Original Article

Risk Factors And Outcome of Pancreatic Fistula after Consecutive Pancreaticoduodenectomy with Pancreaticojejunostomy for Patients with Malignant Tumor

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ABSTRACT

Objective: Pancreatic fistula (PF) is a common complication after pancreaticoduodenectomy (PD) and there is no consensus regarding the criteria to define PF. The study was undertaken to determine the risk factors for PF according to the definition of the International Study Group on Pancreatic Fistula (ISGPF) and to delineate its impact on patient outcome.

Methods: Between March 1994 and May 2009, data from 153 consecutive patients with malignant tumors underwent a PD with pancreaticojejunostomy in the Peking University People's Hospital were recorded prospectively. A total of 24 factors were examined with univariate analysis and multivariate logistic regression analysis was used to estimate relative risks, and their 95% confidence intervals (95% CI) and odds ratio (OR).

Results: Our institution belonged to medium-volume center and PF occurred in 30 patients (19.6%). Pancreatic texture, early postoperative hemorrhage and pancreatic pathologies correlated with PF rates significantly in univariate analyses. But in multivariate regression, soft gland (OR, 4.934; 95% CI, 1.132–7.312) and early postoperative hemorrhage with conservative therapy (OR, 4.130; 95% CI, 1.057–21.112) were predictive. The mean postoperative length of stay in patients with PF was longer (32.7±23.9 versus 60.5±56.2 days) than patients without PF (P=0.001). Overall 30-day mortality was not affected by the development of PF (P=0.657). There was no difference in reoperation rates between patients with and without PF (10.0% versus 6.5%, P=0.787). Concerning the sum of postoperative complications, there were 36 complications for 30 patients with PF, while 64 for 123 patients without PF. When patients with distal cholangiocarcinoma, ampullary and duodenal cancer were considered as a whole for survival analysis, the median survival for patients with PF was 20 months, whereas the median survival for patients without PF was 26 months. Kaplan-Meier survival curves for patients with and without PF were not statistically different (P=0.903).

Conclusion: Soft texture and early postoperative hemorrhage with conservative therapy are independent correlates of increased rate of PF. Anastomotic technique for pancreaticojejunostomy does not have impact on the development of PF in our experience. PF contributes to early postoperative morbidity and the length of hospital stay, but it dose not affect postoperative 30-day mortality, reoperation rate and overall survival.

Key words: Pancreaticoduodenectomy; Pancreatic fistula; Morbidity; Mortality; Surgical outcome

INTRODUCTION

Although improved operative technique and postoperative care decrease mortality after pancreaticoduodenectomy (PD)[1], the rate of pancreatic fistula (PF) is not improved in recent large series which have reported failure of the pancreaticoenteric anastomosis in 10.2%–26.7% of patients worldwide[2–6]. The rate of PF is considered intolerable when compared with leak

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rates of most other gastrointestinal anastomoses. Prior retrospective analyses of surgical series have indicated several important risk factors for PF after PD: surgical volume[7], general health, pancreatic fibrosis, and pancreatic pathology[8]. A number of methods for reducing the incidence of PF have been proposed and analyzed. Many of these involve technical features of the anastomosis, including site of reconstruction[9], anastomotic technique[10], and use of somatostatin analogue[2]. Some investigators even advocated omitting the anastomosis entirely, with occlusion of the remnant duct[3]. To further determine the risk factors for PF in patients who underwent PD with pancreatico-duodenostomy for malignant tumors and to define its effects on outcomes, a univariate and multivariate analysis was conducted using a prospective single-institutional database.

MATERIALS AND METHODS

Patient Selection

Between March 1994 and May 2009, 153 consecutive patients with malignant tumors underwent a PD with pancreaticojejunostomy. The patient was not included when acute pancreatitis was found simultaneously in operation. Details of these patients were entered into a prospective database. There were 106 men (69.3%) and 47 women (30.7%), with a mean age of 58.5±10.5 years (range from 26 to 80 years). All patients had elective operations after full workup and control of preoperative conditions. Indications for PD were malignant diseases (Table 1).

