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Retrospective Cohort Study

Prognostic factors of minimally invasive surgery for gastric cancer:
Does robotic gastrectomy bring oncological benefit?

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Abstract

BACKGROUND

Gastric cancer is the third leading cause of cancer-related death worldwide and surgical resection remains the sole curative treatment for gastric cancer. Minimally invasive gastrectomy including laparoscopic and robotic approaches has been increasingly used in a few decades. Thus far, only a few reports have investigated the oncological outcomes following minimally invasive gastrectomy.

AIM

To determine the 5-year survival following minimally invasive gastrectomy for gastric cancer and identify prognostic predictors.

METHODS

This retrospective cohort study identified 939 patients who underwent gastrectomy for gastric cancer during the study period. After excluding 125 patients with non-curative surgery ($n = 77$), other synchronous cancer ($n = 2$), remnant gastric cancer ($n = 25$), insufficient physical function ($n = 13$), and open gastrectomy ($n = 8$), a total of 814 consecutive patients with primary gastric cancer who underwent minimally invasive R0 gastrectomy at our institution between 2009 and 2014 were retrospectively examined. Accordingly, 5-year overall and recurrence-free survival were analyzed using the Kaplan-Meier method with the log-rank test and Cox regression analyses, while factors associated with survival were determined using multivariate analysis.

RESULTS

Our analysis showed that age > 65 years, American Society of Anesthesiologists

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(ASA) physical status 3, total or proximal gastrectomy, and pathological T4 and N positive status were independent predictors of both 5-year overall and recurrence-free survival. Accordingly, the included patients had a 5-year overall and recurrence-free survival of 80.3% and 78.2%, respectively. Among the 814 patients, 157 (19.3%) underwent robotic gastrectomy, while 308 (37.2%) were diagnosed with pathological stage II or III disease. Notably, our findings showed that robotic gastrectomy was an independent positive predictor for recurrence-free survival in patients with pathological stage II/III [hazard ratio: 0.56 (0.33-0.96), $P = 0.035$]. Comparison of recurrence-free survival between the robotic and laparoscopic approach using propensity score matching analysis verified that the robotic group had less morbidity ($P = 0.005$).

CONCLUSION

Age, ASA status, gastrectomy type, and pathological T and N status were prognostic factors of minimally invasive gastrectomy, with the robot approach possibly improving long-term outcomes of advanced gastric cancer.

Key Words: Laparoscopy; Gastric cancer; Minimally invasive surgery; Prognostic factor; Stomach neoplasms

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Core Tip: This retrospective cohort study on 814 patients undergoing minimally invasive surgery for primary gastric cancer revealed a 5-year overall and recurrence-free survival of 80.3% and 78.2%, respectively. Moreover, our analysis identified age, American Society of Anesthesiologists status, type of gastrectomy, and pathological T and N status as prognostic predictors for overall and recurrence-free survival. The robotic approach was also identified as an independent positive predictor for recurrence-free survival in patients with pathological stage II/III disease, confirmed by the lesser morbidity in the robotic group following propensity score analysis.

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INTRODUCTION

Gastric cancer is the fifth most common malignancy and the third leading cause of cancer-related death worldwide[1]. Surgical resection remains the sole curative treatment for gastric cancer, with regional lymphadenectomy being recommended as a component of radical gastrectomy[2]. Laparoscopic gastrectomy has been increasingly used, considering its better short-term effects and comparable long-term outcomes compared to open gastrectomy[2].

The da Vinci surgical system (DVSS; Intuitive Surgical, Sunnyvale, CA, United States) had been developed to overcome several disadvantages identified for standard minimally invasive laparoscopic surgery[2]. Most laparoscopic surgeons expect that utilizing the DVSS for gastric surgery would allow them to overcome the technical difficulties of laparoscopic gastrectomy, thereby improving its safety, reproducibility, teachability, and long-term outcomes. However, only one large, nonrandomized prospective study (NCT01309256) has compared DVSS with laparoscopic gastrectomy. Accordingly, the study results mentioned above demonstrated that DVSS had higher operative time and cost than laparoscopic gastrectomy with no difference in morbidity, suggesting that DVSS might reduce cost-effectiveness[3]. Concurrently, robotic gastrectomy, which has been actively used for operable patients with resectable gastric cancer at the patient's own expense[2], was introduced at our institution in 2009. Analysis of patient outcomes following robotic gastrectomy had demonstrated that its morbidity was approximately one-fifth of that observed with

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laparoscopic gastrectomy, with such a reduction in morbidity, including decreased incidences of postoperative pancreatic fistula, certainly improving the short-term postoperative course[2]. Moreover, our previous study had compared the oncological outcomes, particularly 3-year survival rates, between robotic gastrectomy and laparoscopic gastrectomy[2]. Thus far, only a few reports have investigated the oncological outcomes following robotic gastrectomy, considering that DVSS remains a relatively new technology. Therefore, the current study aimed to determine the prognostic factors of minimally invasive gastrectomy, including laparoscopic and robotic procedures.

