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Pylorus-Preserving Total Pancreatectomy

Early and Late Results

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Key Words

Pancreatic cancer · Periampullary cancer · Total pancreatectomy · Mortality · Morbidity · Long-term outcome

Abstract

Background/Aims: Preservation of the pylorus is an accepted alternative procedure to the classical Whipple operation for pancreatic head resection but data describing its value for total pancreatectomy are sparse. ***Methods:*** A prospective analysis of 22 total pancreatectomies performed in a consecutive series of 436 pancreatic resections from 1.11.93 to 1.5.99. ***Results:*** 11 patients underwent total pancreatectomy with preservation of the pylorus. Histopathological examination revealed pancreatic adenocarcinoma in 16 cases and duodenal adenocarcinoma in 1 patient, 5 patients had other types of pancreatic neoplasm. In-hospital mortality was 4.5% (n = 1), cumulative morbidity was 59% and reoperations were performed in 9.1% of cases (n = 2). Median follow-up was 37 months (range 5–66). 62% of patients (n = 13) developed tumor recurrence and 13 patients died during the follow-up period with 10 deaths being cancer related. There was no difference concerning postoperative and follow-up morbidity of survival between patients undergoing pylorus-preserving total pancreatectomy or pancreatectomy with gastrectomy. However, postoperative body weight was increased 3, 6, 9 and 12 months following preservation of the pylorus. ***Conclusion:*** Total pancreatectomy with preservation of the pylorus is a feasible type of resection for all types of pancreatic or ampullary tumors, which shows a similar morbidity and long-term survival but improved nutritional recovery compared with standard total pancreatectomy.

Introduction

Originally, total pancreatectomy was introduced as a safer and oncological more radical treatment form for pancreatic cancer in comparison to pancreatic head resection [1–3]. However, several series have shown that perioperative outcome as well as long-term survival was no better than after partial pancreatoduodenectomy [2, 4]. In addition, the value of total pancreatectomy was compromised by the risk of severe metabolic disorders due to the complete loss of pancreatic endocrine and exocrine functions [5]. Therefore, the classical Whipple procedure (cWhipple) is still recommended as the procedure of choice for the treatment of cancer restricted to the head of the pancreas [6, 7]. Due to advances in pancreatic surgery and perioperative intensive care management, pancreatic

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head resections can now be performed with great safety [8–10].

In order to omit the side effects of partial stomach resection [11, 12], the more conservative pylorus-preserving Whipple resection (pp-Whipple) has been introduced by Watson [13] and Traverso and Longmire [14]. Several mostly retrospective studies have shown that preservation of the pylorus does not increase postoperative morbidity and mortality when compared with the cWhipple procedure [12, 15–20]. Moreover, long-term survival was similar after the two procedures in all these studies with the exception of one rather small retrospective series [12, 15–20]. Therefore, pylorus-preserving pancreatoduodenectomy is now considered a valid alternative to the classical Whipple procedure for the treatment of all forms of pancreatic and ampullary cancers.

There remains a minority of cases where total pancreatectomy is indicated in order to achieve radical resection [4, 21]. Although total pancreatectomy with preservation of the pylorus or duodenum has been reported for patients with chronic pancreatitis [22, 23], there exits only sparse information in the literature describing the outcome after pylorus-preserving total pancreatectomy [24, 25]. This prompted an analysis of our series of 22 consecutive patients undergoing total pancreatectomy for pancreatic or ampullary tumors.

