Original Article

Incidence and Risk Factors of Postoperative Pancreatic Fistula after Pancreaticoduodenectomy: A Large Tertiary Center Experience

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Objective: Pancreaticoduodenectomy (PD) is a major operation for the treatment of periampullary and pancreatic cancer, and the number of operations has increased in recent years. Postoperative pancreatic fistula (POPF) remains one of the important complications after PD. The present study aimed to analyze the incidence and risk factors of POPF.

Materials and Methods: The clinical data of 227 patients who underwent PD in Siriraj Hospital between 2011 and 2016 were retrospectively reviewed. POPF was diagnosed and classified into three groups (grade A, B, or C) according to the International Study Group on Pancreatic Fistula (ISGPF). Clinically relevant pancreatic fistula (CR-POPF) takes into account only grade B or C. The risk factors of POPF after PD were analyzed. Univariate and multivariate logistic regression analyses were used to determine the risk factors correlated with POPF.

Results: In total, 227 patients were included in this study. POPF occurred in 96 patients (42.3%), and these were classified into ISGPF grade A patients, 21 (9.3%); grade B, 54 (23.8%); and grade C, 21 (9.3%). The CR-POPF rate was 33.1%. Multivariate analysis revealed soft gland texture [Odds ratio (OR): 6.7, 95% confidence interval (CI): 1.5 to 30.9], small pancreatic duct (P-duct) diameter of ≤3 mm [OR: 4.6, 95% CI: 1.0 to 21.4], and a surgeon's experience of <10 years [OR: 6.5, 95% CI: 1.4 to 30.6] were significant risk factors of POPF. Regarding CR-POPF, these three risk factors were also found to be statistically significant in the multivariate analysis.

Conclusion: Even though the study involved a high volume center, the incidence of POPF after PD was still high, with ISGPF grade B the most common group. Soft gland texture, small P-duct diameter, and low surgeon experience were the key independent risk factors for both POPF and CR-POPF.

Keywords: Postoperative pancreatic fistula, Whipple operation, Pancreaticoduodenectomy, Pancreatic leakage

J Med Assoc Thai 2020;103(Suppl.2): 5-12
Website: http://www.jmatonline.com

Pancreaticoduodenectomy (PD) is the standard operative treatment for benign and malignant tumors in the periampullary area and at the head of pancreas. Even though the mortality rate after PD has continuously declined in recent years, postoperative morbidity is still high. One of the most important complications after PD is postoperative pancreatic fistula (POPF) because of the serious consequences that can occur after leakage, such as intraabdominal collection, intraabdominal bleeding, surgical site infection, and delayed gastric emptying (DGE). Moreover, the mortality rate remains as high as about 40 to 50% in patients with grade C POPF[1,2].

Recent literature has suggested that many factors may have influence on POPF, including gender, a high body mass index (BMI), preoperative jaundice, gland texture, the pancreatic duct diameter, the technique used for pancreaticojejunostomy (PJ) anastomosis, intraoperative blood loss, and the surgeon's experience[2-10].

In Thailand, the number of PD cases is increasing due to the better detection of early stage cancer and as there are more hepatopancreatobilliary (HPB) specialists nowadays. However, there is limited data available and few literature reports on the incidence and risk factors of POPF in a Thai population. Therefore, this study aimed to analyze the incidence and risk factors of POPF following PD.

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Materials and Methods

Patients

Patients who underwent PD in Hepatopancreatobiliary and Transplant Surgery Unit, Department of

How to cite this article: Tovikkai C, Manoontrakul W, Kositamongkol P, Mahawithitwong P, Dumronggittigule W, Sangserestid P, Limsrichamrern S, Sirivatanauksorn Y. Incidence and Risk Factors of Postoperative Pancreatic Fistula after Pancreaticoduodenectomy: A Large Tertiary Center Experience. J Med Assoc Thai 2020;103(Suppl.2): 5-12.

