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Original Article

Short-Term Outcomes of Laparoscopic Total Gastrectomy Performed by a Single Surgeon Experienced in Open Gastrectomy: Review of Initial Experience

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Purpose: Laparoscopic total gastrectomy (LTG) is more complicated than laparoscopic distal gastrectomy, especially during a surgeon's initial experience with the technique. In this study, we evaluated the short-term outcomes of and learning curve for LTG during the initial cases of a single surgeon compared with those of open total gastrectomy (OTG).
Materials and Methods: Between 2009 and 2013, 134 OTG and 74 LTG procedures were performed by a single surgeon who was experienced with OTG but new to performing LTG. Clinical characteristics, operative parameters, and short-term postoperative outcomes were compared between groups.
Results: Advanced gastric cancer and D2 lymph node dissection were more common in the OTG than LTG group. Although the operation time was significantly longer for LTG than for OTG (175.7±43.1 minutes vs. 217.5±63.4 minutes), LTG seems to be slightly superior or similar to OTG in terms of postoperative recovery measures. The operation time moving average of 15 cases in the LTG group decreased gradually, and the curve flattened at 54 cases. The postoperative complication rate was similar for the two groups (11.9% vs. 13.5%). No anastomotic or stump leaks occurred.
Conclusions: Although LTG is technically difficult and operation time is longer for surgeons experienced in open surgery, it can be performed safely, even during a surgeon's early experience with the technique. Considering the benefits of minimally invasive surgery, LTG is recommended for early gastric cancer.

Key Words: Stomach neoplasms, Laparoscopy, Total gastrectomy, Learning curve

Introduction

According to GLOBOCAN 2012, gastric cancer is the fifth most common malignancy and the third most common cause of cancer death worldwide.[1] Although endoscopic resection, chemotherapy, and radiotherapy have improved,[2-5] surgery remains the most important treatment strategy for gastric cancer. Complete surgical resection of tumors with en block lymphadenectomy provides a chance of cure for many patients with gastric cancer.[3]

Since Kitano et al.[6] reported the first case of laparoscopic gastrectomy (LG) for gastric cancer; LG has gained popularity for early stage gastric cancer, especially in Korea and Japan. LG has several advantages over conventional open total gastrectomy (OTG), including less pain, better cosmetic results, shorter hospital stay, faster postoperative recovery, earlier return to normal activities of daily living, and a better quality of life.[7-11] LG was initially limited to clinically early gastric cancer (EGC) located

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in the distal stomach. The subsequent accumulation of experience and development of surgical techniques and devices have allowed surgeons to expand the indications to include not only locally advanced gastric cancer (AGC) but also proximal gastric cancer. The oncologic safety of LG for AGC remains under debate, but a recent large-scale multicenter, retrospective case-control study showed that the long-term results of LG were similar to those of conventional OTG.[12]

Several studies have reported that laparoscopic distal gastrectomy (LDG) is both safe and feasible.[13-16] Recent studies have shown that short-term outcomes of laparoscopic total gastrectomy (LTG) are comparable to those of conventional OTG.[17-19] However, LTG is likely to be more complicated than LDG, especially for less experienced surgeons, because it is difficult to perform an esophagojejunostomy and lymph node dissection around the splenic hilum and left paracardial areas. Nevertheless, few studies have provided information about the learning curve for LTG.[20]

In this study, we evaluated the short-term outcomes of the initial consecutive LTG cases performed by a single surgeon with substantial previous experience in performing OTG and used these cases to determine the learning curve for LTG.

Materials and Methods

1. Patients

We reviewed the data of 74 consecutive patients who underwent LTG performed by a single surgeon with curative intent between April 2009 and December 2013 at Severance Hospital. The surgeon trained as a clinical fellow for 3 years at a gastric cancer specialized center where more than 1,000 cases of gastric cancer surgery were done annually, and had assisted on many cases of OTG and approximately 20 laparoscopic surgeries. In addition, laparoscopic surgery training in animal models was provided once a year. As such, at the time of the first case of LTG in this study, the surgeon already had experience performing >100 cases of OTG and 15 cases of LDG. LTG was initially used only patients with early stage of gastric cancer; thereafter, the indication was expanded to cases of locally AGC. All data were collected prospectively in a unique database. Data were also reviewed for patients who underwent OTG for proximal gastric cancer during the same period by the same surgeon to provide reference data. This study was approved by Severance Hospital's institutional review board (4-2014-0513).