Operation and Postoperative Care

PD was performed without pylorus preservation, and reconstruction was performed by intussusception with an end-to-side or end-to-end pancreaticojejunostomy for all patients. Hepatico-jejunostomy was located about 12 cm distal to pancreaticojejunostomy. Gastrojejunostomy or jejunojejunostomy was located about 40 cm distal to hepaticojejunostomy. The jejunal limb was brought up to the supramesocolic region through an avascular zone of the transverse mesocolon. If possible, a fine silastic tube was placed in the pancreatic duct with several perforations and fixed at the edge of transected pancreas with 10 cm left in the jejunal loop. In the year of 2003 and 2004, the tube was brought out of the jejunal wall to the outside with the aim of diverting pancreatic secretions from the body for the majority of patients. Lymphadenectomy was routinely performed with skeletonization of the hepatic artery from the hepatic pedicle to the celiac axis. Closed drains were placed in the vicinity of the pancreatic and biliary anastomosis, and they were removed when the volume of drainage was less than 5 ml for continuous 3 d. Somatostatin analogues were given for 7 days in 135 patients as prophylaxis for PF. After induction of anesthesia, intravenous antibiotic prophylaxis was administrated for all patients and repeated every 4 hours during the operative procedure. All patients had nasogastric aspiration for at least 7 d. Oral diet was initiated 7 days after operation if there was no PF or other intraabdominal complications.

Definitions of PF

According to selected North American standards[11], high-volume centers were defined as those operating on 20 patients or more per year, medium-volume centers operated on between 5 and 19 patients per year, low-volume centers operated on between 1 and 4 patients per year, and very low-volume centers operated on less than 1 patients per year. Mortality and morbidity were defined, respectively, as death or complication occurring within 30 d after operation. PF was defined, according to the International Study Group on Pancreatic Fistula (ISGPF)[12], as a drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase concentration greater than three times the serum amylase activity. Three different grades of PF (Grade A, B, and C) were defined according to the clinical impact on the patient's hospital course[12]. Patients with PF would be asymptomatic (Grade A) or poorly symptomatic requiring conservative treatment (Grade B), whereas others would develop abscesses, peritonitis, sepsis, and hemorrhage with a high mortality rate which necessitate interventional procedures (Grade C). Delayed gastric emptying (DGE) was defined as the need for nasogastric decompression after postoperative day 10[13]. Wound infection was defined as presence of pus requiring wound opening. Intraabdominal collection was defined as postoperative fluid collection treated by puncture or drainage. Pulmonary infection was defined as a suggestive radiographic study with fever and requirement for antibiotics. Sepsis was diagnosed when systemic inflammatory response syndrome with positive peripheral blood culture appeared[14]. Infectious complications were proved bacteriologically by positive culture. The parenchyma texture was divided in two groups according to the operating surgeon and the progression of the pancreatic fibrosis of the resected specimens. The “soft” group was characterized by an absence of fibrosis, presence of pancreatic edema, and slight inflammatory cell infiltration into the parenchyma of the pancreas. The “hard” group was characterized by periductal or intralobular fibrosis, acinar necrosis, and severe inflammatory cell infiltration. The main pancreatic duct was classified as being less than or greater than 3 mm in diameter. Early postoperative hemorrhage was defined as bleeding from the surgical site within postoperative day 7 with a drop in hemoglobin concentration ≥3 g/dL in 24 h, evidence of bleeding ≥200 ml through either the surgical drain or the nasogastric tube, a requirement of blood transfusion of ≥2 units of packed red blood cells (PRBCs) during resuscitation, or evidence of peripheral circulatory impairment[15−17].

Statistical Analysis

Values were expressed as $\bar{x}\pm s$. Statistical analysis was performed using SPSS software (version 13.0 SPSS, Inc). Categorical variables were analyzed by chi-square test or Fischer’s exact test, as appropriate. Continuous variables were analyzed by Student *t*-test for mean values or Mann-Whitney test for medians, as appropriate. A difference was considered statistically significant when $P<0.05$. Multivariate analysis was done by a nonconditional logistic regression model expressed in odds ratio (OR). To test the independence of the risk factors, significant variables ($P<0.05$) in the univariate analyses were entered into a multivariate logistic regression model with likelihood ratio forward selection with a criterion of $P<0.05$.

RESULTS

Grades of PF in the Study

Of the 153 evaluable patients with malignant tumors undergoing pancreaticoduodenectomy between 1994 and 2009, PF occurred in 30 patients (19.6%) classified as grade A (n=14), grade B (n=9), and grade C (n=7). Details regarding the numbers of PF with various grade per year are listed in Table 2. Our institution belonged to medium-volume center according to selected North American standards. Overall 30-day mortality was 6.5%, and overall morbidity (any complication) was 44.4%. Mean postoperative length of hospital stay was 38.2±34.4 days. Although surgical volume in the latter 8 years (12 patients per year) was nearly double of what it was in the former 8 years (7 patients per year), there was no statistically significant decrease in the PF rate between the two periods (Table 3).

