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Four hundred fifty-three consecutive pancreaticoduodenectomies with pancreaticogastrostomy

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ABSTRACT

Background: Patients who undergo pancreaticoduodenectomy (PD) have the pancreatic remnant (PR) anastomosed to the jejunum. In this study, all patients had the PR anastomosed to the stomach. Our aims are to evaluate postoperative outcomes of patients undergoing PD with pancreaticogastrostomy (PG).
Methods: There was 453 patients who underwent PD with PG. Preoperative characteristics, intraoperative data, and postoperative outcomes were analyzed using univariate and multivariate models.
Results: The patient cohort had a median age of 67 years and underwent resection for pancreatic (40.8%), ampullary (15.9%), duodenal (6.6%), distal bile duct (6.4%) cancers. Multivariate analysis revealed poor prognosis was related to age, tumor diameter, lymph node ratio, perineural invasion, and tumor differentiation in patients with periampullary adenocarcinoma.
Conclusions: This series of patients undergoing PD with PG shows that the operation can be performed safely with excellent outcomes for a variety of malignant and benign conditions.

Introduction

When the one-stage pancreaticoduodenectomy (PD) was first introduced as treatment for tumors of the pancreas and periampullary region, it was associated with high mortality and morbidity.[1] The primary cause of morbidity and mortality is related to leakage from the pancreaticoenteric anastomosis. Because of this several other approaches have been suggested to minimize leak from the pancreaticoenteric anastomosis. These include suture ligation of the pancreatic duct, total pancreatectomy, pancreatic duct injection with neoprene, modifications of the pancreaticojejunostomy (PJ), and pancreaticogastrostomy (PG).[2–8]

This study aims to evaluate the trends in four hundred and fifty-three PD's with PG with emphasis on pathology, complications and long-term endocrine and exocrine function.

Methods

Study design

This was a retrospective cohort study of data that was collected prospectively at Loyola University Medical Center and Edward Hines, Jr. VA Hospital from June 1990 to May 2014. This study received institutional review board approval by the Loyola University Chicago.

Study population and data elements

The analysis cohort included adult patients who underwent PD with PG. Ninety-five percent of the PD were done between June 1995 and May 2014. Data gathered included patient demographics, presenting symptoms, indications for PD, and intraoperative factors such as estimated blood loss (EBL), blood transfusion, and operative time. Postoperative data including pathology, mortality, morbidity, reoperation, length of hospital stay (LOS), and readmissions. Most pathology specimens were read by a single pathologist, supported by a second according to departmental protocol.

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Surgical technique and postoperative care

The surgical technique used has been described previously.[9] A classic PD with distal gastrectomy and a standard lymph node dissection was performed in all patients (Fig. 1A) The PG is the first anastomosis to be performed. The pancreatic remnant (PR) is elevated off the splenic vessels for a distance of at least 4–5 cm. In the soft pancreas, 5 cm is preferred. The anastomosis is made 5 or more cm from the cut end of the stomach. Single layer sutures of 3–0 silk are taken from the posterior superior gastric wall to the anterior pancreas. The sutures in the pancreas must be at least 2–3 cm from the cut edge of the pancreas. Sutures are placed 3–4 mm apart, and the number sutures is dependent on the width of the remnant (Fig. 1B). A gastrotomy is made. It is crucial that the length of the gastrotomy be less than the width of the remnant. This allows for a snug invagination of the remnant into the stomach. Sutures are taken from the posterior inferior gastric wall to the posterior pancreas. In the soft pancreas with a small duct, a stent is placed in the duct to make sure it is not occluded (Fig. 1C). Then, 2–3 cm, at minimum, of the pancreas is invaginated into the stomach (Fig. 1D). A 3 cm invagination is preferred for the soft pancreas. The completed anastomosis (Fig. 1E). The importance of mobilizing the pancreatic remnant for 4–5 cm especially in the soft remnant cannot be overemphasized. Vagotomy and tube gastrotomy is never performed. A drain is placed near the biliary anastomosis and another near the pancreatic anastomosis. Tube jejunostomy is done in patients with borderline nutritional status. In this study, Octreotide was used in the perioperative period in the early years of this study but was abandoned in 2002 after data was published that it did not prevent postoperative pancreatic fistula (POPF).[10] Octreotide was used postoperatively if the patient developed a fistula.

