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Original Article

Short-term Outcomes of Pylorus-Preserving Gastrectomy for Early Gastric Cancer: Comparison Between Extracorporeal and Intracorporeal Gastrogastrostomy

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ABSTRACT

Purpose: This study aimed to compare the surgical and oncological outcomes between totally laparoscopic pylorus-preserving gastrectomy (TLPPG) with intracorporeal anastomosis and laparoscopy-assisted pylorus-preserving gastrectomy (LAPPG) with extracorporeal anastomosis.
Materials and Methods: A retrospective analysis was performed in 258 patients with cT1N0 gastric cancer who underwent laparoscopic pylorus-preserving gastrectomy using two different anastomosis methods: TLPPG with intracorporeal anastomosis (n=88) and LAPPG with extracorporeal anastomosis (n=170). The following variables were compared between the two groups to assess the postoperative surgical and oncological outcomes: proximal and distal margins, number of resected lymph nodes (LNs) in total and in LN station 6, operation time, postoperative hospital stay, and postoperative morbidity including delayed gastric emptying (DGE).
Results: The average length of the proximal margin was similar between the TLPPG and LAPPG groups (2.35 vs. 2.73 cm, P=0.070). Although the distal margin was significantly shorter in the TLPPG group than in the LAPPG group (3.15 vs. 4.08 cm, P=0.001), no proximal or distal resection margin-positive cases were reported in either group. The average number of resected LN was similar in both groups (36.0 vs. 33.98, P=0.229; LN station 6, 5.72 vs. 5.33, P=0.399). The operation time was shorter in the TLPPG group than in the LAPPG (200.17 vs. 220.80 minutes, P=0.001). No significant differences were observed between the two groups in terms of postoperative hospital stay (9.38 vs. 10.10 days, P=0.426) and surgical complication rate (19.3% vs. 22.9%), including DGE (8.0% vs. 11.8%, P=0.343).

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Conclusions: The oncological safety and postoperative complications of TLPPG with intracorporeal anastomosis are similar to those of LAPPG with extracorporeal anastomosis.

Keywords: Function-preserving gastrectomy; Early gastric cancer; Intracorporeal anastomosis; Extracorporeal anastomosis

INTRODUCTION

Patients with early gastric cancer (EGC) has a low recurrence rate and prolonged survival time after treatment [1]. Therefore, two surgical approaches are widely used to treat EGC: minimally invasive and function-preserving surgery to improve the post-treatment quality of life (QoL) [2].

Pylorus-preserving gastrectomy (PPG) has been widely applied in the treatment of middle-third EGCs and has become one of the treatment options for lesions with appropriate depth and location based on the Japanese and Korean gastric cancer treatment guidelines [3,4].

PPG can be a good treatment option even for EGC in the upper third of the stomach in technically feasible locations (proximal tumor border of >3 cm from the esophagogastric junction). PPG has better functional outcomes, lower postoperative morbidity, and the same oncological safety as distal gastrectomy and total gastrectomy [5].

Patients with PPG had fewer subjective postprandial symptoms than those who underwent distal gastrectomy with Billroth I anastomosis. In addition, they have a lower incidence of dumping syndrome, bile reflux gastroesophagitis, and nutritional deficit [6].

The safety and feasibility of laparoscopy-assisted pylorus-preserving gastrectomy (LAPPG) with hand-sewn gastrogastrostomy through mini-laparotomy for the treatment of EGC have been reported [7-9].

Delayed gastric emptying (DGE) is the most common complication of PPG [10-12]. It was more frequent in LAPPG than in laparoscopy-assisted distal gastrectomy (LADG) (7.8% vs. 1.7%); however, the risk of other complications was significantly higher in LADG than in LAPPG [10]. Intraoperative manual dilatation of the pylorus during PPG is a simple and effective procedure for the prevention of DGE caused by pyloric spasms [13]. Fluoroscopy-guided balloon dilation is an effective first-line treatment for DGE following PPG. In addition, retrievable stent placement can be a safe alternative for patients who are refractory to balloon dilations [14].