Table 1. Indications for PD and rates of PF

Pathology	No. of patients	No. of patients with PF	Rates of PF (%)
Pancreatic adenocarcinoma	55	8	14.5
Distal cholangiocarcinoma	38	6	15.8
Ampullary carcinoma	30	10	33.3
Duodenal carcinoma	25	4	16.0
Others invading pancreas	5	2	40.0

Putative Risk Factors for PF

Putative risk factors for PF were conceptually divided into three broad categories[8]: (1) patient-related factors, such as age, gender, and the presence of comorbidities; (2) surgeon-related factors, such as operative time, estimated blood loss, intraoperative blood transfusions, pancreatic anastomotic technique, and preoperative and postoperative biliary stenting; and (3) specimen-related factors, including the texture of the pancreatic remnant at the transection site, dilation of pancreatic duct, and the pathologic diagnosis.

Patient-Related Factors

Univariate analyses of patient-related factors are summarized in Table 4. Figures in parentheses represent the ratio of patients developing PF to total at-risk patients within that category. Rate of PF among female gender was only 12.8%, compared with 22.6% among male gender, but this difference was not statistically significant ($P=0.057$). There was no difference between patients with and without PF (a mean age of 59.2±10.5 years versus 58.4±10.6, P=0.719). Among comorbidities, a history of hypertension, diabetes mellitus (DM) or coronary artery disease (CAD) tended to be associated with higher PF rates, but again this difference was not statistically significant. The serum level of total bilirubin (T-BIL), alkaline phosphatase (ALP), albumin (ALB), creatinine (CRE), fibrinogen (FIB), and γ glutamyltranspeptidase (GGT) did not correlate with PF rates. In addition, preoperative percutaneous transhepatic cholangial drainage (PTCD) did not decrease postoperative PF rate (31.3% versus 18.2% in patients without PTCD, P=0.365).

Surgeon-Related Factors

Univariate analyses of surgeon-related factors are summarized in Table 5. As the same as in Table 1, Figures in parentheses represent the ratio of patients developing PF to total at-risk patients within that category. First, we searched for correlations between specific technical decisions and PF rates. There was no correlation between PF rates and the performance of an end-to-end versus an end-to-side pancreaticojejunal anastomosis (19.4% versus 20.1%, P=1.0). No statistically significant difference in PF rates was found between patients with or without pancreatic duct stenting (20.9% versus 10.5%, P=0.449), nor the pancreatic duct stenting to the outside. Postoperative PF rate among patients with intraoperative biliary drainage by T-tube was 17.7%, compared with 30.4% among patients without biliary drainage, but this difference was not statistically significant (P=0.257). In addition to technical decisions, overall operative complexity was considerable. We chose operative time, estimated blood loss, and units of intraoperative red blood cell transfusions as gross surrogates of increased complexity. Neither of them was found to correlate with increased rates of PF. We also investigated the relationship between postoperative hemorrhage in the first 7 days and the rates of PF.A total of 15 patients experienced early postoperative hemorrhage, 8 of them underwent reoperation and the others received conservative therapy. No difference was found in PF rates between patients with reoperation for hemorrhage and without early postoperative hemorrhage (12.5% versus 18.1%, P=1.0). Patients receiving conservative therapy had a significantly higher PF rate (57.1%) than patients without such complication (18.1%, P=0.042) (Table 2). Finally, there was no difference in PF rates between patients with and without administration of somatostatin analogues.

Disease-Related Factors

Univariate analyses of disease-related factors are summarized in Table 6. The texture of the gland remnant at the site of transection correlated strongly with subsequent postoperative PF rates. Data on gland texture were recorded for all patients.

Table 2. Grade A, B, and C of PF after PD per year

Year	Patients (n)	Grade A	Grade B	Grade C	PF patients n (%)
1994	5	0	0	0	0 (0.0)
1995	6	1	0	0	1 (16.7)
1996	6	0	0	1	1 (16.7)
1997	9	0	0	1	1 (11.1)
1998	6	0	2	0	2 (33.3)
1999	10	1	0	1	2 (20)
2000	5	2	1	0	3 (60)
2001	11	3	1	0	4 (36.4)
2002	8	0	0	0	0 (0)
2003	7	0	0	0	0 (0)
2004	14	2	0	0	2 (14.3)
2005	10	2	0	1	3 (30)
2006	16	0	0	0	0 (0)
2007	13	0	1	0	1 (7.8)
2008	15	3	1	1	5 (33.3)
2009	12	0	3	2	5 (41.7)
Total	153	14	9	7	30 (19.6)

