

## Retrospective Cohort Study

**Non-robotic minimally invasive gastrectomy as an independent risk factor for postoperative intra-abdominal infectious complications: A single-center, retrospective and propensity score-matched analysis**

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**Author contributions:** Shibasaki S, Suda K, and Uyama I made substantial contributions to conception and design of the study; Shibasaki S, Nakauchi M, Nakamura K, Kikuchi K, and Inaba K contributed to acquisition, analysis, or interpretation of the data; Shibasaki S and Nakauchi M performed the statistical analysis; Shibasaki S, Suda K, and Uyama I drafted the article and made critical revisions related to important intellectual content of the manuscript; all the authors have read and approved the final version to be published.

**Institutional review board**

**statement:** This study was approved by the institutional review board of Fujita Health University.

**Informed consent statement:**

Informed consent was obtained from all patients.

**Conflict-of-interest statement:** All the authors except for I. U. have no commercial association with or financial involvement that might pose a conflict of interest in connection with the submitted

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**Abstract****BACKGROUND**

Minimally invasive surgery for gastric cancer (GC) has gained widespread use as a safe curative procedure especially for early GC.

**AIM**

To determine risk factors for postoperative complications after minimally invasive gastrectomy for GC.

**METHODS**

Between January 2009 and June 2019, 1716 consecutive patients were referred to our division for primary GC. Among them, 1401 patients who were diagnosed with both clinical and pathological Stage III or lower GC and underwent robotic gastrectomy (RG) or laparoscopic gastrectomy (LG) were enrolled. Retrospective chart review and multivariate analysis were performed for identifying risk factors for postoperative morbidity.

**RESULTS**

Morbidity following minimally invasive gastrectomy was observed in 7.5% of the patients. Multivariate analyses demonstrated that non-robotic minimally invasive surgery, male gender, and an operative time of  $\geq 360$  min were significant independent risk factors for morbidity. Therefore, morbidity was compared between RG and LG. Accordingly, propensity-matched cohort analysis revealed that the RG group had significantly fewer intra-abdominal infectious complications than the LG group (2.5% vs 5.9%, respectively;  $P = 0.038$ ), while no significant differences were noted for other local or systemic complications.

article. I. U. has received lecture fees from Intuitive Surgical, Inc.. K. S. and K. K. have been funded by Mediaroid, Inc. in relation to Collaborative Laboratory for Research and Development in Advanced Surgical Technology. K.S. has also received advisory fees from Mediaroid, Inc. outside of the submitted work.

**STROBE statement:** Authors have read the STROBE Statement checklist of items and the manuscript was prepared and revised accordingly.

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**Manuscript source:** Invited manuscript

**Received:** November 15, 2019

**Peer-review started:** November 15, 2019

**First decision:** February 14, 2019

**Revised:** March 5, 2020

**Accepted:** March 9, 2020

**Article in press:** March 9, 2020

**Published online:** March 21, 2020

**P-Reviewer:** Fusaroli P, Li Y, Petrucciani N, Wang DR, Guerra F

**S-Editor:** Wang YQ

**L-Editor:** A

**E-Editor:** Ma YJ



Multivariate analyses of the propensity-matched cohort revealed that non-robotic minimally invasive surgery [odds ratio = 2.463 (1.070–5.682);  $P = 0.034$ ] was a significant independent risk factor for intra-abdominal infectious complications.

## CONCLUSION

The findings showed that robotic surgery might improve short-term outcomes following minimally invasive radical gastrectomy by reducing intra-abdominal infectious complications.

**Key words:** Stomach neoplasms; Gastrectomy; Robotic surgical procedure; Minimally invasive procedures; Morbidity; Pancreatic fistula

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**Core tip:** This study aimed to determine risk factors for postoperative complications after minimally invasive gastrectomy for gastric cancer. Accordingly, multivariate analysis identified non-robotic minimally invasive surgery as an independent risk factor for postoperative complications. Propensity score matching analysis showed that the robotic gastrectomy group had a significantly lower incidence of intra-abdominal infectious complications compared to the laparoscopic gastrectomy group. Additionally, multivariate analyses in the propensity score-matched cohort showed that non-robotic minimally invasive surgery was a significant independent risk factor for intra-abdominal infectious complications.