Patients and Methods

From 1.11.93 to 1.5.99, all patients undergoing pancreatic resections were recorded prospectively in a statistical database (SPSS, Chicago, Ill., USA). Standard work-up in patients with suspicion of pancreatic or periampullary cancer included contrast CT or MRI to stage tumor and perioperative risk assessment consisted of ASA score determination [26, 27] in combination with spirometry and ergometry. Patients with signs of biliary obstruction underwent endoscopic retrograde cholangiopancreaticography (ERCP) to insert an endoscopic stent into the common bile duct (CBD). If no contraindications for major surgery were detected, these patients underwent surgical exploration. The abdominal cavity was explored through a midline incision in order to exclude metastatic or locally advanced disease. If no contraindication for resection was found, a 'Kocher maneuver' was performed, the lesser sac was opened and biopsies from suspicious peripancreatic lymph nodes were taken. The superior mesenteric vein (SMV) was dissected from the neck of the pancreas and the gastroduodenal artery was ligated near its origin. Cholecystectomy was followed by complete lymphadenectomy of the hepatoduodenal ligament and the common bile duct was dissected proximal to the cystic duct. The pancreas was resected in total together with the spleen in order to ensure radicality. En bloc resection was performed together with the duodenum, the peripancreatic lymph nodes and the distal stomach in classic pancreaticoduodenectomy procedures (cTotal). The pylorus was preserved if the proximal duodenal resection margin was tumor-free; a 4-cm postpyloric duodenal segment was available for anastomosis and peripyloric lymph nodes showed no tumor infiltration. In these cases (ppTotal), the gastroepiploic vessels as well as the vagal branches to the pylorus were preserved. Lymphadenectomy was completed along the celiac and superior mesenteric vessels and the retropancreatic region of the aorta. Reconstruction after total pancreatectomy consisted of an interrupted end-to-side hepaticojejunal anastomosis in a single-layer technique using the first jejunal loop. An end-to-side anastomosis of the duodenal remnant with the jejunal loop was done in a two layer fashion in cases with ppTotal or an end-to-side interrupted two-layer gastro-jejunostomy was performed in a retrocolic omega-loop-fashion in cTotal. A drainage was placed near the biliary and enteral anastomosis and the abdomen was closed with a running suture in anatomical layers. Antithrombotic prophylaxis consisted of subcutaneous application of low-molecular-weight heparin once a day (3,000 IU/day s.c.). Antibiotics (Piperacillin 4 g and Metronidazole 500 mg or Piperacillin 4 g in combination with Tazobactam 500 mg, American Home products) were given immediately preoperatively and were continued for 48 h postoperatively.

Postoperatively, patients were transferred to the ICU. Abdominal drainage was removed when the secreted fluid measured less than 100 ml/day or at day 5 at the latest. All patients underwent a gastric contrast study at day 5 after surgery and thereafter solid food intake was started. Blood glucose concentrations were measured in 4 to 6-hour intervals and regulated by intravenous administration of insulin (Actrapid®, Novo Nordisk Pharma AG, Küssnacht, Switzerland). After starting oral food intake, patients received either semi-long acting insulin (Mixtard®, Novo Nordisk Pharma AG) or a combination of long-acting insulin as baseline therapy (Insulotard®, Novo Nordisk Pharma AG) in combination with short-acting insulin (Actrapid®) before the meals. Patients were instructed to measure blood glucose levels and to inject insulin by themselves. All patients received pancreatic enzymes (Creon forte®, Kali-Duphar Pharma AG, Bern, Switzerland) in order to treat exocrine pancreatic insufficiency.

Adverse events occurring within 30 days after surgery were recorded as early outcome results. Curative resection was defined as no residual tumor and microscopically clear resection margins. Delayed gastric emptying (DGE) was defined as the inability to tolerate oral food intake for more than 10 days after surgery. Postoperative bleeding was defined as the occurrence of blood loss either through the abdominal drains or by hematemesis in combination with a decrease in systemic hemoglobin content of more than 20 g/l to a value of under 80 g/l within 24 h, requiring at least two units of blood to prevent further blood loss. After discharge, all patients were followed every three months thereafter in combination with our nutritional and diabetic services. The registered data included survival, tumor recurrence, course of pain and body weight as well as capability to work. In addition, any adverse event leading to readmission to the hospital was registered. Insulin requirements and blood glucose levels were recorded and insulin regime was adjusted by the patient's primary care physician in collaboration with the department of diabetology. Persisting diarrhea was defined as the occurrence of more than 3 bowel movements per day for more than 3 months after surgery. Malnutrition was recorded if oral or parenteral hyperalimentation was needed. For statistical analyses, a χ^2 test, a Fisher's exact test or Mann-Whitney U test were applied where appropriate. Analysis of survival was calculated according to Kaplan-Meier and the levels of significance were tested with a log-rank test. Differences were considered significant at $p < 0.05$.

Table 1. Patients' characteristics (median ± range)

Demographics	Total (n = 22)		cTotal (n = 11)		ppTotal (n = 11)		p value
	n	%	n	%	n	%	
Male	13	59	8	73	5	46	n.s.
Female	9	41	3	27	6	54	n.s.
Age, years	63	45–81	63	46–81	59	45–76	n.s.
ASA I–II	17	77	9	82	8	73	n.s.
III–IV	5	23	2	18	3	27	n.s.
Jaundice[1]	5	23	2	18	3	27	n.s.

