Circular versus linear stapling in esophagojejunostomy after laparoscopic total gastrectomy for gastric cancer: a propensity score-matched study

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ABSTRACT

Purpose: We used propensity score matching to compare the complication rates after laparoscopic total gastrectomy (LTG) with esophagojejunostomy (EJS) performed using a circular or a linear stapler.

Methods: We retrospectively enrolled all patients who underwent curative LTG between November 2004 and March 2016. Patients were categorized into the circular and linear groups according to the stapler type used for the subsequent EJS. Patients in the groups were matched using the following propensity score covariates: age, sex, body mass index, American Society of Anesthesiologists physical status, extent of lymph node dissection, and Japanese Classification of Gastric Carcinoma stage. Clinicopathological characteristics and surgical outcomes were compared.

Results: We identified 66 propensity score-matched pairs among 379 patients who underwent LTG. There was no significant between-group difference in the median operative time, extent of lymph node dissection, number of lymph nodes resected, rate of conversion to open surgery, or number of surgeries performed by a surgeon certified by the Japanese Society of Endoscopic Surgery. In the circular and linear groups, the rate of all complications (Clavien-Dindo (CD) classification ≥ I; 21% vs. 26%, respectively; p = 0.538), complications more severe than CD grade III (14% vs. 14%, respectively; p = 1.000), and occurrence of EJS leakage and stenosis more severe than CD grade III (5% vs. 2%, p = 0.301; and 9% vs. 8%, p = 0.753, respectively) were comparable.

Conclusions: There is no difference in the postoperative complication rate related to the type of stapler used for EJS after LTG.

Keywords

Gastric cancer, Laparoscopic total gastrectomy, Esophagojejunostomy, Postoperative complications, Propensity score matching

Author Contributions

- Study conception and design: Noriaki Kyogoku, Yuma Ebihara
- Acquisition of data: Noriaki Kyogoku, Fumitaka Nakamura, Katsuhiko Murakawa, Takayuki Morita, Shunichi Okushiba
- Analysis and interpretation of data: Noriaki Kyogoku
- Drafting of manuscript: Yuma Ebihara
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INTRODUCTION

Since the first report of laparoscopy-assisted distal gastrectomy (LADG) for gastric cancer (GC) in 1994 [1], the number of patients undergoing laparoscopic gastrectomy (LG) in East Asia has increased rapidly. Two randomized control trials (RCTs) verified the safety and efficacy of LADG for early gastric cancer (EGC) [2, 3], and two large-scale case-controlled studies demonstrated that long-term oncological outcomes after LADG for EGC were similar to those after open gastrectomy [3, 4]. Recently, two RCTs verified the safety of LG for advanced gastric cancer (AGC) [5, 6], and our multicenter retrospective study reported satisfactory short- and long-term outcomes after LG for AGC [7]. Furthermore, three RCTs evaluating the short- and long-term outcomes after LADG for AGC are ongoing [5, 8, 9].

On the other hand, laparoscopic total gastrectomy (LTG) is much less frequently performed than laparoscopic distal gastrectomy (LDG) because the subsequent esophagojejunostomy (EJS) is technically difficult. While several studies have evaluated the safety of LTG [12-19], only a few have examined long-term outcomes [20-22]. A study to validate the safety of minimally invasive EJS is ongoing in Japan [23], but there is no RCT investigating short- or long-term outcomes after LTG for GC.

EJS is one of most important surgical procedures in LTG because it is associated with the risk of anastomotic leakage and stenosis [14, 15]. Various EJS methods including the single stapling technique [10, 23], double stapling technique (DST) [10], hemi-double stapling technique [20], functional end-to-end anastomosis [24], and overlap [25] and hand-sewn [11] methods have been reported and selected at the discretion of individual surgeons. Our affiliated hospitals usually employ the DST using a circular stapler, functional end-to-end anastomosis, or the overlap method using a linear stapler. However, which procedure results in the lowest incidence of EJS-related complications after LTG is unknown because there are few studies comparing these techniques. Thus, we used a propensity score-matching method to compare the complication rates after EJS performed using a circular versus a linear stapling device.

MATERIALS and METHODS

Patients

We retrospectively assessed the medical records of all patients who underwent LG for the treatment of GC at Hokkaido University Hospital or an affiliated hospital (Teine Keijinkai, Obihiro-Kosei General, Hokkaido Gastroenterology, and Tonan Hospitals) from November 1998 to March 2016. All patients who underwent curative LTG were included for analysis. After excluding those who underwent jejunal pouch reconstruction or multiple organ resections, the remainder were evaluated for propensity score matching.

