Does Braun anastomosis have an impact on the incidence of delayed gastric emptying and the extent of intragastric bile reflux following pancreatoduodenectomy?: A randomized controlled study.

Hironori Fujieda, MD., Yukihiro Yokoyama, MD., Akihiro Hirata, MD., Hiroaki Usui, MD., Yayoi Sakatoku, MD., Masahide Fukaya, MD., and Masato Nagino, MD.

Division of Surgical Oncology, Department of Surgery,

Nagoya University Graduate School of Medicine, Nagoya, Japan.

Running head: The impact of Braun anastomosis Twenty-four-hour intragastric bilirubin monitoring

Key words:, intragastric bile reflux, pancreatic fistula, twenty-four-hour intragastric bilirubin monitoring

Address correspondence to:

Yukihiro Yokoyama, MD

Division of Surgical Oncology, Department of Surgery

Nagoya University Graduate School of Medicine

65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550, Japan

E-mail address: yyoko@med.nagoya-u.ac.jp

Tel: +81 52-744-2222

Fax: +81 52-744-2230

Original Papers

ABSTRACT

Background/Aims: This study investigated the impact of Braun anastomosis on the incidence of delayed gastric emptying (DGE) and on the intragastric bile reflux after pancreatoduodenectomy with Child reconstruction.

Methods: Sixty-eight patients who underwent subtotal stomach-preserving pancreatoduodenectomy were included. Patients were randomly assigned to a group with or without Braun anastomosis intraoperatively. Twenty-four-hour intragastric bilirubin monitoring was performed to investigate the extent of intragastric bile reflux after surgery. The incidence of DGE and other complications were also monitored.

Results: There were no differences between the non-Braun and Braun groups in terms of patient characteristics. The incidence rate of DGE was 29.4% (n=10/34) in the non-Braun group and 20.6% (n=7/34) in the Braun group (P=0.401). Forty-six of the 68 patients consented to intragastric bilirubin monitoring. The fraction time of intragastric bilirubin reflux was comparable between the two groups. Although the fraction time of intragastric bilirubin reflux had no impact on the incidence of DGE, the incidence of pancreatic fistula was significantly higher in patients with DGE than those without DGE (47.1% vs. 21.6%, p=0.043).

Conclusion: The addition of Braun anastomosis after pancreatoduodenectomy did not effectively reduce the intragastric bile reflux and had minor impact in reducing the incidence of DGE.

INTRODUCTION

Pancreatoduodenectomy is the standard treatment for malignant and benign diseases in the pancreatic head, duodenum, and periampullary region. This treatment is a highly invasive surgical procedure that exhibits a high incidence of postoperative complications [1]. Delayed gastric emptying (DGE) is one of the most common postoperative complications with an reported incidence rate of 19% to 57% [2-5]. DGE is not a life-threatening condition, but it leads to a longer hospital stay [6] and aggravate quality of life in the postoperative period [7].

Two meta-analyses on the impact of Braun anastomosis on the incidence of DGE after pancreatoduodenectomy were published recently [8, 9]. Both studies concluded that the Braun anastomosis was beneficial in reducing the incidence of DGE and shortening postoperative hospital stay, but all of the studies included in these meta-analyses were retrospective ones, and no randomized-controlled trial was included. Some previous studies speculated that the prevention of bile reflux by Braun anastomosis may be involved in the mechanism of the reduced incidence of DGE [7, 10]. However, no previous report compared the extent of real-time bile reflux into the stomach between pancreatoduodenectomy procedures with and without Braun anastomosis [7, 10-12].

The present study randomly assigned patients who underwent pancreatoduodenectomy into groups with and without Braun anastomosis and the impact of Braun anastomosis on the incidence of DGE was investigated. Additionally, in some consented patients, twenty-four-hour intragastric bilirubin concentration was monitored after

surgery to determine the impact of Braun anastomosis on bile reflux into the stomach.

PATIENTS AND METHODS

Patients

All patients who were scheduled to undergo pancreatoduodenectomy at the First Department of Surgery, Nagoya University Hospital from August 2011 to February 2016 were eligible to participate in this study. Written informed consent for participation was obtained from each patient prior to enrollment. The Human Research Review Committee of Nagoya University Hospital approved the study, and it is registered in the University Hospital Medical Information Network (http://www.umin.ac.jp; registration number ID 000006093). The following exclusion criteria were used: young patients (less than 20 years old), patients with severe comorbidities, and patients who declined to participate. Patients were randomized to the with or without Braun anastomosis group. For patients who agreed to participate to the study, randomization was performed during surgery when an operating surgeon decided the case was possible to resect. The primary endpoint was the incidence of DGE. The secondary end points were intragastric bilirubin reflux, operation time, intraoperative bleeding, the incidence of other postoperative complications, including pancreatic fistula, and hospital stay after surgery.

