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Laparoscopic pylorus preserving gastrectomy vs distal gastrectomy for early gastric cancer; A multicenter randomized controlled trial (KLASS-04)

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ABSTRACT

Objective: To evaluate the long-term outcomes of laparoscopic pylorus preserving gastrectomy (LPPG) with laparoscopic distal gastrectomy (LDG) for early gastric cancer (EGC).

Summary Background Data: PPG is considered as a function preserving surgery for EGC. However, there has been no multicenter randomized controlled trial comparing PPG with DG until now,

Methods: A multicenter randomized controlled trial (KLASS-04) with 256 patients with cT1N0M0 gastric cancer located in the mid portion of the stomach was conducted. The primary endpoint was the incidence of dumping syndrome at postoperative 1 year. Secondary endpoints included survival and recurrence, gallstone formation, nutritional parameters, gastroscopic findings, and quality of life (QOL) for 3 years.

Results: In the intention-to-treat analyses, there was no difference in the incidence of dumping syndrome at one year postoperatively (13.2% in LPPG vs. 15.8% in LDG, p=0.622). Gallstone formation after surgery was significantly lower in LPPG than in LDG (2.33% vs. 8.66%, p=0.026). Hemoglobin (+0.01 vs -0.76 gm/dL, p<0.001) and serum protein (-0.15 vs -0.35 gm/dL, p=0.002) were significantly preserved after LPPG. However, reflux esophagitis (17.8% vs. 6.3%, p=0.005) and grade IV delayed gastric emptying (16.3% vs. 3.9%, p=0.001) were more common in LPPG. Changes in body weight and postoperative QOL were not significantly different between groups. Three-year overall survival and disease-free survival were not different (1 case of recurrence of in each group, p=0.98).

Conclusions: LPPG can be used as an alternative surgical option for cT1N0M0 gastric cancer in the mid portion of the stomach.

Trial Registration: ClinicalTrials.gov identifier: NCT02595086

Introduction

Gastric cancer is the 5th most common cancer worldwide (1). In Korea and Japan, due to the screening program with gastroscopy, the majority of gastric cancer is detected at its earlier stage, compared to the western country (2). In this early stage of gastric cancer, the survival after treatment is excellent, therefore the quality of life (QOL) and the presence of postgastrectomy symptoms of individual patients are considered as more important (3).

The pylorus is a short muscular structure at the gastroduodenal junction, and it controls the outflow from the stomach to the duodenum and also prevents the backflow from the duodenum to the stomach. Removal of the pylorus leads to a variety of disorders such as dumping syndrome, reflux gastritis, gallstone formation, and malnutrition. However, preservation of pylorus also induces the delayed gastric emptying (DGE) immediately after surgery (4).

Pylorus preserving gastrectomy (PPG) was originally introduced in Japan for the treatment of peptic ulcer, and was later applied to the treatment of early gastric cancer (EGC) (5-7). PPG is considered as an applicable treatment option for EGC, when the distal tumor margin is placed at least 4-5 cm from the pylorus (8, 9).

Several case-control studies have demonstrated the functional advantages of PPG over distal gastrectomy (DG), such as lower incidence of dumping syndrome, reflux gastritis, gallstone formation, and malnutrition (10-12). However, these advantages of PPG over DG have not yet been confirmed by a multicenter randomized controlled trial. The aim of this Korean Laparoendoscopic Gastrointestinal Surgery Study Group (KLASS)-04 was to evaluate the functional benefits and oncologic safety of laparoscopic PPG (LPPG) over laparoscopic DG (LDG). The short-term results showed that LPPG had a comparable surgical complication rate, compared to LDG (13). Herein, we report the final long-term results of the KLASS-04 trial.

Methods

Study Design, Inclusion Criteria, and Randomization

KLASS-04 is an investigator-initiated, multicenter randomized controlled trial comparing LPPG with LDG for cT1N0M0 gastric cancer in the mid portion of the stomach. The study was approved by the institutional review board (IRB) (H-1502–058-648) of Seoul National University Hospital, followed by each investigator's IRB.

Inclusion criteria included (1) patient's age between 20 and 80 years with Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; (2) histologically confirmed gastric adenocarcinoma; (3) tumor of cT1N0M0 in preoperative gastroscopy, endoscopic ultrasound, and abdominal computed tomography; (4) tumor which was at least 5 cm away from the pylorus and resectable by distal gastrectomy, meaning that the proximal margin was at least 4-5 cm from the gastroesophageal junction.

Patients with a history of other cancers, synchronous EGC or adenoma of the antrum,

previous gastric surgery including gastrojejunostomy, and the presence of other malignancies within 5 years (except for cured basal cell carcinoma or in situ cervical cancer) were excluded. Patients with gallbladder stone, assessed by ultrasonography or non-contrast abdominal computed tomography (CT), were also excluded.

Randomization was performed intraoperatively immediately after diagnostic laparoscopy. It is performed in a 1:1 ratio with each investigator as the stratification factor. Block randomization method with mixed block sizes of 2 and 4 within each stratum is performed using SAS 9.2.

Surgical Quality Control

Only surgeons who had performed at least 50 cases of both LDG and open DG, whose institute had more than 80 cases of gastrectomy per year, and who had performed at least 5 LPPG were eligible to participate in KLASS-04. At least one unedited video of LPPG was reviewed by 2 or more reviewers experienced in LPPG, using a standardized evaluation form.

Surgical procedures and follow-up

After randomization, patients were assigned to either LPPG group or LDG group. Common procedures for both groups included (a) tumor localization by preoperative gastroscopic clip or intraoperative gastroscopy; (b) laparoscopic D1+ lymph node dissection based on current treatment guidelines (8, 9); (c) laparoscopic partial omentectomy; and (d) intraoperative frozen biopsy for both resection margins.

