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ORIGINAL ARTICLE

Possibly more favorable short-term outcomes with minimally invasive surgery than with open surgery in total gastrectomy for locally advanced gastric cancer: A single high-volume center study

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Abstract

Background: Minimally invasive total gastrectomy (MTG) requires advanced surgical skills and is still associated with a higher rate of postoperative complications than other types of gastrectomy. Additionally, the short-term outcomes of MTG compared to open total gastrectomy (OTG) for locally advanced gastric cancer have yet to be demonstrated.

Methods: We retrospectively compared short-term outcomes between MTG and OTG for locally advanced gastric and esophago-gastric junctional cancer, performed at the Cancer Institute Hospital, Tokyo, during the period from January 2017 to March 2024. Propensity score matching (PSM) was conducted to adjust for potential confounders.

Results: In total, 359 patients were included, with 190 remaining after PSM, resulting in 95 in each group. The MTG group experienced a significantly lower incidence of postoperative complications of Clavien–Dindo classification (C-D) ≥3 than the OTG group (3.2% vs. 11.6%, $p = 0.026$). Moreover, the rate of postoperative intra-abdominal infectious complications (IAIC) was significantly lower in the MTG than in the OTG group (C-D ≥ 2; 7.4% vs. 17.9%, $p = 0.029$ and C-D ≥ 3; 2.1% vs. 9.5%, $p = 0.030$, respectively). Subgroup analyses showed the odds ratios for IAIC with C-D ≥ 2 to be more favorable for the MTG than the OTG group in male patients, those ≥70 years of age, patients without esophageal invasion, those without neoadjuvant chemotherapy, those diagnosed with cT≥3, and patients not undergoing combined resection of other organs except for the gallbladder or spleen.

Conclusions: MTG for locally advanced gastric cancer may provide improved short-term outcomes compared to OTG, when performed or supervised by surgeons with high proficiency in laparoscopic techniques.

KEYWORDS
gastric cancer, locally advanced cancer, minimally invasive surgery, postoperative complications, total gastrectomy

1 | INTRODUCTION

Gastric cancer, being the fifth most common cancer worldwide and also ranking fifth as a cause of cancer-related deaths, remains a significant global public health concern.[1] In the treatment of gastric cancer, surgical resection is still the mainstay for achieving curative intent.[2] For resectable gastric cancer, apart from early lesions that can be removed endoscopically, gastrectomy with systematic lymphadenectomy is considered to be the standard treatment.[3]

In recent years, there has been remarkable progress in minimally invasive techniques for gastric cancer surgery, including laparoscopic and robot-assisted surgeries, which have yielded major benefits such as reduced postoperative pain due to smaller incisions and earlier recovery of intestinal motility.[4] Furthermore, randomized controlled trials (RCTs) have recently demonstrated the oncological non-inferiority of laparoscopic surgery as compared to open surgery in distal gastrectomy, not only for early-stage but also for advanced stages of the disease.[5–9] Due to these advancements, minimally invasive distal gastrectomy for gastric cancer has become established as a standard treatment.

Minimally invasive total gastrectomy (MTG) requires advanced surgical techniques and is known to pose a higher risk of postoperative complications than distal gastrectomy via a minimally invasive approach.[10,11] For cStage I gastric cancer, the non-inferiority of laparoscopic total gastrectomy (LTG) as compared to open total gastrectomy (OTG), in terms of postoperative complication rates, was demonstrated in an RCT conducted in China.[12] However, it is still recommended that these technically demanding procedures be performed by surgeons with sufficient skills and experience.[13]

On the other hand, robust evidence regarding the safety of MTG for locally advanced gastric cancer remains insufficient. In fact, national data from Japan have shown higher rates of postoperative anastomotic leakage and reoperation in LTG than OTG for locally advanced cancer.[14] However, considering the favorable short-term outcomes of LTG for early gastric cancer in the aforementioned RCT[12] and the fact that minimally invasive distal gastrectomy has become safer than the open approach for advanced cancer with improved proficiency in surgical techniques,[15] MTG for advanced gastric cancer might achieve lower complication rates than OTG when the advantages of laparoscopy are leveraged by skilled surgeons.

Herein, we hypothesized that MTG potentially has safety preferable to that of OTG for locally advanced gastric cancer and compared short-term outcomes between these two procedures.