MATERIALS AND METHODS

Patients

This single-center retrospective cohort study included patients who underwent curative gastrectomy for gastric cancer at our institution between January 2009 and September 2014. The inclusion criteria were patients with primary gastric adenocarcinoma who underwent curative resection using minimally invasive surgery (MIS). The exclusion criteria were patients with other synchronous cancer and those whose resection was limited due to poor physical functioning. Among the 939 patients who underwent gastrectomy for gastric cancer during the study period, 125 were excluded due to non-curative surgery ($n = 77$), other synchronous cancer ($n = 2$), remnant gastric cancer ($n = 25$), insufficient physical function ($n = 13$), and open gastrectomy ($n = 8$). Thus, the 814 patients who satisfied the study criteria were ultimately analyzed. The clinicopathological variables collected included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status classification, date of surgery, type of approach, histologic type, lymphovascular invasion status, TNM staging (Japanese Gastric Cancer Association classification, 14th edition), number of harvested lymph nodes, postoperative complications determined by Clavien-Dindo (C-D) classification[4], date of the first recurrence, and date and status of the last follow-up. The extent of gastrectomy and lymphadenectomy was defined based on Japanese gastric cancer treatment guidelines[5]. Overall survival (OS) was calculated from the date of resection to the date of the last follow-up or death of any cause. Recurrence-free survival (RFS) was calculated from the date of resection to the date of first recurrence, last follow-up, or death of any cause, whichever occurred first. Details regarding indications for radical gastrectomy, including the selection of laparoscopic or robotic approach, surgical procedures, perioperative management, adjuvant chemotherapy, and oncologic follow-up, have been previously reported[2]. Neoadjuvant chemotherapy (NAC) (S-1 80 mg/m² days 1-21 + CDDP 60 mg/m² day 8 or S-1 80 mg/m² days 1-28) was offered to patients with clinical T ≥ 2 , tumor size ≥ 5 cm, and/or swollen locoregional lymph nodes ≥ 1.5 cm[2]. All patients were uniformly offered robotic surgery without considering their backgrounds, including physical and oncological status. Patients who agreed to the uninsured use of the surgical robot underwent robotic gastrectomy, whereas those who wished for insured treatment underwent laparoscopic gastrectomy[2]. All patients were completely involved in the decision-making process and provided informed consent prior to participation. All surgical procedures were performed or guided by surgeons qualified by the Japanese Society for Endoscopic Surgical Skill Qualification System, initiated in 2004 by the Japanese Society for Endoscopic Surgery to develop a tool for the reliable and reproducible evaluation of trainees' surgical techniques[6]. All procedures were supervised by an expert gastric surgeon (I.U.) who had performed more than 1500 Laparoscopic gastrectomies and 400 robotic gastrectomies. This study was approved by the institutional review board of Fujita Health University.

Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics 25 (IBM Corporation, Armonk, NY, United States). Long-term outcomes were analyzed using the Kaplan-Meier method with the log-rank test and Cox regression analyses. Considering our relatively small sample size, multivariate analysis was conducted using all variables determined to be significant ($P < 0.1$) during univariate analysis as independent variables. Data were expressed as median, interquartile range, or hazard ratio (HR) with the 95% confidence interval (CI) unless otherwise stated. A P value of < 0.05 (two-tailed) was considered statistically significant. Propensity score matching analysis was used to reduce selection bias with regard to potential confounding factors when establishing the laparoscopic and robotic groups. Possible confounders were

selected based on their potential association with the outcome of interest according to clinical knowledge. Therefore, clinicopathological characteristics (age, BMI, sex, ASA status, pathological T and N factor, type of surgery, tumor size, and NAC) were used to adjust differences between the laparoscopic and robotic groups through one-to-one pair matching using optimal match without replacement. Propensity scores were matched using a caliper width 1/5 Logit of the standard deviation. The absolute standardized difference was used to measure covariate balance, in which an absolute standardized mean difference above represented a meaningful imbalance[7]. Independent continuous variables were compared using the Mann-Whitney *U* test or Kruskal-Wallis test. Categorical variables were compared using the χ^2 test or Fisher's exact test.

RESULTS

Patient characteristics

Table 1 summarizes the characteristics of all patients included herein. Accordingly, the included patients had a median age of 68 years, among whom 31.4% ($n = 256$) were diagnosed with clinical stage II or more disease, while 14.6% ($n = 119$) underwent NAC. Laparoscopic and robotic gastrectomy was performed in 657 (80.7%) and 157 (19.3%) patients, respectively. None of the patients required intraoperative conversion to open procedure from MIS. Pathological stage II and III disease was diagnosed in 160 (19.7%) and 148 (18.2%) patients, respectively. Morbidity of C-D grade \geq III was observed in 72 patients (8.8%).

Survival outcomes

The median follow-up period was 59.5 mo, while the 5-year OS and RFS were 80.3% and 78.2%, respectively (**Figure 1A** and **B**). Patients with pStage I, II, and III had a 5-year OS of 91.9%, 76.3%, and 43.7%, and a 5-year RFS of 91.6%, 74.7%, and 36.0%, respectively.

