

A comparative study on the complications of conventional and end-to-side inserting pancreatojejunostomy after pancreaticoduodenectomy

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Abstract

Purpose Pancreatico-digestive anastomosis is important in ensuring the safety of pancreaticoduodenectomy. This study compared the postoperative complications of a newly developed method of inserting end-to-side pancreatojejunostomy with the conventional pancreatojejunostomy after pancreaticoduodenectomy.

Methods From April 2012 to December 2015, 108 consecutive patients underwent pancreaticoduodenectomy at Kumamoto University Hospital. A modified child's reconstruction was performed with the inserting or conventional pancreatojejunostomy. The clinical course and the incidence of postoperative complications were retrospectively evaluated.

Results Five patients were excluded, four who underwent hepato-pancreatoduodenectomy and one who did not require pancreatojejunostomy because of an atrophic pancreatic remnant. Of the 103 patients that were included in the analysis, 41 and 62 underwent surgery with the inserting and conventional methods, respectively. The incidence of postoperative Clavien–Dindo grade > II complications was similar in the two groups [36.6 % (15/41) vs 27.4 % (17/62)]. However, the rates of grade C postoperative pancreatic fistula [7.3 % (3/41) vs 0 % (0/62) $P = 0.030$] and re-operation for postoperative complications [14.6 % (6/41) vs 3.2 % (2/62), $P = 0.034$] were significantly higher in the

inserting group than in the conventional group. There were no in-hospital deaths in either group.

Conclusions The conventional pancreatojejunostomy is safer than the end-to-side inserting pancreatojejunostomy, as the latter is associated with a risk of severe complications. Improvements in pancreatico-digestive anastomosis techniques are required.

Keywords Pancreaticoduodenectomy · Pancreatojejunostomy · Complication · Pancreatic fistula

Introduction

Improvements in surgical techniques and perioperative management have reduced operative mortality rates after pancreaticoduodenectomy (PD) to less than 5 % in high-volume centers [1–5]. However, the morbidity rates remain high, ranging from 30 to 40 % [6–8]. Postoperative pancreatic fistula (POPF), which contributes to prolonged hospitalization and mortality, is the most common complication after PD [1, 9–11]. Thus, pancreatico-digestive anastomosis is important for ensuring the safety of PD.

The normal pancreas is soft and extremely vulnerable to any handling. A smaller number of stitches and avoiding the excessive tightening of sutures have been reported to reduce the incidence of pancreatic injury in rats [12]. In general, multiple stitches are used in pancreatico-digestive anastomosis. A recently developed method of pancreatico-digestive anastomosis, called binding pancreatojejunostomy (PJ), involves the insertion of the pancreatic stump into the jejunum in an end-to-end manner, resulting in fewer stitches than the conventional duct-to-mucosa PJ [13–15]. Pancreatic juice, which is secreted by the transected pancreatic duct branches facing the pancreatic

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stump, drains into the jejunal lumen [14]. As a modification of this method, we introduced a new method of end-to-side inserting PJ, in which the pancreatic stump is deeply inserted into the jejunum in an end-to-side manner and tightened with a purse string suture, independent of the size of the pancreas and jejunum [16]. However, we noticed that end-to-side inserting PJ was associated with a possible risk of severe complications (as described in this study) and , therefore, decided to discontinue inserting PJ and to adopt the conventional PJ.

This historical cohort study compared the postoperative complications of end-to-side inserting PJ with the conventional PJ performed in patients undergoing PD.

Patients and methods

Patients and data collection

Between April 2012 and December 2015, 108 consecutive patients underwent subtotal stomach preserving PD at the Department of Gastroenterological Surgery of Kumamoto University Hospital. Each patient provided written informed consent prior to surgery. All the procedures in this study were in accordance with the guidelines of the Declaration of Helsinki.