Surgery, Faculty of Medicine Siriraj Hospital, between January 2011 and December 2016, were included in the present study. Patients who underwent total complete pancreatectomy after distal pancreatectomy (without PJ anastomosis) were excluded. The following demographic and clinical data, including pathological reports, were collected for analysis. Preoperative data consisted of age, sex, BMI, underlying diseases, clinical presentation, preoperative hematocrit level, white blood cell count, liver function test, tumor markers, and preoperative biliary drainage. Intraoperative data included the type of operation (pyloric preserving or pyloric resecting PD), pancreatic duct diameter, gland texture, and the technique utilized for PJ anastomosis. Postoperative data consisted of drain amylase volume and level, postoperative complications, therapeutic intervention for complications, duration of hospital and intensive care unit (ICU) stay.

POPF was diagnosed and classified according to the definition of POPF given by the International Study Group on Pancreatic Fistula (ISGPF) into three groups: grade A, B, or C[1,11]. Patients were divided for the analyses into two groups: POPF and non-POPF groups. Additional analysis of clinically relevant pancreatic fistula (CR-POPF) was also performed. Here, CR-POPF took into account only grades B and C, while non-CR-POPF included grade A and non-POPF.

Operative procedure

Patients underwent pylorus preserving PD or pyloric resecting PD, and some additional procedures were performed, such as superior mesenteric vein (SMV) or portal vein (PV) resection and reconstruction because of evidence of vascular invasion of the tumor. By the stage of reconstruction, there were subsequently three anastomoses, composed of pancreatico-jejunostomy (PJ), hepatico-jejunostomy, and gastro-/duodeno-jejunostomy. The technique used for PJ anastomosis was either the "duct-to-mucosa" or "dunking" technique depending on the surgeon's preference. The suture materials utilized for pancreatico-jejunostomy were either absorbable (polyglactin) or non-absorbable sutures (polyprolylene). Pancreatic duct stent was placed in selected patients; however, when a pancreatic duct stent was decided on, only an internal plastic stent was placed. Gland texture was documented according to the surgeon's opinion. The size of the pancreatic duct (P-duct) diameter was measured intraoperatively. If P-duct size could not retrieved from the operative note, it would be measured from preoperative radiological imaging.

Study design and statistical analysis

Quantitative data are reported as the mean $\pm$ standard deviation (SD). Continuous variables were compared using the independent sample student's t-test. Categorical variables were compared using the Chi-square test or Fisher exact test, where appropriate. All the variables were tested by univariate analysis, then those with a p-value <0.2 were analyzed by multivariate analysis. Multivariate logistic regression analysis was performed to determine the independent risk factors of POPF. Risk factors for CR-POPF were also identified using the same methods. All the statistical analyses were performed with Stata version 15.0 (StataCorp, College Station, TX, USA). A p-value <0.05 was considered statistically significant.

Results

In total, 227 patients who underwent PD were included in the study. The average age of patients was 62.8 years old. There were 115 (50.7%) male and 112 (49.3%) female patients. The average BMI of the cohort was 22.6 kg/m^2, and 25.6% of the patients had diabetes mellitus (DM), while 10.1% of the patients had a history of smoking. Obstructive jaundice was the most common presentation, with an incidence of 67.0%; among these, 25.1% of the patients underwent preoperative biliary drainage. The demographic data were comparable between the POPF and non-POPF groups as shown in Table 1.

Regarding operative information, 22 patients (9.7%) had concomitant PV/SMV resection and reconstruction. Pyloric preserving PD (69.2%) was more common than pyloric resecting PD or classical Whipple (30.8%) in the present study. The duct-to-mucosa PJ anastomosis technique was performed in 82.8% of the patients, compared to 17.2% operated with the dunking technique. Internal pancreatic stent was used in 31.7% of the patients. The average operative time was 372 minutes. These operative data were comparable between the POPF and non-POPF groups. However, the pancreatic duct diameter in the POPF group was significantly smaller than in the non-POPF group (3.3 mm vs. 4.7 mm, p<0.001). The most common pathological diagnoses in the POPF group were ampullary carcinoma (31.3%) and other pathologies (18.8%), such as neuroendocrine tumor or pancreatic metastases, whereas the most common pathological diagnosis in the non-POPF group was pancreatic ductal adenocarcinoma (49.6%).

Incidence of POPF

Of the 227 patients, 96 patients (42.3%) developed POPF after PD, comprising 21 patients (9.3%) with grade A, 54 patients (23.8%) with grade B, and 21 patients (9.3%) with grade C. The incidence of CR-POPF, including only grade B and C POPF, was 33.1%.

