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Comparison of the long-term outcomes of robotic radical gastrectomy for gastric cancer and conventional laparoscopic approach: a single institutional retrospective cohort study

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Abstract
Background Robotic gastrectomy (RG) for gastric cancer (GC) has been increasingly performed over the last decade. The technical feasibility and safety of RG for GC, predominantly early GC, have previously been reported; however, few studies have evaluated the oncological outcomes. This study aimed to determine the long-term outcomes of RG for GC compared with those of conventional laparoscopic gastrectomy (LG).
Methods Of the 521 consecutive patients with GC who underwent radical gastrectomy at our institution between 2009 and 2012, 84 consecutive patients who underwent RG and 437 patients who received LG were enrolled in this study. Long-term outcomes including the 3-year overall survival (3yOS) and 3-year recurrence-free survival rates (3yRFS) were examined retrospectively.
Results In the RG group, the 3yOS rates stratified by pathological stage according to the Japanese classification of gastric carcinoma (IA, IB, II, and III) were 94.7, 90.9, 89.5, and 62.5 %, respectively. No differences in 3yOS (RG, 86.9 % vs. LG, 88.8 %; $p = 0.636$) or 3yRFS (RG, 86.9 % vs. LG, 86.3 %; $p = 0.905$) were observed between the groups. 3yOS was strongly associated with cancer recurrence within 3 years ($p < 0.001$), while 3yRFS was associated with tumor size $\geq$ 30 mm ($p < 0.001$), clinical stage $\geq$ IB ($p < 0.001$), estimated blood loss $\geq$ 50 mL ($p = 0.033$), and postoperative pancreatic fistula CD grade $\geq$ III) ($p = 0.035$).
Conclusions RG for GC was feasible and safe from the oncological point of view in a cohort including a considerable number of patients with advanced GC.

Keywords Gastric cancer · Robotic gastrectomy · Retrospective cohort study · Pancreatic fistula · Long-term outcomes

Abbreviations

RG	Robotic gastrectomy
GC	Gastric cancer
JCGC	Japanese classification of gastric carcinoma
CD	Clavien–Dindo classification
POPF	Postoperative pancreatic fistula
LG	Laparoscopic gastrectomy
3yOS	3-Year overall survival rates
3yRFS	3-Year recurrence-free survival rates
LN	Lymph node
RDG	Robotic distal gastrectomy
RTG	Robotic total gastrectomy
LDG	Laparoscopic distal gastrectomy
LTG	Laparoscopic total gastrectomy

Gastric cancer is the fourth most common malignant tumor and second leading cause of cancer-related death worldwide [1]. Surgical resection remains the only curative treatment option, with regional lymphadenectomy recommended as part of radical gastrectomy [2]. Laparoscopic gastrectomy (LG) for gastric cancer (GC) is currently supported by a considerable number of studies that have demonstrated its safety, feasibility, and association with favorable oncological outcomes compared with open surgical procedures [3, 4].

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The Da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) has recently been used to overcome some of the disadvantages of LG. Since Giulianotti performed the first robot-assisted distal gastrectomy in 2001 [5], there have been an increasing number of reports demonstrating the safety and feasibility of robotic gastrectomy (RG) for GC, predominantly focusing on early GC, in terms of short-term outcomes. However, there is a lack of studies reporting the long-term outcomes of RG [6–8]. We have performed more than 240 RGs for GC since 2009, establishing a stable and robust methodology [9, 10]. In our previous retrospective study, in which a considerable number of patients with advanced GC were enrolled, we demonstrated the potential advantage of RG, indicating that the use of robotic assistance may reduce postoperative local complications, including pancreatic fistula, compared with LG [10]. Subsequently, we have continuously evaluated the long-term outcomes of this patient cohort. Thus, the present study was designed to determine the oncological feasibility and safety of RG for GC.