2 | PATIENTS AND METHODS

2.1 | Patients

This study included patients with cT2 or more advanced gastric and esophago-gastric junctional adenocarcinoma who underwent total gastrectomy, either OTG or MTG using laparoscopic or robot-assisted approaches, at the Department of Gastroenterological Surgery, Cancer Institute Hospital, Tokyo, Japan during the period from January 2017 through March 2024. The exclusion criteria for this study were requiring conversion to open surgery and undergoing R2 resection. All procedures were performed by highly experienced surgeons or under their direct supervision. Specifically, laparoscopic and robotic procedures were performed by nine experienced surgeons or under their supervision, all of whom had either performed over 300 laparoscopic gastrectomies for gastric cancer or were certificated by the Japan Society for Endoscopic Surgery. Moreover, five of the nine surgeons were actively involved during the same period, collectively performing an average of more than 350 minimally invasive gastrectomies for gastric cancer annually. This study received approval from the institutional review board of the Cancer Institute Hospital (No. 2023-GB-092).

2.2 | Studied criteria

Patient data, including clinical characteristics, surgical findings, and postoperative outcomes, were retrospectively collected from our database and the hospital's electronic medical records. The clinical characteristics included sex, age, body mass index (BMI), Eastern Cooperative Oncology Group Performance Status (ECOG-PS), clinical TNM (tumor-node-metastasis) staging, and the administration of neoadjuvant chemotherapy. Surgical findings included the surgical approach, the presence of splenectomy or combined resection of other organs except for the gallbladder or spleen, the extent of lymph node dissection, operative time, and intraoperative blood loss. Postoperative outcomes comprised hematological parameters such as white blood cell (WBC) count and C-reactive protein (CRP) levels, the amylase concentration in drained abdominal fluid (D-AMY), and the frequency of each postoperative complication within 30 days after surgery.

2.3 | Assessment of clinical staging and definitions

For evaluating the clinical T factor, a thorough review was conducted, incorporating endoscopic findings assessed by an endoscopist and computed tomography (CT) features interpreted by an experienced radiologist. The final decision regarding the depth of tumor wall invasion was reached through consensus at a gastric cancer team conference, composed of surgeons, endoscopists, and chemotherapists. Regional lymph nodes were classified as clinically metastatic if their long-axis diameter was 10 mm or greater on pre-treatment CT scans. The clinical stage was determined according to the 15th edition of the Japanese Classification of Gastric Carcinoma.[16] Postoperative intra-abdominal infectious complications (IAIC) were defined as the presence of any one of the following: anastomotic leakage, intra-abdominal abscess, or pancreatic fistula. The severity of postoperative complications was graded using the Clavien–Dindo classification (C-D).[17]

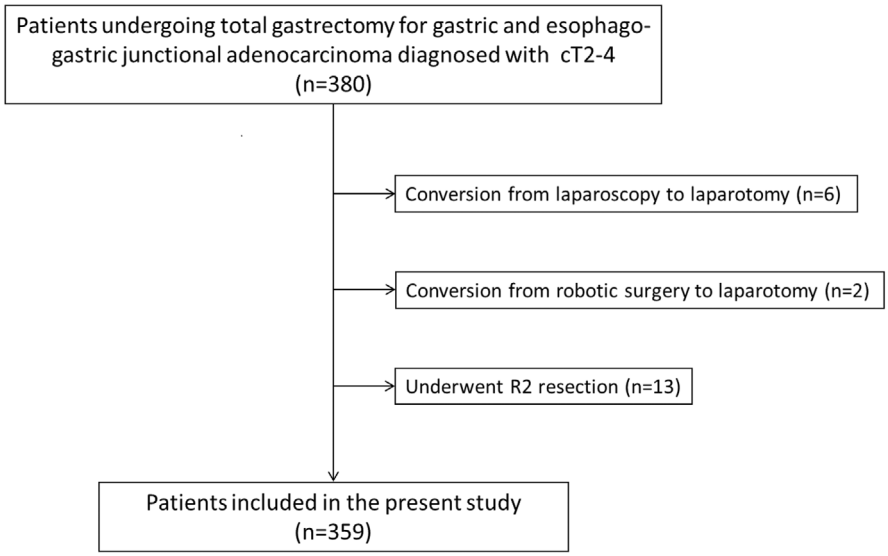

FIGURE 1 Flowchart of patient enrollment.

