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ORIGINAL ARTICLE

The Safety and Feasibility of Single-Port Laparoscopic Gastrectomy for Advanced Gastric Cancer

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Abstract

Background Single-port laparoscopic surgery maximizes the advantages of laparoscopic surgery by reducing damage of the abdominal wall. However, no comparative studies have addressed its application to gastrectomy for advanced gastric cancer (AGC). We therefore aimed to demonstrate the safety and feasibility of single-port laparoscopic gastrectomy (SLG) for the treatment of AGC by comparing it with conventional multi-port laparoscopic gastrectomy (MLG).

Methods We searched the prospective gastric cancer database of our institute for patients with AGC who underwent SLG or MLG between October 2007 and December 2013. Cases of R2 resection with distant metastasis or concurrent surgery for comorbid malignant lesions were excluded. One-to-one propensity score matching was performed to reduce bias from confounding patient-related variables, and the short- and long-term outcomes were compared between the two groups.

Results We identified 216 patients who underwent SLG ($n = 100$) or MLG ($n = 116$). After propensity score matching, we selected 73 pairs of patients who underwent SLG (distal gastrectomy, 49; total gastrectomy, 24) or MLG (distal gastrectomy, 45; total gastrectomy, 28). While the mean operative times were comparable between the groups, the SLG group had less blood loss, a lower postoperative morbidity, and shorter postoperative hospital stays. The 5-year survival rates were 74.2% in the SLG group and 60.2% in the MLG group ($P = 0.081$ by log-rank test).

Conclusions SLG is shown to be safe and feasible for the treatment of AGC, with better short-term results and acceptable oncologic outcomes and may be applicable for AGC treatment.

Keywords Single-port laparoscopic surgery · Distal gastrectomy · Total gastrectomy · Advanced gastric cancer · D2 lymph node dissection

Introduction

Minimally invasive surgery has become increasingly popular for the treatment of both malignant and benign lesions. Since laparoscopic-assisted distal gastrectomy was first reported in 1994 by Kitano et al.,[1] laparoscopic surgeries have been widely used for early gastric cancer.[2,3] These minimally invasive procedures have been associated with less blood loss, less pain, faster recovery, shorter hospital stays, and better cosmetic results than open surgery.[2–6] The indications for laparoscopic approaches for advanced gastric cancers (AGCs) have gradually expanded, with improvements in both surgical techniques and laparoscopic instruments.[6–8]

Current research into minimally invasive surgery has increasingly focused on minimizing surgical trauma by maximizing the benefits of laparoscopic surgery. Transumbilical single-incision or single-port laparoscopic surgery is the goal of minimally invasive surgery in the clinical setting, offering a single extraction site and excellent cosmesis because the scar is concealed in the umbilicus. These advantages have encouraged surgeons to use it in the treatment of many malignant and benign diseases, including gastric cancer, as first reported by Omori et al. in 2011.[9] Retrospective

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studies of pure single-incision laparoscopic distal gastrectomy for the treatment of clinical stage I gastric cancers have since shown that this approach is technically feasible and offers improved cosmesis, reduced postoperative pain, and shortened recovery times compared with conventional multi-port distal gastrectomy.[10–13] More recently, Kim et al. reported similar short-term results in a retrospective study comparing single-port and reduced-port (three-port) laparoscopic distal gastrectomy.[14]

Thus, most previous studies on single-port laparoscopic distal gastrectomy for the treatment of early gastric cancers have had small samples and have focused on the technical feasibility of the approach. However, there are few reports on the application of single-port surgery to more advanced surgeries (e.g., total gastrectomy with splenectomy and distal gastrectomy after neoadjuvant chemotherapy for the treatment of highly AGCs). In addition, no comparative study has been conducted to investigate the efficacy of single-port laparoscopic surgery for AGCs.

We aimed to compare the outcomes of single-port laparoscopic gastrectomy (SLG) with that of conventional multi-port laparoscopic gastrectomy (MLG) to show the feasibility, efficacy, and safety of SLG for AGC.

Methods

Study Design and Patient Selection

This retrospective study was approved by our institutional review board. Signed informed consent was obtained from all patients, who were informed of the surgical and oncological risks preoperatively.

We searched the prospective gastric cancer database of our institute for patients with gastric cancer who underwent gastrectomy between January 2000 and December 2013. First, we excluded patients who underwent surgery by teams before October 2007. The indications of laparoscopic gastrectomy included clinically stages I–III. The first single-port distal laparoscopic gastrectomy for gastric cancer was performed in our institute in 2009, and the first single-port total laparoscopic gastrectomy was performed in 2010. Since then, the indication for SLG included AGCs. The criteria for eligibility were as follows: (1) clinical T2 or over AGC with histologically proven gastric cancer of stages II–IV; (2) laparoscopic distal or total gastrectomy with radical lymphadenectomy; and (3) no co-morbid malignant lesions. Patients were excluded if they underwent R2 resection for residual distant metastasis. Patients with a history of abdominal surgery and R1 resection for positive peritoneal lavage cytology and who had no gross peritoneal dissemination were included, because we routinely performed gastrectomy for P0CY1 stage IV gastric cancer. Preoperative assessment comprised gastroduodenoscopy, abdominal ultrasonography, and computed tomography. Finally, cases were grouped into an SLG group or an MLG group.