Factors related to survival

Univariate analysis identified age > 65 years, ASA status 3, total or proximal gastrectomy, D2 lymphadenectomy, tumor size > 30 mm, lymphovascular invasion, C-D grade \geq III morbidity, NAC administration, adjuvant chemotherapy administration, and higher pT and pN status as factors significantly associated with OS (**Table 2**). However, multivariate analysis revealed that only age > 65 years [HR: 1.62 (1.09-2.40), $P = 0.017$], ASA status 3 [HR: 1.91 (1.18-3.10), $P = 0.009$], total or proximal gastrectomy [HR: 1.45 (1.03-2.05), $P = 0.036$], pT4 [HR: 4.31 (2.37-7.82), $P < 0.001$], and pN positive status were significantly and independently associated with OS (**Table 2**). Similarly, multivariate analysis identified age > 65 years [HR: 1.48 (1.02-2.14), $P = 0.038$], ASA status 3 [HR: 1.62 (1.02-2.60), $P = 0.043$], total or proximal gastrectomy [HR: 1.55 (1.12-2.15), $P = 0.009$], pT4 [HR: 4.20 (2.38-7.41), $P < 0.001$], and pN positive status as factors significantly and independently associated with RFS (**Table 3**). Moreover, multivariate analysis showed that robotic approach could likely be a positive predictor for RFS, although no significant association was observed [HR 0.68 (0.44-1.06), $P = 0.088$] (**Table 3**).

Survival outcomes following the laparoscopic and robotic approach

The laparoscopic and robotic approach had a 5-year OS of 79.4% and 83.4% ($P = 0.243$) and a 5-year RFS of 76.9% and 84.2% ($P = 0.085$), respectively. No significant difference in the 5-year OS and RFS was noted between both groups for patients with pStage I (91.6% *vs* 93.4%, $P = 0.471$ and 91.4% *vs* 92.7%, $P = 0.634$) (**Figure 2A** and **B**). Notably, among patients with pStage II/III, those in the robotic group had significantly better RFS compared to those in the laparoscopic group (74.1% *vs* 51.7%, $P = 0.006$) (**Figure 2D**), although no significant difference in the 5-year OS was observed ($P = 0.071$) (**Figure 2C**).

Factors associated with survival in pStage II/III diseases

Our analysis showed that pT4 [HR: 4.02 (1.21-13.42), $P = 0.024$] and pN positive status were significantly and independently associated with OS. Notably, univariate analysis showed that robotic gastrectomy ($P = 0.007$), total or proximal gastrectomy ($P = 0.004$), tumor size > 30 mm ($P = 0.014$), pT4 ($P = 0.007$), and pN positive status were significantly associated with RFS. Meanwhile, multivariate analysis found that robotic

Table 1 Clinicopathological characteristics of the entire cohort

Variables	<i>n</i> = 814
Age, yr [IQR]	68[61-74]
Sex, <i>n</i> (%)	
Male	562 (69.0)
Female	252 (31.0)
BMI, kg/m ² [IQR]	22.2 [20.0-24.1]
ASA, <i>n</i> (%)	
1	314 (38.6)
2	396 (48.6)
3	104 (12.8)
Clinical stage, <i>n</i> (%)	
I	558 (68.6)
II	125 (15.3)
III	121 (14.9)
IV	10 (1.2)
Neoadjuvant chemotherapy, <i>n</i> (%)	119 (14.6)
Neoadjuvant radiotherapy, <i>n</i> (%)	0 (0)
Approach, <i>n</i> (%)	
Laparoscopic	657 (80.7)
Robotic	157 (19.3)
Type of gastrectomy, <i>n</i> (%)	
Distal	559 (68.7)
Total	238 (29.2)
Proximal	16 (2.0)
Pylorus preserving	1 (0.1)
Lymphadenectomy, <i>n</i> (%)	
D1+	378 (46.4)
D2	436 (53.6)
Dissected nodes, <i>n</i> [IQR]	38[28-48]
Tumor size, mm [IQR]	30[20-50]
pT, <i>n</i> (%)	
1	469 (57.6)
2	87 (10.7)
3	112 (13.8)
4	138 (17.0)
CR	8 (1.0)
pN, <i>n</i> (%)	
0	559 (68.7)
1	98 (12.0)
2	79 (9.7)
3	78 (9.6)
pStage, <i>n</i> (%)	

I	498 (61.2)
II	160 (19.7)
III	148 (18.2)
TCRNany	8 (1.0)
WHO histologic type, <i>n</i> (%)	
Tub/pap	402 (49.4)
Por/sig	352 (43.2)
Mixed/other	60 (7.4)
Lymphovascular invasion, <i>n</i> (%)	531 (65.2)
Adjuvant chemotherapy, <i>n</i> (%)	242 (29.7)
Adjuvant radiotherapy, <i>n</i> (%)	0 (0)
Morbidity (C–D grade \geq III), <i>n</i> (%)	
Anastomotic leakage	22 (2.7)
Pancreatic fistula	30 (3.7)

Categorical and continuous data are presented as *n* (%) and median [IQR], respectively. IQR: Interquartile range; ASA: American Society of Anesthesiologists; BMI: Body mass index; CR: Complete response at the primary site; C-D: Clavien-Dindo classification.

gastrectomy was independently and positively associated with RFS [HR: 0.56 (0.33–0.96), $P = 0.035$]. Apart from robotic gastrectomy, only pT4 and pN positive status were identified as factors independently associated with RFS (Table 4).

