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A Single-site Interventional Study on the Contemporary Relevance of Braun Enteroenterostomy After Pancreaticoduodenectomy

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Abstract. *Background/Aim: Braun enteroenterostomy following pancreaticoduodenectomy is a standard procedure. It has been reported to decrease bile reflux and vomiting, prevent reflux gastritis and delay gastric emptying (DGE). However, some reports suggest that the incidence of DGE is unaffected with this procedure. Therefore, in this study, we aimed to investigate whether Braun enteroenterostomy was effective after pancreaticoduodenectomy. Patients and Methods: A total of 145 patients who underwent pancreaticoduodenectomy were enrolled and divided into 2 groups i.e., 51 patients with Braun enteroenterostomy (B group) and 94 patients without Braun enteroenterostomy (non-B group). We compared the perioperative data of the patients. Patients who reported postoperative symptoms underwent gastrointestinal endoscopic evaluation. Results: The incidence of DGE was 7.4% (7/94) and 1.9% (1/51) in the non-B and B groups, respectively (p=0.36), with no significant difference between the groups. During follow-up, some patients reported symptoms including epigastralgia, nausea and melena. The incidence of these symptoms was 27.7% (26 patients; 26/94) and 23.5% (12 patients; 12/51) in non-B and B groups, respectively. Regarding gastrointestinal endoscopic findings, the incidence of anastomotic ulcer was 7.7% (2/26) and 16.7% (2/12) in non-B and B groups, respectively (p=0.40). Bile reflux incidence was 30.8% (8/26) and 0% (0/12) in non-B and B groups, respectively (p=0.03). Conclusion: Though Braun enteroenterostomy was related to bile reflux, it did not affect the incidence of anastomotic and gastric ulcers or DGE. Therefore, it may not be a necessary procedure after pancreaticoduodenectomy.*

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Key Words: Anastomotic ulcer, Braun enteroenterostomy, child reconstruction procedure, pancreaticoduodenectomy, gastrointestinal endoscopy.

Pancreaticoduodenectomy (PD), first described by Allen Whipple in 1935 (1), is a well-established and effective treatment for operable pancreatic head and periampullary tumors; however, the incidence of postoperative complications is problematic (2). Postoperative pancreatic fistula (POPF) and delayed gastric emptying (DGE) are the two key complications, with the incidence of POPF and DGE reported to be 20-30% (3, 4) and 2-10% (5-7), respectively. DGE may not be life-threatening; however, it affects the length of hospital stay (8) and impairs quality of life in the postoperative period (9). Bile reflux is reported to cause DGE (10). Prevention of bile reflux through Braun enteroenterostomy has been reported to reduce the incidence of DGE (9, 11). Some studies have reported that Braun enteroenterostomy is effective in preventing DGE and shortening the duration of postoperative hospital stay (12, 13), and others have reported that DGE occurred irrespective of whether Braun enteroenterostomy was performed. Therefore, the relevance of Braun enteroenterostomy after PD is questionable. This study investigates whether Braun enteroenterostomy after PD is a necessary procedure and whether it is associated with the incidence of complications.

Patients and Methods

Study design and study population. This is a single-center, prospective interventional study conducted at the Nagasaki University Hospital. Ethical approval was obtained from the hospital ethics committee (approval number: 10112948). Consecutive patients who

underwent PD between August 2010 and November 2015 were enrolled in this study. The follow-up period was 1 year after the surgery. The inclusion criteria were as follows: 1) patients diagnosed with pancreatic, bile duct, and gallbladder cancers; intraductal papillary mucinous neoplasm and carcinoma; Vater papillary, pancreatic neuroendocrine, serous cystic and metastatic pancreatic tumors; 2) patients who underwent PD, pylorus-preserving pancreaticoduodenectomy, and subtotal stomach-preserving pancreaticoduodenectomy. Cases with other organ complications were excluded. Finally, 145 patients were enrolled and the number of patients with Braun enteroenterostomy (B group) and without Braun enteroenterostomy (non-B group) were 51 and 94, respectively. All patients received postoperative H2 blockers or proton pump inhibitors. In addition, endoscopy was performed in patients who complained of postoperative gastrointestinal symptoms.

Operative procedure. In cases of invasive carcinoma of the head of the pancreas with portal invasion, portal vein reconstruction with end-to-end anastomosis was performed. For reconstruction, pancreaticojejunostomy with duct-to-mucosa anastomosis was performed in all patients. In addition, a short 5 Fr stent was inserted in all cases. Choledochojejunostomy *via* retrocolic and gastrojejunostomy *via* antecolic approaches were performed, with vertical mattress and Gambee sutures in the posterior and anterior walls, respectively. Braun enteroenterostomy was randomly performed. Two closed suction drains were placed behind the choledochojejunostomy and near the pancreaticojejunostomy, and brought out through incisions on both sides of the abdominal wall. Laparoscopic procedures were performed for low-grade malignant tumors.