Surgical techniques

All patients underwent a subtotal stomach-preserving pancreatoduodenectomy. The intestinal length between the choledocho-jejunostomy and the gastrojejunostomy was set as

60 cm, and Braun enteroenterostomy was added in the Braun group 20 cm distal to the gastrojejunostomy with an approximately 3 cm anastomotic orifice. Gastrojejunostomy was performed in an antecolic fashion in all patients. A feeding tube was inserted 20 cm distal to the choledochojejunostomy (Supplementary Figure 1A, 1B). In all patients, the stent for choledocho-jejunostomy was not used.

Twenty-four-hour intragastric bilirubin monitoring

Patients who consented to undergo 24-hour intragastric bilirubin monitoring were subjected to this test. Because this is some invasive test with an insertion of monitoring probe into the stomach, the test was performed when patients' food intake was stabilized and other complications such as pancreatic fistula was subsided after surgery. The concentration of intragastric bilirubin was measured using a fiber optic sensor (Bilitec 2000®, Medtronic Functional Diagnostics A/S, Denmark). This system is based on the use of a fiber optic sensor that utilizes the optical properties of bile [13]. The tip of the sensor was installed 7 cm distal to the cardia within the stomach via the nose, and bilirubin absorbance was measured using this sensor. The working range of the sensor is 2.5-100 μmol/l bilirubin concentration, which corresponds to the absorbance values of 0.017 to 0.610 on the fiber optic system [13]. The threshold of the absorbance value for the presence of clinically significant intragastric bilirubin reflux was set as ≥0.14 as previously described [14]. The percentage time with bilirubin absorbance levels during 24 hours was calculated as a fraction time of bilirubin reflux [15].

Analyzed Factors

Preoperative characteristics, including the patient's age, gender, body mass index (BMI), and comorbidities (diabetes mellitus and pancreatitis), were recorded. Intraoperative parameters, such as blood loss, operation time, portal vein resection, and pancreatic texture (soft or hard), were also recorded. The incidence of DGE, pancreatic fistula, and other complications were monitored. DGE and pancreatic fistula was defined according to consensus definition and the clinical grading proposed by the International Study Group of Pancreatic Surgery (ISGPS) [2, 16]. In this study, Grade B or C DGE and pancreatic fistula according to the ISGPS definition were considered as clinically significant DGE and pancreatic fistula, respectively. Other postoperative complications were graded using the Clavien-Dindo classification [17].

Statistical analysis

The number of patients required for this study to achieve statistical validity (2-sided) was calculated based on previous findings of a reduced incidence rate of DGE by adding Braun anastomosis [7]. We assumed that the incidence rate of DGE was reduced from 35% in the non-Braun group to 10% in the Braun group. The α value was set at 0.05, and the β value was set at 0.20 with a power of 80%. The calculations revealed that 34 patients were required in each arm of the study. Continuous data are expressed as medians (range), and results were analyzed using the non-parametric Wilcoxon rank-sum test. The χ^2 test was used to analyze categorical variables. A multivariate analysis was performed using a logistic regression model. Variables with $P < 0.200$ in univariate analyses were used in a multivariate logistic regression analysis to identify independent predictors. A result was considered statistically

significant when P<0.05. The data were analyzed using JMP® version 11 for Windows® (SAS Institute, Cary, North Carolina, USA).

RESULTS

A total of 123 consecutive subtotal stomach preserving pancreatoduodenectomy were performed at the authors' hospital from August 2011 to February 2016. 5 patients were not meeting inclusion criteria, and 50 patients declined to participate in this study. Consent to participate in the study was obtained from 68 patients, and then they were randomized into the non-Braun (n=34) or Braun (n=34) group. Forty-six patients consented to undergo 24-hour bilirubin monitoring (non-Braun, n=22; Braun, n=24) (Figure 1).

Preoperative and intraoperative factors (non-Braun vs. Braun)

There were no statistically significant differences between the non-Braun and Braun groups in preoperative patient characteristics, such as age, gender, BMI, preoperative diagnosis, biliary drainage, history of diabetes, HbA1c levels, pancreatitis, and the main pancreatic duct diameter (Table 1).

Intraoperative blood loss, the rate of intraoperative allogeneic blood transfusion, and operation time were not significantly different between the two groups (Table 1). Operation time was slightly longer in the Braun group than the non-Braun group, but this difference was not statistically significant (P=0.544). The type of pacreaticojejunostomies, the rate of portal vein resection due to cancer invasion, and the rate of soft pancreatic texture were not significantly different between the two groups.