Comparison between robotic and laparoscopic gastrectomy in pStage II/III diseases

To account for confounding factors between both groups, propensity score matching was performed (Table 5). In the prematched cohort of 308 patients with pStage II/III disease, 67 and 241 patients belonged to the robotic and laparoscopic groups, respectively. After matching, each group comprised 61 patients. The matched cohort had a considerably better balance of covariates, with < 0.245 of the cutoff value of an absolute standardized difference. In the postmatched cohort, no differences in clinicopathological variables were observed between the laparoscopic and robotic groups, although the robotic group had lower morbidity (4.9% *vs* 16.4%, $P = 0.04$) (Table 5). Furthermore, the robotic group had significantly better 5-year OS (70.4% *vs* 50.2%, $P = 0.039$) and RFS (74.1% *vs* 44.5%, $P = 0.005$) than the laparoscopic group in the postmatched cohort (Figure 3A and B).

DISCUSSION

The current study clearly identified factors related to survival in patients with gastric cancer who underwent MIS, subsequently presenting three significant findings.

First, the present study highlighted the feasibility and safety of MIS for gastric cancer as determined by the 5-year outcomes. While the long-term outcomes of laparoscopic surgery have been increasingly reported in recent years, only a few studies have investigated the long-term outcomes of the robotic approach[2,8,9]. Consistent with previous studies, including those from our group, the current study demonstrated no significant difference in OS and RFS between the laparoscopic and robotic approaches [2,8,9]. However, among patients with pStage II/III, those in the robotic group demonstrated significantly better RFS than those in the laparoscopic group ($P = 0.006$).

Second, our results showed that pT and pN status was independently associated with both OS and RFS. Currently, multidisciplinary treatment for gastric cancer utilizing various chemotherapeutic options has been developed worldwide. In Western countries, neoadjuvant and adjuvant chemotherapy combined with curative resection has been the standard treatment for advanced gastric cancer[10,11], whereas adjuvant chemotherapy following curative resection remains the standard approach in Japan[5]. Regardless of treatment options, however, evidence has shown that the pN factor is consistently strongly associated with survival following gastric cancer treatment[12–14]. The results of the current study are consistent with those presented

Table 2 Factors associated with overall survival for the entire cohort (*n* = 814)

	Univariate			Multivariate		
	HR	95%CI	P	HR	95%CI	P
Age > 65 yr	1.46	1.04–2.06	0.031	1.62	1.09–2.40	0.017
Female sex	0.75	0.52–1.09	0.129			
BMI > 23 kg/m ²	0.77	0.55–1.07	0.123			
ASA						
1	1			1		
2	0.96	0.68–1.38	0.837	1.06	0.72–1.57	0.753
3	1.97	1.27–3.05	0.003	1.91	1.18–3.10	0.009
Neoadjuvant chemotherapy	1.84	1.27–2.67	0.001	1.34	0.88–2.04	0.166
Robotic approach	0.77	0.50–1.21	0.258			
Type of gastrectomy						
Distal/pylorus-preserving	1			1		
Total/proximal	2.17	1.58–2.99	< 0.001	1.45	1.03–2.05	0.036
D2 lymphadenectomy	1.86	1.32–2.61	< 0.001	0.87	0.57–1.33	0.528
Tumor > 30 mm	3.23	2.20–4.75	< 0.001	1.05	0.66–1.69	0.832
WHO histologic type						
Tub/pap	1			1		
Por/sig/mixed/other	1.54	1.12–2.13	0.009	1.26	0.89–1.78	0.190
Lymphovascular invasion	4.38	2.68–7.17	< 0.001	1.17	0.60–2.26	0.651
pT						
1	1			1		
2	2.82	1.62–4.91	< 0.001	1.72	0.90–3.27	0.099
3	3.03	1.82–5.03	< 0.001	1.54	0.82–2.91	0.184
4	9.78	6.54–14.60	< 0.001	4.31	2.37–7.82	< 0.001
CR	1.67	0.23–12.17	0.613	1.34	0.16–10.97	0.784
pN						
0	1			1		
1	2.76	1.74–4.39	< 0.001	2.02	1.22–3.34	0.007
2	4.05	2.56–6.41	< 0.001	1.97	1.15–3.36	0.013
3	8.08	5.40–12.10	< 0.001	2.92	1.79–4.78	< 0.001
Adjuvant chemotherapy	3.27	2.37–4.50	< 0.001	1.21	0.80–1.82	0.371
Morbidity (C-D grade ≥ III)	1.85	1.18–2.91	0.008	1.27	0.79–2.05	0.325

HR: Hazard ratio; CI: Confidence interval; ASA: American Society of Anesthesiologists; BMI: Body mass index; CR: Complete response at the primary site; C-D: Clavien–Dindo classification.

in previous studies.

Third, the use of the surgical robot was significantly associated with improved RFS among propensity score-matched patients with pStage II/III disease. This could have been attributed to lower morbidity in the robotic gastrectomy group, a causal relationship between morbidity and survival, and higher morbidity in patients undergoing surgery for advanced disease. First, a few studies have shown that robotic gastrectomy was technically safe and feasible but did not have superior morbidity compared to the laparoscopic approach[3]. However, Wang *et al*[15] who compared morbidity between robotic and laparoscopic gastrectomy using propensity score-

Table 3 Factors associated with recurrence-free survival for the entire cohort (n = 814)

