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ORIGINAL ARTICLE

Survival outcomes of laparoscopic versus open total gastrectomy with nodal dissection for gastric cancer in a high-volume Japanese center: A propensity score-matched analysis

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Abstract

Aim: To compare the survival outcomes of laparoscopic total gastrectomy (LTG) with those of open total gastrectomy (OTG) in gastric cancer.

Methods: Using an in-house database, this single-center study reviewed clinical data for patients who underwent surgery for gastric adenocarcinoma in 2008–2018. The patients were divided into an LTG group and an OTG group.

Results: Data for 638 patients were screened. After exclusions, 580 patients (LTG, n = 212; OTG, n = 368) were enrolled. Noting that the OTG group included more advanced tumors, 1:1 propensity score matching was implemented to reduce any selection bias, leaving 326 patients (LTG, n = 163; OTG, n = 163; pStage I/II/III = 147/87/92) for further analysis. The operation time was longer and blood loss was less in the LTG group. The postoperative hospital stay was shorter in the LTG group than in the OTG group (9 d vs 10 d; $P = .040$). There was no significant difference in the incidence of grade III or worse postoperative complications (8.9% vs 11.0%). Five-year overall survival was better in the LTG group (84.9% vs 73.5%; $P = .0010$, log-rank test), but there was no significant difference in overall survival according to pStage (I, 93.0% vs 89.0%; II, 85.8% vs 77.5%; III, 64.1% vs 52.5%). There was a similar trend in relapse-free survival. Distribution of recurrence sites was comparable.

Conclusion: LTG may provide survival outcomes similar to those of OTG when performed by an experienced surgical team. Further evidence is required for final conclusions, especially regarding its efficacy for stage II/III.

KEYWORDS
gastric cancer, laparoscopic total gastrectomy, survival outcome

1 | INTRODUCTION

There is mounting evidence in support of the effectiveness of laparoscopic distal gastrectomy (LDG) in the treatment of gastric cancer. A Korean (KLASS-01)[1] and a Japanese multicenter randomized trial (JCOG0912)[2] found no difference in survival outcomes between LDG and open distal gastrectomy (ODG) in patients with clinical stage (cStage) I gastric cancer. Therefore, LDG is now

recommended as a treatment for cStage I disease in the Japanese guidelines.[3] Furthermore, a Chinese (CLASS-01)[4] and a Korean multicenter randomized trial (KLASS-02)[5] demonstrated that the survival outcomes of LDG were noninferior to those of ODG in patients with cStage II/III gastric cancer. Depending on the final analysis of the results of a parallel-group Japanese trial (JLSSG0901), which will be available in 2022, LDG may be recommended as a standard treatment for cStage II/III gastric cancer in the Japanese guidelines.

Meanwhile, there is still limited high-level evidence for laparoscopic total gastrectomy (LTG), which has more technically challenging components, such as esophagojejunal anastomosis and lymphadenectomy along the splenic artery or at the splenic hilum for D2 dissection. Most of the relevant published studies have been retrospective or have included LDG together with LTG.[6–8] The surgical safety of LTG has been demonstrated by several prospective studies targeting cStage I disease in East Asian countries (KLASS-03, JCOG1401, CLASS-02)[9–11] and in a study targeting cStage II/III disease in Europe (STOMACH).[12] However, even for cStage I disease, no robust comparative data in support of the efficacy of LTG have been published. JCOG1401 was designed as a single-arm confirmatory trial in cStage I disease in Japan,[10] but there are no relevant randomized trials under way. A Korean randomized trial (KLASS-06) in cStage II/III disease is presently in the recruiting phase and will require time to reach a definitive conclusion. Therefore, any current data regarding this issue would be helpful.

We have gradually been expanding the indications for LTG since its introduction at our center in 2010. The aim of this study was to compare the survival outcomes of LTG with those of OTG in our patients with gastric cancer.

2 | METHODS

2.1 | Study design

This study had a single-center retrospective cohort design and compared the clinical outcomes of LTG and OTG using information held in a prospectively maintained in-house database. The possibility of underlying selection bias was controlled for by 1:1 propensity score matching (PSM).

2.2 | Patients

Consecutive patients who underwent surgery for primary gastric adenocarcinoma, including esophagogastric junction cancer, at the National Cancer Center Hospital East from January 2008 to December 2018, were included in the study. The clinical data for these patients were analyzed. The exclusion criteria were as follows: remnant gastric cancer; esophagus-invading cancer requiring a thoracoabdominal approach; the presence of other active malignant disease; and combined pancreatic resection.

2.3 | Surgical procedures

All surgeries were performed or supervised by experienced staff surgeons. LTG was performed only by surgeons who were certified by the endoscopic surgical skill qualification system in Japan.[13] During the study period, the annual surgical volume for gastric cancer at our institution was between 250 and 350 cases. When LTG was first introduced in 2010, its only indication was for cStage I disease but this expanded to include cStage II in 2012, cStage III in 2014, and chemotherapy-pretreated cases in 2016. Total omentectomy was added in cT3–4 cases, with the decision made at the time of surgery. The indication for splenic hilar dissection changed during the study period. Although the extent of lymph node dissection followed the Japanese guidelines,[3] we made a minor change to our dissection strategy for splenic hilar nodes at station 10. Between 2012 and 2015, patients with cT3–4 proximal gastric cancer underwent splenic hilar dissection with splenectomy, regardless of the circumferential tumor location. However, since 2016, when the results of JCOG0110 first became available, we have only performed splenic hilar dissection with splenectomy for tumors that have invaded the greater curvature.[14] Either splenectomy[15] or a spleen-preserving procedure[16] was chosen for dissection of the splenic hilar nodes. However, splenectomy was chosen if the tumor directly infiltrated neighboring organs, such as the pancreas or spleen, or the splenogastric ligament. Furthermore, splenectomy was usually selected if enlargement of the lymph nodes at station 10 was detected before surgery.