2.4 | Transition in surgical approach

Initially, our approach to gastric cancer surgery adhered to the gastric cancer treatment guidelines, restricting laparoscopic surgery only for patients with cT1N0.[18] Subsequently, we expanded the criteria to those with cStage I.[19] In 2018, as part of our clinical study, we started performing laparoscopic distal gastrectomy for locally advanced cancer. The following year, in 2019, we incorporated robotic surgery into our practice. Based on the results of RCT conducted in Japan, we adopted minimally invasive surgery as a standard treatment for locally advanced cancer in the middle of 2022.[9]

2.5 | Propensity score matching

Propensity score matching (PSM) was applied to control for confounding factors. The propensity score was calculated by employing a logistic regression model incorporating the following 10 variables: sex, age, BMI, ECOG-PS, esophago-gastric junctional cancer, clinical T stage, clinical N stage, neoadjuvant chemotherapy, splenectomy, and combined resection of other organs. Optimal matching was conducted at a 1:1 ratio without replacement, using a 0.25 standard deviation of the estimated logit.

2.6 | Statistical analysis

All continuous variables are presented as median values. Continuous variables were analyzed using the Mann–Whitney *U* test, while categorical variables were assessed using either the chi-squared test or Fisher's exact test. Subgroup analyses were conducted to evaluate the risks of intra-abdominal infections of C-D ≥ 2, with calculation of odds ratios (OR) and 95% confidence intervals (CI). All statistical tests were two-sided, and a *p*-value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were performed using JMP Pro 17 (SAS Institute Japan Ltd., Japan) for Windows.

3 | RESULTS

3.1 | Characteristics of patients

Figure 1 is a flowchart illustrating patient enrollment. The core characteristics of the 359 patients included in this study are presented in Table 1. Based on PSM, 190 patients were selected for the analysis, with 95 patients each in the OTG and MTG groups. Table 2 summarizes the patient background data. The clinical characteristics were well-balanced between the two groups.

3.2 | Intraoperative findings

The surgical findings are shown in Table 3. The rates of splenectomy and combined resections, as well as the extent of lymph node dissection and the radicality of the surgery, differed minimally between the two groups. The MTG group had a significantly longer operative time than the OTG group (471 vs. 298 min, $p < 0.001$). Intraoperative blood loss was significantly smaller in the MTG than in the OTG group (63 vs. 330 mL, $p < 0.001$).

3.3 | Postoperative short-term outcomes

Postoperative blood and biochemical findings are summarized in Table 4. The CRP levels on POD 1 and 3 were significantly lower in the MTG than in the OTG group. Additionally, the D-AMY level on POD 1 was also significantly lower in the MTG than in the OTG group.

Table 5 presents postoperative outcomes. The MTG group had a significantly lower incidence of severe postoperative complications with C-D ≥ 3 than the OTG group (3.2% vs. 11.6%, $p = 0.026$).

TABLE 1 Core patient backgrounds (before propensity score matching).

	OTG ($n=233$)	MTG ($n=126$)	p value
Sex, *n* (%)			0.527
Male	157 (67.4)	89 (70.6)	
Female	76 (32.6)	37 (29.4)	
Age, years [IQR]	64 [54–72]	69 [62–75]	0.001
BMI, kg/m^2 [IQR]	22.4 [20.1–24.5]	23.2 [20.5–25.0]	0.086
ECOG-PS, *n* (%)			0.191
0	215 (92.3)	111 (88.1)	
1,2	18 (7.7)	15 (11.9)	
Siewert type II cancer, *n* (%)			<0.001
No	187 (80.3)	118 (93.7)	
Yes	46 (19.7)	8 (6.4)	
Esophageal invasion, *n* (%)	65 (27.9)	19 (15.1)	0.006
Macroscopic type, *n* (%)			<0.001
0	20 (8.6)	25 (19.8)	
1	5 (2.2)	12 (9.5)	
2	58 (24.9)	34 (27.0)	
3	92 (39.5)	34 (27.0)	
4	54 (23.2)	18 (14.3)	
5	4 (1.7)	3 (2.4)	
Tumor size, mm [IQR]	60 [40–90]	60 [40–80]	0.237
Clinical T factor, *n* (%)			<0.001
cT2	22 (9.4)	45 (34.9)	
cT3, 4	211 (90.6)	82 (65.1)	
Clinical N factor, *n* (%)			0.004
cN0	116 (49.8)	77 (61.1)	
cN1-3	117 (50.2)	49 (38.9)	
Clinical stage, *n* (%)			<0.001
cStage I	14 (6.0)	35 (27.8)	
cStage II	104 (44.6)	49 (38.9)	
cStage III	88 (37.8)	32 (25.4)	
cStage IV	27 (11.6)	10 (7.9)	
Neoadjuvant chemotherapy, *n* (%)			<0.001
Absence	143 (61.4)	109 (86.5)	
Presence	90 (38.6)	17 (13.5)	