Data Collection

Data were collected prospectively and recorded in a computer database at our hospital. Age, gender, tumor location, pathological findings, gastrectomy type, reconstruction method, lymph node dissection extent, operative outcomes, morbidity, and conversion to multi-port or open procedures were recorded. In the SLG group, conversion to MLG was defined as the addition of any 5-mm port to the abdominal wall to complete the procedure. An open conversion was defined as any extension of the primary incision for reasons other than specimen extraction or the reconstruction procedure. The indications for conversion were recorded. Morbidity was stratified as recommended by Dindo et al.[15] The Japanese Classification of Gastric Carcinoma, 3rd English Edition (JCGC), was used for TNM staging.[16]

The SLG Procedures

Single-Port Laparoscopic Distal Gastrectomy

We previously reported our surgical procedure for single-port laparoscopic distal gastrectomy.[17] Briefly, the patient was placed in the reverse Trendelenburg position with his or her legs apart, the surgeon positioned between the patient's legs, and an assistant on each side of the patient. A transumbilical laparotomy was created through a 2.5–3.0-cm vertical umbilical incision, and a wound-sealing device was applied. Single-incision laparoscopy was then performed using the glove technique with three or four trocars in separate fingers or via a commercially available access port (SILS™ port; Covidien, MA, USA or EZ access; Hakko, Nagano, Japan). The pneumoperitoneum was established by carbon dioxide insufflation at a pressure of approximately 8–12 mmHg according to the patient's body type. A 10-mm high-definition flexible scope (ENDOEYE flexible HD camera system; Olympus Medical Systems Corp) was used to view the surgical fields.

Conventional straight forceps and an ultrasonic coagulation cutting device (Harmonic scalpel, Ethicon Endosurgery, Cincinnati) were used for gastric mobilization and lymph node dissection. For D2 lymph node dissection, we routinely checked each anatomic landmark according to the JCGC criteria.[16] Finally, reconstruction was performed using the intracorporeal anastomotic technique.[11,12,17]

Single-Port Laparoscopic Total Gastrectomy

Single-port laparoscopic total gastrectomy was performed in a similar way to single-port laparoscopic distal gastrectomy. In addition, station 11d lymph nodes were dissected around the distal splenic artery, and splenectomy was performed to treat advanced cancers in the upper stomach or type IV gastric cancers, allowing dissection of lymph nodes at station 10. The reconstruction procedure was performed intracorporeally using our original purse string stapling technique with a circular stapling device.[18]

The MLG Procedures

We have previously reported our surgical procedure for multi-port laparoscopic distal gastrectomy.[19] Briefly, the patient was placed on a table in the supine position with their legs apart. The initial port was placed via a 2-cm intraumbilical incision made using an open method. A pneumoperitoneum was then established by carbon dioxide insufflation at a pressure of approximately 8–12 mmHg, according to the patient's body type. Standard MLG included five ports (one 12-mm port in the umbilicus, one for liver retraction forceps in the upper midline of the abdomen, one 5-mm port in the right abdomen, and one 12-mm port in the left abdomen). The D2 lymphadenectomy procedure was similar to the SLG procedure. A 2.5–3.0-cm minilaparotomy, made by extending the umbilical incision, allowed extraction of the resected specimen, before reconstruction was performed using the intracorporeal anastomotic technique, as previously reported.[11,12,17–22]

Postoperative Care

The perioperative management protocol was similar for all patients and followed our hospital's clinical pathway. For 48 h after surgery, patients were given basal analgesia by either continuous epidural infusion of ropivacaine plus fentanyl or continuous intravenous infusion of fentanyl, according to the anesthesiologist's preference. Additional analgesia, such as non-steroidal anti-inflammatory drugs or pentazocine, was given if requested by the patient. A soft diet was resumed after the first passage of flatus.

Outcomes

We used one-to-one propensity score matching to ensure that patients in the SLG, and MLG groups were balanced in terms of baseline characteristics. Each patient in the SLG group was matched to a patient in the MLG group based on age, gender, body mass index, American Society of Anesthesiologists score, clinical stage, neoadjuvant chemotherapy use, operation type, reconstruction method, Lauren classification, lymphatic invasion, vascular invasion, and pathological stage.

Next, we calculated the short- and long-term outcomes for comparison between the matched cohorts. These included the short-term operative outcomes (operative time, estimated blood loss, transfusion, conversion to open or multi-port laparoscopic surgery, and number of retrieved lymph nodes), the postoperative complications, the duration of hospitalization, and the 5-year overall and relapse-free survival rates.

