**ORIGINAL ARTICLE** 

# Analysis of procedure-related complications after pancreatodoudenectomy

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#### Abstract

*Purpose* To analyze the procedure-related complications after pancreaticoduodenctomy (PD) and their risk factors.

*Methods* One hundred twenty-six patients underwent pancreatoduodenectomy for diseases at region of pancreatic head were reviewed retrospectively.

*Results* The overall surgical morbidity was 40.5% (51/126). Ten (7.9%) of 51 patients were identified as having pancreatic leakage, others included delayed gastric emptying (8.7%, 11), abdominal infection and abscess (7.9%, 10), abdominal bleeding (5.6%, 7), wound infection (4.8%, 6), wound dehiscence (2.4%, 3), biliary fistula (1.6%, 2) and operative death (1.6%, 2). Other postoperative complications were lung inflammation (3.9%, 5) and newly developed diabetes mellitus, small main pancreatic duct ( $\leq$ 0.5 cm), and surgeon's experience (<10 patients within 5 years) were demonstrated to be independent risk factors by both univariate and multivariate analysis (p < 0.01).

Conclusions Old patients with coexisting diabetes mellitus and small main pancreatic duct undergo

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Shao-liang Han (⊠) E-mail: slhan88@hotmail.com pancreatoduodenectomy by a less experienced surgeon may be at high risk of procedure-related complications.

**Keywords** Pancreaticoduodenectomy · Pancreatic leakage · Complication

#### Introduction

Pancreaticoduodenectomy (PD) is one of the standard treatments for various benign and malignant diseases of the pancreatic head and periampullary region. PD nowadays represents a complex procedure and a challenge for the surgeon. Recently, the operative mortality rate after PD has significantly declined, while the incidence of postoperative morbidity remains high, from 40%–50% [1–6], and a recent series of 650 operations demonstrated a 30-day mortality of 1.4% [7]. The improved mortality is related to improve general management surgeon expertise and higher volume of procedures being performed in a hospital [5].

The complications after PD often lead to prolongation of hospital stay. Pancreatic fistula is the major source of complications, and leakage rate varies from 0-25%, according to recent reports [1, 4–5, 8–10]. Abdominal abscess and hemorrhage are common sequelae of pancreatic anastomotic leakage, which have been associated with a mortality rate of 40% or more [9–11]. The complications after PD were classified as procedure-related (pancreatic leakage, biliary leakage, intraabdominal (IA) abscesses, hemorrhage, delayed gastric emptying) or general (pulmonary and cardiac).

The aim of this study to analyze the risk factors of the procedure-related complications after pancreatoduodenectomy, we reviewed retrospectively 126 cases that underwent PD at our hospital.

#### Patients and materials

#### Patient characteristics

One hundred twenty-six patients with the disease at region of pancreatic head were performed PD at our department from March 1981 to November 2005. There were 87 male and 39 female with a ratio of 2.2:1, the mean age was 61.3 years, ranged from 19 years to 84 years. All of the diseases were confirmed by pathologic examinations, 82 were pancreatic carcinoma, 24 bile duct carcinoma, seven duodenal malignant tumors, six chronic pancreatitis, four traumas of pancreas, two pancreatic benign tumors, and one acute necrotic duodenitis.

### Definitions of postoperative morbidities

The complications after PD are various, such as pancreatic fistulas, and delayed gastric emptying. In this study, pancreatic leakage was defined as: (1) discharge from the postpancreatic drain  $\geq$ 50 ml/d after postoperative day 3, and (2) an amylase level of drainage fluid exceeding three times of the serum concentration. Delayed gastric emptying was defined as intolerance to oral intake and need for nasogastric decompression after the seventh postoperative day. Postoperative mortality was defined as death occurring in the first 30 postoperative days or before discharge from the hospital. Other complications were categorized and defined as any of the following: intra-abdominal abscess (fluid requiring drainage and with positive bacterial culture); wound infection (purulent drainage requiring open packing); postoperative bleeding (requiring transfusion or endoscopic or operative intervention); bile leak (bilious drainage from intraoperatively placed drains or bile collection requiring drainage); biliary stricture (requiring stenting and/or late reoperation); cardiac (myocardial infarction or new-onset arrhythmia requiring intervention); pulmonary (pneumonia, effusion requiring drainage, or reintubation); sepsis (fever, leukocytosis, or bacteremia requiring medical and/or surgical intervention); and reoperation in the first 30 postoperative days or before discharge from the hospital; acute pancreatitis (a more than 3-fold increase in serum or lipase from postoperative day four onward with a compatible clinical course or findings on computed tomography); wound dehiscence (partial or total disruption of the fascial or all the layers of the incision) [12-13].

