



Risk Factor of Pancreatic Fistula after Pancreatoduodenectomy in Patients with Soft Pancreas

Yayoi Matsumoto, Saiho Ko*, Tadataka Takagi, Yuuki Kirihataya, Yasuyuki Nakata, Masanori Matsusaka, Tomohide Mukogawa, Hirofumi Ishikawa and Akihiko Watanabe

Department of Surgery, Nara Prefecture General Medical Center, Japan

Abstract

Background: Pancreatic fistula (PF) is a potentially life-threatening postoperative complication after pancreatoduodenectomy (PD). Soft pancreatic texture is known to be a risk factor of PF. The study tried to elucidate risk factors of PF, especially in patients with soft pancreas.

Methods: One hundred-nine patients underwent PD between 2010 and 2014, excluding cases of PD with major hepatectomy. The diagnoses were: pancreatic carcinoma in 44, cholangiocarcinoma in 23, and carcinoma of the Vater's papilla in 14 and others in 28 patients. Principally, pancreatic duct stent was placed through the duct-to-mucosal pancreatojejunostomy only in patients with soft pancreas and small diameter of the pancreatic duct. PF was defined and scored based on the criteria of the International Study Group on Pancreatic Fistula. Factors influencing development of PF Grade B/C were analyzed. As potential risk factors, age, sex, diagnosis, pancreatic texture, diameter of pancreatic duct, use of pancreatic duct stent, device of dividing the pancreas, blood loss, operation time, and preoperative biliary drainage were included for univariate and multivariate analyses.

Results: PF Grades B and C developed in 8 and 2 patients, respectively. Eight of these patients had soft pancreas. No significant risk factors were determined in the analysis of all patients (n=109). However, small pancreatic duct ($\leq 3\text{mm}$; $p=0.026$), non-pancreatic carcinoma patients ($p=0.0114$), and smaller amount of blood loss ($<1000\text{ml}$; $p<0.0001$) were independent risk factors of PF Grade B/C in patients with soft pancreas (n=68).

Conclusions: Soft pancreas was not a risk factor of PF, probably because of standard use of pancreatic duct stent. Small pancreatic duct, non-pancreatic carcinoma, and the amount of blood loss were significant risk factors of PF in patients with soft pancreas.

Keywords: Pancreatic fistula; Pancreatoduodenectomy; Soft pancreas; Pancreatic duct stent

Introduction

Pancreatic fistula (PF) after pancreatoduodenectomy (PD) can cause serious complications such as intraabdominal hemorrhage and sepsis. Soft pancreas and small pancreatic duct have been reported as significant risk factors. Various cutting and reconstruction methods of the pancreas were tried in many institutions, however, the surgical procedure to minimize the risk of PF has not been standardized.

Although use of pancreatic duct stent is one of the procedures which may reduce the risk and severity of PF, its benefit is still controversial in the literatures [1,2]. Our policy has been to use pancreatic duct stent only in patients with soft pancreas and small pancreatic duct. Our previous study revealed that soft pancreas was not a significant risk factor of PF with such restricted use of pancreatic duct stent to patients with soft pancreas [3]. The purpose of this study is to evaluate the risk factors of PF especially in patients with soft pancreas in whom the pancreatic duct stent has been principally placed.

Materials and Methods

One hundred-nine patients underwent PD excluding cases of PD with major hepatectomy between 2010 and 2014 in our hospital were analyzed. Principally, reconstruction was performed with modified Child's method Pancreatic transaction was performed with scalpel or GIA (Endo GIA Tri-staple™). Pancreas duct-to-jejunum mucosal anastomosis with interrupted suture using 5-0 bio absorbable suture was the standard procedure of pancreatic anastomosis. In case of small

OPEN ACCESS

*Correspondence:

Saiho Ko, Department of Surgery, Nara Prefecture General Medical Center, 1-30-1, Hiramatsu, Nara 631-0846, Japan, Tel: 81-742-46-6001; Fax: 81-742-46-6011;

E-mail: saihoko@naramed-u.ac.jp

Received Date: 18 Jun 2016

Accepted Date: 22 Jul 2016

Published Date: 31 Aug 2016

Citation:

Matsumoto Y, Ko S, Takagi T, Kirihataya Y, Nakata Y, Matsusaka M, et al. Risk Factor of Pancreatic Fistula after Pancreatoduodenectomy in Patients with Soft Pancreas. *Clin Surg*. 2016; 1: 1092.