Risk factors

Clinical factors were analyzed with univariate logistic regression. The risk factors that were statistically significant included soft gland texture (odds ratio (OR): 4.9, 95% confidence interval (CI): 1.8 to 13.1, p = 0.001), pancreatic duct diameter $\leq$3 mm (OR: 2.6, 95% CI: 1.4 to 4.7, p = 0.002), a surgeon's experience of less than ten years (OR: 2.1, 95% CI: 1.2 to 3.8, p = 0.014), pathology of distal cholangiocarcinoma (OR: 9.2, 95% CI: 2.8 to 29.6, p<0.001), adenocarcinoma of the ampulla of Vater (OR: 5.5, 95% CI: 2.5 to 11.8, p<0.001), and adenocarcinoma of duodenum

Table 1. Demographic data in postoperative pancreatic fistula and non-postoperative pancreatic fistula groups

Parameter	Overall (227)	POPF (96, 42.3%)	Non-POPF (131, 57.7%)	*p*-value
Age [year], mean (SD)	62.8 (12.0)	63.0 (12.1)	62.8 (11.9)	0.93
Sex , n (%)				0.52
Male	115 (50.7)	51 (53.2)	64 (48.9)	
Female	112 (49.3)	45 (46.9)	67 (51.1)	
BMI [kg/m^2], mean (SD)	22.6 (3.8)	23.0 (4.0)	22.3 (3.6)	0.17
DM, n (%)				0.10
Yes	58 (25.6)	19 (19.8)	39 (29.8)	
No	169 (74.4)	77 (80.2)	92 (70.2)	
Smoking, n (%)				0.38
Yes	23 (10.2)	8 (8.33)	15 (11.5)	
No	203 (89.8)	87 (90.6)	116 (88.6)	
Obstructive jaundice, n (%)				0.13
Yes	152 (67.0)	59 (61.5)	93 (71.0)	
No	75 (33.0)	37 (38.6)	38 (29.0)	
Preoperative drainage, n (%)				0.56
Yes	57 (25.1)	26 (27.1)	31 (23.7)	
No	170 (74.9)	70 (72.9)	100 (76.3)	
PV resection and reconstruction, n (%)				0.134
Yes	22 (9.7)	6 (6.2)	16 (12.2)	
No	205 (90.3)	90 (93.8)	115 (87.8)	
Pylorus preserving, n (%)				0.64
Yes	157 (69.2)	68 (70.8)	89 (67.9)	
No	70 (30.8)	28 (29.2)	42 (32.1)	
Technique of PJ, n (%)				0.86
Duct to mucosa	188 (82.8)	80 (83.3)	108 (82.4)	
Dunking	39 (17.2)	16 (16.7)	23 (17.6)	
Internal stent, n (%)				0.128
Yes	72 (37.1)	37 (43.0)	35 (32.4)	
No	122 (62.9)	49 (57.0)	73 (67.6)	
Operative time [minute], mean (SD)	372 (100)	383 (114)	363 (87)	0.14
P-duct diameter [mm], mean (SD)	4.1 (2.7)	3.3 (1.7)	4.7 (3.1)	<0.001
Pathology, n (%)				<0.001
Pancreatic ductal adenocarcinoma	82 (36.1)	17 (17.7)	65 (49.6)	
Adenocarcinoma of ampulla of Vater	51 (22.5)	30 (31.3)	21 (16.0)	
Distal cholangiocarcinoma	17 (7.5)	12 (12.5)	5 (3.8)	
Adenocarcinoma of duodenum	27 (11.9)	13 (13.5)	14 (10.7)	
IPMN	10 (4.4)	4 (4.2)	6 (4.6)	
Pancreatitis	9 (4.0)	2 (2.0)	7 (5.4)	
Others*	31 (13.6)	18 (18.8)	13 (9.9)	
Surgeon's experience, n (%)				0.013
≥10 years	75 (33.0)	23 (24.0)	52 (39.7)	
<10 years	152 (67.0)	73 (76.0)	79 (60.3)	