Materials and methods

Patients

We conducted a single-institution retrospective comparative cohort study between January 2009 and December 2012. The patient selection process has been summarized in Fig. 1. All medical records of the 526 patients enrolled in our previous study were precisely reviewed to retrospectively determine preoperative disease stage. As a result, five patients (robotic, $n = 4$ and laparoscopic, $n = 1$) were found to have preoperative Stage IV disease. Thus, 521 patients (robotic, $n = 84$ and laparoscopic, $n = 437$) with preoperative ≤Stage III GC were enrolled in the present study. All patients were evenly offered robotic surgery without considering their backgrounds including physical and oncological status. Patients who agreed to uninsured use of the Da Vinci S HD Surgical System underwent RG ($n = 84$), whereas the remaining patients, who refused non-insured use of the surgical robot, underwent LG with health insurance coverage ($n = 437$). Thus, a patient in RG group had to be charged 2,200,000 JPY during perioperative admission, whereas a patient in LG group was charged 80,100 + (medical expense – 267,000) × 0.01 JPY/month during perioperative admission [11, 12]. Patients were observed for at least 3 years following surgical resection. The following long-term outcomes were assessed: 3-year overall survival rates (3yOS); 3-year recurrence-free survival rates (3yRFS); sites of recurrence; late complications; and short-term surgical outcomes, including clinicopathological characteristics, operative time, estimated blood loss, early complications within 30 days after surgery, length of postoperative hospital stay, and the number of harvested LNs. The primary endpoint was 3yOS. Survival was estimated from the date of initial diagnosis of GC. Short-term outcomes were re-examined in the same manner as reported previously [10, 13]. All operations were supervised by I.U. RG was performed by I.U., S.K., and S.S who had performed more than 100 laparoscopic D2 gastrectomy procedures, whereas LG was either performed or guided by these three surgeons. All participating surgeons had previously performed ≥30 LG procedures. Details of indications for radical gastrectomy, assessment of physical function, operative procedures, perioperative management in radical gastrectomy, extent of gastric resection and LN dissection, type of anastomosis, diagnosis and treatment for pancreatic fistula, and postoperative chemotherapy in addition to oncologic follow-up have previously been reported [10, 13–15]. Patients were completely involved in the decision-making process, and informed consent was obtained from all patients. The present study was approved by the Institutional Review Board of Fujita Health University.

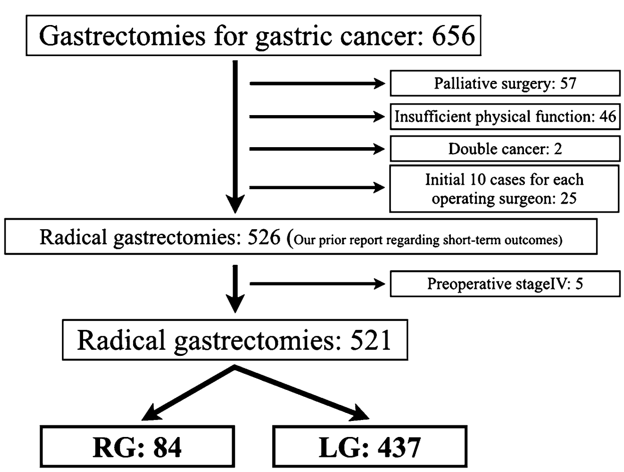

Fig. 1 Flow diagram of the study selection process. *RG* robotic gastrectomy, *LG* laparoscopic gastrectomy

Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics 22 (IBM Corporation, Armonk, NY). Independent continuous variables were compared using the Mann–Whitney *U* test, one-way ANOVA, or Kruskal–Wallis test. Categorical variables were compared using the χ^2 (Chi-square) test or Fisher's exact test. Long-term outcomes were analyzed using the Kaplan–Meier method with the log-rank test and Cox regression analyses. Univariate analyses were performed for all potential confounding variables and effect modifiers. Considering the relatively small sample size, all variables with a significance level of

$p < 0.05$ in the univariate analysis were included as independent variables. Data were expressed as the median (range) or odds/hazard ratio (OR/HR; 95 % confidence interval), unless otherwise stated. p values of <0.05 (two-tailed) were considered to be statistically significant.

Results

Patient characteristics

Patient characteristics have been summarized in Table 1. No significant differences in body mass index, comorbidities (American Society of Anesthesiologists Physical Status (ASA-PS) [16] comorbidities Class $\geq$ 2), history of laparotomy, tumor size, postoperative chemotherapy, and preoperative Japanese classification of gastric carcinoma (JCGC) stage [17] were observed between the RG and LG groups. However, significant differences were indicated in the gender (male vs. female; RG, 48:36 vs. LG, 307:130; $p = 0.018$), age (RG, mean 64 years; range 37–89 years vs. LG, mean 68 years, range 33–87 years; $p = 0.013$), and use of preoperative chemotherapy (RG, 10.7 % vs. LG, 20.4 %; $p = 0.038$).