Several previous studies have reported the safety and feasibility of totally laparoscopic pylorus-preserving gastrectomy (TLPPG) with intracorporeal anastomosis, but these studies did not compare the outcomes of TLPPG to those of LAPPG [15-19]. Hence, the present study aimed to compare the short-term surgical outcomes between patients who underwent TLPPG and those who underwent LAPPG.

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MATERIALS AND METHODS

Patients and indications for PPG

We retrospectively reviewed the database of biopsy-proven clinical T1N0M0 gastric cancer patients who underwent laparoscopic PPG, either LAPPG or TLPPG, between July 2016 and June 2019 in Seoul National University Hospital (SNUH). Those who underwent gastric resection less than standard PPG, such as partial gastrectomy with modified LN dissection or additional major operations other than PPG were excluded from this study. The clinical stage was determined using preoperative computed tomography and endoscopic ultrasonography.

Preoperative endoscopy was performed in all patients for tumor localization and measurement of the distance from the pylorus to the distal margin; metal clips were used to mark the proximal and distal tumor border in both groups. When a distal antrum of >5 cm was secured, PPG was decided, and the type of anastomosis was determined based on the surgeon's preference. Both TLPPG and LAPPG are possible, but in general, surgeons prefer a longer distal antrum for TLPPG to allow a linear stapler (60 mm) to be inserted into the remnant antrum.

Surgical procedure

All procedures were laparoscopically performed by 5 gastrointestinal surgeons at SNUH. The patients were placed in the supine position, and the operator stood on the patient's right side. After induction of general anesthesia, an 11-mm trocar for the camera port was inserted through an infraumbilical incision using an open technique, and pneumoperitoneum was established. The patient was placed in the reverse Trendelenburg position, and four additional trocars were inserted. Stomach mobilization and laparoscopic PPG with D1+ lymphadenectomy were performed as usual [13].

The LNs in the infrapyloric area (LN station 6) were meticulously dissected, preserving the infrapyloric vessels to maintain sufficient blood supply to the pyloric cuff, followed by ligation of the right gastroepiploic vessels distal to the branch of the infrapyloric vessels. The LN at station 5 (suprapyloric LN) was not dissected, and the arcade of the right gastric artery and vein was ligated at approximately 3 cm from the pylorus. Intraoperative frozen sections of the proximal and distal margins were routinely performed in both groups.

LAPPG

A 4- to 5-cm midline skin incision (mini-laparotomy) was made in the epigastric area. The stomach was extracted through the skin incision. After confirming the tumor location by palpating the endoscopic metal clips to ensure adequate proximal and distal margins, the distal stomach was transected, followed by the proximal stomach. Extracorporeal gastro-gastrostomy was performed using hand-sewn sutures.

TLPPG

After lymphadenectomy, intraoperative gastroscopy was routinely performed to verify the tumor location. The location of the preoperative marking clips was confirmed, and distal and proximal stomach transections were performed.

Intracorporeal gastrostomy anastomosis was performed with either delta-shaped intracorporeal anastomosis with closure of the common enterotomy hole using a suture (n=34) [16], delta-shaped intracorporeal anastomosis with closure of the common enterotomy hole using a stapler (n=38) [17], piercing method (n=7) [18], or intracorporeal anastomosis between

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the anterior wall of the proximal stomach and posterior wall of the antrum (Proximal Anterior-Antrum Posterior, PAAP) (n=9) [19]. Each intracorporeal anastomosis technique is a known method, and the detailed procedure is described in reference article [16-19].

Surgical and oncological outcomes

The following clinicopathological data were collected and compared between the LAPPG and TLPPG groups: age, sex, body mass index, anastomosis type, and postoperative Tumor, Node, Metastasis (TNM) stage according to the 8th edition of the American Joint Committee on Cancer TNM classification [20].