[1] Bilirubin level >1 mg/dl.

Results

Out of 436 patients who underwent pancreatic resections, a total of 22 patients received total pancreatectomy (5%). Indications for total pancreatectomy were: tumor extension into the distal pancreas in 19 patients. One patient had a cancer of the pancreatic body with infiltration of the superior mesenteric vein and the retroperitoneum. Two patients with pancreatic head cancer had a frail pancreatic remnant not suitable for performing a safe pancreato-jejunostomy. Demographic data are summarized in table 1. 13 patients underwent preoperative ERCP and a plastic stent was inserted in the common bile duct in 5 patients. Operative findings and length of ICU and hospital stay are depicted in table 2. In patients who underwent cTotal, the proximal duodenum was infiltrated in 4 patients and tumor infiltration was intraoperatively suspected in another 5 patients but not confirmed by histology. Furthermore, distal gastrectomy was performed in 2 patients due to venous stasis in the pyloric region. One patient with pancreatic cancer had a history of total gastrectomy due to gastric cancer. In addition, segmental resection of the colon was performed in 3 patients with locally advanced cancer. An extended retroperitoneal dissection and a left adrenalectomy were carried out in one patient each. Two patients undergoing portal vein resection had intraoperative hemorrhage requiring transfusion while the other 20 patients had no intraoperative complication. Radical resection was achieved in 19 patients (86%). A palliative resection was performed in 2 patients with advanced infiltration of the retroperitoneum and one patient had microscopically positive resection margins.

Table 3 summarizes the results of the histopathological examination and postoperative results are given in table 4. One patient died on day eight due to acute respiratory distress syndrome with progressive heart and renal failure (MOF) resulting in a hospital mortality rate of 4.5% (1/22). 13 patients (59%) encountered a total of 22 postoperative complications (table 4). Two patients were reoperated for intraabdominal bleeding; one of these two patients underwent a second reoperation 26 days after pancreatectomy for an intraabdominal abscess. The other patient died due to MOF as described above. Two patients (9%) developed postoperative cholangitis and were treated with antibiotics. Postoperatively, diabetes could be managed well in all cases with the exception of one patient with transient episodes of hypoglycemia who stayed in the ICU for 6 days. Pancreatic enzymes (Creon forte) were substituted in high doses in all patients.

Follow-up results after discharge are given in table 5. Median follow-up time was 37 months (range 4–66). Patients were placed on a high calorie diet (50 kcal/kg bodyweight per day) consisting of 20% protein, 50% carbohydrate and 30% fat intake. Insulin regimen consisted of administration of semilong acting insulin, a combination of long- and short-acting insulin or an insulin pump system. An average total dose of 24 IU of insulin was given per day (range 20–36 IU) and patients measured their blood glucose levels themselves using a reflectance meter. The postoperative weight course (measured in percentage of pre-disease body weight) is depicted in figure 1. The ppTotal group showed a significantly increased body weight 3, 6, 9 and 12 months following resection compared to cTotal (mean 88 vs. 82%, $p = 0.043$ after 3 months, mean 91 vs. 84%, $p = 0.049$ after 6 months, mean 91 vs. 79%, $p = 0.015$ after 9 months and mean 92 vs. 80% after 12 months, $p = 0.037$, respectively). All but one patient with disease-free survival were able to work regularly. A total of 3 patients (14%) were readmitted to the hospital due to recurrent hypoglycemia. One patient with persistent diarrhea and brittle diabetes died 9 months

Table 2. Intraoperative findings and surgical procedures as well as hospital stay (median ± range)

Parameters (median ± range)	Total (n = 22)	cTotal (n = 11)	ppTotal (n = 11)	p value
Operation time, min	490 (285–750)	495 (380–720)	438 (285–750)	n.s.
Blood loss, ml	1,800 (970–23,000)	1,900 (1,200–22,000)	1,550 (970–23,000)	n.s.
Blood subst., U	4 (1–42)	4 (2–38)	4 (1–42)	n.s.
Splenectomy	19 (86%)	9 (82%)	10 (91%)	n.s.
Portal vein resection	6 (27%)	2 (18%)	4 (36%)	n.s.
Radical resection	19 (86%)	10 (91%)	9 (82%)	n.s.
ICU stay, days	2 (1–8)	2 (1–7)	2 (1–8)	n.s.
Hospital stay, days	20 (4–87)	21 (4–87)	16 (7–45)	n.s.

