Outcome of Esophagojejunostomy During Totally Laparoscopic Total Gastrectomy: A Single-Center Retrospective Study

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Abstract. *Aim: The present study aimed to clarify the safety and feasibility of esophagojejunostomy during totally laparoscopic total gastrectomy (TLTG). Patients and Methods: In 45 consecutive patients who underwent TLTG for gastric cancer, esophagojejunostomy was performed with a functional end-to-end anastomosis (FEEA) using a linear stapler in 24 patients or with a double stapling technique (DST) using a trans-orally inserted anvil (OrVil™) in 21 patients. Results: The DST was more likely to be chosen in patients with tumors located in the upper stomach. In the FEEA group, both the mean length of the operation and the mean postoperative hospital stay were significantly shorter compared to those in the DST group. Two patients in the FEEA group and four patients in the DST group developed postoperative complications but there were no postoperative deaths in either group. Conclusion: Both FEEA and DST in esophagojejunostomy during TLTG are safe and feasible.*

Despite a decrease in its incidence, gastric cancer is still the second most common cancer worldwide (1). In Eastern Asian countries, particularly Korea and Japan, gastric cancer is still the most prevalent malignancy. The proportion of patients with early gastric cancer has increased as a result of improved nation-wide surveillance in both countries (2, 3). Currently, surgical resection using gastrectomy and proper peri-gastric lymphadenectomy is the only treatment option that can enhance the survival rate of patients with gastric cancer (4).

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Since the first laparoscopy-assisted distal gastrectomy for early gastric cancer was performed in 1991 (5), the development of dedicated instruments and surgical techniques has led to the use of laparoscopic distal gastrectomy (LDG) to treat gastric cancer. Many surgeons have described their experience with totally laparoscopic distal gastrectomy (TLDG) and have found it safe and feasible compared to laparoscopic-assisted gastrectomy (LADG) (6, 7). However, laparoscopic total gastrectomy (LTG) for gastric cancer has not become as popular as LDG because the reconstruction is more complex after LTG than after LDG, especially for esophagojejunostomy. The construction of an esophagojejunostomy is technically difficult and serious complications can arise.

Some surgeons have used an extracorporeal approach through a mini-laparotomy, constructing an end-to-side anastomosis with an end-to-end anastomosis stapler (8) as part of laparoscopic-assisted total gastrectomy (LATG). As in intracorporeal anastomotic approaches for esophago-jejunostomy in totally laparoscopic total gastrectomy (TLTG), the double stapling technique (DST) using a trans-orally inserted anvil (OrVil™) (9-11) and a functional end-to-end anastomosis (FEEA) technique using a linear stapler (12) have previously been described. However, no optimal procedure for esophagojejunostomy has yet been established.

Since 2009, we have performed TLTG for 45 patients with gastric cancer as a less invasive total gastrectomy with intracorporeal esophagojejunostomy using either the DST or FEEA. In the present study, we evaluated the safety and efficacy of esophagojejunostomy during TLTG, comparing the treatment outcomes of DST and FEEA in patients who underwent TLTG.

Patients and Methods

Patients. Three hundred and seven patients with gastric cancer were surgically treated in the Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, from

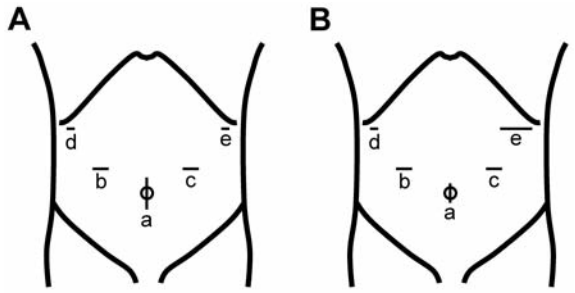

Figure 1. *The positions of the surgical ports. A 12 mm balloon blunt tip trocar was used for the insertion of the laparoscope (a), two 12 mm trocars (b and c) and two 5 mm trocars (d and e) were also inserted. (A) For patients who underwent functional end-to-end esophagojejunostomy, the 12 mm umbilical wound (a) was extended to 30-40 mm to allow the resected specimen to be pulled out. (B) For patients who underwent the DST esophagojejunostomy, the 5 mm left upper wound (e) was extended to 30-40 mm to pull out the resected specimen and allow for the insertion of the circular stapler.*

