J Gastrointest Surg (2016) 20:595–603
DOI 10.1007/s11605-015-2961-6

ORIGINAL ARTICLE

Delayed Gastric Emptying After Stapled Versus Hand-Sewn Anastomosis of Duodenojejunostomy in Pylorus-Preserving Pancreaticoduodenectomy: a Randomized Controlled trial

Yoshihiro Sakamoto[1] · Shutaro Hori[2] · Seiji Oguro[2] · Junichi Arita[3] · Yoji Kishi[2] · Satoshi Nara[2] · Minoru Esaki[2] · Akio Saiura[3] · Kazuaki Shimada[2] · Takeharu Yamanaka[4] · Tomoo Kosuge[2]

Received: 29 July 2015 / Accepted: 16 September 2015 / Published online: 24 September 2015

Abstract

Background A retrospective analysis indicated that the incidence of delayed gastric emptying (DGE) was less after using a circular stapler (CS) for duodenojejunostomy than that after hand-sewn (HS) anastomosis in pylorus-preserving pancreaticoduodenectomy (PpPD). This randomized clinical trial compared the incidence of DGE postoperative after CS duodenojejunostomy with that of conventional HS anastomosis in PpPD.

Methods We randomly assigned 101 patients (age 20–80) undergoing PpPD to receive CS duodenojejunostomy (group CS, n=50) or HS duodenojejunostomy (group HS, n=51) in two Japanese cancer center hospitals between 2011 and 2013. The patients were stratified by institution and size of the main pancreatic duct (<3 or ≥3 mm). The primary endpoint was the incidence of grade B or C DGE according to the international definition with a non-inferiority margin of 5 %. This trial is registered with University hospital Medical Information Network (UMIN) Center: UMIN000005463.

Results Per-protocol analysis of data on 95 patients showed that grade B or C DGE was found in 4 (8.9 %) of 45 patients who underwent CS anastomosis and in 8 (16 %) of 50 patients who underwent HS anastomosis (P=0.015). There were no differences in the overall incidence of DGE (P=0.98), passage of the contrast medium through the anastomosis (P=0.55), or hospital stays (P=0.22).

Conclusions CS duodenojejunostomy is not inferior to HS anastomosis with respect to the incidence of clinically significant DGE, justifying its use as treatment option.

Keywords Delayed gastric emptying · Pylorus-preserving pancreaticoduodenectomy · Circular stapler · Hand-sewn · Randomized controlled trial

Presented at the American College of Surgeons Clinical Congress at San Francisco, on Oct 24, 2014.

✉ Yoshihiro Sakamoto
yosakamo-tky@umin.ac.jp

[1] Hepato-Biliary-Pancreatic Surgery Division, Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

[2] Hepatobiliary and Pancreatic Surgery Division, National Cancer Center Hospital, Chuo-ku, Tokyo, Japan

[3] Department of Gastrointestinal Surgery, Cancer Institute Ariake Hospital, Japanese Foundation for Cancer Research, Koto-ku, Tokyo, Japan

[4] Department of Bioethics, Yokohama City University, Yokohama, Japan

Introduction

Pancreaticoduodenectomy (PD) is the most common surgical procedure for periampullary neoplasms and, 500 PDs are performed per year in the USA according to Surveillance, Epidemiology, and End Results (SEER) database.[1] Delayed gastric emptying (DGE) and pancreatic fistula are the most concerning morbidities associated with prolongation of hospital stay and increased hospital costs. The reported incidence of DGE has a wide range (7–57 %),[2–5] partly because the definition of DGE varies. A recent meta-analysis revealed that perioperative diabetes, pancreatic fistula, and postoperative

complications are significantly associated with an increased risk of DGE, whereas preoperative biliary drainage and antecolic reconstruction are associated with decreased the risk of DGE development.[6] As attempts to prevent DGE, several randomized controlled trials (RCTs) have shown that administration of erythromycin,[2,3] antecolic over retrocolic gastrojejunostomy,[5] pylorus ring resecting PD over pylorus-preserving PD,[7], and Billroth type II reconstruction over Roux-en-Y reconstruction[8] significantly decrease the incidence of DGE.