Copyright © 2016 Saiho Ko. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Table 1: Analyses of risk factors for pancreatic fistula (PF) in all patients (n=109).

Factors	Categories	PF (yes/no)	PF rate	Univariate p value	Multivariate p value
Age	70years>	4/54	7%	0.7522	0.4959
	70years≤	6/45	13%		
Sex	Male	9/60	15%	0.3222	0.173
	Female	1/39	26%		
Diagnosis	pancreatic cancer	2/50	4%	0.0552	0.0998
	others	8/49	16%		
Pancreatic texture	soft	8/60	13%	0.2029	0.3031
	hard	2/39	5%		
Diameter of pancreatic duct	3mm≥	6/53	11%	0.5439	0.4682
	3mm<	4/46	9%		
Pancreatic duct stent	yes	8/55	15%	0.1141	0.109
	no	2/44	5%		
Device of pancreatic transaction	scalpel	7/67	10%	>.9999	0.4501
	GIA*	3/32	9%		
Blood loss	1000ml>	8/73	11%	>.9999	0.6959
	1000ml≤	2/26	8%		
Operation time	420min>	7/58	12%	>.9999	0.3869
	420min≤	3/41	7%		
Preoperative biliary drainage	yes	7/52	13%	0.2206	0.1995
	no	3/47	6%		

*Endo GIA Tri-staple™

pancreatic duct (≤ 3 mm) and soft pancreatic, the incomplete external pancreatic duct stent was placed through the pancreatic duct anastomosis. The closed-suction drains were placed in the anterior and posterior space of the pancreatic anastomosis and Morrison's pouch. All patients received antibiotic therapy intravenously on the day of surgery and 1st postoperative day. Postoperative management was followed clinical pathway and changed appropriately when needed. Operative mortality was defined as death within 90 days.

PF was graded according to the International Study Group on Pancreatic Fistula (ISGPF) and grade B/C was defined as PF in this study [4]. As potential risk factors of PF, age (<70years>, ≥ 70 years), sex (Male, Female), diagnosis (pancreatic carcinoma, others), pancreatic texture (soft, hard), diameter of the pancreatic duct (≤ 3 mm, >3mm), pancreas duct stent (yes, no), device of pancreatic transaction (scalpel, GIA), blood loss (≤ 1000 mL, >1000mL), operation time (<420min, ≥ 420 min), and preoperative biliary drainage (yes, no) were included for univariate and multivariate analyses. The univariate analysis was performed with chi-square test and the multivariate analysis was performed with a logistic regression analysis. $P < 0.05$ was considered as statistically significant.

Results

The demographic data of the patients showed that the median age was 69 (29-82) years old, and the numbers of male and female were 69 and 40, respectively. The final diagnosis were; pancreatic cancer in 44 patients (40%), Cholangiocarcinoma in 23 (21%), Vater's papilla carcinoma in 14 (13%), and others in 28 (26%). Preoperative biliary drainage was done in 59 patients for reduction of obstructive jaundice. The median operation time was 403 (274-826) min. The median intraoperative bleeding was 600 (150-5,380) mL and over

1000mL bleeding were seen in 28 patients. The texture of the pancreas was hard in 41 patients and soft in 68. The diameter of pancreatic duct were small (≤ 3 mm) in 59 patients. The incomplete external pancreatic duct stent was placed in 63 patients. The combined resection was performed in 48 (44%); portal vein in 42, transverse colon in 8, superior mesenteric artery in 4, hepatic artery in 3, and inferior vena cava in 1 patients. The postoperative complications were cholangitis in 9, delayed gastric emptying in 9, chylous ascites in 8 patients. PF (grade B/C) was experienced in 10 (9%) patients, including grade B in 8 (7%) and grade C in 2 (2%) patients. Bleeding from the stump of gastroduodenal artery and common hepatic artery in 2 patients with PF grade C were treated successfully by coil embolization with angiographic approach, and the patients recovered uneventfully thereafter. The median postoperative length of hospital stay was 33 (13-152) days. There was no operative mortality in this series.