	Univariate			Multivariate		
	HR	95%CI	P	HR	95%CI	P
Age > 65 yr	1.33	0.97–1.84	0.076	1.48	1.02–2.14	0.038
Female sex	0.76	0.54–1.06	0.108			
BMI > 23 kg/m ²	0.77	0.56–1.05	0.100			
ASA						
1	1			1		
2	0.95	0.68–1.32	0.761	1.08	0.75–1.55	0.692
3	1.67	1.09–2.55	0.018	1.62	1.02–2.60	0.043
Neoadjuvant chemotherapy	1.91	1.34–2.71	< 0.001	1.39	0.93–2.08	0.104
Robotic approach	0.69	0.45–1.06	0.087	0.68	0.44–1.06	0.088
Type of gastrectomy						
Distal/pylorus-preserving	1			1		
Total/proximal	2.24	1.66–3.02	< 0.001	1.55	1.12–2.15	0.009
D2 lymphadenectomy	2.08	1.50–2.86	< 0.001	0.99	0.66–1.48	0.957
Tumor > 30 mm	3.19	2.23–4.56	< 0.001	0.95	0.61–1.48	0.827
WHO histologic type						
Tub/pap	1			1		
Por/sig/mixed/other	0.54	0.14–2.08	0.005	1.20	0.86–1.66	0.284
Lymphovascular invasion	4.93	3.06–7.94	< 0.001	1.29	0.69–2.43	0.430
pT						
1	1			1		
2	2.87	1.69–4.85	< 0.001	1.57	0.85–2.89	0.148
3	3.42	2.13–5.48	< 0.001	1.60	0.89–2.89	0.120
4	10.62	7.26–15.53	< 0.001	4.20	2.38–7.41	< 0.001
CR	1.41	0.19–10.24	0.737	0.96	0.12–7.77	0.967
pN						
0	1			1		
1	3.08	1.99–4.77	< 0.001	2.23	1.39–3.58	0.001
2	5.01	3.29–7.62	< 0.001	2.24	1.36–3.70	0.002
3	8.92	6.07–13.11	< 0.001	3.32	2.06–5.34	< 0.001
Adjuvant chemotherapy	3.53	2.62–4.77	< 0.001	1.18	0.80–1.73	0.410
Morbidity (C-D grade ≥ III)	1.69	1.09–2.62	0.019	1.04	0.65–1.67	0.868

ASA: American Society of Anesthesiologists; BMI: Body mass index; CR: Complete response at the primary site; C-D: Clavien–Dindo classification; HR: Hazard ratio; CI: Confidence interval.

matched analysis, reported that the robotic group exhibited significantly lower morbidity, particularly with regard to infectious complications (*e.g.*, anastomotic leakage and intra-abdominal abscess)[15]. Furthermore, a multicenter, prospective, single-arm study by our group recently reported that robotic gastrectomy promoted lesser morbidity than laparoscopic gastrectomy among historical controls[2]. Similarly, the present study showed that the robotic group had significantly lesser morbidity compared to the laparoscopic in the postmatched cohort. Second, several studies have demonstrated that morbidity was associated with worse survival in gastric cancer[16–19]. In fact, Jin *et al*[16] reported that patients with and without postoperative complica-

Table 4 Factors associated with recurrence-free survival for patients with pathological stage II/III disease (n = 308)

	Univariate			Multivariate		
	HR	95%CI	P	HR	95%CI	P
Age > 65 yr	1.04	0.73–1.48	0.848			
Female sex	1.08	0.75–1.58	0.673			
BMI > 23 kg/m ²	0.69	0.47–1.00	0.052	0.92	0.62–1.35	0.657
ASA						
1	1					
2	0.82	0.56–1.19	0.297			
3	1.07	0.63–1.80	0.809			
Neoadjuvant chemotherapy	1.37	0.93–2.01	0.114			
Robotic approach	0.50	0.30–0.83	0.007	0.56	0.33–0.96	0.035
Type of gastrectomy						
Distal/pylorus-preserving	1			1		
Total/proximal	1.67	1.18–2.37	0.004	1.32	0.91–1.90	0.145
D2 lymphadenectomy	1.26	0.80–2.00	0.320			
Tumor > 30 mm	2.17	1.17–4.03	0.014	1.34	0.69–2.60	0.303
WHO histologic type						
Tub/pap	1			1		
Por/sig/mixed/other	1.38	0.95–2.00	0.089	1.29	0.88–1.90	0.197
pT						
1	1			1		
2	1.82	0.60–5.53	0.292	1.33	0.42–4.23	0.628
3	1.32	0.47–3.75	0.6	1.45	0.49–4.30	0.505
4	3.96	1.45–10.83	0.007	3.52	1.23–10.07	0.019
pN						
0	1			1		
1	2.07	1.16–3.69	0.014	2.86	1.57–5.24	0.001
2	2.24	1.29–3.90	0.004	2.45	1.38–4.34	0.002
3	3.74	2.21–6.32	< 0.001	3.25	1.88–5.61	< 0.001
Adjuvant chemotherapy	1.37	0.92–2.04	0.119			
Morbidity (C-D grade ≥ III)	1.58	0.97–2.58	0.066	1.22	0.73–2.05	0.453

ASA: American Society of Anesthesiologists; BMI: Body mass index; C-D: Clavien–Dindo classification; HR: Hazard ratio; CI: Confidence interval.

ations had RFS rates of 23% and 40%, respectively ($P < 0.001$). Third, advanced gastric cancer requires complicated procedures, which can cause more complications. Notably, studies have reported that patient with advanced disease had morbidity rates of 8.3%–15.2% following minimally invasive gastrectomy, respectively[20,21]. The aforementioned findings therefore indicate that utilizing surgical robots, which cause less morbidity, might at least partly contribute to the better RFS in patients with advanced gastric cancer, suggesting that surgical robots may be more beneficial for patients with advanced disease. However, although univariate analysis found morbidity to be significantly associated with RFS, multivariate analysis did not identify the same as a significant independent factor associated with RFS in the entire cohort. As such, further investigations are warranted to confirm such findings.