Table 3. Rates of PF in different peroids

Period	No. of patients	Patients with PF	Rates of PF (%)	Statistical value
1994–2001	58	13	22.4	P=0.495 (χ^2 =0.467)
2002–2009	95	17	17.9	
Total	153	30	19.6	

Table 4. Patient-related risk factors for PF

	Patients with PF	Patients without PF	Statistical value
Gender			P=0.156 (χ^2=2.015)
Male	24 (22.6%)	82	
Female	6 (12.8%)	41	
Age	59.2±10.5	58.4±10.6	P=0.719 (t=-0.36)
T-Bil	253.6±199.0	195.2±174.0	P=0.112 (t=-1.60)
ALP	551.7±444.3	477.1±370.3	P=0.358 (t=-0.92)
GGT	862.7±646.1	643.0±509.2	P=0.057 (t=-1.92)
ALB	38.8±5.3	40.0±4.9	P=0.244 (t=1.17)
CRE	71.6±32.0	70.0±21.5	P=0.809 (t=-0.24)
FIB	511.6±154.3	474.2±146.1	P=0.258 (t=-1.14)
Preoperative PTCD			P=0.365 (χ^2=0.822)
Yes	5 (31.3%)	11	
No	25 (18.2%)	112	
Hypertension			P=0.407 (χ^2=0.689)
Yes	9 (24.3%)	28	
No	21 (18.1%)	95	
DM			P=0.865 (χ^2=0.029)
Yes	4 (21.1%)	15	
No	26 (19.4%)	108	
CAD			P=0.394 (χ^2=0.726)
Yes	3 (37.5%)	5	
No	27 (18.6%)	118	

Of these 153 patients, 89 were classified as a soft (normal, friable) gland, 64 as firm (fibrotic, sclerotic). Among patients with a soft gland, 25.8% developed PF, compared with PF rate of only 10.9% among patients with a firm gland (P=0.022).

Impressive trends in PF rate were also evident for individual pathologic diagnoses (Table 6). PF rates were higher among patients with ampullary carcinoma (33.3%) and in patients with tumors invading pancrease (40.0%). PF rates were lower for the other cancers: pancreatic adenocarcinoma, 14.5%; distal cholangiocarcinoma, 15.8%; and duodenal carcinoma, 16.0%. All patients were divided into two groups: patients with ampullary carcinoma and non-ampullary carcinoma. Because of the small number of patients with tumors invading pancrease, they were assigned to the latter. The rates of pancreatic fistula were significantly different among patients with ampullary carcinoma or non-ampullary carcinoma (33.3% versus 16.3%, P=0.035).

A Multivariate Model

Then, we next examined a multivariate model (Table 7) incorporating all the factors with statistically significant correlations in univariate. In this multivariate regression model, only two factors, soft gland (odds ratio, 4.934; 95% CI, 1.132–7.312) and early postoperative hemorrhage with conservative therapy (odds ratio, 4.130; 95% CI, 1.057–21.112) were predictive. Gland texture was the strongest predictor. A soft pancreatic gland implied a 5-fold elevation in risk for postoperative PF (versus a firm gland).

Surgical Outcomes for Patients with or without PF

The development of a postoperative PF complicates a patient's postoperative hospital course, although previous reports emphasized its transformation from the dreaded, mortal complication in the early era of pancreatic surgery to one that is currently typically managed conservatively, or with nonoperative techniques. To better quantify the effects of PF, we examined several measures of patient outcomes (summarized in Table 8).

Table 5. Surgeon-related risk for PF

	Patients with PF	Patients without PF	Statistical value
Pancreatic duct stenting	1176.7±847.6		*P*=0.449 (χ^2=0.573)
Yes	28 (20.9%)	106	
No	2 (10.5%)	17	
Pancreatic duct stenting to the outside			*P*=1.0 (χ^2=0.0)
Yes	3 (18.8%)	13	
No	27 (19.7%)	110	
Type of PJ			*P*=1.0 (χ^2=0.0)
End-to-end	26 (19.4%)	108	
End-to-side	4 (20.1%)	15	
Intra-operative T-tube			*P*=0.257 (χ^2=1.286)
Yes	23 (17.7%)	107	
No	7 (30.4%)	16	
Operative time (hour)	7.3±1.6	7.1±1.5	*P*=0.488 (*t*=-0.70)
Estimated blood loss (ml)	1176.7±847.6	1226.0±746.6	*P*=0.752 (*t*=0.316)
Intraoperative transfusion (units)	4.37±4.44	4.73±4.34	*P*=0.681 (*t*=0.411)
Postoperative hemorrhage in the first 7 d			
Yes + reoperation	1 (12.5%)	7	*P*=1.0 (χ^2=0.0)
Yes + conservation	4 (57.1%)	3	*P*=0.042 (χ^2=4.137)
No	25 (18.1%)	113	
Somatostatin analogues			
Yes	27 (20.0%)	108	*P*=0.985 (χ^2<0.001)
No	3 (16.7%)	15	