Table 3. Histological findings

Characteristics	Total (n = 22)		cTotal (n = 11)		ppTotal (n = 11)		p value
	n	%	n	%	n	%	
Pancreas							
Ductal adenocarcinoma	16	73	9	82	7	64	n.s.
IPMN	2	9.1		0	2	18	n.s.
Cystic tumors	3	14	1	9.1	2	18	n.s.
Duodenum							
Mucinous adenocarcinoma	1	4.5	1	9.1	0		n.s.
Tumor stage (UICC)							
II	6	27	2	18	4	36	n.s.
III	15	68	9	82	6	55	n.s.
No invasive cancer	1	4.5			1	9.1	n.s.

IPMN = Intraductal papillary mucinous neoplasm of the pancreas.

Table 4. In-hospital surgical and medical morbidity

Morbidity	Total (n = 22)		cTotal (n = 11)		ppTotal (n = 11)		p value
	n	%	n	%	n	%	
Cumulative surgical	*8*	*36*	*6*	*55*	*2*	*18*	*n.s.*
Delayed gastric emptying	5	23	4	36	1	9.1	n.s.
Infection (wound/abscess)	3	14	3	27	0		n.s.
Bleeding	2	9.1	1	9.1	1	9.1	n.s.
Cumulative systemic	*7*	*32*	*4*	*36*	*3*	*27*	*n.s.*
Pulmonary	4	18	2	18	2	18	n.s.
Renal	3	14	1	9.1	2	18	n.s.
Cardio-circulatory	2	9.1	0		2	18	n.s.
Other	3	14	2	18	1	9.1	n.s.
Relaparotomy	*2*	*9.1*	*1*	*9.1*	*1*	*9.1*	*n.s.*
Cumulative morbidity	*13*	*59*	*8*	*73*	*5*	*45*	*n.s.*
Mortality	*1*	*4.5*		*0*	*1*	*9.1*	*n.s.*

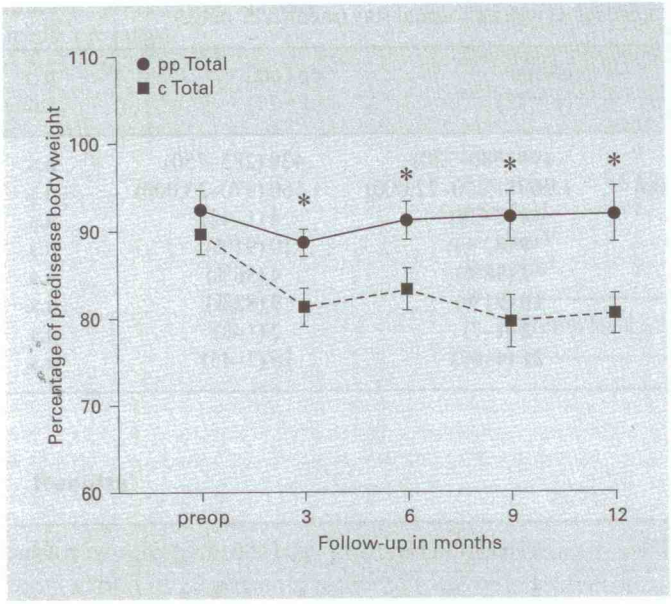

Fig. 1. Postoperative body weight changes in patients surviving pylorus-preserving (ppTotal, n = 10) or classical total pancreatectomy (cTotal, n = 11). Values are expressed as percentages of predisease body weight (mean ± SE). * $p < 0.05$.

after surgery due to lethal hypoglycemia. One patient underwent reoperation due to small bowel obstruction 6 months after surgery. Intraoperatively no signs for recurrence could be detected.

There was no significant difference in survival between the two types of resection (p = 0.48). Actual 3- and 5-year survival rates for patients with pancreatic ductal adenocarcinoma were 11 and 0%, respectively. Actual survival rates for patients with malignancies other than pancreatic ductal adenocarcinoma were 100 and 50% at 3 and 5 years, respectively. The patient who died due to hypoglycemia had no signs of recurrence. Another patient developed metastatic small cell lung cancer and died 36 months after undergoing total pancreatectomy. The autopsy showed no signs for pancreatic cancer recurrence.