All patients were diagnosed with GC by endoscopy, computed tomography, or endoscopic ultrasound. The Japanese Classification of Gastric Carcinoma (JCGC) was used for tumor staging [26]. The primary indication

for LTG was stage I GC based on the Japanese Society of Endoscopic Surgery (JSES) guidelines [27] although, over time, we expanded the indication to include cases of AGC that could be curatively resected. The clinicopathological factors and outcomes of the patients were recorded. The follow-up was defined as the period from the day of operation to the date of death from gastric cancer or other causes. All patients provided informed consent, and the Hokkaido University Hospital Institutional Review Board approved the data collection and analysis (No. 016-0151).

Surgical procedure

The gastric procedure type (resection and reconstruction) was determined by the experience and preference of a surgeon who was accredited through the Endoscopic Surgical Skill Qualification system of the JSES [28]. In cases where the operating surgeon did not possess this qualification, qualified surgeon supervised the operation. The extent of lymph node dissection was determined according to the guidelines of the Japanese Gastric Cancer Association (JGCA) [29]. Patients were divided into three groups defined by the Clavien–Dindo (CD) postoperative complications classification grade [30, 31]. EJS leakage more severe than CD grade III was defined as leakage that required drainage under radiological guidance or re-operation under general anesthesia. EJS stenosis more severe than CD grade III was defined as stenosis that required endoscopic dilatation one or more times during the follow-up period.

Postoperative follow-up

Most patients were seen every three months during the follow-up. Clinical examination and hematologic analysis, including tumor marker assays for carcinoembryonic antigen and carbohydrate antigen 19–9, were performed at each visit. An abdominal computed tomography examination was performed every six months or when recurrence was clinically suspected.

Propensity score matching

Patients were categorized into two groups based on whether their EJS was performed using a circular or linear stapler. The circular group included patients who underwent a DST EJS with a trans-orally or transabdominally inserted anvil. The linear group included patients who underwent EJS by the functional end-to-end anastomosis and overlap method using a linear stapler. Patients in the circular and linear groups were matched using the propensity score method. The propensity score for an individual was calculated using age, sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS), lymph node dissection extent, and the JCGC stage as covariates. Clinicopathological characteristics and surgical outcomes were compared between the two groups.

Statistical analysis

Survival curves were constructed using the Kaplan–Meier method. Group differences in overall survival (OS) were evaluated by the log-rank test. A chi-square test was used to perform a univariate analysis. A P value less than 0.05 was considered statistically significant. All analyses were performed using JMP Pro version 12.0.1 software (SAS Institute Inc., Cary, NC, US).

RESULTS

During the study period, 1916 patients underwent LG for GC. Of these, 379 patients underwent curative LTG and were analyzed. After applying our exclusion criteria, 291 patients were included in the subgroup we evaluated for propensity score matching. Finally, 66 patients in the circular group were individually matched to 66 patients in the linear group (Fig. 1).

Oncologic outcomes

Among the 379 patients who underwent curative LTG, the median follow-up period was 1093 days (range 11– 4177). Fifty-five (14.5%) developed a recurrence in the peritoneum (n = 21, 38.2%), distant lymph nodes (n = 12, 21.8%), liver (n = 12, 21.8%), lung (n = 4, 7.3%), bone (n = 4, 7.3%), or another organ (n = 10, 18.2%). At the time of analysis, 50 patients had died due to a postoperative recurrence (n = 32), another disease (n = 17), or a postsurgical complication (n = 1). The 5-year OS rate for all patients was 81.2%. The 5-year OS rates by pathologic stage were 94.0%, 77.1%, and 43.9% for stages I–III, respectively (Fig. 2). Over five years had elapsed since the operation in 144 patients. The 5-year actuarial OS rates by pathologic stage were 93.1%, 74.4%, and 50.0% for stages I (n = 100), II (n = 30), and III (n = 14), respectively.

Clinicopathological characteristics

The clinicopathological characteristics of the 132 propensity score-matched patients are shown in Table 1. As determined by the study design, the sex, age, BMI, ASA-PS, and clinical JCGC stage distributions in the circular and linear groups were comparable. Further, there were no significant between-group differences in the tumor marker levels, pathological T or N factors, or pathological JCGC stage.

