J Hepatobiliary Pancreat Sci (2016) 23:364–372
DOI: 10.1002/jhbp.349

ORIGINAL ARTICLE

Impact of Braun anastomosis on reducing delayed gastric emptying following pancreaticoduodenectomy: a prospective, randomized controlled trial

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Published online: 24 April 2016

Abstract
Background The present study investigates the clinical impact of Braun anastomosis on delayed gastric emptying (DGE) after pylorus-preserving pancreaticoduodenectomy (PPPD).
Methods From February 2013 to June 2014, 60 patients were recruited for this randomized controlled trial. The incidence of DGE and its risk factors were analyzed according to whether or not Braun anastomosis was used after PPPD.
Results Thirty patients were respectively enrolled in No-Braun group and Braun group. A comparative analysis between the two groups showed no differences in sex, diagnosis, operation time, hospital stay, or postoperative complications, including pancreatic fistula. Overall DGE developed in eight patients (26.7%) in the Braun group and in 14 patients (46.7%) in the No-Braun group ($P = 0.108$). However, clinically relevant DGE (grades B and C) was marginally more frequent in the No-Braun group (23.3% vs. 3.3%, $P = 0.052$). In a multivariable analysis, No-Braun anastomosis was an independent risk factor for developing clinically relevant DGE (odds ratio = 16.489; 95% confidence interval: 1.287–211.195; $P = 0.031$).
Conclusion The overall DGE occurrence was not different between the two groups. However, No-Braun anastomosis was an independent risk factor for developing clinically relevant DGE.

Keywords Braun anastomosis · Delayed gastric emptying · Pancreaticoduodenectomy

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Introduction

Delayed gastric emptying (DGE) is a major complication following pancreaticoduodenectomy (PD) or pylorus-preserving pancreaticoduodenectomy (PPPD), occurring in 14–61% of patients [1–6]. Considering that periampullary tumors, with the exception of benign or borderline pancreatic neoplasms, have a poor prognosis and that PD is a high-morbidity procedure, patients who undergo PD may often feel discouraged, not only because of the disease itself but also because of the difficult recovery. Although DGE is not life-threatening, it results in prolonged hospitalization and increased hospital costs [7]. Consistent intolerable status for appropriate amount of diet could also delay the scheduled adjuvant treatment and lead to patient noncompliance with the entire anti-cancer treatment plan.

Several surgeons have tried to reduce the incidence of DGE with technical modifications while performing PD, including pylorus preservation or pylorus ring resection [8], Billroth II or Roux-en-Y reconstruction for the duodenojejunostomy (DJ) or gastrojejunostomy (GJ) [9, 10], using an antecolic or retrocolic route for the gastroenteric anastomosis [4, 11–13], using subtotal stomach-preserving PD [14, 15] or PPPD, and pylorus dilation [16]. Non-technical factors affecting DGE include older age [12, 17], male sex [9], preoperative diabetes [9, 13, 17–19], preoperative cholangitis [20], use of certain drugs [21–24] (prokinetics or erythromycin), ischemia of the pyloric ring and antrum [25], vagal nerve injury-induced gastric atony or pyloric spasm [16, 26, 27],

absence of motilin due to resection of the duodenum [21, 24, 28], postoperative complications [9, 19, 29–32], and the torsion and angulation of the reconstruction [5, 33].

Some studies investigating the effect of the Braun anastomosis on DGE were recently published [34–37]. Enteroenterostomy between the afferent and efferent limbs distal to the gastroenterostomy site was first reported by Braun over 100 years ago as a method to divert food from the afferent limb and to decrease alkaline reflux gastritis and bile vomiting in the setting of gastric surgery [38]. Theoretically, bile and pancreatic secretions can pass through the Braun anastomosis, diverting to the GJ or DJ site and consequently reducing the pressure on the GJ or DJ site. Food in the afferent limbs can also pass distally through the Braun anastomosis site, preventing afferent loop obstruction. Some authors [34, 35, 37] evaluated the effect of the Braun anastomosis in conventional PD, while another author [36] reported the effects of the Braun anastomosis in PPPD. All of the studies suggested that the Braun enteroenterostomy was beneficial in reducing DGE; however, the studies were all retrospective. A review of the literature indicated that there has been no randomized controlled trial (RCT) to address this issue. Therefore, the purpose of this study was to investigate by means of a prospective RCT the impact of the Braun anastomosis on reducing DGE following PPPD.