**Citation:** Shibasaki S, Suda K, Nakauchi M, Nakamura K, Kikuchi K, Inaba K, Uyama I. Non-robotic minimally invasive gastrectomy as an independent risk factor for postoperative intra-abdominal infectious complications: A single-center, retrospective and propensity score-matched analysis. *World J Gastroenterol* 2020; 26(11): 1172-1184

**URL:** <https://www.wjgnet.com/1007-9327/full/v26/i11/1172.htm>

**DOI:** <https://dx.doi.org/10.3748/wjg.v26.i11.1172>

## INTRODUCTION

Gastric cancer (GC) is the fifth most common malignancy and the third leading cause of cancer-related death worldwide<sup>[1]</sup>. Surgical resection with or without perioperative chemotherapy has remained the only curative treatment option, with regional lymphadenectomy being recommended as part of radical gastrectomy<sup>[2-4]</sup>. Recently, laparoscopic gastrectomy (LG) has gained widespread use as it is a minimally invasive and safe curative procedure for GC especially for early GC<sup>[5-7]</sup>. Since we demonstrated the comparability of the laparoscopic D2 gastrectomy over the open D2 gastrectomy in the short- and long-term outcomes<sup>[8,9]</sup>, minimally invasive surgery (MIS) has been the first choice as the standard radical procedure for GC in our institute<sup>[10]</sup>.

However, several recent studies using the nationwide web-based database of Japan have revealed that LG promoted higher postoperative local complications compared with open gastrectomy (OG)<sup>[11-13]</sup>. Two main reasons may explain such findings. First, LG requires more experience, at least 40–60 surgical procedures, to achieve optimal proficiency compared with OG<sup>[14-17]</sup>. Second, LG has several technical limitations, including limited range of motion with straight forceps and hand tremors, which need to be addressed to further improve surgical outcomes following minimally invasive gastrectomy. Accordingly, two possible measures may help overcome such limitations. First is the Endoscopic Surgical Skill Qualification System (ESSQS), which was launched in 2004 by the Japanese Society for Endoscopic Surgery to develop a tool for the reliable and reproducible evaluation of trainees' surgical techniques<sup>[18]</sup>. In this system, two judges assess non-edited videotapes in a double-blinded fashion using strict criteria. Accordingly, surgeons determined to be qualified by this system experienced less frequent complications following laparoscopic distal gastrectomy (DG) compared with those who failed<sup>[18]</sup>. The second measure involves robotic surgery, which facilitates precise dissection in a confined surgical field with impressive dexterity<sup>[19-21]</sup>. In fact, a number of previous studies have shown that robotic gastrectomy (RG) resulted in significantly lower postoperative complication

rates compared to LG<sup>[20,22,23]</sup>.

Considering the aforementioned discussion, the present study aimed to determine risk factors for postoperative complications after MIS for GC, focusing on the impact of robotics and surgeon qualification by the ESSQS.

## MATERIALS AND METHODS

### Patients

Between January 2009 and June 2019, 1716 consecutive patients were referred to our division for primary GC eligible for surgical treatment. The present study ultimately enrolled 1401 patients (robotic,  $n = 359$  and laparoscopic,  $n = 1042$ ) with both clinical and pathological Stage III or lower GC after excluding 315 patients who had clinical or pathological stage IV GC ( $n = 166$ ), remnant GC ( $n = 53$ ), OG ( $n = 25$ ), double cancer ( $n = 20$ ), and palliative or limited lymphadenectomy ( $n = 51$ ) due to insufficient physical function. The patient selection process is summarized in [Figure 1](#). This study included not only symptomatic patients but also those who were diagnosed as a result of the mass cancer screening programs, which have been executed nationwide and have contributed to earlier detection of GC. In the present study, the stage of the cancer was described according to the 15th edition of the Japanese Classification of Gastric Carcinoma<sup>[24]</sup>. Cancer staging was performed based on the findings of contrast-enhanced computed tomography, gastrography, endoscopic study, and endosonography before the beginning of any treatment and, when applicable, after the completion of chemotherapy, as we previously described<sup>[20]</sup>. Tumor invasion depth was measured ultrasonographically<sup>[25,26]</sup>. The gastric wall was assessed based on the standard five-layer sonographic structure. On the endosonographic image, the mucosal layer is visualized as a combination of the first and second hypoechoic layers, and the submucosal layer corresponds to the third hyperechoic layer. The layer of the muscularis propria is visualized as the fourth hypoechoic layer, and the fifth hyperechoic layer is the serosa, including the subserosa. Initial endoscopic diagnosis regarding invasion depth was confirmed based on the agreement by expert endoscopists at the medical conference prior to therapy. The indication of endoscopic treatment and radical gastrectomy including the extent of systematic lymph node dissection was determined based on the 2014 Japanese Gastric Cancer Treatment Guidelines<sup>[3]</sup>. The microscopic tumor-negative status in the cut end was routinely confirmed by intraoperative frozen section diagnosis as previously reported<sup>[27,28]</sup>, and margins of resection (R0 or R1 resection) was pathologically diagnosed by permanent section diagnosis. In a considerable number of the enrolled patients, *Helicobacter pylori* was examined and systemically eradicated before surgery at each hospital or clinic at which GC of those patients was diagnosed. Details regarding indications for physical function assessment, surgical procedures, perioperative radical gastrectomy management, extent of gastric resection and lymph node dissection, type of anastomosis, and postoperative chemotherapy in addition to oncologic follow-up have been reported previously<sup>[8-10,20,21,29,30]</sup>. This study was approved by the Institutional Review Board of Fujita Health University.