Postoperative factors (non-Braun vs. Braun)

No surgery-related mortality was observed in either group (Table 2). Clinically significant DGE occurred in 17 patients (25.0%). Although the incidence rate of clinically significant DGE was lower (20.6%) in the Braun group compared to that in the non-Braun group (29.4%), the difference did not reach to a statistically significant difference (Table 2). Other complications such as pancreatic fistula, infectious complications, and major complications with a Clavien-Dindo score ≥III were also not significantly different between the non-Braun and Braun groups. Length of hospital stay was also not significantly different between the two groups.

Intragastric bile reflux

A total of 46 patients agreed to undergo 24-hour intragastric bilirubin monitoring (non-Braun, n=22; Braun, n=24). The median (range) time of bilirubin monitoring sensor installation was POD 26 (10-48) in the non-Braun group and POD 24 (13-64) in the Braun group (p=0.724). The median (range) fraction time of clinically significant bilirubin reflux (absorbance ≥0.14) during 24 hours was 78.7% (0-100) in the non-Braun group and 85.3% (6.6-98) in the Braun group (p=0.717). The fraction times above different intragastric bilirubin absorbance thresholds (>0.1～>0.7) were comparable between the non-Braun and Braun groups, which suggests that the extent of bilirubin reflux into the stomach was not different between these two groups (Figure 2A).

When patients were divided into without DGE (non-DGE group, n=51) and with DGE (DGE group, n=17) groups, the median (range) fraction times of clinically significant

bilirubin reflux (absorbance ≥0.14) during 24 hours was 77.2% (3.3-99.1) in the non-DGE group and 80.3% (0-100) in the DGE group (p=0.824). The fraction times above different intragastric bilirubin absorbance thresholds (>0.1～>0.7) were all comparable between the non-DGE and DGE groups, which suggests that the extent of bilirubin reflux was not different between these two groups (Figure 2B).

Analysis for the risk factors of DGE

We finally analyzed the risk factors of DGE with multivariate analysis. Factors that are clinically important and possibly associated with DGE were selected using univariate analysis with a p value <0.200. These factors included age greater than 70 years (p=0.063), male gender (p=0.079), main pancreatic duct diameter <5 mm (p=0.032), intraoperative blood loss >1000 ml (p=0.159), and the incidence of clinically significant pancreatic fistula (p=0.043). Multivariate analysis only identified the main pancreatic duct diameter <5 mm as an independent factor that was significantly associated with the incidence of DGE (Table 3).

DISCUSSION

Braun first performed an anastomosis between the afferent and efferent loops of the jejunum to reduce bile and alkaline reflux into the stomach more than 100 years ago. Retrospective studies by Hochwald et al. [7] and Bin et al. [10] indicated that the addition of the Braun enteroenterostomy to the pancreatoduodenectomy procedure reduced the incidence of DGE and shortened the length of hospital stay. These authors speculated that the reduction of intragastric bile reflux by Braun anastomosis and the prevention of gastric mucosal

irritation prevented the incidence of DGE. However, no previous study actually quantified the extent of bile reflux into the stomach under conditions with or without Braun anastomosis. The present study measured intragastric bilirubin concentrations after pancreatoduodenectomy with or without Braun anastomosis for 24 hours using a continuous bilirubin concentration monitoring system. We also investigated whether the incidence of DGE was associated with the presence or absence of Braun anastomosis or intragastric bilirubin reflux.

Although the incidence rate of DGE was lower in patients with Braun anastomosis (20.6%) compared to those without Braun anastomosis (29.4%), it did not reach to a statistically significant difference. One of the possible reason may be because of underpowered study with small number of patients. It should be noted however, the extent of intragastric bile reflux also showed no difference between the with and without Braun anastomosis groups. Unexpectedly, a certain amount of bile reflux into the stomach was observed regardless of the addition of Braun anastomosis after pancreatoduodenectomy with Child reconstruction. The fraction times of clinically significant bilirubin reflux into the stomach was approximately 80% regardless the addition of Braun anastomosis. This means that the patients who underwent pancreatoduodenectomy with Child reconstruction may have a bile reflux into the stomach most of the time. Moreover, the incidence of DGE was not correlated with the extent of bile reflux into the stomach. These results indicated that the addition of Braun anastomosis has not enough power to reduce the intragastric bile reflux as well as the incidence of DGE. To the best of our knowledge, the present study firstly used a

24-hour continuous bilirubin concentration monitoring system to investigate whether Braun anastomosis has an impact on biliary regurgitation into the stomach.