Methods

Patients

We enrolled patients who were at least 20 years of age and younger than 80 years, who were scheduled to undergo open PPPD for periampullary tumors, and who provided written informed consent to participate between February 2013 and June 2014. In terms of general performance status, patients with a Karnofsky score of at least 70% or ECOG grades 0 to 1 were enrolled. We excluded patients who underwent laparoscopic PPPD or a procedure more extensive than PPPD, such as combined adjacent organ or vessel resection due to tumor invasion, and those who had history of previous transabdominal surgery. Patients were intraoperatively randomly assigned to receive a Braun anastomosis (Braun group) or not to receive a Braun anastomosis (No-Braun group). Two surgeons who have performed more than 40 cases of PPPD per year respectively participated in this trial. Review of case report forms and refresh training of care providers were regularly performed by research meeting in every week. This study was registered at ClinicalTrials.gov (registration number NCT01787955), approved by the Institutional Review Board and Ethical Committee of Severance Hospital, Yonsei University College of Medicine (4-2012-0879), and conducted in accordance with the Declaration of Helsinki.

Trial design and randomization

This study was an open label, and parallel assignment trial. The primary outcome measure was comparison of DGE occurrence between Braun group and No-Braun group. Secondary endpoints included postoperative complications, diet build-up status, clinically relevant DGE rate, and risk factors for DGE. Two surgeons enrolled participants. Patients were randomized intraoperatively to the Braun group or the No-Braun group using a computer-generated random number pattern after the specimen was removed and just before reconstruction. Clinical fellows who did not participate in the operations assigned patients to the interventions according to the random number results.

Surgical procedure

All patients underwent PPPD. The duodenal bulb was resected 3–4 cm distal to and below the pylorus with right gastric artery sacrifice. Lymph nodes (LNs) around the hepatoduodenal ligament and para-aortic area were completely dissected (using standard LN dissection). In cases of pancreatic head or uncinate cancer, the neural tissue around the superior mesenteric artery was dissected (extended LN dissection). A retrocolic Child's type reconstruction was used for end-to-side hepaticojejunostomy (HJ) and end-to-side pancreaticojejunostomy (PJ). PJ was performed in a duct-to-mucosa fashion with an internal short stent placed at the anastomosis site. The antecolic end-to-side DJ was performed approximately 45 to 50 cm distal to the HJ. In the Braun group, a side-to-side jejunojejunostomy was added between the afferent and efferent loops 30 cm below the distal DJ site (Fig. 1).

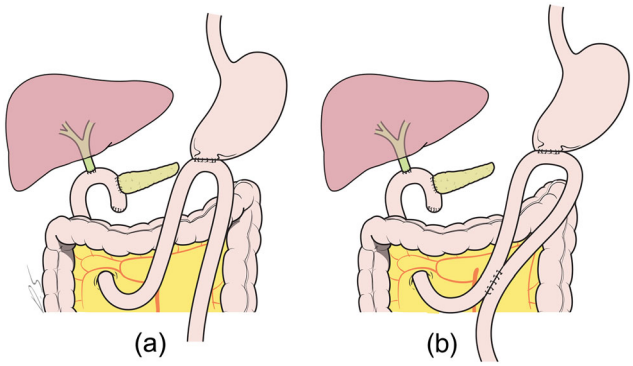

Fig. 1 In the No-Braun group, a Child's type retrocolic end-to-side pancreaticojejunostomy (duct-to-mucosa) and end-to-side hepaticojejunostomy were performed, and antecolic duodenojejunostomy was done (**a**). In the Braun group, in addition to the procedures described in (**a**), a side-to-side jejunojejunostomy between the afferent and efferent loops was performed 30 cm below the distal site of the duodenojejunostomy (**b**)

The DJ and Braun anastomosis were performed in two layers, using interrupted 3–0 polyglactin Lembert sutures for the outer posterior and anterior rows. The inner rows were sewn in a continuous locking fashion posteriorly, and as a Connell stitch anteriorly with 3–0 polyglactin suture. A closed suction drain was placed posteriorly to the PJ site and anteriorly to the HJ site. No patient received a nasogastric tube (NGT) or a feeding jejunostomy tube.

Postoperative management

We did not use routine somatostatin analogs, antiemetic drugs, or prokinetic agents (e.g. erythromycin). The patients could drink water immediately postoperatively; however, patients who experienced nausea as a consequence of anesthesia were allowed sips of water on the first postoperative day (POD). A full liquid diet and solid diet were allowed on the third and fifth PODs, respectively, when the patient was able to tolerate each. For patients who experienced discomfort, the starting day for each diet was delayed until they felt comfortable tolerating it.

Definition of postoperative complications and assessment of diet build-up status

DGE was graded according to the International Study Group of Pancreatic Surgery (ISGPS) consensus definition [6]. Grade A was defined as either NGT insertion after POD 3 or as the inability to tolerate solid diet intake by POD 7. Grade B was defined as using an NGT for 8–14 days, NGT reinsertion after POD 7, or the inability to tolerate a solid diet by POD 14. Grade C was defined as the need to use an NGT for more than 14 days, NGT reinsertion after POD 14, or the inability to tolerate a solid diet by POD 21. DGE of grades B and C was considered to be clinically relevant DGE.

Postoperative pancreatic fistula (POPF) was defined when peritoneal amylase values measured on POD 3 were greater than three times the upper limit of normal for serum amylase values and was graded as A, B, or C based on the International Study Group of Pancreatic Fistula [7]. Overall surgical complications were graded according to the Clavien-Dindo classification system [39].