#### Postoperative management

All patients were managed using a standard postoperative critical pathway. Histamine H2-receptor antagonists were administered to all patients postoperatively as prophylaxis for marginal or stress ulceration. Most patients received erythromycin lactobionate as prophylaxis against early delayed gastric emptying. As part of a now-completed clinical trial evaluating pancreatic fistula, <15% of patients received perioperative octreotide. Operatively placed drains left in the area of the pancreatic and bile duct anastomoses were removed under the direction of the attending surgeon, usually between postoperatively by medical oncology and radiation oncology consultants and were given recommendations regarding treatment with adjuvant chemoradiation and immunotherapy.

### Statistical Analysis

SPSS 13.0 (SPSS Inc., Chicago, IL) was used for statistical analysis. Data were analyzed using the  $\chi^2$  test, student t-test, and Fisher exact test as appropriate. A p < 0.05 was considered statistically significant.

# Results

#### Clinical staging and procedure

Tumors were staged according to American Joint Committee on Cancer (AJCC) staging, 24 patients (25.3%) of malignant tumor of pancreatic head were categorized into stage I, 58(61.0%) into stage II, 13(13.7%) into stage III. Seven patients (29.1%) of malignant tumor of common bile duct were categorized into stage I, 15 (62.5%) into stage II, Two (8.3%) into stage III. 2 patients (28.6%) of malignant tumor of duodenum were categorized into stage I, 3 (42.6%) into stage II, 1 (14.3%) into stage III and 1 (14.3%) into stage IV (Table 1).

In this study, 120 patients underwent standard pancreaticoduodenectomy (PD, i.e., Whipple's procedure), 3 underwent pylorus-preserving pancreaticoduodenectomy (PPPD), 1 underwent hepato - pancreaticoduodenectomy (HPD), and 2 underwent PD combined with resection of portal vein and/or superior mesenteric vein. The 5-year

 Table 1
 Tumor location and TNM staging for pancreatoduodenectomy

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Location	Staging I	Staging II	Staging III	Staging IV
Pancreatic head $(n = 95)$	24	58	13	0
Common bile duct $(n = 24)$	7	15	2	0
Duodenum (n = $7$ )	2	3	1	1
Total	33	76	16	1

# Postoperative complications

The procedure-related postoperative complication data are presented in Table 2. Of the 126 patients, 10 (7.9%) were identified as having pancreatic leakage after operation, other procedure-related postoperative included delayed gastric emptying (8.7%, 11), abdominal infection and abscess (7.9%, 10), abdominal bleeding (5.6%, 7), wound infection (4.8%, 6), wound dehiscence (2.4%, 3), biliary fistula (1.6%, 2) and operative death (1.6%, 2). Other postoperative complications were lung inflammation (3.9%, 5), newly developed diabetes mellitus (2.4%, 3), ketoacidosis (1.6%, 2) and liver-kidney syndrome (0.8%, 1). Indian J Surg (May–June 2010) 72:194–199 Overall surgical morbidity was 40.5% (51/126). Two

patients died of massive abdominal hemorrhage and abdominal abscess associated with pancreatic fistula after operation. The hospital mortality in this series was 1.6% (2/126), the patients required reoperation because of abdominal bleeding or abdominal abscess, pancreaticojejunal anastomotic leakages were found in them.

# Univariate and multivariate analysis

A univariate analysis revealed that age (>60 years), coexisting diabetes mellitus, preoperative serum cretinine (>133 mmol/L), diameter of main pancreatic duct ( $\leq 0.5$  cm), and surgeon's experience (<10 patients within 5 years) were correlated with the procedure-related complications ((p < 0.01) (Table 3). These factors affecting procedure-related complications were further analyzed by

 Table 2
 Postoperative complications after pancreatoduodenectomy

Complications	Cases (%)
Procedure-related complications	
Delayed gastric emptying	11 (8.7%)
Pancreatic fistula	10 (7.9%)
Abdominal infection and abscess	10 (7.9%)
Abdominal hemorrhage	7 (5.6%)
Wound infection	6 (4.8%)
Wound dehiscence	3 (2.4%)
Biliary fistula	2 (1.6%)
Operative death	2 (1.6%)
Other complications	
Lung complication	5 (3.9%)
Newly developed diabetes mellitus	3 (2.3%)
Ketoacidosis	2 (1.6%)
Liver-kidney syndrome	1 (0.8%)

multivariate logistic regression. Age, coexisting diabetes mellitus, small diameter of main pancreatic duct, and surgeon's experience were demonstrated to be independent risk factors (Table 4). Old patients with a coexisting diabetes mellitus and small main pancreatic duct underwent PD by a less experienced surgeon were at high risk of procedurerelated complications.