Statistical Analysis

All statistical calculations were performed using IBM SPSS for Windows, Version 23 (IBM Corp., Armonk, NY, USA). The demographic and clinicopathological characteristics are summarized descriptively. All quantitative values are expressed as means and standard deviations, unless otherwise stated. Student's t tests or Mann–Whitney U tests and Pearson's χ^2 tests were used to compare continuous and categorical variables, respectively. The survival data were estimated using the Kaplan–Meier method. All values were two-tailed, and P values less than 0.05 were considered significant.

Results

Descriptive Data

The flow diagram for patient inclusion is shown in Fig. 1. The cohort of 674 patients who underwent laparoscopic gastrectomy by the same surgical team from October 2007 to December 2013 included 471 distal gastrectomy, 194 total gastrectomy, 7 proximal gastrectomy, and 2 partial gastrectomy cases. After applying the inclusion and exclusion criteria, we identified 100 cases for the SLG group (distal gastrectomy 76, total gastrectomy 24) and 116 cases for the MLG group (distal gastrectomy 54, total gastrectomy 62). Finally,

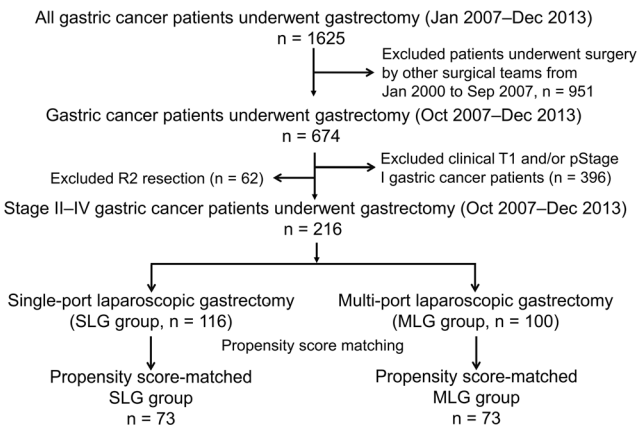

Fig. 1 Patient flow chart. Abbreviations: MLG, multi-port laparoscopic gastrectomy; pStage, pathological stage; SLG, single-port laparoscopic gastrectomy

Table 1 Patient characteristics

	All patients			Propensity-matched patients		
	SLG ($n = 100$)	MLG ($n = 116$)	P value	SLG ($n = 73$)	MLG ($n = 73$)	P value
Age, years, mean ± SD	68.5 ± 10.6	67.0 ± 11.0	0.309	68.4 ± 11.3	67.5 ± 11.4	0.646
Gender: male/female, *n*	68/32	87/29	0.290	51/22	55/18	0.578
BMI, kg/m^2, mean ± SD	22.0 ± 3.4	22.7 ± 3.4	0.123	22.4 ± 3.5	23.1 ± 3.7	0.267
ASA physical status, *n*			0.020			0.258
1	43	33		24	25	
2	53	69		46	40	
3	4	14		3	8	
Main lesion, *n*			0.098			0.935
Upper	34	30		22	23	
Middle	43	44		29	30	
Lower	23	42		22	20	
Maximum tumor size, mm			0.713			0.333
Mean ± SD	54.7 ± 30.0	56.2 ± 27.3		57.8 ± 32.4	53.1 ± 23.0	
Neo-adjuvant chemotherapy			0.118			1.000
Yes	14	26		12	11	
No	86	90		61	62	
Type of operation, *n*			< 0.001			0.604
Distal gastrectomy	76	54		49	45	
Total gastrectomy	24	62		24	28	
Type of reconstruction, *n*			< 0.001			0.270
Billroth I	47	21		26	18	
Roux-en-Y	53	95		47	55	
Degree of lymphadenectomy			0.944			0.730
D1	11	13		10	9	
D2	89	103		63	64	
Clinical T status, n			0.208			0.370
T2	19	19		24	22	
T3	34	35		24	28	
T4a	44	51		22	21	
T4b	3	5		3	2	
Clinical N status, *n*			0.065			1.000
cN0	59	80		44	45	
cN+ (N1/N2/N3)	41 (27/9/5)	36 (20/15/1)		29 (19/6/4)	28 (15/13/0)	
Clinical stage, *n*			0.444			0.370
I	15	17		12	8	
II	52	66		36	41	
III	31	33		23	24	
IV	2	0		2	0	
Pathological T status, *n*			0.717			0.740
pT1	6	4		5	3	
pT2	13	12		10	7	
pT3	37	48		26	29	
pT4	44	52		32 (T4b 1)	34 (T4b 1)	
Pathological N status, *n*			0.417			1.000
pN0	16	25		13	14	
pN+ (N1/N2/N3)	84 (25/23/36)	91 (20/24/47)		60 (20/16/24)	59 (15/11/33)	
Pathological stage, *n*			0.858			0.696

Table 1 (continued)

