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Original Article

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Long-term Oncologic Outcomes of Robotic Total Gastrectomy for Advanced Gastric Cancer

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ABSTRACT

Purpose: Although laparoscopic distal gastrectomy has rapidly replaced open distal gastrectomy, laparoscopic total gastrectomy (LTG) is less frequently performed owing to technical difficulties. Robotic surgery could be an appropriate minimally invasive alternative to LTG because it alleviates the technical challenges posed by laparoscopic procedures. However, few studies have compared the oncological safety of robotic total gastrectomy (RTG) with that of LTG, especially for advanced gastric cancer (AGC). Herein, we aimed to assess the oncological outcomes of RTG for AGC and compare them with those of LTG.
Materials and Methods: We retrospectively reviewed 147 and 204 patients who underwent RTG and LTG for AGC, respectively, between 2007 and 2020. Long-term outcomes were compared using inverse probability of treatment weighting (IPTW).
Results: After IPTW, the 2 groups exhibited similar clinicopathological features. The 5-year overall survival was comparable between the 2 groups (88.5% [95% confidence interval {CI}, 79.4%–93.7%] after RTG and 87.3% [95% CI, 80.1%–92.0%]) after LTG; log-rank P=0.544). The hazard ratio (HR) for death after RTG compared with that after LTG was 0.73 (95% CI, 0.40–1.33; P=0.304). The 5-year relapse-free survival was also similar between the 2 groups (75.7% [95% CI, 65.2%–83.4%] after RTG and 76.4% [95% CI, 67.9%–83.0%] after LTG; log-rank P=0.850). The HR for recurrence after RTG compared with that after LTG was 0.93 (95% CI, 0.60–1.46; P=0.753).
Conclusions: Our findings revealed that RTG and LTG for AGC had similar long-term outcomes. RTG is an oncologically safe alternative to LTG and has technical advantages.

Keywords: Stomach neoplasms; Gastrectomy; Robot surgery; Laparoscopy; Prognosis

INTRODUCTION

Laparoscopic distal gastrectomy (LDG) has emerged as the preferred approach for open distal gastrectomy. This preference is based on its superior short-term outcomes and comparable long-term outcomes demonstrated by high-level evidence from randomized controlled trials [1-8]. Likewise, retrospective studies revealed that laparoscopic total gastrectomy (LTG) has similar long-term survival to open total gastrectomy, with better short-term outcomes [9-13]. The current expectation is that ongoing randomized controlled

Presentation
This work was presented at the 15th International Gastric Cancer Congress (IGCC), Yokohama, Japan, held from June 14 to June 17, 2023.

Conflict of Interest
H.W.J. reports receiving research grants from Medtronic and GC Pharma and is a stockholder and chief executive officer of Hutom. He provided consultancy services to Ethicon and SK Hynix (Wuxi) outside of the submitted work. The other authors have no disclosures to report.

Data Availability Statement
The data presented in this study are available upon request from the corresponding author.

Author Contributions
Conceptualization: H.W.J.; Data curation: H.J., K.K.Y.; Formal analysis: H.W.J., H.J.; Funding acquisition: H.W.J.; Investigation: H.W.J., H.J., K.K., P.S.H., C.M., K.Y.M., K.H.; Methodology: H.W.J., H.J.; Project administration: H.W.J.; Resources: H.W.J.; Supervision: H.W.J.; Validation: H.W.J.; Visualization: H.J.W.; Writing - original draft: H.J., H.J.W.; Writing - review & editing: H.W.J.

trials [14] will substantiate LTG as a viable alternative to open total gastrectomy, providing conclusive evidence for its oncologic safety [15]. Nevertheless, technical complexities have hindered the widespread adoption of LTG compared with LDG.

Compared with laparoscopic surgery, robotic surgery offers a superior operative environment and maintains the advantages of minimally invasive surgery. The implementation of robotic gastrectomy reportedly enhances surgical performance, helping surgeons shift from open to minimally invasive procedures [16,17]. Consequently, robotic total gastrectomy (RTG), which overcomes the technical challenges of LTG, could be a viable alternative, provided that comparable oncological outcomes are verified. However, few studies have explored the oncologic safety of RTG when compared with that of LTG, especially for advanced gastric cancer (AGC). Therefore, in the current study, we aimed to assess the oncological outcomes of RTG for AGC and compare them with those of LTG. Additionally, we evaluated the surgical safety of RTG compared with that of LTG.

MATERIALS AND METHODS

Patients

In a retrospective review of a prospectively collected database, we identified 456 patients diagnosed with clinically advanced gastric adenocarcinoma who had undergone minimally invasive total gastrectomy (either laparoscopic or robotic) at the Department of Surgery, Yonsei University of Medicine, between March 2007 and December 2020. Prior to the procedure, the patients received detailed information regarding the risks and benefits associated with both robotic and laparoscopic surgeries. The patients were also informed about the higher cost of robotic surgery, as the national health insurance system in Korea does not provide coverage for the additional expenses of this procedure. After receiving this comprehensive information, the patients selected the type of operation they wished to undergo, and the selected surgical approach was performed accordingly.