Clinical assessment. General and clinical information such as age, sex, disease type, oral intake start date, and the length of hospital stay were collected from medical records. The surgery type (laparoscopy or open), operation time, and operative blood loss were collected from operative procedure data. Postoperative complications until discharge were evaluated using the Clavien–Dindo Classification system (CDC) (14) that includes five grades ranging from grade I to V. Postoperative complications with a CDC grade of IIIa or more were considered as clinically significant. POPF was defined based on the International Study Group on Pancreatic Fistula criteria (15) and classified into 3 grades as follows: BL, a transient fistula with the patient in good condition; B, fistula leading to infections requiring persistent drainage; and C, fistula resulting in bad prognosis and re-operation. Grade B or C fistulae were considered as clinically relevant POPF. DGE was defined according to the International Study Group for Pancreatic Surgery definition (16) and graded as follows: A, inability to tolerate solid oral intake by postoperative day (POD) 7, usually without vomiting; B, inability to tolerate solid oral intake by POD 14, with or without vomiting; and C, inability to tolerate solid oral intake by POD 21, with or without vomiting. In addition, gastrointestinal endoscopy was performed in patients presenting with postoperative symptoms. Finally, perioperative characteristics of the patients were compared between both groups and the incidence of postoperative gastrointestinal symptoms were considered the primary endpoint, based on the data and results.

Statistical analysis. The difference between the mean values was compared using either Student's *t*-test or the Mann–Whitney *U*-test. *p*-Values less than 0.05 were considered statistically significant.

Results

Patients' demographic and clinical data. The sex ratio (male/female) was 32/19 and 55/39 in the B and non-B groups, respectively. The median age was 70 years in both groups. Table I shows the pre- and intraoperative data.

Table II shows the postoperative data. The incidence of POPF over grade B was 11.7% (11/94) and 7.8% (4/51) in the non-B and B groups, respectively (p=0.77). The total incidence of DGE was 7.4% (7/94) and 1.9% (1/51) in the non-B and B groups, respectively (p=0.36). In fact, the incidence of DGE for Grades A, B, and C in the non-B group was, in order, 3.2%, 2.1%, and 2.1%. On the other hand, the incidence of DGE for Grades A, B, and C in the B group was, in order, 0%, 0%, and 1.9%. There was no significant difference between the groups regarding other complications in CDC (p=0.055). The oral intake start date (median 2 days *vs*. 2 days; p=0.35) and length of hospital stay (median 22 days *vs*. 24 days; p=0.66) were not significantly different between the groups. Finally, there was no significant difference in the incidence of gastrointestinal symptoms between the groups [23.5% (12/51) *vs*. 27.7% (26/94), p=0.59].

Follow-up with gastrointestinal endoscopy. After surgery, 12 (23.5%, 12/51) and 26 (27.7%, 26/94) patients in the B and non-B groups, respectively, underwent gastrointestinal endoscopic evaluation for epigastralgia, anemia, nausea and vomiting, melena, and other symptoms (10, 6, 6, 5 and 3 patients, respectively). As shown in Table III, the incidence of gastric ulcers was 15.4% (4/26) and 0% (0/12) in the non-B and B groups, respectively (p=0.14), while that of anastomotic ulcers was 7.7% (2/26) and 16.7% (2/12) in the non-B and B groups, respectively (p=0.40). The incidence of bile reflux was 30.8% (8/26) and 0% (0/12) in the non-B and B groups, respectively (p=0.03). Although there was a significant difference in the incidence of bile reflux, there was no significant difference in the occurrence of gastric and anastomotic ulcers; hence, bile reflux was unlikely to have caused the development of ulcerative lesions.

Discussion

PD is a curative treatment for operable pancreatic head and periampullary tumors (2). Although the mortality rate of PD was high for several decades, it has gradually improved because of the changes in surgical techniques, instruments, and perioperative management (11, 17). POPF and DGE, which cause longer hospital stays and higher hospital costs, are the two major complications following PD (12, 13). Therefore, reduction of postoperative mortality and morbidity because of complications, including POPF and DGE, is an ever-challenging issue. The reconstruction procedures to reduce POPF and DGE are controversial. The Braun

Table I. *Preoperative and intraoperative data of patients enrolled in the study.*

	B group (n=51)	Non-B group (n=94)	*p*-Value
Age	70 (31-87)	70 (40-85)	0.55
Sex (M/F)	32/19	55/39	0.72
Diseases			
Pancreatic cancer	27	37	0.43
IPMA/IPMC	5	12	
pNEN	0	4	
SCN	1	3	
Chronic pancreatitis	1	4	
Bile duct cancer	9	18	
Gallbladder cancer	1	1	
Vater papilla cancer	4	11	
Duodenal cancer	1	2	
Other	2	2	
Surgical procedure			
PD	4	7	0.94
PPPD	16	31	
SSPPD	31	56	
Open or Laparoscopy			
Lap (Yes/No)	10/41	24/70	0.54
Intraoperative data			
Operative time (min)	456 (309-927)	470 (270-936)	0.69
Blood loss (ml)	850 (50-5,700)	745 (50-6,650)	0.78

IPMA, Intraductal papillary mucinous adenoma; IPMC, intraductal papillary mucinous carcinoma; pNEN, pancreatic neuroendocrine neoplasm; SCN, serous cyst neoplasm; PpPD, pylorus-preserving pancreaticoduodenectomy; PpPD, pylorus-preserving pancreaticoduodenectomy; SSPPD, subtotal stomach-preserving pancreaticoduodenectomy.