For the analysis of surgical and oncological outcomes, data on the operation time, postoperative hospital stay, proximal and distal resection margins, number of resected lymph nodes (LN) in total and in LN station 6, and postoperative complications including DGE were collected. DGE represents the inability to return to a standard diet by the end of the first postoperative week and includes prolonged nasogastric intubation [21]. The severity of complications was classified according to the Clavien–Dindo classification system [22]. The length of antral cuff after PPG was determined by subtracting the distance of "the tumor to the distal resection line (which is the length of the distal resection margin in the pathology result)" from the distance of "the tumor to the pylorus" on preoperative gastroscopy.

Statistics

All statistical analyses were performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA). All continuous data were expressed as mean±standard deviation. Continuous variables were analyzed using the Student's t-test. The patients' characteristics and surgical complications were compared using the χ^2 test and analysis of variance. The risk factors for DGE were analyzed using a logistic regression analysis. A P-value of <0.05 was considered significant.

Ethics statement

This study was conducted in accordance with the ethical principles for medical research involving humans, as outlined in the Declaration of Helsinki, after the approval of the Institutional Review Board of SNUH (No. 1908-176-1059). The requirement for obtaining informed consent was waived due to the retrospective nature of the study.

RESULTS

Patients' characteristics

From July 2016 to June 2019, 261 patients with EGC underwent laparoscopic PPG at our center. After applying the inclusion and exclusion criteria, 258 patients were identified as eligible for the final analysis. Among them, 88 and 170 underwent TLPPG and LAPPG, respectively. The clinicopathological characteristics of the patients are presented in **Table 1**. No significant differences were observed in the clinicopathological characteristics between the 2 groups, except for tumor location, which was more distal in the LAPPG group (P=0.025).

Surgical and oncological outcomes

As shown in **Table 2**, the operation time was shorter in the TLPPG group than in the LAPPG (200.17±43.29 minutes vs. 220.80±46.15 minutes, P=0.001). No significant difference was found in the postoperative hospital stay (9.38±7.94 days vs. 10.10±6.40 days, P=0.426) between the two groups.

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Table 1. Patients' clinicopathological characteristics

Characteristics	TLPPG with intracorporeal anastomosis (n=88)	LAPPG with extracorporeal anastomosis (n=170)	P-value
Age (yr)	58.75±12.05	58.75±12.14	0.932
Age			0.782
≥65	26 (29.5)	48 (28.2)	
<65	62 (70.5)	122 (71.8)	
Sex			0.995
Male	43 (48.9)	82 (48.2)	
Female	45 (51.1)	88 (51.8)	
BMI (kg/m^2)			0.828
<25	28 (31.8)	57 (33.5)	
≥25	60 (68.2)	113 (66.5)	
Pathological T stage			0.277
T1a	48 (54.5)	101 (60.1)	
T1b	32 (36.4)	54 (32.1)	
T2	4 (4.5)	8 (4.8)	
T3	2 (2.3)	2 (1.2)	
T4a	2 (2.3)	0 (0)	
Pathological N stage			0.595
N0	82 (93.2)	160 (94.1)	
N1	4 (4.5)	6 (3.5)	
N2	1 (1.1)	0 (0)	
N3a	1 (1.1)	3 (1.8)	
N3b	0 (0)	1 (0.6)	
TNM stage			0.712
Stage Ia	73 (83.0)	151 (88.8)	
Stage Ib	8 (9.1)	11 (6.5)	
Stage IIa	2 (2.3)	2 (1.2)	
Stage IIb	4 (4.5)	6 (3.5)	
Tumor location (circular)			0.581
LC	26 (29.5)	49 (28.8)	
GC	16 (18.2)	24 (14.1)	
AW	15 (17.0)	40 (23.5)	
PW	31 (35.2)	55 (32.4)	
Tumor location (longitudinal)			0.077
Upper 1/3	7 (8)	8 (4.7)	
Middle 1/3	71 (80.7)	123 (72.4)	
Lower 1/3	10 (11.4)	39 (22.9)	
Tumor location (longitudinal)			0.026*
High body	8 (9.1)	13 (7.7)	
Mid body	36 (40.9)	40 (23.8)	
Low body	40 (45.5)	84 (50)	
Angle	3 (3.4)	21 (12.5)	
Antrum	1 (1.1)	7 (4.2)	