At present, most of gastrointestinal anastomoses are performed using staplers, and this tendency has increased with the introduction of laparoscopic or robotic surgery.[9] The potential advantages of stapled anastomosis are saving of time procedure and less inter-individual differences. We hypothesized that the diversity of hand-sewn (HS) anastomosis may be associated with increased risk of DGE and previously conducted a retrospective study to compare the incidence of DGE after stapled duodenojejunostomy and gastrojejunostomy with those after HS reconstruction for pylorus-preserving PD (PpPD) or classic PD in 387 patients undergoing PD.[10] This study showed that the incidence of DGE was lower after stapled reconstruction (n=70) than that after HS reconstruction (n=317) (7.2 vs. 21 %, P<0.001) and with single-layer anastomosis than with double-layer anastomosis (12 vs. 24 %, P= 0.02). However, these results may have been biased because of the retrospective single institution nature of the study that included a variety of surgical procedures and historical changes. Therefore, we conducted the present dual-institution RCT to compare the incidence of postoperative DGE after duodenojejunostomy using a circular stapler (CS) with that after conventional HS anastomosis in PpPD.

Methods

Trial Design

We conducted this non-inferiority, dual-institution prospective randomized RCT comparing CS and HS duodenojejunostomy in PpPD between April 1, 2011 and July 1, 2013. Two cancer centers in Tokyo, Japan, the National Cancer Center Hospital and Cancer Institute Ariake Hospital, participated in this study. This trial was approved by the Ethics Committees on Clinical Investigation of the two institutions, and all patients provided written informed consent before operation. The trial interventions were duodenojejunostomy using CS and conventional HS anastomosis in PpPD. Classical PD was excluded to simplify the study design. To achieve generalized results for this trial, there was no restriction concerning the particular method of HS anastomosis.

The patient eligibility criteria included undergoing PpPD for periampullary disease, age between 20 and 80 years, and provision of written informed consent. The exclusion criteria included classic PD, total pancreatectomy, with previous gastrectomy, or with major hepatectomy combined with PpPD.

Recruitment and Randomization

All procedures regarding allocation, enrollment, assignment, and announcement of the assignment results to the attending surgeons were performed by two investigators (SH and SO). Enrollment was finally determined intraoperatively at the respective trial centers by the attending physicians. The time from first patient in to last patient out was from April 2011 to April 2013. Randomization was performed intraoperatively after confirmation that surgical resection was feasible, and the patients were assigned to either the CS duodenojejunostomy group (group CS) or the conventional HS method group (group HS) used as the control. Block randomization was performed with stratification by two factors: institution (National Cancer Center Hospital and Cancer Institute Hospital) and size of the main pancreatic duct (<3 and ≥3 mm) at the pancreatic neck evaluated before surgery using computed tomography scans (Fig. 1), because the incidence of DGE is affected by the size of main pancreatic duct with the cutoff value of 3 mm in a retrospective analysis using a large number of patients undergoing PD.[11]

Preoperative Managements

Preoperative biliary drainage in 46 patients (45.5 %) was performed either in a previous hospital or in the present two institutions. The remaining 55 patients underwent surgery without biliary drainage. Surgery was performed when the serum bilirubin concentration decreased to <5 mg/dl. The patients received a second-generation cephalosporin as preoperative intravenous antibiotic prophylaxis.

