneal patch or graft, a cryopreserved homologous, a heterologous, or a prosthetic graft (148-151). The prognosis after venous reconstruction has been largely

favorable, however there are significant differences between each technique. A multicenter retrospective cohort study found the median survival of end-to-end anastomosis, direct suture repair, and interposition grafts to be significantly different (27.6, 18.8, and 13 months respectively) (152). In these three groups, surgical morbidity and mortality were similar. An observational study comparing pancreatectomy with and without venous resection reported comparable overall survival, but significantly different median survival (18.5 *vs.* 25.8 months, respectively), suggesting that venous resection should be limited to patients with no arterial contact and those who also had received adjuvant chemotherapy (153).

Arterial resection during pancreatoduodenectomy is technically complex and requires careful surgical planning. Neoadjuvant therapy is typically recommended prior to resection, and invasion into the arterial space is usually considered a contraindication due to its high morbidity, mortality, and poor oncologic results (154). Multiple studies of arterial resection reported a 3-year survival rate of 8%, however, neoadjuvant chemotherapy was not administered routinely (155). These studies most commonly report results of hepatic artery or celiac axis artery resections. SMA resections are less common, and a systematic review including patients undergoing upfront pancreatectomy with SMA resection concluded that there was no evidence to support SMA resection (156). Perioperative morbidity was 39–91%, with a 25% mortality rate, and median survival of 11 months. In addition, the “TRIANGLE operation” is described as radical tumor removal by sharp dissection along the celiac axis and SMA. If frozen sections along the arterial sheaths are positive, abandoning pancreatectomy and pursuing palliative treatment is indicated (157).

The increasing use of neoadjuvant chemotherapy and/or radiation therapy has also made an impact on the overall survival of patients who undergo arterial resection. Truty *et al.* reported a cohort of patients who received total neoadjuvant therapy followed by resection, 65% of which required combined venous and arterial resection. Overall survival was 58.8 months, and 3-year survival was 62% (158). However, Bachellier *et al.* reported a median overall survival after resection of 13.7 months, although their patient population included 85% with arterial resections and 89% with simultaneous venous resections (159). Arterial resections are very rarely indicated and usually associated with venous resection. As a guideline, an artery first approach should be taken to evaluate any

additional artery involvement when examined by frozen section (160). Careful planning and discussion with a multidisciplinary tumor board at a tertiary center is highly recommended.

## Conclusions

Surgical resection is the only potentially curative treatment for PDAC. Although mortality has gradually decreased in high-volume centers, morbidity remains substantial. Studies on surgical technique to decrease postoperative complications have largely been mixed without clear evidence of benefit. In this study, we attempt to provide a succinct analysis of current data to help achieve safe and technically excellent surgical treatment for PDAC.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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