Patients were excluded from the study based on the following criteria: (1) presence of distant metastasis or palliative surgery; (2) neoadjuvant chemotherapy or radiation therapy; (3) presence of other organ malignancies within 5 years after the operation; (4) clinical or surgical T4b tumors; (5) less than D2 lymph node dissection; and (6) combined organ resection for non-cancer-related causes other than cholecystectomy. After exclusion, 5 patients had an American Society of Anesthesiologists (ASA) classification of IV in the laparoscopic group; no patient in the robotic group had this classification. Therefore, achieving balance in the ASA covariate during the inverse probability of treatment weighting (IPTW) process was deemed infeasible, resulting in the additional exclusion of ASA IV patients from the study cohort. The Institutional Review Board (IRB) of Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, approved this retrospective study (IRB number: 4-2023-1261).

Surgical procedures

Detailed descriptions of the preoperative preparation, patient positioning, port placement, and instrument utilization of LTG and RTG at our institution have been detailed previously [18-22]. Based on these processes, radical total gastrectomy and Roux-en-Y esophagojejunostomy with D2 or D2+10 lymphadenectomy were performed [23]. Total omentectomy was performed when the tumor involved the serosal layer (surgical stage T4a).

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The indications for splenic hilar lymph node dissection at our institution were changed during the study period because the 5th edition of the Japanese Gastric Cancer Treatment Guidelines excluded splenic hilar lymph nodes from the definition of D2 lymph node dissection in total gastrectomy, based on the JCOG 0110 study [24]. Before 2017, all patients with primary tumors accompanied by proper muscle invasion were considered candidates for No. 10 dissection. The current indication for No. 10 dissection with or without splenectomy is the involvement of the tumor on the greater curvature of the serosal layer. Splenectomy was performed when the tumor involved the gastrosplenic ligament or when there was any suspicion of positive lymph nodes in the splenic hilum [19]. During the resection and lymph node dissection phases, all surgeons used ultrasonic shear for both RTG and LTG. In RTG, bipolar devices are used as supplemental energy devices.

During the initial study period, extracorporeal esophagojejunostomy was performed using circular staplers via epigastric mini-laparotomy. In 2008, intracorporeal anastomosis was introduced, in which circular staplers were inserted into the peritoneal cavity through an extended wound at the assistant trocar insertion site. From 2012 onwards, linear staplers have been adopted to perform the intracorporeal overlap method. By 2020, surgeons began employing newly introduced robotic staplers in patients with RTG.

Postoperative management and follow-up

After surgery, all patients received the same standardized postoperative management regardless of the surgical approach. The patients started drinking water on postoperative day 2, consumed a liquid diet on postoperative day 3, ate a soft diet on postoperative day 4, and were recommended to be discharged on postoperative day 5, provided that the patient exhibited tolerance to the soft diet.

After discharge, all patients underwent follow-ups according to the following schedule: 2 weeks after discharge, every 3 months for the first and second years, every 6 months for the subsequent 3 years, and annually thereafter. Interviews regarding subjective symptoms, physical examinations, and laboratory tests, including those for tumor markers, were performed at each visit. Abdominopelvic and chest computed tomography scans were conducted every 6 months for the first 2 years, annually for stage I patients, and every 6 months for 5 years for stage II or higher patients. Upper endoscopy was conducted annually for the initial 3 years and then once every 2 years. For patients diagnosed with stage II or higher disease based on pathological staging, adjuvant chemotherapy with either S-1 monotherapy or a combination of oxaliplatin and capecitabine was recommended.

Statistical analysis

To mitigate the potential bias arising from demographic differences between the RTG and LTG groups, stabilized IPTW was conducted by inverting the propensity scores to determine the weights assigned to each patient [25]. This process created a pseudo-population with an even distribution of confounders. The adjusted covariates included age, sex, year of operation, ASA of classification, body mass index, previous surgical history, clinical T and N stages, tumor size, histological type, and proportion of fluorescent lymphography-guided surgery. The inclusion of the rate of fluorescent lymphography-guided surgery as a covariate was based on previous studies suggesting a potential increase in the number of harvested lymph nodes with fluorescence guidance [26]. Successful covariate balancing was indicated by a standardized mean difference of <10%.

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We employed Student's t-test and χ^2 test for parametric analyses of continuous and categorical variables, respectively. Nonparametric testing of continuous variables was conducted using the Mann-Whitney U test. Logistic regression was applied to categorical variables in which the expected frequency was less than 5 for more than 20% of cells. The Kaplan-Meier method was used for survival analysis. Univariate and multivariate Cox regression analyses were performed to assess the hazard ratios (HRs) for death and recurrence. The proportional hazards assumption was tested based on Schoenfeld residuals, and multicollinearity was assessed using variance inflation factors. All statistical analyses were weighted, and a 2-sided P-value less than 0.05 was considered statistically significant. Analyses were conducted using SPSS (version 26.0; SPSS Inc., Chicago, IL, USA), SAS version 9.4 (SAS Institute, Cary, NC, USA), and R software version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Clinicopathologic characteristics

A total of 456 patients underwent LTG or RTG for AGC. A total of 105 patients were excluded upon meeting the following exclusion criteria: distant metastasis or palliative surgery (n=10); neoadjuvant chemotherapy (n=9); other organ malignancies (n=25); clinical or surgical T4b tumors (n=4); less than D2 lymph node dissection (n=48); combined organ resection (n=4); and ASA classification IV (n=5). The study groups comprised a total of 351 patients (204 with LTG and 147 with RTG) (**Fig. 1**). Before the application of IPTW, notable differences in the clinicopathological characteristics were observed between the 2 groups. Patients in the LTG group were older (P<0.001), had a higher proportion of males (P=0.011), exhibited more underlying diseases with a higher ASA of classification distribution (P=0.004), and received fluorescent lymphography guidance less frequently (P<0.001) than those in the RTG group. Following the IPTW adjustment, the 2 groups were well-balanced, as shown in **Table 1**.