Discussion

Several studies have reported that preservation of the pylorus for pancreatic head resection (ppWhipple) has a similar morbidity and long-term survival compared to the

Table 5. Follow-up after hospital discharge

Morbidity	Total (n = 21)		cTotal (n = 11)		ppTotal (n = 10)		p value
	n	%	n	%	n	%	
Anastomotic ulcer	1	4.8	0		1	10	n.s.
Acute cholangitis	1	4.8	1	9.1	0		n.s.
Poorly controlled diabetes	4	19	2	18	2	20	n.s.
Diarrhea	2	9.5	1	9.1	1	10	n.s.
Reoperation	1	4.8	1	9.1	0		n.s.
Cumulative morbidity	*9*	*43*	*4*	*36*	*5*	*50*	*n.s.*
*Tumor recurrence**	*13*	*62*	*7*	*64*	*6*	*60*	*n.s.*
Local recurrence	7	33	4	36	3	30	n.s.
Distant metastases	12	57	6	54	6	60	n.s.
Diseased	*13*	*62*	*8*	*73*	*5*	*50*	*n.s.*
Recurrence related	10	48	6	54	4	40	n.s.
Other cause	3	14	2	18	1	10	n.s.
Median survival (months)	*16 (4–65)*		*10 (5–31)*		*18 (4–65)*		*n.s.*

* Only patients with malignant disease were included in this analysis, resulting in 11 patients in the cTotal group and 9 patients following ppTotal.

classical Whipple resection (cWhipple) [12, 16–20]. It has been postulated that the ppWhipple procedure improves postoperative nutritional recovery and therefore benefits quality of life [12, 16–20, 28]. At our institution, we favor the pylorus-preserving Whipple resection although at present unbiased scientific evidence is lacking to prove the superiority of either type of resection. Thus, we adapted the principle of preservation of the pylorus also for patients undergoing total pancreatectomy. In the present study, the cTotal and ppTotal groups were comparable in terms of patient demographics and tumor characteristics.

Due to the severe consequences of total pancreatectomy on glucose metabolism and intestinal function, the indication for total resection of the pancreas has to be constrained. Indications for total pancreatectomy in this study were resectable cancer of the pancreatic body or the pancreatic head with tumor extension into the distal pancreas in 20 patients. A friable pancreatic stump, which would make for a hazardous anastomosis was the indication for total pancreatectomy only in two out of 331 consecutive patients (0.6%) undergoing pancreatic head resection at our institution. No patient underwent completion pancreatectomy due to a pancreatic fistula [10] or due to chronic pancreatitis, which should no longer be regarded as an indication for total pancreatectomy [2, 6]. ppTotal is technically a minor variation of the cTotal procedure and operation time and blood loss were similar for the two procedures. Although previous studies have reported a frightening mortality rate following total pancreatectomy, more recent studies as well as our actual series are now reaching values comparable to those reported after the Whipple resection [9, 21, 25, 29–31]. The reasons for this improvement may be a combination of more accurate patient selection, advances in surgical technique and more sophisticated intensive care management. Moreover, markedly fewer patients die due to surgical complications as reported in the past and the same observation was made in our study [25]. In contrast, morbidity following total pancreatectomy continues to be substantial even in newer series [21, 32]. The cumulative morbidity in our series was 59% and was similar for both types of resection. Although our rates may be higher than in other studies, this difference may be explained by the fact that we recorded all relevant data prospectively whereas most published reports are retrospective or used even questionnaires. Moreover, the majority of adverse events was minor and temporary and consisted of cardiopulmonary as well as renal complications typically seen after major abdominal surgery. Therefore, only 4 patients had major surgical complications. This is a favorable result when one takes into account that we followed an aggressive surgical approach even in patients with advanced cancer disease.

Another commonly recorded complication was delayed gastric emptying (DGE) which resolved spontaneously in all patients. The effect of preservation of the pylorus on DGE following pancreatic resection is an ongoing controversy in the surgical literature. Some studies reported a higher incidence of DGE pylorus preservation whereas other authors did not [12, 15–20, 33–35]. Consistent with more recent published studies, we did not observe an increased incidence of DGE after preservation of the pylorus [15, 20, 25, 36, 37]. Reasons for these controversial results may be that most reports are either based on retrospective studies or observations in patients with chronic pancreatitis [20, 35–38]. One obvious problem with retrospective studies is that many factors such as patient selection, surgical technique and perioperative management, may have changed over time and may have influenced the incidence of DGE during the more recent periods. Moreover, multiple problems with bias and patient selection in nonrandomized studies may affect conclusions. Moreover, it seems that the extent of surgery, such as extended lymph node dissection in cancer patients and the occurrence of complications are far more important factors determining the incidence of delayed gastric emptying than preservation of the pylorus alone [10, 38].