2.4 | Postoperative management

The clinical pathway, which included the enhanced recovery after surgery concept, was consistent during the study period regardless of whether LTG or OTG was performed. Intake of fluids was started on postoperative day (POD) 1 and a soft meal was allowed on POD 3. The patient was usually discharged from the hospital between POD 8 and POD 10, provided that there were no complications. Patients with pStage II/III disease received adjuvant S-1 chemotherapy for 1 y. S-1 plus oxaliplatin or S-1 plus docetaxel has been an adjuvant treatment option for patients with pStage III disease since 2016. Neoadjuvant chemotherapy was used only in patients with extensive lymph node metastasis, such as bulky nodal metastasis around the celiac artery. Patients were followed up in the outpatient clinic at 6-mo intervals for at least 5 y after surgery. Recurrent disease was detected mainly on computed tomography scans. In this study, staging categories with T/N factors followed the UICC TNM system, eighth edition.[17] Postoperative complications were graded using the Clavien–Dindo classification,[18] and those who were grade III or worse were considered meaningful.

2.5 | Outcome measurements

The primary study outcome was overall survival (OS). Secondary outcomes were relapse-free survival (RFS), postoperative complications, length of postoperative hospital stay, and sites of recurrence.

2.6 | Statistical analysis

Between-group differences in patient characteristics were assessed using the Student's *t*-test or Fisher's exact test. Kaplan–Meier survival curves were drawn and differences in survival between the two groups were examined using the log-rank test. OS was defined as the interval between surgery and death from any cause and RFS as the interval between surgery and initial relapse or death from any cause. Recurrence was confirmed radiologically or pathologically.

All statistical analyses were performed using JMP software v. 15 (SAS Institute, Cary, NC, USA). PSM was performed using MatchIt (The R Foundation for Statistical Computing, Vienna, Austria). All *P*-values were two-sided and considered statistically significant at $P < .05$.

3 | RESULTS

3.1 | Before propensity score matching

3.1.1 | Patient characteristics and surgical outcomes

Initial screening identified 638 potentially eligible patients in the database. Fifty-eight patients were excluded (remnant gastric cancer, n = 38; left thoraco-abdominal approach required, n = 5; presence of other malignant disease, n = 10; and pancreatic resection, n = 5), leaving 580 patients for inclusion in the study. These patients were divided into an LTG group (n = 212) and an OTG group (n = 368). The baseline characteristics of the entire cohort of patients and their surgical outcomes are summarized in Table 1. Patients in the OTG group had more advanced disease

TABLE 1 Demographic characteristics and surgical data for the original study cohort

	Laparoscopic total gastrectomy (n = 212)	Open total gastrectomy (n = 368)	*P*-value
Male to female sex ratio	157:44	262:106	.459
Age (y)	68 (60, 74)	67 (59, 72)	.383
Body mass index	22.5 (20.6, 24.3)	22.0 (20.0, 24.3)	.292
Clinical T factors			
cT 1/2/3/4	73/54/60/25	73/40/79/176	<.0001
Clinical N factors			
cN0/(+)	154/58	176/192	<.0001
Clinical stage			
I/II/III/IV	110/62/33/7	79/91/153/45	<.0001
Estimated tumor size (mm)	54 (39, 80)	76 (45, 107)	<.0001
Histology (diff./undiff./other)	95/108/9	157/194/17	0.875
Chemotherapy before surgery	16 (7.5%)	79 (21.5%)	<.0001
Combined splenectomy	13 (6.1%)	198 (53.8%)	<.0001
Total omentectomy	90 (42.5%)	183 (50.5%)	.101
Operation time (min)	298 (265, 345)	212 (183, 247)	<.0001
Estimated blood loss (g)	29 (15, 51)	395 (230, 617)	<.0001
Lymph nodes harvested, n	42 (32, 50)	38 (29, 48)	.007
Length of postoperative hospital stay (d)	9 (8, 11)	11 (9, 14)	.212
Adjuvant chemotherapy	102 (48.1%)	248 (61.6%)	<.0001
Pathological T factors			
pT 0/1a/1b/2/3/4a/4b	2/26/51/30/50/51/2	1/13/39/32/104/157/22	<.0001
Pathological N factors			
pN 0/1/2/3a/3b	123/42/19/22/6	108/69/70/68/53	<.0001
Pathological stage			
CR/I/II/III/IV	2/95/59/53/3	1/63/87/168/49	<.0001

Note: Data are shown as the median and interquartile range. Body mass index was calculated as kg/m^2.
Abbreviations: CR, complete response; diff., differentiated; undiff., undifferentiated.