### Decision on procedure selection

Patients were completely involved in the decision-making process, and informed consent was obtained from all patients. However, during the study period, decision making on patient procedures was dependent on circumstances surrounding the national medical insurance coverage. Accordingly, RG had not been included in the national medical insurance coverage in Japan between January 2009 and March 2018, during which patients needed to be charged 2200000 JPY upon perioperative admission to undergo RG<sup>[20]</sup>. All patients were equally offered robotic surgery without considering their backgrounds, including physical and oncological status. Hence, 211 patients who agreed to uninsured da Vinci Surgical System (DVSS) application underwent RG, whereas the remaining 946 patients who refused uninsured DVSS application underwent LG with health insurance coverage. Meanwhile, between October 2014 and January 2017, we organized a multi-institutional, single-arm prospective clinical study approved for Advanced Medical Technology ("Senshiniryō") B<sup>[23]</sup>. Accordingly, 94 patients with cStage I/II GC who were enrolled in our institution's Senshiniryō B trial were also included in the present analysis. Since its approval for national medical insurance coverage based on the outcomes of the Senshiniryō B trial in April 2018, RG has been more favorably indicated for patients diagnosed with advanced GC who required total gastrectomy (TG) or proximal gastrectomy (PG) and desired to undergo RG at our institution. After April 2018, 52 patients underwent RG, whereas 96 underwent LG.

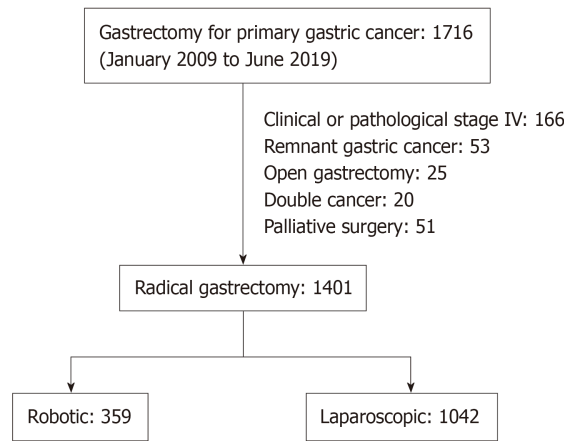


Figure 1 Flow diagram of the study selection process.

### Operating surgeon selection

All LG procedures were performed or guided by the ESSQS-qualified surgeons. Meanwhile, RG was performed by surgeons certified to operate a DVSS console, qualified by the ESSQS, and certified by the Japanese Society of Gastroenterological Surgery. All procedures related to LG and RG were supervised by an expert gastric surgeon (I.U.) who had performed more than 1500 LG and 400 RG procedures.

### Measurements

All patients were observed for 30 d following surgery. The primary endpoint of this single-center retrospective analysis was morbidity. Secondary endpoints comprised clinicopathological characteristics and short-term surgical outcomes, including operative time, surgeon console time, estimated blood loss, number of dissected lymph nodes, complication rates, rates for intra-abdominal infectious complications (including postoperative pancreatic fistulas, leakage, and intra-abdominal abscesses), mortality rate, and length of postoperative hospitalization. All postoperative complications Grade IIIa or above based on the Clavien-Dindo (CD) classification were recorded<sup>[31]</sup> and classified according to the Japan Clinical Oncology Group Postoperative Complications Criteria based on the CD classification ver. 2.0<sup>[32]</sup>. Total operative time was defined as the duration from the start of abdominal incision until complete wound closure, while surgeon console time was defined as the duration of DVSS operation during surgery. Blood loss was estimated by weighing suctioned blood and gauze pieces that had absorbed blood.