Table 6. Specimen-related risk for PF

	Patients with PF	Patients without PF	Statistical value
Pathology			*P*=0.035 (χ^2=2.46)
Ampullary carcinoma	10 (33.3%)	20	
Non-ampullary carcinoma	20 (16.3%)	103	
Texture of gland at transaction site			*P*=0.022 (χ^2=5.247)
Soft	23 (25.8%)	66	
Firm	7 (10.9%)	57	
Dilation of pancreatic duct (≥3 mm)			*P*=0.916 (χ^2=0.011)
Yes	13	53	
No	17	71	

Table 7. Multivariate logistic regression model

	P value	Odds ratio	95% confidence interval
Soft pancreatic texture	0.026	4.934	1.132–7.312
Postoperative hemorrhage with conservative therapy	0.042	4.130	1.057–21.112
Ampullary carcinoma	0.211	1.566	

Early Postoperative Mortality

Overall 30-day mortality was not affected by the development of PF (*P*=0.657). There were three major causes of postoperative mortality (Table 9). Patients with PF, however, were more likely to undergo percutaneous drainage: 10.0% versus 0.8% in patients without PF (*P*=0.024), but no difference was found in reoperation rates between patients with and without PF (10.0% versus 6.5%, *P*=0.787). One of the three reoperations in patients with PF was performed for management of sepsis from a leaking pancreaticojejunostomy and the patient underwent anastomotic repair and wide drainage. The other two reoperations were for wound problems. Mean postoperative length of stay in patients without PF was 32.7±23.9 days, compared with 60.5±56.2 days for patients who developed PF (*P*=0.001).

The Survival of Patients with or without PF

Increased rates of certain postoperative complications were also observed in patients with PF (Table 5). In terms of single complication, patients with PF were more likely to have postoperative pulmonary infection (*P*=0.018). Rates of other complications, such as hemorrhage, intra-abdominal abscess, delayed gastric emptying, bile leak, wound infection, biliary infection ,and general complications were not statistically different in patients with or without PF. Concerning the sum of postoperative complications, there were 36 complications for 30 patients with PF, while 64 for 123 patients without PF. Because of the low incidence of PF (14.5%) and loss of follow-up (n=2) for patients with PF, the available PF data for patients with pancreatic cancer (n=6) was not enough for analysis. Due to the similar prognosis of distal cholangiocarcinoma, ampullary and duodenal cancer, we consider them as a whole (i.e., periampullary cancer) for survival analysis. Of the 93 patients in this study, long-term survival data was available for 69 (15 of 20 patients with PF, 54 of 73 patients without PF). The median survival for patients with PF was 20 m, whereas the median survival for patients without PF was 26 m. Kaplan-Meier survival curves for these two groups of patients are not statistically different (Figure 1: Mantel-Cox log rank test χ^2=0.073, *P*=0.903). Despite the increase in early postoperative complications in patients with PF, the overall survival in patients with periampullary cancer (excluding pancreatic cancer) was not affected by the development of PF.

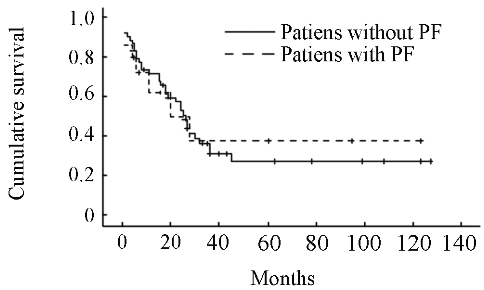

Figure 1. Long-term survival of patients with periampullary cancer is not influenced by the development of PF. Kaplan-Meier survival curves for these two groups of patients are not statistically different.