In the case of LPPG, #6 lymph nodes were carefully dissected to preserve the infrapyloric vessels. #5 lymph node dissection was not performed, and the right gastric arcade was ligated after first branching of the right gastric artery. Distal resection was performed about 3 to 5 cm from the pylorus and proximal resection was performed according to the tumor location after mini-laparotomy. The anastomosis (gastrogastrostomy) was made by an extracorporeal hand-sewn technique. In case of LDG, gastroduodenostomy (Billroth I, BI) or loop gastrojejunostomy (Billroth II, BII) with or without Braun jejunojejunostomy or Roux-en-Y (RY) gastrojejunostomy was performed by extracorporeal or intracorporeal approach. In the control group, the anastomosis method was determined by the location of the tumor and the surgeon's preference.

Patients enrolled in both groups were followed up 1 month after discharge, and then at 6-month intervals for 3 years. Gastroscopy was performed every year, and abdominal sonography and abdominal CT were performed alternately every 6 months. Recurrence, gallstone formation, QOL data, and long-term complications were collected in each visit. This study was not blinded and the patients were informed about the type of procedure after surgery. The detailed protocol has been described previously (13).

Endpoints and sample size calculation

The primary endpoint was the incidence of dumping syndrome according to the Sigstad score (7 or more) at 1 year after surgery (14). For sample size calculation, patients who underwent LPPG and LDG from August 2014 to October 2014 at Seoul National University Hospital

were analyzed for dumping syndrome at 1 year after surgery. Among 95 patients (52 LPPG, 43 LDG), dumping syndrome was observed in 0% (0/52) in LPPG group and in 7.0% (3/43) in LPPG group. The level of significance (α) was 0.05, and the type II error (β) was 0.20, so the power of the test was 80%. Each group required 108 patients to detect a difference in the incidence of dumping syndrome, and with a drop-out rate of 15%, the final calculation was 128 patients in each group and 256 patients in total.

Secondary endpoints included (a) short-term complications within 30 days as defined in previous KLASS trials (15, 16) and the 90-day mortality rate, (b) long-term complications for 3 years, assessed through patient interviews at each outpatient clinic, (c) 3-year overall and disease-free survival, (d) Incidence of gallbladder stone as assessed by ultrasonography or non-contrast abdominal CT, (e) changes in body weight, fat volume as assessed by abdominal CT scan, and other nutritional parameters, (f) gastroscopic findings such as gastritis (yes or no), bile reflux (yes or no), gastric emptying (1 = no food residue, 2 = liquid only, 3 = soft diet residue, 4 = nearly normal diet residue), reflux esophagitis (yes or no), and marginal ulcer (yes or no) (17), and (f) patients' QOL as assessed by EORTC-C30 and STO22.

Statistical Analysis

All patients were included in the intention-to-treat (ITT) analysis. The as-treated (AS) analysis included patients who switched to the other approach (LPPG vs. LDG) after randomization, excluding patients who received total gastrectomy. The per protocol (PP) analysis was also performed after excluding patients who (a) received unassigned surgery, (b) received total gastrectomy (TG) or combined resection, (c) received adjuvant chemotherapy, or (d) had a protocol violation. ITT analysis was given priority over PP analysis, if there were differences in statistical values between ITT and PP analyses.

Chi square test or Fisher's exact test was used to examine the difference in the proportions of patients between two groups. Continuous variables were analyzed by independent t-test or Wilcoxon rank-sum test. Kaplan-Meier method with log-rank test was used for survival and recurrence, and mixed-effects linear regression model was used for QOL analyses. $P<0.05$ was considered statistically significant. Statistical analysis was performed with SAS version 9-4.

Results

Patient demographics, tumor and operative characteristics

After the quality control process for investigators, 16 out of 19 surgeons from 9 institutes were enrolled in KLASS-04 (acceptance rate: 84%). A total of 256 patients (129 LPPG and 127 LDG) from 9 institutions were enrolled from July 2015 to July 2017, and all of them were used for the ITT analysis. The PP analysis included 215 patients (107 LPPG and 108 LDG) (Figure 1). There were no significant differences in patient demographics and tumor characteristics between groups in ITT and PP analyses. In ITT analysis, there was no

combined resection and all patients received R0 resection. The operation time was longer in LPPG group (194.5 min) compared to LDG group (180.9 min, p =0.005), and vagus nerve was more preserved in LPPG group (81.4% for hepatic branch and 24.0% for celiac branch) than in LDG group (14.2% for hepatic branch and 6.3% for celiac branch, p<0.001 and p=0.004, respectively). One patient in LPPG group and 2 patients in LDG group received total gastrectomy due to the positive proximal resection margin. Six patients received DG in LPPG group due to positive distal resection margin (n=2), gross suspicion of advanced cancer during surgery (n=2), and injury of infrapyloric vessel (n=2). The mean number of lymph nodes in both groups was more than 30 (Table 1).

Short and long-term complications

Overall 30-day complication rates were 17.8% and 16.5% in LPPG and in LDG groups, respectively, without statistical significance (p = 0.784). The mean postoperative hospital days were 8.38 and 8.19 days in LPPG and in LDG groups (p = 0.903). There was no 90-day mortality in either group. Detailed data have been reported previously (13).

Regarding long-term complications, reflux occurred more frequently in LPPG (13.7%) than in LDG in AT analysis (3.1%, p = 0.002). There were no differences in stenosis, dumping syndrome, or delayed gastric emptying between groups (Table 2).