Pathologic outcomes

Table 2 presents the unadjusted and adjusted pathological outcomes of RTG and LTG. Before IPTW, the pathological T, N, and overall stages were similar between the 2 groups (P=0.150, P=0.738, and P=0.163, respectively). The median number of retrieved lymph nodes after RTG (58.0 [interquartile range (IQR), 46.0–75.0]) was higher than that after LTG (52.0 [IQR, 43.0–64.0]; P=0.004). After IPTW (**Table 2**), the distribution of pathologic T and N classifications did not differ between the 2 groups (P=0.774 and P=0.665, respectively), and the overall pathologic stage showed no significant difference (P=0.384). The median number of retrieved lymph nodes was 56.0 (IQR, 45.0–71.0) in the RTG group and 54.0 (IQR, 44.0–70.0) in the LTG group (P=0.866). None of the patients in either group had a lymph node yield of less than 16. Retrieval of 30 or more lymph nodes was observed in 98.1% and 95.8% of patients in the RTG and LTG groups, respectively (P=0.234).

Perioperative outcomes

Details of the perioperative outcomes are shown in **Table 2**. Prior to IPTW, the RTG group exhibited a longer operation time (P<0.001) and lower estimated blood loss (P<0.001). After IPTW (**Table 2**), the mean operation time was still longer in the RTG group (287.4±62.1 minutes) than in the LTG group (250.4±55.6 minutes; P<0.001). The median estimated blood loss was lower in the RTG group (70.0 [IQR, 35.0–120.0] mL) than in the LTG group (100.0 [IQR, 60.0–180.0] mL; P=0.001). Conversion to open surgery occurred in 0.5 (0.4%) of the

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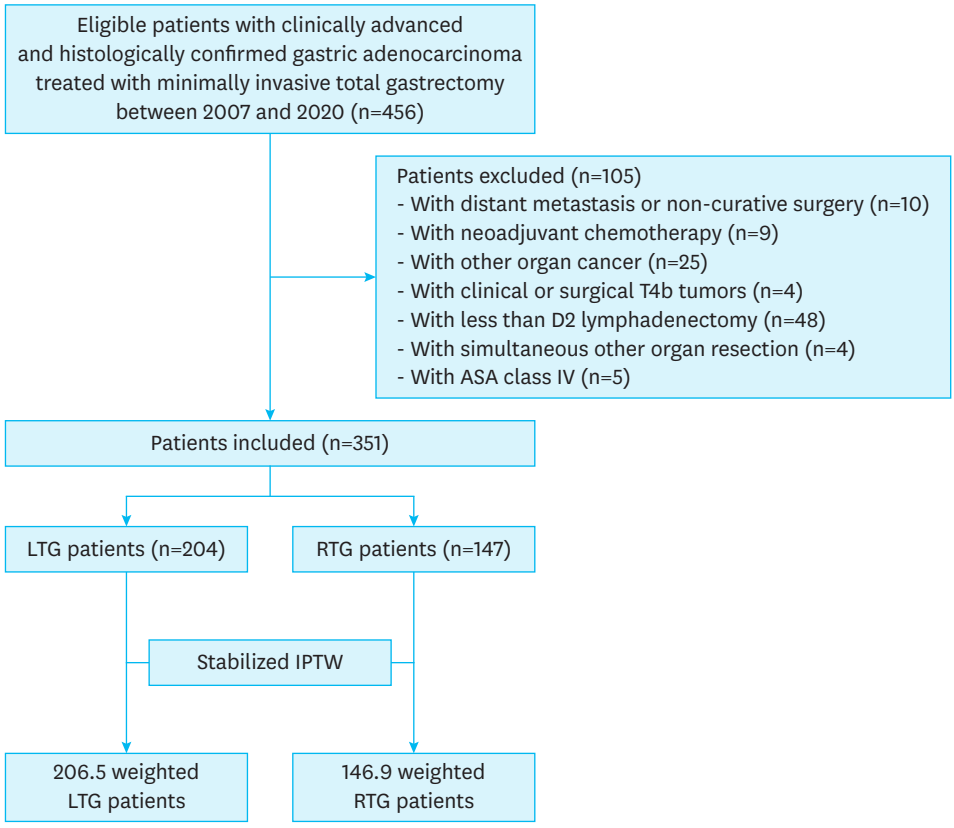

Fig. 1. Study flow chart.
ASA = American Society of Anesthesiologists; LTG = laparoscopic total gastrectomy; RTG = robotic total gastrectomy; IPTW = inverse probability of treatment weighting.