2. Operative procedure

A brief summary of the LTG procedure is as follows. After the induction of general anesthesia, the patient was placed in a supine reverse Trendelenburg position. The surgeon stood on the patient's right side, while the first assistant stood on the opposite side. The camera assistant was positioned on the surgeon's right side. We inserted three 12-mm trocars and two 5-mm trocars. One 12-mm trocar was inserted through an infra-umbilical incision using an open method. After pneumoperitoneum was achieved, two 12-mm trocars were inserted in the right and left flank areas. Two 5-mm trocars were inserted in the right and left upper quadrants 2 cm below both lower rib margins. Laparoscopic coagulation shears (Ethicon, Cincinnati, OH, USA) were used for the lymph node dissection: D1+ or D2 lymph node dissection was performed for clinically EGC, while D2 lymph node dissection was conducted for advanced tumors (D2 lymph node dissection included splenic hilum lymph node dissection). The duodenum was resected below the pyloric ring via intracorporeal approach. After the esophagus was clamped, esophageal resection was performed between the two clamps using laparoscopic coagulation shears. A purse-string suture was created around the esophagus. The resected stomach was removed through a 4-cm mini-laparotomy incision that was formed by extending the incision for the 12-mm trocar in the lower left quadrant. A 25-mm detachable anvil was inserted in the esophageal stump and a purse-string suture was tied over the purse-string tying notch of the anvil. After a jejunojejunostomy was performed through the incision, esophagojejunostomy was conducted with a laparoscopic circular stapler EEA 25 (Covidien, Mansfield, MA, USA), and the jejunal stump was closed with a linear stapler (Fig. 1, Supplementary Video Clip). A closed drain tube was placed along the esophagojejunostomy site.

3. Evaluating postoperative outcomes

The clinical characteristics of the enrolled patients, including age, sex, American Society of Anesthesiologists (ASA) score, history of previous abdominal operation, body mass index (BMI), and tumor classification, were reviewed and compared between the two groups. Factors associated with perioperative outcomes, such as the lymph node dissection extent, presence of combined resection, operation time, intraoperative bleeding, hospital length of stay, time to first flatus, and time to first soft diet were reviewed.

To control postoperative pain, intravenous patient-controlled analgesia (PCA) was provided for patients who underwent LTG