Surgical Procedures of PpPD

The details of our standard surgical PpPD procedure have been described previously.[12] In brief, duodenum was cut at 2 cm distal side of the pylorus ring using linear stapler. After completion of pancreaticojejunostomy and hepaticojejunostomy, the antecolic gastrojejunostomy was performed according to the results of randomization. In group HS, the duodenojejunostomy was performed either by Albert-Lembert method, Gambee anastomosis, or layer-to-layer method with or without Braun anastomosis at the discretion of each attending surgeons (Fig. 2). In group CS, the duodenojejunostomy was made using circular staplers. The details of stapled Roux-en-Y reconstruction have been described previously.[13] In brief, antecolic duodenojejunostomy was performed by Roux-en-Y reconstruction using Proximate ILS™ 25- or 29-mm CS (Ethicon Endo-Surgery, Cincinnati,

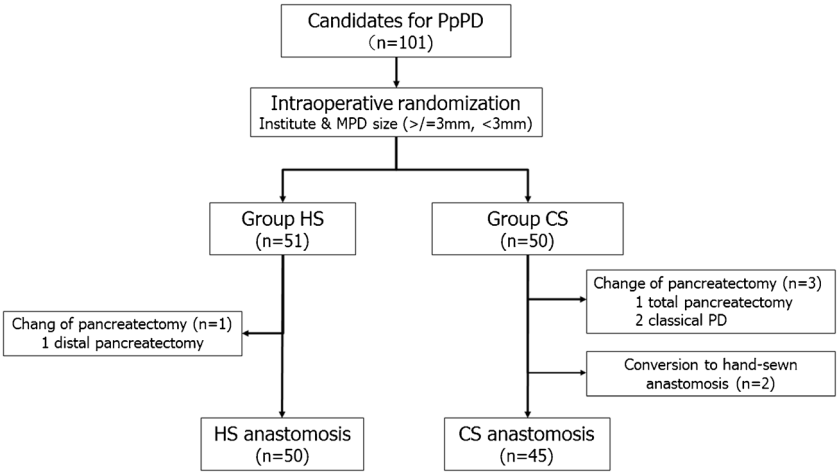

Fig. 1 Randomization and treatments. *PpPD*, pylorus-preserving pancreaticoduodenectomy; *MPD*, main pancreatic duct; *HS*, hand-sewn anastomosis; *CS*, anastomosis using a circular stapler

OH) or EEA 25- or 28-mm CS (US Surgical, Norwalk, CT) in PpPD. Jejunojejunostomy was performed to reconstruct the Roux-en-Y jejunal limb (Fig. 2).

Combined portal vein resection was performed in 19 patients (19 %) out of 101 patients undergoing PD or total pancreatectomy. Pancreaticojejunostomy was performed at the discretion of the attending surgeons, and pancreatic duct was reconstructed by using duct-to-mucosa anastomosis in 77 patients, the dunking method was performed in six patients, and invagination was performed in 16 patients. The pancreatic parenchyma was sewn to the jejunal wall by two-layer anastomosis in 46 patients, by Kakita's method[14] in 36 patients, and by other methods in 17 patients. In one patient, pancreaticojejunostomy was not performed because of total pancreatectomy, and the remaining one patient underwent distal pancreatectomy after randomization.

Postoperative Management

The nasogastric tube was removed on postoperative day (POD) 1. Reinsertion of the gastric tube was performed if the patient complained of nausea or vomiting and/or if severe distension of the stomach was observed on abdominal radiography. Postoperative administration of erythromycin or octreotide was prohibited. In group CS, postoperative administration of proton pump inhibitor was recommended in order to prevent the anastomotic bleeding which was found in 15 % in the preliminary study.[13] The patients were discharged from the hospital, when they could eat almost half of their regular diet and had one abdominal drain left with minimal output.

Sample Size

The hypothesis of the present trial was that the incidence of grade B or C DGE in CS anastomosis is no more than that in HS anastomosis. The trial was designed to have a non-inferiority setting. The assumed incidences of grade B or C DGE after PpPD in CS and HS anastomosis were estimated to be 6 and 20 %, respectively, from an institutional review.[10] The sample size was calculated on the basis of a non-inferiority margin of 5 %, a one-sided alpha level of 0.05, and a power of 80 % and included 49 patients in each arm. Assuming a dropout rate of 2 %, a total of 100 patients were to be allocated in this trial, with a total accrual period of 2 years.