2009 to 2013. One hundred and twenty-eight of these patients (41.7%) underwent totally laparoscopic gastrectomy, defined as a procedure where both the resection and anastomosis are performed intracorporeally with a laparoscopic technique (13-16). The subjects included in this study were 45 patients with gastric cancer who underwent TLTG. We investigated the background clinical data, surgical results and postoperative course of these 45 patients.

Surgical procedures. Total gastrectomy and lymphadenectomy were performed according to the guidelines of the Japanese Gastric Cancer Association (Association JGC, ed. Japanese Classification of Gastric Carcinoma. 13th ed. Tokyo Kanehara 1999). In brief, the patient was placed under general anesthesia in the lithotomy position. A balloon blunt tip trocar was inserted in the umbilical region using a cut-down method, and a laparoscope was inserted through the trocar. The liver was pulled up using a silicone disc by a phi-shaped technique, as reported previously (17). All procedures were performed using two trocars for the operator and two trocars for the assistant (Figure 1). The basic extent of lymphadenectomy in the present series was D1+; however, patients with clinical N1 disease underwent D2 lymphadenectomy. For all 45 patients, reconstruction was performed by the Roux-en Y method. In principle, esophagojejunostomy by the double stapling technique (DST) using a trans-orally inserted anvil (OrVil™) was performed in patients with gastric cancer located at the esophagogastric junction or in the upper stomach with esophageal invasion, whereas a functional end-to-end anastomosis (FEEA) using a linear stapler was performed as the first choice in other patients.

Functional end-to-end anastomosis (FEEA) with a linear stapler. In 24 patients, the esophagojejunostomy was performed by the FEEA technique using linear staplers. Figure 1A shows the positions of the five ports used during TLTG with FEEA reconstruction. A 12-mm balloon blunt tip trocar was for the insertion of the laparoscope, while four other trocars (two 12 mm and two 5 mm) were also inserted. The resected specimen was pulled out through the extended wound at the umbilicus (Figure 1A). Figure 2 shows the esophagojejunostomy with the FEEA technique. The abdominal esophagus was exposed and transected using an Echelon 60 mm linear stapler in the horizontal direction (Figures 2A, B). Thereafter, 5 mm transverse incisions were created at the edges of the tip of the antimesenteric border between the jejunum and the left lateral wall of the abdominal esophagus. Both jaws of a 45 mm linear stapler were inserted into the holes and fired (Figures 2C, D). The entry hole was closed with a 60 mm linear stapler (Figures 2E, F). The functional end-to-end esophagojejunostomy was then accomplished. A side-to-side jejunostomy proceeded at a point 40 cm distal to the esophagojejunostomy using a 60 mm linear stapler. The entry hole for this stapler was closed with a 60 mm linear stapler.

The double stapling technique (DST) with a trans-orally inserted anvil. In 21 patients, esophagojejunostomy was performed using the double stapling technique (DST) using a trans-orally inserted anvil (OrVil; DST Series™ EEA™ OrVil™, 25 mm; Covidien, Mansfield, MA, USA) and a circular stapler, as described previously (9). Figure 1B shows the positions of the five ports used for TLTG with DST reconstruction. A 12-mm balloon blunt tip trocar for insertion of the laparoscope and four other trocars (two 12-mm and two 5-mm) were inserted. The 5 mm left upper wound was extended to allow the resected specimen to be pulled out and the circular stapler to be inserted (Figure 1B).