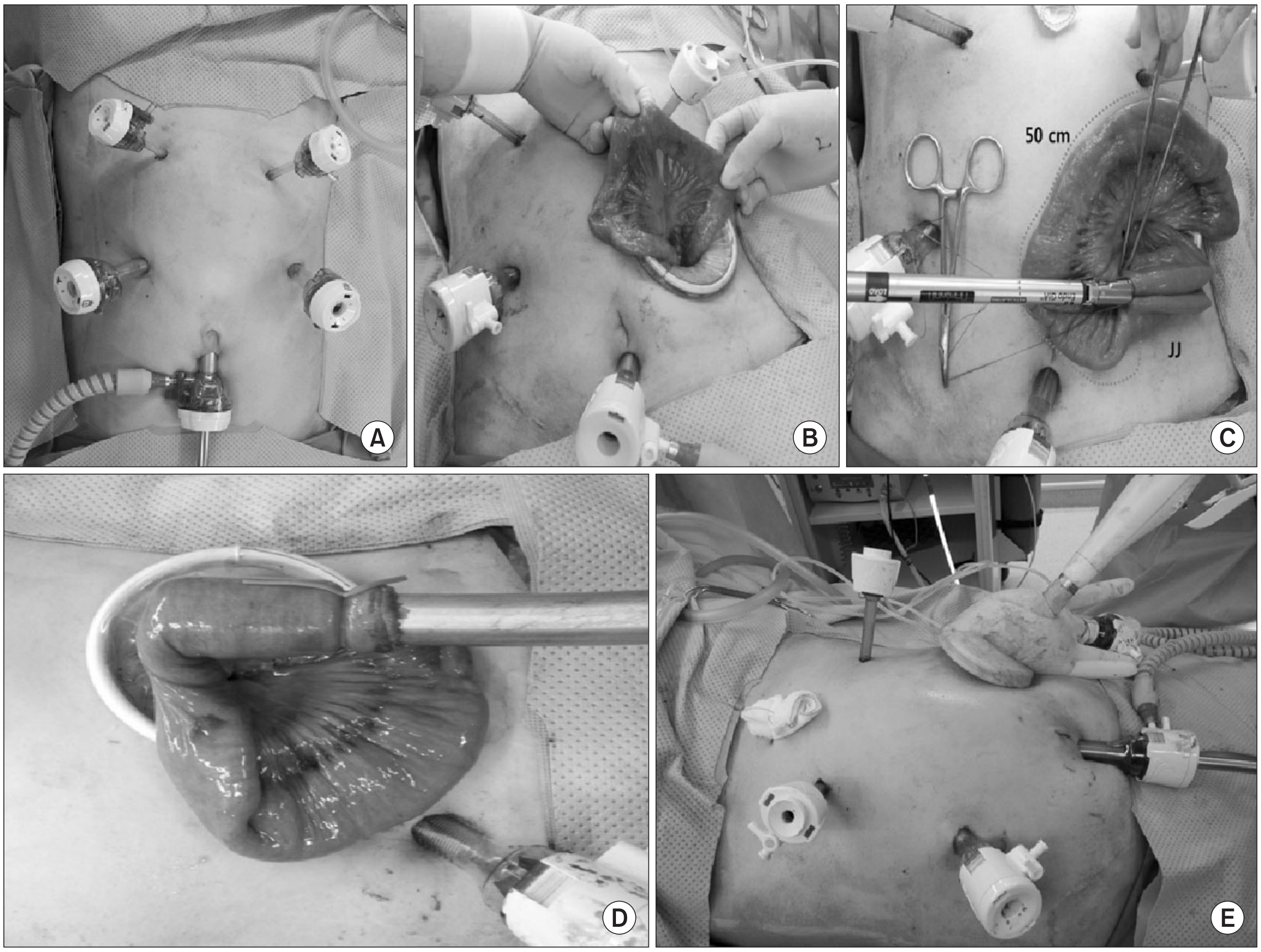

Fig. 1. Trocar locations and extracorporeal procedures for laparoscopic total gastrectomy. (A) Trocar placement. (B) Small bowel extraction through a mini-laparotomy in the lower left quadrant of the abdomen. (C) Jejunojejunostomy (JJ) approximately 50 cm distal to the esophagojejunostomy site. (D) Circular stapler insertion into the jejunum to create the esophagojejunostomy. (E) Circular stapler with jejunum insertion into the intra-abdominal cavity for the esophagojejunostomy.

and epidural PCA was given to those who underwent OTG. If the patient requested more analgesics, additional intravenous or intramuscular analgesics were supplied, and the number of additional doses during the first 7 postoperative days (POD) was recorded. To estimate pain severity after gastrectomy, visual analog scale (VAS) pain scores were recorded on POD 0 to 7. A white blood cell (WBC) count was obtained preoperatively, immediately after surgery (POD 0), and on POD 1, 3, and 5, while a serum C-reactive protein (CRP) level was obtained on POD 1, 3, and 5. Complications were recorded according to the Clavien-Dindo Classification of surgical complications.[21]

4. Statistical methods

IBM SPSS ver. 20.0 (IBM Co., Armonk, NY, USA) was used to analyze the demographics and perioperative outcomes of each group. Pearson's chi-square test was used to compare categorical variables. An independent t-test was used for continuous variables if the data for both groups satisfied the normality criteria; otherwise, Mann-Whitney's U-test was used. To compare longitudinal outcomes, such as VAS pain scores, WBC counts, and serum CRP levels, a linear mixed model was applied, and the outcomes at each time were compared by independent t-tests. To describe the learning curve, the stable operation time was evaluated by the moving average method ('nls2') and non-linear regression model ('bcp' and 'strucchange') using R statistics version 2.12.1 (R Foundation for Statistical Computing, Vienna, Austria). Values of $P<0.05$ were considered statistically significant.