Dumping syndrome

In ITT analysis, there was no significant difference in terms of the incidence of dumping syndrome (13.2% in LPPG and 15.8% in LDG, p = 0.622) at 1 year after surgery. PP analysis also showed a similar result (14.0% in LPPG vs. 13.9% in LDG, p = 0.949). In ITT analysis, the most common dumping symptoms were borborygmia (65.2%), followed by abdominal fullness (61.7%), sleepiness/yawning/apathy (49.2%), weakness/exhaustion (29.7%), dizziness (28.5%), and ‘desire to lie or sit down’ (27.0%). The incidence of all specific symptoms did not differ between groups. Only eructation which is an inverse symptom of dumping syndrome (-1 point) was more frequent after LPPG (72.1% in LPPG vs. 55.1% in LDG, p = 0.005) (Table 3). There was a trend towards a lower dumping score after LPPG than after LDG at 6 months and at 3 years. (Suppl Figure 1, 2, Supplemental Digital Content 1, http://links.lww.com/SLA/F288).

Gallstone formation and nutritional outcomes

In ITT analysis, gallstone formation was significantly less frequent after LPPG, compared to LDG (2.33% in LPPG vs. 8.66% in LDG, p = 0.026). PP analysis showed the similar results (0.93% in LPPG and 9.26% in LDG, p = 0.006).

In terms of nutritional parameters, in ITT analyses, blood hemoglobin levels at 1 and 3 years after surgery were significantly preserved in LPPG group (-0.39 and +0.01 gm/dL) compared to LDG group (-0.73 and -0.76 gm/dL, p = 0.013 and p < 0.001). Serum protein levels at 1 and 3 years were also significantly preserved in LPPG group (-0.10 and -0.15 gm/dL)

compared to LDG group (-0.32 and -0.35 gm/dL, p = <0.001 and p = 0.002). Serum albumin levels at 1 and 3 years after surgery also showed a tendency to be preserved after LPPG (-0.09 and -0.11 gm/dL) compared to LDG group (-0.14 and -0.19 gm/dL, p = 0.09 and p = 0.06). PP analysis showed the similar statistical results (data not shown). However, the body weight loss at 1 and 3 years was not significant between groups (-5.33 and -4.64 kg in LPPG vs. -5.13 and 5.46 kg in LDG, p = 0.390 and p = 0.126) (Figure 2). Loss of abdominal fat, assessed by CT volumetry at 1 year, showed a trend toward less fat volume loss in LPPG group (-132.67 mm^2) compared to LDG group (-163.11 mm^2, p = 0.085).

Gastroscopic findings

In ITT analysis, bile reflux was less frequent in LPPG, compared to LDG (13.2% in LPPG vs. 24.4% in LDG, p = 0.021), but reflux esophagitis and DGE were more frequent in LPPG than in LDG (reflux esophagitis; 17.8% in LPPG vs. 6.3% in LDG, p = 0.005, DGE = 4; 16.3% in LPPG vs. 3.9% in LDG, p = 0.001). Gastritis and ulcer were not significantly different between groups (Table 4).

QOL outcomes

Regarding QOL outcomes, there were no significant differences of postoperative changes in EORTC C30 or STO22 between groups, except for higher dysphagia (STO22) in LPPG compared to LDG for 3 years after surgery in PP analyses (Suppl Figure 3, 4, Supplemental Digital Content 1, http://links.lww.com/SLA/F288). ITT analysis showed the similar statistical results (data not shown).

Survival and Recurrence

In ITT analysis, 243 out of 256 patients completed 3-year follow-up, therefore follow-up rate was 94.9%. There were no significant differences in terms of overall survival and disease-free survival between LPPG and LDG groups for 3 years (Figure 3).

Two patients recurred within 3 years. In one patient with pT1aN0M0 (stage Ia) disease, loco-regional relapse near to anastomosis site occurred at 24 months after LPPG, and the patients received reoperation. In another patient with pT4aN0M0 (stage IIb) disease, peritoneal seeding was detected at 24 months after LDG, and the patients received palliative chemotherapy. Both patients were alive at 3 years after surgery. Two deaths which were not related to gastric cancer occurred in LPPG group, and none in LDG group.

Discussion

This KLASS-04, multicenter randomized controlled trial comparing LPPG with LDG in patients with cT1N0M0 gastric cancer in the mid portion of the stomach, showed that there is

no difference in the dumping syndrome between LPPG and LDG, but showed clinically meaningful benefits of LPPG in terms of less gallstone formation, less nutritional deficit, and less bile reflux.

To our knowledge, only one multicenter randomized controlled trial evaluating PPG was reported previously (18). In this study, 36 open PPG were compared with 38 open DG with BI anastomosis from 1994 to 1996 from 9 Japanese institutions without explanation of the primary endpoint or sample size calculation. The incidence of early dumping syndrome was lower in PPG (8.3%) than in DG (33.3%, p = 0.03). Other outcomes such as surgical morbidity, body weight change, hemoglobin, and total protein levels were not different between groups.

Short-term outcomes of KLASS-04 are quite acceptable. As well as comparable surgical complication to LDG, the mean number of retrieved lymph nodes of LPPG was 38.1 which can be considered as sufficient for the lymph node dissection for EGC. However, DGE caused by pyloric spasm was still an obstacle to PPG. In KLASS-04, DGE has occurred in 5.4% after LPPG. This percentage was comparable with previous reports (10-12, 19). Several approaches have been used to treat or prevent DGE, including balloon dilatation, Botulinum toxin injection, intraoperative manual dilatation, and biodegradable stent placement (20-23).