Values are presented as mean±standard deviation or number (%).
TLPPG = totally laparoscopic pylorus-preserving gastrectomy; LAPPG = laparoscopy-assisted pylorus-preserving gastrectomy; BMI = body mass index; LC = lesser curvature; Gc = greater curvature; AW = anterior wall; PW = posterior wall.
*Statistically significant values.

Although the distal margins were shorter in the TLPPG group than in the LAPPG (3.15±1.82 cm vs. 4.08±2.23 cm, P=0.001), no distal resection margin positive cases were reported in either groups.

The length of proximal margins (2.35±1.66 cm vs. 2.73±1.55 cm, P=0.070) were similar in the TLPPG and LAPPG groups without any case of cancer involvement in the proximal margin in both groups.

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Table 2. Surgical outcome

Characteristics	TLPPG with intracorporeal anastomosis (n=88)	LAPPG with extracorporeal anastomosis (n=170)	P-value
Operation time (min)	200.17±43.29	220.80±46.15	0.001*
Postoperative hospital stay (days)	9.38±7.9	10.1±6.4	0.426
PRM (cm)	2.35±1.66	2.73±1.55	0.070
Positive PRM	0 (0)	0 (0)	
DRM (cm)	3.15±1.82	4.08±2.23	0.001*
Positive DRM	0 (0)	0 (0)	
Number of resected LN			
Total	36.0±13.5	33.98±12.83	0.229
Resected LN in No. 6	5.72±3.3	5.33±3.58	0.399
Length of antral cuff (cm)	5.5±2.4	4.35±1.8	0.001*
<3 cm	8 (9.3)	24 (14.2)	0.000*
3–5 cm	35 (40.7)	107 (63.3)	
>5 cm	43 (50.0)	38 (22.5)	

Values are presented as mean±standard deviation or number (%).
TLPPG = totally laparoscopic pylorus-preserving gastrectomy; LAPPG = laparoscopy-assisted pylorus-preserving gastrectomy; PRM = proximal resection margin; DRM = distal resection margin; LN = lymph node.
*Statistically significant.

TLPPG group had a significantly longer antral cuff than the LAPPG group (5.5±2.4 cm vs. 4.35±1.8 cm, P=0.001).

Postoperative complications

The postoperative morbidity analysis is shown in **Table 3**. No significant differences were observed in the overall surgical and medical complications (19.3% vs. 22.9%, P=0.503). The risk of ileus/motility disorder was higher in the TLPPG group compared with that in the LAPPG group (3.4% vs. 0%, P=0.015), but both groups had similar grades of complications according to the Clavien–Dindo classification, except grade I, which was higher in TLPPG (P=0.048). No in-hospital mortality was observed in either group.

However, DGE only occurred in 8.0% of the TLPPG group, while it occurred in 11.8% of the LAPPG group, which is not significant (P=0.343).

Table 3. Surgery-related complications

Complications	TLPPG with intracorporeal anastomosis (n=88)	LAPPG with extracorporeal anastomosis (n=170)	P-value
Total cases of all complications	17 (19.3)	39 (22.9)	0.503
Wound	1 (1.1)	5 (2.9)	0.362
Fluid collection	3 (3.4)	6 (3.5)	0.960
Intraabdominal bleeding	1 (1.1)	2 (1.2)	0.977
Intraluminal bleeding	1 (1.1)	1 (0.6)	0.634
Ileus/motility disorder	3 (3.4)	0 (0)	0.015*
Anastomosis leakage	1 (1.1)	3 (1.8)	0.699
Other infection	1 (1.1)	3 (1.8)	0.699
Urinary	1 (1.1)	0 (0)	0.164
Pulmonary	2 (2.3)	3 (1.8)	0.779
Delayed gastric emptying	7 (8)	20 (11.8)	0.343
Clavien-Dindo grade			
I	2 (2.3)	0 (0)	0.048*
II	5 (5.7)	11 (6.5)	0.803
IIIa	12 (13.6)	33 (19.4)	0.246
IVa	0 (0)	1 (0.6)	0.471

Values are presented as number (%).
TLPPG = totally laparoscopic pylorus-preserving gastrectomy; LAPPG = laparoscopy-assisted pylorus-preserving gastrectomy.
*Statistically significant.