Surgical outcomes and postoperative course

The surgical outcomes and postoperative complications in the propensity score-matched patients are shown in Table 2. The median blood loss was significantly less in the linear group compared to that in the circular group (50 mL [range 0–600] vs. 97 mL [range 0–1108], p = 0.003). The median postoperative hospital stay was significantly shorter in the circular group compared to that in the linear group (9 days [range 7–82] vs. 14 days

[range 6–108], p = 0.002). There was no significant between-group difference in the median operative time, extent of lymph node dissection, number of resected lymph nodes, rate of conversion to open surgery, or number of surgeries performed by a JSES-qualified surgeon. Furthermore, there was no difference in the rate of postoperative complications of any grade between the two groups. The incidence of EJS leakage and stenosis more severe than CD grade III did not differ between the circular and linear groups.

DISCUSSION

To the best of our knowledge, ours is the first study to use propensity score matching to compare the complication rates of EJS performed using a linear or circular stapler after LTG. Due to a lack of evidence demonstrating the superiority of one treatment over another, the optimal management of GC remains controversial. At our affiliated hospitals, we began treating GC with LTG even before the method was included in the Japanese Gastric Cancer Treatment Guideline [28]. The four affiliated hospitals that participated in this study are high-volume centers in our prefecture and have performed LG for EGC since 1998. After adopting LTG for GC treatment, we determined that the short-term outcomes were comparable to those of open gastrectomy at each hospital. After establishing the efficacy of LDG for EGC, we expanded the indications for LTG to include AGC in 2004.

LTG is less commonly performed than is LDG, in part because the subsequent EJS is technically difficult. Several studies of EJS procedures, including two systematic reviews, have been published. Four of these studies suggested that the use of circular staplers is associated with EJS stenosis [14, 17, 18], while another indicated that the use of a linear stapler might reduce the risk of EJS stenosis [15]. One investigator reported that the use of circular staplers is associated with EJS leakage [28], but another found the incidence of EJS leakage was similar regardless of stapler type (linear vs. circular) [17]. Chen et al. suggested that the use of a circular or linear stapler for EJS is feasible and safe and recommended that the EJS method should be selected on the basis of the tumor location [19].

Studies of several malignant tumors, including breast, colorectal, and periampullary cancers [32–35], have suggested an association between postoperative complications and long-term survival. Further, several reports have indicated that postoperative complications were associated with prognosis in patients with GC [36, 37]. In our multicenter retrospective study evaluating LG in AGC, we showed that postoperative complications were associated with recurrence-free survival [7]. Therefore, ensuring the safety of LG is important to short- and long-term outcomes in patients with GC.

Previous reports indicate that 5.1 to 15.2% of patients undergoing LDG experience morbidity more severe than CD grade III [2–7], while in patients undergoing LTG this rate is higher (5.0 to 26.1%) [7, 12, 14]. In our retrospective multicenter study evaluating LG in AGC, the incidence of morbidity more severe than CD grade III after LTG was significantly higher than that following LDG (18.7% vs. 6.3%, respectively; p = 0.0011) [7].

On the other hand, Lin et al. suggested that the morbidity and mortality rates after LTG were comparable to those after LDG [22]. In the present study, the incidence of morbidity after LTG was 14.0% in both the circular and linear groups and comparable with the previously reported rate.

The results of the present study indicate that neither of the two EJS procedures we evaluated was associated with a lower rate of complications than the other, and EJS-related morbidity was comparable in the circular and linear groups. This was true for all complications (21% vs. 26%, respectively; $p = 0.538$), all complications more severe than CD grade III (14% vs. 14%, respectively; $p = 1.000$), and occurrences of EJS leakage and stenosis more severe than CD grade III (5% vs. 2%, $p = 0.301$; and 9% vs. 8%, $p = 0.753$, respectively). Blood loss was greater in the circular group than in the linear group (97 mL vs. 50 mL, $p = 0.003$). One reason for this difference was the variation in procedure selection between hospitals. In one hospital, many patients underwent EJS with the circular stapling method while the opposite was true at another hospital. Two of the hospitals gradually transitioned from using circular to linear staplers. The number of patients in the circular and linear groups at these hospitals was comparable. However, many of the late cases were included in the linear group. By the time these cases were performed, surgical blood loss had been reduced by the standardization of the operative procedure and device development. The difference in the median postoperative hospital stay between the circular and linear groups was attributed to the policies of the affiliated hospitals and the differences in the operative period described above.

The 5-year OS rate according to the pathological stage was 94.0%, 77.1%, and 43.9% for stages I–III, respectively. These rates were comparable with those after open surgery for tumors of the same stages as reported by the Japanese Association of Clinical Cancer Centers and others [20–22].