RTG group and 3.2 (1.5%) of the LTG group (P=0.327). Total omentectomy was performed in 34.8 (23.7%) patients in the RTG group and 65.1 (31.5%)patients in the LTG group (P=0.107). Splenectomy was performed in 8.2 (5.6%) patients of the RTG group and 10.1 (4.9%) of the LTG group (P=0.758). Complications classified as Clavien-Dindo grade II or higher occurred in 61.9 (42.2%) patients of the RTG group when compared with 75.1 (36.4%) patients of the LTG group (P=0.271). Complications classified as Clavien-Dindo grade III or higher occurred in 13.1 (9.0) patients in the RTG group, compared with 18.2 (8.8) patients in the LTG group (P=0.965). The incidence of each complication did not differ significantly between the 2 groups. Mortality rates within 90 days after surgery were also similar, occurring in 0.8 (0.6%) patients of the RTG group and 2.8 (1.3%) patients of the LTG group (P=0.485). Unplanned re-operations and re-admissions occurred in 1.7 (1.1%) and 14.2 (9.7%) patients of the RTG group, respectively, compared with 1.2 (0.8%) and 13.8 (6.7%) patients of the LTG group (P=0.568 and P=0.310, respectively). The median length of hospital stay was similar between the 2 groups, 6.0 (5.0–8.0) days for both groups (P=0.550). Following surgery, 82.6 (56.2%) patients in the RTG group and 114.9 (55.7%) patients in the LTG group received adjuvant chemotherapy (P=0.922).

Survival outcomes

After IPTW, there was no significant difference in overall (log-rank P=0.544) or relapse-free (log-rank P=0.850) survival between the 2 groups after a median follow-up time of 58.0 months. After excluding postoperative mortalities, the 5-year overall survival rates were

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Table 1. Clinicopathologic characteristics before and after the inverse probability of treatment weighting

Variables	Unadjusted				Adjusted			
	LTG (n=204)	RTG (n=147)	P-value	SMD	LTG (n=206.5)	RTG (n=146.9)	P-value	SMD
Age (yr)*	59.3±13.0	53.1±12.7	<0.001	−0.483	56.1±14.0	56.5±14.1	0.805	0.029
Male	136 (66.7)	78 (53.1)	0.011	0.280	117.7 (57.0)	86.4 (58.8)	0.735	−0.037
Operation year			0.003				0.856	
2007–2013	33 (16.2)	33 (22.4)		−0.159	40.9 (19.8)	28.3 (19.2)		0.014
2014–2018	98 (48.0)	86 (58.5)		−0.211	105.6 (51.1)	71.9 (48.9)		0.045
2019–2020	73 (35.8)	28 (19.0)		0.382	60.0 (29.1)	46.7 (31.8)		−0.063
ASA classification			0.004				0.840	
I	41 (20.1)	52 (35.4)		−0.346	61.0 (29.6)	44.4 (30.2)		−0.016
II	118 (57.8)	74 (50.3)		0.151	109.6 (53.1)	73.9 (50.3)		0.056
III	45 (22.1)	21 (14.3)		0.203	35.8 (17.4)	28.6 (19.5)		−0.055
BMI (kg/m^2)	23.5±3.0	23.0±3.2	0.135	−0.161	23.3±3.0	23.1±3.2	0.486	−0.075
Previous abdominal surgery	57 (27.9)	28 (19.0)	0.059	0.211	46.9 (22.7)	33.7 (22.9)	0.965	−0.005
Clinical T stage			>0.999				0.363	
cT2–3	169 (82.8)	122 (83.0)		−0.004	174.4 (84.5)	118.7 (80.8)		0.098
cT4a	35 (17.2)	25 (17.0)		0.004	32.1 (15.5)	28.2 (19.2)		−0.098
Clinical N stage			0.588	−0.067			0.720	−0.039
cN−	97 (47.5)	65 (44.2)			95.0 (46.0)	64.8 (44.1)		
cN+	107 (52.5)	82 (55.8)			111.5 (54.0)	82.1 (55.9)		
Tumor size (cm)			0.641				0.739	
<2	18 (8.8)	9 (6.1)		0.103	13.8 (6.7)	7.2 (4.9)		0.069
≥2, <4	86 (42.2)	63 (42.9)		−0.014	89.2 (43.2)	62.3 (42.4)		0.016
≥4	100 (49.0)	75 (51.0)		−0.040	103.5 (50.1)	77.4 (52.7)		−0.052
Histology			0.183				0.981	
Differentiated	53 (26.0)	28 (19.0)		0.167	44.7 (21.6)	31.0 (21.1)		0.012
Undifferentiated	128 (62.7)	106 (72.1)		−0.201	142.1 (68.8)	102.5 (69.8)		−0.020
Others	23 (11.3)	13 (8.8)		0.081	19.6 (9.5)	13.3 (9.1)		0.015
Fluorescence lymphography			<0.001	−0.573			0.856	0.020
Not used	147 (72.1)	66 (44.9)			127.5 (61.7)	92.1 (62.7)		
Used	57 (27.9)	81 (55.1)			79.0 (38.3)	54.8 (37.3)		

Values in parentheses are percentages unless indicated otherwise, or mean ± standard deviation.
LTG = laparoscopic total gastrectomy; RTG = robotic total gastrectomy; SMD = standardized mean difference; ASA = American Society of Anesthesiologists; BMI = body mass index.

88.5% (95% CI, 79.4%–93.7%) for the RTG group and 87.3% (95% CI, 80.1%–92.0%) for the LTG group. The 5-year relapse-free survival rates after RTG and LTG were 75.7% (95% CI, 65.2%–83.4%) and 76.4% (95% CI, 67.9%–83.0%) after LTG. Survival analysis after stratification by stage showed comparable outcomes, as shown in **Fig. 2**. No statistically significant differences were observed in the weighted overall and relapse-free survival of stage II patients (log-rank P=0.322 and 0.288, respectively) or stage III patients (log-rank P=0.813 and 0.797, respectively).