	All patients			Propensity-matched patients		
	SLG ($n = 100$)	MLG ($n = 116$)	P value	SLG ($n = 73$)	MLG ($n = 73$)	P value
II (IIA/IIB)	40 (21/19)	43 (27/16)		31 (18/13)	26 (16/10)	
III (IIIA/IIIB/IIIC)	44 (15/19/10)	53 (18/19/16)		31 (11/13/7)	35 (11/13/11)	
IV	16	20		11	12	
Lymphatic invasion			0.028			1.000
−/+	14/86	31/85		14/59	15/58	
Vascular invasion			0.126			1.000
−/+	22/78	37/79		18/55	18/55	
Curability			0.721			0.824
R0	84	95		62	60	
R1	16	21		11	12	
Adjuvant chemotherapy			0.007			0.129
Yes	90	88		64	56	
No	10	28		9	17	
Type of tumor, n			0.683			0.869
Differentiated	48	52		35	37	
Undifferentiated	52	64		36	36	

ASA: American Society of Anesthesiologists, BMI: body mass index, MLG: multi-port laparoscopic gastrectomy, SLG: single-port laparoscopic gastrectomy. TNM staging was based on the Japanese Classification of Gastric Carcinoma, 3nd English edition

propensity score matching identified 73 pairs of patients who underwent SLG (distal gastrectomy 49, total gastrectomy 24) or MLG (distal gastrectomy 45, total gastrectomy 28) ($P = 0.604$). Total gastrectomy with splenectomy was performed in 11 cases per group.

Table 1 shows the demographics of the full ($n = 216$) and propensity score matched ($n = 146$) cohorts. There were no conversions to open surgery in either group, and there were no conversions to the multi-port approach in the SLG group. Several variables were significantly different between the two baseline groups, but the patient distributions were closely balanced after propensity score matching.

Pathologically, there were similar distributions of T stage, node status, and tumor stage according to the JCGC.[16] Between the SLG and MLG groups, the numbers with pathological stage II/III disease (62 and 61, respectively) and stage IV disease (CY1P0; 11 and 12, respectively) were comparable ($P = 0.921$), as was the maximum tumor size (57.8 and 53.1 mm, respectively), and number of patients with serosal invasion (pT4; 32 and 34, respectively). Pathological node-positive disease was present in 60 patients (82%) in the SLG group and 59 patients (81%) in the MLG group ($P = 1.000$).

Surgical Outcomes

All gastrectomies did not require transfusion for intraoperative bleeding and did not require either open conversion (in both groups) or conversion to multi-port laparoscopic surgery, as applicable.

We compared early surgical outcomes between the SLG and MLG groups (Table 2). The mean operative time was similar between the two groups. Notably, the median estimated blood loss was significantly lower in the SLG group compared with the MLG group (0–minimal mL vs. 100 mL, $P < 0.001$). Number of lymph nodes harvested were not significantly differ in the two groups (72 vs. 66; $P = 0.141$).

Next, we performed subset analyses by distal and total gastrectomy in the SLG and MLG groups (Table 3). The short-term results for distal gastrectomy were better in the SLG group than in the MLG group, with similar operative time, less blood loss, fewer complications, and shorter postoperative hospital stays. The similar operative times also implied that SLG was at least non-inferior to MLG in this regard. Concerning total gastrectomy, the operative time and blood loss were comparable between the two groups, but the SLG group had fewer morbidities and shorter postoperative hospital stays.

Morbidity

The overall complication rate was significantly lower in the SLG group than in the MLG group ($P = 0.002$) (Table 2). According to the Clavien–Dindo classification, there were significantly fewer grade II or higher complications in the SLG group compared with the MLG group (4.1% vs.

Table 2 Surgical outcomes in the propensity-matched groups

	SLG ($n = 73$)	MLG ($n = 73$)	P value
Operative time, min, mean ± SD	327 ± 77	329 ± 85	0.850
Estimated blood loss, ml, median (range)	0 (0–530)	100 (0–1900)	< 0.001
Transfusion, *n*	0	0	–
Conversion, *n*	0	0	–
No. of lymph nodes retrieved, *n*	72.7 ± 22.9	66.4 ± 28.3	0.141
Complication, *n* (%)	3 (4.1)	16 (21.9)	0.002
G1			
Wound infection	0	2	
Intraabdominal fluid collection	0	1	
Others	0	2	
G2 or higher	3 (4.1)	11 (15.1)	0.046
Wound infection	0	3	
Intraabdominal fluid collection	1	1	
Anastomotic leak	0	0	
Pancreatic fistula	0	1	
Pancreatitis	0	1	
Ileus	0	0	
Delayed gastric emptying	0	1	
Pulmonary infection	1	0	
Enteritis	0	1	
Cholecystitis	0	1	
Cholangitis	0	1	
Others	1	1	
Postoperative hospital stay			
Days, median (range)	8 (5–31)	12 (6–70)	< 0.001
Postoperative mortality	0	0	–

MLG: multi-port laparoscopic gastrectomy, SLG: single-port laparoscopic gastrectomy

15.1%, $P = 0.046$). Although there is not significantly different, there were fewer grade III complications in the SLG group compared with the MLG group (1.4% vs. 2.7%). In the SLG group, there were no cases of anastomotic leakage, pancreatitis, or pancreatic fistulae, and postoperative hospital stays were significantly shorter (8 vs. 12 days, $P < 0.001$). There was no in-hospital mortality in either group.