The perioperative management of the patients has been described previously [11, 16]. Postoperative complications were defined according to the Clavien–Dindo scale [17]. POPF was assessed according to the definitions of the International Study Group for Pancreatic Surgery [18]. Operative and postoperative data were collected and stored in an electronic database. This historical cohort study analyzed the postoperative complications of PJ in patients undergoing PD.

The surgical technique for PD

Patients with malignant disease underwent D2 lymph node dissection [19, 20]. If invasion of the superior mesenteric and portal veins was observed, the involved vasculature was resected and reconstructed. The pancreatic neck was cut with a surgical scalpel. After resection, the jejunal cut end was moved up retrocolically. PJ was performed as described below. Hepatico-jejunostomy and gastro-jejunostomy were performed distal to the PJ site using a modified Child's reconstruction. A peritoneal drainage tube (a 6.3-mm closed drain) was placed on the ventral side of the PJ site. The amylase levels in the drain output were routinely measured until at least the third postoperative day. When POPF was not observed, the drain was removed on the third postoperative day. The operations, which included PJ in both two groups, were performed by two senior

pancreatic surgeons. Abdominal complications, such as POPF, abdominal abscess, or abdominal hemorrhage, were usually treated by persistent drainage, ultrasonography-guided or computed tomography-guided drainage, or intervention. However, when those treatments were not able to control the complications, we did not hesitate to perform a re-operation before the patients suffered from a severe complication, such as sepsis or shock.

The surgical technique for the end-to-side inserting PJ

End-to-side inserting PJ was performed as described previously [16]. Briefly, the pancreatic stump was isolated from the retroperitoneum with a margin of up to 30 mm. An external pancreatic duct stent tube was inserted into the main pancreatic duct in all the cases. An incision of the same diameter as the pancreatic stump was made on the jejunum. Purse string sutures using absorbable 3-0 monofilament thread were applied around the jejunal incision to seal the site of anastomosis. The pancreatic stump was inserted end-to-side into the jejunal incision. Five-to-six stay sutures of absorbable 4-0 monofilament thread were also applied between the pancreas and the jejunal incision to secure the depth of insertion and to prevent the pancreatic stump from separating from the jejunum. Inserting PJ was performed from April 2012 to October 2013.

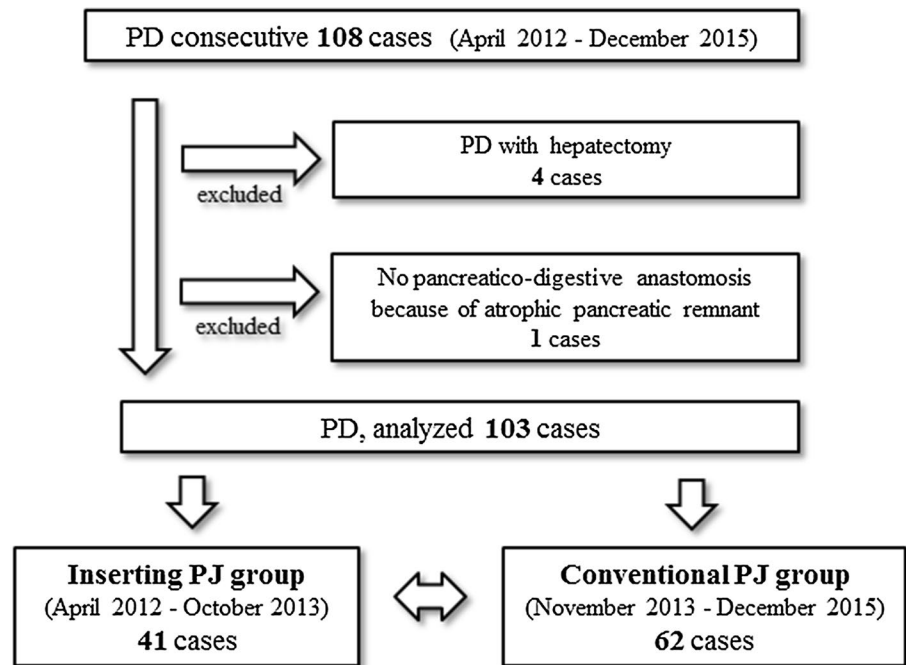
The surgical technique for conventional PJ