The weighted Cox regression analysis revealed that the type of surgery (laparoscopic or robotic) did not significantly affect the risk of mortality or recurrence (**Table 3**). Robotic surgery, compared with laparoscopic surgery, exhibited an HR of 0.73 (95% CI, 0.40–1.33; P=0.304) for death and an HR of 0.93 (95% CI, 0.60–1.46; P=0.753) for recurrence. No significant differences were observed in the recurrence patterns, as shown in **Table 4**. Peritoneal recurrence was the most common type of recurrence in both groups, accounting for 52.9% and 52.7% of the recurrences after RTG and LTG, respectively (P>0.999).

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Table 2. Pathologic and perioperative outcomes

Variables	Unadjusted			Adjusted		
	LTG (n=204)	RTG (n=147)	P-value	LTG (n=206.5)	RTG (n=146.9)	P-value
Operation time (min)	247.0 (210.3–287.0)	270.0 (238.5–327.5)	<0.001	250.4±55.6	287.4±62.1	<0.001
Estimated blood loss (mL)	110.0 (63.0–200.0)	58.0 (30.0–108.5)	<0.001	100.0 (60.0–180.0)	70.0 (35.0–120.0)	0.001
Open conversion	4 (2.0)	1 (0.7)	0.588	3.2 (1.5)	0.5 (0.4)	0.327
Total omentectomy	64 (31.4)	42 (28.6)	0.656	65.1 (31.5)	34.8 (23.7)	0.107
Splenectomy	11 (5.4)	11 (7.5)	0.566	10.1 (4.9)	8.2 (5.6)	0.758
Retrieved lymph nodes	52.0 (43.0–64.0)	58.0 (46.0–75.0)	0.004	54.0 (44.0–70.0)	56.0 (45.0–71.0)	0.866
≥16 lymph nodes	204 (100.0)	147 (100.0)	>0.999	206.5 (100.0)	146.9 (100.0)	>0.999
≥30 lymph nodes	192 (94.1)	144 (98.0)	0.137	197.7 (95.8)	144.1 (98.1)	0.234
Proximal margin (mm)	20.0 (11.0–32.0)	20.0 (10.0–45.0)	0.306	20.0 (11.0–30.0)	20.0 (10.0–45.0)	0.995
Pathologic T stage*			0.150			0.774
T1	56 (27.5)	27 (18.4)		48.7 (23.6)	29.3 (19.9)	
T2	38 (18.6)	24 (16.3)		33.7 (16.3)	28.8 (19.6)	
T3	54 (26.5)	50 (34.0)		56.9 (27.6)	42.4 (28.9)	
T4a	56 (27.5)	46 (31.3)		67.1 (32.5)	46.4 (31.6)	
Pathologic N stage*			0.738			0.665
N0	107 (52.5)	73 (49.7)		98.6 (47.7)	75.3 (51.3)	
N1	32 (15.7)	22 (15.0)		33.3 (16.1)	23.8 (16.2)	
N2	29 (14.2)	19 (12.9)		33.4 (16.2)	16.9 (11.5)	
N3	36 (17.6)	33 (22.4)		41.2 (20.0)	30.9 (21.0)	
Pathologic stage*			0.163			0.384
I	75 (36.8)	40 (27.2)		66.3 (32.1)	44.6 (30.4)	
II	64 (31.4)	51 (34.7)		58.2 (28.2)	51.3 (34.9)	
III	65 (31.9)	56 (38.1)		82.0 (39.7)	51.0 (34.7)	
Total CD ≥ II complications	87 (42.6)	54 (36.7)	0.315	75.1 (36.4)	61.9 (42.2)	0.271
II	64 (31.4)	39 (26.5)		56.9 (27.6)	48.8 (33.2)	
IIIa/b	15 (7.4)	12 (8.2)		11.8 (5.7)	10.8 (7.3)	
IVa/b	3 (1.5)	2 (1.4)		3.6 (1.8)	1.6 (1.1)	
V	5 (2.5)	1 (0.7)		2.8 (1.3)	0.8 (0.6)	
CD ≥ III complications	23 (11.3)	15 (10.2)	0.885	18.2 (8.8)	13.1 (9.0)	0.965
Fluid collection	1 (0.5)	2 (1.4)	0.775	0.7 (0.4)	1.3 (0.9)	0.512
Intra-abdominal abscess	1 (0.5)	0 (0.0)	>0.999	1.4 (0.7)	0.0 (0.0)	0.989
Anastomotic leakage	12 (5.9)	5 (3.4)	0.414	9.3 (4.5)	4.1 (2.8)	0.402
Anastomotic stenosis	4 (2.0)	1 (0.7)	0.588	2.6 (1.3)	1.2 (0.8)	0.693
Intra-abdominal bleeding	2 (1.0)	1 (0.7)	>0.999	1.6 (0.8)	1.0 (0.7)	0.921
Intestinal obstruction	1 (0.5)	1 (0.7)	>0.999	1.2 (0.6)	0.9 (0.6)	0.970
Other surgical complications	1 (0.5)	1 (0.7)	>0.999	0.6 (0.3)	0.7 (0.5)	0.785
Cardiac	0 (0.0)	1 (0.7)	0.869	0.0 (0.0)	0.8 (0.6)	0.987
Pulmonary	1 (0.5)	3 (2.0)	0.401	0.7 (0.3)	3.0 (2.1)	0.169
Re-operation	1 (0.5)	2 (1.4)	0.775	1.2 (0.8)	1.7 (1.1)	0.568
Re-admission	14 (6.9)	11 (7.5)	0.990	13.8 (6.7)	14.2 (9.7)	0.310
Hospital stay (days)	6.0 (5.0–9.0)	6.0 (5.0–9.0)	0.115	6.0 (5.0–8.0)	6.0 (5.0–8.0)	0.550
Adjuvant chemotherapy	104 (51.0)	91 (61.9)	0.054	114.9 (55.7)	82.6 (56.2)	0.922

Values in parentheses are percentages unless indicated otherwise, mean ± standard deviation or median (interquartile range).
LTG = laparoscopic total gastrectomy; RTG = robotic total gastrectomy; CD = Clavien-Dindo grade.
*Union for International Cancer Control (UICC) classification, 8th edition.