Due to persistent diarrhea which may be encountered in some patients after total pancreatectomy and the complete lack of insulin antagonists these patients are more prone to sudden and severe hypoglycemia. Moreover, partial stomach resection may limit the daily calorie intake thus further complicating the metabolic consequences after cTotal. In our study, there was no difference between the two patient groups regarding diabetic management neither in the early postoperative period nor after discharge. Moreover, none of the disease-free survivors suffered from recurrent severe hypoglycemia function during long-term follow-up. Thus, our study seems to confirm that intense patient instruction, regular home glucose monitoring and a high calorie diet distributed in several meals per day can prevent severe hypoglycemia in most patients [5]. In addition, more sophisticated insulin regimens such as a combination of long and short-acting insulin or the use of an insulin pump system may have further facilitated the diabetic management of these patients. Although, the majority of patients complained about some sort of temporary diarrhea after discharge, these symptoms diminished rapidly in both patient groups under high dose enzyme substitution as reported by other authors as well [5, 21, 39]. In contrast, body

weight of patients undergoing ppTotal showed a markedly superior recovery during the first months after surgery compared to patients following cTotal. Thus, our observation seems to confirm that preservation of gastric reservoir function will improve oral calorie intake and accelerate body weight recovery following total pancreatectomy [16, 17, 25].

The most important topic remains the question whether preservation of the pylorus will compromise surgical radicality and therefore reduce long-term survival. Histological observations and studies from autopsies have shown, that the pancreatic resection margin rather than the duodenum or pyloric region is more likely to be infiltrated by cancer [40–43]. Our series revealed no difference in survival between the two groups and thus confirmed a most recent study [25]. It is also a well-known fact that survival following resection for pancreatic but also ampullary cancer is compromised by a high incidence of local tumor recurrence. In our series, only 33% of patients had local failure whereas 57% developed distant metastases. However, the recurrence pattern was not different between the two procedures. Overall, we consider a median survival of 12 months for the patients undergoing total pancreatectomy for pancreatic adenocarcinoma still a respectable result since the majority of these patients had stage III disease according to the UICC classification. More aggressive resection procedures such as regional pancreatectomy and radical lymph node dissection have not improved survival [44–46]. Therefore, ppTotal is a valid surgical treatment for pancreatic cancer and similar results after cTotal or ppTotal have been recently reported [25, 29, 30, 32]. Moreover, in patients with less aggressive cancers such as pancreatic IPMN or cystic pancreatic a tumor, functional outcome is of major concern and accordingly, ppTotal is a particularly good indication for these lesions.

In conclusion, total pancreatectomy with preservation of the pylorus is a feasible treatment for most patients with pancreatic or periampullary cancer when partial resection is no more possible. Preservation of the pylorus goes along with a similar morbidity and mortality but facilitates early nutritional recovery without compromising long-term survival. Therefore, total pancreatectomy with partial or total gastrectomy should be restricted to when tumor either involvement of the pyloric region is suspected or neurovascular innervation of the pylorus is compromised.