We recorded the first day on which patients were able to tolerate a solid diet. However, the assessment of "tolerance to solid diet intake" could be individually subjective in patients, so we also recorded the day on which patients were able to eat more than half of the solid oral intake amount. Additionally, the use of prokinetics or antiemetic drugs was evaluated.

Sample size calculation and statistical analysis

To calculate the appropriate sample size, we hypothesized that surgery with a Braun anastomosis would be superior to the conventional procedure in reducing DGE following PPPD. The sample size was based on the overall DGE incidence of 30% for PPPD cases without Braun anastomosis from the most recent 5 years selected from the trial center database and an expected reduction of DGE incidence to 4.2% in the Braun anastomosis group, based on the results of a previous study [35]. The difference in the DGE occurrence proportion between the two groups was 0.258 under the alternative hypothesis. To demonstrate such a difference with the two-sided Z-test with a power of 80% (β of 20%) and a two-sided α of 5%, a sample size of at least 29 patients in each group was necessary. We planned to enroll a total of 30 patients for each arm. The significance level of the test was targeted at 0.05. PASS version 2008 (NCSS statistical software, Kaysville, UT, USA) was used for the power calculation. Continuous variables are expressed as the mean ± standard deviation. Differences between groups for continuous variables were tested using the Student's *t*-test. Categorical variables are expressed as number (percentage). Associations between different categorical variables were tested with the χ^2 test or Fisher's exact test. To investigate the independent associations of the risk factors for DGE, multivariable logistic regression analysis was performed. Statistical significance was defined as a $P < 0.05$. Statistical analyses were performed using SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Patient enrollment and demographics

Between February 2013 and June 2014, a total of 135 patients were assessed for study eligibility. Among them, 28 did not meet the inclusion criteria, and 47 declined to participate. Finally, 60 patients were randomized to the Braun ($n = 30$) or No-Braun ($n = 30$) anastomosis group. No patient withdrew or was lost to follow-up during study period. Because there was no postoperative mortality in either group, all participating patients were included in the final analysis (Fig. 2).

There were no significant difference between the two groups in terms of sex, comorbidity, presence of diabetes mellitus (DM), preoperative serum albumin level, total bilirubin level, and final pathologic diagnosis. However, patients in the Braun group were found to be older than were those in the No-Braun group (69 ± 8 vs. 63 ± 9 years, $P = 0.005$, Table 1).

