ORIGINAL ARTICLE

Changes in Morbidity After Pancreatic Resection

Toward the End of Completion Pancreatectomy

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Hypothesis: Advances in specialized centers for pancreatic diseases have improved surgical morbidity and outcome. In the past, postoperative local complications (pancreatic fistulae) were causing most of the mortality. Now, more patients experience postoperative complications related to their comorbidity.

Design: To report a prospective audit of a single center's experience with pancreatic resection during an 8-year period.

Setting: Tertiary referral center focused on pancreatic diseases.

Patients and Interventions: Six hundred seventeen consecutive patients underwent pancreatectomy between November 1, 1993, and August 31, 2001. The series included 468 pancreatic head resections (76%), 25 total pancreatectomies (4%), 88 left-sided resections (14%), and 36 others (6%).

Main Outcome Measures: Morbidity after pancreatic resection.

Results: Postoperative in-hospital mortality was 1.6%, and the additional operation rate was 4.1%. Four patients died of surgical complications and 6 of systemic complications. Systemic morbidity was 18% and consisted primarily of cardiopulmonary complications (13%). The most frequent postoperative complication was delayed gastric emptying (14%), which caused significant prolongation of the hospital stay. No patients died of a postoperative pancreatic fistula, which occurred in 3.2%, and no completion pancreatectomies were necessary.

Conclusions: Pancreatic resections can be performed with considerable safety and a low rate of pancreatic complications. More patients die of systemic complications than in the past, which increases the demand for precise preoperative patient selection. Completion pancreatectomy should no longer be considered in patients with a pancreatic fistula.

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PANCREATIC SURGERY has changed substantially during the past 20 years. Pancreatic resection remains an intervention of particular significance, often technically challenging and with logistic demands for preoperative diagnostics and perioperative management. Recently, the value of centralization of pancreatic surgery in high-volume institutions has been demonstrated.[1-4] The current mortality rate after pancreatic resection is less than 5%[5-10] in specialized surgical centers, which is significantly lower than that in units with a low frequency of pancreatic surgery.[11] Pancreatic anastomosis was long considered to be the critical step in pancreatic surgery, and it represented the main cause of morbidity and death. At a center for pancreatic surgery in Switzerland, we conducted a prospective audit with special attention to the recording of specific surgical and systemic morbidity after pancreatic resections. The aim of this study is to report a single center's experience with a high caseload during an 8-year period.

See Invited Critique at end of article

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METHODS

Between November 1, 1993, and August 31, 2001, pancreatic resections were performed in 617 consecutive patients at the Department of Visceral and Transplantation Surgery, University of Bern. All data were prospectively recorded on a standardized form.[6] Two surgeons (M.W. and H.F.) monitored the completeness and consistency of data. A standardized preoperative diagnostic workup of the pancreas was performed by abdominal computed tomography (95%) and endoscopic retrograde cholangiopancreatography (67%) and, during the past

4 years, increasingly by magnetic resonance tomography (24%) and simultaneous magnetic resonance cholangiopancreatography. The preoperative risk assessment was performed by ergometry and spirometry and was graded according to the American Society of Anesthesiologists classification.

Patients received operative antibiotic prophylaxis (piperacillin-metronidazole or tazobactam) for 48 hours, a weight-adapted thrombosis prophylaxis with low-molecular-weight heparin combined with compression stockings, and a pancreatic secretion inhibitor (octreotide, 300-600 µg/d subcutaneously for 7 days).[12,13] In most cases, postoperative pain treatment was by peridural analgesia for 3 to 7 days. All patients were monitored postoperatively in the intensive care unit or the surgical intermediate care unit for at least 1 night.