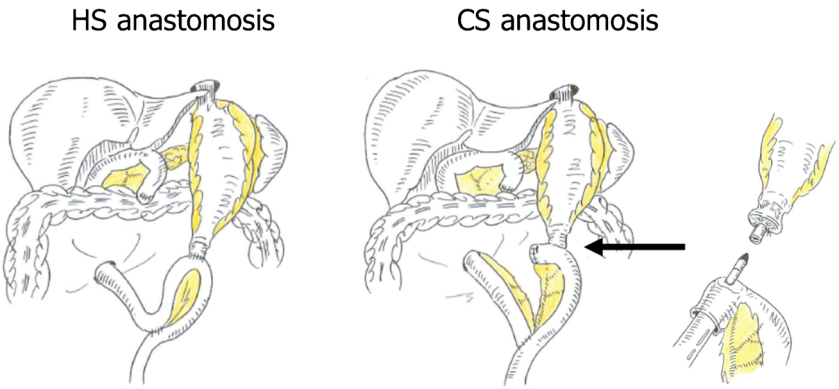

Fig. 2 Schematic representation of hand-sewn anastomosis versus anastomosis using a circular stapler. *HS*, hand-sewn; *CS*, circular stapler

Outcome Measures

The primary endpoint was the incidence of grade B or C DGE defined according to the International Study Group on Pancreatic Surgery classification.[15] The secondary endpoints were as follows: (1) reconstruction time (min), (2) passage of the contrast medium on PODs 4–7, (3) the incidence of all grades of DGE, and (4) the length of hospital stay (days).

DGE was classified into grades A, B, and C according to the definition proposed by the International Study Group of Pancreatic Surgery[15]: in brief, grade A, unable to tolerate solid oral intake by POD 7 and usually no vomiting; grade B, unable to tolerate solid oral intake by POD 14 with/without vomiting: and grade C, unable to tolerate solid oral intake by POD 21 with/without vomiting. Reinsertion of the gastric tube or opening of the gastrostomy on or after POD 7 was considered to be indicative of DGE. Because the timing of serving food was influenced by the preference of each attending surgeon, grade A was not considered to be a clinically relevant complication.

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

The reconstruction time included not only the time for duodenojejunostomy by HS or CS anastomosis but also the time for jejunojejunostomy in Roux-en-Y reconstruction and the time for Braun anastomosis in conventional Billroth II reconstruction.

Definition of Other Outcome Measures

Postoperative pancreatic fistula (POPF) was defined according to the definition proposed by the International Study Group on Pancreatic Fistula;[16] in brief, POPF was diagnosed when the amylase concentration of the drain fluid obtained on or after POD 3 was >3 times the upper range of serum amylase concentration. POPF was classified into grades A, B, and C according to severity: in brief, grade A fistula was a "transient fistula" not associated with a delay in hospital discharge; grade B fistula led to a delay in discharge, with persistent drainage for >3 weeks; and grade C fistula was usually associated with major complications. Grade B or C fistula was considered to constitute clinically relevant POPF. Complications other than POPF and DGE were classified according to the criteria proposed by Clavien and Dindo,[17] and only complications classified as grade 2 or above were recorded.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows statistical software (SPSS Inc., Chicago, IL). The chi-square test or Fisher's exact test was used for univariate analysis, and the Mann–Whitney *U* test was used to compare the variables between the two groups. A multivariate analysis of the risk factors for DGE was performed using logistic regression analysis. Data were expressed as the median and range. A P value of <0.05 was considered to indicate statistical significance.

Results

Between April 2011 and April 2013, 101 patients were randomly assigned to group CS and group HS (Fig. 1). None of the 101 patients died in the hospital as a result of surgery.