### Perioperative management of postoperative pancreatic fistula

Diagnosis and grading of pancreatic fistula were determined according to CD classification<sup>[31]</sup> as mentioned above. Our perioperative management for postoperative pancreatic fistula was conducted as follows<sup>[20,33]</sup>: Although pancreatic fistula is defined as output *via* an operatively placed drain (or a subsequently placed percutaneous drain) of any measurable volume of drain fluid on or after postoperative day 3, with an amylase level at least over 3 times as high as the upper normal range of the serum level, it was comprehensively diagnosed according to not only drain amylase levels, but also changes in the properties of the drain and the clinical, laboratory, and imaging findings including computed tomographic scans. Patients with high drain amylase level and no abnormal physical and laboratory findings were observed without any treatment (CD Grade I). The abdominal drainage tube was removed basically after the drain amylase level was sufficiently recovered. Patients with high drain amylase level accompanied by abnormal findings such as fever, abdominal pain, and high inflammatory markers, were intensively treated with antibiotics, octreotide acetate, and parenteral nutrition while the drainage tube position was urgently confirmed using computed tomographic scans and radiographic contrast study (CD Grade II). When the drainage tube position was not appropriate, an additional or alternative drainage tube was placed into the fluid cavity using percutaneous computed tomography or ultrasonography-guided technique (CD Grade IIIa), and irrigation and drainage with saline was performed. Parenteral nutrition was gradually switched to enteral nutrition without delay, once pancreatic fistula had been confined to a certain space and inflammatory response had settled.

### Propensity score-matched analysis

Propensity score-matched (PSM) analysis was used to limit confounders and overcome possible patient selection bias. Propensity scores for all patients were calculated using a logistic regression model based on the following variables: Age, gender, body mass index (BMI), American Society of Anesthesiologist (ASA) classification, presence of neoadjuvant chemotherapy, history of laparotomy, cT, cN, cStage, pT, pN, pStage, type of gastrectomy, extent of lymph node dissection, and splenectomy. Consequently, rigorous adjustment for significant differences in the baseline characteristics of PSM patients was performed using nearest neighbor matching without replacement and a caliper width of 0.2 logit of the standard deviation. An absolute standardized difference (SD) was used to measure covariate balance, in which an absolute standardized mean difference above 0.1 indicated a meaningful imbalance<sup>[11,12]</sup>.

### Statistical analysis

All analyses were conducted using IBM SPSS Statistics 23 (IBM Corporation, Armonk, NY, United States). Between-group comparisons were performed using the  $\chi^2$  test or Mann-Whitney *U* test. Univariate  $\chi^2$  test and multivariate logistic regression analysis were used to determine risk factors for the occurrence of postoperative complications. Data were expressed as median (range) or odds ratio (OR) (95% confidence interval) unless otherwise specified.  $P < 0.05$  (two-tailed) was considered statistically significant.

## RESULTS

### Clinicopathological features and surgical outcomes after minimally invasive gastrectomy

Patient characteristics and surgical outcomes of MIS for GC are summarized in [Table 1](#). Accordingly, 939 (67%) and 856 (61%) patients had cStage I and pStage I disease, respectively, while 120 (8.6%) received preoperative chemotherapy. A total of 359 and 1042 patients underwent RG and LG, while 993 (70.9%), 89 (6.4%), and 319 (22.8%) underwent DG, PG, and TG, respectively. Moreover, 767 and 634 patients underwent D1+ and D2 dissection, respectively. The rates for conversion to open procedure, reoperation within 30 d, in-hospital mortality within 30 d, and morbidity within 30 d after operation were 0.1%, 1.1%, 0.3% and 7.5%, respectively ([Table 1](#)). All patients completed successfully R0 resection.

### Risk factors for morbidity after minimally invasive gastrectomy

Univariate analysis identified seven significant factors for postoperative CD grade IIIa or more complications, including non-robotic MIS, male gender, cStage II or higher, type of gastrectomy (PG and TG), splenectomy, operative time  $\geq 360$  min, and estimated blood loss  $\geq 50$  mL. Multivariate analysis determined that non-robotic MIS [OR = 2.591 (1.418–4.717);  $P = 0.002$ ], male gender [OR = 1.969 (1.142–3.390);  $P = 0.015$ ], and operative time  $\geq 360$  min [OR = 1.800 (1.098–2.952);  $P = 0.020$ ] were significant independent risk factors for morbidity ([Table 2](#)).