SURGICAL TECHNIQUES

All pancreatic resections were performed in accordance with standardized procedures described elsewhere.[6,14-17] Pancreatic anastomosis after pancreatic head resection is performed as a 2-layer pancreaticojejunostomy (5/0 PDS [ETHICON ENDO-SURGERY, Division of Johnson & Johnson AG, Spreitenbach, Switzerland] or 5/0 Novafil [Davis & Geck, Division of American Cyanamid Co, Danbury, Conn], external suture rows: seromuscular onto the pancreatic capsule and parenchyma; internal suture rows: mucosa to mucosa of the pancreatic duct). Initially (1993-1994), end-to-end anastomoses (n=34; 7%) to the pancreatic stump were carried out. Later, end-to-side anastomoses were performed exclusively (n=434; 93%).[18] Furthermore, in the case of duodenum-preserving pancreatic head resections, 150 additional side-to-side anastomoses to the remaining rim of the pancreatic head were performed. Reconstruction during pancreaticoduodenectomy was always performed with a single retrocolic jejunal Roux-en-Y loop. The pancreas, bile duct, and stomach (or duodenum in the case of pylorus-preserving pancreatic head resection) were anastomosed in consecutive order. No stents were used for the pancreatic or biliary anastomoses.

Left-sided pancreatic resections were usually performed without anastomoses (88%; 77/88). In 11 patients, an end-to-end (n=4) or an end-to-side (n=7) pancreaticojejunostomy was carried out.

In case of malignant periampullary tumors, a standardized lymphatic dissection was performed in the hepatoduodenal ligament, along the celiac trunk and the common hepatic artery to the right side of the superior mesenteric artery, behind the pancreatic head (cava and aorta), and along the portal and superior mesenteric veins. For tumors of the pancreatic body and the pancreatic tail, dissection of the lymph nodes was performed in the region of the celiac trunk and the superior mesenteric artery and vein, as well as behind the pancreas along the left side of the renal vein and the left adrenal gland. In each patient, 1 soft drainage was placed close to the pancreatic anastomosis or stump.

COMPLICATIONS

Mortality was defined as the total number of in-hospital deaths. *Gastric emptying delay* was defined as the necessity to leave the nasogastric tube in for more than 10 days after surgery or the need for nasogastric tube reinsertion after day 10. A *pancreatic fistula* was defined as a persisting secretion of more than 30 mL/d of drainage fluid with a high level of amylase (>5000 U/mL) for more than 10 days or the later reoccurrence of amylase-rich fluid via the drainage canal. A *biliary fistula* was diagnosed when fluid with a high level of bilirubin was secreted for more than 5 days. *Postoperative bleeding* was defined as the necessity to transfuse more than 2 U of packed red blood cells more than 24 hours after surgery or as the need for an additional operation because of hemorrhage.

Table 1. Demographic Characteristics of 617 Patients Undergoing Pancreatic Resection

Characteristic	No. (%)
Sex	
M	359 (58)
F	258 (42)
Age, mean (range), y	67 (18-87)
ASA classification	
I-II	493 (80)
III-IV	124 (20)
Diabetes mellitus	92 (15)
Cardiac comorbidity	99 (16)
Chronic obstructive pneumopathy	49 (8)
Jaundice*	105 (17)

Abbreviation: ASA, American Society of Anesthesiologists.
*Jaundice is indicated by a bilirubin level greater than 5.8 mg/dL (>100 µmol/L).

Table 2. Pathological Diagnoses in 617 Pancreatic Resections

Pathological Diagnosis	Malignant Disease, No. (%) (n = 346)	Benign Disease, No. (%)	
		Neoplastic (n = 57)	Nonneoplastic (n = 214)
Periampullary tumors			
Pancreas	205 (59)	1 (2)	0
Ampulla	30 (9)	15 (26)	0
Common bile duct	26 (8)	2 (4)	0
Duodenum	9 (3)	7 (12)	0
Cystic tumors	14 (4)	25 (44)	0
Neuroendocrine tumors	29 (8)	6 (11)	0
Other tumors	33 (10)	1 (2)	0
Chronic pancreatitis	0	0	197 (92)
Other indications	0	0	17 (8)

STATISTICS

For statistical comparisons of the individual patient groups, either a 2-sided χ^2 test with the Yates correction for continuity or a Fisher exact test was used. Quantitative variables were tested by means of the Kruskal-Wallis H test or a Mann-Whitney test. Values of $P<.05$ were considered significant. All calculations were performed using a statistical program (SPSS for Windows; SPSS Inc, Chicago, Ill).

