CHAPTER 105

Prevention and Management of Complications of Pancreatic Surgery

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Mortality after pancreatic resection has greatly decreased in comparison with historical series, from 33% following Whipple's initial reports to currently less than 2% in most high-volume centers,[1] resulting in the recognition that assessment of surgical quality for these high-acuity patients warrants further refinement.[1] Birkmeyer et al. have demonstrated the impact of hospital volume on actual operative mortality for pancreatic cancer resections, among other high-acuity operations,[2] but these two measures accounted for only half of the hospital-level variation in mortality. Moreover, van der Geest et al. found that the volume-outcome relationship persists in the highest-volume centers (≥40 procedures annually),[3] yet overall morbidity remains high for pancreatic resections, in the range of 35% to 55%.[1,4] Previously published outcomes after pancreatic resection in a high-volume institution are demonstrated in Table 105.1; the three most common complications were delayed gastric emptying (DGE) in 14%, wound infection in 7%, and pancreatic fistula in 5%.[5] This chapter will also discuss postpancreatectomy hemorrhage (PPH).

Initial efforts to better understand perioperative mortality after pancreatic resection demonstrated the impact of hospital volume on outcome, with a threefold to fourfold greater operative mortality at low-volume hospitals versus high-volume hospitals.[6–8] Fong et al. also demonstrate an ongoing survival benefit (6% at 2 years) for patients undergoing pancreatic cancer resection at a high-volume institution.[8] A recent single-institution study reports that higher surgeon volume is associated with shorter operative time, less intraoperative blood loss, and higher lymph node harvest (for cancer cases).[9] However, surgeon experience mitigated these differences, with experienced surgeons (>50 pancreaticoduodenectomies [PDs]) having significantly lower morbidity compared with less experienced surgeons and, in particular, less blood loss, shorter operative time, and a lower postoperative pancreatic fistula (POPF) rate.[9] Twenty PDs were required to equalize the experienced and inexperienced surgeons. However, adequacy of oncologic resection did not differ based on experience.

This chapter will focus on technical and clinical means of preventing and managing pancreatic surgical complications, but the import of surgeon and hospital volume, as well as experience, on complications and overall outcome after pancreatic resection should not be lost on the reader. Schmidt et al. also emphasize the importance of the institution's systems support for the diagnosis and management of postoperative complications (i.e., interventional radiology and gastroenterology, intensive care, and surgical team members).[9]

POSTPANCREATECTOMY HEMORRHAGE

Hemorrhage associated with pancreatic resection (PPH) occurs in up to 8% of cases but may account for 11% to 38% of mortality.[10–13] Because of the potential consequences of this problem, a consensus definition was developed by the International Study Group of Pancreatic Surgery (ISGPS) in 2007[14] and is seen in Table 105.2. This definition was validated and has been found to correlate well with duration of hospital stay, morbidity, and mortality.[13] It may occur intraoperatively, early in the postoperative period, or late (more than 24 hours postoperatively). Intraoperative hemorrhage may be more likely to occur in the event of aberrant vasculature particularly when not preoperatively identified.[15] Fig. 105.1 demonstrates normal peripancreatic vasculature, as seen on computed tomography (CT) angiography.[15] The common variations include a replaced right hepatic artery (11% to 21%), replaced left hepatic artery (4% to 10%), accessory right or left hepatic artery (<1% to 8%), and celiac artery stenosis (2% to 8%).[15]

Intraoperative vascular complications are known to adversely affect ultimate outcome,[16] including in-hospital mortality and survival rate; thus efforts to delineate vasculature preoperatively by means of a pancreatic protocol CT including arterial, venous, and portal venous phases[15] should allow the surgeon to be better prepared intraoperatively and limit the occurrence of intraoperative hemorrhage related to an unexpected encounter with abnormal vascular anatomy. These efforts should continue intraoperatively by inspection and palpation of the operative field to further define the vascular anatomy. For example, a replaced right hepatic artery may be appreciated by palpation of a pulse posterior and lateral to the bile duct and portal vein. Intraoperative hemorrhage may also occur in the setting of tumor infiltration that involves the relevant vasculature.

To obtain intraoperative control of hemorrhage, direct pressure should be applied initially to allow for mobilization of appropriate anesthetic and surgical resources, such as blood products, vascular sutures, and clamps, and appropriate surgical assistance. Aberrant vasculature, such as a replaced right hepatic artery, may need to be reconstructed or anastomosed to an alternate vessel to preserve hepatic arterial blood flow. Doppler ultrasonography may be useful to determine whether there is already alternate arterial flow. Venous injuries may be able to be addressed with venorrhaphy or with patch venoplasty. In exsanguinating, uncontrolled hemorrhage, portal vein ligation has been described, with a potential for survival, when accompanied by a "second-look" laparotomy in 24 hours

ABSTRACT

Mortality after pancreatic resection has greatly decreased in comparison with historical series, from 33% following Whipple's initial reports to currently less than 2% in most high-volume centers, resulting in the recognition that assessment of surgical quality for these high-acuity patients warrants further refinement. The impact of hospital volume on actual operative mortality is significant for pancreatic cancer resections, but these two measures accounted for only half of the hospital-level variation in mortality. The three most common complications after pancreatectomy are delayed gastric emptying, wound infection, and pancreatic fistula. This chapter will also discuss postpancreatectomy hemorrhage. Initial efforts to better understand perioperative mortality after pancreatic resection demonstrated the impact of hospital volume on outcome and an ongoing survival benefit (6% at 2 years) for patients undergoing pancreatic cancer resection at a high-volume institution. However, great effort has since been expended to better define, describe, and categorize postpancreatectomy complications, as well as to understand risk factors for the complications and management strategies. This chapter will focus on technical and clinical means of preventing and managing pancreatic surgical complications, but the import of surgeon and hospital volume, as well as experience, on complications and overall outcome after pancreatic resection should not be lost on the reader.