Abbreviations: BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IQR, interquartile range; MTG, minimally invasive total gastrectomy; OTG, open total gastrectomy.

Moreover, the rate of postoperative IAIC with C-D ≥ 2 was significantly lower in the MTG than in the OTG group (7.4% vs. 17.9%, $p=0.029$). Specifically, the incidences of pancreatic fistula (2.1% vs. 9.5%, $p=0.030$) and intra-abdominal abscess (5.3% vs. 15.8%, $p=0.018$) were significantly lower in the MTG than in the OTG group. The MTG group also had a significantly lower rate of postoperative IAIC with C-D ≥ 3 than the OTG group (2.1% vs. 9.5%, $p=0.030$). Additionally, the median hospital stay for the MTG group was significantly shorter than that of the OTG group.

3.4 | Subgroup analyses for the risk of intra-abdominal infectious complications

The forest plots of ORs for IAIC with C-D ≥ 2 are presented in Figure 2. The ORs were significantly lower in the MTG than in the OTG groups in male patients, those ≥70 years of age, patients without esophageal invasion, those not given neoadjuvant chemotherapy, those diagnosed with cT≥3, and patients who did not undergo combined resection of other organs.

TABLE 2 Characteristics of patients (after propensity score matching).

	OTG ($n=95$)	MTG ($n=95$)	p value
Sex, *n* (%)			1.000
Male	64 (67.4)	64 (67.4)	
Female	31 (32.6)	31 (32.6)	
Age, years [IQR]	68 [59–74]	69 [56–75]	0.731
BMI, kg/m^2 [IQR]	23.1 [21.2–25.4]	22.7 [20.4–24.4]	0.277
ECOG-PS, *n* (%)			1.000
0	85 (89.5)	85 (89.5)	
1.2	10 (10.5)	10 (10.5)	
Siewert type II cancer, *n* (%)			1.000
No	87 (91.6)	87 (91.6)	
Yes	8 (8.4)	8 (8.4)	
Esophageal invasion, *n* (%)	18 (19.0)	19 (20.0)	0.855
Macroscopic type, *n* (%)			0.185
0	16 (16.8)	8 (8.4)	
1	4 (4.2)	8 (8.4)	
2	17 (17.9)	28 (29.5)	
3	38 (40.0)	32 (33.7)	
4	18 (19.0)	16 (16.8)	
5	2 (2.1)	3 (3.2)	
Tumor size, mm [IQR]	50 [40–75]	60 [45–90]	0.064
Clinical T factor, *n* (%)			0.852
cT2	18 (19.0)	17 (17.9)	
cT3,4	77 (81.1)	78 (82.1)	
Clinical N factor, *n* (%)			0.305
cN0	58 (61.1)	51 (53.7)	
cN1-3	37 (39.0)	44 (46.3)	
Clinical stage, *n* (%)			0.422
cStage I	13 (13.7)	13 (13.7)	
cStage II	49 (51.6)	40 (42.1)	
cStage III	22 (23.2)	32 (33.7)	
cStage IV	11 (11.6)	10 (10.5)	
Neoadjuvant chemotherapy, *n* (%)			0.852
Absence	77 (81.1)	78 (82.1)	
Presence	18 (19.0)	17 (17.9)	

Abbreviations: BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IQR, interquartile range; MTG, minimally invasive total gastrectomy; OTG, open total gastrectomy.

