

Analysis of Risk Factors for Delayed Gastric Emptying (DGE) after 387 Pancreaticoduodenectomies with Usage of 70 Stapled Reconstructions

Yoshihiro Sakamoto · Yusuke Yamamoto ·
Shojiro Hata · Satoshi Nara · Minoru Esaki ·
Tsuyoshi Sano · Kazuaki Shimada · Tomoo Kosuge

Received: 10 December 2010 / Accepted: 23 March 2011 / Published online: 9 August 2011
© 2011 The Society for Surgery of the Alimentary Tract

Abstract

Background Delayed gastric emptying (DGE) is one of the most troublesome complications after pancreaticoduodenectomy (PD).

Methods Between 2004 and 2009, 387 patients underwent PD and of these, 302 patients (78%) underwent pylorus-preserving PD. The stapled reconstruction of duodeno- or gastrojejunostomy was introduced in 2006, and 70 patients (18%) underwent stapled Roux-en-Y reconstruction. Postoperative DGE was defined based on the International Study Group on Pancreatic Surgery classification, and grade B or C DGE was considered to be clinically relevant. Risk factors for DGE were evaluated using univariate and multivariate analyses.

Results Four patients died in the hospital (1.0%). Postoperative DGE was found in 70 patients (18%). DGE was less frequently seen in stapled reconstruction than in hand-sewn reconstruction (7.2% vs. 21%, $P<0.001$), and in single-layer anastomosis than in double-layer anastomosis (12% vs. 24%, $P=0.02$). The multivariate logistic regression analysis revealed that the independent risk factors for DGE were postoperative pancreatic fistula (risk ratio [RR] 2.4, $P=0.002$), hand-sewn reconstruction (RR 2.9, $P=0.03$) and male (RR 2.2, $P=0.02$).

Conclusion The method of alimentary reconstruction affected the occurrence of DGE. The incidence of DGE was less in stapled reconstruction than in hand-sewn reconstruction.

Keywords Pancreaticoduodenectomy · Delayed gastric emptying · Stapled reconstruction · Hand-sewn reconstruction

Introduction

The recent advances in imaging studies, surgical techniques, and perioperative management have decreased the mortality rate of pancreaticoduodenectomy (PD) to less than 2% in high-volume centers.^{1,2} However, the morbidity rate still remains high, and postoperative pancreatic fistula (POPF) and delayed gastric emptying (DGE) have been the leading complications.^{3,4}

DGE after PD, otherwise known as “gastroparesis,”⁵ was originally noted by Warshaw et al. in 1985.⁶ DGE is not a fatal complication, but sometimes results in a significant prolongation of hospital stay and increase in hospital costs. The reported incidence of DGE has a wide range (7–45%),^{7–10} partly because there was no standard definition of this complication. Very recently, the International Study Group of Pancreatic Surgery defined DGE¹¹ and the

This work is supported in part by Grant-in-Aid for scientific research from the Ministry of Health and Welfare of Japan.

Y. Sakamoto (✉) · Y. Yamamoto · S. Hata · S. Nara · M. Esaki ·
K. Shimada · T. Kosuge
Hepatobiliary and Pancreatic Surgery Division,
National Cancer Center Hospital,
5-1-1 Tsukiji, Chuo-ku,
Tokyo 104-0045, Japan
e-mail: yosakamo-tky@umin.ac.jp

T. Sano
Department of Gastroenterological Surgery,
Aichi Cancer Center Hospital,
Nagoya, Aichi, Japan

incidence of DGE is now widely evaluated using the universal criteria.¹²

We previously reported the preliminary results of stapled reconstruction during PD.¹³ Alimentary reconstruction using staplers during gastric and colorectal surgery is a widely accepted technique.^{14,15} The use of circular staplers in esophagojejunostomy is more convenient and safer than hand-sewn suturing. Colorectal anastomoses using the double stapling technique have also become popular, especially since the advent of laparoscopic surgery.¹⁶ Recent advances in laparoscopic surgery allow PD to be performed under laparoscopic guidance¹⁷; thus, it has become necessary to establish the feasibility of stapled alimentary reconstruction. To our knowledge, the clinical efficacy of stapled reconstruction using staplers during PD has not been elucidated.

The primary objective of this study is to analyze the risk factors for relevant DGE among 387 patients who underwent PD in 2004–2009 in a Japanese high-volume center. In this study, we defined DGE on the basis of the international definition and analyzed the clinicopathological variables that influenced the occurrence of grade B or C DGE. The secondary objective is to study the clinical impact of stapled reconstruction on the occurrence of DGE.