KEYWORDS

Pancreatectomy, complications, pancreatic surgery, delayed gastric emptying, postpancreatectomy hemorrhage, pancreatic fistula

TABLE 105.1 Mortality and Morbidity After Pancreaticoduodenectomy and Distal Pancreatectomy in 616 Patients

	Overall (*N* = 616)	Pancreaticoduodenectomy/Total Pancreatectomy (*n* = 564)	Distal Pancreatectomy (*n* = 52)	*P* Value
Perioperative mortality	2.3%	2.3%	1.9%	NS
Overall complications	30%	31%	25%	NS
SPECIFIC COMPLICATIONS				
Reoperation	3%	3%	4%	NS
Delayed gastric emptying	—	14%	—	—
Cholangitis	—	3%	—	—
Bile leak	—	2%	—	—
Wound infection	7%	7%	5%	NS
Pancreatic fistula	5%	5%	8%	NS
Intraabdominal abscess	3%	3%	4%	NS
Pneumonia	1%	1%	0%	NS
Pancreatitis	1%	1%	0%	NS
POSTOPERATIVE LENGTH OF STAY				
Mean ± SE	13.7 ± 0.4 days	14.0 ± 0.4 days	11.5 ± 2.2 days	.08
Median	11 days	11 days	7 days	—

NS, Not significant.
From Sohn TA, Yeo CJ, Cameron JL, et al. Resected adenocarcinoma of the pancreas—616 patients: results, outcomes, and prognostic indicators. *J Gastrointest Surg*. 2000;4:567.

TABLE 105.2 Classification of PPH: Clinical Condition and Diagnostic and Therapeutic Consequences

Grade	Time of Onset, Location, Severity and Clinical Impact of Bleeding		Clinical Condition	Diagnostic Consequence	Therapeutic Consequence
A	Early, intraluminal or extraluminal, mild	—	Well	Observation, blood count, ultrasonography and, if necessary, computed tomography	No
B	Early, intraluminal or extraluminal, severe	Late, intraluminal or extraluminal, mild*	Often well/ intermediate, very rarely life-threatening	Observation, blood count, ultrasonography, computed tomography, angiography, endoscopy†	Transfusion of fluid/blood, intermediate care unit (or ICU), therapeutic endoscopy,† embolization, relaparotomy for early PPH
C		Late, intraluminal or extraluminal, severe	Severely impaired, life-threatening	Angiography, computed tomography, endoscopy†	Localization of bleeding, angiography and embolization (endoscopy†), *or* relaparotomy, ICU

*Late, intraluminal or extraluminal, mild bleeding may not be immediately life-threatening to patient but may be a warning sign for later severe hemorrhage ("sentinel bleed") and is therefore grade B.
†Endoscopy should be performed when signs of intraluminal bleeding are present (melena, hematemesis, or blood loss via nasogastric tube).
ICU, Intensive care unit; *PPH,* postpancreatectomy hemorrhage.
From Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH)—an International Study Group of Pancreatic Surgery definition. *Surgery*. 2007;142:20.

to evaluate for signs of ischemia.[17] A more recent paper reports on a small series of patients undergoing damage control laparotomy (DCL) for pancreatic surgery,[18] primarily for portal vein injury, with the goal of allowing intensive care unit (ICU) resuscitation to reverse the accompanying hypothermia, acidosis, and coagulopathy. They describe initial venous compression to allow for identification/visualization of the site of injury, as well as for preparation of the surgical and anesthetic teams. Useful maneuvers for compression included the Kocher maneuver and sponge sticks. The pancreas was then divided and the specimen quickly extirpated when possible. Other techniques used to shorten operating time included external drainage, packing, stapled bowel closure, and rapid abdominal closure.[18] The authors emphasize that there was significant resource use but no mortality. Other risk factors for PPH have been identified including age, pancreatic fistula, pancreatoduodenectomy, and the nutritional risk index (NRI).[16]

Management of early and late PPH is addressed by the ISGPS classification schema.[13,14] Early PPH is most often a result of technical failure to achieve appropriate hemostasis at the index operation or else secondary to underlying coagulopathy. When significant and thought to be technical

FIGURE 105.1 Computed tomography angiography of normal peripancreatic arterial anatomy. (From Shukla PJ, Barreto SG, Kulkarni A, Nagarajan G, Fingerhut A. Vascular anomalies encountered during pancreatoduodenectomy: do they influence outcomes? *Ann Surg Oncol*. 2010;17:186.)

failure, prompt relaparotomy is mandated.[19] PPH occurring later than the first postoperative day and up to several weeks postoperatively is often a result of other postoperative complications, such as fistula, anastomotic ulceration, or pseudoaneurysm.[11,14,20] PPH may represent bleeding from intraluminal or extraluminal sources: unsecured vessels, vessels with pseudoaneurysm, anastomotic suture lines or ulceration, resection cut surfaces, or hemobilia. Named vascular structures that may be the source of bleeding are the gastroduodenal, hepatic, or splenic artery, branches of the superior mesenteric artery, or the splenic vein stump.[13,14] The classification system for PPH is described in Table 105.2.