# Discussion

In recent years, PD has been used increasingly as a safe method of resection in patients with malignant and benign disorders of the pancreas and periampullary region [13–15]. Wu et al. [14] reported that the success rate of pancreatoduodenectomy was 10.1%, and the postoperative

1–3- and 5-year survival rates for carcinoma of head of pancreas were 67.5%, 36% and 5.6%, respectively, and the median survival time was 7 months in patients with unresectable tumor who received radiotherapy and/ or chemotherapy. Our results indicated that the 5-year survival rates were 12.6%, 20.8% and 15.4% for pancreatic carcinoma, bile duct carcinoma and duodenal carcinoma, respectively.

Yeo et al. [7] reported that the most common complications for 650 patients undergoing PD were early delayed gastric emptying (19%), pancreatic fistula (14%), and wound infection (10%). Twenty-three patients required reoperation in the immediate postoperative period (3.5%), most commonly for bleeding, abscess, or dehiscence. Aslam et al. [1] reported that out of 30 patients, three patients died in early postoperative period

 Table 3
 Results of univariate analysis of risk factors for procedure-related complications

Factors	Procedure-related complications		
	Yes/No	p value	
Age		0.018	
$\leq 60$ years n = 79	21/58		
>60 years (n = 57)	30/17		
Gender		0.818	
Male (n = 87)	37/50		
Female $(n = 39)$	14/25		
Coexisting diabetes mellitus		0.000	
Yes $(n = 31)$	28/3		
No (n = 95)	23/95		
Total bilirubin		0.816	
$\geq$ 34.2 µmol/L (n = 90)	41/50		
$<34.2 \ \mu mol/L \ (n = 36)$	10/36		
Serum cretinine		0.001	
>133 mmol/L (n = 32)	24/32		
$\leq 133 \text{ mmol/L} (n = 94)$	27/94		
Tumor location		0.783	
Pancreatic head $(n = 84)$	39/45		
Periampullary region $(n = 42)$	12/30		
Preoperative drainage of jaundice		0.892	
Yes $(n = 34)$	12/22		
No (n = 92)	39/53		
Operation method		0.0632	
Whipple procedure $(n = 120)$	47/73		
Non-standard PD* $(n = 6)$	4/2		
Volume of blood transfusion		0.915	
$\geq 800 \text{ ml} (n = 30)$	14/16		
<800 ml (n = 96)	37/59		
Diameter of main pancreatic duct		0.001	
$\leq 0.5 \text{ cm} (n = 25)$	14/11		
>0.5 cm (n = 121)	37/84		
Surgeon's experience		0.000	
$\geq 10$ patients within 5 years (n = 87)	17/68		
<10 patients within 5 years (n = 39)	32/7		

\*Non-standard PD, including 3 PPPD, 1 HPD and 2 PD with combined resection

with 10% mortality while 26.7% had wound infection, 16.7% had chest complications, 13.3% developed IA collections, 10% had hemorrhage, 3.3% had delayed gastric emptying, 3.3% had pancreatic fistula and 3.3% had organ failure. Pancreatic anastomosis leakage remains a major cause of postoperative morbidity after PD, and it contributes significantly to operative mortality. Lin et al. [2] retrospectively reviewed 1891 patients undergoing PD, 216 of those patients (11.4%) developed a postoperative pancreaticocutaneous fistula. Hosotani et al. [16], reviewed 161 patients who had undergone PD and reported a fistula rate of 11% (17/161), finding that pancreaticojejunostomy anastomotic technique, pancreatic texture and pancreatic duct size were substantial risk factors for pancreatic leakage after PD. In a study of Marcus et al. [17], male sex was found to be a significant factor predisposing pancreatic fistula. A recent study from Yeh et al. [18], identified jaundice, creatinine clearance abnormality, and intraoperative blood loss as significant risk factors for leakage. Matsusue et al. [19], found that

5	1		
Risk factors	p value	Relative risk	95% confidence interval
Age (>60 years)	0.046	2.47	1.12-5.98
Coexisting diabetes mellitus	0.004	3.69	1.51-8.98
Serum cretinine >133 mmol/L	0.002	1.03	1.03-2.04
Small pancreatic duct (≤0.5 cm)	0.005	0.09	0.02-0.47
Surgeon's experience (<10 patients within 5 years)	0.009	0.31	0.13-0.76