Oncologic Outcomes

Patients were followed for 58.9 (range = 4.2–72.7) months postoperatively, corresponding to 60.0 (range = 8.7–72.7) months in the SLG group and 54.0 (range = 4.2–64.4) months in the MLG group ($P = 0.054$). Figure 2 shows the cumulative survival curves for patients undergoing SLG and MLG after propensity score matching. Overall survival was not significantly different between the two groups, but survival from stage II–IV gastric cancers appeared to be better in the SLG group than in the MLG group (74.2% vs. 60.2%; $P = 0.081$ by log-rank test). Figure 3 shows the overall and relapse-free survival curves for patients with stage II/III disease. The overall survival rates were 79.7 and 65.8% in the SLG and MLG groups, respectively ($P = 0.091$ by log-rank test, Fig. 3a); the corresponding relapse-free survival rates were 75.2 and 61.9% ($P = 0.125$ by log-rank test, Fig. 3b).

Subgroup analysis was then conducted for overall survival based on pathological stage, as summarized in Fig. 4. The overall survival of patients with stage II disease was not significantly different between the SLG and MLG groups ($P = 0.685$, Fig. 4a). The overall survival from stage III cancer was 76.1% in the SLG group and 57.6% in the MLG group, respectively ($P = 0.099$, Fig. 4b). The overall survival from stage IV cancer was similar between the SLG and MLG groups ($P = 0.578$, Fig. 4c).

Discussion

With advances in both laparoscopic instruments and surgical techniques, multi-port laparoscopic approaches have been applied to more complex procedures (e.g., radical D2 gastrectomy and total gastrectomy) and the treatment of

Table 3 Surgical outcomes in the propensity-matched subgroups

	SLDG ($n = 49$)	MLDG ($n = 45$)	*P* value	SLTG ($n = 24$)	MLTG ($n = 28$)	*P* value
Operative time, min, mean ± SD	299 ± 65	316 ± 77	0.240	383 ± 70	350 ± 95	0.164
Estimated blood loss, ml, median (range)	0 (0–530)	100 (0–1900)	< 0.001	100 (0–350)	150 (0–1050)	0.516
No. of lymph nodes retrieved, *n*	67.7 ± 22.0	63.2 ± 26.9	0.383	83.1 ± 21.5	71.6 ± 30.3	0.125
Complication, *n* (%)	1 (2.0)	7 (15.6)	0.026	2 (8.3)	9 (32.1)	0.046
G1						
Wound infection	0	2		0	0	
Intraabdominal fluid collection	0	0		0	1	
Others	0	2		0	0	
G2 or higher	1 (2.0)	3 (6.7)	0.346	2 (8.3)	8 (28.6)	0.086
Wound infection	0	1		0	2	
Intraabdominal fluid collection	0	0		1	1	
Anastomotic leak	0	0		0	0	
Pancreatic fistula	0	0		0	1	
Pancreatitis	0	1		0	0	
Ileus	0	0		0	0	
Delayed gastric emptying	0	1		0	0	
Pulmonary infection	0	0		1	0	
Enteritis	0	0		0	1	
Cholecystitis	0	0		0	1	
Cholangitis	0	0		0	1	
Others	1	0		0	1	
Postoperative hospital stays						
Days, median (range)	8 (6–19)	11 (6–26)	< 0.001	9.5 (5–31)	15 (8–70)	0.001
Postoperative mortality	0	0		0	0	

MLDG: multiple-port laparoscopic distal gastrectomy, MLTG: multiple-port laparoscopic total gastrectomy, SLDG: single-port laparoscopic distal gastrectomy, SLTG: single-port laparoscopic total gastrectomy

AGC.[6–8,19,23,24] Based on success in expanding the indications for laparoscopic approaches, reduced-port surgery has recently been developed to minimize abdominal wall damage caused by multiple-port approaches when treating gastric cancer. The technical feasibility of reduced-port approaches compared to conventional five-port approaches has been demonstrated.[25–29] SLG, in which the procedure is performed via one extraction site, is the ultimate aim of such approaches. Supporting this, Kim et al. reported that single- and reduced-port distal gastrectomy provided comparable short-term results when treating early gastric cancer.[14] Although their cohort was small overall, with more female and fewer obese patients in the single-port group, they concluded that single-port distal gastrectomy could be a treatment option in this limited subset of patients with early gastric cancer.