Conversion of the Surgical Procedure or the Anastomotic Method in Six Patients

After randomization, surgical procedures were changed in four patients, and they were excluded from the per-protocol analysis. One patient in group HS underwent distal pancreatectomy, and another patient in group CS underwent total pancreatectomy to completely eradicate pancreatic cancer. Two patients in group CS underwent classic PDs; one patient underwent PD to increase the chance of cure. In another patient in group CS, the duodenum was lacerated because of size mismatch between the shaft and orifice of the duodenum. The antrum of the stomach was resected, and HS gastrojejunostomy was performed.

In two patients undergoing PpPD assigned to group CS, duodenojejunostomy was performed by HS anastomosis; one case with size mismatch between the shaft and orifice of the duodenum and another patient with trouble in making a purse-string suture. These two patients were excluded from the per-protocol analysis.

Further analysis of the surgical complications was performed by excluding the above six patients because the ratio of these deviation was relatively high (5.9 %), and the results of the six patients might have had a large influence on the primary endpoint. Excluding six patients from of the per-protocol analysis, no significant difference was found in the baseline characteristics of the 95 patients in per-protocol analysis (Table 1). Operative outcomes showed that there was no significant difference in overall operative time, blood loss, incidence of blood transfusion, extent of nodal dissection, incidence of SMA nerve dissection or portal vein resection, and methods of pancreato-jejunostomy (Table 2). Braun

Table 1 Baseline characteristics of the 95 patients in per-protocol analysis

	HS group (n=50)	CS group (n=45)	P value
Age, years	64.0 (32–79)	67.5 (38–80)	0.16
Gender (male/female)	30/20	22/23	0.28
BMI	22.1 (17.5–27.1)	21.6 (16.1–31.4)	0.12
Preoperative biliary drainage (yes/no)	19/31	25/20	0.09
Diabetes (yes/no)	11/39	16/29	0.14
Pancreatitis (yes/no)	9/41	8/37	0.98
Albumin (mg/dl)	4.2 (2.9–4.8)	4.0 (2.9–5.0)	0.06
Creatinine (mg/dl)	0.7 (0.1–1.1)	0.7 (0.4–1.2)	0.31
Total cholesterol (mg/dl)	193 (92–285)	183 (109–279)	0.81
Cholinesterase (IU/l)	274 (145–419)	291 (134–446)	0.52
CRP (mg/dl)	0.13 (0–2.06)	0.12 (0.02–5.89)	0.92
CA19-9 (U/ml)	20.0 (1–1,827)	21.0 (1–5,650)	0.93
HbA1c (%)	5.5 (4.1–10.0)	5.7 (4.2–9.7)	0.13
Diameter of main pancreatic duct (≥3 mm/<3 mm)	26/24	23/22	0.93
Institution (NCCH/CIH)	39/11	35/10	0.98
Diseases			
Pancreatic adenocarcinoma	15	19	0.13
Bile duct carcinoma	9	4	
Ampullary adenocarcinoma	5	8	
Intraductal papillary mucinous neoplasm	13	4	
Pancreatic neuroendocrine neoplasm	3	1	
Duodenal cancer	2	3	
Others	3	6	

HS hand-sewn, *CS* circular stapler, *NCCH* National Cancer Center Hospital, *CIH* Cancer Institute Hospital, *BMI* body mass index, *CRP* C-reactive protein, *CA19-9* carbohydrate antigen 19-9, *HbA1c* hemoglobin A1c

anastomosis was added in 29 (57 %) out of the 50 patients in group HS while none in group CS.

Primary Endpoint

In the per-protocol analysis, grade B or C DGE was found in eight (16 %) patients in group HS and three (6.7 %) patients in group CS. Non-inferiority of group CS compared with group HS was demonstrated (P= 0.015). In chi-square analysis, superiority of group CS was not proved (P=0.16) (Table 3).

Secondary Endpoints

The reconstruction time was longer in group CS (35± 7.2 min) than in group HS (24.5±9.6 min, P<0.001). In group HS, 29 of the 50 anastomoses were performed with Braun anastomosis. The mean reconstruction time of the 29 patients with Braun anastomosis was 30.1±7.6 min, which was not significantly different from that of group CS (35.0±7.2 min). Upper gastrointestinal study was performed in 40 (80 %) out of 50 patients in group HS and in 38 (84 %) out of 45 patients in group CS. There was no significant difference in the passage of the contrast medium. Including grade A, DGE was found in ten (20 %) patients in group HS, and nine (20 %) patients in group CS (P=0.20). There was no significant difference in the length of hospital stay between the two groups (Table 3).