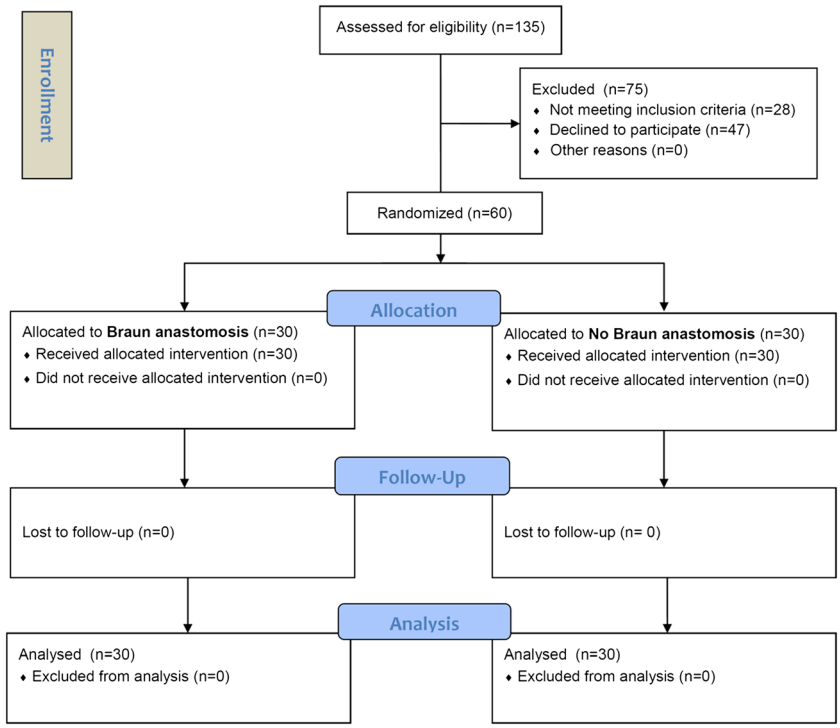

Fig. 2 Patient enrollment flowchart

Table 1 Patient demographics between the Braun and No-Braun groups

	Braun (n = 30)	No-Braun (n = 30)	P-value
Age (years), mean ± SD	69 ± 8	63 ± 9	0.005
Sex (male/female)	19 (63.3%)/11 (36.7%)	19 (63.3%)/11 (36.7%)	1.000
Underlying medical history			0.168
DM	13 (43.3%)	10 (33.3%)	0.426
DM only	4 (13.3%)	5 (16.7%)	
DM + HiBP	8 (26.7%)	3 (10%)	
DM + Tbc	1 (3.3%)	1 (3.3%)	
DM + Hepatitis	0 (0%)	1 (3.3%)	
Hypertension	6 (20%)	5 (16.7%)	
Hypertension + Tbc	2 (6.7%)	0 (0%)	
Old Tbc	2 (8.7%)	0 (0%)	
Preop. albumin (g/dL), mean ± SD	3.7 ± 0.6	3.8 ± 0.5	0.435
Preop. t. Bilirubin (mg/dL), mean ± SD	3.5 ± 4.6	3.3 ± 4.1	0.865
Diagnosis			0.893
Pancreatic cancer	10 (33.3%)	11 (36.7%)	
CBD cancer	8 (26.7%)	8 (26.7%)	
AoV cancer	7 (23.3%)	8 (26.7%)	
Benign/borderline pancreatic tumor	5 (16.7%)	3 (10%)	
IMPN	4 (13.4%)	2 (6.7%)	
NET	1 (3.3%)	0 (0%)	
SPT	0 (0%)	1 (3.3%)	

Data are presented as n (%) unless otherwise noted. *AoV* ampulla of Vater, *CBD* common bile duct, *DM* diabetes mellitus, *HiBP* hypertension, *preop* preoperative, *IPMN* intraductal papillary mucinous neoplasm, *NET* neuroendocrine tumor, *SD* standard deviation, *SPT* solid pseudopapillary tumor, *t.* total, *Tbc* pulmonary tuberculosis

Surgical outcomes

No significant differences were observed in operative time, intraoperative bleeding, intraoperative transfusion, extent of LN dissection, and hospitalization length between the two groups. There were no statistical differences in postoperative complications, such as POPF, bile leakage, chyle leakage, wound complications, intra-abdominal abscess, bleeding, and Clavien-Dindo classification grade ($P > 0.05$, Table 2).

Postoperative course and incidence of delayed gastric emptying

The starting day for the full liquid diet, gas out day, vomiting event, addition of other medications (prokinetics or antiemetics), and NGT insertion were not significantly different between the two groups. A solid diet was given earlier to the Braun group, but this difference was not significant (6 ± 4 vs. 9 ± 8 days, $P = 0.091$), and the day when the patients could eat half of the oral intake amount was marginally significantly earlier in the Braun group (9 ± 5 vs. 12 ± 9 days, $P = 0.054$).

The overall DGE incidence ($P = 0.108$) and DGE grade ($P = 0.181$) were not significantly different between the two groups. However, it was found that clinically relevant DGE was marginally significantly more frequent in the No-Braun group (3.3% vs. 23.3%, $P = 0.052$, Table 3).

Risk factors for DGE

When we analyzed the risk factors for clinically relevant DGE development, age, sex, presence of DM, POPF, and other postoperative complications did not affect clinically relevant DGE development. However, not receiving a Braun anastomosis significantly ($P = 0.049$) affected the development of clinically relevant DGE (grades B and C) in the univariable analysis. Multivariable logistic regression analysis showed that not receiving a Braun anastomosis significantly affected clinically relevant DGE (odds ratio [OR] = 16.489, 95% confidence interval [CI]: 1.287–211.195, $P = 0.031$, Table 4).

DGE incidence for the Braun and No-Braun groups divided by median age

Because patients in the Braun group were found to be older than those in the No-Braun group (Table 1), an age-adjusted analysis was added. All patients were divided in two groups based on being older or younger than the mean age (≤65.7 vs. >65.7 years). The overall incidences of DGE and clinically relevant DGE were not different between the two groups adjusted for age (Table 5).

Discussion

Various efforts to reduce DGE after PD have been proposed by surgeons. In previously published retrospective studies [34–37], Braun enteroenterostomy was shown to prevent DGE. This was the first prospective RCT to investigate the effect of Braun anastomosis on DGE following PPPD, and we showed a marginally significantly lower incidence of clinically relevant DGE (grades B and C) in the Braun group compared to that in the No-Braun group (3.3% vs. 23.3%, $P = 0.052$). There were three patients with grade C DGE, and they were all in the No-Braun group. Hochwald et al. [34] first reported the usefulness of Braun enteroenterostomy for decreasing the sequelae of DGE following conventional PD in 2010. They reported that clinically relevant DGE incidence was low in the Braun group (7% vs. 31%, $P = 0.003$). Nikfarjam et al. [35] also reported the effectiveness of the Braun anastomosis for reducing clinically relevant DGE (4.2% vs. 35%, $P = 0.008$). Xu et al. showed similar results (6.7% vs. 26.87%, $P < 0.001$). The different incidence rates of clinically relevant DGE between the Braun and No-Braun groups was 20% in the current trial, a similar result to those in previous retrospective studies (20.17–30.8%).