Figure 3 shows the esophagojejunostomy by the DST technique. The abdominal esophagus was exposed and transected using a 60 mm linear stapler, as shown in Figures 2A and B. The OrVil™ anvil was passed transorally through the larynx to the stapled esophageal stump. A small hole was created using an ultrasonic knife at the corresponding position of the stapled esophageal stump, and the tube was pulled out into the abdominal cavity through the hole until the white plastic rubber ring was fully revealed. The connecting thread was cut and the tube was disconnected from the anvil (Figsures 3A, B). Then, a 25-mm circular stapler was inserted into the distal limb of the jejunum and introduced into the abdominal cavity from an extended left upper incision. The anvil and circular stapler were connected and an end-to-side esophagojejunostomy anastomosis was made (Figures 3C, D). The entry hole of the circular stapler was closed with a 60-mm linear stapler (Figures 3E, F). Similar to FEEA, a side-to-side jejunostomy was then performed.

Staging of the tumor and statistical analyses. The staging of the tumor was based on the Japanese Classification of Gastric Carcinoma (Association JGC, Japanese Classification of Gastric Carcinoma. 13th ed. Tokyo, Kanehara, 1999) and the depth of invasion and lymph node metastasis were defined by the pathological findings. The data were analyzed using the Graphpad Prism software program, v5.0 (Graphpad Software Inc, San Diego, CA, USA). A difference of $p<0.05$ was considered to be significant.

Results

Table I shows the clinicopathological characteristics of the 45 patients who underwent TLTG. The mean age was 63.7 years (range=38-85 years) and 30 (66.7%) male and 15 (33.3%) female patients underwent TLTG. Thirty-three tumors (73.3%) were located in the upper-third of the stomach or around the esophagogastric junction, while 12 tumors were

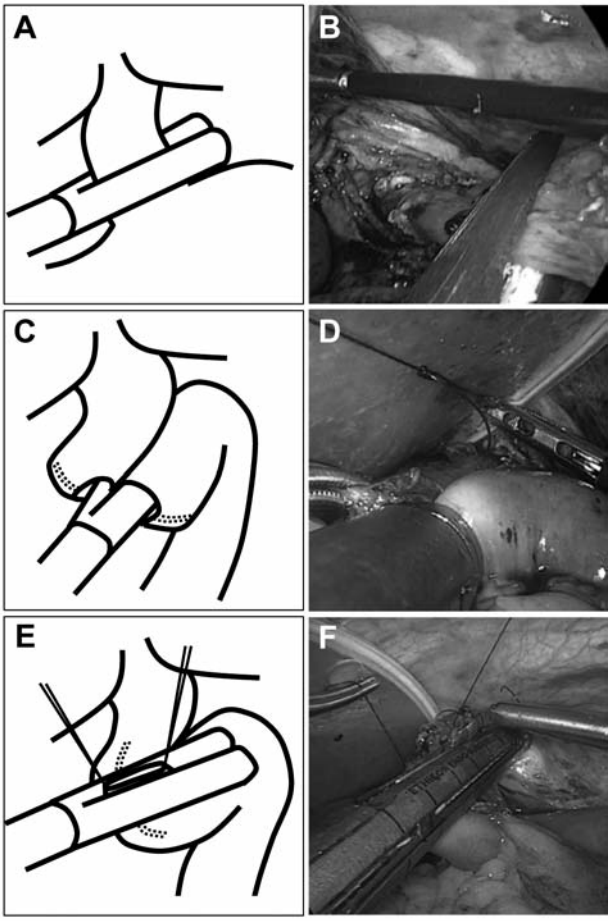

Figure 2. *Esophagojejunostomy by functional end-to-end anastomosis (FEEA) with a linear stapler. (A, B) The abdominal esophagus was exposed and transected using an Echelon 60-mm linear stapler in the horizontal direction. (C, D) 5-mm transverse incisions were created at the edges of the tip of the antimesenteric border between the jejunum and the left lateral wall of the abdominal esophagus. Both jaws of a 45-mm linear stapler were inserted into the holes and fired. (E, F) The entry hole was closed with a 60-mm linear stapler.*