### Patient background factors stratified according to type of procedure

Our analysis subsequently focused on the comparison between RG and LG. Patient characteristics according to type of procedure are summarized in [Table 3](#). Although no differences in BMI, history of laparotomy, tumor size, cT, cN, cStage, pT, pN, pStage, and number of metastatic lymph nodes were observed between the RG and LG group, significant differences were found in age [RG 67 (30–89) vs LG 70 (24–93);  $P < 0.001$ ], gender (M:F, RG 233:126 vs LG 740:302;  $P = 0.033$ ), ASA classification (1:2:3, RG 160:168:31 vs LG 340:565:137;  $P < 0.001$ ), preoperative chemotherapy (RG 5.3% vs LG 9.7%;  $P = 0.010$ ), type of resection (DG:PG:TG, RG 250:42:67 vs LG 743/47/252;  $P < 0.001$ ), and extent of lymphadenectomy (D1+:D2, RG 178:181 vs LG 589:453;  $P = 0.023$ ). Factors having an SD over 0.1 included age, gender, BMI, ASA classification, tumor size, use of preoperative chemotherapy, type of resection, extent of lymphadenectomy, and splenectomy ([Table 3](#)). To compensate for such differences, PSM analysis was used. The average and standard deviation of the propensity score was 0.256 and 0.111, respectively, thus yielding a caliper width of 0.02 for this study. After propensity score matching, 354 patients were included in each group ([Figure 2](#)). Propensity score distributions for each case before and after matching are presented in [Figure 2](#). After matching, the SD for age, gender, BMI, ASA classification, presence of neoadjuvant chemotherapy, history of laparotomy, tumor size, cT, cN, cStage, pT, pN, pStage, type of resection, extent of lymph node dissection, and splenectomy decreased

**Table 1 Patient backgrounds and surgical outcomes following minimally invasive gastrectomy at our institution, *n* = 1401**

Clinicopathological characteristics		Surgical outcomes	
Age (yr)	69 (24–93)	No. of operators (certified surgeon)	33 (19)
Gender (M:F)	973:428	Qualified:non-qualified surgeons	925:476
Body mass index (kg/m <sup>2</sup> )	22.3 (1.4.3–37.3)	Procedure (RG:LG)	359:1042
ASA grade (1:2:3)	500:733:168	Type of resection (DG:PG:TG)	993:89:319
History of laparotomy, <i>n</i> (%)	263 (18.8)	Extent of lymphadenectomy (D1+:D2)	767:634
Tumor size (mm)	30 (0–180)	Splenectomy, <i>n</i> (%)	40 (2.9)
cT <sup>1</sup> (1:2:3:4a)	751:264:224:162	Total operative time (min)	348 (147–942)
cN <sup>1</sup> (-:~)	1093:308	Estimated blood loss (mL)	30 (0–2150)
cStage <sup>1</sup> (I:IIA:IIIB:III)	939:76:154:232	No. of dissected LNs	35 (6–114)
pT <sup>1</sup> (1:2:3:4a)	797:164:178:262	Conversion to open procedure, <i>n</i> (%)	1 (0.1)
pN <sup>1</sup> (0:1:2:3)	949:174:137:141	Reoperation rate, <i>n</i> (%)	15 (1.1)
pStage <sup>1</sup> (I:II:III)	856:280:265	In-hospital mortality, <i>n</i> (%)	4 (0.3)
No. of metastatic LNs	0 (0–63)	Morbidity, <i>n</i> (%)	105 (7.5)
Use of preoperative chemotherapy, <i>n</i> (%)	120 (8.6)	Hospital stay following surgery (d)	13 (2–195)

<sup>1</sup>Japanese Classification of Gastric Carcinoma, 15<sup>th</sup> edition. Data are presented as median with range unless otherwise specified. ASA: American Society of Anesthesiologist; LNs: Lymph nodes; RG: Robotic gastrectomy; LG: Laparoscopic gastrectomy; DG: Distal gastrectomy; PG: Proximal gastrectomy; TG: Total gastrectomy.

to < 0.10, indicating that a sufficient balance was achieved (Table 3).

#### **Surgical and short-term outcomes stratified according to type of procedure**

Surgical outcomes and short-term postoperative courses of the entire cohort and the PSM cohort are summarized in Table 4. Accordingly, 8 and 33 operating surgeons performed RG and LG, respectively. Moreover, 100% of the RG cases and only 56.5% (572/1042) of the LG cases ( $P < 0.001$ ) were handled by qualified surgeons. The RG group had a significantly shorter duration of hospitalization following surgery compared to the LG group [RG 12 (2–195) d *vs* LG 13 (3–177) d;  $P < 0.001$ ], despite having a slightly greater total operative time [RG 360 (174–942) min *vs* LG 342 (147–937) min;  $P < 0.001$ ] and estimated blood loss [RG 36 (0–935) mL *vs* LG 29 (0–2150) mL;  $P < 0.001$ ]. No significant differences were observed in the number of dissected lymph nodes, conversion to open procedure, and reoperation rate. In-hospital mortality was sufficiently low (RG 0.6% *vs* LG 0.3%;  $P = 0.578$ ) throughout this series. After propensity score matching, results similar to those for the entire cohort were obtained (Table 4).