Dumping syndrome is a common but underdiagnosed complication of gastric surgery (24). Dumping syndrome is reported to develop in 25 to 50% of patients after gastrectomy, and up to 70% after bariatric surgery (24-26). Sigstad score, which was used as the primary endpoint of KLASS-04, is one of the most accurate and widely used systems for the diagnosis of dumping syndrome (24). Sigstad score is distinctive as it has been validated by laboratory findings, such as changes of plasma volume and blood sugar index (14). However, contrary to our expectation, the incidence of dumping syndrome was not different between groups, and KLASS-04 did not show the decreased incidence of dumping syndrome after LPPG, compared to LDG. The incidence of dumping syndrome in our study was 13% after LPPG and 16% after LDG. We can assume that the result may be different if other diagnostic measurements such as continuous glucose monitoring were used (24). For example, Ri et al reported that PPG had the lowest incidence of dumping syndrome among various types of gastrectomy using continuous glucose monitoring (26).

Gallstone formation is another important long-term sequelae after gastrectomy. One Japanese study reported that gallstone after gastrectomy was 8 to 28% depending on the type of resection and anastomosis (27). One Korean multicenter prospective study reported that 25 (16.7%) out of 150 patients had gallstone after gastrectomy, and 4 (2.7%) of them had symptomatic cholecystitis or cholangitis for 1 year after surgery (28). In KLASS-04, gallstone formation was significantly less after LPPG compared to LDG, showing a clear benefit of PPG over DG which was consistent with the previous reports (10, 29).

Nutritional parameters are also considered an important advantage of PPG over DG. Accordingly, KLASS-04 showed that hemoglobin, total protein, and albumin levels were significantly higher after LPPG than LDG. This may be related to the “physiologic passage” of food through the duodenum after PPG, which was not after BII or RY. Hemoglobin preservation after LPPG may be related to longer food contact with gastric acid, and higher gastric acidity in LPPG may promote the absorption of iron in the duodenum (12). Other

reports comparing BI with BII or RY also showed the benefit of anemia and nutritional factors after BI anastomosis (30). In contrast, body weight and fat volume were not significantly preserved after PPG. Perhaps the food intake itself was not different between two groups, and it may mainly affect our results. More studies are needed for the mechanism of weight loss and for the solution against weight loss after gastrectomy in the future (31, 32).

Prospective observation of gastroscopy after PPG has rarely been reported. Several retrospective studies consistently reported that bile reflux was less but DGE was more common than DG-BII at 1 year after surgery (12, 33, 34). Our results showed similar results in DGE, but the higher incidence of reflux esophagitis than DG was also noted, which may be related to DGE after PPG. Regular gastroscopic follow-up and proper management after PPG are required to minimize the problem related to postoperative reflux esophagitis.

Regarding postoperative QOL, KLASS-04 did not find any differences between LPPG and LDG. Recently, several prospective single-center observational studies using EORTC C30 and STO22 were reported from Korea and China, but the results were inconsistent (12, 35, 36). Recently, new QOL modules focusing on postgastrectomy syndrome were developed and widely applied in the clinical practice, and this approach is expected to reveal the real difference in QOL between PPG and other procedures more accurately (37, 38).

The oncologic safety of PPG in EGC was well established when PPG was performed under the strict indication criteria of cT1N0M0 cancer (7-9, 44). KLASS-04 also showed comparable overall and disease-free survival with PPG versus DG. However, dissection of #6 lymph node is very important as lymph node metastasis of #6 area is not uncommon (39), therefore the surgeon should be familiar with dissecting the infrapyloric area without injuring infrapyloric vessels. In our KLASS-04 study, injury to infrapyloric artery and vein occurred in only 3 (2.3%) and 6 (4.7%) cases, respectively (13). The strict qualification of the surgeons in KLASS-04 may be one of the reasons for this favorable outcome. Considering the technical challenges of infrapyloric area dissection, LPPG should be cautiously applied by experienced surgeons in regions where the advanced gastric cancer is prevalent. In addition, it should be noticed that the application of LPPG in advanced gastric cancer has not been evaluated until now.

Our study has several limitations. First, the follow-up period was 3 years, therefore the long-term outcome at 5 years was not measured. Second, when assessing postoperative anemia, serum levels of iron or vitamin B12, nor their supplementation status were not checked during the follow-up period. Third, this study is not a blinded trial, therefore all of patient-reported outcomes such as incidence of dumping syndrome and postoperative QOL may be significantly biased. Fourth, because we applied a strict surgeon qualification process, our results cannot be simply extrapolated to general practice but only to experienced surgeons. Lastly, anastomosis method was not standardized in the control group. Since the anastomosis method after DG may affect clinical outcomes, such as nutrition, anemia, bile reflux, or gastritis, care should be taken when interpreting the results. Whereas, in LPPG group, only extracorporeal gastrogastrostomy was allowed for the standardization of procedure. Recently, intracorporeal gastrogastrostomy was also performed with the support of intraoperative gastroscopy and the surgical outcomes were reported to be comparable with extracorporeal gastrogastrostomy (40, 41).

In conclusion, LPPG has the advantages of less gallstone formation, less nutritional deficit, and less bile reflux compared to LDG without compromising complications or recurrence. However, the incidence of dumping syndrome and postoperative QOL were not different. LPPG also has disadvantages of more DGE and reflux esophagitis. PPG can be used as an alternative option for cT1N0M0 gastric cancer in the mid portion of the stomach when performed by experienced surgeons in regions where EGC is prevalent.