The results obtained in this prospective randomized study are not consistent with the results of two currently published meta-analyses that reported a benefit of Braun anastomosis in reducing the incident of DGE after pancreatoduodenectomy. However, these two meta-analyses included only retrospective analyses and no randomized controlled studies were included. In fact, there is only one report that performed randomized controlled study to investigate the impact of Braun anastomosis on the incidence of DGE after pancreatoduodenectomy [18]. This recently published report comparing the non-Braun group and Braun group in pancreatoduodenectomy included 30 patients in each group. Similar to our observations, the results indicated that the overall DGE tended to be lower in the Braun group but the difference did not reach to a statistically significant difference. Based on the results of the present study, we currently do not add Braun anastomosis routinely in the procedure of subtotal stomach-preserving pancreatoduodenectomy. However, a larger scale multiple institutional prospective randomized study should be designed to clarify the real benefit of Braun anastomosis on the incidence of DGE.

The results of our study indicated that the incidence of DGE was not associated with Braun anastomosis as well as the intragastric bile reflux. In contrast, the incidence of DGE was significantly associated with the incidence of pancreatic fistula, which is a well-recognized risk factor of DGE [11, 19]. The incidence of DGE was also associated with the small main pancreatic duct diameter, which is a major risk factor for pancreatic fistula [20].

Hocking et al. previously reported that peripancreatic inflammation may result in gastric dysrhythmia, which may explain one of the mechanisms of DGE [21]. Although it may be difficult to prove the exact mechanistic link between the peripancreatic inflammation and the incidence of DGE, the results in this study may imply that inflammation outside of the stomach (i.e., from pancreatic fistula) have a greater impact than the inflammation of inside of the stomach (i.e., from biliary regurgitation) on the occurrence of DGE. This hypothesis should be tested in a future study.

This study was designed to investigate the impact of Braun anastomosis on a short-term outcome after pancreatoduodenectomy, but the long-term outcome is not known. Future studies should monitor and compare the recovery of nutritional status, incidence of gastric ulcers in the remnant stomach, and the incidence of regurgitating gastritis between Braun and non-Braun groups. It also should be noted that the timing of intragastric bilirubin monitoring was performed on widely-ranged postoperative day. The timing of test may have a significant impact on the gastric motility and the reflux of bile into the stomach. However, it was ethically difficult to perform bilirubin monitoring test if patients have a trouble of eating. Therefore, the test was performed when patients' oral intake was stabilized.

In conclusion, this randomized study indicated that the addition of Braun anastomosis to the pancreatoduodenectomy procedure with Child reconstruction may have a minor impact on the reduction of intragastric bile reflux and the incidence of DGE.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Topal B, Fieuws S, Aerts R, Weerts J, Feryn T, Roeyen G, Bertrand C, Hubert C, Janssens M, Closset J, Belgian Section of H, Pancreatic S: Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction after pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre randomised trial. Lancet Oncol 2013;14:655-62.
2. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Traverso LW, Yeo CJ, Buchler MW: Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2007;142:761-8.
3. 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: Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg 1997;226:248-57; discussion 57-60.
4. Izbicki JR, Bloechle C, Broering DC, Knoefel WT, Kuechler T, Broelsch CE: Extended drainage versus resection in surgery for chronic pancreatitis: a prospective randomized trial comparing the longitudinal pancreaticojejunostomy combined with local pancreatic head excision with the pylorus-preserving pancreatoduodenectomy. Ann Surg 1998;228:771-9.
5. Martignoni ME, Friess H, Sell F, Ricken L, Shrikhande S, Kulli C, Buchler MW: Enteral nutrition prolongs delayed gastric emptying in patients after Whipple resection. Am J Surg 2000;180:18-23.

6. Fabre JM, Burgel JS, Navarro F, Boccarat G, Lemoine C, Domergue J: Delayed gastric emptying after pancreaticoduodenectomy and pancreaticogastrostomy. Eur J Surg 1999;165:560-5.
7. Hochwald SN, Grobmyer SR, Hemming AW, Curran E, Bloom DA, Delano M, Behrns KE, Copeland EM, Vogel SB: Braun enteroenterostomy is associated with reduced delayed gastric emptying and early resumption of oral feeding following pancreaticoduodenectomy. J Surg Oncol 2010;101:351-5.
8. Xu B, Zhu YH, Qian MP, Shen RR, Zheng WY, Zhang YW: Braun Enteroenterostomy Following Pancreaticoduodenectomy: A Systematic Review and Meta-Analysis. Medicine 2015;94:e1254.
9. Huang MQ, Li M, Mao JY, Tian BL: Braun enteroenterostomy reduces delayed gastric emptying: A systematic review and meta-analysis. Int J Surg 2015;23:75-81.
10. Xu B, Meng H, Qian M, Gu H, Zhou B, Song Z: Braun enteroenterostomy during pancreaticoduodenectomy decreases postoperative delayed gastric emptying. Am J Surg 2015;209:1036-42.
11. Liu QY, Li L, Xia HT, Zhang WZ, Cai SW, Lu SC: Risk factors of delayed gastric emptying following pancreaticoduodenectomy. ANZ J Surg 2016;86:69-73.
12. Watanabe Y, Ohtsuka T, Kimura H, Matsunaga T, Tamura K, Ideno N, Aso T, Miyasaka Y, Ueda J, Takahata S, Tanaka M: Braun enteroenterostomy reduces delayed gastric emptying after pylorus-preserving pancreatoduodenectomy: a retrospective review. Am J Surg 2015;209:369-77.