Results

1. Baseline characteristics

The patients' characteristics are shown in Table 1. The mean age was 58.5 years in the OTG group and 55.9 years in the LTG group (P=0.151). Sex, BMI, and previous abdominal surgical history were similar between the two groups. Patients in the OTG group had a significantly higher ASA score and were more likely to have AGC than those in the LTG group (P=0.003 and <0.001, respectively).

2. Perioperative outcomes

Table 2 shows perioperative outcomes for each group. In the OTG group, 92.5% of patients underwent D2 lymph node dissection; in contrast, D2 lymph node dissection was used for only 32.4% of the 74 patients in the LTG group, and fewer lymph nodes were retrieved in the LTG than OTG group (P=0.020). The percentages of patients who underwent combined resection were similar for the two groups. The operation time was longer in the LTG group than in the OTG group (217.5 minutes vs. 175.7 minutes, P<0.001), but estimated blood loss was less in the LTG group (80.8 g vs. 130.0 g, P<0.001).

Although the time to first flatus was statistically shorter in the LTG group than in the OTG group (3.5 days vs. 3.8 days, P<0.001), the difference was of dubious clinical significance. Length of hospital stay and time to first soft diet were similar between the two groups. VAS scores were lower on POD 1 to 4 in the LTG group than in the OTG group and fewer additional analgesic doses were required during the first 7 POD in the LTG group, but the overall pain scores during the first 7 days after

Table 1. Patients' clinical characteristics

Clinical characteristic	OTG (n=134)	LTG (n=74)	P-value
Age (yr)	58.5±12.3	55.9±11.7	0.151
Sex			0.218
Male	94 (70.1)	45 (60.8)	
Female	40 (29.9)	29 (39.2)	
BMI (kg/m^2)	22.7±3.7	22.9±3.0	0.659
ASA score			0.003
I	70 (52.2)	41 (55.4)	
II	41 (30.6)	30 (40.5)	
III	23 (17.2)	2 (2.7)	
IV	0	1 (1.4)	
Previous abdominal surgery			0.210
No	90 (67.2)	56 (75.7)	
Yes	44 (32.8)	18 (24.3)	
Tumor classification*			<0.001
EGC	21 (15.7)	57 (77.0)	
AGC	113 (84.3)	17 (23.0)	

Values are presented as mean±standard deviation or number (%). OTG = open total gastrectomy; LTG = laparoscopic total gastrectomy; BMI = body mass index; ASA = American Society of Anesthesiologists; EGC = early gastric cancer; AGC = advanced gastric cancer. *Classification according to the standard of Japanese Classification of Gastric Carcinoma 3rd English edition on gastric cancer staging system.

Table 2. Operative and postoperative outcomes of OTG and LTG

Variable	OTG (n=134)	LTG (n=74)	P-value
Extent of lymph node dissection*			<0.001
D1+b	10 (7.5)	50 (67.6)	
D2	124 (92.5)	24 (32.4)	
No. of retrieved lymph node	44.8±18.2	39.9±11.8	0.020
Combined resection	29 (21.6)	11 (14.9)	0.273
Operation time (min)	175.7±43.1	217.5±63.4	<0.001
Intraoperative blood loss (g)	130.0±126.5	80.8±60.4	<0.001
Hospital stay after surgery (d)	9.0±3.1	8.3±3.4	0.097
First flatus passage (d)	3.8±0.8	3.5±0.7	<0.001
Soft diet initiated (d)	6.0±1.9	5.7±2.0	0.252
No. of additional pain killers used for POD 7	7.7±5.8	4.7±4.0	<0.001
VAS			0.873
POD 0	5.4±2.0	5.5±1.9	0.850
POD 1	5.6±2.1	4.8±1.9	0.010
POD 2	5.9±1.8	4.8±1.9	<0.001
POD 3	5.5±1.9	4.5±1.8	0.001
POD 4	4.5±2.0	3.8±1.9	0.012
POD 5	4.0±1.9	3.7±1.9	0.254
POD 6	3.5±1.9	3.0±1.6	0.056
POD 7	2.9±1.7	2.7±1.5	0.513
WBC			0.521
Preoperative	6.5±2.3	6.5±1.9	0.881
POD 0	12.6±4.5	14.0±3.1	0.007
POD 1	10.9±3.3	11.1±3.2	0.709
POD 3	7.5±3.0	7.2±2.4	0.454
POD 5	6.4±2.1	6.6±2.0	0.542
Serum C-reactive protein (mg/ml)			0.202
POD 1	56.2±31.6	63.4±27.6	0.103
POD 3	101.6±58.1	98.5±59.3	0.721
POD 5	60.2±50.6	57.4±51.0	0.717