4 | DISCUSSION

We compared the short-term outcomes of MTG and OTG for locally advanced gastric cancer using PSM, and obtained the following findings. First, there were significant declines in CRP and D-AMY levels in the early postoperative period in the MTG group. Second, the MTG group experienced significantly lower postoperative incidences of all complications with C-D ≥ 3 and IAIC with C-D ≥ 2 or C-D ≥ 3, specifically pancreatic fistula and intra-abdominal abscess, than the OTG group. Third, subgroup analyses suggested that the ORs for IAIC with C-D ≥ 2 were more favorable for the MTG than the OTG group in male patients, those ≥70 years of age, patients without esophageal invasion, those not given neoadjuvant chemotherapy, patients diagnosed with cT≥3, and those not undergoing combined resections other than the gallbladder or spleen. Therefore, with sufficient laparoscopic skills, MTG has the potential to achieve better short-term outcomes than OTG in patients suffering from locally advanced gastric cancer.

As mentioned earlier, evidence regarding distal gastrectomy for gastric cancer is accumulating. A recent meta-analysis, including eight RCTs, showed that minimally invasive approaches for distal gastrectomy in advanced gastric cancer significantly reduce

TABLE 3 Intraoperative findings.

	OTG ($n=95$)	MTG ($n=95$)	p value
Splenectomy, n (%)	18 (19.0)	15 (15.8)	0.566
Combined resection of other organs[a], n (%)	4 (4.2)	6 (6.3)	0.516
Extent of lymph node dissection, n (%)			0.614
D2 or less	70 (73.7)	73 (76.8)	
D2+	25 (26.3)	22 (23.2)	
Residual tumor, n (%)			0.120
R0	92 (96.8)	87 (94.6)	
R1	3 (3.2)	8 (8.4)	
Operative duration, min [IQR]	298 [239–358]	471 [401–558]	<0.001
Intraoperative blood loss, mL [IQR]	330 [140–610]	60 [20–150]	<0.001
No. of retrieved lymph nodes, n [IQR]	59 [52–68]	64 [52–78]	0.151

Abbreviations: IQR, interquartile range; MTG, minimally invasive total gastrectomy; OTG, open total gastrectomy.

[a]Except the gallbladder or spleen.

TABLE 4 Postoperative blood and biochemical findings.

	OTG ($n=95$)	MTG ($n=95$)	p value
WBC on POD 1, $*10^3$ u/L [IQR]	10.1 [7.6–12.1]	10.4 [8.4–12.9]	0.199
WBC on POD 3, $*10^3$ u/L [IQR]	8.2 [6.6–11.3]	8.2 [6.6–10.0]	0.458
CRP on POD 1, mg/L [IQR]	8.8 [7.3–11.0]	6.5 [4.9–7.4]	<0.001
CRP on POD 3, mg/L [IQR]	13.7 [9.9–17.7]	11.0 [7.1–15.5]	0.003
D-AMY on POD 1, U/L [IQR]	727 [386–1493]	456 [270–784]	0.001
D-AMY on POD 3, U/L [IQR]	288 [114–548]	221 [126–360]	0.112

Abbreviations: CRP, C-reactive protein; D-AMY, amylase in drained abdominal fluid; IQR, interquartile range; MTG, minimally invasive total gastrectomy; OTG, open total gastrectomy; POD, postoperative day; WBC, white blood cell.

TABLE 5 Postoperative complications.

	OTG ($n=95$)	MTG ($n=95$)	p value
All complications (C-D ≥ 2), n (%)	25 (26.3)	16 (16.8)	0.113
All complications (C-D ≥ 3), n (%)	11 (11.6)	3 (3.2)	0.026
IAIC (C-D ≥ 2), n (%)	17 (17.9)	7 (7.4)	0.029
Leakage, n (%)	1 (1.1)	3 (3.2)	0.312
Pancreatic fistula, n (%)	9 (9.5)	2 (2.1)	0.030
Intra-abdominal abscess, n (%)	15 (15.8)	5 (5.3)	0.018
IAIC (C-D ≥ 3), n (%)	9 (9.5)	2 (2.1)	0.030
Leakage, n (%)	1 (1.1)	1 (1.1)	1.000
Pancreatic fistula, n (%)	6 (6.3)	1 (1.1)	0.054
Intra-abdominal abscess, n (%)	7 (7.4)	1 (1.1)	0.030
Wound infection, n (%)	1 (1.1)	0 (0)	0.316
Pneumonia, n (%)	0 (0)	1 (1.1)	0.316
Postoperative hospital stays, days [IQR]	11 [9–15]	9 [8–10]	<0.001