 Table 4
 Multivariate analysis of risk factors for procedure-related complications

advanced age (>70 years) was an adverse factor for pancreatic leakage. A retrospective study was carried out by Wu et al. [14] to evaluate 178 patients suffering from carcinoma of head of pancreas, they found the following factors related to pancreatic anastomotic leakage, such as pancreatic texture, pancreatic pathology, pancreatic duct size, pancreatic juice output, intraoperative blood loss, operative techniques and age and jaundice. Our result demonstrated that age (>60 years), coexisting diabetes mellitus, small diameter of main pancreatic duct (≤0.5 cm), and surgeon's experience (<10 patients within 5 years) were demonstrated to be independent risk factors by both univariate analysis and multivariate analysis (p < 0.01). This implies that old patients with a coexisting diabetes mellitus and small main pancreatic duct underwent pancreatoduodenectomy by a less experienced surgeon were at high risk of procedurerelated complications.

One of the most common morbidities after PD is delayed gastric emptying with rates of 15-40% [20-21]. Advances in surgical skills and postoperative care have resulted in mortality rates of <5% [22-23]. The Whipple procedure involves resection of the head of the pancreas and the entire duodenum, and the pancreas is reconstructed with a pancreaticojejunostomy, choledochojejunostomy, and gastrojejunostomy. The operation classically involves removal of the pylorus and antrum; however recently, surgeons have used a pylorus-preserving Whipple procedure to lower the incidence of postgastrectomy symptoms, such as delayed gastric emptying. Both methods - the standard and the pylorus-preserving Whipple-have their advocates, but each method continues to have gastroparesis as a postoperative problem [4, 10, 20-21]. In our study, 11 (8.7%) of 126 patients underwent PD complicated delayed gastric emptying after operation.

Hemorrhage after pancreatoduodenectomy is a severe, life-threatening complication. Balachandran et al. [8] reported that 44 (20.2%) patients after PD had a bleeding complication, Of these, 25 patients had an IA bleed and 21 had gastrointestinal (GI) bleed (two had both IA and GI bleed). And significant postoperative bleeding occurred in 21 (4.6%) of 456 patients who had undergone pancreatoduodenectomy according to Yoon et al. [24]. Molino et al. [4] retrospectively analyzed 121 patients underwent pancreatic resection with radical intent, they found that average recovery time was 24 days (range 12–65); operative mortality was 5.8% (7/121); general morbidity, including medical and surgical complications, was observed in 47 patients (38.8%). Pancreatic fistula occurred in 16 patients (13.2%); ten of these underwent a second operation. In our study, 5.6% PD patients complicated abdominal bleeding, and one died of massive abdominal hemorrhage.

Bassi et al. [5] reported that the mortality in PD patients was 3/150 (2%) with a re-operation rate of 5/150 (3.3%). The median duration of the postoperative hospital stay was 10 days (range, 5–155 days) according to Sledzianowski et al. [22], two patients (3%) died postoperatively; 12(20%) had one or more IA complications with re-operation necessary in 3 (5%): 6 pancreatic fistula (10%), 11 IA collections (18%), one postoperative hemorrhage (2%). In our study, the hospital mortality in this series was 1.6% (2/126), the patients required reoperation because of abdominal bleeding or abdominal abscess, pancreaticojejunal anastomotic leakages were found in them.

Taken together, old patients with a coexisting diabetes mellitus and small main pancreatic duct underwent pancreatoduodenectomy by a less experienced surgeon were at high risk of procedure-related complications.

## References

- Aslam T, Masood R, Maher M (2005) Early complications following pancreatico - duodenectomy. J Coll Physicians Surg Pak15:708–711
- Lin JW, Cameron JL, Yeo CJ, Riall TS, Lillemoe KD (2004) Risk factors and outcomes in postpancreaticoduodenectomy pancreaticocutaneous fistula. J Gastrointest Surg 8:951–959
- Adam U, Makowiec F, Riediger H, Schareck WD, Benz S, Hopt UT (2004) Risk factors for complications after pancreatic head resection. Am J Surg187:201–208
- Molino D, Perrotti P, Napoli V, Antropoli C, Perrotta S, Presta L, Gargano E, Bocchetti R, D'Antonio D (2002) Surgical complications following pancreaticoduodenectomy: Results of a single center experience. G Chir 23:405–412
- Bassi C, Falconi M, Salvia R, Mascetta G, Molinari E, Pederzoli P (2001) Management of complications after pancreaticoduodenectomy in a high volume centre: results on 150 consecutive patients. Dig Surg18:453–457
- Schlitt HJ, Schmidt U, Simunec D, Jäger M, Aselmann H, Neipp M, Piso P (2002) Morbidity and mortality associated with pancreatogastrostomy and pancreatojejunostomy