Methods

From 2004 to 2009, 387 patients underwent PD at our institute. Diseases included invasive pancreatic cancer in 202 patients, bile duct cancer in 50 patients, intraductal papillary mucinous neoplasm in 37 patients, ampullary or duodenal cancer in 53 patients, neuroendocrine tumor in eight patients, gallbladder or cystic duct cancer in seven patients, solid pseudopapillary tumor or gastrointestinal tumor in six patients, metastatic cancers in four patients, pancreatitis or autoimmune disease in seven patients, and other diseases in 13 patients. Six attending surgeons (TK, KS, TS, YS, ME, and SN) performed or controlled all the surgeries; of these six surgeons, three had more than 20 years of surgical experience, while the remaining three surgeons had less than 20 years of experience. One chief resident and four residents attended the surgical management in turn.

Surgical Procedures of PD

The details of our standard surgical procedure of PD have been described elsewhere.¹⁸ Preoperative biliary drainage in 187 patients (48%) was performed either in the previous hospital or in our institute: only percutaneous biliary drainage (PTBD) in 103 patients, only

endoscopic retrograde biliary drainage in 63 patients, and both PTBD and retrograde biliary drainage in 21 patients. The remaining 200 patients underwent PD without biliary drainage. PD was performed when the serum bilirubin concentration decreased less than 5 mg/dL. Patients received preoperative intravenous antibiotic prophylaxis, using a second-generation cephalosporin. After the removal of the pancreatic head, we routinely wrapped the stump of the gastroduodenal artery using the falciform ligament to prevent the bleeding caused by the pancreatic leakage.¹⁹ Surgical procedures included pylorus-preserving PD (PPPD) in 296 patients, classical Whipple procedure (CW) or subtotal stomach-preserving PD (SSPPD) in 83 patients, PPPD plus limited hepatic resection in one patient, CW plus limited hepatic resection in two patients, and PPPD plus extended right hemihepatectomy in five patients. CW and SSPPD were not strictly distinguished, and the resection of the pyloric ring and antrum was performed according to the tumor extension or to the preference of the attending surgeon. The combined portal vein resection was performed in 83 patients (21%) out of 387 patients. In 382 patients, pancreaticojejunostomy was performed by duct-to-mucosa anastomosis in 342 patients, dunking method in 36 patients, and other methods in four patients. The pancreatic parenchyma was sewn to the jejunal wall by two-layer anastomosis in 324 patients, by Kakita's method²⁰ in 39 patients, and by other methods in 19 patients. In five patients, pancreaticojejunostomy was not performed.

Stomach Reconstruction by Conventional Hand-Sewn Method

Duodenojejunostomy was performed in PPPD in 249 patients, gastrojejunostomy in 67 patients undergoing CW or SSPPD, and jejunoejunostomy in one patient who had previously undergone total gastrectomy. Duodenojejunostomy and gastrojejunostomy were performed by the Gambee anastomosis in 84 patients, Albert–Lembert anastomosis in 198 patients, and layer-to-layer anastomosis in 31 patients. A Braun jejunoejunostomy was performed to prevent direct exposure of bile and pancreatic juice to the anastomotic site.

Stapled Roux-en-Y Reconstruction

All of the stapled reconstruction was performed by one of the authors (YS) since August 2006, and YS performed all of the alimentary reconstruction using staplers since then. The details of stapled Roux-en-Y reconstruction have been described elsewhere.¹³ Briefly, an antecolic duodenojejunostomy was performed by Roux-en-Y reconstruction

using a circular stapler in 53 PPPDs (Proximate ILS™ 25 or 29 mm, Ethicon Endo-Surgery, Cincinnati, OH [$n=19$], EEA circular stapler, 25 or 28 mm, US Surgical, Norwalk, CT [$n=34$]). An antecolic gastrojejunostomy was performed by Roux-en-Y reconstruction using a linear stapler (ENDO-GIA ROTICULATOR™ 60, US Surgical, Norwalk, CT) in six CWs. A circular stapler was used to perform a gastrojejunostomy on the posterior wall of the stomach in 10 SSPPDs. In the remaining one patient who underwent total gastrectomy and PD, an esophagojejunostomy was performed using a circular stapler.

Postoperative Management

Two closed drains (8 or 10 mm in diameter) were inserted beside the pancreatojejunostomy and the drainage fluid was intermittent suctioned. The nasogastric tube was removed on postoperative day (POD) 1. The reinsertion of the gastric tube or opening of the gastrostomy was performed if the patient complained of nausea or vomiting and/or if severe distention of the stomach was observed on abdominal radiography. No patient was administered erythromycin or octreotide postoperatively. Patients were discharged from the hospital when they could eat almost half of their regular diet and had one abdominal drain left with minimal output.

Definition of Outcome Measures

POPF was defined according to the definition proposed by the International Study Group on Pancreatic Fistula,²¹ i.e., when the amylase concentration of the drain fluid obtained on or after POD 3 was greater than three times the upper range of serum amylase concentration. POPF was classified into grades A, B, and C according to severity: briefly, grade A, fistula was a “transient fistula” not associated with a delay in hospital discharge; grade B, fistula led to a delay in discharge, with persistent drainage for more than 3 weeks; and grade C, fistula was usually associated with major complications. Grade B or C fistulae were considered to constitute clinically relevant POPF.