Table 8. Pancreaticocutaneous fistula and surgical outcome

	Patients with PF	Patients without PF	Statistical value
Postoperative 30-day mortality	3/30 (10.0%)	7/123 (5.7%)	*P*=0.657 (χ^2=0.197)
Percutaneous drainage rate	3/30 (10.0%)	1/123 (0.8%)	*P*=0.024
Reoperation rate	3/30 (10.0%)	8/123 (6.5%)	*P*=0.787 (χ^2=0.073)
Postoperative length of stay (d)	60.5±56.2	32.7±23.9	*P*=0.001 (t=-4.166)
Complications	36	64	
GI hemorrhage	6	11	*P*=0.160 (χ^2=1.971)
Intra-abdominal hemorrhage	4	4	*P*=0.077 (χ^2=3. 121)
Intra-abdominal abscess	5	14	*P*=0.632 (χ^2=0. 229)
DGE	3	7	*P*=0.691 (χ^2=0.158)
Bile leak	1	3	*P*=0.586
Wound infection	7	7	*P*=0.08 (χ^2=7.032)
Pulmonary infection	5	4	*P*=0.018 (χ^2=5.603)
Biliary infection	3	3	*P*=0.165 (χ^2=1.928)
General complication	2	15	*P*=0.589 (χ^2=0.292)

Table 9. The causes for early postoperative mortality

Causes	Number	Percentage (%)
Grade C PF	3	30
Intra-abdominal infection	4	40
Intra-abdominal hemorrhage	1	10
Gastric-intestinal hemorrhage	2	20

DISCUSSION

During the past two decades, despite many improvements in operative technique and postoperative management, PF continues to be a common complication following PD, occurring in 19.6% of patients with malignant tumors at our institution. Although a growing number of evidences demonstrate that high surgical volumes translate into improved patient outcomes for this procedure[5, 18], we have not observed a significant decline in the rate of PF. The frequency of PF after PD is documented in the international literature with a wide range from 0% to 26.7%[2–5, 19, 20]. These differences might partially arise from PF definition[12], which has significantly weakened important meta-analyses regarding PF. In our study, a consensus definition from an International Study Group for pancreatic fistula[12] is adopted, allowing accurate comparison of other surgical experiences.

Univariate analysis of correlations between risk factors and PF identified three statistically significant correlates. Two risk factors, texture of the pancreatic remnant and early postoperative hemorrhage with conservative therapy, are easily accepted as correlating with increased PF rates. The third risk factor of pathology, though, is less easily understood. Previous studies reported the rate of PF was lower among patients with pancreatic adenocarcinoma, when compared with other periampullary cancers[8, 21]. Generally, pancreatic adenocarcinoma is typically associated with firm, fibrotic, easily sutured glands, whereas other periampullary cancers are often associated with a soft, normal, friable gland. But how to explain the high incidence of PF only among patients with ampullary cancer at our institution?

In our next multivariate regression analysis, we found that only the former two risk factors are independent correlates of increased PF rates, while ampullary cancer was not an independent correlate. Soft texture of the pancreatic remnant is the major risk factor for PF reported in the literature. Anastomotic technique for pancreaticojejunostomy (end-to-end versus end-to-side) does not have a statistically significant impact on the development of a postoperative PF in our current study. In addition, choices controllable in operation regarding other anastomotic technique (pancreaticojejunal versus pancreaticogastric; duct-to-mucosa or mucosa-to-mucosa) did not statistically correlate with PF rates[4]. It appears that the texture of the gland is more important than the types of anastomosis. The explanation for increased PF rates with soft texture seems obvious, because a normal, soft pancreatic remnant holds sutures poorly and has normal exocrine function, which are two easily accepted reasons. However, Binding pancreaticojejunostomy, as a new technique of anastomosis, avoids direct connection of pancreas with jejunum by suture and decreases the incidence of PF apparently[12, 22]. The reasons why postoperative hemorrhage with conservative therapy would be associated with a high incidence of PF are obvious too. Early postoperative hemorrhage decreases visceral perfusion and leads to anastomotic ischemia, if it is treated immediately through reoperation, visceral perfusion and anastomotic ischemia can be improved rapidly. As a result of fact, the rates of PF between patients with postoperative early hemorrhage who underwent reoperation for hemostasis and patients without postoperative hemorrhage had no significant differences. When conservative therapy is performed, the condition of anastomotic ischemia will continue for a period of time and compromise anastomotic healing inevitably. Similarly, previous coronary artery disease was identified as a risk factor for PF in the literatures[23]. In fact, these risk factors work through the decreased blood supply of pancreaticojejunal anastomosis[24].