After PPH becomes apparent, evaluation must occur in a timely fashion and may include a variety of modalities depending on the hemodynamic status of the patient and apparent location of the bleeding (intraluminal or extraluminal): endoscopy, angiography, CT scan, or reoperation.[14] Early extraluminal PPH requires reexploration. Intraluminal bleeding may manifest as extraluminal if there is associated anastomotic breakdown,[13] and this may be amenable to angiographic intervention when involving the pancreaticojejunostomy. Bleeding from the gastrojejunostomy or duodenojejunostomy may first be excluded by endoscopy. Over time, conservative management has become more successful for late PPH but surgical intervention has continued to be the mainstay of treatment. Mortality in patients with late PPH is much higher than for the routine pancreatic resection, with rates of 16% to 27%,[13–21] but is strongly associated with a bleed in the setting of a septic complication, such as pancreatic fistula. Patients present with septic complications and/or a sentinel bleed. Radiographic embolization has become a more successful modality, with up to 80% success,[13] but is limited by the initially intermittent nature of the bleeding.[20] Furthermore, key factors are the recognition of the sentinel bleed, the presence of pancreatic fistula, and a long gastroduodenal artery stump with radiopaque marker for an effective embolization.[21] Reexploration is indicated when angiographic intervention is not technically feasible or successful or when the site is not visualized on angiography and the patient is hemodynamically unstable.[13]

PANCREATIC FISTULA

POPF continues to be the nemesis of pancreatic resection. Occurring in up to 33% of cases, even in the setting of vast improvements in the safety and efficacy of pancreatic surgery overall as mentioned earlier, fistula rates have failed to decrease significantly.[22–24] One must first recall the definition of *fistula* as "an abnormal communication from one epithelialized surface to another" compared with that of *leakage*, referring to "an abnormal escape of fluid through an orifice or opening."[23]

In addition, POPF occurs with the leakage of amylase-rich fluid from the transection margin of the gland and/or from the pancreatic-enteric anastomosis. Although many literature reports have been devoted to studying the diagnosis, management, and effect of POPF on patient outcome, comparison of these studies has been difficult because there was previously no uniform definition available. To better understand POPF, the ISGPF developed a classification scheme that is presented in Table 105.3.[25] POPF was defined as inclusive of all peripancreatic fluid collections, abscesses, leaks, or fistulas and diagnosed by virtue of drain amylase, output, imaging, and clinical picture (well versus septic).[25] According to the classification scheme, grade A fistulas are biochemical only and not clinically relevant, whereas grades B and C fistulas are clinically relevant, requiring further evaluation and management, such as antibiotics, nutritional support, octreotide, and percutaneous drainage (grade B) or surgical exploration (grade C) in the setting of sepsis.[25] Subsequent efforts to validate this classification scheme demonstrate that grade A fistulas comprise nearly half of all POPF yet have no apparent significant effect on outcome. However, grade B/C fistulas occur less often (40% and 11%, respectively) but are associated with higher resource use (ICU stay, nursing services post discharge, readmission), longer hospital stay, more complications, and, accordingly, increase in cost, grade for grade.[22,24]

RISK STRATIFICATION

Prevention of POPF relates to appropriate risk stratification[26] according to endogenous, perioperative, and operative risk factors.[22] A soft gland or diagnoses of ampullary, duodenal, cystic, or islet cell pathologies increases the risk of POPF development by up to 10-fold.[26,27] Pancreatic duct size is also crucial, with small ducts up to 3 mm in diameter conferring increased risk of POPF,[26,28] with an odds ratio greater than 3. The Fistula Risk Score has been developed and validated as a predictive tool for surgeons, taking the above factors into account.[29,30] As for other endogenous risk factors, conflicting information

TABLE 105.3 Criteria for Grading Pancreatic Fistula (International Study Group of Pancreatic Surgery Classification Scheme)

Criteria	No Fistula	Grade A Fistula	Grade B Fistula	Grade C Fistula
Drain amylase	<3 times normal serum amylase	>3 times normal serum amylase	>3 times normal serum amylase	>3 times normal serum amylase
Clinical conditions	Well	Well	Often well	Ill appearing/bad
Specific treatment	No	No	Yes/No	Yes
Ultrasonography/Computed tomography (if obtained)	Negative	Negative	Negative/positive	Positive
Persistent drainage (>3 weeks)	No	No	Usually yes	Yes
Signs of infection	No	No	Yes	Yes
Readmission	No	No	Yes/No	Yes/No
Sepsis	No	No	No	Yes
Reoperation	No	No	No	Yes
Death related to fistula	No	No	No	Yes

Note: Signs of infection include elevated body temperature >38°C, leukocytosis, and localized erythema, induration, or purulent drainage. Readmission is any hospital admission within 30 days following hospital discharge from the initial operation. Sepsis is the presence of localized infection and positive culture with evidence of bacteremia (i.e., chills, rigors, elevated white blood cell count) requiring intravenous antibiotic treatment, or hemodynamic compromise as demonstrated by high cardiac output and low systemic vascular resistance within 24 hour of body temperature >38°C.
Modified from Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group definition. *Surgery*. 2005;138:8.