An upper gastrointestinal (UGI) study using an oral contrast medium was conducted between POD 4 and 7 at the discretion of the attending surgeon. A UGI score was calculated according to the degree of passage of the contrast medium grade A, good passage of the medium without stasis in the stomach; grade B, mild dilatation of the remnant stomach or formation of niveau in the stomach and passage of the medium maintained when the patient changes the position; and grade C, severe dilatation of the remnant stomach or no passage of the contrast medium to the jejunum.

DGE was classified into grades A, B, and C according to the definition proposed by the International Study Group of Pancreatic Surgery¹¹: grade A, unable to tolerate solid oral intake by POD 7 and usually no vomiting; grade B, unable to tolerate solid oral intake by POD 14 with/without vomiting; and grade C, unable to tolerate solid oral intake by POD 21 with/without vomiting. Reinsertion of the gastric tube or opening of the gastrostomy on or after POD 7 was considered to be indicative of DGE. Because the timing of serving food was influenced by the preference of each attending surgeon, grade A was not considered to be a clinically relevant complication, but grade B and C DGE were. The complications other than POPF and DGE were classified according to the criteria proposed by Clavien and Dindo,²² and only the complications related grade 2 above were recorded.

Univariate and Multivariate Analysis of Risk Factors for DGE

The univariate analysis of risk factors for DGE (grade B or C) was performed in relation to the following clinicopathological variables: operative period (2004–2006 vs. 2007–2009), age (≥ 65 , < 65 years), gender, body mass index (≥ 25 , < 25 kg/m²), presence of diabetes mellitus, performance of preoperative biliary drainage, disease (pancreatic cancer vs. others), presence of background pancreatitis, size of the main pancreatic duct (≥ 3 mm, < 3 mm), surgical procedures (PPPD vs. CW or SSPPD), combined portal vein resection, intraoperative radiation therapy, method of pancreaticojejunostomy (duct-to-mucosa anastomosis vs. dunking method), method of duodeno-/gastrojejunostomy (stapled vs. hand-sewn reconstruction), surgical experience of the attending surgeons (≥ 20 years, < 20 years), operative time (≥ 500 min, < 500 min), blood loss (≥ 750 ml, < 750 ml), results of bile juice culture on day 1, and POPF (absent or grade A vs. grade B or C). The thresholds of age, operative time, and blood loss were determined on the basis of the median value of each parameter. Multivariate analysis was performed using the significant factors in the univariate analysis.

Statistical Analysis

Analysis was performed using SPSS for Windows statistical software (SPSS Inc., Chicago, IL). The chi-square test or Fisher’s exact test was used for univariate analysis, and the Mann–Whitney U test was used to compare the variables between the two groups. A multivariate analysis of the risk factors for DGE was performed using logistic regression analysis. Data were expressed as median and range. A P value of less than .05 was considered statistically significant.

Results

Four patients (1.0%) died in the hospital as a result of the surgery: massive bleeding caused by POPF in two patients, Guillain–Barre syndrome in one patient, and congestion of the portal venous system in one patient. The overall surgical complications are summarized in Table 1. Reoperation was performed in eight patients (2%). Other than the complications in Table 1, one patient who underwent hand-sewn reconstruction developed anastomotic leak, and four patients who underwent stapled reconstruction developed anastomotic bleeding on POD 1 in one, POD 9 in two, and POD 16 in one. No anastomotic leakage was found in the group of stapled reconstruction. All four patients underwent endoscopic clipping of the bleeding points, and they recovered conservatively.

Table 1 Summary of postoperative complications of 387 patients who underwent pancreaticoduodenectomy

	Grade	<i>n</i>	(%)
POPF (<i>n</i> =197, 51%)	A	56	15
	B	129	33
	C	12	3
DGE (<i>n</i> =188, 49%)	A	118	31
	B	38	9.8
	C	32	8.3
Wound infection (<i>n</i> =38, 9.8%)	2	32	8.3
	3a	1	0.3
	3b	1	0.3
Pneumonia (<i>n</i> =15, 3.9%)	2	10	2.6
	3a	2	0.3
	4a	2	0.3
	5	1	0.3
Intra-abdominal bleeding (<i>n</i> =11, 2.8%)	3a	1	0.3
	3b	2	0.5
	4a	5	0.3
	4b	1	0.3
	5	2	0.5
Intra-abdominal abscess (<i>n</i> =62, 16%)	2	31	8
	3a	22	1.3
	3b	2	0.3
	4a	4	0.3
	4b	1	0.3
	5	2	0.5
Diarrhea (<i>n</i> =17, 4.4%)	2	17	4.4

Other complications are defined according to the classification of Clavien and Dindo²²