The univariate and multivariate analyses of all patients (n=109) showed no significant risk factor for the development of PF (Table 1). While univariate analysis of patients with soft pancreas (n=68) showed no significant risk factor of PF, multivariate analysis of these 68 patients indicated that small pancreatic duct (≤ 3 mm; $p=0.026$), non-pancreatic carcinoma ($p=0.0114$), smaller amount of blood loss (<1000ml; $p<0.0001$) were independent risk factors for the development of PF (Table 2).

Discussion

PD is a standard surgical procedure for pancreatic head carcinoma and lower bile duct carcinoma currently. In spite of progress in operative procedure and perioperative management, postoperative complication rate is still high with 20-65% [5-8]. Especially, PF is

Table 2: Analyses of risk factors for pancreatic fistula (PF) in patients with soft pancreas (n=68).

Factors	Categories	PF (yes/no)	PF rate	Univariate p value	Multivariate p value
Age	70years>	3/34	8%	0.4538	0.3031
	70years≤	5/26	16%		
Sex	Male	6/36	14%	0.7008	0.1239
	Female	2/24	8%		
Diagnosis	pancreatic cancer	1/20	5%	0.419	0.0114
	others	7/40	15%		
Diameter of pancreatic duct	3mm≥	7/42	14%	0.4265	0.0026
	3mm<	1/18	5%		
Pancreatic duct stent	yes	8/42	16%	>.9999	0.0026
	no	0/18	0%		
Device of pancreatic transaction	scalpel	5/36	12%	0.0986	0.1239
	GIA*	3/24	11%		
Blood loss	1000ml>	7/51	12%	0.4531	<0.0001
	1000ml≤	1/9	10%		
Operation time	420min>	5/36	12%	>.9999	0.1239
	420min≤	3/24	11%		
Preoperative biliary drainage	yes	5/30	14%	0.7102	>.9999
	no	3/30	9%		

*Endo GIA Tri-staple™

a potentially life-threatening postoperative complication after PD and it may cause serious complications including intraabdominal infection and bleeding. As outbreak mechanism for intraabdominal bleeding in grade C pancreatic fistula is considered as followings: pancreatic enzyme from the pancreatic fistula causes self-digestion of blood vessels around the pancreatic fistula, which results in formation of aneurysms and its rupture. According to the past literatures, the mortality rate of postoperative bleeding caused by PF after PD was 30-58% [5-8]. After PD, biological defense mechanism may be deteriorated. Insufficient drainage easily causes sepsis and abdominal abscess, which may promote self-digestion of the blood vessels due to leaked pancreatic enzyme. Since 2005, PF were graded to Grade A to C according to the ISGPF. The overall PF rate was 16-32%, Grade B was 3.6-26%, and Grade C was 1-5.7% in the literatures [4,9]. In this study, the rates of Grade B and C were 8 (7%) and 2 (2%), which were rather favorable comparing to other literatures.

Risk factors influencing PF were reported to be soft pancreas, small pancreatic duct (≤ 3 mm), lower bile duct carcinoma and Vater's papilla carcinoma, and intraoperative bleeding (≥ 1000 mL). Among them, most important risk factors were soft pancreas and small pancreatic duct. However, univariate and multivariate analysis of the present study identified no significant risk factor of PF. This might be because of our restricted use of external pancreatic duct stent to the patients with soft pancreas and small pancreatic duct. Uchida et al. [10] studied the cut-end of the pancreatic remnant histologically for its grade of fibrosis in comparison with the exocrine activity of the pancreatic remnant (EAPR) which was calculated by the value of the product of volume of drained pancreatic juice and its amylase activity. And the histological grade of fibrosis of the pancreatic stump was inversely correlated with EAPR. The incidence of leakage of pancreatojejunal anastomosis was significantly higher in the patients with high values of EAPR ($p < 0.05$).

In the analysis of patients with soft pancreas, placement of

pancreatic duct stent was another independent risk factor of PF. This result showed that external pancreatic duct stent could not completely prevent PF, while it might decrease severity of PF. The similar finding was reported by Suzuki Y et al. [11].