Nikfarjam et al. [35] reported that Braun anastomosis was the only significant independent factor associated with reduced DGE after PD ($P = 0.025$), as did Xu et al. [37] (OR: 4.485, $P < 0.001$). Watanabe et al. [36] found that the omission of a Braun anastomosis was the only independent factor associated with DGE after PPPD (OR: 5.04, 95% CI: 1.59–19.66, $P < 0.01$). We also observed that not receiving a Braun anastomosis was an independent risk factor affecting clinically relevant DGE after PPPD in a multivariate analysis (OR = 16.489, 95% CI: 1.287–211.195, $P = 0.031$).

Since Warshaw and Torchiana [1] first described DGE after PD in the 1980s, several definition systems were used for evaluating DGE incidence before the consensus definition of ISGPS was published [6]. Although several authors [3, 30, 40] have validated the ISGPS definition of DGE, the actual tolerance to oral intake could sometimes be confused according to the researchers to define DGE. Akizuki et al. [40] measured total dietary intake in addition to DGE incidence based on the ISGPS definition to analyze postoperative oral intake tolerance. They recorded the amount of oral intake because, even if the same oral diet begins on the same POD for patients, the amount of the intake differs among individuals. It is also possible that even patients without DGE would not sufficiently tolerate an oral diet. They found that a high body mass index, postoperative intra-abdominal infection, and DGE were risk factors for low oral intake. In this study, we

Table 2 Surgical outcomes between the Braun and No-Braun groups

	Braun (n = 30)	No-Braun (n = 30)	P-value
Operation time (min), mean ± SD	406 ± 81	413 ± 109	0.768
Bleeding (ml), mean ± SD	556 ± 248	528 ± 468	0.778
Transfusion	5 (16.7%)	5 (16.7%)	0.635
LN dissection			0.589
Standard/Extended	21 (70%)/9 (30%)	22 (73.3%)/8 (26.7%)	
Hospital stay (days), mean ± SD	20 ± 7	21 ± 11	0.773
POPF			0.347
No/Yes	25 (83.3%)/5 (16.7%)	22 (73.3%)/8 (26.7%)	
POPF grade			0.510
A	3 (10%)	7 (23.3%)	
B	2 (6.7%)	1 (3.3%)	
C	0	0	
Bile leakage		1.000	
No/Yes	30 (100%)/0	29 (96.7%)/1 (3.3%)	
Chyle leakage			0.706
No/Yes	25 (83.3%)/5 (16.7%)	27 (90%)/3 (10%)	
Wound complication			0.424
No/Yes	25 (83.3%)/5 (16.7%)	27 (93.1%)/2 (6.9%)	
Intra-abdominal abscess			1.000
No/Yes	29 (96.7%)/1 (3.3%)	29 (96.7%)/1 (3.3%)	
Bleeding			1.000
No/Yes	30 (100%)/0	29 (96.7%)/1 (3.3%)	
Clavien-Dindo classification			0.734
Grade I–II	17 (80.9%)	17 (85%)	
Grade IIIa–IIIb	4 (19%)	3 (15%)	
Grade IVa–V	0	0	

Data are presented as n (%) unless otherwise noted. *LN* lymph node, *POPF* postoperative pancreatic fistula, *SD* standard deviation

also noted the first day that patients could eat more than half of the oral intake amount in order to add information for analyzing oral intake tolerance. That day was marginally earlier in the Braun group (9 ± 5 vs. 12 ± 9, P = 0.054).

Many clinical factors have been suggested as independent risk factors for DGE, including patient's age [12, 17], male sex [9], preoperative cholangitis [20], intraoperative bleeding [40], and postoperative complications (especially, POPF [9, 13, 19, 30, 32]). Lermite et al. [17] reported that old age (>70 years) was an independent factor influencing DGE after PD. In this study, even though the mean age was older in the Braun group, which may have been due to the small number of patients included in this RCT, age was not associated with DGE. When we performed an age-adjusted analysis, the incidences of overall DGE and clinically relevant DGE were not different between the Braun and No-Braun groups. Qu et al. [19] reported the risk factors for DGE based on a meta-analysis; they found that preoperative diabetes, pancreatic fistula, and postoperative complications were significantly associated with an increased risk of DGE. Other authors have reported that preoperative diabetes was independent risk factor for DGE [9, 13, 17–19]. In our study, diabetes was not associated with DGE. Several other studies have also shown that postoperative complications, especially POPF [9, 13, 19, 30, 32], were related to DGE. POPF has been shown to be associated with intra-abdominal bleeding and infection. Gastric dysrhythmias might develop secondarily to intra-abdominal local inflammation or abscess and consequently cause DGE [41]. The rate of clinically relevant POPF in the studies suggesting POPF as a risk factor for DGE ranged from 17% to 36%. However, Nikfarjam et al. [13] reported that POPF was not associated with increased DGE. The overall POPF incidence in their study was 19%, and clinically relevant POPF was 14.6%. In our study, the grade C POPF rate was 0% in both groups, and overall clinically relevant POPF (grade B only) was observed in only 5%. Intra-abdominal abscess was observed in one patient (3.3%) in each group. There was no in-hospital mortality. These postoperative outcomes with low morbidity in the present study might not affect the DGE occurrence in both groups.