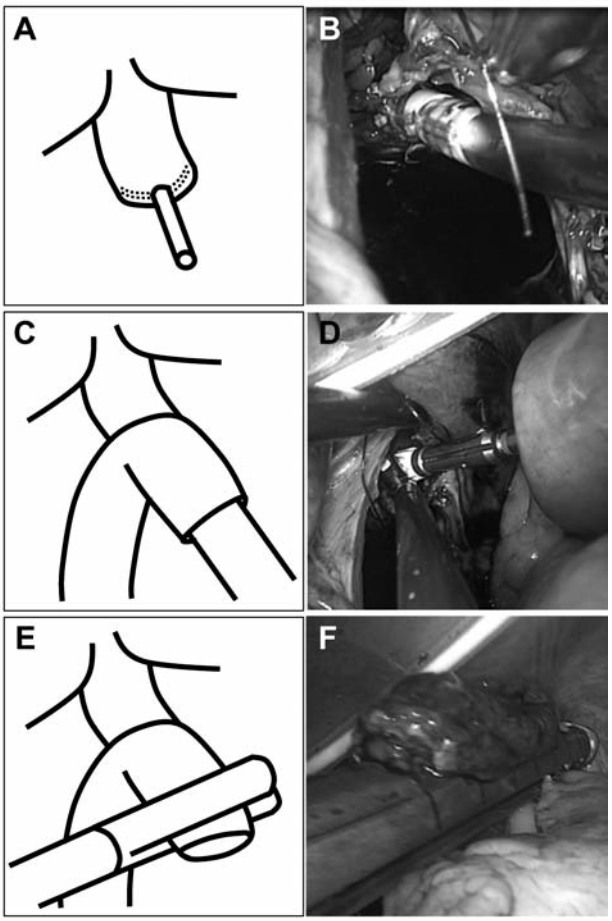

Figure 3. *Esophagojejunostomy by the double stapling technique (DST) with a trans-orally inserted anvil (OrVil™). (A, B) After transection of the abdominal esophagus, the OrVil™ anvil was passed transorally through the larynx to the stapled esophageal stump. A small hole was created using an ultrasonic knife on the corresponding position of the stapled esophageal stump and the tube was pulled out into the abdominal cavity through the hole until the white plastic rubber ring was fully revealed. The connecting thread was cut and the tube was disconnected from the anvil. (C, D) A 25-mm circular stapler was inserted into the distal limb of the jejunumand introduced into the abdominal cavity from the extended left upper incision. The anvil and circular stapler were connected and an end-to-side esophagojejunostomy anastomosis was made. (E, F) The entry hole of the circular stapler was closed with a 60-mm linear stapler.*

located in the middle-third or lower-third of the stomach. The mean tumor size was 57.1 mm (range 7-150 mm). The depth of invasion of 20 tumors (44.4%) was T3-4, while that of 25 tumors (55.6%) was T1-2. Lymph node metastasis was detected in 28 patients (62.2%) and eight patients showed distant metastasis (cytology-positive: 4, peritoneal dissemination: 3 and liver metastasis: 1). Twenty-nine tumors (64.4%) were TNM stage I-II, while 16 (35.6%) were stage III-IV. In the DST group, 19 of 21 (90.5%) tumors were located in the upper stomach (EG or U), while 14 of the 24 (58.3%) tumors in the FEEA group were located in the upper stomach (p=0.0199). There were no significant differences in the other factors between the two groups.

Table II shows the results of the comparison of the surgical and postoperative outcomes. In the FEEA group, both the mean length of the operation and the mean postoperative hospital stay were significantly shorter compared to those in the DST group (313 min *vs*. 382 min: p=0.0140, 11.5 days *vs*. 17.4 days: p=0.003, respectively). There were no significant differences in the mean blood loss (95 ml *vs*. 174 ml) and mean day of resuming oral intake

Table I. *The clinicopathological characteristics of 45 patients who underwent TLTG.*