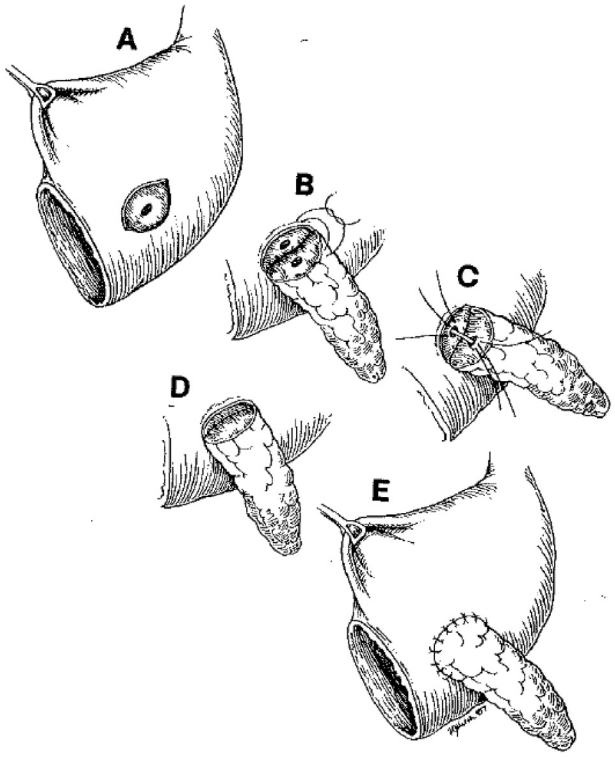

Fig. 1. Pancreaticogastrostomy surgical technique
A) Distal gastrectomy and gastrotomy. B) Pancreatic suture placement. C) Stent placement (if soft pancreas with small duct. D) Pancreas is invaginated into the stomach. E) Completed anastomosis.

A nasogastric tube (NGT) is used mainly to decompress the stomach to allow the pancreas to heal to the gastric wall. On the fourth post-op day, erythromycin intravenously is initiated.[11] In the absence of bilious drainage, the right drain is removed on the fifth postoperative day. Amylase in the fluid from the intraoperatively placed pancreatic drain is measured daily. In the absence of a POPF defined as amylase-rich fluid three times greater than the serum amylase after one solid meal, the left drain was removed. Parameters set forth by the International Study Group on Pancreatic Fistula (ISGPF) are used to grade POPF. Grade A fistulae are those in which patients are well with no evidence of infection and the fistula managed by the drain placed at surgery. Grade B fistulae are those in which the patients are often well but manifested signs of infection and had a positive CT requiring a new drain. Grade C fistulae are those patients who appeared ill, had signs of infection and sepsis, had a positive CT and required reoperation or in whom death is related to POPF. Delayed gastric emptying (DGE) is defined as the need for the NGT to stay in for ten days or if the NGT had to be reinserted after being removed and the patient needs to go on parenteral nutrition. A bile leak is defined as persistent bilious drainage from the right subhepatic drain on postsurgical day five and after. An intraabdominal infection (IAI) is defined as purulent drainage from a closed suction drainage system placed at surgery or purulent drainage from a drain placed postoperatively by CT guidance. All patients are seen after discharge in the surgical clinic and are then cleared. The patients with malignancy are seen in the Multidisciplinary GI Oncology clinic for discussion of adjuvant therapy. Borderline resectable pancreas cancer patients are treated with neoadjuvant FOLFIRINOX (leucovorin, 5-fluorouracil, irinotecan, and oxaliplatin) followed by treatment with concomitant radiation therapy to the tumor bed and fluoropyrimidine and resection if appropriate.[12]

Long-term pancreatic function and survival

Personal interviews were conducted with 90 patients who underwent PD with PG between 1995 and 2010 to assess long-term endocrine and exocrine function. A diagnosis of diabetes mellitus (DM) was made when a patient exhibited a hemoglobin A1C greater than 6.5%. Patients who required or did not require exocrine pancreatic enzyme therapy were also recorded. A diagnosis of steatorrhea is made when a patient began to have frequent, foul-smelling, floating stools. Patient follow up, and survival was obtained from the electronic and paper medical records, and by using the Social Security Death Index, the Center for Medicare and Medicaid Services (CMS), and the cancer registries at respective tertiary care centers patients are cared for.