Values are presented as number (%) or mean±standard deviation. OTG = open total gastrectomy; LTG = laparoscopic total gastrectomy; POD = postoperative day; VAS = visual analogue scale; WBC = white blood cell. *Classification according to the Japanese gastric cancer treatment guidelines 2010 (ver. 3).

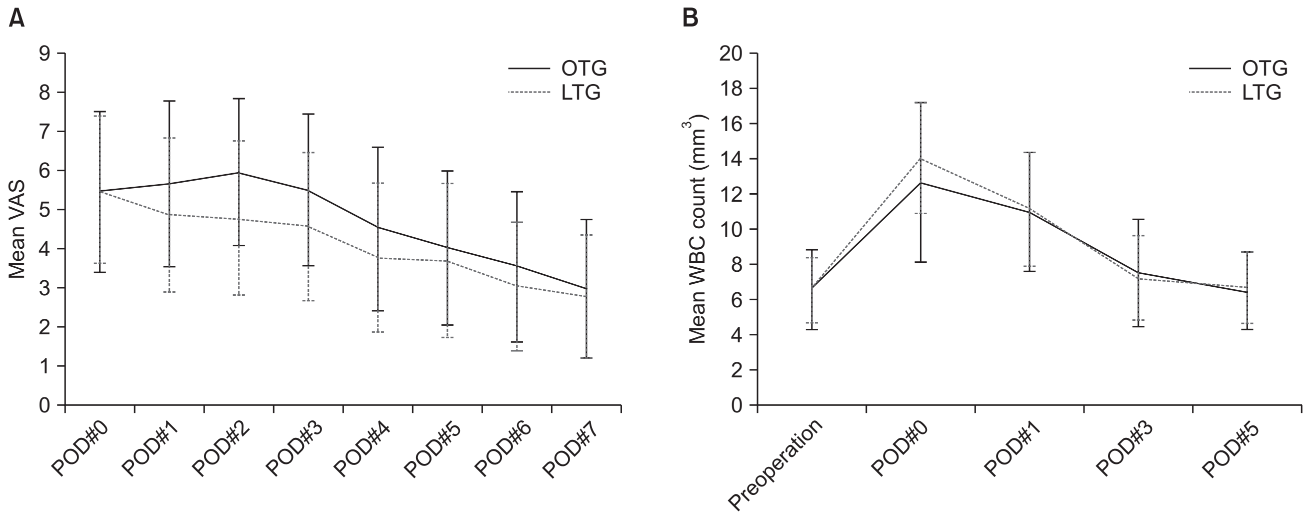

Fig. 2. Mean visual analog scale (VAS) scores (A) and white blood cell (WBC) counts (B) after laparoscopic total gastrectomy (LTG) and open total gastrectomy (OTG). POD = postoperative day.

Table 3. Postoperative complications after OTG and LTG

Grade*	OTG (n=134)	LTG (n=74)	P-value
Grade I	Wound problem (n=2) Chylous ascites (n=3)	Wound problem (n=2) Hematochezia (n=1)	-
Grade II	Wound infection (n=2) Intra-abdominal complicated fluid collection (n=4) Respiratory problem (n=2) Leg DVT (n=1)	Intra-abdominal complicated fluid collection (n=4) Intra-abdominal hematoma (n=1) Respiratory problem (n=1) Cellulitis (n=1)	-
Grade III-a	Complicated fluid collection (n=2)	-	-
Total (n)	16 (11.9%)	10 (13.5%)	0.660

OTG = open total gastrectomy; LTG = laparoscopic total gastrectomy; DVT, deep vein thrombosis. *Classification according to the Clavien-Dindo classification.

gastrectomy did not differ between the two groups (Table 2, Fig. 2A). Inflammatory markers such as WBC counts and serum CRP levels were generally similar between the two groups. Except for a higher WBC in the LTG group on the day of surgery (P=0.007), the WBC and CRP levels did not differ significantly between groups (Table 2, Fig. 2B).