The conventional PJ was also performed using end-to-side anastomosis. A small incision, of the same size as the main pancreatic duct, was made on the jejunal wall. Eight sutures of 5-0 monofilament thread were applied through the pancreatic duct and pancreatic parenchyma, followed by the entire layer of the jejunum. An external pancreatic duct stent tube was inserted into the main pancreatic duct in all the cases, prior to the tying of the duct-to-jejunum sutures. Four sutures of 2-0 monofilament thread were inserted through the entire thickness of the pancreas and the seromuscular layer of the jejunum. These sutures were tied to secure a tight fit between the jejunal wall and the pancreatic cut end. The conventional PJ was performed from November 2013 to December 2015.

Statistical analysis

Descriptive statistics are presented as the median (range) or the number (percentage), as appropriate. All the statistical analyses were performed using the SAS software program (version 9.1; SAS Institute, Inc., Cary, NC, USA). The parameters in the patient groups were compared using the Mann–Whitney *U* test or the Chi-squared test. *P* values of <0.05 were considered to indicate statistical significance.

Fig. 1 Diagram of the patient flow in the present study. *PJ* pancreaticojejunostomy, *PD* pancreaticoduodenectomy



Results

Patient characteristics

Of the 108 consecutive patients who underwent PD during the study period, five were excluded, four who underwent PD with hepatectomy, and one who did not require PJ because of an atrophic pancreatic remnant (Fig. 1). The 103 patients who were analyzed included 41 who underwent inserting PJ and 62 who underwent the conventional PJ. Table 1 shows the demographic and clinical characteristics of these patients. The inserting PJ group included 25 men and 16 women with a median age of 68 years (range 34–85 years) and a median body mass index (BMI) of 23.0 kg/m² (range 15.8–32.0 kg/m²). The conventional PJ group included 37 men and 25 women with a median age of 71 years (range 32–85 years) and a median BMI of 22.35 kg/m² (range 16.2–35.8 kg/m²). There were no significant differences between the groups in age, sex, or BMI. The distribution of the performance status was also similar in the inserting and conventional groups, as were the rates of prior laparotomy (17.1 vs 12.9 %) and preoperative bile duct drainage (39.0 vs 43.5 %). There were no significant differences in the patients' comorbidities (diabetes mellitus, ischemic heart disease, and respiratory disease) or diagnoses. The diagnoses of the inserting PJ group included pancreatic cancer ($n = 18$, 43.9 %), bile duct cancer ($n = 9$, 22.0 %), and other conditions ($n = 14$). The diagnoses of the conventional group included pancreatic cancer ($n = 27$ patients, 43.5 %), bile duct cancer ($n = 12$, 19.4 %), and other conditions ($n = 23$).

Operative findings

The intraoperative parameters are shown in Table 2. The inserting and conventional PJ groups had similar median operating times of 426 min (range 291–840 min) and 450 min (range 353–802 min), respectively, and a median intraoperative blood loss of 602 g (range 77–3623 g) and 676 g (range 110–3389 g), respectively. Three patients (7.1 %) in the inserting group and 12 (19.4 %) in the conventional group underwent superior mesenteric and portal vein resection and reconstruction, and 11 (26.8 %) and 16 (25.8 %) patients, respectively, received blood transfusion; the differences between the groups were not statistically significant. The pancreatic texture was soft in 23 (56.1 %) patients in the inserting group and 32 (51.6 %) in the conventional group. The median diameter of the main pancreatic duct remnant was 3 (range 2–6 mm) and 3 mm (range 2–7 mm), in the inserting and conventional groups, respectively. The median time required for PJ was significantly shorter in the inserting group (17 min, range 12–24 min) than in the conventional group (24 min, range 18–35 min; $P = 0.008$).