Statistical analysis

The primary outcome of interest was postoperative and long-term complications, and survival. Patient demographics, intraoperative and postoperative course and pathologic findings were evaluated by univariate and multivariate analyses to determine their relationship to survival. In 0.8% of patients ($n = 4$), pathology reports could not be traced and in 1.5% ($n = 7$) patients were lost to follow up. Differences in survival between patient subsets were compared using the log-rank test. Multivariate analysis was performed with Cox proportional hazards models. Significance was accepted for $p < .05$. The analysis was performed using StataCorp. 2015. (Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Results

Four hundred and fifty-three consecutive patients underwent PD with PG. The mean age of the patients was 65.7 years (SD = 12), and males accounted for 58.3% (N = 264) of the patients. The three most common presenting symptoms were jaundice, weight loss, and abdominal pain. The mean intraoperative EBL was 1009 ml (SD = 757), and the median number of red blood cell units transfused was 0 (IQR = 0–7) with a median operative time of 6 h (IQR = 4–13). Adenocarcinomas accounted for the greatest proportion of cases with the following distribution: pancreas 40.8% (N = 185), ampulla 15.9% (N = 72), duodenum 6.6% (N = 30), and bile duct 6.4% (N = 29). Pancreatitis, neuroendocrine tumors (NET), intrapancreatic mucinous neoplasms (IPMN), mucinous cystadenocarcinomas (MCAC), gastrointestinal stromal tumors (GIST), serous cystadenomas, and other benign pathologies accounted for the remaining 30.3% of cases (Table 1).

Next, we evaluated postoperative complications. There was 12.8% (N = 58) patients who developed a POPF with 9.5% grade A, 2.9% grade B, and 0.4% grade C fistulas. Higher fistula rates occurred in those with a soft pancreatic remnant (19%; $p < .05$) and a pancreatic duct diameter in the remnant of less than 3 mm (17.2%; $p < .05$). Regarding tumor type, the rate of developing a POPF with a diagnosis of pancreatic adenocarcinoma was 5.4% compared to 23.3% for ampullary carcinoma and 26.7% for duodenal carcinoma ($p < .05$). Other complications included; DGE (9.5%), surgical site infection (SSI) (5.3%), IAI (4.0%), return to the operating room (1.7%), cardiopulmonary (4.6%), early postoperative hemorrhage (2.4%), small bowel obstruction (1.5%), bile (0.9%), and gastric leak (0.7%). Thirteen percent of patients (N = 59) were readmitted within 30 days of discharge, and the combined in-hospital and 30 day-mortality rate was 1.3% (N = 6) and 90 day-mortality rate was 3.3% (N = 15). The median postoperative LOS was nine days (IQR: 8–11). (Tables 2 and 3).

Next, we evaluated the development of new-onset postoperative DM and steatorrhea. The median time between PD and the diagnosis of DM was 2.9 years (SD 2.7 years). The overall prevalence was 23.4% (N = 18) and developed in younger patients (58.1 years versus 65.8 years; $p = .021$). Forty-seven (52.8%) patients developed symptomatic steatorrhea requiring pancreatic enzyme therapy. Patients who developed steatorrhea underwent PD with PG at a younger age 61.4 (IQR = 28–82) compared to those who did not 67 (IQR = 42–91).

Lastly, we evaluated survival in the setting of periampullary cancer; univaraiable analysis was conducted for 304 patients (post-op deaths and those lost to follow up excluded). Parameters influencing survival were age (HR = 1.02; $p < .001$), reoperation (HR = 2.47; $p = .05$), tumor diameter (HR = 1.22; $p < .001$), positive lymph nodes (HR = 2.22; $p < .001$), lymph node ratio (OR = 22.10; $p < .001$), lymphovascular invasion (HR = 2.12; $p < .001$), perineural invasion (OR = 2.38; $p < .001$), positive margins (HR = 1.37; $p < .001$), and tumor located in pancreas (HR = 1.89; $p < .001$). Using a Cox proportional hazards model, a multivariate analysis was undertaken. Predictors of poor survival were age (HR = 1.02; $p < .001$), tumor diameter (HR = 1.21; $p < .001$), lymph node ratio (HR = 17.77; $p < .001$), perineural invasion (HR = 1.89; $p < .001$), moderately (HR = 1.60; $p < .04$) and poor tumor differentiation (HR = 1.82; $p < .02$). (Tables 4–6, Fig. 2).

Table 1
453 Consecutive pancreaticoduodenectomies: demographics and intraoperative characteristics.