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Figure 1. Flowchart of patient enrollment

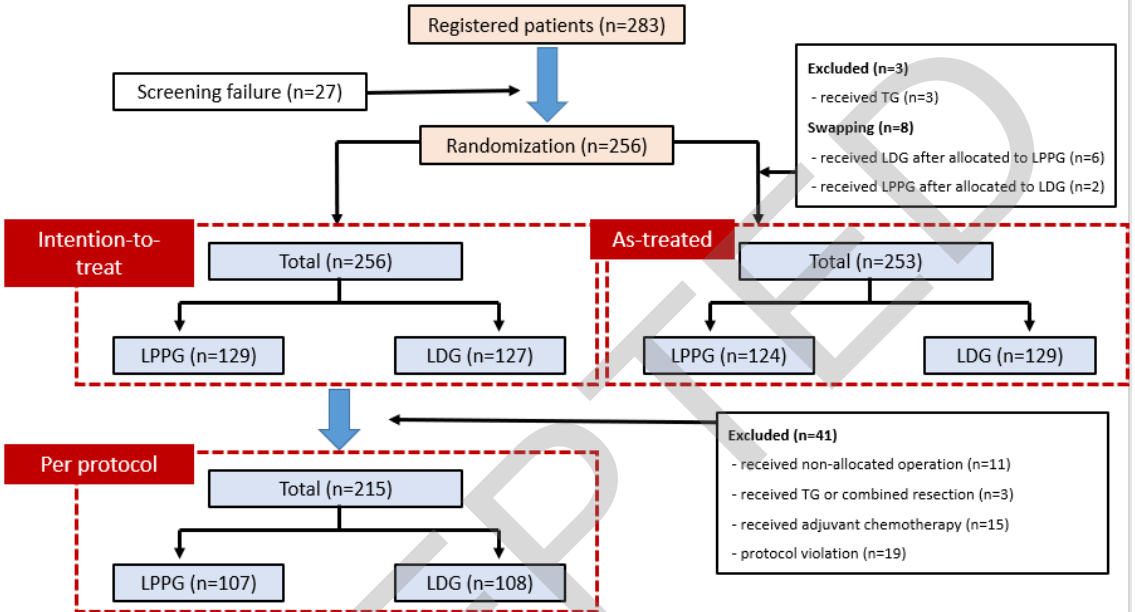


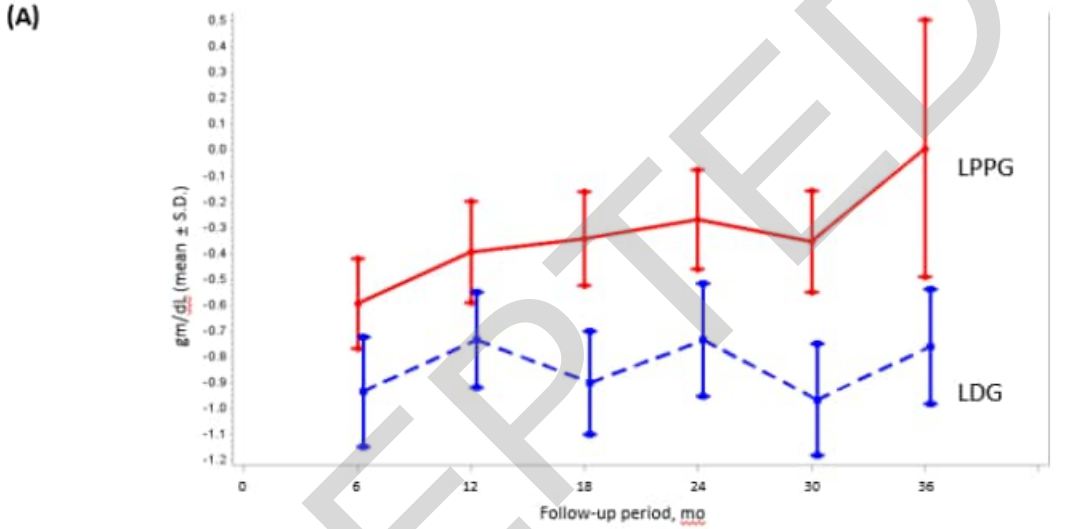
Figure 2. Nutritional parameters after LPPG versus LDG for 3 years after surgery in intention-to-treat populations

(A) Change in hemoglobin (gm/dL)

(B) Change in total protein (gm/dL)

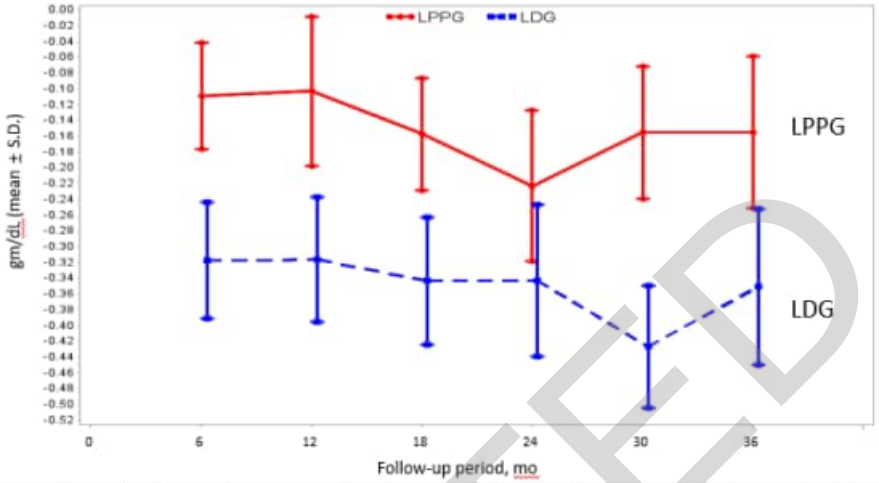
(C) Change in albumin (gm/dL)

(D) Change in body weight (kg)