TABLE 2 Postoperative complications and sites of disease recurrence in the original cohort

	Laparoscopic total gastrectomy (n = 212)	Open total gastrectomy (n = 368)	*P*-value
Morbidity ≥ CD grade III, *n* (%)			
Overall	19 (9.0)	33 (9.0)	1.000
Anastomotic leak	6 (2.8)	8 (2.2)	1.000
Anastomotic bleeding	1 (0.4)	1 (0.3)	1.000
Pancreatic fistula	4 (1.9)	14 (3.8)	.226
Intraabdominal abscess	5 (2.4)	6 (1.6)	.541
Intraabdominal bleeding	2 (0.8)	3 (0.8)	1.000
Cholecystitis	1 (0.4)	2 (0.5)	1.000
Bowel obstruction	4 (1.9)	3 (0.8)	.265
Pleural effusion	0 (0)	2 (0.5)	.535
90-Day mortality, *n* (%)	0 (0)	1 (0.3)	1.000
Sites of recurrence, *n* (%)			
Overall	43	139	
Bone	2 (4.7)	3 (2.2)	.338
Lung	3 (7.0)	8 (5.8)	.723
Liver	7 (16.3)	19 (13.7)	.627
Nodal	9 (20.9)	28 (20.1)	1.000
Peritoneal	17 (39.5)	69 (49.6)	.295
Local	5 (11.6)	12 (8.6)	.555

Abbreviation: CD, Clavien–Dindo.

and larger tumors. Perioperative chemotherapy was administered more frequently in the OTG group; combined splenectomy was also performed more often in this group. The ratios of total omentectomy to omentum-preservation were equivalent between the two groups. The operation time was longer in the LTG group, but with less intraoperative blood loss. More lymph nodes were harvested in the LTG group. There was no significant between-group difference in the frequency of grade III or worse postoperative complications or in mortality (Table 2).

3.1.2 | Survival outcomes

The median follow-up duration was 58 mo (interquartile range [IQR] 42, 72) in the LTG group and 51 mo (IQR 20, 67) in the OTG group ($P = .012$). The curves for OS are shown in Figure 1. OS was better in the LTG group regardless of stage (83.1% vs 54.5%; $P < .0001$, log-rank test), reflecting the heterogeneity in stage. When the patients were stratified according to pStage, OS was similar between the groups for pStage I disease (93.4% vs 90.1%; $P = .1515$, log-rank test) but was slightly better in the LTG group for pStage II (82.5% vs 70.4%; $P = .0226$, log-rank test) and III disease (67.5% vs 45.2%; $P = .0010$, log-rank test). RFS curves showed a similar tendency (Figure 2). When the patients were stratified by stage, RFS was better in the subset with pStage III disease in the LTG group (54.1% vs 37.9%; $P = .0076$, log-rank test). The sites of recurrence were similar between the two groups (Table 2).

3.2 | After propensity score matching

Potentially confounding factors were adjusted for between the LTG and OTG groups using 1:1 PSM to minimize any patient selection bias. The following covariates among preoperative factors were used for matching: age, sex, macroscopic appearance (whether type 4 or not), body mass index, tumor size, preoperative chemotherapy, the cT factor, and the cN factor. The caliper width was 0.2. Finally, data for 163 matched pairs (326 patients in total) were extracted for comparative analyses.

3.2.1 | Patient characteristics and surgical outcomes

The baseline preoperative patient characteristics or tumor factors were well balanced in the propensity score-matched cohort, as shown by values of standardized mean differences (Table 3). Combined splenectomy was slightly more frequently done in the OTG group, but total omentectomy was equally performed. As a result, still the operation time was longer with more lymph nodes harvested but less intraoperative blood loss in the LTG group. The postoperative length of stay was 1 d shorter in the LTG group. In terms of pathological stage, more advanced disease was included in the OTG group, even though preoperative factors were well balanced by PSM. There was no significant between-group difference in the frequency of grade III or worse postoperative complications or mortality (Table 4).