RESULTS

The demographic patient data are summarized in **Table 1**. There were 403 resections (65%) for neoplasia and 214 operations (35%) for nonneoplastic diseases of the pancreas. Data regarding the specific pathological diagnoses of the diseases are given in **Table 2**. A total of 468 pancreatic head resections (76%), 25 total pancreatectomies (4%), 88 left-sided resections (14%), and 36 atypical resections (6%), including segmental resections and tumor enucleations, were performed. Nine surgeons performed the pancreatic resections. The median length of stay for all patients was 14 days (range,

Table 3. Intraoperative Findings in 581 Patients Undergoing Pancreatic Resection*

Finding	Pancreatic Head Resection (n = 468)	Left-Sided Pancreatic Resection (n = 88)	Total Pancreatectomy (n = 25)
Intraoperative data, median (range)			
Blood loss, mL	1200 (200-22 000)	1100 (300-1800)	1900 (500-2200)
Transfusion, erythrocyte concentration	2 (0-40)	2 (0-42)	4 (0-38)
Surgery time, min	410 (220-780)	300 (130-670)	480 (285-730)
Vascular resection, No. (%)			
Tumor infiltration	22 (5)	3 (3)	9 (36)
Technical causes	11 (2)	0	0
Pancreaticojejunostomy, No. (%)			
End-to-end	34 (7)	4 (5)	0
End-to-side	434 (93)	7 (8)	0
Side-to-side	150 (32)†	0	0

*Enucleations and atypical resections were not included in this analysis.
†Side-to-side anastomoses in patients undergoing a duodenum-preserving pancreatic head resection.

Table 4. Causes of the 10 Cases of Hospital Mortality in 617 Consecutive Patients Undergoing Pancreatic Resection

Operation	Day of Death	Cause of Death
Pylorus-preserving Whipple	6	Acute heart failure
	8	Acute heart failure
	11	Sepsis
	42	Biliary fistula
Classic Whipple	11	ARDS, multiple-organ failure
	60	MRSA sepsis
Duodenum-preserving resection	16	Multiple-organ failure
Left-sided pancreatic resection	6	Intestinal necrosis
	39	Sepsis
Total pancreatectomy	8	Multiple-organ failure

Abbreviations: ARDS, adult respiratory distress syndrome; MRSA, methicillin-resistant *Staphylococcus aureus*.

4-118 days). The hospital stay was longest after total pancreatectomy (median, 20 days) and shortest after duodenum-preserving pancreatic head resection (median, 12 days) ($P<.001$).

INTRAOPERATIVE VARIABLES

Operative time, blood loss, and blood transfusion requirements are summarized in **Table 3**. The length of surgery was significantly shorter for left-sided pancreatic resections compared with pancreatic head resections ($P<.001$), whereas blood loss and blood substitution volumes were identical. Compared with total pancreatectomy, operative time ($P<.001$), blood loss ($P=.001$), and blood transfusions ($P=.002$) were significantly lower for left-sided pancreatic resection. Likewise, clear differences were evident when total pancreatectomy was compared with pancreatic head resection (length of surgery: $P=.01$; blood loss: $P=.001$; and blood substitution: $P<.001$). Duodenum-preserving pancreatic head resection entailed shorter surgery times ($P<.04$) and less blood loss ($P=.001$) and blood substitution ($P<.01$) than the Whipple operation.