This study had several limitations. First, it was a retrospective, observational, nonexperimental study. Second, we included patients who underwent either laparoscopy-assisted total gastrectomy (LATG) or total laparoscopic total gastrectomy (TLTG). We initially began treating patients with LATG with reconstruction through a mini-laparotomy. We then gradually transitioned to providing TLTG with intracorporeal reconstruction. Intracorporeal reconstruction could ensure a larger working space and a better view of the surgical field than extracorporeal reconstruction. Therefore, the EJS after TLTG may be safer and easier than that following LATG. An analysis excluding patients who underwent LATG might lead to different results than we found. A well-designed RCT is required to validate our findings.

CONCLUSION

There is no difference in the postoperative complication rate related to the type of stapler used for EJS after LTG. The surgeon’s preference and experience should determine the selection of the EJS procedure.

Compliance with Ethical Standards

Ethical standards

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and its later versions. Informed consent for study inclusion was obtained from all patients.

Conflicts of interest

The authors declare that they have no conflict of interest.

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Table 1 Clinicopathological characteristics of propensity score-matched patients

	Circular (n = 66)	Linear (n = 66)	*p*-value
Sex			0.455
Male	43	47	
Female	23	19	
Age (years)	67 (40-88)	68 (35-88)	0.626
BMI (kg/m^2)	23.0 (15.0-34.6)	22.7 (16.9-33.4)	0.711
ASA-PS			1.000
1-2	63	63	
3-4	3	3	
Tumor marker			
CEA (ng/mL)	1.9 (0.2-9.3)	2.3 (0.5-31.9)	0.077
CA19-9 (U/mL)	7.9 (0.6-404)	5.0 (0.6-14812)	0.236
Clinical JCGC stage			0.842*
I	58	56	
II	7	8	
III	1	2	
Pathological T			0.434
pT1-2	50	46	
pT3-4	16	20	
Pathological N			1.000
pN (+)	19	19	
pN (-)	47	47	
Pathological JCGC stage			0.399
I	48	41	
II	9	14	
III	9	11	

*Fisher's exact test. ASA-PS, American Society of Anesthesiologists physical status; BMI, body mass index; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9; JCGC, Japanese Classification of Gastric Carcinoma

Table 2 Surgical outcomes and postoperative course in propensity score-matched patients

	Circular (n = 66)		Linear (n = 66)		*p*-value
	Number	%	Number	%	
Operative time (min)	328 (197-627)		303 (171-494)		0.165
Blood loss (mL)	97 (0-1108)		50 (0-600)		0.003
Extent of lymph node dissection					
D1	20		22		0.709
D1+	46		44		
Number of lymph nodes resected	34 (3-90)		41 (1-93)		0.080
Conversion to open surgery	2	3	0	0	0.154
Postoperative complication					
CD ≧ I	14	21	17	26	0.538
CD ≧ IIIa	9	14	9	14	1.000
EJS leakage[a]	3	5	1	2	0.301
EJS stenosis[a]	6	9	5	8	0.753
Qualified surgeon[b]	33	50	42	57	0.114
Postoperative hospital stay (day)	9 (7-82)		14 (6-108)		0.002

[a]Clavien-Dindo (CD) grade ≧ IIIa. [b]Accredited through the endoscopic surgical skill qualification system of the Japanese Society of Endoscopic Surgery. EJS, esophagojejunostomy