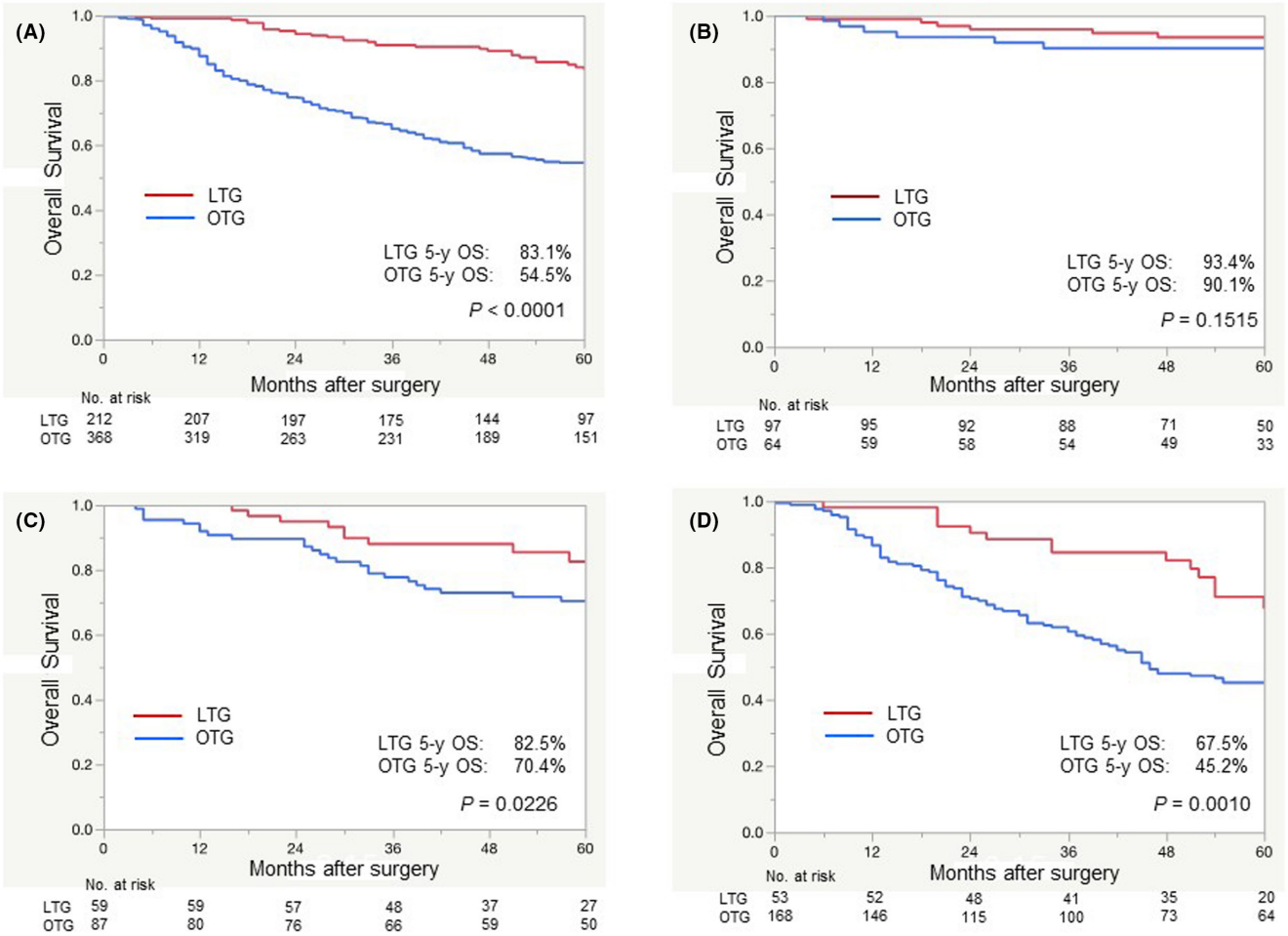

FIGURE 1 Overall survival curves for the original cohort. (A) All pathological stages, (B) pStage I, (C) pStage II, and (D) pStage III. LTG, laparoscopic total gastrectomy; OS, overall survival; OTG, open total gastrectomy

3.2.2 | Survival outcomes

The median follow-up duration was 56 mo (IQR 42, 70) in the LTG group and 59 mo (IQR 29, 69) in the OTG group ($P = .2097$) which were well balanced. The OS curves are shown in Figure 3. Even after PSM, OS remained slightly better in the LTG group (84.9% vs 73.5%; $P = .0010$, log-rank test) possibly due to heterogeneity in pStage, but the differences became much smaller than before PSM. In the subsets stratified according to pStage, there was no statistically significant difference in OS; in pStage I (93.0% vs 89.0%; $P = .1211$, log-rank test), pStage II (85.8% vs 77.5%; $P = .1787$, log-rank test), and pStage III (64.1% vs 52.5%; $P = .1344$, log-rank test). RFS curves are shown in Figure 4. A similar tendency was observed with no statistically significant difference in RFS according to pStage. There was no significant between-group difference in the distribution of sites of recurrence (Table 4).

4 | DISCUSSION

This study compared real-life clinical data between patients who underwent LTG and those who underwent OTG at a high-volume cancer center. The sample size appears to have been adequate and the surgery is likely to have been of high-quality in view of the abundant experience of the surgical team. PSM was used to balance underlying preoperative factors known to be a source of selection bias between the two groups. The follow-up periods seemed enough and were well balanced. The OS and RFS rates after LTG were noninferior to those after OTG, whether the disease stage was pathological I, II, or III. Distribution of sites of recurrence were very similar. These findings suggest that LTG is oncologically feasible and effective when performed by an experienced surgical team in selected patients.

LTG involves several technically challenging aspects that are not found in LDG. Therefore, the surgical safety of LTG should be fully assessed. In this study, complications that were grade III or worse occurred in 9.0% in the original study cohort of patients who underwent LTG, which was comparable with the complication rate in OTG. Similar morbidity rates were reported in several key prospective studies of the safety of LTG for Stage I cancer, such as 9.4% in KLASS-03[9] and 7.6% in CLASS-02.[11] Taking into account the fact that more than half of our patients had advanced disease, our findings seem to be acceptable. Similarly, when compared in detail with