13. Bechi P, Pucciani F, Baldini F, Cosi F, Falciai R, Mazzanti R, Castagnoli A, Passeri A, Boscherini S: Long-term ambulatory enterogastric reflux monitoring. Validation of a new fiberoptic technique. Dig Dis Sci 1993;38:1297-306.

14. Kauer WK, Burdiles P, Ireland AP, Clark GW, Peters JH, Bremner CG, DeMeester TR: Does duodenal juice reflux into the esophagus of patients with complicated GERD? Evaluation of a fiberoptic sensor for bilirubin. Am J Surg 1995;169:98-103; discussion - 4.

15. Vaezi MF, Richter JE: Role of acid and duodenogastroesophageal reflux in gastroesophageal reflux disease. Gastroenterology 1996;111:1192-9.

16. 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.

17. 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;240:205-13.

18. Hwang HK, Lee SH, Han DH, Choi SH, Kang CM, Lee WJ: Impact of Braun anastomosis on reducing delayed gastric emptying following pancreaticoduodenectomy: a prospective, randomized controlled trial. Journal of hepato-biliary-pancreatic sciences 2016;23:364-72.

19. Sakamoto Y, Yamamoto Y, Hata S, Nara S, Esaki M, Sano T, Shimada K, Kosuge T: Analysis of risk factors for delayed gastric emptying (DGE) after 387

pancreaticoduodenectomies with usage of 70 stapled reconstructions. J Gastrointest Surg 2011;15:1789-97.

20. Yokoyama Y, Ebata T, Igami T, Sugawara G, Ando M, Nagino M: Proposal for a Pancreatic Configuration Index for Determining Patients at High Risk of Pancreatic Fistula Following Pancreatoduodenectomy. Dig Surg 2016;33:169-76.

21. Hocking MP, Harrison WD, Sninsky CA: Gastric dysrhythmias following pylorus-preserving pancreaticoduodenectomy. Possible mechanism for early delayed gastric emptying. Dig Dis Sci 1990;35:1226-30.

FIGURE LEGENDS

Figure 1.

Study flow chart.

Figure 2.

A. The fraction times above different intragastric bilirubin absorbance thresholds (>0.1～>0.7) in the non-Braun and Braun groups.

B. The fraction times above different intragastric bilirubin absorbance thresholds (>0.1～>0.7) in the non-DGE and DGE groups.

Supplementary figure 1.

Schema of the reconstruction with (A) and without Braun anastomosis (B) after pancreatoduodenectomy.

Table 1. Preoperative and intraoperative factors (non-Braun vs. Braun)

	Non-Braun (n=34)	Braun (n=34)	P value
Preoperative factors			
Age, median (range) [years]	72 (45-83)	66 (55-78)	0.160
Male gender, n [%]	24 (70.6)	20 (58.8)	0.310
BMI, median (range) [kg/m^2]	21.0 (16.8-27.0)	21.3 (16.5-28.7)	0.348
Diagnosis, n (%)			0.463
Pancreatic cancer	11 (32.4)	12 (35.3)	
Bile duct cancer	8 (23.5)	9 (26.5)	
Duodenal papilla cancer	7 (20.6)	4 (11.8)	
IPMN	7 (20.6)	5 (14.7)	
Other malignancies	0	3 (8.8)	
Benign diseases	1 (2.9)	1 (2.9)	
Biliary drainage, n (%)	20 (58.8)	21 (61.8)	0.804
Diabetes, n (%)	12 (35.3)	6 (17.6)	0.168
HbA1c, median (range) [%]	5.7 (4.2-8.5)	5.5 (4.5-8.2)	0.451
Pancreatitis, n (%)	3 (8.8)	3 (8.8)	1.000
MPD diameter*, median (range) [mm]	3.8 (1.8-13.8)	4.1 (1.9-17.1)	0.736
Intraoperative factors			
Blood loss, median (range) [ml]	978 (342-1959)	867 (188-4018)	0.466
Intraoperative BTF, n (%)	13 (38.2)	6 (17.6)	0.059
Operation time, median (range) [min]	470 (336-698)	508 (298-710)	0.544
Pancreatojejunostomy, n (%)			0.163
Duct-to-mucosa	33 (97.1)	30 (88.2)	
Invagination	1 (2.9)	4 (11.8)	
Portal vein resection, n (%)	8 (23.5)	4 (11.8)	0.203
Soft pancreas, n (%)	20 (58.8)	19 (55.9)	0.806

BMI, body mass index; IPMN, intraductal papillary mucinous neoplasm; MPD, main pancreatic duct; BTF; allogeneic blood transfusion

* The MPD diameter were measured on axial images of computed tomography.