Factor	Total (n=45)	FEEA (n=24)	DST (n=21)	*p*-Value[3]
Mean age (range)	63.7 (38-85)	65.6 (49-85)	61.5 (38-82)	NS
Gender				
Male/Female	30/15	13/11	17/4	NS
Location of tumor[1]				
EG-U/M-L	33/12	14/10	19/2	0.0199
Mean tumor size, mm (range)	57.1 (7-150)	61.1 (7-150)	52.4 (10-130)	NS
Depth of tumor invasion				
T1-2/T3-4	25/20	12/12	13/8	NS
Lymph node metastasis				
Negative/Positive	28/17	16/8	12/9	NS
Distant metastasis[2]				
M0/M1	37/8	18/6	19/2	NS
TNM stage				
Stage I-II/Stage III-IV	29/16	14/10	15/6	NS

[1]EG: within 2 cm of the esophagogastric junction, U: upper-third of the stomach except for EG tumors, M: middle-third of the stomach, L: lower-third of the stomach. [2]Distant metastasis including cytology-positive cases: 4, peritoneal dissemination: 3, and liver metastasis: 1. [3]The chi-squared test, Fisher's exact test and the Mann-Whitney *U*-test were used.

Table II. *Comparison of operative and postoperative outcomes.*

Factor	FEEA (n=24)	DST (n=21)	*p*-Value[1]
Mean length of operation			
min (range)	313 (196-431)	382 (219-719)	0.0140
Mean amount of blood loss			
ml (range)	95 (1-281)	174 (1-530)	NS
Mean day of resuming oral intake			
Postoperative day (range)	4.8 (3-9)	8.4 (3-37)	NS
Mean postoperative hospital stay			
Day (range)	11.5 (8-18)	17.4 (9-50)	0.0033
Postoperative complication			
Anastomotic leakage	0	2	
Pulmonary complication	0	2	NS
Bleeding	1	0	
Pancreatic fistula	1	0	
Mortality	0	0	NS

[1]The Chi-square test, Fisher's exact test and Mann-Whitney *U*-test were used.

(4.8 days *vs*. 8.4 days) between the two groups. A total of six patients developed postoperative complications; two patients in the FEEA group (postoperative bleeding: 1, pancreatic fistula: 1) and four patients in the DST group (anastomotic leakage: 2, pulmonary complications: 2). Hemostasis was performed as a re-operation for the patient who developed postoperative bleeding, while the other complications recovered with conservative treatment. There were no postoperative deaths in either group.

Discussion

In the present retrospective study, we evaluated the safety and efficacy of esophagojejunostomy in 45 patients who underwent TLTG in our institute and compared the treatment outcomes of FEEA and DST. The DST was more likely to be chosen in patients with tumors located in the upper stomach or gastroesophageal junction, while the other background data were similar between the two groups. The esophagojejunostomy

by the DST was associated with a longer operation and longer postoperative hospital stay. Although two patients in the FEEA group and four patients in the DST group developed postoperative complications, all of them recovered and there was no procedure-related death in either group.

At present, esophagojejunostomy by the DST technique using the OrVil™ anvil is the most common method for TLTG (18-21). We had started performing TLTG with esophagojejunostomy by the DST in 2009. However, the intra-abdominal application of a circular stapler and anastomosis were often challenging because of the narrow space and limited laparoscopic view. Okabe *et al*. noted that a circular stapler has not been specifically designed for endoscopic surgery and the existing staplers have usually been extracorporeally applied because of the difficulties associated with applying them under a limited laparoscopic view (22). If force is applied to a relatively large anvil, the mucosa can slip-off and rupture the esophageal wall, which would result in serious complications (23). In contrast, a linear stapler can be easily manipulated intra-abdominally and a recent study demonstrated the safety and feasibility of esophagojejunostomy by FEEA during TLTG (12). Therefore, we currently choose to perform esophago-jejunostomy by FEEA as the first choice. However, the FEEA is not appropriate for patients with tumors that have invaded the esophagus because the abdominal esophagus should be resected in such patients. Since these patients would no longer have a sufficient length of abdominal esophagus to accomplish FEEA, patients with tumors located at the esophagogastric junction or in the upper stomach with esophageal invasion are principally treated with esophagojejunostomy by the DST. That is why the ratio of tumors located in the upper stomach was significantly higher in the DST group than in the FEEA group in the present study.