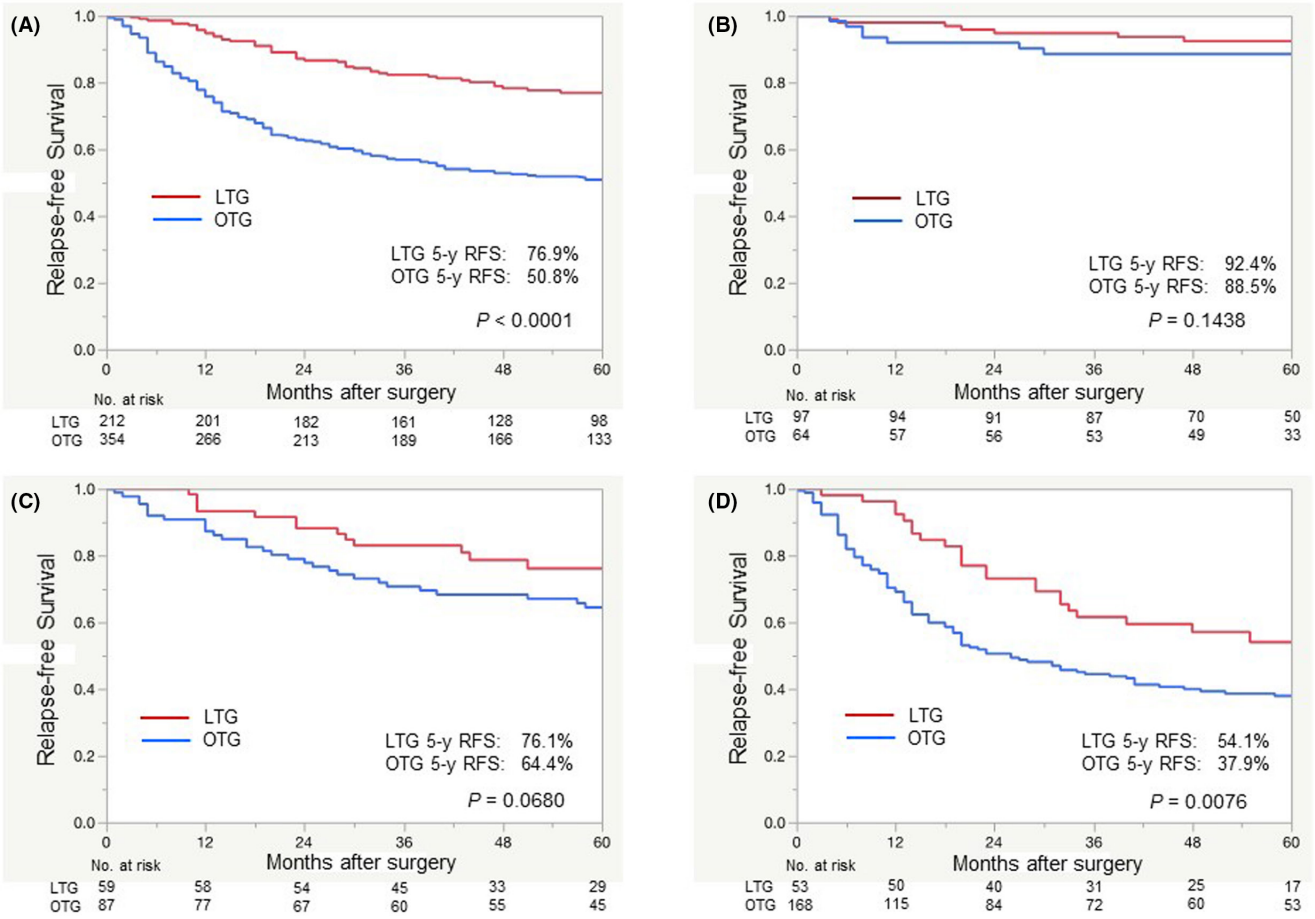

FIGURE 2 Relapse-free survival curves for the original cohort. (A) All pathological stages, (B) pStage I, (C) pStage II, and (D) pStage III. LTG, laparoscopic total gastrectomy; OTG, open total gastrectomy; RFS, relapse-free survival

a Japanese single-arm prospective study of LTG for cStage I disease (JCOG1401),[10] the incidence rates of pancreatic fistula (our study vs JCOG1401; 1.9% vs 2.6%), anastomotic leak (2.8% vs 2.6%), abdominal abscess (2.4% vs 4.6%), and intraabdominal bleeding (0.8% vs 0.5%) were also similar. In addition, there have been two pivotal large-scaled studies using the Japanese national clinical database (NCD) to compare short-term outcomes of LTG and OTG.[19,20] Especially, the retrospective cohort study using data of 2012 and 2013 demonstrated significantly higher incidences of anastomotic leak in LTG (LTG vs OTG; 5.4% vs 3.6% in a Stage I cohort, 5.7% vs 3.6% in a Stage II-IV cohort), which indicated the necessity of careful implementation of LTG in clinical practice.[20] Nonetheless, in this study the incidences of anastomotic leak were equivalent between LTG and OTG (2.8% vs 2.2%). Understandably, more recent cases were included in this study compared to the NCD study, as the patients who underwent LTG between 2010 and 2018 were enrolled. Presumably, the considerable difference as found in the NCD study has shrunk due to standardization of surgical procedure and technical advances.

In terms of a comparison to Western studies, STOMACH[12] was a randomized European trial that compared the outcomes of LTG and OTG after neoadjuvant chemotherapy. Compared with our study, morbidity (our study vs STOMACH; 9.0% vs 12.2%) and mortality (0% vs 4%) rates were higher, and blood loss was greater (29 mL vs 171 mL); however, a similar number of lymph nodes was harvested (42.0 vs 41.7). Arguably, these data should not be compared, given the differences in body habitus (body mass index 22.5 vs 26.5) and administration of preoperative chemotherapy (7.5% vs 100%) in the two study groups. Furthermore, considering the small proportions of patients with early-stage cancer, these differences suggest that there were more challenging cases in the study performed in Western countries.