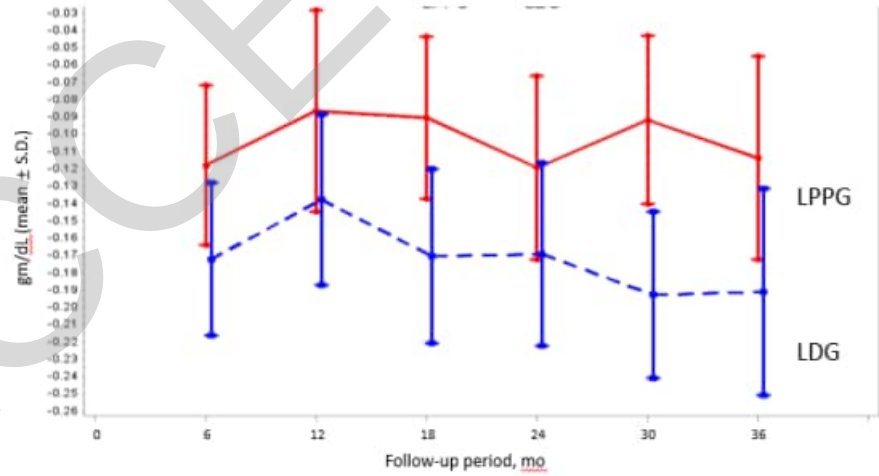
		Preop	6 mo	12 mo	18 mo	24 mo	30 mo	36 mo
Change in hemoglobin (gm/dL)	LPPG	-	-0.59±0.99	-0.39±1.12	-0.34±1.03	-0.27±1.08	-0.35±1.09	0.01±2.8
	LDG	-	-0.93±1.19	-0.73±1.03	-0.9±1.1	-0.74±1.19	-0.97±1.16	-0.76±1.2
	P-value	-	0.013	0.013	<0.001	<0.001	<0.001	<0.001
No. at risk	LPPG	129	129	127	126	124	122	124
	LDG	127	123	124	119	118	114	114

(B)



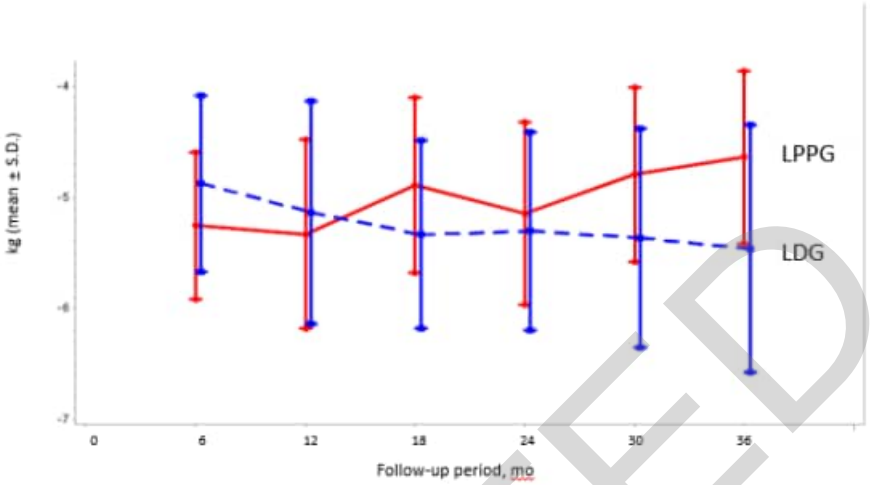
		Preop	6 mo	12 mo	18 mo	24 mo	30 mo	36 mo
Change in total protein (gm/dL)	LPPG	-	-0.11±0.39	-0.1±0.53	-0.16±0.4	-0.22±0.53	-0.15±0.47	-0.15±0.54
	LDG	-	-0.32±0.41	-0.32±0.44	-0.34±0.44	-0.34±0.52	-0.43±0.42	-0.35±0.53
	P-value	-	<0.001	<0.001	0.001	0.003	<0.001	0.002
No. at risk	LPPG	129	127	124	123	123	122	124
	LDG	127	121	123	118	116	113	113

(C)



		Preop	6 mo	12 mo	18 mo	24 mo	30 mo	36 mo
Change in albumin (gm/dL)	LPPG	-	-0.12±0.26	-0.09±0.33	-0.09±0.27	-0.12±0.3	-0.09±0.27	-0.11±0.33
	LDG	-	-0.17±0.25	-0.14±0.28	-0.17±0.28	-0.17±0.29	-0.19±0.26	-0.19±0.32
	P-value	-	0.042	0.093	0.038	0.167	0.001	0.056
No. at risk	LPPG	129	128	127	126	124	122	124
	LDG	127	123	124	119	118	114	114

(D)



		Preop	6 mo	12 mo	18 mo	24 mo	30 mo	36 mo
Change in Body weight (kg)	LPPG	-	-5.25±3.77	-5.33±4.82	-4.89±4.39	-5.14±4.5	-4.79±4.3	-4.64±4.16
	LDG	-	-4.87±4.35	-5.13±5.57	-5.34±4.63	-5.3±4.73	-5.37±5.09	-5.46±5.77
	P-value	-	0.801	0.390	0.194	0.352	0.122	0.126
No. at risk	LPPG	129	127	126	121	118	118	113
	LDG	127	118	121	117	111	104	106

Figure 3. (A) Overall and (B) disease-free survivals of patients who received laparoscopic pylorus preserving gastrectomy versus laparoscopic distal gastrectomy in intention-to-treat populations
LPPG, laparoscopic pylorus preserving gastrectomy; LDG, laparoscopic distal gastrectomy