Despite a certain protective effect of incomplete external pancreatic duct stent for duct-to-mucosa anastomosis, PF from the small branches of the pancreatic duct can not be prevented. To reduce the PF from pancreatic duct branches, several techniques have been reported. While treating the pancreatic stump by using soft coagulation device or ultrasonic coagulation device to occlude pancreatic ductal branches on the pancreatic stump, adding jejunal seromuscular layers adhesion anastomosis to the pancreatic stump (the modified Kakita's procedure), and using pancreatogastrostomy are possible procedure to reduce the risk of PF, these have shown no definite advantage [5-7,12]. In the present study, soft pancreas was not a significant risk factor of PF, and the PF rate was rather low comparing to other literatures. These results suggest that pancreatic duct stent successfully reduce PF. In patients with soft pancreas, however, PF could not prevented sufficiently in cases of small pancreatic duct.

In conclusions, the policy to use pancreatic duct stent only for patients with soft pancreas would be reasonable. Small pancreatic duct should be recognized as a risk factor even with pancreatic duct stent in patients with soft pancreas.

References

1. Winter JM, Cameron JL, Campbell KA, Chang DC, Riall TS, Schulick RD, et al. Does pancreatic duct stenting decrease the rate of pancreatic fistula following pancreaticoduodenectomy? Results of a prospective randomized trial. *J Gastrointest Surg.* 2006; 10: 1280-1290.
2. Poon RT, Fan ST, Lo CM, Ng KK, Yuen WK, Yeung C, et al. External drainage of pancreatic duct with a stent to reduce leak rate of

- pancreaticojejunostomy after pancreaticoduodenectomy. A prospective randomized trial. *Ann Surg.* 2007; 246: 425-435.
3. Matsumoto Y, Ko S, Takagi T, et al. Risk factors of postoperative pancreatic fistula after pancreaticoduodenectomy. *J Nara Gen Med C.* 2016; 20: 62-65. (in Japanese).
 4. Pratt WB, Maithel SK, Vanounou T, Huang ZS, Callery MP, Vollmer CM Jr. Clinical and economic validation of the International Study Group of Pancreatic Fistula (ISGPF) classification scheme. *Ann Surg.* 2007; 245: 443-451.
 5. C J Yeo, J L Cameron, M M Maher, P K Sauter, M L Zahurak, M A Talamini, et al. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. *Ann Surg.* 1995; 222: 580-588.
 6. Bassi C, Falconi M, Moliari E, Salvia R, Butturini G, Sartori N, et al. Reconstruction by Pancreaticojejunostomy Versus Pancreaticogastrostomy Following Pancreatectomy. *Ann Surg.* 2005; 242: 767-771.
 7. Duffas JP, Suc B, Msika S, Fourtanier G, Muscari F, Hay JM, et al. A controlled randomized multicenter trial of pancreatogastrostomy or pancreaticojejunostomy after pancreatoduodenectomy. *Am J Surg.* 2005; 189: 720-729.
 8. Fernández-Cruz L, Cosa R, Blanco L, López-Boado MA, Astudillo E. Pancreatogastrostomy with gastric partition after pylorus-preserving pancreatoduodenectomy versus conventional pancreaticojejunostomy: a prospective randomized study. *Ann Surg.* 2008; 248: 930-938.
 9. Liang TB, Bai XL, Zeng SS. Pancreatic fistula after pancreaticoduodenectomy: diagnosed according to International Study Group Pancreatic Fistula (ISGPF) definition. 2007; 7: 325-331.
 10. Uchida E, Tajiri T, Nakamura Y, Aimoto T, Naito Z. Relationship between grade of fibrosis in pancreatic stump and postoperative pancreatic exocrine activity after pancreaticoduodenectomy: with special reference to insufficiency of pancreaticointestinal anastomosis. *J Nippon Med Sch.* 2002; 69: 549-556.
 11. Suzuki Y, Fujino Y, Ajiki T, Ueda T, Sakai T, Tanioka Y, et al. No mortality among 100 consecutive pancreaticoduodenectomies in a middle-volume center. *World J Surg.* 2005; 29: 1409-1414.
 12. Kakita A, Takahashi T, Yoshida M, Furata K. A simpler and more reliable technique of pancreaticojejunal anastomosis. *Surg Today.* 1996; 26: 532-535.