There are few reference data to allow comparison of long-term oncological outcomes. However, 5-y survival rates in surgically resected cases are available in the 2011 Japanese National Clinical Database Gastric Cancer Registry report.[21] When stratified by pStage, 5-y OS were reported to be 88.5% for pStage I, 73.5% for pStage II, and 44.5% for pStage III[19]. Even considering the historical differences, the survival outcomes in our study seem to be acceptable. For patients with Stage I, LTG has been theoretically considered as the standard treatment, with extrapolating the long-term outcomes of JCOG 0912 (randomized phase-III trial in Japan, LDG vs ODG).[2] However, in fact the comparative data of LTG and OTG regarding long-term outcomes for this population has been lacking.

TABLE 3 Demographic characteristics and surgical data for the propensity score-matched cohort

	Laparoscopic total gastrectomy (n = 163)	Open total gastrectomy (n = 163)	*P*-value	Standardized mean difference
Male to female sex ratio	130:33	134/29	.136	.09
Age (y)	69 (62, 74)	67 (60, 74)	.468	.07
Body mass index	22.2 (20.5, 24.4)	22.4 (20.2, 24.6)	.268	.09
Clinical T factors				
cT 1b/2/3/4	46/37/46/34	45/35/39/44	.538	.06
Clinical N factors				
cN 0/(+)	112/51	106/57	.457	.08
Clinical stage				
I/II/III/IV	73/51/31/8	72/36/46/9	.133	.08
Estimated tumor size (mm)	55 (38, 85)	56 (37, 85)	.605	.06
Histology (diff./undiff./other)	91/68/5	86/71/6	.863	.06
Chemotherapy before surgery	16 (9.8%)	17 (10.4%)	.854	.02
Combined splenectomy	12 (7.4%)	26 (14.7%)	.016	
Total omentectomy	79 (48.5%)	85 (52.1%)	.58	
Operation time (min)	296 (263, 350)	210 (178, 242)	<.0001	
Estimated blood loss (g)	26 (15, 47)	368 (224, 561)	<.0001	
Lymph nodes harvested, n	41 (31–50)	34 (25–43)	.0001	
Postoperative hospitalization (d)	9 (8, 12)	10 (9, 14)	.041	
Adjuvant chemotherapy	68 (41.7%)	88 (54.0%)	.027	
Pathological T factors				
pT 0/1a/1b/2/3/4a/4b	26/49/13/27/46/2	13/32/26/47/43/2	.03	
Pathological N factors				
pN 0/1/2/3a/3b	106/25/13/13/6	81/32/28/16/6	.04	
Pathological stage				
I/II/III	91/33/39	56/54/53	.03	

Note: Data are shown as the median and interquartile range. Body mass index was calculated as kg/m^2.
Abbreviations: diff., differentiated; undiff., undifferentiated.

Our study seems to be valuable to cover this point. On the other hand, the efficacy of LTG for patients with Stage II/III has been more debatable, although two phase-III trials of LDG vs ODG (CLASS-01, KLASS-02)[4,5] have revealed the noninferiority of LDG. The survival rate in patients who have undergone total gastrectomy is generally worse than that in those who have undergone distal gastrectomy (56.9% vs 76.8% in the above-mentioned registry data[21]), which tendency may be enhanced in advanced disease. One Japanese multicenter cohort study (LOC-A) previously demonstrated the non-inferior survival outcomes of laparoscopic surgery to open surgery in patients with cStage II/III.[7] In that trial, around 40% of patients in the laparoscopic group underwent LTG and its noninferiority was also shown in the subgroup analysis. In fact, the survival outcomes in our patients with pStage II/III disease are in line with 5-y OS in CLASS-01[5] (LDG vs ODG; 79.1% vs 84.5% in pStage II, 58.6% vs 59.5% in pStage III), which suggests that LTG is effective even for Stage II/III. Surely, statistical power in the subset of Stage II/III does not seem enough due to the small sample size (112 LTGs in the original cohort, 72 LTGs in the matched cohort). However, considering the absence of evidence for this population, the outcomes of this study seem to have a certain degree of impact. To further assess the efficacy of LTG for Stage II/III, the long-term outcomes of JLSSG0901 with the subgroup analysis (eg, Stage III, node-positive cases, T4 cases) will provide some insights or studies with a larger sample size specific to LTG are required. Furthermore, the results of the ongoing Korean randomized trial (KLASS-06), which started in April 2018 and has the primary endpoint of 3-y RFS, are awaited.

In terms of site of recurrence, the peritoneum was the most common site in both groups, which is consistent with previous reports.[5,6] Locoregional recurrence (including around the splenic hilum) is not common after LTG, which suggests appropriate local control. However, liver metastasis was seen slightly more often after LTG and warrants further examination.

This study has several limitations. First, despite its large sample size, the study design was retrospective in nature. Even after PSM, we could not completely exclude the possibility of underlying patient selection bias. We have strictly conducted PSM using covariates prior to the surgical intervention. Consequently, the

TABLE 4 Postoperative complications and sites of recurrence in the propensity score-matched cohort

	Laparoscopic total gastrectomy (n = 163)	Open total gastrectomy (n = 163)	*P*-value
Morbidity ≥ CD III, *n* (%)			
Overall	14 (8.9)	18 (11.0)	.577
Anastomotic leak	3 (1.8)	3 (1.8)	1.000
Anastomotic bleeding	0 (0)	1 (0.6)	1.000
Pancreatic fistula	3 (1.8)	5 (3.1)	.723
Intraabdominal abscess	4 (2.4)	4 (2.4)	1.000
Intraabdominal bleeding	1 (0.6)	3 (1.8)	.623
Cholecystitis	1 (0.6)	0 (0)	1.000
Bowel obstruction	2 (1.2)	1 (0.6)	1.000
Pleural effusion	0 (0)	1 (0.6)	1.000
90-Day mortality, *n* (%)	0 (0)	0 (0)	1.000
Sites of recurrence, *n* (%)			
Overall	30	47	
Bone	2 (6.7)	2 (4.3)	.641
Lung	2 (6.7)	2 (4.3)	.641
Liver	4 (13.3)	6 (4.2)	1.000
Nodal	6 (2.0)	13 (27.7)	.59
Peritoneal	14 (46.7)	19 (40.4)	.642
Local	2 (6.7)	4 (8.5)	1.000

Abbreviation: CD, Clavien–Dindo.