There was no significant difference in the incidence of complications other than DGE between the two groups (Table 4). A forest plot of the effect of each treatment on DGE suggested that there were no confounding factors between the significant variables and the effect of each treatment (Fig. 3).

Discussion

The present study demonstrated that the incidence of grade B or C DGE after CS duodenojejunostomy was non-inferior to that after HS duodenojejunostomy in PpPD (6.7 vs. 16 %, P=0.015). Two (4 %) of the 50 patients assigned to group CS required conversion to HS anastomosis because of size mismatch between the duodenal orifice and anvil head. One (2 %) patient in group CS was converted to group HS because of the failure of the purse-string suture around the anvil head.

Table 2 Operative parameters of the 95 patients in per-protocol analysis

	Group HS (n=50)	Group CS (n=45)	P value
Operator (staff/resident)	40/10	36/9	1.00
Operative time (min)	453 (318–689)	490 (269–703)	0.23
Estimated blood loss (ml)	622 (160–1,830)	645 (75–2,734)	0.85
Red cell transfusion (yes/no)	2/48	2/43	0.91
Pancreatic parenchyma			
Soft	33	27	0.40
Intermediate	6	10	
Hard	11	8	
Lymph node dissection (D1/D2)	10/40	7/38	0.57
Dissection of SMA nerve plexus (yes/no)	14/36	15/30	0.57
Portal vein resection (yes/no)	7/43	10/35	0.30
Anastomotic method for duodenojejunostomy			
Circular stapler	0	45	<0.001
Albert-Lembert	6	0	
Gambee	27	0	
Layer-to-layer	17	0	
Braun anastomosis or Roux-en-Y limb (yes/no)	29/21	45/0	<0.001
Pancreato-jejunostomy (duct)			
Duct-to-mucosa	39	34	0.96
Dunking method	3	3	
Invagination	8	8	
Pancreato-jejunostomy (parenchyma)			
2-layer method	20	24	0.36
Kakita's method	21	13	
Invagination	9	8	

SMA spinal muscular atrophy

However, surgical mortality, bleeding at the anastomotic site, or other severe complications associated with the introduction of CS[13] were not found in this trial. Contrary to the findings of our previous retrospective study, superiority of CS reconstruction over HS reconstruction in terms of the incidence of DGE was not shown, but non-inferiority was proved in this trial. These results indicate that duodenojejunostomy using a CS could be accepted as a safe and acceptable option that did not increase the risk of DGE.

Table 3 Postoperative outcome measures as for endpoints of the 95 patients in per-protocol analysis

	Group HS (n=50)	Group CS (n=45)	P value[a]
Time needed to perform duodenal reconstruction (min)	24.5 (10–50)	35.0 (23–50)	<0.001
Upper gastrointestinal study (performed/not performed)	40/5	38/7	0.42
A	32	29	0.55
B	12	7	
C	1	2	
Total DGE (yes/no)	10/40	9/36	0.98
None	40	36	0.51
A	2	6	
B	4	1	
C	4	2	
DGE grade B or C (yes/no)	8/42	3/41	0.16
NG reinsertion (yes/no)	5/45	3/42	0.56
Diet started day (days)	6 (4–32)	6 (4–74)	0.68
Hospital stay (days)	23.5 (10–75)	27.0 (14–108)	0.33

[a] P value is analyzed by chi-square analysis, not the non-inferior setting

Table 4 Postoperative complications other than DGE of the 95 patients in per-protocol analysis