Surgical outcomes and short-term postoperative courses

Surgical outcomes and short-term postoperative courses are summarized in Table 1. In the RG group, operative times were slightly longer (RG, 378 min vs. LG, 361 min; $p = 0.010$), estimated blood loss was greater (RG, 44 mL vs. LG, 33 mL; $p = 0.045$), and hospital stays were shorter (RG, 14 days vs. LG, 15 days; $p = 0.017$) compared with the LG group. The extent of resection, lymphadenectomy, and type of reconstruction were similar between groups. There were no cases requiring conversion to open procedures in either group. No differences in the number of dissected lymph nodes, number of metastatic lymph nodes, pathological JCGC stage, reoperation rate, and mortality were observed between groups. No patients required repeat surgery in the RG group, whereas seven (1.6 %) patients underwent repeat surgery in the LG group.

Table 1 Characteristics, surgical outcomes, and pathological findings of enrolled patients

	RG $n = 84$	LG $n = 437$	p value
Patients characteristics			
Gender (M/F)	48/36	307/130	0.018**
Age (y/o)	64 [37–89]	68 [33–87]	0.013***
Body mass index (kg/m^2)	22.6 [14.7–30.5]	21.8 [14.5–35.3]	0.620***
Comorbidity [n (%)]	43 (51.2)	243 (55.6)	0.456**
History of laparotomy [n (%)]	17 (20.2)	112 (25.6)	0.294**
Tumor size (mm)	30 [3–190]	30 [0–190]	0.618***
Neoadjuvant chemotherapy [n (%)]	9 (10.7)	89 (20.4)	0.038**
Adjuvant chemotherapy [n (%)]	28 (33.3)	135 (30.9)	0.687**
Clinical JCGC* stage (IA/IB/II/III/IV)	43/18/10/12/1	240/70/80/42/5	0.336**
Surgical outcomes			
Extent of resection (DG/TG)	57/27	301/136	0.853**
Lymphadenectomy (D1/D2)	35/49	232/205	0.055**
Type of reconstruction (RY/BI/BII)	30/27/27	183/165/89	0.059**
Operative time (min)	378 [200–853]	361 [147–779]	0.010***
Console time (min)	322 [154–785]	None	
Estimated blood loss (mL)	44 [1–935]	33 [0–1017]	0.045***
No. of dissected LNs	40 [17–95]	38 [8–109]	0.113***
Conversion to open procedure [n (%)]	0 (0)	0 (0)	
Hospital stay (days)	14 [2–31]	15 [8–136]	0.017***
Reoperation [n (%)]	0 (0.0)	7 (1.6)	0.290**
In-hospital mortality [n (%)]	1 (1.2)	1 (0.2)	0.297**
Pathological findings			
No. of metastatic LNs	0 [0–35]	0 [0–37]	0.534***
Pathological JCGC* stage (CR/IA/IB/II/III/IV)	0/38/11/19/16/0	6/239/41/80/71/0	0.363**

* Japanese classification of gastric carcinoma 14th; ** χ^2 test; *** Mann–Whitney test

Early and late postoperative complications

Postoperative complications have been summarized in Table 2. Within 30 days following surgical treatment, the rates of overall complications classified according to Clavien–Dindo classification (CD) grade [18] ≥III (RG, 2.4 % vs. LG, 11.7 %; $p = 0.010$), local complications (RG, 1.2 % vs. LG, 10.1 %; $p = 0.008$), and pancreatic fistula (RG, 0 % vs. LG, 4.2 %; $p = 0.033$) were significantly greater in the LG group than in the RG group. No significant differences in anastomotic leakage (RG, 0 % vs. LG, 2.5 %; $p = 0.142$) or intra-abdominal abscess (RG, 0 % vs. LG, 0.9 %; $p = 0.494$) were observed between groups. Rates of systemic complications were similar between the two groups. One patient in each group died after surgery (one case of pulmonary embolism in the RG group and one case of intra-abdominal bleeding in the LG group). Regarding late complications classified as CD grade ≥ III, internal hernia occurred in 5 (1.1 %) patients in the LG group; all these patients required surgical treatments. In contrast, no late complications were observed in the RG group.