3. Postoperative morbidities

Postoperative morbidities occurred in 10 of the 74 patients (13.5%) in the LTG group and 16 of the 134 patients (11.9%) in the OTG group (Table 3). The morbidities in the LTG group included grade II intra-abdominal complicated fluid collection (n=4), hematoma (n=2), respiratory complication (n=1), and cellulitis controlled by antibiotics (n=1). The morbidities in the OTG group included wound infection (n=2), intra-abdominal complicated fluid collection (n=4), respiratory complication (n=2), and deep vein thrombosis (n=1). Two patients in the OTG group required postoperative external drainage for their complicated intra-abdominal fluid collection; these cases were graded as III-a complications. There were no cases of anastomotic or stump leaks in either group.

4. Learning curve

To determine the learning curve for LTG, the operation time was evaluated using the moving average method. Fig. 3A shows that the operation time for LTG cases gradually decreased after the first case, whereas the operation time for OTG cases performed in the same period as the LTG cases exhibited no overall decrease (each point represents the operative time of each case, the lines represent its serial pattern in LTG and OTG, and the

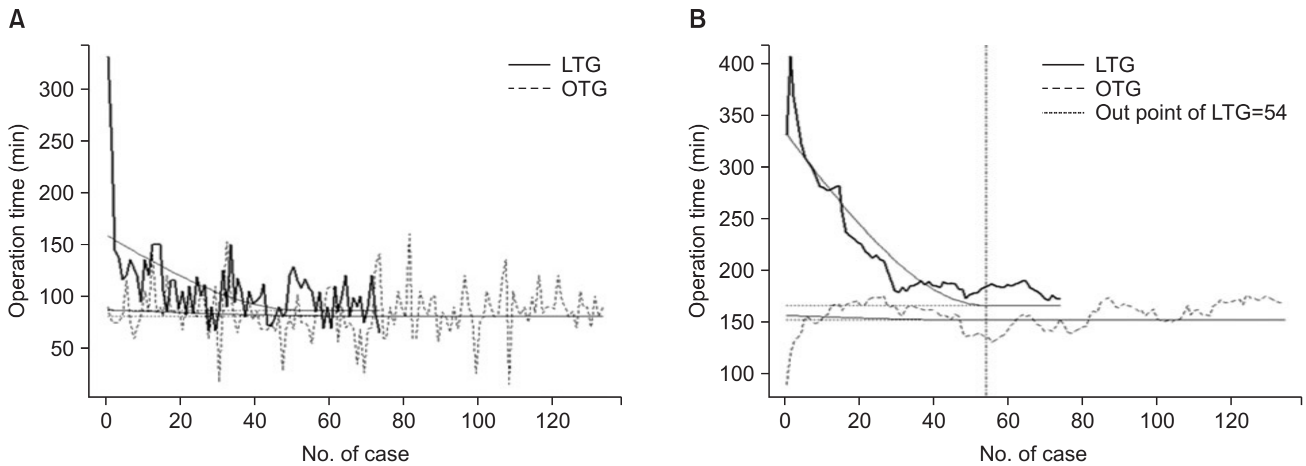

Fig. 3. Operation time and learning curves for laparoscopic total gastrectomy (LTG) and open total gastrectomy (OTG). (A) Changes in operation time with the accumulation of case experiences. (B) A graph of the consecutive 15 cases showing its sequential average through the moving average method.

curved line is the trend line). Fig. 3B is a graph of the consecutive 15 cases that shows its average sequentially through the moving average method. The operation time moving average of 15 cases in the LTG group decreased gradually, and the curve converged to a flat line after 54 cases as analyzed by the non-linear regression model. In the OTG group, a cut-off point could not be calculated, and it converged from its initial case because the surgeon was already past the learning curve (Fig. 3B). Overall morbidity in the pre- versus post-learning curve of LTG was not statistically different (13.0% and 15.0% in pre- and post-learning curve, respectively, Fisher's exact test; P=0.543)