DISCUSSION

In this study, we demonstrated that the surgical and oncological outcomes did not differ between LTG and RTG for AGC. Although RTG was associated with a longer operation time and less intraoperative blood loss than LTG, other surgical outcomes did not differ, including open conversion rate, length of hospital stay, incidence of complications, and pathologic outcomes. The weighted 5-year overall survival rates were also similar between the 2 groups, not only across the entire study population but also across each TNM stage. Recurrence rates and patterns after RTG were comparable to those after LTG.

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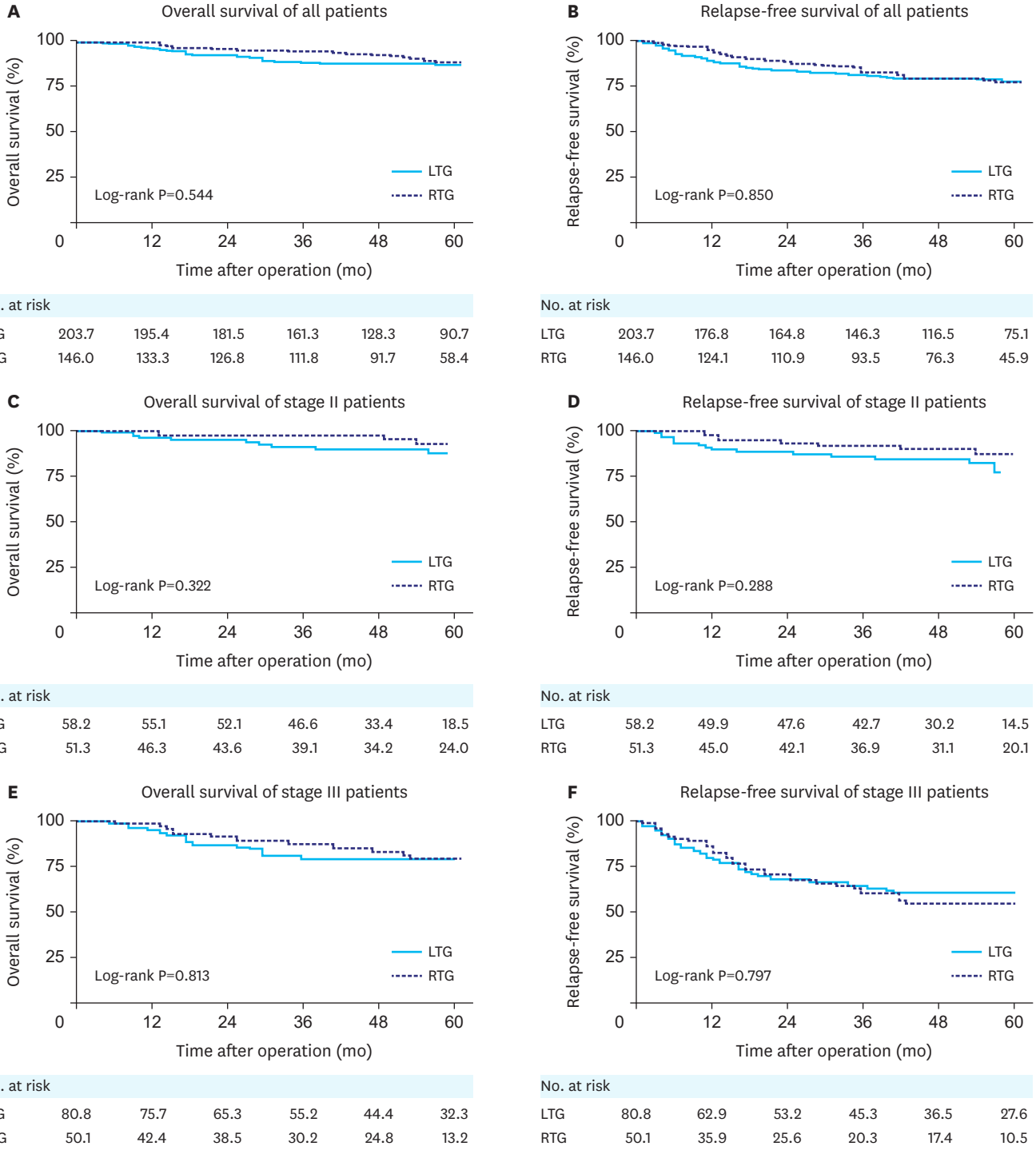

No. at risk						
LTG	203.7	195.4	181.5	161.3	128.3	90.7
RTG	146.0	133.3	126.8	111.8	91.7	58.4

No. at risk						
LTG	203.7	176.8	164.8	146.3	116.5	75.1
RTG	146.0	124.1	110.9	93.5	76.3	45.9