Table II. *Postoperative data of patients enrolled in the study.*

	B group (n=51)	Non-B group (n=94)	*p*-Value
No complications	4 (7.8%)	9 (9.6%)	0.055
CDC-I	24 (47.1%)	32 (33.3%)	
CDC-II	16 (31.4%)	26 (27.7%)	
CDC-IIIa	5 (9.8%)	19 (20.2%)	
CDC-IIIb	1 (1.9%)	6 (6.4%)	
CDC-IVa	0	0	
CDC-IVb	0	1 (1.1%)	
CDC-V	1 (1.1%)	1 (1.1%)	
POPF (-/BL/B/C)	35/12/3/1	63/20/11/0	0.77
DGE(-/A/B/C)	50/0/0/1	87/3/2/2	0.36
Oral-intake start date	2 (2-28)	2 (2-70)	0.35
Length of hospital stay	22 (10-109)	24 (10-137)	0.66
Incidence of gastro-intestinal symptoms	12 (23.5%)	26 (27.7%)	0.59

IPMA, Intraductal papillary mucinous adenoma; IPMC, intraductal papillary mucinous carcinoma; pNEN, pancreatic neuroendocrine neoplasm; SCN, serous cyst neoplasm; PD, pancreaticoduodenectomy; PpPD, pylorus-preserving pancreaticoduodenectomy; SSPPD, subtotal stomach-preserving pancreaticoduodenectomy, CDC, Clavien–Dindo classification; POPF, postoperative pancreatic fistula; DGE, delayed gastric emptying.

Table III. *Gastrointestinal endoscopic findings after pancreaticoduodenectomy.*

	B group (n=12)	Non-B group (n=26)	*p*-Value
Gastric ulcer	0 (0%)	4 (15.4%)	0.15
Anastomotic ulcer	2 (16.7%)	2 (7.7%)	0.40
Bile reflux	0 (0%)	8 (30.8%)	0.03

enteroenterostomy, which was introduced more than a century ago, is considered a useful procedure for reducing mortality and morbidity, especially in the case of DGE (18). It is an anastomosis between the afferent and efferent limbs that are distal to a gastroenterostomy or duodenoenterostomy (18, 19), and is designed to divert pancreatic and biliary juices from the afferent to the efferent limb, thereby decreasing reflux into the stomach. Meta-analyses have reported that although Braun enteroenterostomy is beneficial in reducing the incidence of DGE and shortening the length of the postoperative hospital stay, the incidence of gastrointestinal symptoms or ulcerative lesions are unclear (12, 13). Other studies have reported that the incidence of DGE is equivalent, regardless of whether Braun enteroenterostomy is present or absent (20, 21). Our investigation to determine whether Braun enteroenterostomy is a necessary procedure revealed that it did not affect the incidence of complications, including gastrointestinal symptoms and ulcerative lesion.

Although bile reflux was confirmed in the non-B group by gastrointestinal endoscopy and there was a significant difference in bile reflux between the B and non-B groups, the incidence of ulcerative lesions or DGE was not correlated with bile reflux. These results showed that Braun enteroenterostomy did not affect the development of postoperative symptoms, including the incidence of DGE and POPF. Our data is not consistent with the results of a few meta-analyses that showed a positive benefit of Braun anastomosis in reducing the incidence of DGE after PD. Notably, these included only retrospective analyses. A recent study reported the impact of Braun anastomosis on the incidence of DGE after PD in a randomized controlled study with two groups *i.e.*, non-Braun and Braun groups, with 30 patients in each group (20). Similarly to our results, the incidence rate of DGE was lower in the Braun group with no statistically significant difference. Based on our own data and this report, we currently do not perform Braun anastomosis as a routine procedure after PD in our hospital.

However, our study has some limitations. First, the statistical analysis was limited because of the small sample size. Therefore, a large-scale multi-institutional prospective randomized study is needed in the future to clarify whether Braun enteroenterostomy is indeed a necessary procedure. Second, future studies should include nutritional status and gastrointestinal endoscopic findings for all cases after PD to clearly elucidate the long-term treatment outcomes.

Conclusion

In conclusion, though Braun enteroenterostomy was related to bile reflux, our study indicated that it did not affect the incidence of anastomotic and gastric ulcers or DGE and the addition of Braun anastomosis after PD may not affect the short-term outcomes. Therefore, it may not be an essential procedure. However, more prospective randomized studies should be designed to clarify not only the short-term outcomes but also the long-term outcomes.

Conflicts of Interest

The Authors who have taken part in this study declare that they do not have anything to disclose regarding funding or conflicts of interest with respect to this manuscript.

Authors' Contributions

TT, MH, TA, and SE designed and drafted the manuscript. HM, HI, KN, TH, KN, and AS collected data and assisted in preparing the manuscript. All Authors read and approved the final manuscript.

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