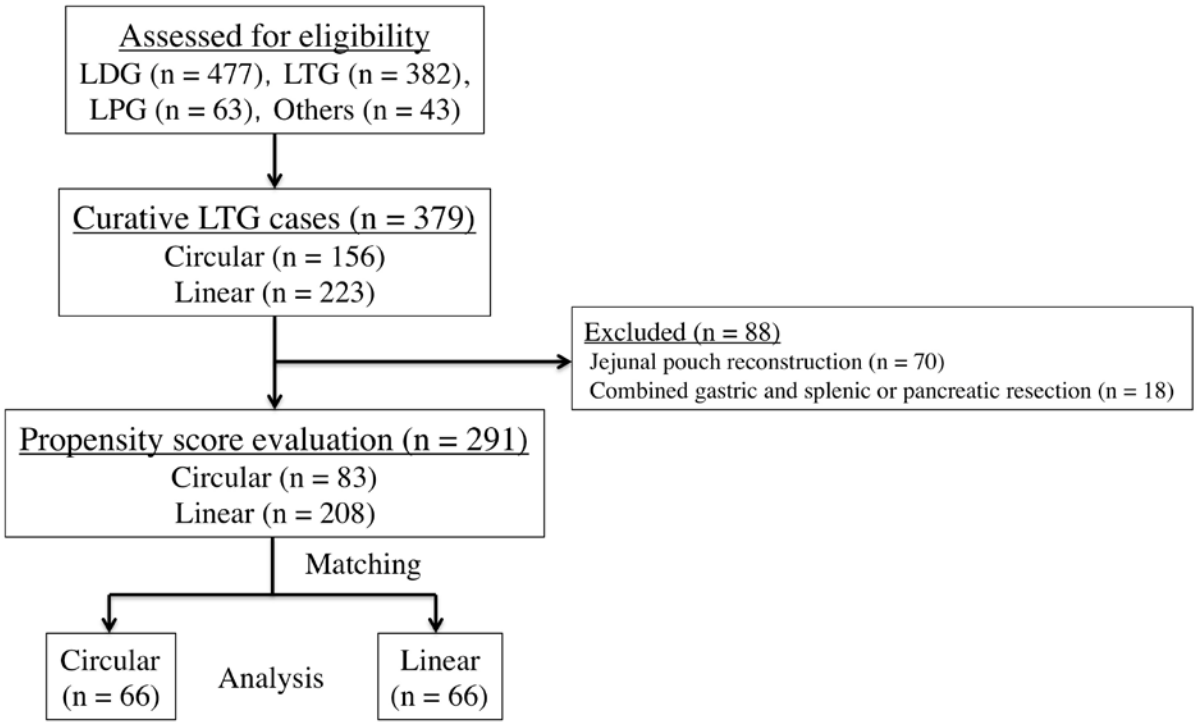

Fig. 1 Study enrollment. LDG, laparoscopic distal gastrectomy; LPG, laparoscopic proximal gastrectomy; LTG, laparoscopic total gastrectomy

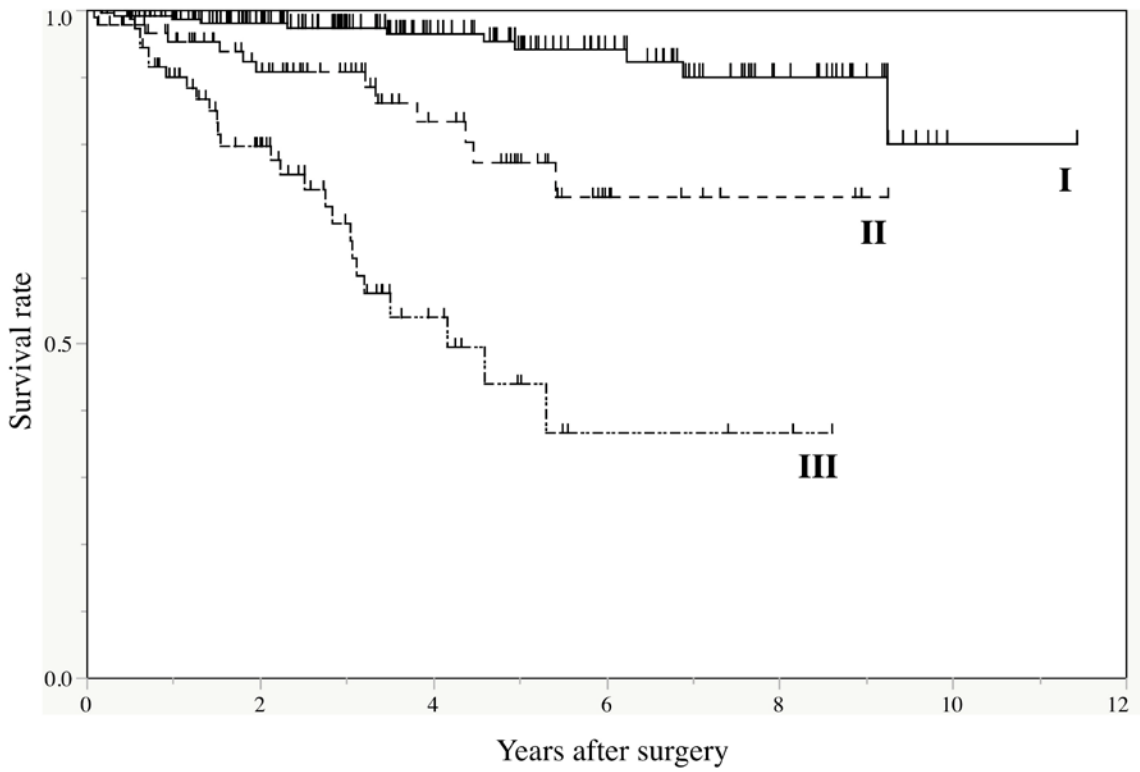

Fig 2. Oncologic outcomes after laparoscopic total gastrectomy in 379 patients