Three-year long-term outcomes

Three-year long-term outcomes are shown in Fig. 2. Fifty-one patients were censored (RG, $n = 10$; LG, $n = 41$, $p = 0.467$). The follow-up period was 40.5 months (range 1.1–75.8 months) in the RG group and 42.2 months (range 1.7–78.9 months) in the LG group ($p = 0.437$). Cumulative 3yOS rates in the RG and LG groups were 86.9 and 88.8 %, respectively ($p = 0.636$). Two patients in the RG group and nine patients in the LG group died during follow-up, with no relation to cancer recurrence. Cumulative 3yRFS rates in the RG and LG groups were 86.9 and 86.3 %, respectively ($p = 0.905$). 3yOS rates stratified according to the pathological JCGC stage (pIA, pIB, pII, and pIII) were 94.7, 90.9, 89.5, and 62.5 % in the RG group, and 96.2 % ($p = 0.653$), 95.1 % ($p = 0.597$), 83.8 % ($p = 0.543$), and 64.8 % ($p = 0.989$) in the LG group, respectively. 3yRFS rates stratified according to the pathological JCGC stage (pIA, pIB, pII, and pIII) were 100.0, 81.8, 89.5, and 56.3 %, in the RG group and 98.7 % ($p = 0.491$), 97.6 % ($p = 0.051$), 76.3 % ($p = 0.205$), and 47.9 % ($p = 0.629$) in the LG group, respectively. Collectively, no significant differences in long-term outcomes were observed between the LG and RG groups.

Sites of tumor recurrence

Sites of tumor recurrence within 3 years following surgical resection have been given in Table 3. In the RG group, 11 (13.1 %) patients developed tumor recurrence compared with 60 (13.7 %) in the LG group ($p = 0.908$). Peritoneal dissemination was the most common type of recurrence in both groups (RG, 7.1 % vs. LG, 7.6 %). Similar profiles for sites of recurrence were observed between groups. Notably, no local recurrence or loco-regional LN metastasis was observed in the RG group.

Factors associated with 3-year long-term outcomes

To investigate the factors determining long-term outcomes, univariate and multivariate analyses were conducted. Univariate analyses revealed that age (≥70 years old; $p = 0.025$), history of laparotomy ($p = 0.022$), tumor size (≥30 mm; $p < 0.001$), clinical stage (≥IB; $p < 0.001$), estimated blood loss (≥50 mL; $p < 0.001$), duration hospital stay (≥15 days; $p = 0.006$), extent of resection ($p < 0.001$), type of lymphadenectomy ($p = 0.034$), type

Table 2 Early and late complications (Clavien–Dindo grade ≥ III)

	RG	LG	p value*
Early complications [n (%)]	2 (2.4)	51 (11.7)	0.01
Local [n (%)]	1 (1.2)	44 (10.1)	0.008
Anastomotic leakage [n (%)]	0 (0)	11 (2.5)	0.142
Pancreatic fistula [n (%)]	0 (0)	19 (4.3)	0.033
Intra-abdominal abscess [n (%)]	0 (0)	4 (0.9)	0.494
Small bowel obstruction [n (%)]	1 (1.2)	4 (0.9)	0.586
Wound infection [n (%)]	0 (0)	1 (0.2)	0.839
Systemic [n (%)]	1 (1.2)	11 (2.5)	0.398
Pneumonia [n (%)]	0 (0)	6 (1.4)	0.346
Pulmonary embolism [n (%)]	1 (1.2)	2 (0.5)	0.411
Cardiac disease [n (%)]	0 (0)	1 (0.2)	0.839
Late complication (internal hernia) [n (%)]	0 (0)	5 (1.1)	0.414