#### **Postoperative complications**

Postoperative complications are summarized in Table 5. Briefly, the RG group had a significantly better morbidity rate than the LG group (RG 3.6% *vs* LG 8.8%;  $P = 0.002$ ). Robotic surgery promoted better attenuation of intra-abdominal infectious complications compared to non-robotic surgery (RG 2.5% *vs* LG 6.3%;  $P = 0.005$ ), while no significant differences in other local (RG 0.8% *vs* LG 1.3%;  $P = 0.632$ ) or systemic (RG 0.3% *vs* LG 1.6%;  $P = 0.091$ ) complication rates were observed. After PSM analysis, results remained almost same (Table 5), with the RG group showing a significantly better morbidity rate than the LG group (RG 3.7% *vs* LG 7.6%;  $P = 0.033$ ). Robotic surgery promoted better attenuation of intra-abdominal infectious complications compared to non-robotic surgery (RG 2.5% *vs* LG 5.9%;  $P = 0.038$ ), while no significant differences in other local (RG 0.6% *vs* LG 1.1%;  $P = 0.682$ ) or systemic (RG 0.3% *vs* LG 1.1%;  $P = 0.369$ ) complication rates were observed.

#### **Risk factors for intra-abdominal infectious complications among the propensity score-matched cohort**

Univariate analysis identified several significant risk factors for intra-abdominal infectious complications, including non-robotic MIS, male gender, PG or TG, operative time  $\geq 360$  min, estimated blood loss  $\geq 50$  mL, and non-qualified surgeons (Table 6). Multivariate analysis clearly demonstrated that non-robotic MIS [OR 2.463 (1.070–5.682);  $P = 0.034$ ], male gender [OR 3.937 (1.157–13.333);  $P = 0.028$ ], and operative time  $\geq 360$  min [OR 2.779 (1.003–7.701);  $P = 0.049$ ] were significant independent risk factors for intra-abdominal infectious complications.

**Table 2 Risk factors for morbidity after minimally invasive gastrectomy, n = 1401**

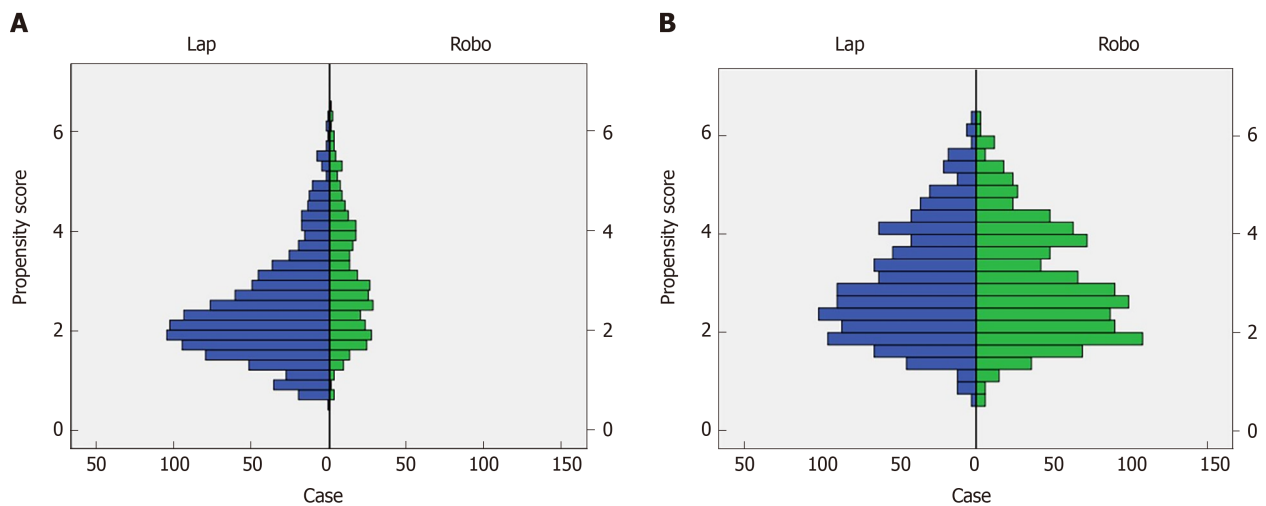
Factors	Univariate analysis, OR (95%CI)	P value	Multivariate analysis, OR (95%CI)	P value
Non-robotic minimally invasive surgery	2.438 (1.381–4.304)	0.002	2.591 (1.418–4.717)	0.002
Age ≥ 70 yr	1.020 (0.706–1.474)	0.920		
Male	2.277 (1.372–3.779)	0.001	1.969 (1.142–3.390)	0.015
Body mass index ≥ 23 kg/m <sup>2</sup>	1.138 (0.763–1.698)	0.538		
ASA score 2 or higher	1.069 (0.703–1.625)	0.832		
cT2 <sup>1</sup> or higher	1.296 (0.870–1.930)	0.222		
cN <sup>1</sup> positive	1.183 (0.745–1.879)	0.540		
cStage II <sup>1</sup> or higher	1.649 (1.102–2.467)	0.017	1.247 (0.809–1.922)	0.318
Proximal or total gastrectomy	1.847 (1.230–2.772)	0.004	1.208 (0.753–1.937)	0.433
D2 lymph node dissection	1.204 (0.809–1.792)	0.415		
Splenectomy	2.734 (1.179–6.339)	0.026	1.360 (0.542–3.408)	0.512
History of laparotomy	1.083 (0.658–1.783)	0.795		
Operative time ≥ 360 min	2.449 (1.613–3.718)	< 0.001	1.800 (1.098–2.952)	0.020
Estimated blood loss ≥ 50 mL	2.039 (1.367–3.042)	< 0.001	1.368 (0.873–2.143)	0.209
Tumor size ≥ 30 mm	1.119 (0.703–1.782)	0.721		
pT2 <sup>1</sup> or higher	1.378 (0.926–2.052)	0.125		
pN <sup>1</sup> positive	1.155 (0.761–1.753)	0.516		
pStage II <sup>1</sup> or higher	1.471 (0.987–2.192)	0.061		
Use of neoadjuvant chemotherapy	1.274 (0.662–2.452)	0.467		
Non-qualified surgeons	1.148 (0.785–1.679)	0.521		