5

Table 2. Postoperative factors (non-Braun vs. Braun)

	Non-Braun (n=34)	Braun (n=34)	P value
Mortality, n (%)	0 (0)	0 (0)	1.000
Clinically significant DGE, n (%)	10 (29.4)	7 (20.6)	0.401
Clinically significant pancreatic fistula, n (%)	11 (32.4)	8 (23.5)	0.418
Infectious complications, n (%)	9 (26.5)	13 (38.2)	0.300
Clavien-Dindo score (≥III), n (%)	17 (53.3)	19 (55.9)	0.627
In-hospital day, median (range) [days]	31 (11-56)	28 (10-96)	0.859

DGE; delayed gastric emptying

Table 3. Factors associated with the incidence of DGE

Variables	No. of patients	No. of patients with DGE (%)	Univariate		Multivariate	
			Odds ratio (95% C.I.)	*P* value	Odds ratio (95% C.I.)	*P* value
Age						
≤70 years	41	7 (17.1)	1.00	0.063	1.00	0.154
>70 years	27	10 (37.0)	2.86 (0.93-8.83)		2.51 (0.71-9.38)	
Gender						
Female	24	3 (12.5)	1.00	0.079	1.00	0.078
Male	44	14 (31.8)	3.27 (0.83-12.80)		3.46 (0.87-17.99)	
MPD diameter						
≥5 mm	27	3 (11.1)	1.00	0.032	1.00	0.042
<5 mm	41	14 (34.2)	4.15 (1.06-16.21)		4.98 (1.05-31.48)	
Blood loss						
≤1000 ml	38	7 (18.4)	1.00	0.159	1.00	0.368
>1000 ml	30	10 (33.3)	2.21 (0.72-6.77)		1.90 (0.47-8.11)	
Clinically significant pancreatic fistula						
No	49	9 (18.4)	1.00	0.043	1.00	0.721
Yes	19	8 (42.1)	3.23 (1.01-10.34)		1.31 (0.29-5.50)	