The current study has several limitations worth noting. First, this study was retrospective in nature and involved only a single institution. Moreover, the sample

Table 5 Clinicopathological characteristics of pStage II/III patients in the pre- and postmatched cohort

	Prematched			Postmatched			
	Lap (n = 241)	Robotic (n = 67)	P	ASD	Lap (n = 61)	Robotic (n = 61)	P ASD
Sex, n (%)			0.132	0.204			0.580 0.100
Male	174 (72.2)	42 (62.7)			35 (57.4)	38 (62.3)	
Female	67 (27.8)	25 (37.3)			26 (42.6)	23 (37.7)	
Age, yr [IQR]	69 [61–75]	65 [60–77]	0.134	0.235	68 [61–75]	65 [60–77]	0.824 0.042
BMI, kg/m ² [IQR]	21.6 [19.2–23.7]	23.1 [20.0–24.8]	0.008	0.329	22.6 [20.4–24.9]	23.0 [20.0–24.9]	0.810 0.007
ASA, n (%)			0.074	0.315			0.959 0.052
1	89 (36.9)	35 (52.2)			31 (50.8)	30 (49.2)	
2	118 (49.0)	24 (35.8)			23 (37.7)	23 (37.7)	
3	34 (14.1)	8 (11.9)			7 (11.5)	8 (13.1)	
Neoadjuvant chemotherapy, n (%)	61 (25.3)	11 (16.4)	0.128	0.220	10 (16.4)	11 (18.0)	0.810 0.043
Type of gastrectomy, n (%)			0.075	0.329			1 < 0.001
Distal	136 (56.4)	48 (71.6)			42 (68.9)	42 (68.9)	
Total	104 (43.2)	19 (28.4)			19 (31.1)	19 (31.1)	
Proximal	1 (0.4)	0 (0)			0 (0)	0 (0)	
Tumor size, mm [IQR]	50[35–70]	40[30–63]	0.026	0.265	50 [35–77]	43 [30–65]	0.192 0.187
pT, n (%)			0.042	0.391			0.860 0.158
1	11 (4.6)	8 (11.9)			4 (6.6)	6 (9.8)	
2	35 (14.5)	4 (6.0)			4 (6.6)	4 (6.6)	
3	85 (35.3)	27 (40.3)			21 (34.4)	23 (37.7)	
4	110 (45.6)	28 (41.8)			32 (52.5)	28 (45.9)	
pN, n (%)			0.15	0.338			0.617 0.244
0	65 (27.0)	24 (35.8)			16 (26.2)	22 (36.1)	
1	48 (19.9)	15 (22.4)			17 (27.9)	13 (21.3)	
2	68 (28.2)	10 (14.9)			9 (14.8)	10 (16.4)	
3	60 (24.9)	18 (26.9)			19 (31.1)	16 (26.2)	
pStage, n (%)			0.246				0.716
II	121 (50.2)	39 (58.2)			32 (52.5)	34 (55.7)	
III	120 (49.8)	28 (41.8)			29 (47.5)	27 (44.3)	
Dissected nodes, n [IQR]	44 [35–53]	43 [35–51]	0.858		45 [35–54]	43 [30–65]	0.556
WHO histological type, n (%)			0.667				0.229
Tub/pap	88 (36.5)	27 (41.8)			17 (27.9)	26 (42.6)	
Por/sig	129 (53.5)	34 (50.7)			37 (60.7)	30 (49.2)	
Mixed/other	24 (10.0)	5 (7.5)			7 (11.5)	5 (8.2)	
Lymphovascular invasion, n (%)	241 (100)	66 (98.5)	0.218		61 (100)	60 (98.4)	0.5
Adjuvant chemotherapy, n (%)	161 (66.8)	47 (70.1)	0.605		38 (62.3)	43 (70.5)	0.338
Morbidity (C-D grade ≥ III), n (%)	31 (12.9)	3 (4.5)	0.053		10 (16.4)	3 (4.9)	0.04

Categorical and continuous data are presented as n (%) and median [IQR], respectively. ASA: American Society of Anesthesiologists; BMI: Body mass

index; CR: Complete response at the primary site; C-D: Clavien-Dindo classification; ASD: Absolute standardized mean difference.