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Table 4. Logistic regression analysis of the risk factors for delayed gastric emptying

Risk factors	B	SE	OR (95%CI)	P-value
Age	−0.032	0.020	0.968 (0.930–1.008)	0.118
Sex				
(Female†:male)	1.182	0.498	3.260 (1.229–8.643)	0.018*
BMI	0.001	0.077	1.001 (0.860–1.165)	0.992
Length of antral cuff	−0.032	0.113	0.968 (0.776–1.208)	0.774
Tumor location (longitudinal)				
(Mid body†:Lower body)	1.073	0.617	2.924 (0.873–9.796)	0.082
(Mid body†:Angle)	1.233	0.805	3.423 (0.708–16.623)	0.126
(Mid body†:High body)	−0.258	1.189	0.772 (0.075–7.946)	0.828
Anastomosis type				
(Delta anastomosis, suture closure†:Delta anastomosis, stapled closure)	0.212	0.951	1.236 (0.192–7.972)	0.823
(Delta anastomosis, suture closure†:PAAP)	1.063	1.352	2.894 (0.204–40.990)	0.432
(Delta anastomosis, suture closure†:Hand sewn)	0.250	0.809	1.284 (0.263–6.265)	0.757
Constant	−1.789	2.316	0.167	0.440

B = unstandardized regression coefficient; SE = standard error; OR = odds ratio; CI = confidence interval; BMI = body mass index.
*Significant P≤0.05; †Reference category.

Table 5. Surgical outcomes of different types of intracorporeal anastomosis

Surgical outcomes	Delta anastomosis, suture closure (n=34)	Delta anastomosis, stapled closure (n=38)	Piercing method (n=7)	PAAP method (n=9)	P-value
Operation time (min)	197.06±40.3	200±47.8	200±40.2	212.78±40.6	0.924
Postoperative stay (days)	8.79±7.7	10.21±8.8	10.14±9.2	7.44±1.4	0.842
Complications					
Total cases of all complications	4 (11.8)	9 (23.7)	2 (28.6)	2 (22.2)	0.543
Wound	0	1 (2.6)	0	0	0.722
Fluid collection	0	2 (5.3)	0	1 (11.1)	0.325
Intraabdominal bleeding	0	1 (2.6)	0	0	0.722
Intraluminal bleeding	0	1 (2.6)	0	0	0.722
Ileus/motility disorder	1 (2.9)	2 (5.3)	0	0	0.805
Anastomosis leakage	1 (2.9)	0	0	0	0.685
Other infection	0	0	1 (14.3)	0	0.008
Urinary	0	1 (2.6)	0	0	0.722
Pulmonary	0	1 (2.6)	1 (14.3)	0	0.134
Delayed gastric emptying	2 (5.9)	4 (10.5)	0 (0)	1 (11.1)	0.736
Clavien-Dindo grade					
I	1 (2.9)	1 (2.6)	0 (0)	0 (0)	0.927
II	0 (0)	3 (7.9)	1 (14.3)	1 (11.1)	0.277
IIIa	3 (8.8)	7 (18.4)	1 (14.3)	1 (11.1)	0.692

Values are presented as mean±standard deviation or number (%).
PAAP = proximal anterior-anterior posterior.

Table 4 provides an overview of risk factors for DGE after PPG. Although the risk of DGE was significantly higher in men than in women (odds ratio, 3.260; 95% confidence interval, 1.229–8.643), antral cuff length, tumor location, and anastomosis method were not significant risk factors for DGE.