The development of PF is associated with a greater number of other postoperative complications and prolonged hospital stay is well demonstrated[8, 25, 26]. In our study, PF contributes to early postoperative morbidity and the length of hospital stay. It dose not affect hospital mortality, reoperation rate and overall survival. The conclusion is drawn that PF is a common, low-risk local complication, as is documented in the international literature[27]. After all, PF accounts for a third of major early postoperative mortality causes and that is a vital reason for identification of risk factors with an aim of intervention. There is another fact that the majority of patients with PF after PD will heal with appropriate conservative measures[2], such as drainage, fasting, nasogastric suction, partial or total parenteral nutrition, enteral nutrition, antibiotics, and somatostatin analogue, only partial patients with severe state of illness need to be managed differently[12, 28]. At present, the classification and severity of PF after PD which were defined by Bassi et al. are available[12]. What the present study tells us is that in patients with PF after PD, about 23% will develop grade C PF and about 43% of the latter will decease. All the patients with grade A and B PF will recover without death related to PF. Actually, it is more meaningful to identify the risk factors for grade C PF, although it is a pity that conclusions cannot be drawn in our study because of the small sample size of the patients with grade C PF (n＝7). Results of study of 111 patients with postoperative PF showed that 30% of them had grade C PF with a mortality rate of 40% and demonstrated 3 discriminant risk factors (preoperative soft pancreatic parenchyma, preoperative transfusion, and postoperative bleeding) for identification of high-risk patients with grade C PF[28]. All these patients should been offered active conservative treatments[25] and closed monitoring for occurrences of enlarged abdominal collections, pseudoaneurysms, and infection. Some of these complications can be treated preventively through imaging-guided percutaneous drainage and arterial embolization[29, 30]. When unsuccessful drainage, septic shock, or hemorrhage with hemodynamic instability occurs, reoperation should been performed and the options include anastomotic revision with wide drainage, conversion to isolated Roux-en-Y pancreaticojejunostomy with wide drainage, conversion to pancreaticogastrostomy with wide drainage, or completion pancreatectomy[4, 28, 31]. The latter is considered to be a last resort when there is pancreatic necrosis[32]. To avoid postoperative diabetes mellitus after completion pancreatectomy, pancreatectomy with conservation of a 5-cm pancreatic remnant was developed[33].

In conclusion, postoperative PF after PD, as a local complication, dose not have impact on 30-day mortality and reoperation rate, but it accompanies with increased other complications and prolonged hospital stay. It is of great importance to identify risk factors for PF, especially life-threatening grade C PF. PD should be performed with considerable attention in patients with soft gland. Early postoperative hemorrhage also should be dealed with active attitude. It is critical that each surgeon knows the risk factors so as to take corresponding measures for each patient.

REFERENCES

[1] Yeo CJ, Cameron JL, Sohn TA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes [J]. Ann Surg 1997; 226:248−57.

[2] Yeo CJ, Cameron JL, Lillemoe KD, et al. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial [J]. Ann Surg 2000; 232:419−29.

[3] Suc B, Msika S, Fingerhut A, et al. Temporary fibrin glue occlusion of the main pancreatic duct in the prevention of intra-abdominal complications after pancreatic resection: Prospective randomized trial [J]. Ann Surg 2003; 237:57−65.

[4] Aranha GV, Aaron JM, Shoup M, et al. Current management of pancreatic fistula after pancreaticoduodenectomy [J]. Surgery 2006; 140:561−8.

[5] Cheng Q, Zhang B, Zhang Y, et al. Predictive factors for complications after pancreatico-duodenectomy [J]. J Surg Res 2007; 139:22−9.

[6] Reid-Lombardo KM, Farnell MB, Crippa S, et al. Pancreatic anastomotic leakage after pancreaticoduodenectomy in 1,507 patients: a report from the Pancreatic Anastomotic Leak Study Group [J]. J Gastrointest Surg 2007; 11:1451−8.

[7] Goonetilleke KS, Siriwardena AK. Nationwide questionnaire survey of the contemporary surgical management of pancreatic cancer in the United Kingdom & Ireland [J]. Int J Surg 2007; 5:147−51.

[8] Lin JW, Cameron JL, Yeo CJ, et al. Risk factors and outcomes in postpancreaticoduodenectomy pancreaticocutaneous fistula [J]. J Gastrointest Surg 2004; 8:951−9.

[9] Duffas JP, Suc B, Msika S, et al. A controlled randomized multicenter trial of pancreato-gastrostomy or pancreatojejunostomy after pancreatoduodenectomy [J]. Am J Surg 2005; 189:720−9.