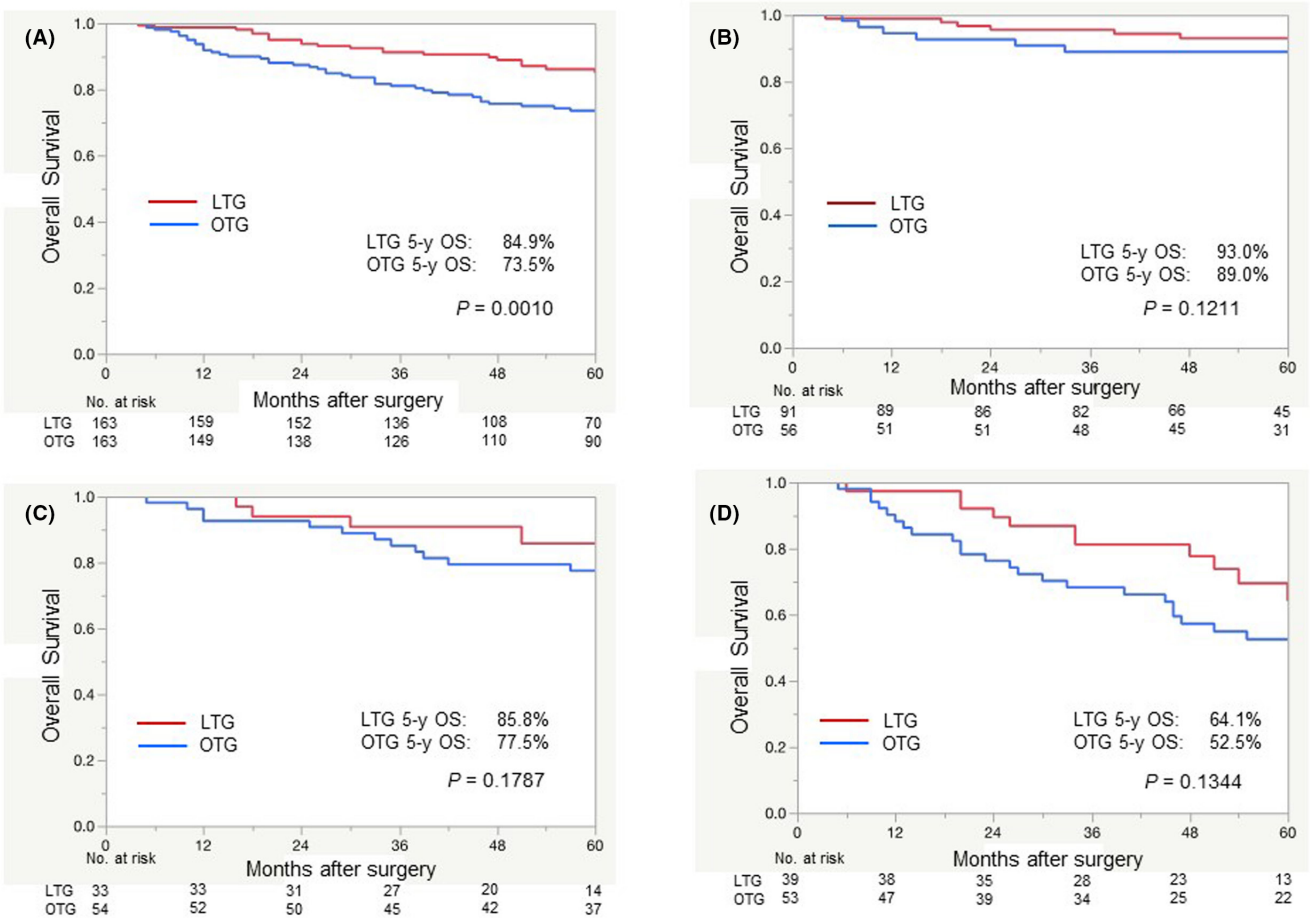

FIGURE 3 Overall survival curves for the propensity score-matched cohort. (A) All pathological stages, (B) pStage I, (C) pStage II, and (D) pStage III. LTG, laparoscopic total gastrectomy; OS, overall survival; OTG, open total gastrectomy