POPF postoperative pancreatic fistula—graded according to the definition proposed by an International Study Group on Pancreatic Fistula (ISGPF)²¹. *DGE* delayed gastric emptying—defined by the International Study Group of Pancreatic Surgery (ISPGS)¹¹

Risk Factors for Grade B or C DGE

DGE was found in 188 patients (49%): grade A in 118 (31%) patients, grade B in 38 (9.8%), and grade C in 32 (8.3%), excluding four patients who died as a result of surgery and one patient who did not undergo alimentary reconstruction. In univariate analysis, male sex, hand-sewn reconstruction, blood loss (≥ 750 mL), and POPF (grade B or C) were identified as significant risk factors for grade B or C DGE (Table 2). Median hospital stay of patients without relevant DGE (*n*=312) and with relevant DGE (*n*=70) was 22 (9–84) days and 43 (20–324) days, respectively ($P < 0.001$). Multivariate analysis also revealed hand-sewn reconstruction, male sex, and grade B or C POPF as independent risk factors (Table 3).

Comparison of the Results According to Methods of Alimentary Reconstruction

There was a significant difference between stapled and hand-sewn reconstructions in blood loss, incidence of re-gastric drainage, days until regular diet, incidence of DGE, and hospital stay (Table 4). Operative time was significantly shorter in the group of double-layer anastomosis than in the group of single-layer anastomosis. In hand-sewn reconstruction, the incidences of DGE and re-gastric drainage were significantly lower in single-layer anastomosis (Gambée anastomosis, *n*=84) than in double-layer anastomosis (Albert–Lembert or layer-to-layer anastomosis, *n*=229; 12% vs. 24%, $P=0.02$). Days until regular diet and hospital stay were significantly shorter in single-layer anastomosis than those in double-layer anastomosis, although there were no differences in sex, disease, operative procedure, results of UGI study, and POPF between the 2 groups.

Discussion

DGE after PD is a unique complication, which is rarely seen after distal pancreatectomy or distal gastrectomy. DGE has been reported to be affected by several factors including gastric dysrhythmias due to intra-abdominal complications,^{10,23} gastric atony after duodenal resection in response to reduction in motilin levels,^{7,24,25} pylorospasm secondary to vagotomy,²⁶ angulation of the reconstructed alimentary tract²⁷ and continuous enteral nutrition.^{3,28} Several comparative retrospective studies have revealed that antemesenteric reconstruction,¹⁰ vertical reconstruction,²⁹ and antecolic reconstruction^{30,31} were associated with a decreased risk for DGE. Furthermore, some prospective randomized trials have reported that erythromycin,^{7,24} cyclic enteral feeding, rather than continuous enteral

Table 2 Summary of clinicopathological factors of patients with and without delayed gastric emptying

		Without DGE (<i>n</i> =312)	With DGE (<i>n</i> =70)	<i>P</i> value
Patient characteristics				
Operative period	2004–2006	157	28	0.12
	2007–2009	155	42	
Age	<65	147	28	0.28
	≥65	165	42	
Sex	Male	176	55	0.001*
	Female	136	15	
Body mass index	<25	294	63	0.20
	≥25	18	7	
Diabetes mellitus	Absent	221	45	0.28
	Present	91	25	
Preoperative biliary drainage	Not performed	160	35	0.85
	Performed	152	35	
Diseases	Pancreatic cancer	165	35	0.66
	Others	147	35	
Background pancreatitis	Absent	189	36	0.16
	Present	123	34	
Size of main pancreatic duct	<3 mm	127	36	0.10
	≥3 mm	185	34	
Surgical parameters				
Operative procedure	CW or SSPPD ^a	64	19	0.22
	PPPD	248	51	
Portal vein resection	Not performed	244	55	0.95
	Performed	68	15	
IORT	Not performed	276	60	0.67
	Performed	35	9	
Pancreaticojejunostomy	Duct-to-mucosa	281	58	0.21
	Dunking	28	11	
Braun anastomosis	Braun or Roux-en-Y	244	62	0.054
	No Braun	67	8	
Duodeno/gastrojejunostomy	Hand-sewn	248	65	0.009*
	Stapled	64	5	
Experience of the attending surgeons	<20 years	163	28	0.06
	≥20 years	149	28	
Operative time	<500 min	159	30	0.22
	≥500 min	153	40	
Blood loss	<750 mL	165	24	0.005*
	≥750 mL	147	46	
Postoperative factors				
Bile juice culture on day 1	Negative	132	29	0.31
	Positive	94	28	
POPF	Absent or grade A	214	30	<0.001*
	Grade B or C	98	40	