Age (yr.), *mean (SD)*	67	21–91
Male, *n (%)*	264	58.3%
Presenting symptoms, *n (%)*		
Jaundice	286	63.1%
Weight Loss	141	31.1%
Pain	144	31.8%
ASA, *n (%)*		
1	4	0.9%
2	123	27.2%
3	265	58.5%
4	13	2.9%
Intraoperative Factors, *median (IQR)*		
Blood loss (mL)	800	150–7500
Transfusions (units red cells)	0	0–7
Operative Time (hours)	6	4–13
Pathology, *n (%)*		
Pancreatic adenocarcinoma	185	40.8%
Ampullary adenocarcinoma	72	15.9%
Duodenal adenocarcinoma	30	6.6%
CBD adenocarcinoma	29	6.4%
Pancreatitis	30	6.6%
Neuroendocrine tumor	18	4.0%
IPMN	39	8.6%
Mucinous cystadenocarcinoma	16	3.5%
Serous cystadenoma	7	1.5%
Other	25	5.5%

American Society of Anesthesiologist physical status classification (ASA); common bile duct (CBD); intraductal papillary mucinous neoplasm (IPMN).

Discussion

Pancreaticoduodenectomy, commonly referred to as the Whipple procedure, remains the most complex operation that a surgeon can perform on the gastrointestinal (GI) tract. Recently the published mortality from high volume centers is less than 2%. Several studies have shown that the operation can be done safely and without mortality.[13–17] In this series, 197 consecutive patients underwent PD without mortality, although, morbidity remains high. Morbidity is mainly related to the anastomosis of the pancreatic remnant to the GI tract. In this study, the pancreatic remnant was invaginated into the posterior stomach. Several theoretical, anatomical, and technical advantages have been proposed to explain the safety of PG.[18]

In this study, mortality was 1.3%. The deaths in this series were from different causes, but in at least two, autopsies would suggest that late bleeding was the cause, though the exact site could not be identified. Delayed bleeding as a cause for postoperative mortality was seen in 13 of 2000 consecutive PD's published by Cameron and He and Cheng et al.[19,20] The authors correctly point out that delayed bleeding after PD has become a major challenge. In delayed bleeding after PD, our policy is to send the patient for a CT angiogram (CTA) and look for subtle bleeding or a small aneurysm. In these cases, we find the CTA can expedite and focus the catheter angiogram considerably. We believe this CTA first protocol screens out the readily identifiable pseudoaneurysms and limits angiographic catheter time and contrast exposure while maximizing the ability to diagnose and treat an arterial bleeding source quickly. The role of the interventional radiologist in managing complications after PD has been delineated.[21] In this series, 5.7% (n = 26) patients had a percutaneous transhepatic catheter placed for biliary anastomotic leak, percutaneous drainage of abdominal fluid for SSI or fluid collection, and placement of new drains or change of drains for Grade A fistula becoming a Grade B fistula, for example, or an angiogram for pseudoaneurysm.

Another cause of late bleeding is ulceration at the gastrojejunal anastomosis. Of the four patients in whom this occurred, two were unstable and required reoperation to control bleeding. Two patients who were stable had the bleeding controlled with endoscopy. It is the authors' practice to keep patients on proton pump inhibitors (PPIs) for 6 months to one year postoperatively. Whether patients with PD should be left on PPIs for a longer time is open to further study.

Table 2
453 Consecutive pancreaticoduodenectomies: postoperative outcomes.

Postoperative Complications, *n (%)*		
None	299	66.0%
Fistula	58	12.8%
Grade A	43	74.1%
Grade B	13	22.4%
Grade C	2	3.4%
Delayed Gastric Emptying	43	9.5%
Wound Infection	24	5.3%
Cardiopulmonary Complication	21	4.6%
Surgical Site infection	18	4.0%
Hemorrhage	11	2.4%
Small bowel obstruction	7	1.5%
Bile Leak	4	0.9%
Gastric Leak	3	0.7%
Mortality	6	1.3%
90-day mortality	15	3.3%
Reoperation	8	1.7%
Hospital Readmission	59	13.0%
Length of Hospitalization (days), mean (SD)	11	6.6

Postoperative complication data were collected from inpatient medical records for each patient. Readmissions occurred within 30 days of discharge from the index operation. Mean data reported as mean ± standard deviation.