	Group HS (n=50)	Group CS (n=45)	P value
Other complications			
Pancreatic fistula (yes/no)	27/23	21/24	0.48
None	23	24	
A	8	4	
B	16	14	
C	3	3	
POPF grade B or C (yes/no)	19/31	17/28	0.98
Wound infection	6	3	0.41
Bile leakage	1	0	0.36
Pneumonia	1	0	0.36
Ascites	0	2	0.12
Abdominal abscess	4	2	0.53
Intra-abdominal hemorrhage	1	0	0.36
Gastrointestinal hemorrhage	0	0	NS
Anastomotic bleeding	0	0	NS
Diarrhea	5	4	0.93
Administration of proton pump inhibitor (yes/no)	12/32	37/1	<0.001
Rate of body weight loss at discharge (%)	6.5 (−1.1 to 18.2)	6.5 (−0.8 to 20.2)	0.47
Mortality	0	0	NS

NS not significant

DGE after PD is a unique complication that is rarely seen after distal pancreatectomy or distal gastrectomy. DGE has been reported to be affected by several factors including gastric dysrhythmias due to intra-abdominal complications,[4,18] gastric atony after duodenal resection in response to reduction in motilin levels,[2,3,19] pylorospasm secondary to vagotomy,[20] angulation of the reconstructed alimentary tract,[21] and continuous enteral nutrition.[22,23] Several comparative retrospective studies have revealed that antemesenteric reconstruction,[4] vertical reconstruction,[24] and antecolic reconstruction[25,26] are associated with a decreased risk of DGE. Several randomized studies have shown that administration of erythromycin,[2,3] antecolic reconstruction,[5] resection of the pylorus ring,[7] and Billroth II rather than Roux-en-Y reconstruction[8] are associated with improved results for DGE; however, DGE is still a troublesome complication, and the treatment strategy for DGE has not been established. On the basis of our previous study,[10,13] a hypothesis can be drawn that anastomotic ischemia or edema may provoke the initial occurrence of stasis of the gastric juice, which may lead to subsequent DGE. In the

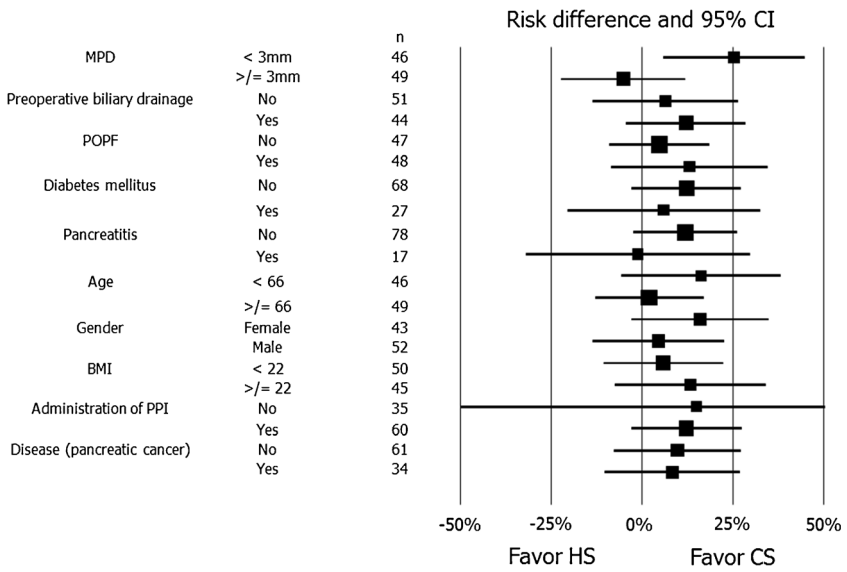

Fig. 3 Forest plot of the effect of treatment on the occurrence of grade B or C delayed gastric emptying in subgroup analysis. The size of squares is proportional to the size of the corresponding subgroup. *MPD*, main pancreatic duct; *POPF*, postoperative pancreatic fistula; *BMI*, body mass index; *HS*, hand-sewn; *CS*, circular stapler

present study, CS anastomosis for duodenojejunostomy in PpPD offered stable passage and minimized inter-individual variations at the anastomotic site, which helped to prevent an increase in the rate of DGE. In fact, the incidence of grade B or C DGE was 6.7 %, which was similar with that (7.2 %) of previous retrospective study, indicating the stability of stapled anastomosis.