Discussion

Although the benefits of LTG in gastric cancer surgery are widely accepted, technical difficulty is one of the main reasons surgeons may be reluctant to perform it. Especially for surgeons experienced with OTG, starting to perform LTG can be accompanied by a longer operation time and the potential risk of surgical complications. Therefore, here we analyzed the initial experience with LTG of a single surgeon who was previously experienced with OTG. As shown by our results, LTG can be performed safely, even during a surgeon's initial use of the technique, and 54 cases are necessary to overcome the learning curve as assessed by operation time.

The technical steps for laparoscopic esophagojejunostomy are shown in Fig. 1 and the Supplementary Video Clip. Resected stomach extirpation, anvil insertion, jejunojejunostomy creation, and circular stapler insertion were performed through a mini-laparotomy in the lower left quadrant. Some surgeons recently used a linear stapler for esophagojejunostomy,[22] which can be inserted through a 12-mm trocar without the need for an additional incision. Although using a linear stapler for esophagojejunostomy can avoid a mini-laparotomy, we used a circular stapler both because we were familiar with it and it is also used for OTG.

Postoperative morbidity and mortality are important factors for assessing short-term surgical outcomes. We found that the complications incidence, type, and grade after gastrectomy were similar for OTG and LTG. No anastomotic or stump leaks and no mortality occurred after OTG or LTG, while no grade III complications occurred after LTG. Although the operation time was longer for LTG than OTG, all patients recovered safely without major complications. Admittedly, the differences in tumor characteristics (EGC vs. AGC) and the extent of lymph node dissection (D1+ vs. D2) between OTG and LTG may have influenced our results comparing short-term outcomes and operation-related factors between the two groups. Nevertheless, our data appear to demonstrate the technical safety of LTG.

Analysis of the operation time learning curve for LTG showed that it converged to a flat line after 54 cases. Comparing our results to previous reports of the learning curve for LDG for gastric cancer,[23] more experience seems to be required to perform LTG. In this study, the surgeon had adequate experience with OTG before starting to perform LTG. Thus, the operation time was significantly shorter for OTG than for LTG and there was no learning curve for OTG. Because LTG was usually performed for clinical EGC, D1+ lymph node dissection was more common used than D2 dissection during LTG. To ensure an adequate D2 lymph node dissection, including hilar lymph node dissection, more experience with LTG would be necessary.

Although postoperative complications and overall recovery were similar between the LTG and OTG groups, LTG showed the benefits of being a minimally invasive surgery, such as less blood loss, shorter time to first flatus, less pain, and less analgesic use. Therefore, LTG is a good surgical option for upper-third EGC, and if surgeons follow basic surgical principles for gastric cancer surgery, they can perform LTG safely, even during their initial experience with the technique.

Our study had limitations. Because it was a retrospective cohort study, the tumor characteristics and lymph node dissection extent differed between the LTG and OTG groups. In addition, we did not analyze the oncological outcomes of LTG and only discussed the technical safety of LTG because the indications for LTG and OTG are different. The oncological safety of LTG in AGC would be another issue that could be addressed in future studies. Moreover, the learning curve for LTG for a completely novice surgeon is unknown because the surgeon in this study had already performed more than 100 OTG and 15 LDG procedures. Moreover, during the learning curve period of LTG, the initial 54 cases here, the surgeon performed LDG more than four times more commonly than LTG. Experience with LDG can contribute to the surgeon overcoming the learning curve of LTG. If no case of LDG is accompanied, the number of procedures required to overcome the LTG learning curve would be greatly increased. The changed indication of LTG from EGC to AGC is another limitation.

In conclusion, LTG was safely and feasibly performed here by a surgeon experienced with OTG with comparable outcomes. The learning curve of LTG for a surgeon experienced with OTG seemed to exceed 50 cases.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Electronic Supplementary Material

This online version of this article (doi: 10.5230/jgc.2015.15.3.159) contains supplementary materials.

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