HOSPITAL MORTALITY

Ten patients (2%) died in the hospital (**Table 4**). Analysis of the causes of death showed that 4 patients died of surgical complications. Of these, 2 patients died of an abscess in the pancreatic region with subsequent multiple-organ failure, 1 developed small bowel necrosis after enteral alimentation (percutaneous catheter jejunostomy), and 1 died of septic complications after a postoperative biliary fistula. Six patients died of systemic complications: 3 of multiple-organ failure, with no surgical complications as documented by autopsy; 2 of acute heart failure; and 1 of a systemic methicillin-resistant *Staphylococcus aureus* catheter infection (central venous catheter). Regarding mortality, no statistical difference was evident among the various surgical procedures. Mortality was lowest in the group having duodenum-preserving pancreatic head resection (0.7%) and highest after total pancreatectomy (4%).

POSTOPERATIVE MORBIDITY

Total morbidity was 36%, that is, 221 of 617 patients had 1 or more complications. The surgical complications (26%) are listed in **Table 5**. The most frequent complication was gastric emptying delay (14%). The incidence of postoperative pancreatic fistulae was 3.2% (n=20), and it was highest after left-sided pancreatic resection (5/88; 5.7%). No patient with a pancreatic fistula died. One patient underwent another operation owing to a high-output pancreatic fistula (>200 mL/d) after duodenum-preserving pancreatic head resection. Two patients underwent an interventional drainage procedure after developing a low-output fistula and a simultaneous perianastomotic abscess. In the remaining 17 patients, the fistulae healed with conservative treatment without additional interventions, and no patient with a pancreatic fistula had to undergo completion pancreatectomy. Additional operations were performed on 4 of the 11 patients with an intra-abdominal abscess; the remaining patients were treated by interventional radiology. Aside from septic complications, postoperative bleeding was the most frequent cause of additional surgery, but none of the 10 patients who underwent another surgery for postoperative bleeding died. Mortality after the sec-

ond operation (16%) was significantly higher than that in the group without surgical revision (1%) ($P<.001$).

Systemic complications were mainly cardiopulmonary (**Table 6**). Systemic morbidity was highest after total pancreatectomy (32%).

COMMENT

Elective pancreatic resections have developed into safe surgical procedures, and mortality in specialized centers has decreased to 2% to 5%.[1-4,6,8,19,20] This rate is consistent with that of the present series of 617 pancreatic resections performed during the past 8 years. Pancreatic surgery today is performed by a variety of techniques, which allows the surgeon to use a more tailored, disease-directed approach depending on the localization, extent, and gravity of the underlying disease.[14,17,21-23] We prefer organ preservation when feasible oncologically, and we adapted the various techniques into clinical routine with mortality less than 2% for the entire group and 0.7% for patients with chronic pancreatitis.

Several concepts to increase the safety of pancreatic surgery have been assimilated into clinical routine, including the formation of pancreatic centers with high patient volumes (caseload[4]); standardized perioperative management, including the inhibition of pancreatic secretion; and various methods to increase the safety of pancreatic resection, reconstruction, and anastomotic techniques.[6,24-28] Their relative importance with respect to safety remains to be tested. Centralization as a concept to improve results has been demonstrated in many surgical fields, including the pancreas,[4,19] and may be more important for the postoperative outcome than differences in surgical technique. However, surgical advances pioneered by individual surgeons during the past 30 years allowed the current trend toward minimal mortality and the currently reported "acceptable morbidity."

Mortality and morbidity rates seem to be good in many large centers despite considerable differences in technique and complication rates (eg, pancreatic fistula rates of 2%-15%). Factors such as the technique of pancreatic anastomosis, including ductal drainage, type of reconstruction, the need for preoperative biliary drainage, and intraoperative drain placement, have been debated for many years. Their relative importance needs to be assessed in light of publications that demonstrate that a preoperative biliary drain[29-31] may be a risk factor for infectious complications[32-35] and that the placement of drains in the surgical area to allow postoperative wound drainage is not related to local complications.[36] Our previous analysis of more than 250 consecutive patients undergoing pancreatic head resection could not document a positive effect of a preoperative biliary drain on morbidity, mortality, infection, and long-term survival rates. On the other hand, a multivariant regression analysis identified the presence of jaundice (bilirubin level >5.8 mg/dL [>100 µmol/L]) as a significant risk factor for postoperative hemorrhage.[37]