Table 3 Postoperative course and DGE incidence

	Braun (n = 30)	No-Braun (n = 30)	P-value
Full liquid diet (day), mean ± SD	3 ± 1	5 ± 5	0.152
Solid diet (day), mean ± SD	6 ± 4	9 ± 8	0.091
Gas out (day), mean ± SD	4 ± 2	5 ± 3	0.222
Half of oral intake amount (day), mean ± SD	9 ± 5	12 ± 9	0.054
Vomiting event			0.222
No/Yes	25 (83.3%)/5 (16.7%)	21 (70%)/9 (30%)	
Adding prokinetics or antiemetic drugs			0.592
No/Yes	20 (66.7%)/10 (33.3%)	18 (60%)/12 (40%)	
NGT insertion			1.000
No/Yes	27 (90%)/3 (10%)	26 (86.7%)/4 (13.3%)	
DGE			0.108
No/Yes	22 (73.3%)/8 (26.7%)	16 (53.3%)/14 (46.7%)	
DGE grade			0.181
A	7 (23.3%)	7 (23.3%)	
B	1 (3.3%)	4 (13.3%)	
C	0 (0%)	3 (10%)	
Clinically relevant DGE			0.052
No & grade A	29 (96.7%)	23 (76.7%)	
Grades B & C	1 (3.3%)	7 (23.3%)	

Data are presented as n (%) unless otherwise noted. *DGE* delayed gastric emptying, *NGT* nasogastric tube, *SD* standard deviation

Table 4 Logistic regression analysis for risk factors influencing clinically relevant DGE

	Clinically relevant DGE					
	Univariable analysis			Multivariable analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age (> 67 vs. ≤ 67)	0.926	0.209–4.104	0.919			
Sex (male vs. female)	1.889	0.422–8.457	0.406			
DM (Yes vs. No)	1.737	0.389–7.756	0.470			
Braun anastomosis (No vs. Yes)	8.826	1.012–76.960	0.049	16.489	1.287–211.195	0.031
POPF (Yes vs. No)	2.520	0.514–12.343	0.254			
POPF, Clinical (Yes vs. No)	3.571	0.285–44.718	0.324			
Wound complication (Yes vs. No)	3.067	0.483–19.452	0.234	8.717	0.710–107.107	0.091
Intraabdominal abscess (Yes vs. No)	7.286	0.408–130.074	0.177			
Clavien-Dindo classification (≥ IIIa vs. no complication and I–II)	3.133	0.494–19.866	0.226			

Clinically relevant DGE was defined as DGE grades B and C. Clinically relevant POPF was defined as POPF grades B and C. Chyle leakage and postoperative bleeding were not available for logistic regression analysis. *CI* confidence interval, *DGE* delayed gastric emptying, *DM* diabetes mellitus, *OR* odds ratio, *POPF* postoperative pancreatic fistula

The hospital stay for the No-DGE group was 20 days, similar to that for the DGE group (21 days) and longer than that in Europe and the United States. This difference may relate to differences in healthcare costs and medical insurance systems among countries. Medical costs in Western countries are considerably higher than are those in Korea. Most patients in Korea refuse discharge when they feel any minor physical discomfort.

There are some limitations to the present study. One weakness is the small number of patients. According to the reference study's result (i.e. the difference in DGE incidence rates between the Braun and No-Braun groups was 30.8%) [35], our calculated sample size was small. However, in order to avoid unnecessary randomization, we tried to limit the sample size to the minimum required for statistical analysis. It is expected that a larger RCT will be

Table 5 Age-adjusted DGE incidence between the Braun and No-Braun groups

	Age ≤ 65.7 years (n = 26)			Age > 65.7 years (n = 34)		
	Braun (n = 10)	No-Braun (n = 16)	P-value	Braun (n = 20)	No-Braun (n = 14)	P-value
DGE			0.683			0.163
No	7 (70%)	9 (56.2%)		15 (75%)	7 (50%)	
Yes	3 (30%)	7 (43.8%)		5 (25%)	7 (50%)	
Clinically relevant DGE			0.136			0.283
No & grade A	10 (100%)	12 (75%)		19 (95%)	11 (78.6%)	
Grades B & C	0	4 (25%)		1 (5%)	3 (21.4%)	

Clinically relevant DGE was defined as DGE grades B and C. *DGE* delayed gastric emptying

conducted based on the current encouraging data to prove the beneficial effect of the Braun anastomosis for reducing clinically relevant DGE following PPPD. In addition, it was interesting to note that, even though this study was designed as an RCT, approximately 40% of eligible patients did not agree with enrollment. As patients' awareness about the potential risks and ethical issues of RCTs is increasing, patients seem hesitant to get actively involved in them. This issue needs to be considered in planning future RCTs. If effective patient's enrollment were not feasible, the power of the RCT may be limited, and even randomization would not be possible.