The rate of POPF development in this series was 12.8%, which is within range of most studies. Most fistulae were Grade A (75.5%), followed by Grade B (20.5%) and Grade C (3.7%). If one separates patients with a soft pancreatic remnant and a duct diameter of less than 3 mm the fistula rate was 19% and 17.2%, respectively. Patients with pancreatic and distal bile duct cancer with a firm or hard remnant had a much lower postoperative fistula rate when compared to those with ampullary and duodenal carcinoma where the remnant was soft. One theoretical anatomical advantage to performing a PG is that the thick wall and excellent blood supply of the stomach are better able to hold the sutures from the stomach to the soft pancreas.[18] In our study, only 3.4% (N = 2) of patients developed a Grade C fistula. Both had surgery and survived. In a worldwide study of 4301 PD's with PJ McMillan et al. found that patients 1.8% (N = 79) developed Grade C, POPF's.[22] Of the 79 patients, deaths occurred in 35% (N = 25) and reoperation was needed in 72.2% of cases. Other studies have also identified PG to be associated with less severe fistulas.[23] One theory that leads to less lethal Grade C fistulae and thus do not require re-laparotomy or lead to death has to do with gastrointestinal physiology.[24] Pancreatic proteolytic enzymes are secreted as proenzymes and require enterokinase for activation. Enterokinase is secreted from the wall of the duodenum and jejunum although absent in the stomach. The activation of these proteolytic enzymes requires an alkaline environment. Therefore, the emptying of pancreatic secretions into the acidic gastric lumen precludes the digestive action of the pancreatic anastomosis by activated proteolytic enzymes. The acid is neutralized by the alkaline secretions brought to the stomach by the gastrojejunostomy.[9] All the Grade A and Grade B fistulae in this study were treated conservatively with success which has also been noted by other authors.[24] We experienced very few chylous leaks, contained leaks at the gastrointestinal anastomosis, or leaks at the biliary anastomosis which has noted by Bassi et al.[25] Another common postoperative complication after PD is DGE, which occurred in 9.3% of patients. It is important to note that DGE often occurs in the presence of IAI which should be ruled out in all cases.[26] We attribute our low DGE rate to having a low rate of IAI of 4%. These findings are consistent with those of others.[25]

In a tertiary, high volume pancreatic surgery center like ours, most patients with jaundice are referred with endoscopic biliary stents and occasionally trans-hepatic stents. We compared patients with stents and those with no stents and found no differences in mortality or morbidity in either group.

The 30-day readmission rate in this study was 13%. We found that the addition of a Nurse Practitioner (NP) was very useful.[27] With the hiring of an NP to work with three surgeons we found that more patients went home with nursing, physical therapy, and occupational therapy. In addition, there was a 50% reduction in unnecessary ER visits and possible readmissions. The latter we believe was due to the regular calls made by the NP to the patients postoperatively and before their first postoperative clinic visit.

Table 3
Rates and odds ratios for developing pancreatic fistula postoperatively by selected pancreatic features.

	Rate of fistula formation	Odds Ratio	P value
Pancreatic Texture			
Firm (reference)	9.3%	–	–
Soft	19.0%	4.42	0.00
Hard	2.8%	0.43	0.43
Pancreatic Duct Diameter			
> 3 mm (reference)	2.3%	–	–
< 3 mm	17.2%	8.84	0.00
Periampullary adenocarcinoma		0.73	0.29
Pancreatic adenocarcinoma	5.4%	0.22	0.00
Ampullary adenocarcinoma	23.3%	3.40	0.00
Duodenal adenocarcinoma	26.7%	3.24	0.01
CBD adenocarcinoma	7.1%	0.56	0.44

Results of univariate logistic regression models. Odds ratio for fistula formation for all periampullary adenocarcinoma patients in comparison to the rest of the cohort was calculated; in addition, each adenocarcinoma was individually analyzed against others with periampullary adenocarcinoma. CBD, common bile duct.

Table 4
Univariate and multiple variable regressions for parameters influencing survival in 304 patients with periampullary adenocarcinoma.