TABLE 105.4 The Impact of Increasing Number of Risk Factors for Pancreatic Fistulas

Outcomes	No Risk Factors ($n = 63$)	1 Risk Factor ($n = 88$)	2 Risk Factors ($n = 66$)	3 Risk Factors ($n = 13$)	4 Risk Factors ($n = 3$)	*P* value
Clinically relevant fistulas (%)	1 (2)	7 (8)	16 (24)	4 (31)	3 (100)	<.001
Nonfistulous complications (%)	22 (35)	38 (43)	38 (58)	6 (42)	2 (67)	.113
Hospital duration (median, days)	8	8	8	9	19	.001
Total hospital costs (median)	$16,969	$17,797	$20,179	$26,776	$40,517	.002
Total cost increase (beyond no risk factors)	—	$828	$3210	$9807	$23,548	—

Risk factors for pancreatic fistulas consist of (1) small pancreatic duct size (<3 mm); (2) pancreatic parenchyma of soft texture; (3) ampullary, duodenal, cystic, or islet cell pathology; and (4) increased intraoperative blood loss (>1000 mL).
Modified from Pratt WB, Callery MP, Vollmer CM Jr. Risk prediction for development of pancreatic fistula using the International Study Group of Pancreatic Surgery classification scheme. *World J Surg*. 2007;32:419.

exists in the literature. Some investigators have identified older age, male gender, coronary artery disease, diabetes mellitus, jaundice, and low creatinine clearance as predictors of POPF.[22,27,31,32] However, even though studies have found a correlation between male gender and POPF, these results are weakened by the design of these studies.[22,28] Moreover, explanations for the impact of gender are still lacking.[22] Interestingly, as a perioperative factor, neoadjuvant therapy appears to reduce the risk of fistula.[22,33] Operative risk factors for POPF include blood loss higher than 1000 mL, the anastomotic technique, routine drain placement, transanastomotic stents, and longer operative time.[22,26,28,31] Importantly, there appears to be an additive effect of these risk factors, whereby the percentage of patients developing a POPF increases sequentially as the number of risk factors increases,[26] as seen in Table 105.4, and is associated with increased cost and hospital stay.

Although the incidence of POPF seems to be similar after distal and central pancreatectomy versus proximal pancreatectomy, the clinical course in the setting of a distal resection is milder.[34] However, risk factors particular to distal resections remain poorly understood. Again, a soft gland is predictive of POPF, as well as primary pancreatic pathology and splenic preservation.[35] Division of the pancreas at the body rather than the neck and failure to ligate the main pancreatic duct were also identified as predictors of POPF after distal pancreatectomy.[36] Furthermore, there was no difference in fistula rate for stump closure with suture versus stapler, nor for any demographic measures.[35]

PREVENTIVE MEASURES

Many technical variations have been studied with the hope of decreasing the incidence of POPF. For PD, both the type of anastomosis and the technique used have been evaluated. The pancreatic-enteric anastomosis may be to the jejunum or to the stomach. For the more typical pancreaticojejunal anastomosis, a duct-to-mucosa or invagination technique may be used, as demonstrated in Figs. 105.2 and 105.3, respectively.[37] Most groups have found the duct-to-mucosa technique to be superior in terms of fistula rates, according to a large meta-analysis by Poon et al. published in 2002 and reflecting the studies of the 1990s.[38] Additional variations include the use of a single- or double-layer anastomosis, as well as the choice between continuous and interrupted suture. The binding pancreaticojejunostomy, in which invagination is used with ablation of the overlapping jejunal mucosa, has been

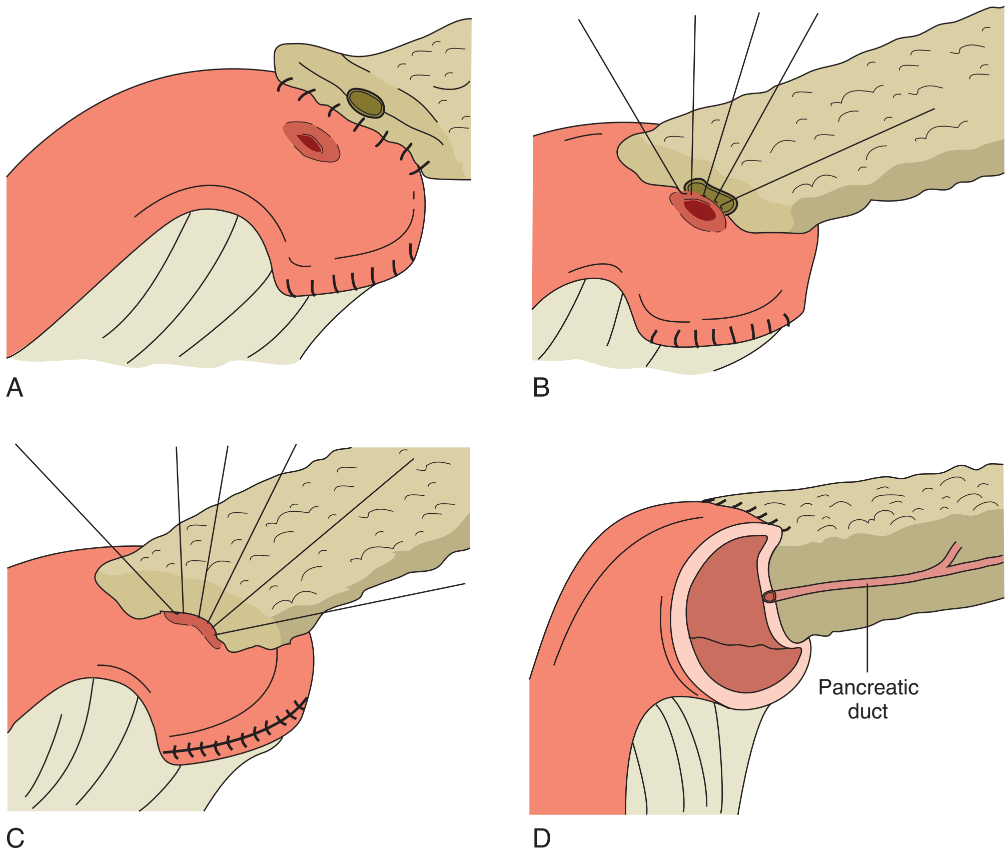

FIGURE 105.2 Duct-to-mucosa pancreaticojejunostomy. (A) Posterior outer row of interrupted silk sutures. (B) Posterior inner layer of duct-to-mucosa sutures. (C) Anterior inner layer of duct to mucosa interrupted sutures have been placed and tied. (D) Side view of completed anastomosis. Note in this trial, indwelling stents were not used. (Modified from Cameron JL, Sandone C. *Atlas of Gastrointestinal Surgery*. Vol. 1. 2nd ed. Hamilton, Ontario: Decker; 2007:296 [Figs. 26, 27, 30, and 31].)