To the best of our knowledge, the present study was the first RCT to evaluate the effectiveness of the Braun anastomosis in reducing DGE after PPPD, and this trial was performed with a relatively short study period (16 months) facilitating well controlled RCT with uniform operative technique and postoperative management. Based on the current RCT, it was demonstrated that Braun anastomosis could reduce clinically relevant DGE (grades B and C) with marginal statistical significance, and that not receiving a Braun anastomosis was an independent risk factor affecting clinically relevant DGE following PPPD.

Acknowledgments The authors would like to express their special appreciation to Dong-Su Jang (Medical Illustrator, Medical Research Support Section, Yonsei University College of Medicine, Seoul, Korea) for his excellent illustrations in the manuscript.

Conflict of interest None declared.

Author contributions Conception and design: HK Hwang and CM Kang. Acquisition, analysis, and interpretation of data: HK Hwang, SH Lee, DH Han, SH Choi and CM Kang. Drafting of the manuscript: HK Hwang, SH Lee, DH Han, SH Choi and CM Kang. Critical revision of the manuscript for important intellectual content: HK Hwang, CM Kang and WJ Lee. Statistical analysis: HK Hwang and CM Kang.

References

1. Warshaw AL, Torchiana DL. Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. Surg Gynecol Obstet. 1985;160:1–4.
2. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg. 1997;226:248–57.
3. Welsch T, Borm M, Degrate L, Hinz U, Buchler MW, Wente MN. Evaluation of the International Study Group of Pancreatic Surgery definition of delayed gastric emptying after pancreatoduodenectomy in a high-volume centre. Br J Surg. 2010;97:1043–50.
4. Eshuis WJ, van Eijck CH, Gerhards MF, Coene PP, de Hingh IH, Karsten TM, et al. Antecolic versus retrocolic route of the gastroenteric anastomosis after pancreatoduodenectomy: a randomized controlled trial. Ann Surg. 2014;259:45–51.
5. Itani KM, Coleman RE, Meyers WC, Akwari OE. Pylorus-preserving pancreatoduodenectomy. A clinical and physiologic appraisal. Ann Surg. 1986;204:655–64.
6. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007;142:761–8.
7. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery. 2005;138:8–13.
8. Kawai M, Tani M, Hirono S, Miyazawa M, Shimizu A, Uchiyama K, et al. Pylorus ring resection reduces delayed gastric emptying in patients undergoing pancreatoduodenectomy: a prospective, randomized, controlled trial of pylorus-resecting versus pylorus-preserving pancreatoduodenectomy. Ann Surg. 2011;253:495–501.
9. Sakamoto Y, Yamamoto Y, Hata S, Nara S, Esaki M, Sano T, et al. 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.
10. Shimoda M, Kubota K, Katoh M, Kita J. Effect of billroth II or Roux-en-Y reconstruction for the gastrojejunostomy on delayed gastric emptying after pancreaticoduodenectomy: a randomized controlled study. Ann Surg. 2013;257:938–42.
11. Tani M, Terasawa H, Kawai M, Ina S, Hirono S, Uchiyama K, et al. Improvement of delayed gastric emptying in pylorus-preserving pancreaticoduodenectomy: results of a prospective, randomized, controlled trial. Ann Surg. 2006;243:316–20.
12. Gangavatiker R, Pal S, Javed A, Dash NR, Sahni P, Chattopadhyay TK. Effect of antecolic or retrocolic reconstruction of the gastro/duodenojejunostomy on delayed gastric emptying after pancreaticoduodenectomy: a randomized controlled trial. J Gastrointest Surg. 2011;15:843–52.
13. Nikfarjam M, Kimchi ET, Gusani NJ, Shah SM, Sehmbey M, Shereef S, et al. A reduction in delayed gastric emptying by classic pancreaticoduodenectomy with an antecolic gastrojejunal anastomosis and a retrogastric omental patch. J Gastrointest Surg. 2009;13:1674–82.