No. at risk						
LTG	58.2	55.1	52.1	46.6	33.4	18.5
RTG	51.3	46.3	43.6	39.1	34.2	24.0

No. at risk						
LTG	58.2	49.9	47.6	42.7	30.2	14.5
RTG	51.3	45.0	42.1	36.9	31.1	20.1

No. at risk						
LTG	80.8	75.7	65.3	55.2	44.4	32.3
RTG	50.1	42.4	38.5	30.2	24.8	13.2

No. at risk						
LTG	80.8	62.9	53.2	45.3	36.5	27.6
RTG	50.1	35.9	25.6	20.3	17.4	10.5

Fig. 2. Overall and relapse-free survival by surgical approach. (A) Overall survival of all patients, (B) relapse-free survival of all patients, (C) overall survival of stage II patients, (D) relapse-free survival of stage II patients, (E) overall survival of stage III patients, and (F) relapse-free survival of stage III patients.
LTG = laparoscopic total gastrectomy; RTG = robotic total gastrectomy.

These findings are consistent with those of previous studies demonstrating comparable survival outcomes across different surgical approaches [1-5,7,8,27]. The oncological safety of gastric cancer surgery is determined by radical resection with thorough lymph node dissection, adequate margins, and proper tissue and organ handling during the procedure.

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Table 3. Cox proportional hazard analysis for overall survival and relapse-free survival

Variables	Overall survival				Relapse-free survival			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Type of surgery								
Laparoscopic	Ref.		Ref.		Ref.		Ref.	
Robotic	0.80 (0.44–1.46)	0.470	0.73 (0.40–1.33)	0.304	0.95 (0.61–1.48)	0.818	0.93 (0.60–1.46)	0.753
Age	1.00 (0.98–1.03)	0.749			1.00 (0.99–1.02)	0.644		
Sex								
Female	Ref.				Ref.			
Male	1.41 (0.77–2.58)	0.261			0.95 (0.62–1.47)	0.832		
ASA								
I	Ref.				Ref.			
II	0.88 (0.47–1.66)	0.701			1.18 (0.73–1.90)	0.506		
III	0.63 (0.22–1.79)	0.386			0.74 (0.34–1.59)	0.436		
BMI	0.96 (0.87–1.06)	0.454			0.97 (0.90–1.05)	0.480		
Pathologic T stage*								
pT1	Ref.		Ref.		Ref.		Ref.	
pT2	1.02 (0.26–4.00)	0.977	1.02 (0.26–4.01)	0.979	0.88 (0.28–2.81)	0.832	0.84 (0.26–2.72)	0.768
pT3	1.74 (0.56–5.39)	0.334	1.00 (0.26–3.84)	0.998	3.04 (1.31–7.03)	0.009	1.63 (0.60–4.42)	0.339
pT4a	5.30 (1.97–14.31)		2.87 (0.75–10.98)	0.124	6.33 (2.87–13.94)		3.11 (1.11–8.74)	0.031
Pathologic N stage*								
pN0	Ref.		Ref.		Ref.		Ref.	
pN1	0.84 (0.28–2.57)	0.766	0.56 (0.17–1.80)	0.330	1.20 (0.55–2.63)	0.652	0.85 (0.37–1.96)	0.704
pN2	0.85 (0.27–2.70)	0.787	0.61 (0.18–2.05)	0.428	1.86 (0.92–3.75)	0.084	1.39 (0.65–3.00)	0.400
pN3	5.38 (2.82–10.25)	<0.001	3.27 (1.54–6.94)	0.002	6.97 (4.17–11.65)	<0.001	3.90 (2.14–7.11)	<0.001
Histology								
Differentiated	Ref.				Ref.			
Undifferentiated	1.48 (0.68–3.25)	0.318			1.06 (0.63–1.81)	0.821		
Others	0.69 (0.15–3.24)	0.639			0.45 (0.14–1.41)	0.170		
Tumor size (cm)								
<2	Ref.				Ref.		Ref.	
≥2, <4	1.53 (0.27–8.63)	0.628			2.37 (0.44–12.92)	0.318	1.42 (0.25–8.08)	0.691
≥4	3.55 (0.66–19.02)	0.139			6.87 (1.31–36.16)	0.023	2.02 (0.35–11.63)	0.430
Adjuvant chemotherapy								
Not received	Ref.		Ref.		Ref.		Ref.	
Received	3.33 (1.63–6.83)	0.001	1.37 (0.45–4.22)	0.582	3.38 (1.98–5.78)	<0.001	0.99 (0.47–2.09)	0.978

HR = hazard ratio; CI = confidence interval; ASA = American Society of Anesthesiologists; BMI = body mass index.
*Union for International Cancer Control (UICC) classification, 8th edition.

Table 4. Recurrence patterns

Variables	Unadjusted			Adjusted		
	LTG (n=45)	RTG (n=30)	P-value	LTG (n=45.4)	RTG (n=23.9)	P-value
Recurrence types			0.587			0.865
Peritoneal	24 (53.3)	16 (53.3)		23.9 (52.7)	12.6 (52.9)	>0.999
Hematogenous	6 (13.3)	5 (16.7)		4.8 (10.5)	3.8 (15.7)	0.947
Lymphatic	5 (11.1)	6 (20.0)		4.8 (10.7)	3.5 (14.5)	0.464
Locoregional	2 (4.4)	1 (3.3)		3.6 (8.0)	0.7 (3.0)	>0.999
Mixed	8 (17.8)	2 (6.7)		8.2 (18.1)	3.3 (13.9)	0.298

Values in parentheses are percentages unless otherwise indicated.
LTG = laparoscopic total gastrectomy; RTG= robotic total gastrectomy.