BMI = body mass index, DM = diabetes mellitus, IPMN = intraductal papillary mucinous neoplasm, P-duct = pancreatic duct, PJ = pancreaticojejunostomy, POPF = postoperative pancreatic fistula, PV = portal vein, SD = standard deviation
* Others diagnoses included duodenal gastrointestinal stromal tumor, solid pseudopapillary neoplasm, neuroendocrine tumor, serous cystadenoma, gallbladder cancer, choledochal cyst, metastatic renal cell carcinoma, liposarcoma at head of pancreas

(OR: 3.6, 95% CI: 1.4 to 9.0, p = 0.007) compared to pancreatic ductal adenocarcinoma. The following variables with a p-value less than 0.2 were selected for multivariate logistic regression analysis: BMI >25 kg/m^2, DM, obstructive jaundice, PV resection and reconstruction, internal pancreatic stent, pancreatic duct diameter, gland texture, pathology, and a surgeon's experience. Only three risk factors were found to be significantly associated with POPF, namely soft gland texture (OR: 6.7, 95% CI: 1.5 to 30.9, p = 0.02), P-duct diameter ≤3 mm (OR: 4.6, 95% CI: 1.0 to 21.4, p = 0.05), and a surgeon's experience of less than ten years (OR: 6.5, 95% CI: 1.4 to 30.6, p = 0.02). The univariate and multivariate logistic regression analyses for the risk factors of POPF after PD are shown in Table 2.

Complications, intervention, and mortality

Among the complications after PD, intraabdominal collection (27.1% vs. 3.8%, p<0.001), postoperative bleeding

Table 2. Univariate and multivariate logistic regression analysis of postoperative pancreatic fistula risk factors

Risk factors	Univariate		Multivariate	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age				
<70 years	1	0.65		
≥70 years	1.14 (0.6 to 2.0)			
Sex				
Male	1	0.52		
Female	0.84 (0.5 to 1.4)			
BMI				
≤25 kg/m^2	1	0.09	1	0.16
>25 kg/m^2	1.67 (0.9 to 3.1)		3.24 (0.6 to 16.5)	
DM				
No	1	0.09	1	0.64
Yes	0.58 (0.3 to 1.1)		1.6 (0.4 to 7.2)	
Smoking				
No	1	0.48		
Yes	1.15 (0.8 to 1.8)			
Obstructive jaundice				
No	1	0.13	1	0.55
Yes	0.65 (0.4 to 1.1)		0.56 (0.1 to 3.6)	
Preoperative drainage				
No	1	0.55		
Yes	1.19 (0.7 to 2.2)			
PV resection and reconstruction				
No	1	0.12	1	0.24
Yes	0.47 (0.2 to 1.3)		0.21 (0.1 to 2.8)	
Pylorus preserving				
No	1	0.64		
Yes	1.14 (0.6 to 2.0)			
Technique of PJ				
Dunking	1	0.86		
Duct-to-mucosa	0.93 (0.5 to 1.9)			
Internal stent				
No	1	0.13	1	0.21
Yes	1.57 (0.9 to 2.8)		2.83 (0.6 to 14.2)	
P-duct diameter				
>3 mm	1	0.002	1	0.05
≤3 mm	2.57 (1.4 to 4.7)		4.63 (1.0 to 21.4)	
Operative time				
<360 min	1	0.28		
≥360 min	1.33 (0.8 to 2.3)			
Gland texture				
Hard	1	0.001	1	0.02
Soft	4.86 (1.8 to 13.1)		6.69 (1.5 to 30.9)	
Pathology				
Pancreatic ductal adenocarcinoma	1		1	
Adenocarcinoma of ampulla of Vater	5.46 (2.55 to 11.8)	<0.001	0.18 (0.02 to 1.8)	0.14
Distal cholangiocarcinoma	9.18 (2.8 to 29.6)	<0.001	0.58 (0.1 to 6.3)	0.65
Adenocarcinoma of duodenum	3.55 (1.4 to 9.0)	0.007	1.00 (0.1 to 8.7)	1.00
IPMN	2.54 (0.7 to 10.1)	0.18	0.11 (0.003 to 3.3)	0.21
Pancreatitis	1.09 (0.2 to 5.7)	0.92	N/A	N/A
Others	5.29 (2.2 to 12.9)	<0.001	0.37 (0.03 to 4.0)	0.41
Surgeon's experience				
≥10 years	1	0.014	1	0.02
<10 years	2.09 (1.2 to 3.8)		6.52 (1.4 to 30.6)	