	Odd Ratio	P value
Univariable Analysis		
Age	1.02	<0.01
Reoperation	2.47	0.05
Tumor diameter	1.22	<0.01
Lymph node positive	2.22	<0.01
Lymph node ratio	22.10	<0.01
Lymphovascular invasion	2.12	<0.01
Perineural invasion	2.38	<0.01
Positive margin	1.37	0.05
Tumor location		
Pancreas	1.89	<0.01
Duodenum	0.59	0.03
Ampulla	0.50	<0.01
Common bile duct	1.18	0.42
Tumor differentiation		
Well	0.66	0.05
Moderately	1.10	0.45
Poorly	1.10	0.47
Multivariable Analysis		
Age	1.02	<0.01
Tumor diameter	1.21	<0.01
Lymph node ratio	17.77	<0.01
Perineural invasion	1.89	<0.01
Tumor differentiation		
Well	1.00	–
Moderately	1.60	0.04
Poorly	1.82	0.02

Results of univariate and multiple variable logistic regression models. Odds ratio for tumor differentiation are reported using well differentiated tumors as the baseline. Each adenocarcinoma was individually analyzed. Against all others with periampullary adenocarcinoma.

When considering just the four periampullary tumors, the most common indication for PD was pancreatic cancer, followed by ampullary cancer, duodenal cancer, and distal bile duct cancer. In a study of 242 patients with periampullary adenocarcinoma, Yeo, et al. found four factors to adversely affect survival: 1) tumor diameter; 2) the presence of positive resection margins; 3) lymph node metastases; and 4) the presence of poorly differentiated histology.[28] Their findings agree with ours in terms of tumor diameter, lymph node metastases, and tumor differentiation. In addition, we found lymph node ratio was a powerful predictor of prognosis.

Adjuvant chemoradiation therapy (CRT) for resected pancreatic adenocarcinoma was established when the results from the Gastrointestinal Tumor Study Group (GITSG) concluded that the combined use of radiation therapy and fluorouracil was effective in prolonging survival when compared to no adjuvant therapy.[29] Early patients in our series received fluorouracil and radiation as adjuvant therapy in resected pancreatic cancer. The adjuvant paradigm shifted to treatment with gemcitabine-based chemotherapy with or without concomitant chemoradiation with the demonstration of similar efficacy and better tolerability of gemcitabine-based adjuvant therapy compared to fluoropyrimidine therapy in the adjuvant setting.[30,31] The role of newer combination chemotherapy regimens in the adjuvant treatment of pancreas cancer is being studied. The value of radiation therapy in the adjuvant treatment of resected adenocarcinoma of the pancreas has been questioned, and RTOG 0848 is accruing resected patients to answer this critical question.[32] In our series of patients reported in this paper, the median survival for those patients with pancreatic adenocarcinoma who received adjuvant therapy was 25.5 months and for those not receiving CRT was 10.7 months. Adjuvant CRT was also used in patients with ampullary, bile duct, and duodenal adenocarcinomas based on pathologic stage and specific pathologic features (size, poor differentiation, lymph node status, and lymphovascular and perineural invasion). Suffice it to say that in some instances of periampullary cancers, surgery alone, and in the clear majority, surgery and CRT, gives patients their best chance of survival.

While short-term complications following PD have received much attention, few have reported on the long-term outcomes of endocrine and exocrine function following these operations. In our study 90 patients underwent long-term follow up after PD.[33] Thirteen (14.4%) were excluded because they developed diabetes before surgery. Of the remaining 77 patients 23.4% developed DM postoperatively. Patients who developed DM postoperatively tended to have their operation at a young age (58.1 years) than those who did not develop DM (65.8 years). While the survival in both groups did not significantly differ, the small difference in survival is one possible explanation for this observation. Those who developed DM had a median survival or follow up of 6.6 years, while those who did not develop DM had median survival or follow up of 6.0 years. Additionally, we hypothesize that younger patients are less likely to modify their diet to maintain glycemic control. In contrast, older patients may be willing to control their glucose intolerance with diet alone. While glycemic control maybe problematic in long-term survivors of PD, exocrine insufficiency manifested by steatorrhea is also quite problematic in these patients. We found that 52.8% of patients developed pancreatic exocrine insufficiency significant enough to cause symptomatic steatorrhea postoperatively requiring pancreatic enzyme therapy. It has been suggested that the acidic environment in the stomach denatures pancreatic secretions, leading to exocrine insufficiency in patients with PG compared to those undergoing PJ.[18,34] However since the gastrojejunostomy introduces alkaline biliary secretions into the

Table 5
Survival after pancreaticoduodenectomy for periampullary adenocarcinoma and other pathologies.