Abbreviations: C-D, Clavien–Dindo classification; IAIC, intra-abdominal infectious complication; IQR, interquartile range; MTG, minimally invasive total gastrectomy; OTG, open total gastrectomy.

postoperative complications as compared to open surgery.[15] On the other hand, only one RCT compared the short-term outcomes of LTG to OTG for early-stage gastric cancer.[12] In that RCT, the postoperative complication rates were 17.4% for OTG and 18.1% for LTG, demonstrating the non-inferiority of LTG; however, these rates are not particularly low in either group. Retrospective studies have suggested that LTG yields better outcomes in terms of wound infections and pneumonia, likely due to the smaller incision as compared to OTG.[20,21] Nevertheless, concern persists regarding the higher incidence of anastomotic leakage with LTG than with OTG.[22,23] These procedures should be performed by skilled surgeons,[14] considering the favorable outcomes regarding anastomotic leakage after laparoscopic distal gastrectomy when conducted by surgeons qualified in surgical skills.[24]

Recent reports on LTG for locally advanced gastric cancer have demonstrated variable short-term outcomes when compared to OTG.[14,25–27] Feng et al., using PSM, reported that LTG for locally advanced gastric cancer produced better short-term outcomes than OTG.[27] However, even after PSM, the OTG group had larger tumors and a higher incidence of pT4 than the LTG group in their study. Conversely, Jeong et al. suggested a higher complication rate for LTG with D2 lymphadenectomy than for OTG, although their study had a relatively small sample size of just 81 patients.[25] Kodera et al. used a nationwide database to show LTG for cStage II-IV to be associated

Subgroup		Number of OTG / MTG	OR	95% CI	*p* value
Sex	Female	31 / 31	0.64	0.10-4.15	0.641
	Male	64/ 64	0.30	0.10-0.90	0.025
Age	<70 years	53 / 52	0.64	0.21-1.94	0.426
	≥70 years	42/ 43	0.10	0.01-0.85	0.015
BMI	<25 kg/m^2	70 / 78	0.41	0.13-1.27	0.113
	≥25 kg/m^2	25 / 17	0.34	0.06-1.90	0.271
Esophageal invasion	No	77 / 76	0.25	0.08-0.80	0.022
	Yes	18 / 19	0.93	0.16-5.34	0.942
Neoadjuvant chemotherapy	No	77 / 78	0.28	0.10-0.82	0.015
	Yes	18 / 17	1.07	0.13-8.56	0.952
Clinical T	2	18 / 17	-	-	-
	3, 4	77 / 78	0.38	0.15-0.97	0.039
Clinical N	0	58 / 51	0.46	0.15-1.44	0.178
	1, 2, 3	37 / 44	0.25	0.05-1.30	0.133
Clinical stage	I, II	62 / 53	0.38	0.11-1.27	0.164
	III, IV	33 / 42	0.35	0.08-1.51	0.170
Splenectomy	No	77 / 80	0.49	0.17-1.39	0.171
	Yes	18 / 15	0.14	0.02-1.36	0.095
Combined resection of other organs	No	91 / 89	0.37	0.14-0.99	0.042
	Yes	4 / 6	0.20	0.01-3.66	0.500

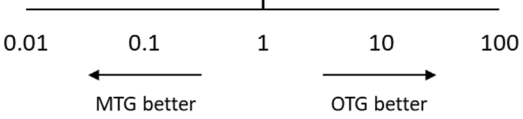

FIGURE 2 Forest plot of odds ratios for the risk of intra-abdominal infectious complications (C-D ≥ 2) in subgroup analyses. For specific subgroups, the MTG group had significantly lower odds ratios (ORs) for intra-abdominal infectious complications than the OTG group. Significant differences were observed in male patients (OR = 0.30, 95% CI = 0.10–0.90; $p = 0.025$), those ≥70 of age (OR = 0.10, 95% CI = 0.01–0.85; $p = 0.015$), those without esophageal invasion (OR = 0.25, 95% CI = 0.08–0.80; $p = 0.022$), patients not given neoadjuvant chemotherapy (OR = 0.28, 95% CI = 0.10–0.82; $p = 0.015$), those diagnosed with cT ≥3 (OR = 0.38, 95% CI = 0.15–0.97; $p = 0.039$), and patients not requiring combined resections other than the gallbladder or spleen (OR = 0.37, 95% CI = 0.14–0.99; $p = 0.042$). BMI, body mass index; CI, confidence interval; C-D, Clavien–Dindo classification; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; MTG, minimally invasive total gastrectomy; OR, odds ratio; OTG, open total gastrectomy.