<sup>1</sup>Japanese Classification of Gastric Carcinoma, 15<sup>th</sup> edition. The  $\chi^2$  test was used for univariate analysis. Multivariate logistic regression was used for multivariate analyses of factors having a *P* value of < 0.05 during univariate analysis. ASA: American Society of Anesthesiologist; OR: Odds ratio; CI: Confidence interval.

## DISCUSSION

The present study sought to identify risk factors for complications after MIS for GC. Accordingly, multivariate analysis revealed that non-robotic MIS was among the independent risk factors for complications. To determine whether a cause-effect relationship existed between non-RG and morbidity, short-term outcomes between RG and LG were compared using PSM analysis. Subsequent results showed that the RG group had a significantly lower incidence of intra-abdominal infectious complications compared to LG group and was more likely to be handled by an ESSQS-qualified surgeon. However, multivariate analysis of the PSM cohort showed that non-robotic MIS, but not the lack of ESSQS surgeon qualification, was a significant independent risk factor for intra-abdominal infectious complications. These findings clearly suggest that robotic surgery is at least more effective in reducing morbidity after MIS for GC than ESSQS qualification. The results presented herein support our previous evidence suggesting that the use of a robotic system significantly reduced postoperative complications<sup>[18]</sup>. In addition, the present study yielded three major findings.

First, the current study observed a 3.6% and 2.5% incidence rate for CD grade IIIa or higher morbidity and intra-abdominal infectious complications following RG, respectively. This finding was comparable to results from other prospective trials in Japan (2.5%–5.0% and 0.6%–3.3%, respectively)<sup>[23,34,35]</sup> or in other countries (reported as a range from 1.0% to 8.9%)<sup>[36]</sup>. In particular, RG seemed to have greater beneficial effects against pancreatic fistulas and intraperitoneal abscesses rather than anastomotic leakage compared to LG, although no significant difference was observed. This may be partly attributed to the meticulousness and high-definition magnified three-dimensional image of the robotic systems, which could be more effective in pancreas-protective radical lymph node dissection rather than intracorporeal alimentary tract reconstruction<sup>[30,37]</sup>. Actually, according to **Table 5**, there is a trend towards decrease in intraperitoneal abscess as well as pancreatic fistula in the RG group. Since intraperitoneal abscess could be induced by subclinical pancreatic fistula, the following speculation has taken place considering the results of our previous study in which RG significantly reduced pancreatic fistula: Robotic articulating forceps in combination with the magnified vivid three dimensional image enable operating surgeons to conduct radical lymph node dissection with little touch



**Figure 2** Mirrored histogram of propensity scores. A: Before matching; B: After matching, showing the distributions of laparoscopic gastrectomy (lap, blue-bar) and robotic gastrectomy (robo, green-bar).