* χ^2 test

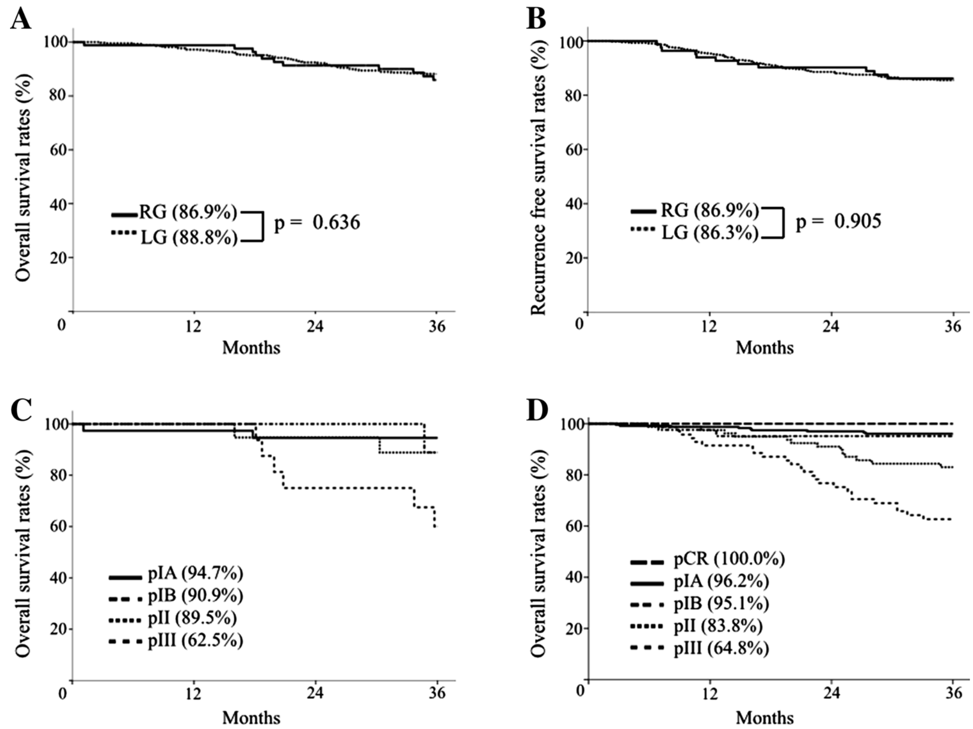

Fig. 2 3yOS and 3yRFS (Kaplan–Meier method, log-rank test). **A** 3yOS in RG and LG groups; **B** 3yRFS in RG and LG groups; **C** 3yOS stratified according to pathological stage in the RG group; **D** 3yOS stratified according to pathological stage in the LG group. *OS* overall survival, *RFS* recurrence-free survival

Table 3 Recurrence sites

	RG	LG	*p* value*
Total	11 (13.1)	60 (13.7)	0.908
Peritoneum [*n* (%)]	6 (7.1)	33 (7.6)	0.896
Liver [*n* (%)]	2 (2.4)	12 (2.7)	0.601
Distant lymph nodes [*n* (%)]	1 (1.2)	7 (1.6)	0.621
Local site [*n* (%)]	0 (0)	1 (0.2)	0.839
Regional lymph nodes [*n* (%)]	0 (0)	1 (0.2)	0.839
Lung [*n* (%)]	0 (0)	1 (0.2)	0.839
Bone [*n* (%)]	1 (1.2)	2 (0.5)	0.411
Others [*n* (%)]	1 (1.2)	3 (0.7)	0.506

* χ^2 test

of reconstruction ($p = 0.001$), morbidity (CD grade $\geq$ III; $p = 0.025$), early postoperative local complications (CD grade $\geq$ III; $p = 0.018$), postoperative pancreatic fistula (CD grade $\geq$ III; $p = 0.046$), postoperative intra-abdominal abscess (CD grade $\geq$ III; $p = 0.016$), and any tumor recurrence $\leq$ 3 years following surgical resection ($p < 0.001$) were associated with 3yOS. Multivariate analysis demonstrated that tumor recurrence $\leq$ 3 years following surgical resection was the only significant factor associated with 3yOS (HR 40.635; 95 % CI 21.026–78.533; $p < 0.001$). Regarding the 3yRFS, univariate analyses demonstrated that tumor size ($\geq$30 mm; $p < 0.001$), clinical stage ($\geq$IB, $p < 0.001$), estimated blood loss ($\geq$50 mL; $p < 0.001$), operative time ($\geq$400 min; $p = 0.003$), hospital stay ($\geq$15 days; $p = 0.006$), the number of dissected lymph nodes ($\geq$40; $p = 0.017$), extent of resection ($p < 0.001$), type of lymphadenectomy ($p < 0.001$), type of reconstruction ($p = 0.001$), early postoperative local complications (CD grade $\geq$ III, $p = 0.019$), and postoperative pancreatic fistula (CD grade $\geq$ III, $p = 0.013$) were associated with 3yRFS. Multivariate analysis demonstrated tumor size $\geq$30 mm (HR 4.328; 95 % CI 1.950–9.604; $p < 0.001$), clinical stage $\geq$ IB(HR 8.022; 95 % CI 3.406–18.896; $p < 0.001$), estimated blood loss $\geq$ 50 mL (HR 1.684; 95 % CI 1.044–2.717; $p = 0.033$), and postoperative pancreatic fistula (CD grade $\geq$ III; HR 2.480; 95 % CI 1.068–5.760; $p = 0.035$) as factors significantly associated with 3yRFS.