MPD, main pancreatic duct

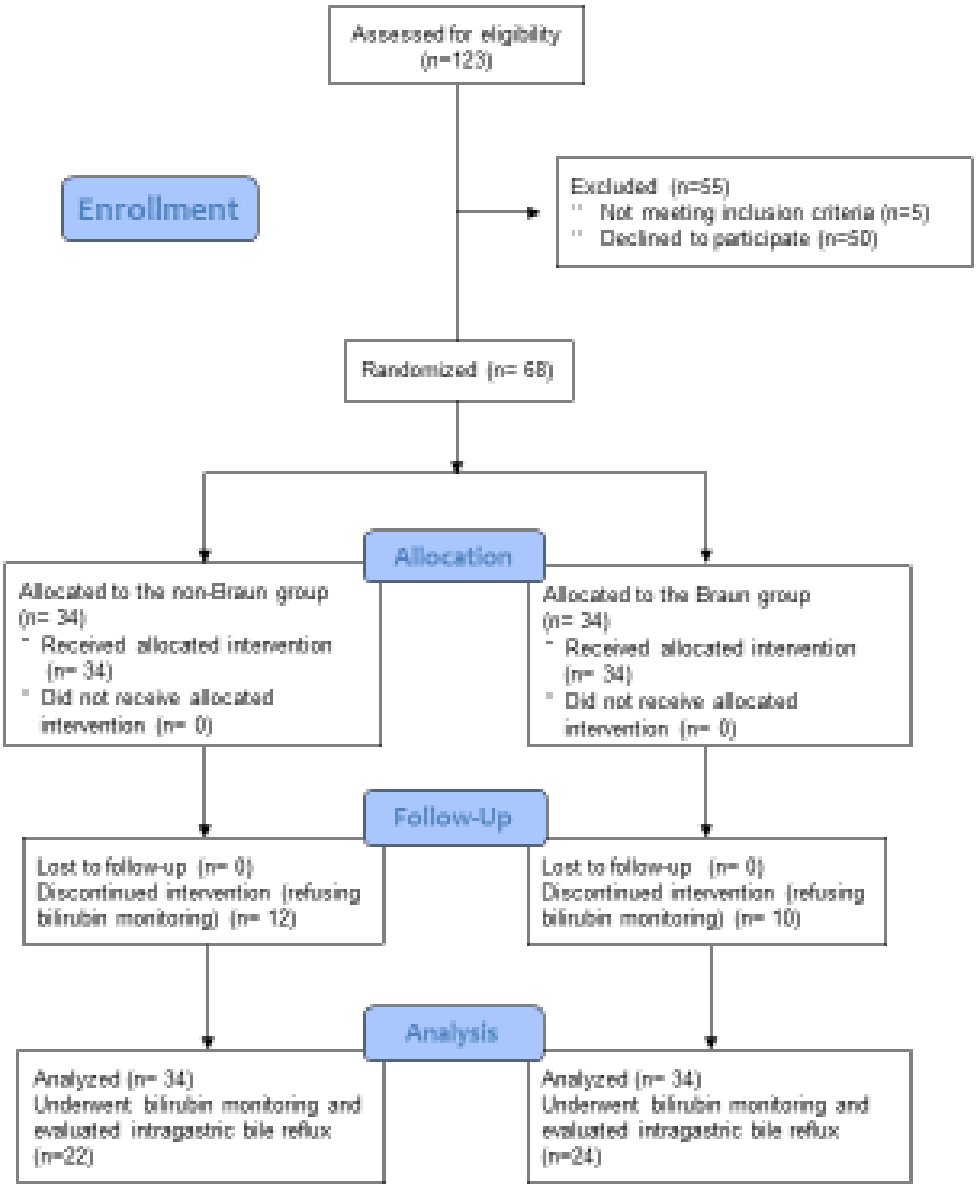


Fig 1. Study flow chart

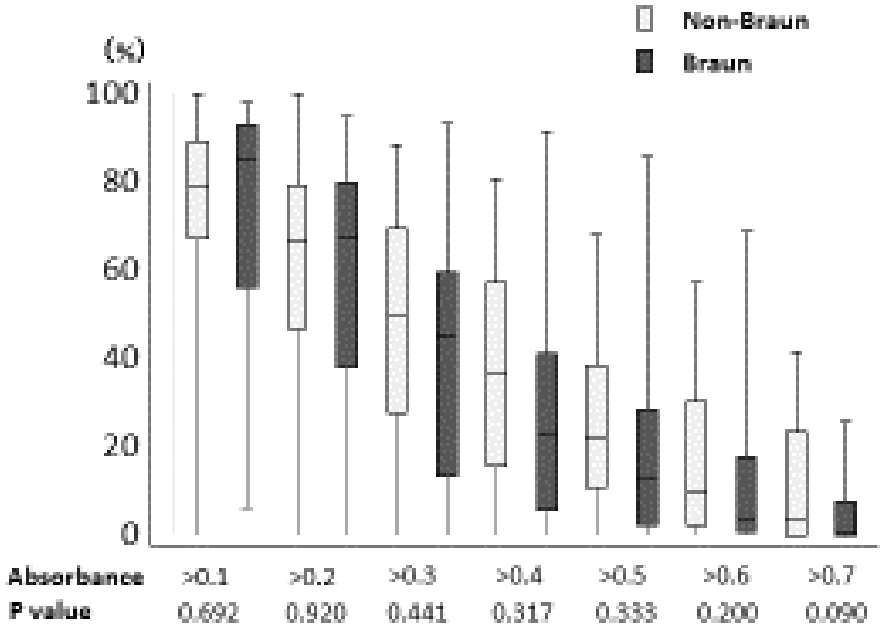


Fig 2A. The fraction times above different intragastric bilirubin absorbance thresholds (>0.1～>0.7) in the non-Braun and Braun groups.