[10] Suzuki S, Kaji S, Koike N, et al. Pancreaticojejunostomy of duct to mucosa anastomosis can be performed more safely without than with a stenting tube [J]. Am J Surg 2009; 198:51−4.

[11] Gouma DJ, van Geenen RC, van Gulik TM, et al. Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume [J]. Ann Surg 2000; 232:786−95.

[12] Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international

study group (ISGPF) definition [J]. Surgery 2005; 138:8–13.
[13] Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS) [J]. Surgery 2007; 142:761–8.
[14] Vincent JL. Sepsis definitions [J]. Lancet Infect Dis 2002; 2:135.
[15] Blanc T, Cortes A, Goere D, et al. Hemorrhage after pancreaticoduodenectomy: when is surgery still indicated? [J] Am J Surg 2007; 194:3–9.
[16] Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition [J]. Surgery 2007; 142:20–5.
[17] Choi SH, Moon HJ, Heo JS, et al. Delayed hemorrhage after pancreaticoduodenectomy [J]. J Am Coll Surg 2004; 199:186–91.
[18] Gordon TA, Bowman HM, Bass EB, et al. Complex gastrointestinal surgery: impact of provider experience on clinical and economic outcomes [J]. J Am Coll Surg 1999; 189:46–56.
[19] Rosso E, Bachellier P, Oussoultzoglou E, et al. Toward zero pancreatic fistula after pancreatico-duodenectomy with pancreaticogastrostomy [J]. Am J Surg 2006; 191:726–32.
[20] Peng S, Mou Y, Cai X, et al. Binding pancreaticojejunostomy is a new technique to minimize leakage [J]. Am J Surg 2002; 183: 283–5.
[21] Poon RT, Lo SH, Fong D, et al. Prevention of pancreatic anastomotic leakage after pancreatico-duodenectomy [J]. Am J Surg 2002; 183: 42–52.
[22] Peng SY, Wang JW, Lau WY, et al. Conventional versus binding pancreaticojejunostomy after pancreaticoduodenectomy: a prospective randomized trial [J]. Ann Surg 2007; 245: 692–8.
[23] Lermite E, Pessaux P, Brehant O, et al. Risk factors of pancreatic fistula and delayed gastric emptying after pancreaticoduodenectomy with pancreaticogastrostomy [J]. J Am Coll Surg 2007; 204:588–96.
[24] Strasberg SM, Drebin JA, Mokadam NA, et al. Prospective trial of a blood supply-based technique of pancreaticojejunostomy: effect on anastomotic failure in the Whipple procedure [J]. J Am Coll Surg 2002; 194:746–58.
[25] Munoz-Bongrand N, Sauvanet A, Denys A, et al. Conservative management of pancreatic fistula after pancreaticoduodenectomy with pancreatico-gastrostomy [J]. J Am Coll Surg 2004; 199:198–203.
[26] Grobmyer SR, Rivadeneira DE, Goodman CA, et al. Pancreatic anastomotic failure after pancreatico-duodenectomy [J]. Am J Surg 2000; 180:117–20.
[27] Beger HG, Gansauge F, Schwarz M, et al. Pancreatic head resection: the risk for local and systemic complications in 1315 patients-a monoinstitutional experience [J]. Am J Surg 2007; 194:S16–S9.
[28] Fuks D, Piessen G, Huet E, et al. Life-threatening postoperative pancreatic fistula (grade C) after pancreaticoduodenectomy: incidence, prognosis, and risk factors [J]. Am J Surg 2009; 197: 702–9.
[29] Harvey J, Dardik H, Impeduglia T, et al. Endovascular management of hepatic artery pseudoaneurysm hemorrhage complicating pancreaticoduodenectomy [J]. J Vasc Surg 2006; 43:613–7.
[30] de Castro SM, Busch OR, Gouma DJ. Management of bleeding and leakage after pancreatic surgery [J]. Best Pract Res Clin Gastroenterol 2004; 18:847–64.
[31] Van Berge Henegouwen MI, De Wit LT, Van Gulik TM, et al. Incidence, risk factors, and treatment of pancreatic leakage after pancreaticoduodenectomy: drainage versus resection of the pancreatic remnant [J]. J Am Coll Surg 1997; 185:18–24.
[32] de Castro SM, Busch OR, Van Gulik TM, et al. Incidence and management of pancreatic leakage after pancreatoduodenectomy [J]. Br J Surg 2005; 92:1117–23.
[33] Ihse I, Anderson H, Andrén-Sandberg. Total pancreatectomy for cancer of the pancreas: is it appropriate? [J] World J Surg 1996; 20: 288–93.