Subgroup analyses

To examine the learning curve effect, subgroup analysis was conducted by dividing each group into two groups. The first half of the series (G1) comprised 42 RGs and 218 LGs. The second half of the series (G2) comprised 42 RGs versus 219 LGs. There were no differences in the operating surgeons' level of experience [no. of the patients who operated by the expert (three RG surgeons who are more experienced in minimally invasive surgery) versus those who operated by the non-expert surgeons (the remaining surgeons)], clinical stage, type of resection, extent of lymph node dissection, total complication, and postoperative pancreatic fistula between G1 and G2

Table 4 Comparison between the first group (G1) and the second group (G2): a differences in backgrounds and short-term outcomes between G1 and G2; b differences in operative time and estimated blood loss between G1 and G2 stratified by the type of operation

a	G1 ($n = 260$)	G2 ($n = 261$)	p value*
Expert:non-expert	113:147	94:167	0.082
cStage I:II:III	185:47:23:5	186:43:31:1	0.093
DG:TG	187:73	171:90	0.115
D1 + :D2	138:122	129:132	0.404
Total complications [n (%)]	25 (9.6)	28 (10.7)	0.674
Postoperative pancreatic fistula [n (%)]	9 (3.5)	10 (3.8)	0.822

b	Operative time (min)			Estimated blood loss (mL)		
	G1	G2	p value**	G1	G2	p value**
RDG [28 (G1) versus 29 (G2)]	373 [200–592]	325 [255–490]	0.009	47 [4–147]	32 [1–97]	0.027
LDG [159 (G1) versus 142 (G2)]	313 [147–634]	352 [182–585]	0.007	35 [0–702]	23 [0–460]	>0.001
RTG [14 (G1) versus 13 (G2)]	477 [352–853]	511 [429–667]	0.488	67 [32–935]	78 [10–403]	0.458
LTG [59 (G1) versus 77 (G2)]	415 [256–779]	470 [228–765]	0.004	80 [0–1017]	50 [0–621]	0.034

Expert cases shows no. of the patients who operated by the expert (three RG surgeons who are more experienced in minimally invasive surgery), whereas non-expert cases demonstrates those who operated by the non-expert surgeons (the remaining surgeons). * χ^2 test

** Mann–Whitney test

RDG robotic distal gastrectomy, *LDG* laparoscopic distal gastrectomy, *RTG* robotic total gastrectomy, *LTG* laparoscopic total gastrectomy

(Table 4a). Operative time and estimated blood loss were analyzed by stratifying according to the extent of resection (G1, 28 RDGs, 159 LDGs, 14 RTGs, and 59 LTGs; G2, 29 RDGs, 142 LDGs, 13 RTGs, and 77 LTGs; Table 4b). Operative time in the RDG group was significantly reduced from G1 to G2 (373 min vs. 325 min; $p =$ 0.004), whereas the operative time markedly increased in the LDG group (313 min vs. 352 min; $p = 0.007$). Regarding estimated blood loss, significant reductions were observed in the RDG (47 mL vs. 32 mL; $p = 0.027$), LDG (35 mL vs. 23 mL; $p < 0.001$) and LTG (80 mL vs. 50 mL; $p = 0.034$) groups. No significant differences in either factor were observed in the RTG group.