^a Including two patients undergoing total gastrectomy for gastric cancer

**P*<0.05

DGE delayed gastric emptying, *CW* classical Whipple procedure, *SSPPD* subtotal stomach preserving pancreaticoduodenectomy, *PPPD* pylorus-preserving pancreaticoduodenectomy, *IORT* intraoperative radiation therapy, *POPF* postoperative pancreatic fistula—graded according to the definition proposed by an international study group on pancreatic fistula (ISGPF)²¹

feeding,³² and antecolic reconstruction³³ were effective for reducing the incidence of DGE. The present study is the first to highlight the anastomotic method and show through multivariate analysis that the method of alimentary recon-

struction of duodenojejunostomy or gastrojejunostomy strongly influences the occurrence of DGE. The present result implied that DGE could be initiated by anastomotic edema or stenosis following a disturbance in blood supply,

Table 3 Multivariate logistic regression of risk factors for delayed gastric emptying (grade B or C)

Variables	Risk ratio	95% CI	<i>P</i> value
Hand-sewn reconstruction	2.888	1.094–7.623	0.03*
Sex (male)	2.189	1.145–4.183	0.02*
POPF (grade B or C)	2.371	1.365–4.117	0.002*

**P*<0.05

POPF postoperative pancreatic fistula—graded according to the definition proposed by an international study group on pancreatic fistula (ISGPF)²¹

which in turn may accelerate the progression of gastroparesis. Stapled reconstruction rather than hand-sewn reconstruction and single-layer anastomosis rather than double-layer anastomosis were associated with decreased risks for DGE and shorter hospital stay.

In this study, the definitions of POPF and DGE were determined on the basis of the international definition recently proposed by the International Study Group of Pancreatic Surgery^{11,21} to avoid detection bias resulting from the previously unclear definition. We regard grade A DGE as a non-relevant complication because the slight delay in starting a regular diet can be attributed to the discretion of the attending staff. When a patient has a high fever with relevant POPF in an early postoperative period, the patient may be prohibited from oral feeding irrespective of the presence of DGE, but this secondary fasting could not be clearly distinguished from real DGE in a retrospective analysis. Therefore, we considered only grade B or C DGE as a relevant complication.

Stapled alimentary reconstruction is now widely used in gastric, colorectal, or esophageal surgery.^{14–16} The possible advantages of stapled reconstruction are: standardized approach irrespective of the operating surgeon, institution, or surgical approach (open vs. laparoscopic); easy in performing the reconstruction; and possible avoidance of anastomotic edema and subsequent stricture formation. On the other hand, its disadvantages include: high cost, risk of bleeding at the anastomotic site, and mass-production of industrial waste.¹³ Notably, in our previous study, the operative costs were higher in the stapled group, but the overall hospital costs were higher in the hand-sewn group.¹³ Recent advances in laparoscopic surgery have made it possible to perform PD for lower grade malignancies and invasive cancer.¹⁷ Reconstruction of the stomach using circular a stapler can become an indispensable step of laparoscopic PD, and it is therefore mandatory to have a clear grasp of the results of employing stapled alimentary reconstruction during open PD.

Several authors have reported that some reconstructive procedures, such as antecolic reconstruction,^{30,31,33} antemesenteric reconstruction,¹⁰ and vertical reconstruction^{29,30,}

reduce the incidence of DGE. In some historical studies, the incidence of DGE was lower in the CW or SSPPD group than in the PPPD group.^{34,35} A possible reason for a higher incidence of DGE in the PPPD group is that duodenojejunostomy is narrower than gastrojejunostomy, while the remnant stomach is larger in the PPPD group than in the CW group, which might disturb the passage of the food. However, three prospective randomized trials and a meta-analysis have negated the advantage of the CW over PPPD groups.^{8,9,36,37} In our study, the incidence of DGE was comparable between CW (or SSPPD) and PPPD groups (23% vs. 17%, *P*=0.22). Based on a review of the literature and present results, it seems that PPPD is not inferior to CW or SSPPD, and that the operative procedure itself is not an essential factor for the occurrence of DGE.

In the multivariate analysis, POPF was an independent risk factor for DGE. Numerous researchers have reported that DGE develops more frequently in patients with POPF or peritonitis compared to those without such inflammatory complications.^{3,5,10,12,23,39} POPF remains the leading lethal complication after PD. The incidence of POPF (grade B or C, 36%) in our series is much higher than those of the previously reported series. This may be partly because the amylase concentration in the drain fluid was measured repeatedly until it decreased, and the decision to remove the drain was made carefully and gradually. Such prolonged drain placement may evoke retrograde infection in the surgical site and may increase the risk for POPF. The hospital stay of patients in this study was longer than that of patients in the United States and Europe, which may be attributed to the difference in insurance systems. However, the mortality rate in our 387 cases of PD was 1%, which is an acceptable rate and supports the safety of our perioperative management.

In the multivariate analysis, sex was also an independent risk factor for DGE; DGE was found more often in men than in women. This finding is supported by those of other reports,^{31,39} but the underlying pathogenesis remains unclear. In our institute, POPF was more frequent in men than in women,³⁸ which could be attributed to the increased incidence of DGE in men.