14. Akizuki E, Kimura Y, Nobuoka T, Imamura M, Nishidate T, Mizuguchi T, et al. 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.
15. 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.
16. Fischer CP, Hong JC. Method of pyloric reconstruction and impact upon delayed gastric emptying and hospital stay after pylorus-preserving pancreaticoduodenectomy. J Gastrointest Surg. 2006;10:215–9.
17. Lermite E, Pessaux P, Brehant O, Teyssedou C, Pelletier I, Etienne S, et al. Risk factors of pancreatic fistula and delayed gastric emptying after pancreaticoduodenectomy with pancreaticogastrostomy. J Am Coll Surg. 2007;204:588–96.
18. van Berge Henegouwen MI, van Gulik TM, DeWit LT, Allema JH, Rauws EA, Obertop H, et al. Delayed gastric emptying after standard pancreaticoduodenectomy versus pylorus-preserving pancreaticoduodenectomy: an analysis of 200 consecutive patients. J Am Coll Surg. 1997;185:373–9.
19. Qu H, Sun GR, Zhou SQ, He QS. Clinical risk factors of delayed gastric emptying in patients after pancreaticoduodenectomy: a systematic review and meta-analysis. Eur J Surg Oncol. 2013;39:213–23.
20. 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.
21. Matsunaga H, Tanaka M, Naritomi G, Yokohata K, Yamaguchi K, Chijiwa K. Effect of leucine 13-motilin (KW5139) on early gastric stasis after pylorus-preserving pancreatoduodenectomy. Ann Surg. 1998;227:507–12.
22. Ohwada S, Satoh Y, Kawate S, Yamada T, Kawamura O, Koyama T, et al. Low-dose erythromycin reduces delayed gastric emptying and improves gastric motility after Billroth I pylorus-preserving pancreaticoduodenectomy. Ann Surg. 2001;234:668–74.
23. Takahata S, Ohtsuka T, Nabae T, Matsunaga H, Yokohata K, Yamaguchi K, et al. Comparison of recovery of gastric phase III motility and gastric juice output after different types of gastrointestinal reconstruction following pylorus-preserving pancreatoduodenectomy. J Gastroenterol. 2002;37:596–603.
24. Yeo CJ, Barry MK, Sauter PK, Sostre S, Lillemoe KD, Pitt HA, et al. Erythromycin accelerates gastric emptying after pancreaticoduodenectomy. A prospective, randomized, placebo-controlled trial. Ann Surg. 1993;218:229–37.
25. Gauvin JM, Sarmiento JM, Sarr MG. Pylorus-preserving pancreaticoduodenectomy with complete preservation of the pyloroduodenal blood supply and innervation. Arch Surg. 2003;138:1261–3.
26. Tanaka A, Ueno T, Oka M, Suzuki T. Effect of denervation of the pylorus and transection of the duodenum on acetaminophen absorption in rats; possible mechanism for early delayed gastric emptying after pylorus preserving pancreatoduodenectomy. Tohoku J Exp Med. 2000;192:239–47.
27. Kim DK, Hindenburg AA, Sharma SK, Suk CH, Gress FG, Staszewski H, et al. Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy? Ann Surg Oncol. 2005;12:222–7.
28. Tanaka M, Sarr MG. Role of the duodenum in the control of canine gastrointestinal motility. Gastroenterology. 1988;94:622–9.
29. Riediger H, Makowiec F, Schareck WD, Hopt UT, Adam U. Delayed gastric emptying after pylorus-preserving pancreatoduodenectomy is strongly related to other postoperative complications. J Gastrointest Surg. 2003;7:758–65.
30. Park JS, Hwang HK, Kim JK, Cho SI, Yoon DS, Lee WJ, et al. 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.
31. Hashimoto Y, Traverso LW. Incidence of pancreatic anastomotic failure and delayed gastric emptying after pancreatoduodenectomy in 507 consecutive patients: use of a web-based calculator to improve homogeneity of definition. Surgery. 2010;147:503–15.
32. Malleo G, Crippa S, Butturini G, Salvia R, Partelli S, Rossini R, et al. Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy: validation of International Study Group of Pancreatic Surgery classification and analysis of risk factors. HPB (Oxford). 2010;12:610–8.
33. Ueno T, Tanaka A, Hamanaka Y, Tsurumi M, Suzuki T. A proposal mechanism of early delayed gastric emptying after pylorus preserving pancreatoduodenectomy. Hepatogastroenterology. 1995;42:269–74.
34. Hochwald SN, Grobmyer SR, Hemming AW, Curran E, Bloom DA, Delano M, et al. Braun enteroenterostomy is associated with reduced delayed gastric emptying and early resumption of oral feeding following pancreaticoduodenectomy. J Surg Oncol. 2010;101:351–5.
35. Nikfarjam M, Houli N, Tufail F, Weinberg L, Muralidharan V, Christophi C. Reduction in delayed gastric emptying following non-pylorus preserving pancreaticoduodenectomy by addition of a Braun enteroenterostomy. JOP. 2012;13:488–96.
36. Watanabe Y, Ohtsuka T, Kimura H, Matsunaga T, Tamura K, Ideno N, et al. Braun enteroenterostomy reduces delayed gastric emptying after pylorus-preserving pancreatoduodenectomy: a retrospective review. Am J Surg. 2015;209:369–77.
37. 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.
38. Braun H. Ueber die Gastro-enteostomie and Gleichzeutig Ausgefuhrte. Arch Klin Chir. 1893;45:361.
39. 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.
40. Akizuki E, Kimura Y, Nobuoka T, Imamura M, Nagayama M, Sonoda T, et al. 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.
41. 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.