Despite its benefits, the single-port laparoscopic approach requires advanced surgical skill due to crowded instrumentation and limited forceps movement. Furthermore, single-port laparoscopic D2 gastrectomy is extremely challenging because of the complexity in creating a secure surgical field that has appropriate countertraction, especially when manipulating bulky gastric lesions and lymph nodes. Ann et al. reported a small case series showing that mid-pancreas mobilization was a simple and feasible method for single-port D2 gastrectomy in clinical stage I gastric cancer.[30] We have also described a secure procedure for pure D2 distal SLG, in which instruments and laparoscope were positioned to maintain good surgical views and gain proper countertraction in each surgical field.[11,17] In a retrospective study by Omori et al. comparing D2 distal SLG and distal MLG, the SLG procedure was safe and feasible for the treatment of gastric cancer.[31] However, we were unable to identify any reports of the efficacy of single-port approaches for AGC or cancer located in the upper stomach. This may be because the reconstruction procedure (D2 suprapancreatic lymphadenectomy) and manipulation of huge gastric tumors or bulky lymph nodes are made difficult by the restricted number of access ports, the limited view, the limited range of forceps motion, and the crowding of the laparoscope and other instruments.

In the present study, we compared SLG with conventional MLG for the treatment of clinically AGC with pathologically

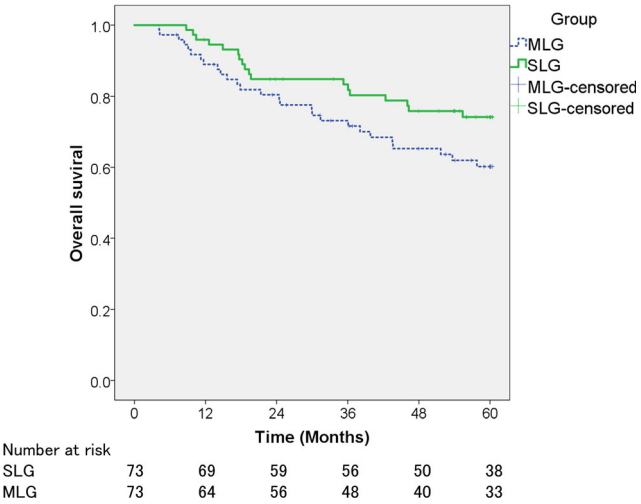

Fig. 2 Cumulative survival curve of patients undergoing SLG and MLG for pStage II–IV gastric cancer, after propensity score matching. The 5-year survival rates were 74.2 and 60.2% in the SLG ($n = 73$) and MLG ($n = 73$) groups, respectively ($P = 0.081$ by log-rank test). The two groups did not differ significantly. Abbreviations: MLG, multi-port laparoscopic gastrectomy; SLG, single-port laparoscopic gastrectomy

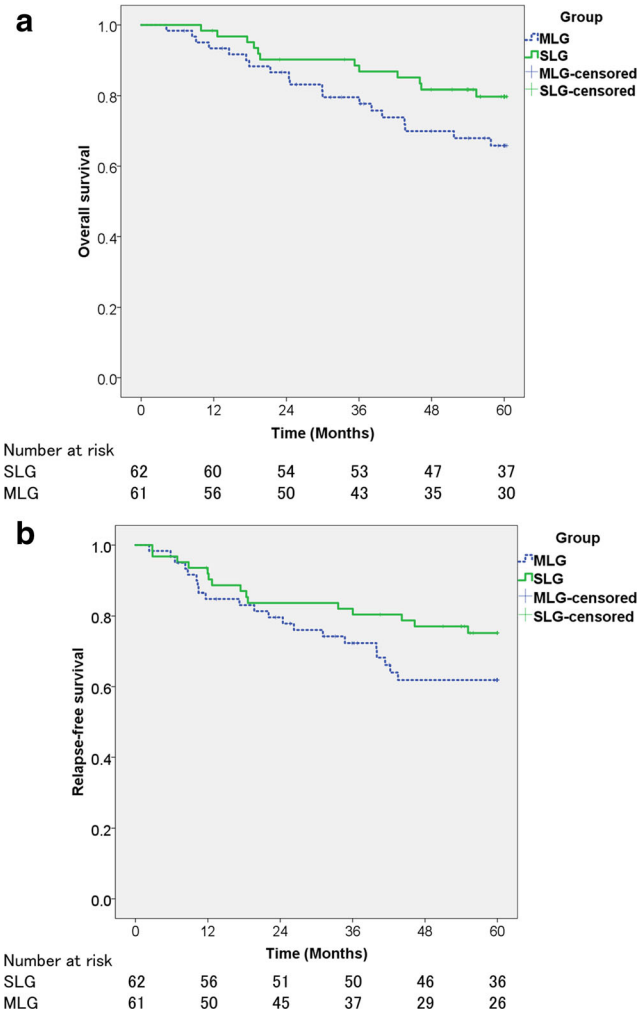

Fig. 3 Cumulative and relapse-free survival curves of patients undergoing SLG and MLG for pStage II/III gastric cancer. **a** Cumulative overall survival curve: The 5-year survival rates were 79.7 and 65.8% in the SLG ($n = 62$) and MLG ($n = 61$) groups, respectively ($P = 0.091$ by log-rank test). The two groups did not differ significantly. **b** Relapse-free survival curve: The 5-year relapse-free survival rates were 75.2 and 61.9%, respectively ($P = 0.125$ by log-rank test). The two groups did not differ significantly. Abbreviations: MLG, multi-port laparoscopic gastrectomy; pStage, pathological stage; SLG, single-port laparoscopic gastrectomy

proven AGC. Cases underwent distal or total gastrectomy, with or without splenectomy. Our results showed that SLG and MLG had comparable operative times, but that there was reduced blood loss, reduced morbidity, and shortened hospital stays in the SLG group, without compromising oncologic adequacy. In a subgroup analysis of patients who underwent total gastrectomy, we showed that both the operative time and blood loss were comparable between the groups, but that the morbidity rate was lower in the SLG group. Compared with conventional MLG, we therefore concluded that SLG was a feasible and safe approach for the treatment of AGC in both total and distal gastrectomy.