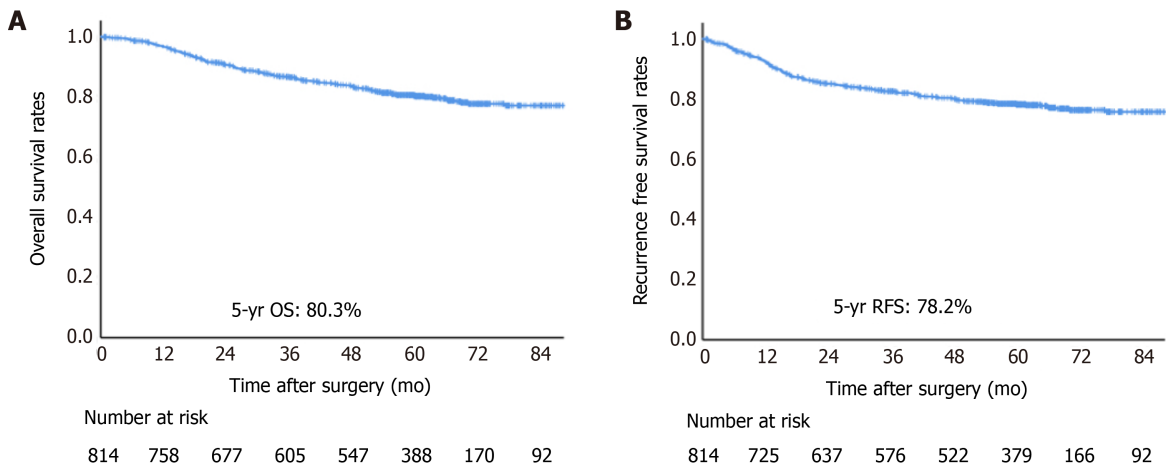


Figure 1 Kaplan-Meier curves. Kaplan-Meier estimates in the entire cohort A: Overall survival probability; B: Recurrence-free survival probability. OS: Overall survival; RFS: Recurrence-free survival.

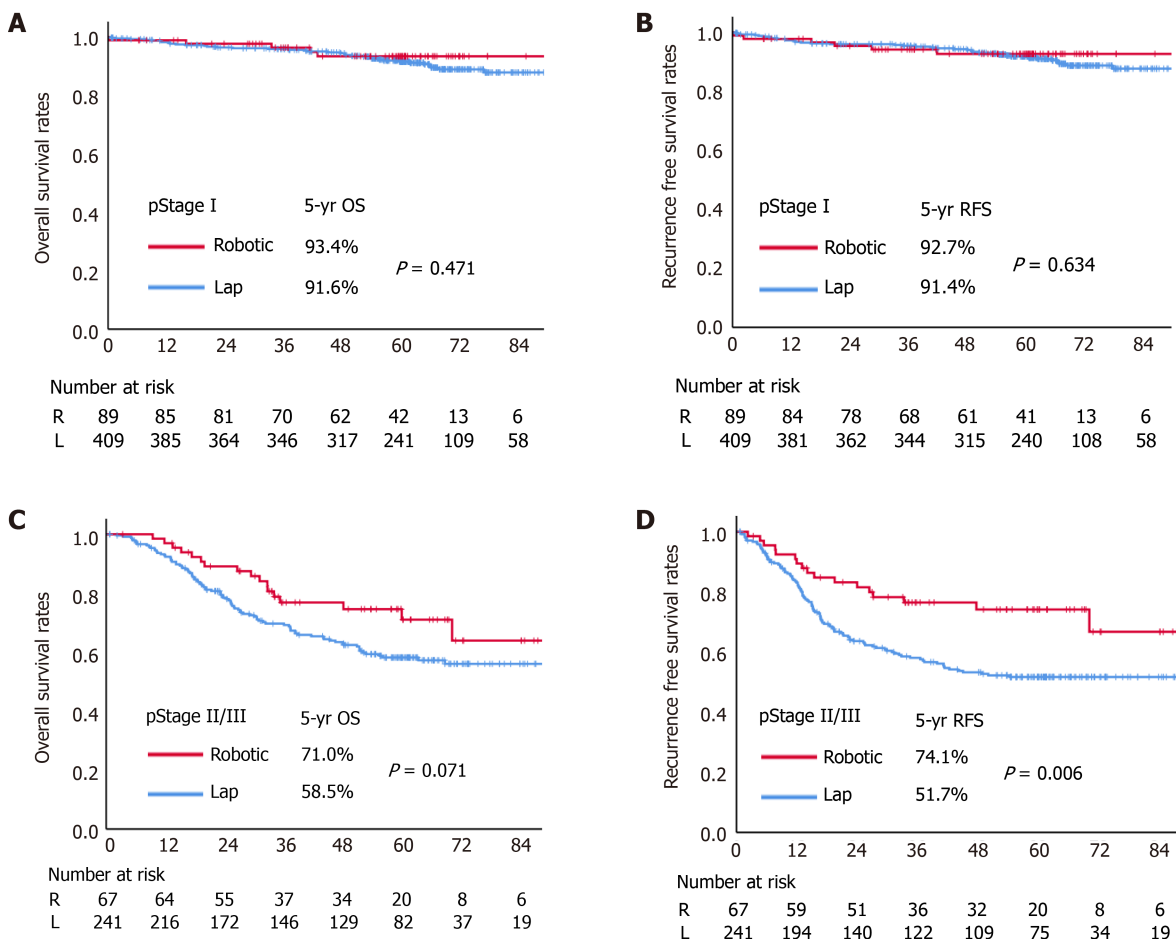


Figure 2 Kaplan-Meier curves. A and C: Kaplan-Meier estimates of overall survival probability for pathological stage I and II/III, B and D: Kaplan-Meier estimates of recurrence-free survival probability for pathological stage I and II/III. OS: Overall survival; RFS: Recurrence-free survival.

size, particularly that of the robotic group, was relatively small. Therefore, given that biases may exist in our data, the overall results should be interpreted with caution. As described in our previous reports[2,6], patients were selected according to whether they agreed to the uninsured use of robot-assisted surgery, which may have caused