	N	Median Survival (months)	1-Year Survival (%)	3-Year Survival (%)	5-Year Survival (%)	10-Year Survival (%)	15-Year Survival (%)	20-Year Survival (%)
Entire cohort	440	40	81	53	40	19	7	1
Periampullary adenoca.	304	27	75	38	25	10	4	1
IPMN	38	88	97	92	76	26	8	0
Pancreatic cystadenoma	23	136	91	83	78	57	22	0
Neuroendocrine tumor	18	70	94	83	61	28	6	0
Villous adenoma	10	132	100	90	80	60	0	0
GIST	4	130	100	75	75	50	25	0
Pancreatic cystadenoca.	2	78	50	50	50	50	0	0

Unadjusted mean survival and percentage of patients surviving at each time point, excluding postoperative mortalities. Median survival is listed in years; percentage survival in each pathologic group at each time point is listed. Adenoca, adenocarcinoma; cystadenoca, cystadenocarcinoma; IPMN, intraductal papillary mucinous neoplasm; GIST, gastrointestinal stromal tumor.

Table 6
Survival after pancreaticoduodenectomy for periampullary adenocarcinoma and other pathologies by node status.

Number of Cases	Periampullary		Pancreatic		Duodenal		Ampullary		Common Bile Duct	
	112	193	50	130	14	10	34	36	11	17
Node status	−	+	−	+	−	+	−	+	−	+
Median Survival	43.2	32.4*	34.8	16.8*	51.6	22.8*	87.6	24.0*	24	30
Survival Intervals:										
1 year	88.4	65.3	88.0	60.8	92.9	80.0	88.2	72.2	81.8	65.3
3 year	57.1	24.9	48.0	23.1	50.0	10.0	73.5	30.6	45.5	24.9
5 year	41.1	15.0	32.0	13.1	35.7	0.0	58.8	19.4	27.3	15.0
10 year	16.1	5.2	8.0	4.6	14.3	0.0	29.4	8.3	0.0	5.2
15 year	8.0	1.0	4.0	0.8	14.3	0.0	8.8	0.0	0.0	1.0
20 year	1.8	0.0	0.0	0.0	0.0	0.0	5.9	0.0	0.0	0.0

Unadjusted mean survival and percentage of patients surviving at each time point, excluding postoperative mortalities. Median survival is listed in years; percentage survival in each pathologic group at each time point by lymph node status.

stomach and perioperative and long-term use of PPI also reduced acid secretions, other explanations need to be found to explain this high incidence of steatorrhea after PG. The group that required pancreatic enzyme therapy was significantly younger than the group that did not require enzyme therapy (61.4 years versus 67.0 years). As in the development of DM in younger patients, we hypothesize that this may also be due to younger patients being less willing to modify their diet. Beger et al. recommended that duodenal sparing pancreatic resections can be performed in premalignant or tumors with low malignant potential of the pancreas. This could be an option in younger patients with these tumors and benign disease.[35] If PD is required in young patients it is possible that PG be avoided. One interesting finding was that 59.1% of patients requiring enzymes for pancreatic insufficiency had PD for pancreatic cancer in contrast to 20.8% who underwent PD for ampullary cancer. We hypothesize that patients with pancreatic adenocarcinoma of the head have ductal obstruction which may eventually lead to atrophy of the body and tail, while the pancreatic remnant in the remnant of patients with ampullary adenocarcinoma are not as atrophied and these patients experience less pancreatic insufficiency.

The major limitation of this study is that even though the oncologic outcomes are favorable, it should be noted that various adjuvant treatments were used during the study period.

Conclusion

This study presents a large number of patients who underwent PD with PG at two institutions. In this series, the postoperative mortality was 1.3%. Postoperative pancreatic fistula rate was 12.8%.