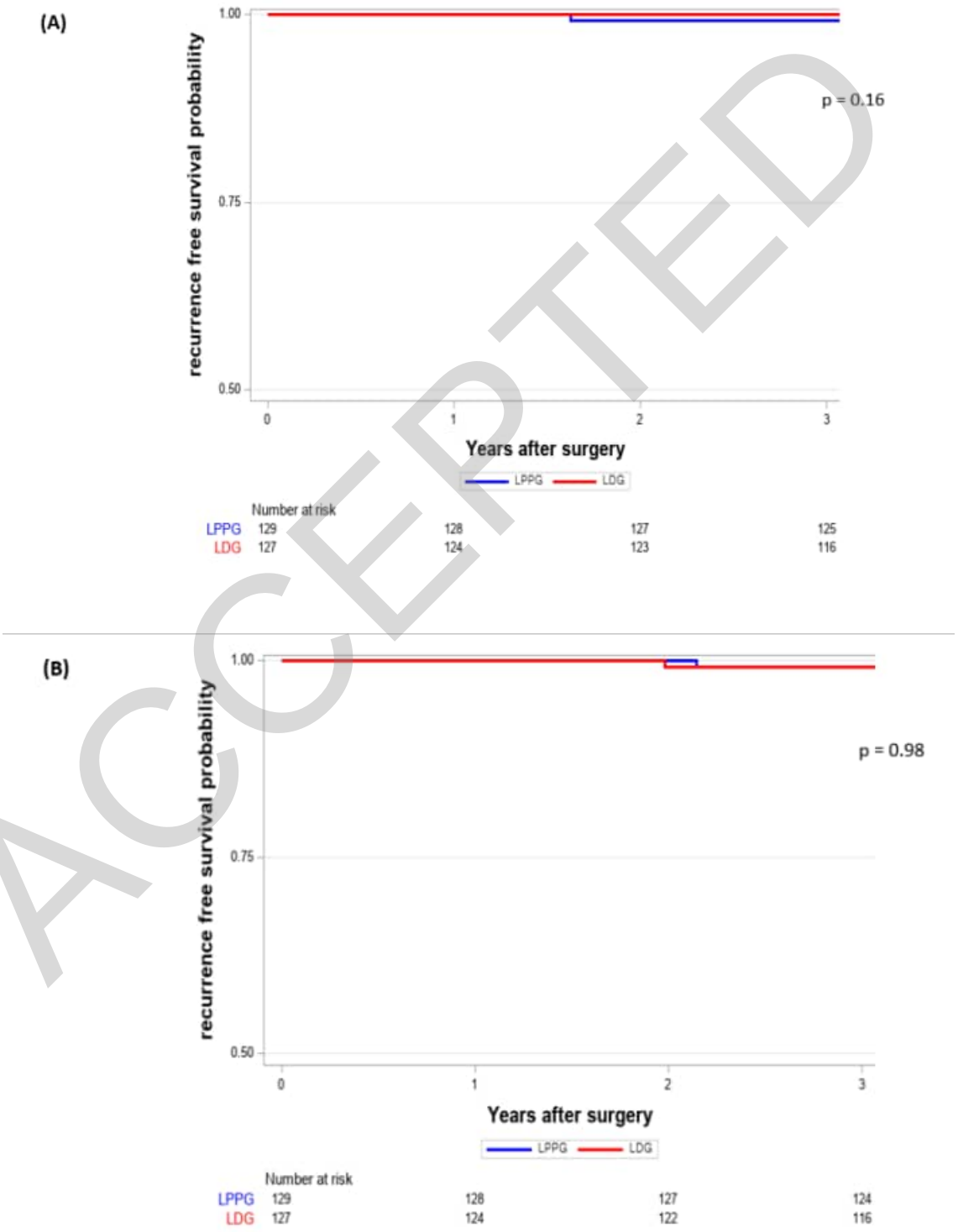


Table 1. Patients' demographics, tumor characteristics, and surgical data

Characteristics	Patients, No (%)					
	Intention-to-treat analysis			Per-protocol analysis		
	LPPG (n=129)	LDG (n=127)	p-value	LPPG (n=107)	LDG (n=108)	p-value
Sex (M : F)	63 : 66	63 : 64	0.902	52 : 55	55 : 53	0.733
Age, years, mean (SD)	55.6 (10.6)	57.7 (10.4)	0.186	56.0 (10.8)	58.2 (10.2)	0.126
BMI, kg/m^2, mean (SD)	23.5 (2.6)	23.7 (2.8)	0.809	23.6 (2.5)	23.7 (2.8)	0.921
Operation type			<0.001			<0.001
PPG	122 (94.6)	2 (1.6)		107 (100)	0	
DG	6 (4.7)	123 (96.9)		0	108 (100)	
TG	1 (0.8)	2 (1.6)		0	0	
Anastomosis			<0.001			<0.001
Gastrogastrostomy	122 (94.6)	2 (1.6)		107 (100)	0	
Gastroduodenostomy (Billroth I)	2 (1.6)	57 (44.9)		0	52 (48.1)	
Gastrojejunostomy (Billroth II)	3 (2.3)	40 (31.5)		0	34 (31.5)	
Gastrojejunostomy (Roux-en-Y)	1 (0.8)	26 (20.5)		0	22 (20.4)	
Esophagojejunostomy	1 (0.8)	2 (1.6)		0	0	
Retrieved LNs, mean (SD)	38.1 (14.4)	45.2 (20.9)	0.005	38.3 (14.6)	43.8 (19.9)	0.048
pT stage			0.652			0.813
T1	122 (94.5)	114 (89.8)		102 (95.3)	105 (97.2)	
T2	4 (3.1)	8 (6.3)		4 (3.7)	3 (2.8)	
T3/T4a	2 (1.6)	4 (3.1)		0	0	
pN stage			0.451			0.108
N0	115 (89.2)	116 (91.3)		98 (91.6)	104 (96.3)	
N1	10 (7.8)	4 (3.2)		9 (8.4)	3 (2.8)	
N2/3	4 (3.2)	6 (4.7)		0	1 (0.5)	

Abbreviations: LPPG, laparoscopic pylorus preserving gastrectomy; LDG, laparoscopic distal gastrectomy; BMI, body mass index; LN, lymph node