shown to have equivalent fistula rates versus duct-to-mucosa but increased incidence of PPH.[22] There is one recent report of superiority of the invagination technique over the duct-to-mucosa technique in terms of fistula rate,[39] but the usual practice of the surgeons involved is taken into account; thus the results are difficult to interpret, and, at this point, duct-to-mucosa continues to be the preferred technique.

Pancreaticogastrostomy has been postulated to be advantageous with respect to POPF occurrence, because of the thickness and blood supply of the gastric wall, its proximity to the pancreas, and incomplete activation of pancreatic enzymes in the presence of gastric acid.[23,34] Yeo et al.[40] completed a prospective randomized trial comparing pancreaticojejunostomy to pancreaticogastrostomy (Fig. 105.4), which failed to demonstrate any benefit to either technique because the fistula rate was approximately 12% in both groups, which were similar in terms of gland texture and operative characteristics. Of note, surgeon volume did affect fistula rate.[39] There have been several nonrandomized similar studies and two meta-analyses that have concluded that pancreaticogastrostomy does indeed have a lower fistula rate when compared with pancreaticojejunostomy.[22,41] Furthermore, long-term patency and functional results may be problematic with this variation, as described in smaller case series.[38] Thus pancreaticojejunostomy continues as the mainstay of the reconstruction, although there may be some merit to performing the invagination technique or pancreaticogastrostomy when the duct is very small and/or difficult to delineate, and other high-risk factors are present, or when the surgeon is more practiced with those techniques.

In summary and at a most fundamental level, a successful pancreaticoenteric anastomosis requires a tension-free anastomosis with properly placed and tied sutures, preserved blood supply to the pancreatic remnant and jejunum, and unobstructed flow from the pancreas into the gastrointestinal tract, whatever the chosen technique may be.

Neither internal stenting nor creation of an isolated Roux loop has been found to positively affect fistula rate.[22] However, there is one randomized trial that demonstrates a significantly lower rate of POPF formation with external stenting compared with no stent (6% vs. 22%, respectively).[42] In theory, such external drainage might be advantageous because it should completely divert the pancreatic secretions away from the anastomosis.[42] Moreover, a meta-analysis also concluded that there was a benefit when stents are used; however, further studies need to be performed before asserting this benefit.[43]

After distal pancreatectomy, fistula rates have been studied to compare stapled versus sutured pancreatic

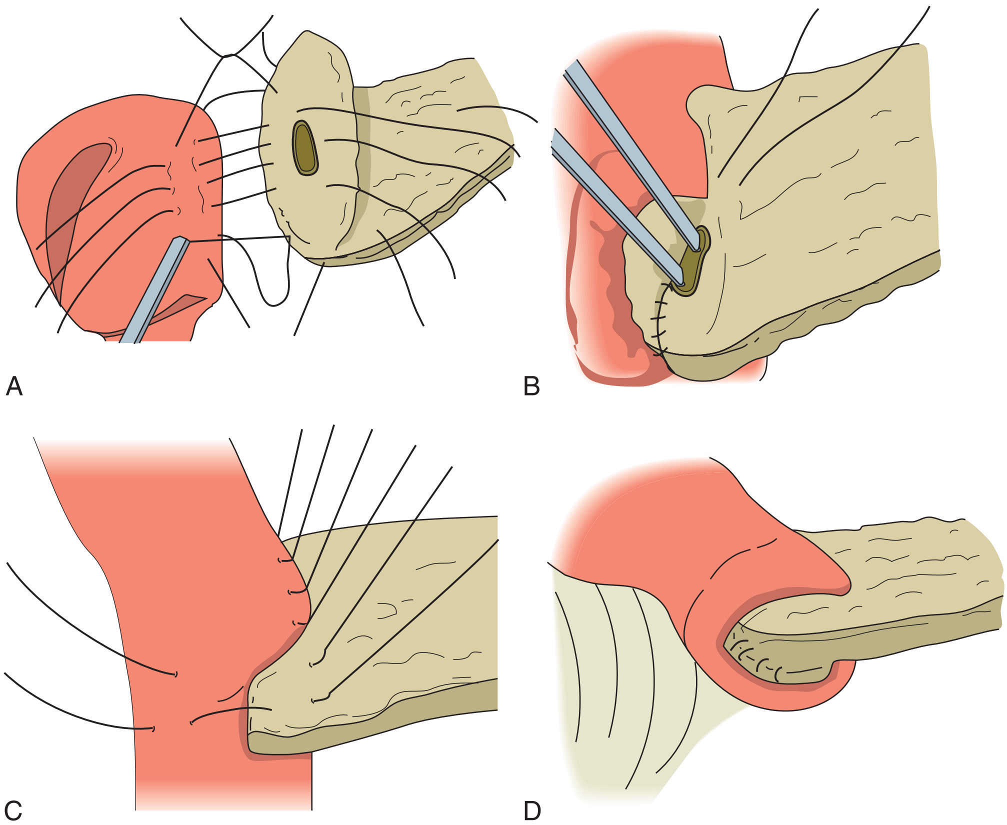

FIGURE 105.3 Invagination pancreaticojejunostomy. (A) Posterior outer row of silk interrupted sutures. (B) Inner continuous suture. (C) Outer layer of interrupted silk sutures. (D) Completed anastomosis demonstrating the "dunking" of the pancreatic remnant. (Modified from Cameron JL, Sandone C. *Atlas of Gastrointestinal Surgery*. Vol. 1. 2nd ed. Hamilton, Ontario: Decker; 2007:294 [Figs. 21, 23, 24, and 25].)