Postoperative outcomes

The postoperative short-term outcomes are shown in Table 2. There was no significant difference in the incidence of postoperative Clavien–Dindo grade > II complications in the inserting (36.6 %, 15/41) and conventional (27.4 %, 17/62) groups. Table 3 shows the details of postoperative complications according to the Clavien–Dindo

Table 1 Demographic and clinical characteristics of the included patients

	Inserting group (<i>n</i> = 41)	Conventional group (<i>n</i> = 62)	<i>P</i> value
Male:female, <i>n</i>	25:16	37:25	0.895
Median age (range), years	68 (34–85)	71 (32–85)	0.370
Performance status (0:1:2), <i>n</i>	30:10:1	49:13:0	0.945
Median body mass index (range), kg/m ²	23.0 (15.8–32.0)	22.35 (16.2–35.8)	0.290
Previous laparotomy, <i>n</i> (%)	7 (17.1)	8 (12.9)	0.763
Preoperative bile duct drainage, <i>n</i> (%)	16 (39.0)	27 (43.5)	0.649
Comorbidities, <i>n</i> (%)			
Diabetes mellitus	8 (19.5)	15 (24.2)	0.751
Ischemic heart disease	4 (9.8)	5 (8.1)	0.953
Respiratory disease	4 (9.8)	7 (11.3)	0.937
Final diagnosis, <i>n</i> (%)			
Pancreatic cancer	18 (43.9)	27 (43.5)	0.999
Bile duct cancer	9 (22.0)	12 (19.4)	
IPMN	4 (9.8)	5 (8.1)	
Vater's papilla cancer	3 (7.3)	8 (12.9)	
NET	3 (7.3)	6 (9.7)	
Metastasis from other organs	1 (2.4)	1 (1.6)	
GIST	1 (2.4)	1 (1.6)	
Chronic pancreatitis	1 (2.4)	0	
SPT	1 (2.4)	0	
Duodenal cancer	0	2 (3.2)	

GIST gastrointestinal stromal tumor, *IPMN* intraductal papillary mucinous neoplasm, *NET* neuroendocrine tumor, *SPT* solid pseudopapillary tumor

Table 2 Operative findings and postoperative outcomes

	Inserting group (<i>n</i> = 41)	Conventional group (<i>n</i> = 62)	<i>P</i> value
Median (range) operation time, min	426 (291–840)	450 (353–802)	0.136
SMV-PV resection and reconstruction, <i>n</i> (%)	3 (7.1)	12 (19.4)	0.158
Median (range) intraoperative bleeding, g	602 (77–3623)	676 (110–3389)	0.432
Blood transfusions, <i>n</i> (%)	11 (26.8)	16 (25.8)	0.909
Median (range) diameter of main pancreatic duct, mm	3 (2–6)	3 (2–7)	0.171
Pancreatic texture (soft:hard)	23:18	32:30	0.807
Median (range) time needed for PJ, min	17 (12–24)	24 (18–35)	0.008
Complications (Clavien–Dindo > II), <i>n</i> (%)	15 (36.6)	17 (27.4)	0.325
Re-laparotomy for complication, <i>n</i> (%)	6 (14.6)	2 (3.2)	0.034
Median (range) postoperative day of removal of the abdominal drain	4 (3–41)	4 (3–45)	0.017
Median (range) postoperative hospital stay, days	23 (13–46)	25 (13–53)	0.446
In-hospital mortality	0	0	–

SMV-PV superior mesenteric and portal vein

scale. The grades complications that occurred in the inserting group were classified as Clavien–Dindo grade II in 3 patients, grade III in 11 patients, and grade IV in 1 patient. In contrast, grades complications that occurred in the conventional group were classified as Clavien–Dindo grade II in 2 patients and grade III in 15 patients. The most frequent complication in both groups was grade B or C POPF.