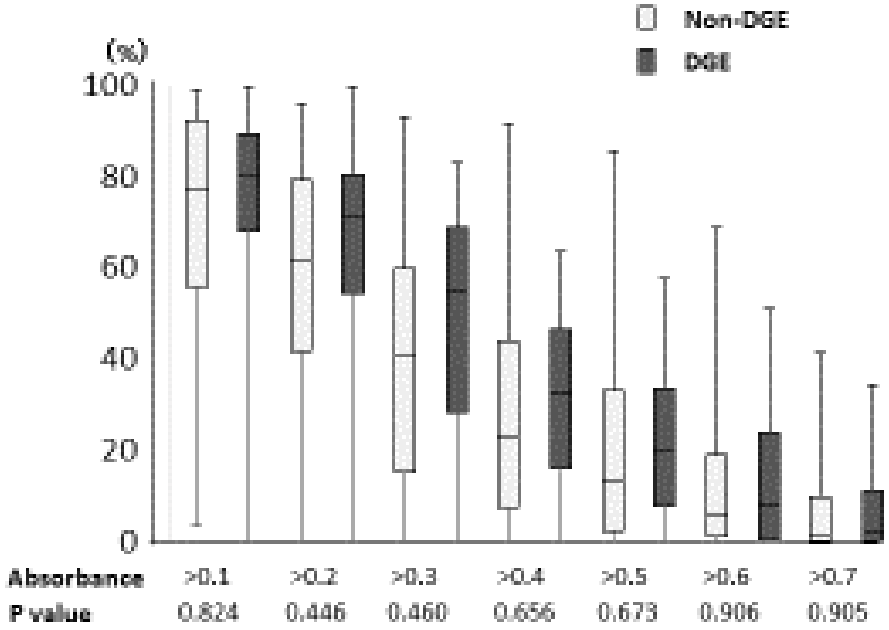
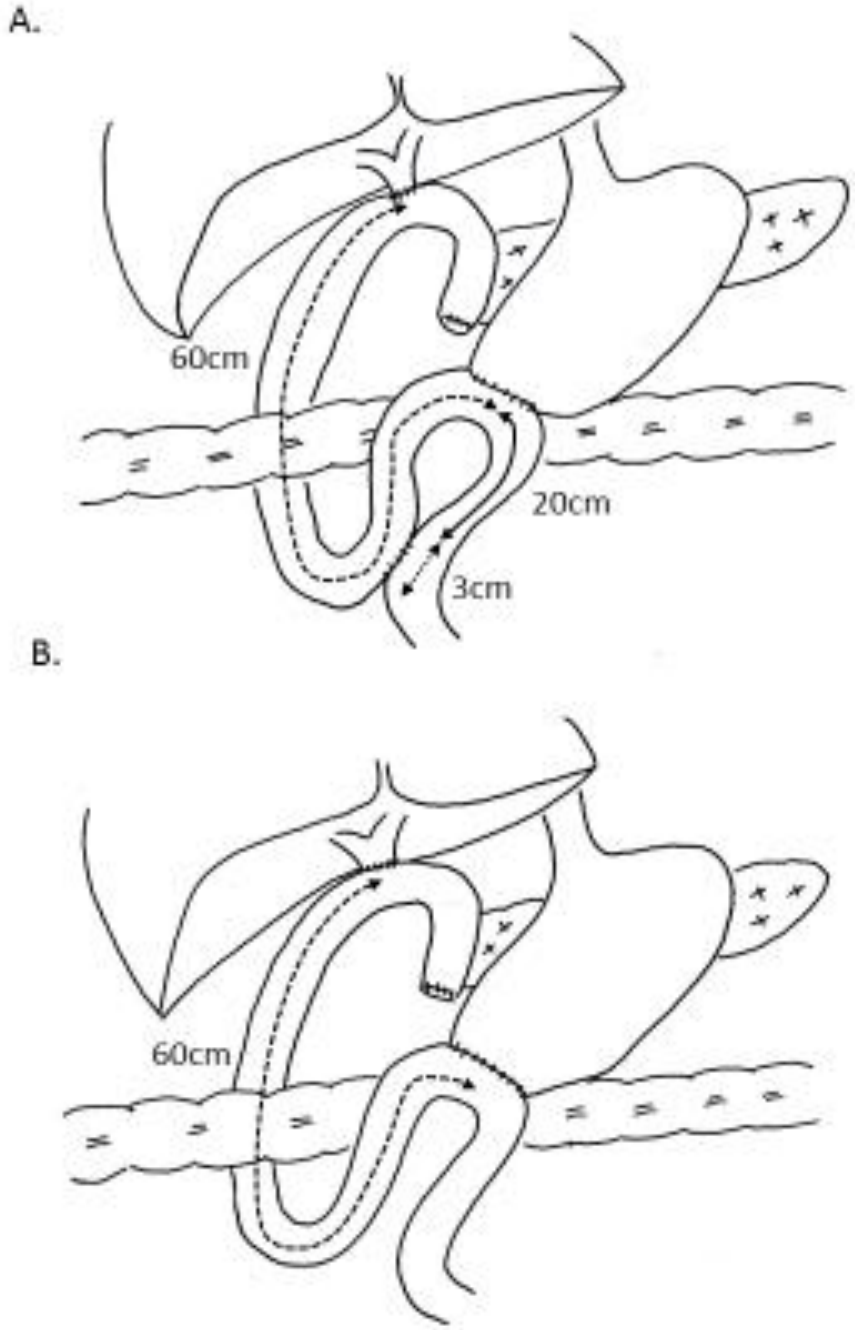


Fig 2B. The fraction times above different intragastric bilirubin absorbance thresholds (>0.1～>0.7) in the non-DGE and DGE groups.



Supplementary Fig 1. Schema of the reconstruction with (A) and without Braun anastomosis (B) after pancreatoduodenectomy.