RTG and LTG showed equal radicality when considering the extent of lymph node dissection, with similar pathological and postoperative outcomes. Moreover, approximately 9% of Clavien-Dindo grade III or higher complications in both RTG and LTG are comparable with those reported in previous studies that explored the safety of LTG [12,28-30]. The techniques used in LTG to accomplish these goals are similarly applicable to RTG. The only differences were in the surgical environment and instruments. Consequently, the similar oncological outcomes observed between RTG and LTG are unpredictable. It has been consistently

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suggested that LTG yields equivalent oncologic outcomes to those of open total gastrectomy for AGC [9-13,30-31]. Ongoing randomized controlled trials are expected to align with these findings. Upon establishing oncologic comparability between LTG and open total gastrectomy in an ongoing randomized controlled trial [14], similar conclusions can be drawn regarding the oncologic comparability between RTG and open total gastrectomy.

Despite the anticipated validation of the oncologic safety and potentially superior short-term outcomes of LTG compared to those of open total gastrectomy, its widespread adoption appears to be challenging. The primary obstacle contributing to its limited penetration is related to the technical complexities. Therefore, LTG is unlikely to replace open total gastrectomy as rapidly as LDG replaced open distal gastrectomy. The application of robotics, as an evolved form of laparoscopic surgery, can overcome the technical complexities of LTG for gastric cancer, as observed in other organ oncologic surgeries such as prostate, kidney, pancreas, and colorectal surgeries [32]. Consequently, establishing the oncologic safety of RTG compared with that of LTG for AGC, as evidenced in this study, would provide an alternative minimally invasive surgical option for total gastrectomy, particularly for surgeons who are more accustomed to open surgery and aim to transition from open to minimally invasive surgery.

The superior surgical environment provided by the robotic surgery system, including features such as tremor filtration, 3-dimensional magnified visualization, and ergonomic design, enables more meticulous lymph node dissection in technically demanding areas, such as along the splenic vessels and splenic hilum. Reportedly, RTG can facilitate the harvesting of a larger number of lymph nodes in the extraperigastric, suprapancreatic, splenic vessel, and splenic hilar areas than LTG [19]. Additionally, the robotic approach alleviates the difficulties associated with esophagojejunostomy, which often leads to a higher incidence of anastomotic leakage after LTG [33]. RTG may potentially ease this process by facilitating suturing, anastomotic line alignment, and access to the mediastinal space [34]. Moreover, as a cutting-edge platform, robotic surgery has great potential for additional functions that can further enhance the surgical environment, such as the integration of 3-dimensional vascular anatomy navigation and real-time audiovisual mentoring systems [35,36]. Although the superior surgical environment did not yield improved oncological or surgical outcomes in this study, it could reduce physical strain and mitigate technical challenges for novice surgeons [37,38]. Therefore, employing a robotic approach could facilitate the transition from open to minimally invasive total gastrectomy.

This study had several limitations. First, this was a retrospective study conducted at a single high-volume institution, potentially limiting the generalizability of the obtained results. However, propensity score matching of potential confounding factors with IPTW was used to minimize selection bias. Second, almost one-third of patients initially diagnosed with clinically AGC were postoperatively classified as having pathologic stage I. However, we aimed to evaluate the oncologic safety of RTG with D2 dissection for clinically, not pathologically, advanced cancer, making this result more reflective of real-world scenarios. Third, all surgeons in this study had experience in both LTG and RTG. The inclusion of their learning curves over the study period may have impacted the short-term outcomes of the 2 groups during the initial phase. The advantages of the robotic approach in terms of surgical environment and shorter learning curves could have been more pronounced if the surgeons were inexperienced in both LTG and RTG. Fourth, this study exclusively focused on patients who underwent upfront surgery. Additional research is required to assess the outcomes of

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RTG and LTG after neoadjuvant chemotherapy. Finally, this study did not identify the direct benefits of robotic surgery. Given the high cost and extended operative time associated with robotic surgery, numerous studies have evaluated its potential advantages over laparoscopic surgery. Although the robotic system was expected to have benefits for complex, technically demanding procedures rather than simple ones, this study did not demonstrate the superiority of RTG over LTG. However, this is the first study confirming the safety and feasibility of RTG as an alternative to LTG.

To the best of our knowledge, this is the first matched analysis to compare survival outcomes between RTG and LTG, specifically for locally AGC. Previous studies on RTG have predominantly focused on the short-term outcomes of RTG in patients with AGC [34,38-41]. One prior study investigating the long-term outcomes of RTG for AGC was an unmatched analysis limited to patients who underwent spleen-preserving total gastrectomy without clinical evidence of serosal involvement [19]. In contrast, this study employed IPTW for matched analysis, including patients with serosal involvement, and did not exclude total gastrectomy accompanied by splenectomy.

In conclusion, this study demonstrated that RTG can be an oncologically safe alternative to LTG while offering technical advantages to surgeons. Based on the oncological validity of RTG in this study and the convenience of performing lymphadenectomy for technically demanding lymph node stations and esophagojejunostomy during RTG reported previously, the adoption of a robotic approach would expedite the transition of surgeons from open to minimally invasive total gastrectomy. Our findings provide essential evidence for future randomized controlled trials comparing RTG and LTG for AGC.

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