Importantly, the incidence of re-laparotomy for postoperative complications was significantly higher in the inserting than in the conventional group [14.6 % (6/41) vs 3.2 % (2/62), *P* = 0.034] (Table 2). Three patients in the inserting group underwent re-laparotomy due to grade C POPF, two for abdominal abscesses and one for repeated hemorrhage from the pancreatic cut end into the jejunum. In

Table 3 Details of the postoperative complications

	Inserting group (n = 41)	Conventional group (n = 62)	P value
Complication n (%) (Clavien–Dindo scale)			
Grade B or C POPF	5 (12.2) (III 4, IV 1)	11 (17.7) (III 11)	0.930
Abdominal abscess	5 (12.2) (II 1, III 4)	2 (3.3) (III 2)	
Abdominal hemorrhage	2 (4.9) (II 1, III 1)	2 (3.3) (II 1, III 1)	
Delayed gastric emptying	1 (2.4) (II 1)	0	
Venous thrombosis	1 (2.4) (III 1)	1 (1.6) (II 1)	
Pneumoniae	1 (2.4) (III 1)	0	
Bile leakage	0	1 (1.6) (III 1)	

POPF postoperative pancreatic fistula

comparison, one patient each underwent re-laparotomy due to bile leakage and abdominal abscess in the conventional group. The median day of abdominal drain removal was postoperative day 4 (3–41) in the inserting group and postoperative day 4 (3–45) in the conventional group; the difference was not statistically significant. The median duration of postoperative hospital stay did not differ to a statistically significant extent in the inserting (23 days; range 13–46 days) and conventional (25 days; range 13–53 days) groups. There were no in-hospital deaths in either group.

Details of POPF

Figure 2 shows the amylase levels in the drain output. The amylase levels were high in both groups on postoperative day 1 and gradually decreased on postoperative days 2 and 3. The median amylase levels were significantly lower in the inserting group than in the conventional group on postoperative days 1 ($P = 0.043$), 2 ($P = 0.029$), and 3 ($P = 0.006$).

Figure 3 shows the incidence of POPF in each group. Although the incidence of total POPF (grades A, B, and C) was similar in the inserting (17.1 %, 7/41) and conventional (27.4 %, 17/61) groups ($P = 0.328$), the incidence of grade C POPF in the inserting group was significantly higher than that in the conventional group (7.3 vs 0 %, $P = 0.030$).

Discussion

This study compared postoperative outcomes of the inserting and conventional PJ. Despite the retrospective design of this study, the patient characteristics and conditions

Amylase concentration of drain output (IU/l)

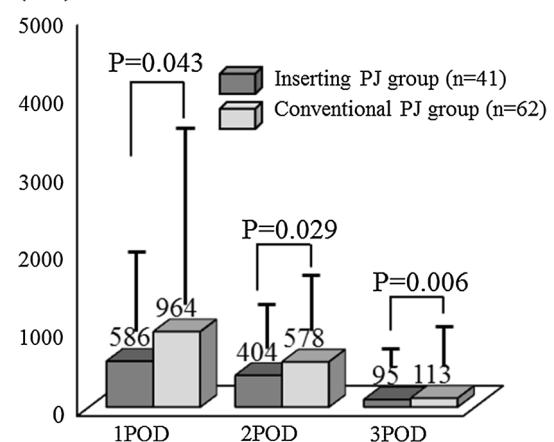
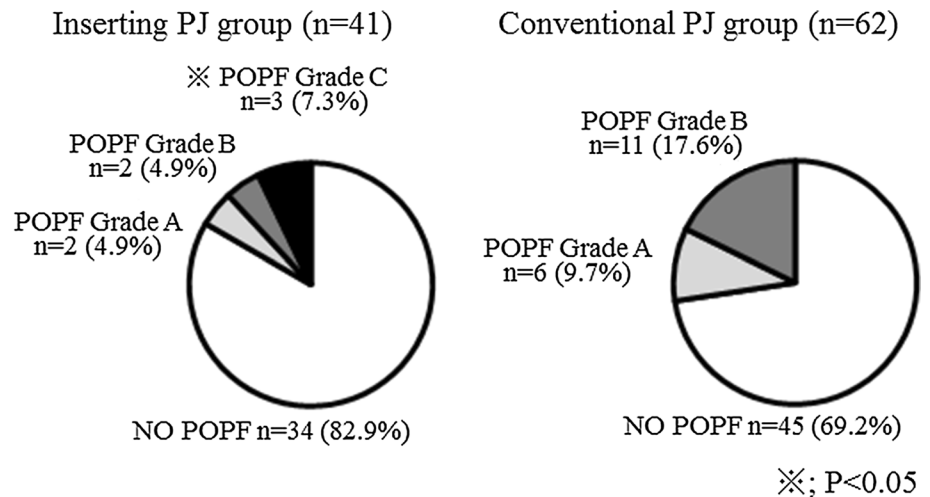