remnant[35] without clear demonstration of benefit with one technique over another found in evaluating the various papers in the literature[35,36]; thus either approach is acceptable. Investigation of the success of fibrin glue for preventing POPF has been marred by bias, and thus no conclusion has been reached as regards its utility.[23]

Octreotide, a long-lasting analogue of somatostatin, inactivates gastric and pancreatic exocrine secretion and may thus support a fragile pancreaticojejunostomy[23] or soft remnant after distal pancreatectomy. Studies of the utility of octreotide for decreasing POPF have been conflicting.[23,35,36] Some authors have found octreotide to be effective for distal[35] or local resection but not helpful in PD.[38] However, the benefit is clearer for high-risk glands[38] after PD. Prophylactic octreotide was efficacious and cost efficient when given to patients at high risk for POPF, with the criteria as listed previously,[26] and thus may be used selectively for those patients. No benefit was found for low-risk patients. On the other hand, a Cochrane review found no benefit in reducing fistula rates.[22] Furthermore, McMillan et al. found that octreotide was associated with higher rates of clinically relevant POPF, specifically in the presence of risk factors, including soft pancreatic parenchyma, high-risk pathologies, small duct diameter (≤4 mm), and elevated intraoperative blood loss.[44] However, a randomized trial found that pasireotide, a longer-acting somatostatin analogue, reduced the rates of clinically relevant POPF.[45]

MANAGEMENT

Management of clinically relevant pancreatic fistulas hinges on timely diagnosis. Especially because latent leaks or fistulas may develop and the patient may be home already, with the operative drain out, it is critical to acknowledge and respond to patient reports of worsening abdominal pain, fever, failure to thrive, or inability to tolerate a diet. According to the ISGPF classification, diagnosis requires drain amylase measurement, as well as clinical and imaging data. Furthermore, a sinister character of drain effluent, or output greater than 200 mL/day after postoperative day 5 may be associated with clinically relevant POPF.[23] Grade A fistulas are not of clinical consequence.[24] Patients having had a proximal or central pancreatectomy are more likely to require aggressive resuscitation and/or intervention than are patients after distal pancreatectomy.[34]

Much of the treatment of clinically relevant POPF is empiric. Initial management often includes hydration, being "nil per os" (NPO), supplemental nutrition, and antibiotics when patients present with signs and symptoms of infection (i.e., fever, leukocytosis). Octreotide may be given for high-output fistulas. Patients with amenable collections may undergo radiology-guided drainage, particularly if the operative drain has already been removed or if it is not adequately draining the site of the collection.

Reexploration is rarely required but may be necessary in the setting of clinical decline, undrainable fistula/abscess, or for the suspicion of pancreaticojejunal anastomotic dehiscence (Fig. 105.5). Options include wide drainage, anastomotic revision or conversion to alternate pancreatic duct drainage site, completion pancreatectomy, or use of a bridge-stent technique,[46] as depicted in Fig. 105.6. Pancreaticojejunal anastomotic dehiscence following PD is a rare but difficult problem to manage. The previously mentioned traditional surgical options are associated with significant morbidity and mortality. With a patient who is already compromised physiologically, the goal is a safe, efficient reoperation. The bridge-stent technique allowed a small group of patients to recover to hospital discharge with limited long-term sequelae[46] and is another option in the armamentarium to deal with this complex problem. However, specifically for patients with grade C POPF, a significant burden is incurred for patients, and aggressive clinical management, including reoperation when indicated (approximately 72% reported in this series), did not impact 90-day mortality.[47]

Patients with clinically relevant POPF are known to have longer hospital stays, more additional complications, ICU requirements, transfusion requirements, and need for services or rehabilitation placement on discharge.[24] Accordingly, total costs increase significantly as the grade of fistula increases.[24]

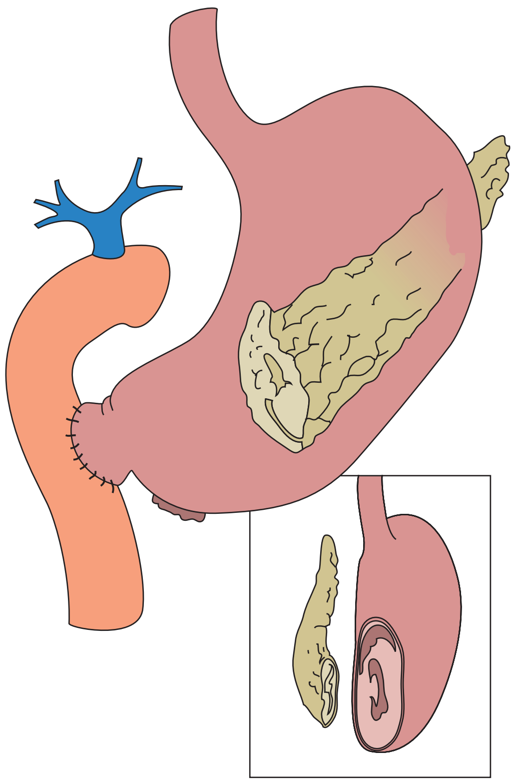

FIGURE 105.4 Pancreaticogastrostomy illustration, with anastomosis of the pancreas to the posterior gastric wall. (From Yeo CJ, Cameron JL, Maher MA, et al. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. *Ann Surg*. 1995;222:580.)