95% CI = 95% confidence interval, BMI = body mass index, DM = diabetes mellitus, IPMN = intraductal papillary mucinous neoplasm, N/A = not applicable, OR = odds ratio, P-duct = pancreatic duct, PJ = pancreaticojejunostomy, POPF = postoperative pancreatic fistula, PV = portal vein

* Others diagnoses included duodenal gastrointestinal stromal tumor, solid pseudopapillary neoplasm, neuroendocrine tumor, serous cystadenoma, gallbladder cancer, choledochal cyst, metastatic renal cell carcinoma, liposarcoma at head of pancreas

(15.6% vs. 3.8%, $p = 0.002$), and surgical site infection (37.5% vs. 22.9%, $p = 0.02$) were statistically significantly higher in the POPF group. Nevertheless, sepsis (10.4% vs. 4.6%, $p = 0.10$), delayed gastric emptying (28.1% vs. 19.1%, $p = 0.11$), and chyle leakage (15.6% vs. 13.0%, $p = 0.57$) were slightly, but not significantly, higher in the POPF group. Percutaneous drainage for intraabdominal collection had been performed significantly more in the POPF group compared to in the non-POPF group (16 patients vs. 2 patients, $p<0.001$). The re-operation rate was also significantly higher in the POPF group (12.5% vs. 3.1%, $p<0.001$). Overall mortality in this cohort was 6.1% (14 patients), which was significantly higher in the POPF group (10.4% vs. 3.0%, $p = 0.02$). Complication rates according to the POPF and non-POPF groups are shown in Figure 1.

Length of stay was longer in higher grade POPF. Patients with POPF grade C stayed an average ±SD of 46.6±30.3 days in hospital, while patients without POPF stayed only 15.2±9.2 days on average. Patients with POPF grade C also stayed longer in ICU, with an average ±SD of 15.8±17.1 days, whereas patients in the others groups stayed in ICU less than 1 day on average. The length of hospital stay and length of ICU stay are shown in Figure 2.

Clinically relevant POPF

In the subgroup analysis for CR-POPF, which constituted only grade B and C POPF, the multivariate analysis also found that soft gland texture (OR: 3.7, 95% CI: 1.0 to 13.4, $p = 0.05$), P-duct diameter ≤3 mm (OR: 7.6, 95% CI: 1.7 to 34.1, $p = 0.008$), and a surgeon's experience of <10 years (OR: 10.1, 95% CI: 2.1 to 48.7, $p = 0.004$) were the three significant risk factors for developing CR-POPF.

Discussion

POPF remains the most common and serious complication after PD that probably contributes to subsequent terrible outcomes or death in admission, even in high volume centers. In recent studies, the POPF rate was reported to range from 5% to 64%[2-9,12-23], and the risk factors of POPF were stated as multifactorial, including male, obstructive jaundice, intraoperative blood loss, soft gland texture, and small P-duct[2-4,6-10,12]. In the present study, the incidence of POPF was 42.3%, comparable with recent studies. The risk factors for POPF from the multivariate regression analysis were soft gland texture, P-duct diameter ≤3 mm, and a surgeon having experience of less than 10 years.

Soft gland consistency was a risk factor of POPF in the present study with an OR of 4.9 (95% CI: 1.8 to 13.1, $p = 0.001$) in the univariate analysis and an OR of 6.7 (95% CI: 1.5 to 30.9, $p = 0.02$) in the multivariate analysis. These values correspond to many previous studies[4,6,7,9,10,12,14]. Nevertheless, pancreatic gland texture is subjective and only classified by surgeons from intraoperative palpation, and there is currently no obvious standard scale. The soft pancreatic consistency is mostly related with a fatty pancreas[4,24]. Gaujoux et al used histological assessment