References

1 Remine WH, Priestley JT, Judd ES, King JN: Total pancreatectomy. Ann Surg 1970;172: 595–604.
2 Sarr MG, Behrns KE, van Heerden JA: Total pancreatectomy: An objective analysis of its use in pancreatic cancer. Hepatogastroenterology 1993;40:418–421.
3 Pedrazzoli S, Pasquali C, Sperti C: General aspects of surgical treatment of pancreatic cancer. Dig Surg 1999;16:265–275.
4 McAfee MK, van Heerden JA, Adson MA: Is proximal pancreatoduodenectomy with pyloric preservation superior to total pancreatectomy. Surgery 1989;105:347–351.
5 Dresler CM, Fortner JG, McDermott K, Bajorunas DR: Metabolic consequences of (regional) total pancreatectomy. Ann Surg 1991;214: 131–140.
6 Ihse I, Anderson H, Andren S: Total pancreatectomy for cancer of the pancreas: Is it appropriate? World J Surg 1996;20:288–293, discussion 294.
7 Jones L, Russell C, Mosca F, Boggi U, Suton R, Slavin J, et al: Standard Kausch-Whipple pancreatoduodenectomy. Dig Surg 1999;16:297–304.
8 van Berge Henegouwen MI, Gouma DJ: Low mortality following resection for pancreatic and periampullary tumours in 1026 patients: UK survey of specialist pancreatic units (letter). Br J Surg 1998;85:425–426.
9 Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, et al: Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: Pathology, complications, and outcomes. Ann Surg 1997;226:248–257, discussion 257–260.
10 Büchler MW, Friess H, Wagner M, Kulli C, Wagener V, Z'graggen K: Pancreatic fistula after pancreatic head resection: analysis of 331 consecutive patients. Br J Surg 2000;87:883–889.
11 Itani KMF, Coleman RE, Meyers WC, Akwardi OE: Pylorus-preserving pancreatoduodenectomy. A clinical and physiologic appraisal. Ann Surg 1986;204:655–664.
12 Takada T, Yasuda H, Amano H, Yoshida M, Ando H: Results of a pylorus-preserving pancreatoduodenectomy for pancreatic cancer: A comparison with results of the Whipple procedure. Hepatogastroenterology 1997;44:1536–1540.
13 Watson K: Carcinoma of the ampulla of Vater: Successful radical resection. Br J Surg 1944;31: 368–373.
14 Traverso LW, Longmire WP: Preservation of the pylorus in pancreaticoduodenectomy. Surg Gynecol Obstet 1978;146:959–962.
15 Roder JD, Stein HJ, Hüttl W, Siewert JR: Pyloruspreserving versus standard pancreaticoduodenectomy: An analysis of 110 pancreatic and perriampullary carcinomas. Br J Surg 1992;79:152–155.
16 Klinkenbijl JHG, van der Schelling GP, Hop WCJ, van Pel R, Bruining HA, Jeekel J: The advantages of pylorus-preserving pancreatoduodenectomy in malignant disease of the pancreas and the periampullary region. Ann Surg 1992;216:142–145.
17 Kozuschek W, Reith HB, Haarmann W: The role of pylorus-preserving duodenopancreatic head resection; in Beger HG, Büchler MW, Malfertheiner P (eds): Standards in Pancreatic Surgery. Berlin, Springer, 1993, pp 414–424.
18 Büchler MW, Ebert M, Beger HG: Grenzen chirurgischen Handelns beim Pankreaskarzinom. Langenbecks Arch Chir Suppl 1993;75: 460–464.
19 Mosca F, Giulianotti PC, Balestracci T, Di Candio G, Pietrabissa A, Sbrana F, et al: Long-term survival in pancreatic cancer: Pylorus-preserving versus Whipple pancreatoduodenectomy. Surgery 1997;122:553–566.