Stapled alimentary reconstruction is now widely used in gastric, colorectal, or esophageal surgery.[27–29] Surgical stapling instruments were first developed in Russian in the 1950s,[30] and Dr. Ravitch applied the device in the field of gastrointestinal tract.[31] There were two types of surgical devices, a linear stapler and a CS for the anastomosis of the alimentary tract. Use of a CS for end-to-end anastomosis did not begin in the USA until 1974. Nance et al. reported the initial results of 57 anastomoses in 42 patients.[32] Use of a CS was first introduced for low anterior resection in case of rectal cancer or for esophagogastric anastomoses following resection of the lower esophagus at the end of 1970s.[33] Currently, it is reported to be more convenient and safer than HS suturing. Colorectal anastomoses using the double stapling technique have also become popular, particularly since the advent of laparoscopic surgery.[34] Recently, laparoscopic approach has been utilized to perform PD, and some aggressive surgeons reported that the morbidity and mortality rate of laparoscopic PD was comparable with those of open PD.[35] On the other hand, with respect to reconstruction after esophageal resection, in a RCT, esophagojejunostomy using CS did not increase the rate of leakage but increased the risk of benign stricture to four times that associated with HS one-layer anastomosis.[36] Stapler anastomosis after colectomy was associated not only with a decreased incidence of anastomotic leakage but also with decreased anastomosis recurrence and cancer-specific survivals in a large RCT.[37] Thus, use of a CS for alimentary anastomosis is debatable, but the present RCT showed acceptable outcomes for preventing DGE.

The study had several limitations. First is diversity of the anastomosis method in group HS consisting of three types of anastomosis measures with (n=29) or without (n=21) Braun anastomosis. In the study by Shimoda et al., the incidence of DGE was higher with Roux-en-Y reconstruction than with Billroth II reconstruction with Braun anastomosis.[8] Even if we adopt these results in the present RCT, we can say that the stapled duodenojejunostomy itself would not increase the incidence of DGE in comparison with hand-sewn duodenojejunostomy, because Roux-en-Y anastomosis was performed in all patients of group CS. Logically, the incidence of DGE should be decreased in group CS, when the same reconstruction method is applied in both groups. Second, the time needed for reconstruction was not shortened in group CS. The reconstruction time, including that for jejunojejunostomy, was longer in group CS than in group HS, because the reconstruction time in group CS included the time for jejunojejunostomy. In group HS, 29 of the 50 anastomoses were performed with Braun anastomosis. The mean reconstruction time of the 29 patients with Braun anastomosis was 30.1±7.6 min, which was not significantly different from that of group CS (35.0±7.2 min). This may be partly because of the learning curve of the stapling technique. The third limitation is the rationale for the non-inferiority design. Considering the cost and time of the present stapling anastomosis, this randomized study should have been designed as a superiority trial. However, in our previous study, we already had good reason to consider that stapled reconstruction was easier, more comfortable, and more stable than HS anastomosis on the basis of experience of performing 70 anastomoses using staplers.[10]

In conclusion, the results of this RCT showed that use of a CS for duodenojejunostomy in PpPD is an acceptable option that did not increase the risk of DGE.

Acknowledgments The authors express deep gratitude to *Dr. Katsuhiko Uesaka*, Department of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center Hospital, *Dr. Masaru Konishi* and *Dr. Naoto Gotohda*, Department of Hepatobiliary and Pancreatic Surgery, National Cancer Center Hospital East, and *Dr. Masaji Hashimoto*, Department of Digestive Surgery, Toranomon Hospital, for their critical review of the trial design and manuscripts.

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

Competing Interests The authors declare that they have no competing interests.

Disclosure Information Nothing to disclose

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