Matsui *et al*. and Lee *et al*. concluded that esophagojejunostomy by FEEA after total gastrectomy is convenient, safe, reliable and can be performed independent of the esophagus and depth of the esophageal hiatus (24, 25). Although esophagojejunostomy by FEEA after total gastrectomy in open surgery has become accepted, laparoscopic esophagojejunostomy seems to be quite rare. Recently, Ebihara *et al*. (12) demonstrated the outcome of esophagojejunostomy by FEEA in 65 patients who underwent TLTG. The mean length of the operation was 271.5 min and the mean blood loss was 85.2 g. Ten patients (15.4%) developed postoperative complications, including three (4.6%) cases of anastomotic stenosis at the region of the esophagojejunostomy. Comparing these findings with our results, the length of the operation and blood loss were similar to those of our 24 cases, however, we have not experienced any cases of postoperative stenosis of the esophagojejunostomy. Ebihara *et al*. recommended using a 45 mm linear stapler because they experienced anastomotic stenosis when they used a 60 mm linear stapler. They insisted that the 60 mm linear stapler lacks grasping power, perhaps because the esophageal mucosa could slip off and became shortened before firing, and the abdominal esophagus did not stretch during functional end-to-end esophagojejunostomy when they used a 60-mm linear stapler. We have also used a 45 mm linear stapler for esophagojejunostomy and have not experienced any cases of stenosis. These findings imply that the 45 mm linear stapler is suitable for this anastomosis.

Several previous studies have reported the outcomes of esophagojejunostomy using the OrVil™ anvil in LTG. Ito *et al*. (10) reported that the mean length of the operation was 243 min, the mean blood loss was 79 ml, the incidence of anastomotic leakage was 1.7% and the incidence of stenosis was 1.7% in 117 patients who underwent TLTG. Kunisaki *et al*. (21) reported that the length of the operation was significantly shorter (209.8 min *vs*. 261.4 min) and the intraoperative blood loss was significantly lower (111.0 g *vs*. 173.3 g) in TLTG using the OrVil™ anvil (n=30) than in LATG (n=15). Anastomotic leakage was seen in one patient (3.3%) in that study. Zuiki *et al*. (19) reported that the incidence of anastomotic leakage was 1.9% and that of stenosis was 21.2% (75% with an anvil size of 21 mm and 17.0% with an anvil size of 25 mm) in their study of 52 patients who underwent TLTG. In the present study of 21 patients who underwent TLTG with esophagojejunostomy by the DST using the OrVil™ anvil, the mean length of the operation was longer (382 min), the mean blood loss was higher (174 ml) and the incidence of anastomotic leakage was higher (9.5%) than those of previous reports. One possible explanation for these findings is that 10 of the 21 (47.6%) patients who underwent esophagojejunostomy by the DST had gastric cancer at the esophagogastric junction or in the upper stomach with esophageal invasion, and the difficulty of a higher anastomosis in such patients might result in a higher incidence of leakage. Nonetheless, the DST using an OrVil™ circular stapler is a useful method, especially for higher esophagojejunostomy, because FEEA is thought to be very difficult in such cases.

A comparison of the surgical and postoperative outcomes is shown in Table II and revealed that esophagojejunostomy by the DST was associated with a longer operation and a longer postoperative hospital stay. As described above, the DST was more likely to be chosen for patients with tumors located in the upper stomach or gastroesophageal junction. In such patients, the abdominal esophagus and lower thoracic esophagus needed to be mobilized with surrounding lymph node dissection before the anastomosis could be performed, therefore, the operation tended to be longer. Moreover, the difficulties associated with the higher anastomosis of DST could be a risk factor for anastomotic leakage and could prolong the postoperative hospital stay.

Although the long-term outcomes of esophagojejunostomy during TLTG remain unknown, we consider both FEEA and the DST to be safe and feasible. Notably, the DST enables a higher anastomosis for patients with tumors at the

gastroesophageal junction or in the upper stomach with esophageal invasion. However, higher esophagojejunostomy in such cases might be a risk factor for anastomotic leakage. Therefore, anastomosis must be carefully performed, while keeping this possible complication in mind.

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