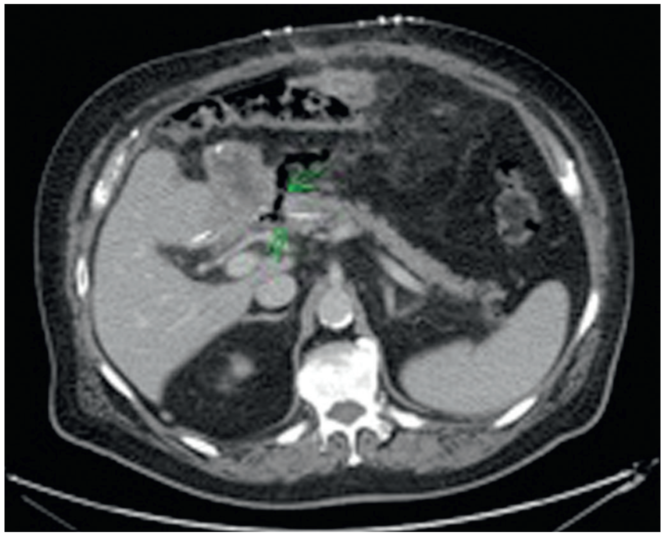

FIGURE 105.5 *Arrows* demonstrate gap between the pancreas and the jejunum, with associated peripancreatic gas. (From Kent TS, Callery MP, Vollmer CM. The bridge-stent technique for salvage of pancreatico-jejunal anastomotic dehiscence. *HPB [Oxford]*. 2010;12:577.)

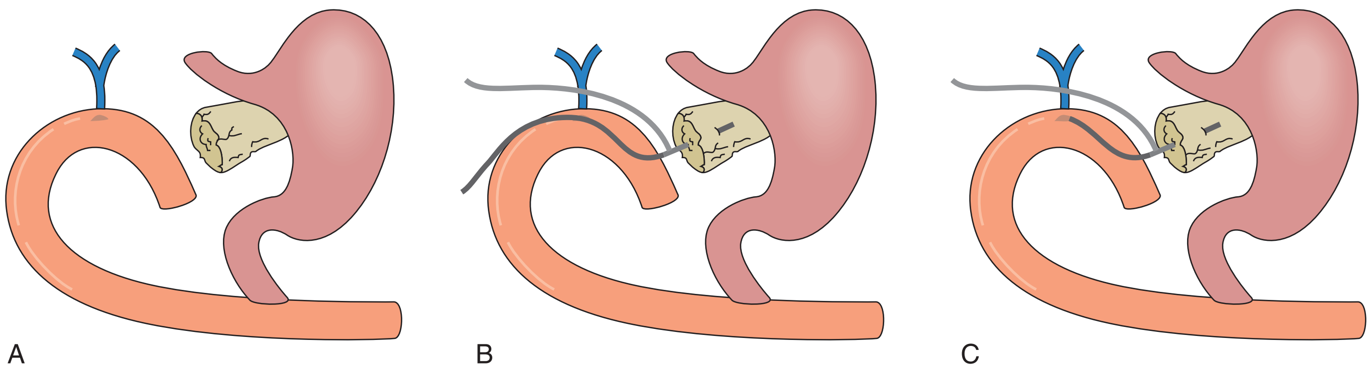

FIGURE 105.6 (A) Dehiscence of the pancreaticojejunal anastomosis is illustrated, with a gap between the pancreatic remnant and jejunum. (B) Bridge-stent technique with externalized stent plus external drain. (C) Bridge-stent technique with internal stent and external drain adjacent to gap. (From Kent TS, Callery MP, Vollmer CM. The bridge-stent technique for salvage of pancreatico-jejunal anastomotic dehiscence. *HPB [Oxford]*. 2010;12:577.)

DELAYED GASTRIC EMPTYING

Although DGE is rarely life-threatening and typically is self-limited, it can increase the length of hospital stay, likelihood of readmission, other complications, and ultimately cost.[48,49] Until 2007 there was no standard definition of DGE, and thus it was difficult to compare the multitude of literature reports on the topic, which described an incidence after PD of 6% to more than 50%.[5,48–51] The ISGPS has now created a definition (Table 105.5) of DGE, dividing it into grades of severity. Similar to the consensus definitions for PPH and POPF, this effort resulted in a standardized classification scheme based on duration of NGT decompression required, time until solid food is tolerated, the presence of vomiting or gastric distention, and the use of prokinetics.[47,51]

PREVENTIVE MEASURES

DGE is likely multifactorial but may be related to the decrease in plasma motilin that occurs following duodenal resection, vagal innervation to the pylorus and antrum with gastric atony, and/or relative devascularization of the pylorus.[48] Thus attempts to prevent DGE have centered on technical modifications to modulate the previously mentioned factors.