It is reasonable to expect that the increased difficulty of SLG may lead to prolonged operative times, increased blood losses, and higher morbidity rates. However, compared with the MLG group, not only were postoperative complication rates significantly lower in our SLG group but also operative times were comparable. Specifically, there were no anastomotic leakages or pancreas-related complications in the SLG group. A large, multi-institutional, prospective randomized study reported an overall postoperative complication rate of 15.2% when using MLG to treat AGC.[24] In a multi-institutional prospective phase II feasibility study, MLG with D2 lymphadenectomy for AGC was associated with either anastomotic leakage or pancreatic fistula in 4.7% and grade III systemic and local complications in 5.8%.[23] In our study, the overall postoperative complication rate was significantly lower in the SLG group than in the MLG group, and the severe morbidity rate in the SLG group was lower compared with that reported for MLG in this and previous reports. Indeed, the SLG procedure may be a more precise, delicate, and efficient by tracing the layer between the organ and the lymph node. This minimal and careful manipulation of preserved tissues/organs likely accounted for the reduced tissue/organ damage, decreased blood loss, and lower morbidity seen with the less-invasive single-port approach.

Minimally invasive surgery has been associated with shorter hospital stays. Consistent with this, the mean postoperative hospital stay in our SLG group was significantly shorter than that in our MLG group. When interpreting this result, however, it should be remembered that the length of hospital stay may be affected by medical insurance and clinical pathways, so does not necessarily reflect an implicit benefit of minimally invasive surgery. Nevertheless, it does confirm the feasibility of SLG for the treatment of AGC.