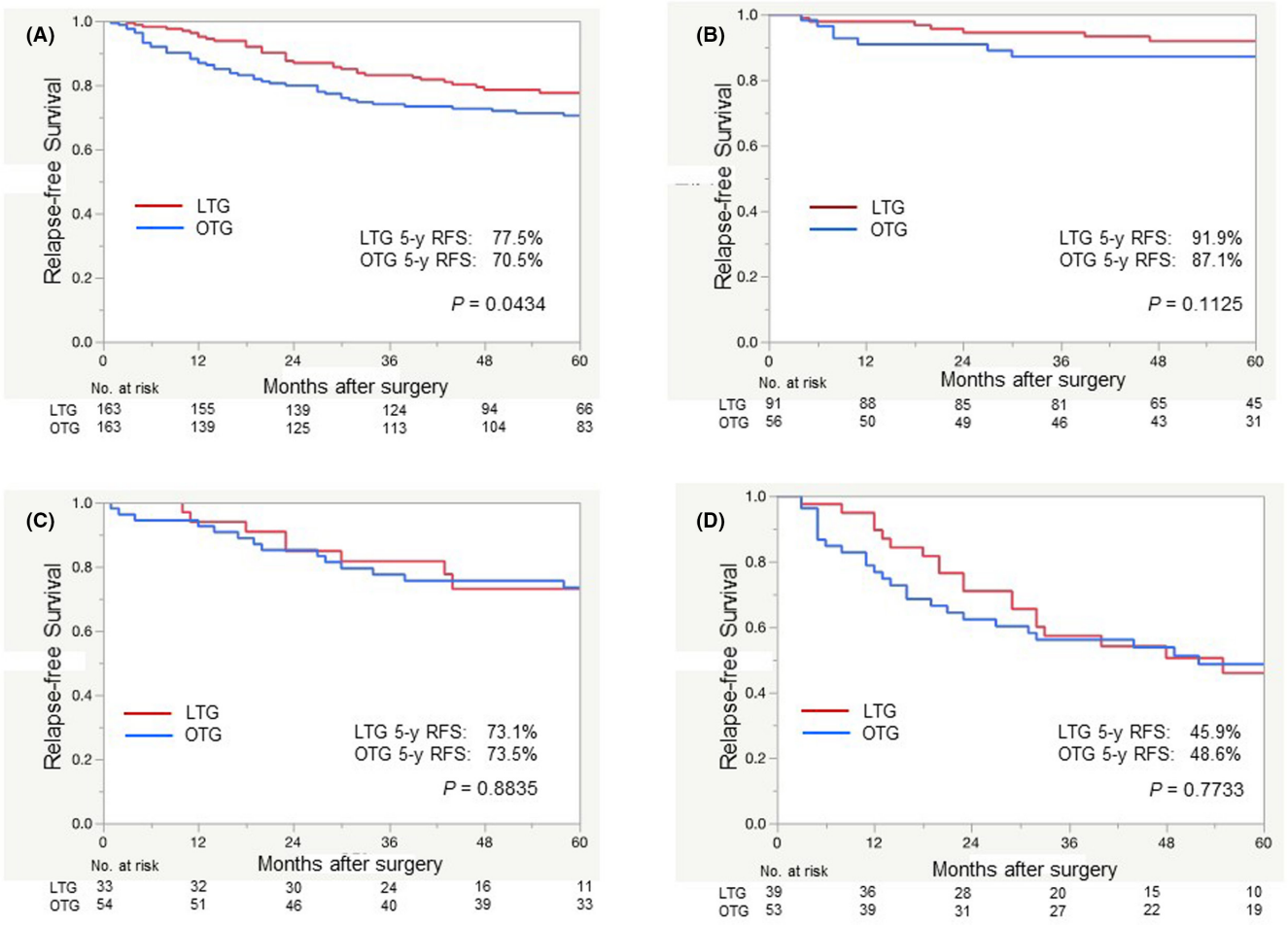

FIGURE 4 Relapse-free survival curves for the propensity score-matched cohort. (A) All pathological stages, (B) pStage I, (C) pStage II, and (D) pStage III. LTG, laparoscopic total gastrectomy; OTG, open total gastrectomy; RFS, relapse-free survival

OTG group included slightly more pathologically advanced disease. To avoid misinterpretations attributable to the stage distribution, we compared the survival curves stratified by pStage before and after PSM. As a result, the survival outcomes of LTG were not inferior to OTG consistently in each pStage. From a statistical point of views, these facts indicate no serious misinterpretation occurred in this study. Second, it was a single-center study performed in a high-volume cancer center in East Asia, where conditions are different from those in centers in Western countries. Therefore, the findings of this study should be extrapolated with caution, and generalization worldwide may be inappropriate. In this regard, we await the long-term outcome of a European randomized trial (STOMACH, LOGICA).[8,12] Third, the 10-y study period seems rather long considering the rapid improvements in surgical techniques and instruments over this time. Furthermore, the recommendations for chemotherapeutic regimens in cases with recurrence have been modified following the emergence of key evidence. Small effects arising as a result of different historical backgrounds cannot be denied. Moreover, the strategies used to perform splenic hilar dissection, routine splenectomy, and spleen preservation had changed during the study period. Laparoscopy is expected to allow spleen-preserving splenic hilar dissection, and such procedures are included in this study cohort. A phase-II multicenter study (JCOG1809) is under way in Japan[22] to determine the safety and efficacy of laparoscopic spleen-preserving splenic hilar dissection for proximal advanced gastric cancer that invades the greater curvature.

In conclusion, the findings of this study suggest that the survival outcome after LTG is equivalent to that after OTG, regardless of disease stage in appropriately selected patients. However, more robust evidence is required before any definitive conclusions can be drawn, especially regarding its efficacy for Stage II/III disease.

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Registry and the registration no. of the study: N/A, owing to the retrospective nature of the study.

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