Regarding neoadjuvant chemotherapy (NAC), the present series demonstrated that greater pathological efficacy of NAC was associated with increased survival (NAC effect grade, 0, 1a, 1b, 2, and 3; 3yOS, 66.7, 66.7, 82.6, 88.2, and 100.0 %, respectively; 3yRFS, 66.7, 54.5, 60.9, 88.2, and 100.0 %, respectively). Pathological responders to NAC (grade $\geq$ 1b) had better 3yOS ($p = 0.026$) and 3yRFS ($p = 0.047$) compared with non-responders to NAC (grade 0 or 1a).

To investigate the influence of the operating surgeon's level of experience on the outcomes, short- and long-term outcomes were compared between the expert surgeons and the non-expert surgeons. Then, no significant differences were observed in short- and long-term outcomes given in Table 5.

Discussion

This retrospective comparison study, which comprised a considerable number of patients with advanced GC (RG group, 41.7 %; LG group, 34.6 %; overall, 35.7 %), clearly demonstrates the potential advantages of RG according to short- and long-term outcomes [19–22]. Four major findings were yielded by the present study.

First, RG demonstrated similar long-term outcomes with lower early morbidity compared with LG. To date, a considerable number of studies, including our previous reports, have investigated the short-term outcomes of RG for GC [6, 10, 19–21, 23–25]. According to previous reports, the use of robot assistance resulted in increased operative durations [6, 10, 19–21, 24, 25], smaller estimated blood loss [6, 19–21, 23–25], comparable in-hospital stay durations [6, 19, 24], and similar [20, 25] or decreased morbidity [6, 10, 19] compared with LG. The results of the present study corroborate these previous studies, except that estimated blood loss in the RG group was slightly greater than that in the LG group. RG slightly increased blood loss, possibly because we preferably used the bipolar devises in RG in order to fully utilize the robotic dexterity with articulating function. Actually, bipolar cautery has relatively lower hemostability compared with the ultrasonic laparoscopic coagulation shears and the vessel sealing systems, which we usually use in LG [10, 27]. However, median blood loss of 44 mL in RG was deemed to be acceptable considering the results of the previous

Table 5 Comparison of the outcomes between the expert and non-expert surgeons

	Expert surgeons ($n = 207$)	Non-expert surgeons ($n = 314$)	p value
Short-term outcomes [n (%)]			
Total complication	19 (9.2)	34 (10.8)	0.542*
Local complication	16 (7.7)	29 (9.2)	0.549*
Pancreatic fistula	8 (3.9)	11 (3.5)	0.829*
Leakage	3 (1.4)	8 (2.5)	0.300*
Intra-abdominal abscess	0 (0)	4 (1.3)	0.131*
Systemic complication	4 (1.9)	8 (2.5)	0.445*
Long-term outcomes			
3yOS (%)	85.5	90.4	0.098**
3yRFS (%)	83.6	88.2	0.156**

3yOS, 3-year overall survival rates; 3yRFS, 3-year recurrence-free survival rates

* Mann–Whitney test; ** log-rank test

studies [6, 19–21, 23–25]. It is particularly striking that there were no cases of pancreatic fistula in the RG group in the present study. In contrast, there have been only a few studies reporting the long-term outcomes of RG, at least partly because only a decade has passed since the development of this technology [6–8]. Consistent with previous studies, the present study demonstrated similar 3yOS and 3yRFS between the RG and LG groups; these are acceptable outcomes considering previous reports [8, 26]. Regarding tumor recurrence, recurrence rates stratified according to stage and recurrence sites were similar between the two groups. These results indicate that RG for GC was at least as feasible and safe as LG from both surgical and oncological perspectives.

Second, the only important factor associated with 3yOS was tumor recurrence according to the results of multivariate analysis. Thus, 3yRFS rates were assessed to remove the influence of tumor recurrence on survival. Accordingly, oncological factors including tumor size ($\geq$30 mm) and clinical stage of $\geq$ IB and surgical factors including postoperative pancreatic fistula (CD grade $\geq$ III) were found to be associated with 3yRFS. These results were consistent with those of our previous report demonstrating that postoperative local complications may negatively affect long-term outcomes [27], indicating the oncological as well as surgical importance of preventing pancreatic fistula. Large prospective studies are required to determine the efficacy of robotic gastrectomy in reducing pancreatic fistula and potential of improving long-term outcomes.