Table 5 shows the surgical outcomes according to the intracorporeal anastomosis type. No significant differences were found in the operation time, postoperative stay, or total complications, including DGE.

DISCUSSION

PPG is a function-preserving surgery for treating EGC, intended to decrease the complication rate and improve the postoperative QoL [6,10]. The oncological safety of PPG has been

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demonstrated in many retrospective studies [10,12,23,24]. Kong et al. [25] suggested that PPG is safe for early gastric cancer within ≥5 cm from the pylorus, which is located not only in the middle third but also in the lower third of the stomach.

Totally laparoscopic distal gastrectomy can reduce the intraoperative estimated blood loss and postoperative pain and enhance bowel motility in gastric cancer surgery [26]. Several previous studies have also reported the safety and feasibility of TLPPG [16-20].

Robot-assisted gastrectomy has recently been introduced as a treatment option for patients with early gastric cancer. Robot-assisted pylorus-preserving gastrectomy is a safe treatment option for EGC in the middle third of the stomach in terms of surgical complications and oncologic outcomes; however, it has no benefit over LAPPG [26]. In our institution, robotic gastrectomy has also been performed using two different anastomosis methods, intracorporeal and extracorporeal anastomosis, according to the surgeon's preference and/or surgical cases. Further studies on this topic are warranted.

The oncological safety of TLPPG was comparable to that of LAPPG; no positive proximal or distal margins were observed in either study groups. The location of tumors was verified easily during the LAPPG procedure by palpating the marking clips placed preoperatively through the mini-laparotomy site; however, location of tumors during TLPPG is quite tricky. In this procedure, marking clips are placed preoperatively, and an intraoperative gastroscopy is performed. Intraoperative frozen section margins were routinely performed in both groups.

We also evaluated the operation time, postoperative stay, number of resected LN, number of examined LN at station #6, and postoperative complication rates in both groups. In this study, the operation time was shorter in the TLPPG group than in the LAPPG group. However, the postoperative stay, number of resected LN, and number of examined LN at #6 stations were not significantly different between the TLPPG and LAPPG groups. The postoperative complications were not different between the two groups; specifically, DGE was observed in the early postoperative period in 8% (7/88) of patients who underwent TLPPG and in 11.8% (20/170) of patients who underwent LAPPG.

The risk of DGE was significantly higher in male patients. However, the different types of intracorporeal anastomosis did not increase the risk of DGE. The length of the antral cuff was not a significant risk factor of DGE; this finding is similar to the results of a previous Japanese study, which stated that the length of the pyloric cuff showed no significant differences in terms of symptoms, such as dumping syndrome or bowel emptying disturbances [27].

Among the different methods of intracorporeal anastomosis, the rate of delayed DEG DGE in delta-shaped intracorporeal anastomosis with stapled closure in the common entry group was somewhat higher than that in the other groups, although the difference was not significant (**Table 5**). Closure of the common entry using a stapler is suspected to cause acute angulation, which disturbs appropriate gastric emptying. Therefore, some surgeons participating in this study prefer to perform delta anastomosis with suture closure as they have noticed this problem. However, further studies are needed to determine whether delta anastomosis with stapled closure has a direct effect on DGE.

The Korean multicenter randomized controlled trial (KLASS-04), which compared LAPPG and LADG as treatment for EGC in the middle third of the stomach, has finished

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recruitment, and the follow-up is ongoing; this trial will provide more precise evidence about the functional outcome and oncologic safety of PPG [3,28].

This study has some limitations. First, it was designed as a single-institutional, retrospective study. A prospective observational or randomized interventional study can provide a better comparison. However, future studies should explore the long-term safety, including cancer recurrence and disease-free survival rates.

In conclusion, the present study demonstrated that TLPPG with intracorporeal anastomosis has oncological safety and postoperative complications similar to those of LAPPG with extracorporeal anastomosis.

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