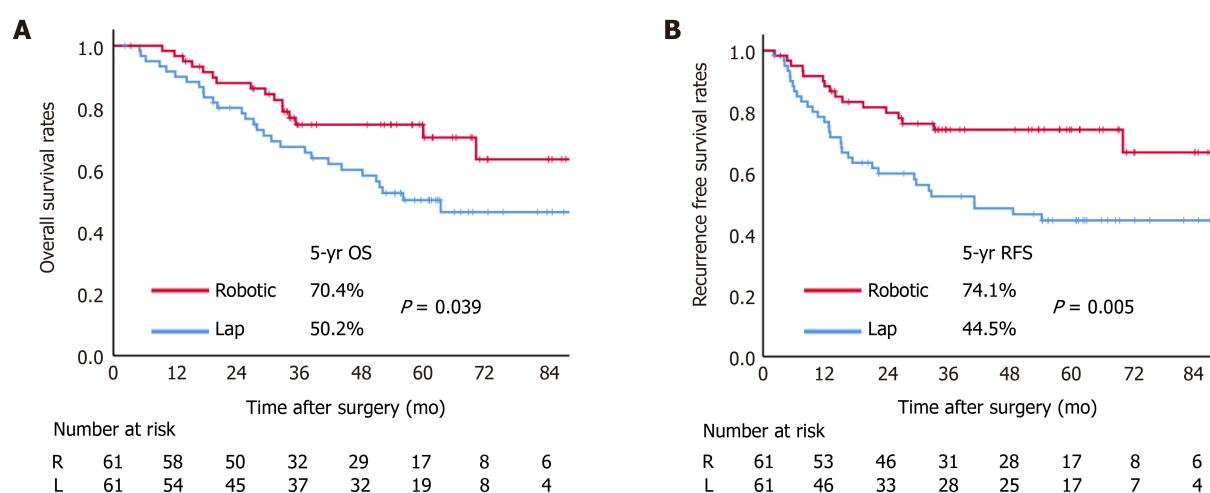


Figure 3 Kaplan-Meier curves. Kaplan-Meier estimates in the postmatched cohort. A: Overall survival probability; B: Recurrence-free survival probability. OS: Overall survival; RFS: Recurrence-free survival.

selection bias due to a possible preference for robotic gastrectomy in patients of higher economic status. However, this was an inherent limitation at the time of study enrollment considering that the DVSS was not covered by the medical insurance in Japan at the time the enrolled patients underwent gastrectomy, whereas conventional laparoscopic gastrectomy was covered. Second, propensity score matching between the laparoscopic and robotic group did not account for adjuvant chemotherapy administration given that, similarly to postoperative complications, adjuvant chemotherapy was determined after robotic or laparoscopic gastrectomy was conducted. Considering that both adjuvant chemotherapy and postoperative complications may affect prognosis[2,6,21], well-designed prospective trials are needed to determine a cause-effect relationship between robotic or laparoscopic gastrectomy and postoperative complications, as well as adjuvant chemotherapy administration.

CONCLUSION

In conclusion, the current study identified age, ASA status, type of gastrectomy, and pathological T and N status are prognostic factors of minimally invasive gastrectomy for gastric cancer. Moreover, the use of robotic assistance was associated with reduced early morbidity, as well as potentially better oncological outcomes in advanced gastric cancer.

ARTICLE HIGHLIGHTS

Research background

Minimally invasive surgery (MIS) including laparoscopic and robotic approaches for gastric cancer has been increasingly used because of its beneficial short-term effects over the open approach. However, oncological outcomes are not established.

Research motivation

There have been few reports on the oncological outcomes of MIS for gastric cancer patients, especially for the robotic approach, because a surgical robot remains a relatively new technology. Therefore, this study aimed to determine the prognostic factors of minimally invasive gastrectomy, including laparoscopic and robotic approaches.

Research objectives

This study aimed to determine the prognostic factors of minimally invasive gastrectomy, including laparoscopic and robotic approaches.

Research methods

This single-institutional retrospective cohort study included 814 consecutive patients with primary gastric cancer who underwent minimally invasive R0 gastrectomy between 2009 and 2014. We retrospectively examined 5-year overall survival and recurrence-free survival and investigated factors related to survival.

Research results

Age > 65 years, American Society of Anesthesiologists (ASA) physical status 3, total or proximal gastrectomy, and pathological T4 and N positive status were independent predictors of overall survival and recurrence-free survival. The five-year overall survival and recurrence-free survival were 80.3% and 78.2%, respectively. Of all 814 patients, 157 patients (19.3%) underwent robotic gastrectomy and 308 (37.2%) were diagnosed with pathological stage II or III disease. Robotic gastrectomy was an independent positive predictor for recurrence-free survival in pathological stage II/III patients (hazard ratio: 0.56 [0.33-0.96], $P = 0.035$). Comparison of recurrence-free survival between robotic and laparoscopic approach using propensity score matching analysis verified that with less morbidity in the robotic group ($P = 0.005$).

Research conclusions

Age, ASA status, type of gastrectomy, and pathological T and N status were prognostic factors of minimally invasive gastrectomy for gastric cancer, and the use of a surgical robot may improve its long-term outcomes for advanced gastric cancer.

Research perspectives

Future studies to better prove the efficacy of robotic gastrectomy for advanced gastric cancer patients are warranted.

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