Third, several reports have demonstrated the short learning curve of RG. Eleven to 25 five cases of surgical experiences are required to overcome the learning curve of RG [28]. This positive effect was at least partly corroborated in the present study as demonstrated by the significant reductions in operative duration after performing 28 robotic distal gastrectomies, although the initial 10 cases of each operating surgeon were excluded from the present study.

Fourth, RG may be more compatible with multimodal treatment than LG. In the present cohort, NAC was identified as a significant risk factor determining postoperative complications in the LG group, but not in the RG group [10]. Although NAC was not found to contribute to long-term outcomes in the present study, future improvements in response rates to NAC may lead increased survival durations as NAC responders were observed to have better outcomes than non-responders.

There were several limitations to the present study. This study was conducted at a single-institution in a retrospective manner. The sample size, particularly in the RG group, was relatively small, and the observation period was relatively short. Therefore, data may be biased and the overall results should be interpreted with caution. First, as described in our prior report [10], patient selection was achieved based on whether or not the patient agreed with the uninsured use of robot-assisted surgery, which may have caused selection bias induced by a possibility of preference for RG in patients with higher economic status; however, this was the best we could do at the time of study enrollment, because the use of the Da Vinci Surgical System was not covered by medical insurance in Japan, whereas conventional laparoscopic gastrectomy was covered. In fact, the Japanese government prohibits joint provision of medical treatments covered by public health insurance and those not covered. Therefore, only the patients in the RG group were required to pay for all the medical fees charged during the perioperative hospital stay. Second, there were some between-group differences in patient backgrounds such as gender, age, and the use of neoadjuvant chemotherapy, which might be confounders in this study. To control for this confounding, multivariate analysis was conducted to determine the factors contributing to long-term outcomes. Third, there might be a concern for a bias possibly induced by the difference in operating surgeons' level of experience. No significant differences were observed in short- and long-term outcomes at least between the expert and non-expert surgeons.

In this form of single-institution retrospective study with limited sample size, it is quite difficult to eliminate these biases even by using a case–control model matching not only patients' physical and oncological factors but also operating surgeons' factors, which may provide with more statistically reliable outcomes. Therefore, based on the outcomes of our present study, we have been conducting a multi-institutional single-arm prospective trial which has been approved for Advanced Medical Technology ("senshiniryo") by the Japanese Ministry of Health, Labor and Welfare since the beginning of October 2014. This clinical trial is designed to determine the impact of the use of the robot, for minimally invasive radical gastrectomy to treat resectable GC, on short-term outcomes, mainly focusing on postoperative complications, as well as long-term outcomes and cost [29]. The specific hypothesis of this study is that the use of the robot in patients with cStage I or II diseases reduces the morbidity of 6.4 % down to 3.2 %. To prove this hypothesis, a single-arm study will be conducted using the historical control (morbidity of 6.4 % in LG previously performed in three leading hospitals in our country). In the prospective arm, RG will be done for consecutive patients with cStage I or II GC. The sufficient sample size is calculated to be 330. All the patients will be registered in 2 years after starting this trial and followed up for 3 years; thus, the expected study period should be 5 years in total. Interim analyses will be done once the initial 220 cases are registered. To control for the safety and quality of robotic operations, the institutions and the operating surgeons have to meet the following requirements: institutions, at least one year after launching RG, performed more than 20 RGs including not less than 5 total gastrectomies, performed more than 50 LGs during the past 4 years, morbidity (C–D Grade $\geq$ III) in LGs during the past 4 years $\leq$ 12 %; operating surgeons, endoscopic surgical skill qualification system: qualified surgeon (Japan Society for Endoscopic Surgery), Board Certified Surgeon in Gastroenterology (the Japanese Society of Gastroenterological Surgery), Certificate of Da Vinci Surgical System Off-Site Training as a Console Surgeon, performed more than 10 RGs including not less than 1 RTG. The operating surgeon's level of robotic skill is also examined by reviewing a non-edited video recording RTG before participating in the trial.

In conclusion, RG for GC was found to be feasible and safe from both surgical and oncological perspectives. The use of robotic assistance is associated with decreased early morbidity, particularly reduced risk of pancreatic fistula, and comparable long-term outcomes. As RG may be more compatible with multimodal treatment, RG represents a promising minimally invasive approach for the treatment of advanced GC.

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Compliance with ethical standards

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