The cause of postoperative deaths has changed considerably. Four of the 10 patients died as a result of surgical complications. Six patients died of systemic complications. Previously, mortality was primarily attributed to complications from pancreatic anastomoses.[38-40] Although local complications decrease with increasing experience in pancreatic surgery, systemic complications, caused by the patient's comorbidity, need to be addressed by careful preoperative evaluation and perioperative management.

Table 5. Surgical Morbidity in 617 Patients Undergoing Pancreatic Resection

Variable	Patients, No. (%)	Additional Operations, No.
Mortality	10 (2)	0
Additional operation	25 (4)	0
Surgical morbidity	158 (26)	0
Gastric emptying delay	85 (14)	1
Septic complications		
Wound infection	22 (4)	0
Intra-abdominal abscess	11 (2)	4
Fistula		
Pancreas	20 (3)	0
Colon	3 (0.5)	3
Biliary	4 (1)	2
Hemorrhage	20 (3)	10
Cholangitis	11 (2)	0
Postoperative ileus	7 (1)	3
Liver necrosis	5 (1)	1
Neurologic complications	4 (1)	0
Obstructive jaundice	1 (0.2)	1
Chyloascites	1 (0.2)	0

Table 6. Systemic Morbidity in 617 Patients Undergoing Pancreatic Resection

Variable	Patients, No. (%)
Systemic morbidity	112 (18)
Cardiopulmonary	82 (13)
Renal	22 (4)
Neurologic	14 (2)
Catheter sepsis	10 (2)
Other	14 (2)

Standardized resections and improvement of the anastomotic technique may explain reduced local morbidity rates. In the present series, the postoperative rate of pancreatic fistula was 3.2%, including a 5.7% fistula rate in left-sided pancreatic resections. Only 1 (5%) of 20 patients, who had a high-output fistula, required a second operation, on the seventh day, after a duodenum-preserving pancreatic head resection. We therefore propose that the pancreatic fistula should be treated conservatively as long as it is not accompanied by organ failure.[41-44] The concept of a second operation might be abandoned in patients with a pancreatic fistula, and we have not seen an indication to perform completion pancreatectomy during the past 8 years.

The morbidity rate after pancreatic resection remains high. The most frequent surgical complication was gastric emptying delay. Although this complication seldom occurs after left-sided resection and after duodenum-preserving pancreatic head resection, we recorded delayed gastric emptying in 23% of the patients after pancreatoduodenectomy. Gastric emptying delay has clinical and economic relevance, as the affected patients remained in the hospital for more than a week longer, often requiring additional feeding. The positive effect of administration of erythromycin in the early postopera-

tive period on gastric emptying after pancreatoduodenectomy was documented in a randomized study.[45] However, delayed gastric emptying remains the unsolved postoperative complication, and, in the future, the method of resection and reconstruction needs to be studied.[46]

Left-sided pancreatic resections without anastomoses have significantly higher fistula rates compared with pancreatic head resections. The risk of a pancreatic leak from a directly closed pancreas is higher than from a technically correct pancreatic anastomosis. Although the rate of pancreatic fistula may be reduced by performing an anastomosis after left-sided resection, these fistulae without anastomosis regularly heal with external drainage and seem to have less potential for additional complications (erosive hemorrhage), perhaps because the pancreatic secretion is not activated through contact with intestinal enzymes.

In conclusion, this study underlines that pancreatic resections can be performed with considerable safety and low pancreatic complication rates. Under the present circumstances, completion pancreatectomy has probably lost its indications.

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This article is dedicated to Hans G. Beger, MD, for his lifetime achievements in pancreatic surgery.

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