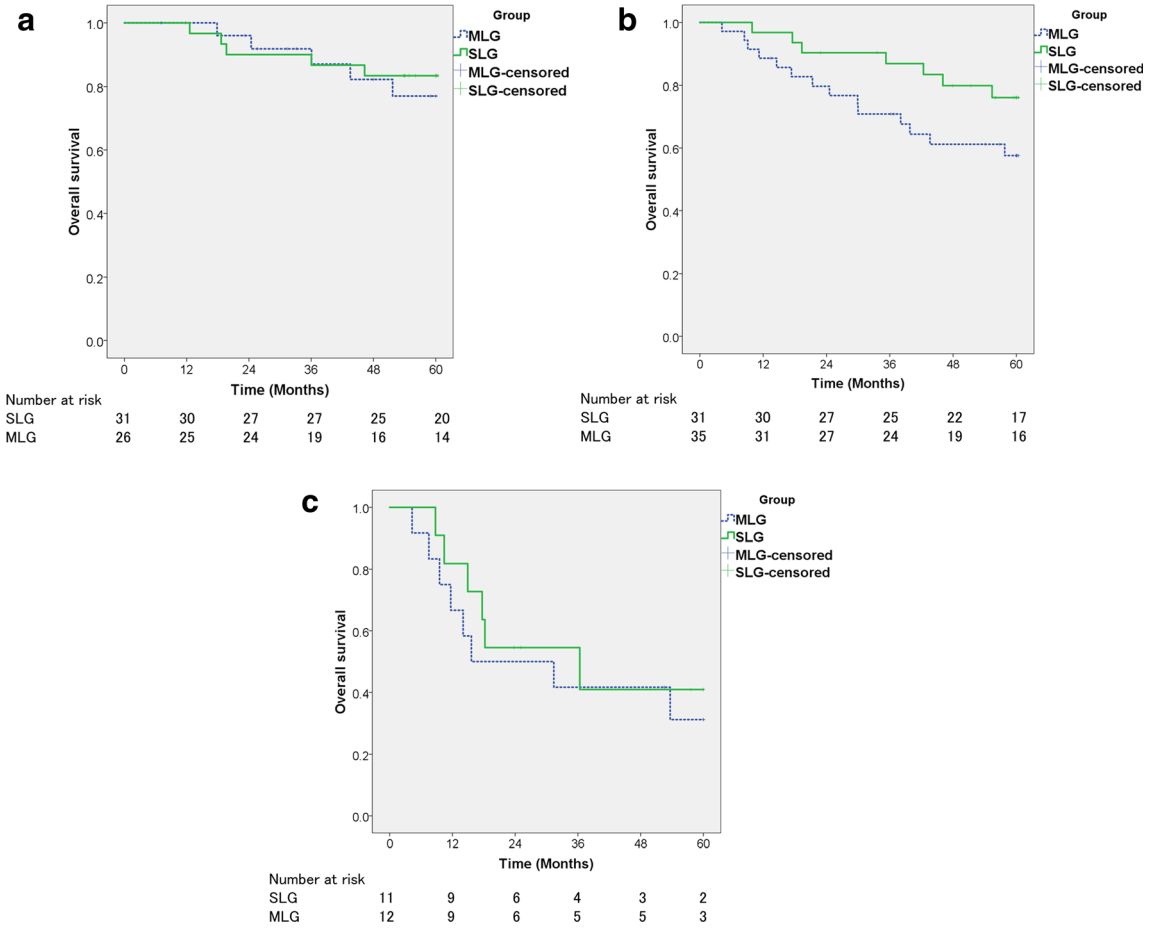

Fig. 4 Cumulative Survival Curves for SLG and MLG by pStage. **a** Cumulative survival curve for pStage II gastric cancer: There was no significant difference between the SLG ($n = 31$) and MLG ($n = 26$) groups (83.3 and 77.0%, respectively; $P = 0.685$ by log-rank test). **b** Cumulative survival curve for pStage III gastric cancer: The survival rate tended to be higher in the SLG group ($n = 31$) than MLG group ($n = 35$) (76.1% vs. 57.6%; $P = 0.099$ by log-rank test). **c** Cumulative survival curve for pStage IV gastric cancer: The survival rate was similar between the SLG ($n = 11$) and MLG ($n = 12$) groups (40.9% vs. 31.3%; $P = 0.578$ by log-rank test). Abbreviations: MLG, multi-port laparoscopic gastrectomy; pStage, pathological stage; SLG, single-port laparoscopic gastrectomy

In terms of oncologic safety, several retrospective and prospective studies have shown that long-term outcomes for AGC, including the 5-year overall survival, are comparable between laparoscopic and open gastrectomy.[19,32–36] In the present study, the overall survival did not differ significantly between the SLG and MLG groups either for all pathological stages, but survival in AGCs appeared to be better in the SLG group than in the MLG group (Fig. 2) or individually for pathological stages III (Fig. 4b). Although the reasons for this result are difficult to explain, it has been reported that postoperative complications seem to be an independent prognostic factor after gastric cancer treated with curative resection.[37] In our study, the 5-year overall survival was lower in patients with morbidity ($n = 19$) than in those without morbidity ($n = 127$) ($P < 0.001$, data not shown). The overall postoperative complication rate was significantly lower in the SLG group than in the MLG group. Thus, single-port approaches might help improve long-term outcomes by reducing complication rates compared with multi-port approaches.

This study has several limitations that should be considered when interpreting the data. First, although the analyses were performed after propensity score matching, residual confounding could have been introduced by other differences between the two groups, such as a period of operation. The first single-incision laparoscopic distal gastrectomy for gastric cancer was performed in our institute in 2009. Since then, the indications for single incision laparoscopic gastrectomy included all of gastric cancer. The frequency of SLG increased during the study period, whereas the frequency of MLG decreased. Therefore, during the analyzed period, MLG was performed mainly in the early period (2007–2009) and SLG performed mainly in the late period (2010–2013). Second, this study was retrospective and had a small sample size, requiring further evaluation of long-term outcomes. Ideally, a large-scale randomized controlled study is needed to confirm the oncological feasibility of single-port approach.

In conclusion, distal or total SLG with radical lymph node dissection is shown to be a safe and feasible procedure for

patients with AGC. Specifically, SLG facilitates reduced surgical invasiveness, minimal scarring, and faster postoperative recovery, with acceptable oncologic outcomes. Although SLG may be an attractive minimally invasive option for the treatment of AGC, large-scale prospective randomized trials are required to confirm its feasibility and effectiveness.

Author Contribution Omori designed the study and wrote the initial draft of the manuscript. Omori and Fujiwara contributed to the interpretation of the data and to the critical revision of the manuscript for important intellectual content. All the other authors (Yamamoto, Yanagimoto, Sugimura, Masuzawa, Kishi, Takahashi, Yasui, Miyata, Ohue, Yano, and Sakon) contributed to data collection and interpretation and critical review of the manuscript. All the authors have read and approved the final version of the manuscript and have agreed to the accountability of all aspects of the study, ensuring that any queries related to the accuracy or integrity of any part of the work are answerable.

Compliance with Ethical Standards

This study was approved by the Institutional Review Board of the Osaka Police Hospital. All patients signed a written informed consent. Data collection and analysis were performed in compliance with the Helsinki Declaration of 1975.

Conflict of Interests Drs. Takeshi Omori, Yoshiyuki Fujiwara, Kazuyoshi Yamamoto, Yoshitomo Yanagimoto, Keijirou Sugimura, Toru Masuzawa, Kentarou Kishi, Hidenori Takahashi, Masayoshi Yasui, Hiroshi Miyata, Masayuki Ohue, Masahiko Yano, and Masato Sakon have no conflicts of interest or financial ties to declare.

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