There is an argument that not stapled anastomosis, but Roux-en-Y limb reconstruction or Braun reconstruction might influence on the incidence of DGE. In patients with Braun anastomosis or Roux-en-Y limbs, pancreatic and the bile juice are diverted through the jejunal limb away from the stomach. However, no significant difference was found in the incidence of DGE between Braun or Roux-en-Y group and no-Braun group (Table 2). It is difficult to speculate the clinical impact of jejunal limb reconstruction on the occurrence of DGE in this study.

Table 4 Methods of duodenojejunostomy or gastrojejunostomy and surgical outcomes of pancreaticoduodenectomy

	Stapled reconstruction (n=69)		Hand-sewn reconstruction (n=313)		Hand-sewn reconstruction (n=313)		Hand-sewn reconstruction (n=313)		P value (stapled vs. hand-sewn)	Hand-sewn reconstruction (n=84)		Hand-sewn reconstruction (n=229)		P value (Single-layer vs. two-layer)
		n	%	n	%	Single-layer anastomosis (n=84)		Double-layer anastomosis (n=229)		Albert-Lembert anastomosis (n=198)	Layer-to-layer anastomosis (n=31)			
						n	%	n				%		
Gender, male	43	62%	188	60%	51	61%	116	59%	21	68%	0.73	21	68%	0.89
Disease, pancreatic cancer	28	41%	154	49%	40	48%	97	49%	17	55%	0.19	17	55%	0.74
Operative procedure														
PPP	52		247		68		151		28		0.52	28		0.59
CW or SSPD	17		66		16		47		3			3		
Operative time (min)	510	(240–990)	480	(210–1000)	540	(240–790)	510	(300–990)	360	(300–680)	0.82	360	(300–680)	0.04*
Blood loss, ≥750 mL	26	(38%)	167	(53%)	47	(56%)	106	(54%)	14	(45%)	0.02*	14	(45%)	0.58
Re-gastric drainage	2	(2.9%)	45	(14%)	3	(9.7%)	35	(17.7%)	7	(22.6%)	0.009*	7	(22.6%)	0.001*
POPF (grade B or C)	19	(27.5%)	119	(38%)	36	(42.9%)	72	(36.3%)	11	(35.5%)	0.10	11	(35.5%)	0.29
Results of UGI study														
Grade A	38		47		23		10		14		0.95	14		0.35
Grade B	10		12		3		6		3			3		
Grade C	5		5		2		1		2			2		
Days until regular diet (days)	5	(4–35)	8	(4–59)	6	(4–34)	8	(5–59)	7	(5–40)	<0.001*	7	(5–40)	<0.001*
DGE (grade B or C)	5	(7.2%)	65	(21%)	10	(11.9%)	48	(24.2%)	7	(22.6%)	0.009*	7	(22.6%)	0.02*
Hospital stay (days)	18	(10–60)	25	(9–324)	21	(10–84)	26	(9–324)	25	(14–60)	<0.001*	25	(14–60)	0.001*

* P<0.05

CW classical Whipple procedure, SSPD subtotal stomach preserving pancreaticoduodenectomy, PPPD pylorus-preserving pancreaticoduodenectomy, POPF postoperative pancreatic fistula—graded according to the definition proposed by an international study group on pancreatic fistula (ISGPF)²¹, Re-gastric drainage reinserion of nasogastric tube or opening the gastrostomy tube, UGI study upper gastrointestinal study using oral contrast medium, DGE delayed gastric emptying—defined by the International Study Group of Pancreatic Surgery (ISPGS)¹¹

This is a single institutional, retrospective cohort study of DGE in 387 patients who had undergone PD. We performed a multivariate analysis using logistic regression model and found that hand-sewn reconstruction was an independent risk factor of the occurrence of DGE. But we must concede that the large variability regarding the surgical procedures and techniques in our institute might make it difficult to detect the influence of a single variation on the occurrence of DGE. A multi-institutional, prospective randomized trial is necessary to objectively evaluate the clinical significance of stapled reconstruction during PD.

We experienced 5.7% anastomotic bleeding in four out of 70 patients who underwent stapled reconstruction, while 0% in 317 patients who underwent hand-sewn reconstruction, which should be a significant complication. Since the initial four bleeding events, we routinely performed intraoperative hemostasis on the anastomotic site via the jejunal loop, and thereafter, we experienced no bleeding in the subsequent 50 patients. Stapled reconstruction would be beneficial not only for patients by reducing DGE, but also for surgeons because it is a simple and easy method.

In conclusion, POPF, hand-sewn reconstruction, and sex (male) were independent risk factors for DGE in the present study on the cohort of 387 patients who had undergone PD. The method of alimentary reconstruction affected the occurrence of DGE. The incidence of DGE was more frequent in patients with hand-sewn reconstruction than in those with stapled reconstruction in our setting. A multi-institutional, prospective randomized trial is necessary to objectively evaluate the clinical significance of stapled reconstruction during PD.