following partial pancreatoduodenectomy. Br J Surg 89: 1245–1251

- Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, Hruban RH, Ord SE, Sauter PK, Coleman J, Zahurak ML, Grochow LB, Abrams RA (1997) Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg 226: 248–260
- Balachandran P, Sikora SS, Raghavendra Rao RV, Kumar A, Saxena R, Kapoor VK (2004) Hemorrhagic complications of pancreaticoduodenectomy. ANZ J Surg 74:945–950
- Tien YW, Lee PH, Yang CY, Ho MC, Chiu YF (2005) Risk factors of massive bleeding related to pancreatic leak after pancreaticoduodenectomy. J Am Coll Surg 201:554–559
- Schmidt CM, Powell ES, Yiannoutsos CT, Howard TJ, Wiebke EA, Wiesenauer CA, Baumgardner JA, Cummings OW, Jacobson LE, Broadie TA, Canal DF, Goulet RJ Jr, Curie EA, Cardenes H, Watkins JM, Loehrer PJ, Lillemoe KD, Madura JA (2004) Pancreaticoduodenectomy: a 20-year experience in 516 patients. Arch Surg 139:718–727
- Butturini G, Marcucci S, Molinari E, Mascetta G, Landoni L, Crippa S, Bassi C (2006) Complications after pancreaticoduodenectomy: the problem of current definitions. J Hepatobiliary Pancreat Surg 13:207–211
- Yekebas EF, Wolfram L, Cataldegirmen G, Habermann CR, Bogoevski D, Koenig AM, Kaifi J, Schurr PG, Bubenheim M, Nolte-Ernsting C, Adam G, Izbicki JR (2007) Postpancreatectomy hemorrhage: diagnosis and treatment: an analysis in 1669 consecutive pancreatic resections. Ann Surg 246:269–280
- Peng SY, Wang JW, Lau WY, Cai XJ, Mou YP, Liu YB, Li JT (2007) Conventional versus binding pancreaticojejunostomy after pancreaticoduodenectomy: a prospective randomized trial. Ann Surg 245:692–698
- Wu J, Shao Y, Rong W, Shan Y, Gao J, Wu T (2002) Diagnosis and treatment of 178 patients with carcinoma of the head of pancreas. Zhonghua Zhong Liu Za Zhi 24:497–500
- 15. Huguier M, Barrier A, Gouillat C, Suc B, Jaeck D, Launois

B (2008) Pancreaticoduodenectomy for cancer of the head of the pancreas. J Chir (Paris)145:9–15

- Hosotani R, Doi R, Imamura M (2002) Duct-to-mucosa pancreatic-ojejunostomy reduces the risk of pancreatic leakage after pancreatoduodenectomy. World J Surg 26: 99–104
- Marcus SG, Cohen H, Ranson JH (1995) Optimal management of the pancreatic remnant after pancreaticoduodenectomy. Ann Surg 221:635–648
- Yeh TS, Jan YY, Jeng LB, Hwang TL, Wang CS, Chen SC, Chao TC, Chen MF (1997) Pancreaticojejunal anastomotic leak after pancreaticoduodenectomy-multivariate analysis of perioperative risk factors. J Surg Res 67:119–125
- Matsusue S, Takeda H, Nakamura Y, Nishimura S, Koizumi S (1998) A prospective analysis of the factors influencing pancreatico-jejunostomy performed using a single method, in 100 consecutive pancreaticoduodenectomies. Surg Today 28:719–726
- Park YC, Kim SW, Jang JY, Ahn YJ, Park YH (2003) Factors influencing delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. J Am Coll Surg 196:859–865
- Gouma DJ, van Geenen RC, Van Gulik TM, De Haan RJ, De Wit LT, Busch OR, Obertop H (2000) Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. Ann Surg 232:786–795
- Sledzianowski JF, Duffas JP, Muscari F, Suc B, Fourtanier F (2005) Risk factors for mortality and intra-abdominal morbidity after distal pancreatectomy. Surgery 137:180–185
- Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M (2005) International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery138:8–13
- Yoon YS, Kim SW, Her KH, Park YC, Ahn YJ, Jang JY, Park SJ, Suh KS, Han JK, Lee KU, Park YH (2003) Management of postoperative hemorrhage after pancreatoduodenectomy. Hepatogastroenterology 50:2208–2212