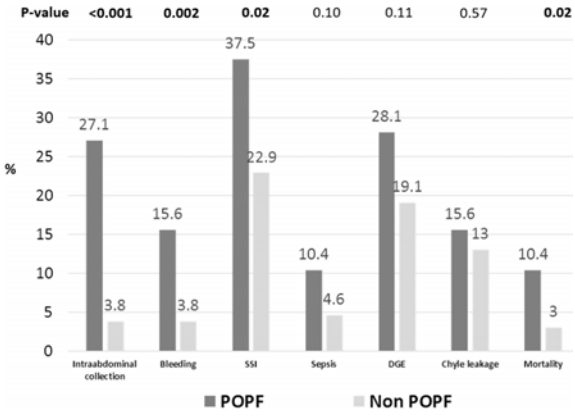

Figure 1. Complications after pancreaticoduodenectomy according to postoperative pancreatic fistula.

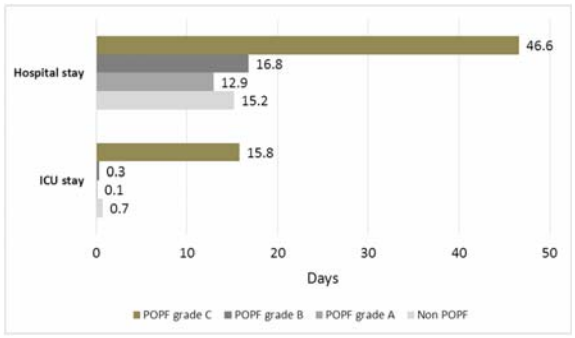

Figure 2. Length of hospital stay and intensive care unit stay after pancreaticoduodenectomy according to postoperative pancreatic fistula.

in an attempt to precisely classify pancreatic consistency. They considered scoring for fatty infiltration and fibrosis to identify a fatty pancreas. They reported a fatty pancreas was found more frequently in soft pancreas, and it was a significant predictive factor of POPF in multivariate analysis[4]. This correlation may be the reason why a "soft" gland texture is a risk factor of POPF, but there is currently no prospective study confirming the correlation between the texture estimate by a surgeon and histological fatty infiltration. In terms of scoring, Ansorge et al classified gland consistency before anastomosis completion into four grades: very hard (PC1), hard (PC2), soft (PC3), and very soft (PC4). They found that the incidences of POPF were significantly higher in higher grades of pancreatic consistency ($p<0.001$)[14]. However, this classification was still subjective and based on intraoperative palpation by a surgeon. Several hypotheses of soft gland causing POPF have been proposed. One is that exocrine function is mostly preserved in the soft pancreas, leading to rich proteolytic enzymes causing

autolysis of the pancreatic tissue. Another is that soft gland is more susceptible to fragile or tear during dissection or suturing.

Small P-duct diameter is widely recognized as another risk factor of POPF[2,3,7-10,12]. In the present study, the average pancreatic duct diameter in the POPF group was significantly smaller than in the non-POPF group (3.3 mm vs. 4.7 mm, $p<0.001$). The risk of POPF in patients with a P-duct diameter ≤3 mm was significantly higher than those with a P-duct diameter >3 mm, with an OR of 2.6 (95% CI: 1.4 to 4.7, $p = 0.002$) in the univariate analysis and an OR of 4.6 (95% CI: 1.0 to 21.4, $p = 0.05$) in the multivariate analysis. A dilated P-duct, mostly arising from pathologic obstruction due to a tumor or chronic pancreatitis, was identified clearly after resection and was sutured easily during PJ anastomosis. A dilated P-duct diameter >3 mm is related with pancreatic fibrosis, caused from long-standing pancreatic obstruction, where pancreatic fibrosis is a protective factor against POPF[4,14]. A dilated P-duct was more commonly found in some types of pathology, such as adenocarcinoma of the ampulla of Vater, because the obstruction was below the common channel of the main P-duct connecting to the common bile duct, thus contributing to the dilated P-duct; whereas the obstruction level was only at the distal common bile duct in distal cholangiocarcinoma and the P-duct was not affected. Therefore, the risk of POPF was significantly higher in distal cholangiocarcinoma than in adenocarcinoma of the ampulla of Vater in the univariate analysis in this study. However, the risk became not statistically significant when adjusted to the P-duct diameter and other factors in the multivariate analysis. This may be due to a correlation between the pathology and P-duct diameter. Barreto et al reviewed 18 studies involving 2,150 patients in total in a meta-analysis and found that the most significant parameters used to predict the development of POPF could be based on the preoperative imaging features of a fatty or fibrotic pancreas and the main P-duct diameter. They also demonstrated that a large P-duct diameter measured preoperatively was linked to a lower risk of developing POPF[25].