References

1. Bassi C, Falconi M, Salvia R, Mascetta G, Molinari E, Pederzoli P. Management of complications after pancreaticoduodenectomy in a high volume centre: results on 150 consecutive patients. *Dig Surg* 2001; 18:453–7.
2. Buchler MW, Wagner M, Schmied BM, Uhl W, Friess H, Z'Graggen K. Changes in morbidity after pancreatic resection: toward the end of completion pancreatectomy. *Arch Surg* 2003; 138:1310–4.
3. Lermite E, Pessaux P, Brehant O, Teyssedou C, Pelletier I, Etienne S, Arnaud JP. Risk factors of pancreatic fistula and delayed gastric emptying after pancreaticoduodenectomy with pancreaticogastrostomy. *J Am Coll Surg* 2007; 204:588–96.
4. DeOliveira ML, Winter JM, Schafer M, Cunningham SC, Cameron JL, Yeo CJ, Clavien PA. Assessment of complications after pancreatic surgery: A novel grading system applied to 633 patients undergoing pancreaticoduodenectomy. *Ann Surg* 2006; 244:931–7.
5. Tanaka M. Gastroparesis after a pylorus-preserving pancreatoduodenectomy. *Surg Today* 2005; 35:345–50.
6. Warshaw AL, Torchiana DL. Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. *Surg Gynecol Obstet* 1985; 160:1–4.
7. Yeo CJ, Barry MK, Sauter PK, Sostre S, Lillemoe KD, Pitt HA, Cameron JL. Erythromycin accelerates gastric emptying after pancreaticoduodenectomy. A prospective, randomized, placebo-controlled trial. *Ann Surg* 1993; 218:229–38.
8. Lin PW, Lin YJ. Prospective randomized comparison between pylorus preserving and standard pancreaticoduodenectomy. *Br J Surg* 1999; 86:603–7.
9. Seiler CA, Wagner M, Sadowski C, Kulli C, Buchler MW. Randomized prospective trial of pylorus-preserving vs. classic duodenopancreatectomy (Whipple procedure): initial clinical results. *J Gastrointest Surg* 2000; 4:443–52.
10. Park YC, Kim SW, Jang JY, Ahn YJ, Park YH. Factors influencing delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. *J Am Coll Surg* 2003; 196:859–65.
11. Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Yeo CJ, Büchler MW. Delayed gastric emptying (DGE) after pancreatic surgery: definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2007; 142:761–8.
12. Park JS, Hwang HK, Kim JK, Cho SI, Yoon DS, Lee WJ, Chi HS. Clinical validation and risk factors for delayed gastric emptying based on the International Study Group of Pancreatic Surgery (ISGPS) Classification. *Surgery* 2009; 146:882–7.
13. Sakamoto Y, Kajiwara T, Esaki M, Shimada K, Nara S, Kosuge T. Roux-en-Y reconstruction using staplers during pancreaticoduodenectomy: results of a prospective preliminary study. *Surg Today* 2009; 39:32–7.
14. Nomura S, Sasako M, Katai H, Sano T, Maruyama K. Decreasing complication rates with stapled esophagojejunostomy following a learning curve. *Gastric Cancer* 2000; 3:97–101.
15. Hansen O, Schwenk W, Hucke HP, Stoch W. Colorectal stapled anastomoses. Experiences and results. *Dis Colon Rectum* 1996; 39:30–6.
16. Köckerling F, Rose J, Schneider C, Scheidbach H, Scheuerlein H, Reymond MA, Reck T, Konradt J, Bruch HP, Zornig C, Bärlechner E, Kuthe A, Szinicz G, Richter HA, Hohenberger W. Laparoscopic colorectal anastomosis: risk of postoperative leakage. Results of a multicenter study. Laparoscopic Colorectal Surgery Study Group (LCSSG). *Surg Endosc* 1999; 13:639–44.
17. Kendrick ML, Cusati D. Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. *Arch Surg* 2010; 145:19–23.
18. Shimada K, Sano T, Sakamoto Y, Kosuge T. Clinical implications of combined portal vein resection as a palliative procedure in patients undergoing pancreaticoduodenectomy for pancreatic head carcinoma. *Ann Surg Oncol* 2006; 13:1569–78.
19. Sakamoto Y, Shimada K, Esaki M, Kajiwara T, Sano T, Kosuge T. Wrapping the stump of the gastroduodenal artery using the falciform ligament during pancreaticoduodenectomy. *J Am Coll Surg* 2007; 204:334–6.
20. Kakita A, Yoshida M, Takahashi T. History of pancreaticojejunostomy in pancreaticoduodenectomy: development of a more reliable anastomosis technique. *J Hepatobiliary Pancreat Surg* 2001; 8:230–7.
21. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005; 138:8–13.
22. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; 240(2):205–13.
23. van Berge Henegouwen MI, van Gulik TM, DeWit LT, Allema JH, Rauws EA, Obertop H, Gouma DJ. Delayed gastric emptying