Fig. 2 Postoperative amylase levels of the abdominal closed drains. Peritoneal closed drains were placed near the PJ of patients, and the amylase levels in the inserting PJ (dark gray bars) and conventional PJ (light gray bars) groups were measured on postoperative days 1, 2, and 3. P values of <0.05 were considered to indicate a statistically significant difference. PJ pancreaticojejunostomy

for PJ, such as the pancreatic texture and diameter of the pancreatic duct, were well-balanced in the two groups. The technique used for inserting PJ is simple to perform and requires fewer stitches than the conventional PJ [16]. Similarly, although the total operating time was similar in the two groups, this study found that the time required for inserting PJ was significantly shorter than that required for the conventional PJ.

Following inserting PJ, pancreatic secretions from the transected cut end drain into the jejunal lumen [14, 16]. This study showed that the level of amylase in the drain

Fig. 3 Details of POPF. The incidence of each grade of POPF, as defined by the International Study Group for Pancreatic Surgery, was determined in the inserting PJ (*left panel*) and conventional PJ (*right panel*) groups. *P* values of <0.05 were considered to indicate a statistically significant difference. *PJ* pancreaticojejunostomy, *POPF* postoperative pancreatic fistula



output with the inserting method was significantly lower than that with the conventional method. Although the incidence of total POPF was lower in the inserting group, this difference was not statistically significant. However, the risks of grade C POPF and re-laparotomy were significantly higher with the inserting method. This was likely due to the large incision made in the jejunum causing severe leakage following the development of POPF. In contrast, the conventional method requires only a small incision in the jejunum and thus minimizes the risk of severe leakage.

One patient who underwent inserting PJ developed repeat hemorrhage from the pancreatic cut end into the jejunal lumen. The walls of the blood vessels at the pancreatic cut end can be digested by trypsin, elastase, and other pancreatic exocrine enzymes, causing late hemorrhage [21]. During the conventional PJ, but not inserting PJ, the pancreatic cut end was fit tightly to the jejunal wall. This may be a reason for repeated hemorrhage into the jejunal lumen in patients undergoing inserting PJ.

The major limitation of this study was its retrospective design. Prospective trials in larger cohorts are needed to fully evaluate the efficacy and safety of inserting PJ in comparison to the conventional PJ after PD. In addition, inserting PJ could be compared to other types of pancreatico-digestive anastomoses, such as pancreatico-gastrostomy (PG). Recently, several clinical reports have argued that PG is superior to PJ for the prevention of POPF [22]. It is suggested that inserting PG is a useful technique for the pancreatico-digestive anastomoses after PD [23]. On the other hand, the scientific evidence to support the use of pancreatico-digestive anastomosis has not been sufficiently established. The efficacy and safety of PJ have been analyzed in animal models, including dog and porcine models [24, 25]. However, no animal studies have compared PG with PJ.

In conclusion, the conventional PJ was apparently safer than inserting PJ, as the latter was associated with a higher risk of severe complications, despite the shorter anastomosis time and reduced drain amylase level. Improvements in pancreatico-digestive anastomosis are thus needed.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest in association with the present study.

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