20 Schoenberg MH, Gansauge F, Kunz R: Die Wertigkeit der pyloruserhaltenden partiellen Duodenopankreatektomie beim duktalen Pankreascarcinom. Chirurg 1997;68:1262–1267.
21 Swope TJ, Wade TP, Neuberger TJ, Virgo KS, Johnson FE: A reappraisal of total pancreatectomy for pancreatic cancer: Results from US Veterans Affairs hospitals, 1987–1991. Am J Surg 1994;168:582–585, discussion 585–586.
22 Lambert MA, Lincham IP, Russell RCG: Duodenum preserving total pancreatectomy for endstage chronic pancreatitis. Br J Surg 1987; 74:35–39.
23 Easter DW, Cuschieri A: Total pancreatectomy with preservation of the duodenum and pylorus for chronic pancreatitis. Ann Surg 1991; 214:575–580.
24 Hunt DR, McLean R: Pylorus preserving pancreatectomy: Functional results. Br J Surg 1989;76:173–176.
25 Sugiyama M, Atomi Y: Pylorus-preserving total pancreatectomy for pancreatic cancer. World J Surg 2000;24:66–70, discussion 70–71.
26 Dripps RD, Lamont A, Eckenhoff JE: The role of anesthesia in surgical mortality. JAMA 1961;178:261–266.
27 Vacanti CJ, Van Houton RJ, Hill RC: A statistical analysis of the relationship of physical status to postoperative mortality in 63,388 cases. Anesth Analg 1970;49:564–566.
28 Tsao JI, Rossi RL, Lowell JA: Pylorus-preserving pancreatoduodenectomy. Arch Surg 1994; 129:405–412.
29 Brooks JR, Brooks DC, Levine JD: Total pancreatectomy for ductal cell carcinoma of the pancreas. An update. Ann Surg 1989;209:405–410.
30 Launois B, Franci J, Bardaxoglou E, Ramee MP, Paul JL, Malledant Y, et al: Total pancreatectomy for ductal adenocarcinoma of the pancreas with special reference to resection of the portal vein and multicentric cancer. World J Surg 1993;17:122–126, discussion 126–127.
31 Bottger TC, Junginger T: Factors influencing morbidity and mortality after pancreaticoduodenectomy: Critical analysis of 221 resections. World J Surg 1999;23:164–171, discussion 171–172.
32 Baumel H, Huguier M, Manderscheid JC, Fabre JM, Houry S, Fagot H: Results of resection for cancer of the exocrine pancreas: A study from the French Association of Surgery. Br J Surg 1994;81:102–107.
33 Warshaw AL, Torchiana DL: Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. Surg Gynecol Obstet 1985; 160:1–4.
34 Braasch JW, Rossi RL, Watkins E, Deziel DJ, Winter PF: Pyloric and gastric preserving pancreatic resection. Ann Surg 1986;204:411–418.
35 Jimenez R, Fernandez-del Castillo C, Rattner D, Chang Y, Warshaw A: Outcome of pancreaticoduodenectomy with pylorus preservation or with antrectomy in the treatment of chronic pancreatitis. Ann Surg 2000;231:293–300.
36 Zerbi A, Balzano G, Patuzzo R, Calori G, Braga M, Di Carlo V: Comparison between pylorus-preserving and Whipple pancreatoduodenectomy. Br J Surg 1995;82:975–979.
37 van Berge Hengouwen MI, van Gulik TM, De-Wit LT, Allema JH, Rauws EA, Obertop H, et al: Delayed gastric emptying after standard pancreaticoduodenectomy versus pylorus-preserving pancreaticoduodenectomy: An analysis of 200 consecutive patients. J Am Coll Surg 1997;185:373–379.
38 Büchler MW, Friess H, Müller MW, Wheatley AM, Beger HU: Randomized trial of duodenum-preserving pancreatic head resection versus pyloruspreserving Whipple in chronic pancreatitis. Am J Surg 1995;169:65–70.
39 Kayahara M, Nagakawa T, Ueno K, Ohta T, Tsukioka Y, Miyazaki I: Surgical strategy for carcinoma of the pancreas head area based on clinicopathologic analysis of nodal involvement and plexus invasion. Surgery 1995;117: 616–623.
40 Cubilla AC, Fortner J, Fitzgerald P: Lymph node involvement in carcinoma of the head of the pancreas area. Cancer 1978;41:880–887.
41 Newman KD, Braasch JW, Rossi RL, O'Campo-Gonzales S: Pyloric and gastric preservation with pancreatoduodenectomy. Am J Surg 1985;145:152–156.
42 Nagai H, Kuroda A, Morioka Y: Lymphatic and local spreading of T1 and T2 pancreatic cancer. Ann Surg 1986;204:65–71.
43 Martin RF, Rossi RL: Pylorus-preserving pancreatoduodenectomy for cancer: Is it an adequate operation; in Hanyu F, Takasaki K (eds): Pancreatoduodenectomy. Tokyo, Springer, 1997, pp 107–114.
44 Fortner JG, Klimstra DS, Senie RT, Maclean BJ: Tumor size is the primary prognosticator for pancreatic cancer after regional pancreatectomy. Ann Surg 1996;223:147–153.
45 Pedrazzoli S, DiCarlo V, Dionigi R, Mosca F, Pederzoli P, Pasquali C, et al: Standard versus extended lymphadenectomy associated with pancreatoduodenectomy in the surgical treatment of adenocarcinoma of the head of the pancreas: A multicenter, prospective, randomized study. Lymphadenectomy Study Group. Ann Surg 1998;228:508–517.
46 Henne-Bruns D, Vogel I, Luttges J, Kloppel G, Kremer B: Ductal adenocarcinoma of the pancreas head: Survival after regional versus extended lymphadenectomy. Hepatogastroenterology 1998;45:855–866.