- after standard pancreaticoduodenectomy versus pylorus-preserving pancreaticoduodenectomy: an analysis of 200 consecutive patients. *J Am Coll Surg* 1997; 185:388–95.
24. Ohwada S, Satoh Y, Kawate S, Yamada T, Kawamura O, Koyama T, Yoshimura S, Tomizawa N, Ogawa T, Morishita Y. Low-dose erythromycin reduces delayed gastric emptying and improves gastric motility after Billroth I pylorus-preserving pancreaticoduodenectomy. *Ann Surg* 2001; 234:668–74.
 25. Tanaka M, Sarr MG. Role of the duodenum in the control of canine gastrointestinal motility. *Gastroenterology* 1988; 94:622–9.
 26. Kim DK, Hindenburg AA, Sharma SK, Suk CH, Gress FG, Staszewski H, Grendell JH, Reed WP. Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy? *Ann Surg Oncol* 2005; 12:222–7.
 27. Ueno T, Tanaka A, Hamanaka Y, Tsurumi M, Suzuki T. A proposal mechanism of early delayed gastric emptying after pylorus preserving pancreatoduodenectomy. *Hepatogastroenterol* 1995; 42:269–74.
 28. Martignoni ME, Friess H, Sell F, Ricken L, Shrikhande S, Kulli C, Büchler MW. Enteral nutrition prolongs delayed gastric emptying in patients after Whipple resection. *Am J Surg* 2000; 180:18–23.
 29. Murakami H, Yasue M. A vertical stomach reconstruction after pylorus-preserving pancreaticoduodenectomy. *Am J Surg* 2001; 181:149–52.
 30. Sugiyama M, Abe N, Ueki H, Masaki T, Mori T, Atomi Y. A new reconstruction method for preventing delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. *Am J Surg* 2004; 187:743–6.
 31. Hartel M, Wente MN, Hinz U, Kleeff J, Wagner M, Müller MW, Friess H, Büchler MW. Effect of antecolic reconstruction on delayed gastric emptying after the pylorus-preserving Whipple procedure. *Arch Surg* 2005; 140:1094–9.
 32. van Berge Henegouwen MI, Akkermans LM, van Gulik TM, Masclee AA, Moojen TM, Obertop H, Gouma DJ. Prospective, randomized trial on the effect of cyclic versus continuous enteral nutrition on postoperative gastric function after pylorus-preserving pancreatoduodenectomy. *Ann Surg* 1997; 226:677–87.
 33. Tani M, Terasawa H, Kawai M, Ina S, Hirono S, Uchiyama K, Yamaue H. Improvement of delayed gastric emptying in pylorus-preserving pancreaticoduodenectomy. Results of a prospective, randomized, controlled trial. *Ann Surg* 2006; 243:316–20.
 34. Hayashibe A, Kameyama M, Shinbo M, Makimoto S. The surgical procedure and clinical results of subtotal stomach preserving pancreaticoduodenectomy (SSPPD) in comparison with pylorus preserving pancreaticoduodenectomy (PPPD). *J Surg Oncol* 2007; 95:106–9.
 35. Akizuki E, Kimura Y, Nobuoka T, Imamura M, Nishidate T, Mizuguchi T, Furuhashi T, Hirata K. Prospective nonrandomized comparison between pylorus-preserving and subtotal stomach-preserving pancreaticoduodenectomy from the perspectives of DGE occurrence and postoperative digestive functions. *J Gastrointest Surg* 2008; 12:1185–92.
 36. Tran KT, Smeenk HG, van Eijck CH, Kazemier G, Hop WC, Greve JW, Terpstra OT, Zijlstra JA, Klinkert P, Jeekel H. Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure. A prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. *Ann Surg* 2004; 240:738–45.
 37. Diener MK, Knaebel HP, Heukauffer C, Antes G, Büchler MW, Seiler CM. A systematic review and meta-analysis of pylorus-preserving versus classical pancreaticoduodenectomy for surgical treatment of periampullary and pancreatic carcinoma. *Ann Surg* 2007; 245:187–200.
 38. Kajiwara T, Sakamoto Y, Morofuji N, Nara S, Esaki M, Shimada K, Kosuge T. An analysis of risk factors for pancreatic fistula after pancreaticoduodenectomy: clinical impact of bile juice infection on day 1. *Langenbecks Arch Surg* 2010; 395:707–12.
 39. Akizuki E, Kimura Y, Nobuoka T, Imamura M, Nagayama M, Sonoda T, Hirata K. Reconsideration of postoperative oral intake tolerance after pancreaticoduodenectomy: prospective consecutive analysis of delayed gastric emptying according to the ISGPS definition and the amount of dietary intake. *Ann Surg* 2009; 249:986–94.