with significantly higher rates of leakage and reoperation than OTG, while also tending to result in higher rates of all complications with C-D ≥ 3. However, there was no difference between the two groups in all complications with C-D ≥ 2.[14] Therefore, the safety of MTG for locally advanced gastric cancer remains a topic of considerable debate.

However, the findings of the present study suggest that, under the performance or supervision of skilled surgeons, MTG may achieve favorable outcomes, potentially even surpassing those of OTG, for locally advanced cancer. Indeed, the results of our present study are consistent with the short-term outcomes of LTG for cStage I gastric cancer in the prospective study conducted by the Japan Clinical Oncology Group (JCOG) in Japan.[28] On the other hand, according to another RCT conducted by JCOG, the short-term outcomes for OTG in locally advanced gastric cancer were reportedly as follows: postoperative morbidity 16.7%, leakage 3.2%, pancreatic fistula 2.4%, and abdominal abscess 4.0%, rates very similar to those of MTG in our study.[29] Considering that the results of the RCT are for OTG without splenectomy, MTG is potentially more advantageous in preventing postoperative complications. This advantage might be attributable to several factors, such as the enhanced visualization provided by laparoscopic technology, less extensive intra-abdominal manipulation, and more precise handling techniques acquired through experience.[30,31]

Among the factors found to be favorable for MTG in the subgroup analysis, male sex, advanced age, and advanced T stage have all been recognized risk factors for postoperative complications in gastric cancer surgery, as demonstrated by national data and

RCTs.[32,33] Since these known risk factors improve more with MTG than with OTG, the minimally invasive approach may hold promise for reducing complications after total gastrectomy for advanced gastric cancer. Particularly among elderly patients, who likely have a high proportion of frail individuals, providing minimally invasive surgery may facilitate postoperative recovery and thus be beneficial in preventing postoperative complications.[34] Additionally, the tendency for MTG to show better outcomes than OTG in patients with splenectomy may be due to the minimal manipulation of the pancreatic body and tail during MTG. On the other hand, the better outcomes for MTG in patients without esophageal invasion, not given neoadjuvant chemotherapy, or without combined resections may be attributable to the fact that, among patients with these conditions, there are individuals who require extremely advanced surgical techniques for the performance of minimally invasive surgery.

This study has several limitations. First, this study was retrospectively conducted at a single institution, leading to a limited sample size. Despite the application of PSM, the potential for selection bias and residual confounding remains, particularly regarding anastomosis methods, where MTG typically involves side-to-side anastomosis using a linear stapler, while OTG employed a more heterogeneous approach, utilizing either circular or linear staplers. Second, considering that MTG was gradually applied to increasing numbers of the advanced lesions during the study period, time-related bias may have influenced the results, such as the gradual improvement of minimally invasive surgical techniques. Third, since the MTG group included different surgical approaches such as laparoscopic and robotic, the consistency of the characteristics within the MTG group may have been compromised. Although both laparoscopic and robotic surgeries tended to yield better short-term outcomes than open surgery (data not shown), including both approaches may have further contributed to the heterogeneity of the population. Finally, we were not able to compare long-term survival between the two groups due to the very recent study period. Given that postoperative complications have been identified as risk factors that worsen long-term outcomes,[35] the favorable short-term outcomes of MTG observed in this study might also improve survival. The results of the ongoing RCT in South Korea (KLASS06; NCT03385018) are eagerly awaited.

In conclusion, MTG for locally advanced gastric cancer may yield superior short-term outcomes as compared to OTG when performed or supervised by surgeons highly skilled in laparoscopy, thereby fully leveraging its inherent advantages. This also suggests that MTG might be a superior surgical procedure, potentially offering oncological benefits.

AUTHOR CONTRIBUTIONS

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The authors declare no conflicts of interest to this article.

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