The experience of a surgeon is another interesting risk factor found in this study. A surgeon's experience was classified into two groups: experience <10 years and ≥10 years. Less experienced surgeons had a higher rate of POPF, with an OR of 2.1 (95% CI: 1.2 to 3.8, $p = 0.014$) in the univariate analysis and an OR of 6.5 (95% CI: 1.4 to 30.6, $p = 0.02$) in the multivariate analysis. Analyzing the data of 1,003 patients who underwent PD by one of 19 surgeons in a single center, Schmidt et al reported that the accumulated surgeon's experience irrespective of their annual volume had a significant effect on the outcomes. The cumulative PD cases of an individual surgeon remained an important determinant of morbidity, pancreatic leakage, operating time, and intraoperative blood loss[5]. In the present study, the average number of PD cases per year per surgeon was 7.2. Therefore, an individual surgeon should have an accumulated experience of more than 72 cases in his/her career to overcome the learning curve in order to reduce the POPF rate. Similarly, Roberts et al explored the cumulative sum analysis to assess individual surgeon's pancreatic fistula outcomes and found that POPF rate would be steadily improved after 50 to 70 cases[26].

There are several factors that were analyzed in the present study and found to be not significant for POPF. The technique utilized for PJ anastomosis was one of those factors. Recent meta-analyses reported no difference between the duct-to-mucosa and dunking techniques of PJ. Sun et al analyzed seven randomized controlled trials (RCT) of 850 participants and found no significant difference in the rates of POPF, reoperation, and morbidity. Kilambi et al analyzed eight RCTs of 1,043 participants and similarly found no significant difference between the two techniques[27,28]. In the present study institution, the technique utilized for PJ anastomosis depends on a surgeon's preference, and here, the dunking technique was performed in only a small portion of the patients. Recently, a meta-analysis was performed that compared PJ and PG in terms of their impact on the POPF rate. Menahem et al analyzed seven RCTs of 562 patients who underwent PG and 559 who underwent PJ. The pancreatic fistula rate was significantly lower in the PG group than in the PJ group (OR = 0.53; 95% CI: 0.38 to 0.75, $p<0.001$)[29,30]. However, PG anastomosis had not been performed in any patients in the present study. Male gender, high BMI, obstructive jaundice, and intraoperative blood loss are significant risk factors reported in several recent studies. Nevertheless, these factors were not significant risk factors in the present study.

The presence of POPF was related to higher mortality ($p = 0.02$) and morbidity after PD. The morbidities were found to be significantly higher in the POPF group, including intraabdominal collection ($p<0.001$), bleeding ($p = 0.002$), and surgical site infection ($p = 0.02$), also in accordance with the findings from other recent studies[2,9]. In addition, the present study found that the length of hospital stay and length of ICU stay were longer in patients who had POPF, especially those with POPF grade C.

Some limitations in this study need to be highlighted. First, the retrospective nature of the study meant it often suffered from missing data. Second, in terms of the surgical procedure, the technique utilized for PJ, the suture material, or the internal stent used depended on the surgeon's preference. Third, pancreatic gland texture or P-duct diameter determination were subjective and may not have been accurately recorded. However, regarding the P-duct diameter, preoperative imaging was reviewed to confirm the size of the P-duct diameter.

In conclusion, even though the present study involved patients in a high volume center, the incidence of POPF after PD was still high and ISGPF grade B was the most common group. Soft gland texture, small P-duct diameter, and a surgeon's experience were independent risk factors for both POPF and CR-POPF.

What is already known on this topic?

POPF is one of the most important risks after PD,

and it can lead to other complications, including postoperative mortality. Many preoperative and intraoperative factors may have an impact on POPF.

What this study adds?