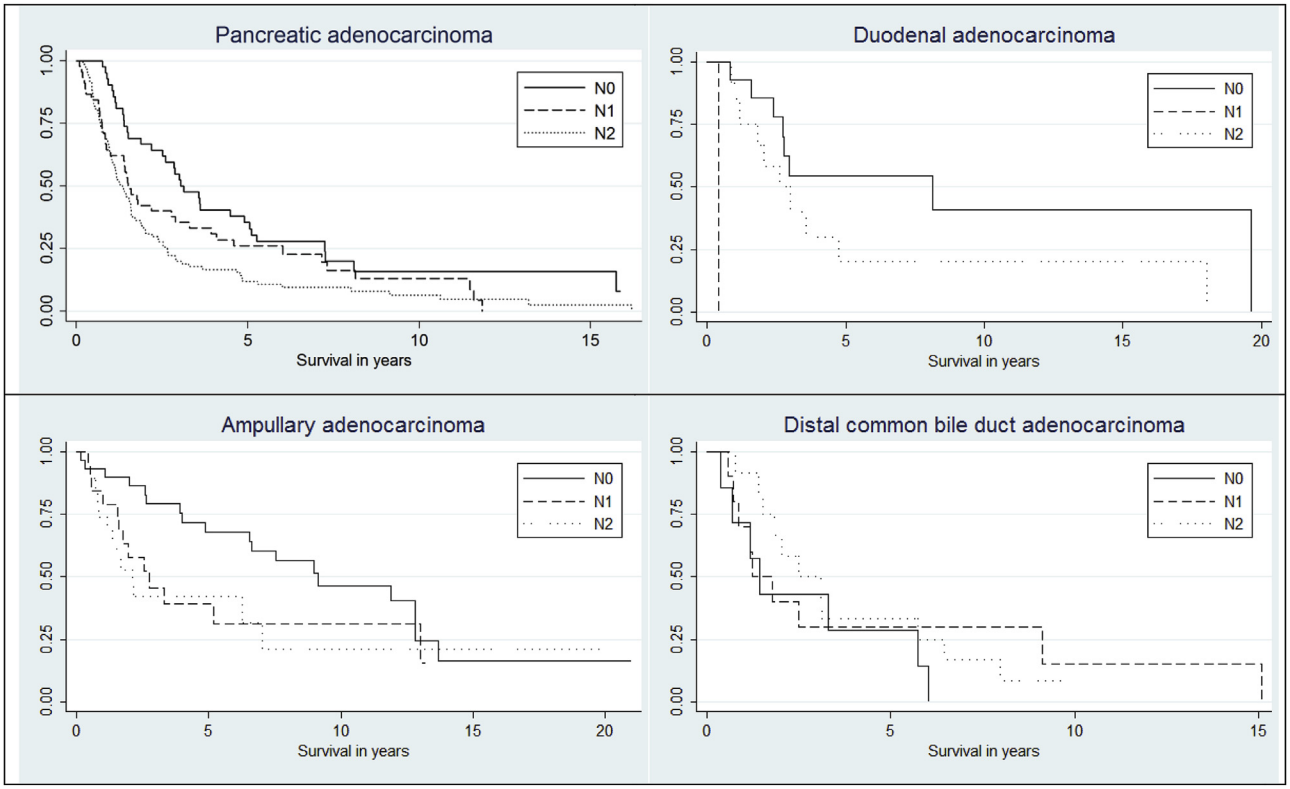

Fig. 2. Kaplan-Meier survival curves for 304 PDs with PG for periampullary neoplasms, by tumor type.
Kaplan-Meier survival curves for 304 patients that underwent PD with PG, excluding postoperative deaths and those lost to follow-up, by lymph node status. N0 designates those patients with no positive lymph nodes on final pathologic examination; N1 designates those with 1–2 lymph nodes positive, and N2 designates those with 3 or more lymph nodes positive.

In the soft pancreas with small ducts, the fistula rates were 17% and 19%, respectively. A study comparing PJ to PG in the soft pancreas with small ducts in relation to postoperative fistula formation is needed. Wound infections, SSI, and DGE, were also low in our study. Early postoperative bleeding occurred in 1.5% of patients, and they were treated by surgery, endoscopy, and interventional radiology with no deaths. This shows the importance of having the gastroenterologist and interventional radiologists as support personnel to the pancreatic surgeon. About a quarter of patients developed new onset diabetes and fifty percent developed steatorrhea requiring therapy. New onset diabetes and pancreatic insufficiency was observed in younger patients. Readmissions occurred in 13% of patients and were mainly due to dehydration and a failure to thrive. The presence of an NP who counseled patients on what to expect reduced the number of readmissions. In conclusion, PD with PG can be done with low mortality, low rates of CR-POPF, surgical site, and wound infections, DGE, and reoperation, and an acceptable length of hospital stay and rate of readmission. Survival in patients with the four major periampullary adenocarcinomas compared favorably with published data from other institutions.

Disclosure information

No conflicts of interest to disclose amongst the authors.

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Appendix A. Supplementary data

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