Table 2. Short and long term complications

Characteristic	Patients, No (%)					
	Intention-to-treat analysis			As-treated analysis		
	LPPG (n=129)	LDG (n=127)	p-value	LPPG (n=124)	LDG (n=129)	p-value
Short-term complications						
Overall morbidity	23 (17.8)	21 (16.5)	0.784	24 (19.3)	20 (15.5)	0.419
Pyloric stenosis	7 (5.4)	1 (0.8)	0.014	8 (6.5)	0 (0.0)	0.003
Complications except pyloric stenosis (DGE)	16 (13.1)	21 (16.5)	0.448	16 (13.8)	20 (15.5)	0.706
Grade of complications						
I	9 (7.0)	8 (6.3)	0.828	9 (7.3)	8 (6.2)	0.737
II	8 (6.2)	6 (4.7)	0.603	8 (6.4)	6 (4.7)	0.531
IIIa	12 (9.3)	7 (5.5)	0.247	13 (10.5)	6 (4.7)	0.078
IIIb	0 (0.0)	2 (1.6)	0.245	0 (0.0)	2 (1.6)	0.498
Postoperative hospital stay, days, mean (SD)	8.38 (6.1)	8.19 (6.5)	0.903	8.54 (6.3)	8.08 (6.4)	0.688
Readmission within 30 days	2 (1.6)	5 (3.9)	0.279	3 (2.4)	4 (3.1)	>0.999
Reoperation within 90 days	0 (0.0)	1 (0.8)	0.496	0 (0.0)	1 (0.8)	>0.999
Death with 90 days	0 (0.0)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	1.000
Long-term complications						
Stenosis	0 (0.0)	1 (0.8)	0.496	0 (0.0)	1 (0.8)	>0.999
Reflux	16 (12.4)	5 (3.9)	0.014	17 (13.7)	4 (3.1)	0.002
Dumping syndrome	10 (7.8)	18 (14.2)	0.100	10 (8.1)	18 (14.0)	0.136
Delayed gastric emptying	3 (2.3)	1 (0.8)	0.622	3 (2.4)	1 (0.8)	0.362
Others	3 (2.3)	2 (1.6)	>0.999	2 (1.6)	3 (2.3)	>0.999

Abbreviations: LPPG, laparoscopic pylorus preserving gastrectomy; LDG, laparoscopic distal gastrectomy

Table 3. Incidence of each dumping symptoms observed for 3 years after surgery in ITT population

	Score	LPPG	LDG	Total	p-value
Shock	+5	0 (0.00)	1 (0.79)	1 (0.39)	0.4961
Syncope, unconsciousness	+4	-	-	-	-
Desire to lie or sit down	+4	37 (28.68)	32 (25.20)	69 (26.95)	0.5298
Dyspnea	+3	12 (9.30)	6 (4.72)	18 (7.03)	0.152
Weakness, exhaustion	+3	36 (27.91)	40 (31.50)	76 (29.69)	0.5297
Sleepiness, yawning, apathy	+3	62 (48.06)	64 (50.39)	126 (49.22)	0.7091
Palpitation	+3	24 (18.60)	25 (19.69)	49 (19.14)	0.8261
Restlessness	+2	6 (4.65)	4 (3.15)	10 (3.91)	0.749
Dizziness	+2	36 (27.91)	37 (29.13)	73 (28.52)	0.8279
Headache	+1	15 (11.63)	18 (14.17)	33 (12.89)	0.5434
Sweating, pallor, clammy skin	+1	21 (16.28)	25 (19.69)	46 (17.97)	0.4779
Nausea	+1	24 (18.60)	27 (21.26)	51 (19.92)	0.5949
Abdominal fullness	+1	81 (62.79)	77 (60.63)	158 (61.72)	0.7221
Borborygmia	+1	84 (65.12)	83 (65.35)	167 (65.23)	0.9681
Eructation	-1	93 (72.09)	70 (55.12)	163 (63.67)	0.0048
Vomiting	-4	18 (13.95)	14 (11.02)	32 (12.50)	0.4785

Abbreviations: ITT, intention-to-treat; LPPG, laparoscopic pylorus preserving gastrectomy; LDG, laparoscopic distal gastrectomy

Table 4. Gastroscopic findings for 3 years after surgery

Characteristic	Patients, No (%)					
	Intention-to-treat analysis			Per-protocol analysis		
	LPPG (n=129)	LDG (n=127)	p-value	LPPG (n=107)	LDG (n=108)	p-value
Gastritis	56 (43.41)	50 (39.37)	0.5117	45 (42.06)	45 (41.67)	0.9539
Bile reflux	17 (13.18)	31 (24.41)	0.0213	13 (12.15)	27 (25.00)	0.0155
reflux esophagitis	23 (17.83)	8 (6.30)	0.0047	16 (14.95)	6 (5.56)	0.0230
Gastric emptying						
no food residue	113 (87.60)	121 (95.28)	0.0284	95 (88.79)	104 (96.30)	0.0359
liquid only	10 (7.75)	7 (5.51)	0.4717	9 (8.41)	7 (6.48)	0.5898
soft diet remained	47 (36.43)	27 (21.26)	0.0074	42 (39.25)	23 (21.30)	0.0042
nearly normal diet residue	21 (16.28)	5 (3.94)	0.0011	18 (16.82)	5 (4.63)	0.0038
Ulcer						
anastomosis site	6 (4.65)	4 (3.15)	0.749	5 (4.67)	4 (3.70)	0.7480
other stomach	4 (3.10)	1 (0.79)	0.3701	4 (3.74)	1 (0.93)	0.2122

Abbreviations: LPPG, laparoscopic pylorus preserving gastrectomy; LDG, laparoscopic distal gastrectomy