Some groups have found a decreased rate of DGE with pylorus-preserving versus classic PD, but more recent studies have found the opposite, leaving no clearly better technique at this point in time.[48–52] Still other surgeons advocate pylorus-preserving PD with the addition of a pyloric dilation or pyloromyotomy to decrease the incidence of DGE.[4,48,53] These studies have been difficult to interpret in light of variable DGE definitions and variation in the diagnoses of included cases, and recent reviews conclude equivalency.[54,55] Another decision point is the location (retrocolic or antecolic) of the gastrojejunostomy or duodenojejunostomy. Nikfarjam et al. found a significant decrease in the rate of DGE when they switched from retrocolic to antecolic gastrojejunostomy or duodenojejunostomy.[56] This finding was supported by a meta-analysis in which the incidence of DGE in antecolic duodenojejunostomy was lower when compared with the retrocolic approach (risk ratio: 0.260).[57]

Promotility agents have also been evaluated as to their efficacy at decreasing the incidence of DGE after pancreatic resection. A prospective study in 1993 found that erythromycin, a motilin agonist, was associated with a 37% reduction in the incidence of DGE, and with a significant reduction in the percentage liquid retention in gastric emptying studies.[58] Another similar study supported this finding.[59] Metoclopramide is often used instead of, or in addition to erythromycin, but is not well studied in this patient population. Octreotide also may have an adjunctive role in decreasing DGE in terms of its ability to limit POPF.

TABLE 105.5 Consensus Definition of DGE After Pancreatic Surgery

DGE Grade	NGT Required	Unable to Tolerate Solid Oral Intake by POD	Vomiting/ Gastric Distention	Use of Prokinetics
A	4–7 days or reinsertion > POD 3	7	±	±
B	8–14 days or reinsertion > POD 7	14	+	+
C	>14 days or reinsertion > POD 14	21	+	+

Note: To exclude mechanical causes of abnormal gastric emptying, the patency of either the gastrojejunostomy or the duodenojejunostomy should be confirmed by endoscopy or upper gastrointestinal gastrograph in series.
DGE, Delayed gastric emptying; *NGT,* nasogastric tube; *POD,* postoperative day.
From Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery. *Surgery*. 2007;142:761.

MANAGEMENT

Nearly all patients with DGE resolve with conservative management, consisting of nasogastric tube decompression and nutritional support, either with a feeding jejunostomy tube or with total parenteral nutrition (TPN) until symptoms resolve and a regular diet can be tolerated. In addition, management of the primary associated problem (i.e., pancreatic fistula) is crucial.

In summary, many technical modifications have been investigated with respect to limiting DGE. Again, the ability to draw meaningful conclusions from most of these published reports is limited by the lack of uniform definition and by, in general, longer time to remove the nasogastric tube or initiate diet in the older studies. Furthermore, when one technical aspect was compared, many other factors varied, again limiting comparison. However, the use of an antecolic duodenojejunostomy does seem to be consistently associated with decreased DGE rates.[55,57] Most important in the prevention of DGE is the avoidance of other complications, namely POPF, as discussed earlier, because such complications are clearly associated with a secondary DGE.[48,49]

INFECTIOUS COMPLICATIONS

Infectious complications occur frequently following pancreatectomy. In a review of our own data, infections occurred in nearly one-third of patients, including both proximal and distal resections, and accounted for a nearly 40% increase in total cost, as well as one extra hospital day. Among major infections, infected pancreatic fistula was responsible for 28%, followed by wound infection at 24%. Other major infections included pneumonia (17%), abscess (15%), urinary tract infection (10%), and sepsis (6%). Many patients with at least one infection incurred multiple infections. A study found that patient-related characteristics including intraoperative blood transfusion, diabetes, and use of steroids were risk factors for surgical site infections following gastrointestinal surgery.[60] Thus infectious complications, of both minor and major significance, occur frequently following pancreatic resections and are most commonly wound infections and infected pancreatic fistulas. These are responsible for a significant burden to patients, practitioners, and systems alike. Their common occurrence in the setting of excellent adherence to infection control regulations emphasizes the need to discover better process improvements to decrease the incidence of infectious complications, including reevaluating the effectiveness of chosen antimicrobial prophylaxis regimens and adjusting the regimens according to various risk profiles. Fong et al. found discordance between antimicrobial prophylaxis and wound infection cultures in a multicenter study.[61] They suggest that bile cultures should be obtained in patients who undergo preoperative endoscopic retrograde cholangiopancreatography because the identified microorganisms matched the ones found on wound cultures.[61]

SUMMARY

Pancreatic resection remains a high-acuity operation that can be safely performed by appropriately trained and experienced surgeons, in adequately equipped facilities. Although mortality has declined, morbidity remains high. Major potential complications as discussed here include POPF, PPH, and DGE. Other, more generic, complications remain prevalent as well, particularly wound infections, which have been reported at 7% to 15%, and in association with fistulas.[5,40,56]

Aside from efforts to prevent and appropriately manage individual complications, the system of care delivery for pancreatic surgical patients plays a crucial role in improving outcomes overall. Adequate system-wide support for the diagnosis and management of complications must be sufficient to provide the appropriate level of care.[9] For example, services available should include ICU level of care, adequate blood bank, interventional radiology and gastroenterology, nurses accustomed to managing complex postoperative care and drains, and case management. Standardized care plans have been developed to care for postpancreatectomy patients. "Critical" or "clinical" pathways, presently known as enhanced recovery after surgery (ERAS) protocols, have been defined as "structured multidisciplinary care plans that detail essential steps (process measures) in the care of patients with specific problems."[62] Such structured plans have been shown to positively impact outcomes without compromising morbidity and mortality for these patients.[63,64] Multiple studies have confirmed the decreased resource use, readmission, and cost and increased bed/operation theater availability[64,65] and also demonstrated fewer deviations from the expected postoperative course after initiation of the clinical pathway.[23,66] As a result of these data, it has been suggested that development and maintenance of such pathways or protocols should be a requirement for institutions to serve as referral centers.[64,65]

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