Even in the high volume tertiary center, POPF after PD remains high, which is consistent with other previous studies with a POPF rate of 43.3% and CR-POPF rate of 33.1%. Soft gland texture, P-duct diameter ≤3 mm, and a surgeon's experience of less than 10 years were significant risk factors for both POPF and CR-POPF.

Acknowledgements

The authors would like to express appreciation to Miss Onchira Acharayothin for her help in collecting and recording the data for the analyses.

Potential conflicts of interest

The authors declared no conflicts of interest.

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อุบัติการณ์และปัจจัยเสี่ยงในการเกิดภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัด Pancreaticoduodenectomy: ประสบการณ์ในโรงพยาบาลตติยภูมิขนาดใหญ่

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วัตถุประสงค์: Pancreaticoduodenectomy (PD) เป็นการผ่าตัดรักษาโรคมะเร็งบริเวณ periampullary และมะเร็งหัวตับอ่อน จำนวนการผ่าตัดชนิดนี้เพิ่มมากขึ้นในช่วงปีหลัง ภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัด (postoperative pancreatic fistula) ยังเป็นภาวะแทรกซ้อนที่สำคัญของการผ่าตัดนี้ การศึกษานี้มีวัตถุประสงค์เพื่อวิเคราะห์หาอุบัติการณ์และปัจจัยเสี่ยงในการเกิดภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัด

วัสดุและวิธีการ: ข้อมูลทางคลินิกของผู้ป่วย 227 รายที่เข้ารับการผ่าตัด PD ในโรงพยาบาลศิริราชระหว่างปี พ.ศ. 2554 ถึง พ.ศ. 2559 ได้รับการทบทวน ภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดได้รับการวินิจฉัยและแยกเป็นสามระดับ (ระดับ A, B และ C) ตามเกณฑ์ของ International Study Group on Pancreatic Fistula ภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดที่สำคัญทางคลินิก (clinically relevant postoperative pancreatic fistula) นับรวมเฉพาะระดับ B และ C เท่านั้น Univariate และ multivariate logistic regression analysis ใช้ในการวิเคราะห์หาปัจจัยเสี่ยงในการเกิดภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัด

ผลการศึกษา: การศึกษานี้รวบรวมผู้ป่วยทั้งหมด 227 ราย ภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดเกิดในผู้ป่วย 96 ราย นับเป็นร้อยละ 42.3 แบ่งเป็น ระดับ A 21 ราย (ร้อยละ 9.3) ระดับ B 54 ราย (ร้อยละ 23.8) และระดับ C 21 ราย (ร้อยละ 9.3) อัตราการเกิดภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดที่สำคัญทางคลินิกเท่ากับร้อยละ 33.0 การวิเคราะห์แบบ multivariate logistic regression พบว่าเนื้อตับอ่อนที่นุ่ม [Odds ratio (OR): 6.7, 95% confidence interval (CI): 1.5 ถึง 30.9], ท่อตับอ่อนที่มีขนาดเส้นผ่าศูนย์กลางน้อยกว่าหรือเท่ากับ 3 มิลลิเมตร [OR: 4.6, 95% CI: 1.0 ถึง 21.4] และประสบการณ์ของศัลยแพทย์น้อยกว่า 10 ปี [OR: 6.5, 95% CI: 1.4 ถึง 30.6] เป็นปัจจัยเสี่ยงของการเกิดภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัด และทั้งสามปัจจัยเป็นปัจจัยเสี่ยงของการเกิดภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดที่สำคัญทางคลินิกด้วย

สรุป: แม้ในสถาบันที่มีการผ่าตัด pancreaticoduodenectomy ในปริมาณมาก อุบัติการณ์ของภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดยังคงสูง และภาวะน้ำย่อยตับอ่อนรั่วซึมในระดับ B พบได้มากที่สุด เนื้อตับอ่อนที่นุ่ม ท่อตับอ่อนขนาดเล็ก และประสบการณ์ของศัลยแพทย์ที่น้อย เป็นปัจจัยเสี่ยงในการเกิดภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดและภาวะน้ำย่อยตับอ่อนรั่วซึมภายหลังการผ่าตัดที่สำคัญทางคลินิกด้วย