on the pancreas, leading to reduction in postoperative intra-abdominal infectious complications including clinical and subclinical pancreatic fistula. In addition, the “double bipolar” method characterized by simultaneous use of Maryland bipolar forceps (bipolar forced coagulation, 420172, Intuitive) with the right hand and Fenestrated bipolar forceps (bipolar soft coagulation, 420205, Intuitive) with the left hand might also facilitate pancreas-protective dissection in RG<sup>[20,23]</sup>. However, there has been little evidence that minimally invasive gastrectomy is contributed to the reduction in postoperative pancreatic fistula, as shown in previous meta-analyses based on retrospective studies<sup>[38,39]</sup>. Therefore, further studies including multi-center randomized controlled trial are desired to establish solid evidence on RG.

Second, multivariate analysis showed that surgeon non-qualification was not an independent risk factor for morbidity. Two possible reasons may explain such a result. First is that a qualified surgeon could have guided the non-qualified surgeon performing the surgery. Second is that the qualified surgeons are able to perform high-quality surgeries even on technically demanding cases. In fact, our results showed that qualified surgeons were more likely to be in charge of more difficult procedures, including PG, TG, and D2 dissection, and there were no significant differences in morbidity rate of LG between the qualified and non-qualified surgeons (data not shown). Therefore, we still believe that ESSQS has played an important role in securing the safety and quality of MIS for GC.

Third, our findings showed that RG increased total operative time, a result consistent with those presented in many previous reports or meta-analyses<sup>[36]</sup>. In contrast, total operative time  $\geq 360$  min was identified as an independent risk factor for postoperative intra-abdominal infectious complications. This reduction in complications despite prolonged operative time with RG suggest its potential efficacy for addressing or overcoming certain factors that may induce complications in association with prolonged operative time. Considering that more technically-demanding procedures, such as PG/TG or D2 dissection, as well as complicated patient backgrounds, such as more advanced diseases, higher BMI, and use of preoperative chemotherapy, would likely extended operative time, they would constitute good indications for RG.

The present study has several limitations that need consideration. First, this study employed a single-center, retrospective, and non-randomized design. Moreover, financial resources necessary for RG had been changed from each patient’s own expense, Senshinriyo B, to the national insurance coverage. Therefore, considering possible data biases, overall results should be interpreted cautiously. Since October 2018, all patients who underwent RG using the national medical insurance must be prospectively registered to the web-based registry of the National Clinical Database<sup>[40]</sup>. Thus, large real-world data from this prospective registry would reveal actual outcomes of RG, including intraoperative and postoperative adverse effects and long-term oncologic outcomes. Second, this study has concerns regarding operator bias given that almost half of the LG cases were performed by non-qualified surgeons, while all RG procedures were performed by qualified surgeons. Accordingly, it remains largely unclear whether the protective effects of RG on morbidity observed herein could be extrapolated to RG conducted by a non-qualified surgeon. To address



**Table 3 Patient characteristics and clinicopathological features by each type of procedure**

	Entire cohort (n = 1401)		P value	SD	Propensity-score matched cohort (n = 708)		P value	SD
	RG (n = 359)	LG (n = 1042)			RG (n = 354)	LG (n = 354)		
Age (yr)	67 (30–89)	70 (24–93)	< 0.001	0.24	67 (30–89)	66 (24–90)	0.315	0.10
Gender (M:F)	233:126	740:302	0.033	0.12	230:124	230:124	1.000	0
Body mass index (kg/m <sup>2</sup> )	22.9 (14.3–32.0)	22.2 (14.5–37.3)	0.021	0.12	22.8 (14.3–32.0)	22.4 (14.9–37.3)	0.752	0.03
ASA grade (1:2:3)	160:168:31	340:565:137	< 0.001	0.25	155:168:31	149:174:31	0.905	0.03
History of laparotomy, n (%)	66 (18.4)	197 (18.9)	0.876	0.01	65 (18.4)	59 (16.7)	0.621	0.04
Tumor size (mm)	30 (0–170)	30 (0–180)	0.013	0.14	30 (0–170)	30 (0–180)	0.208	0.09
cT <sup>1</sup> (1:2:3:4a)	198:75:56:30	553:189:168:132	0.131	0.04	195:74:55:30	204:70:48:32	0.834	0.05
cN <sup>1</sup> (-:~)	287:72	806:236	0.337	0.06	284:70	289:65	0.702	0.04
cStage <sup>1</sup> (I:II:III)	249:62:48	690:168:184	0.183	0.07	246:61:47	252:59:43	0.962	0.04
pT <sup>1</sup> (1:2:3:4a)	210:36:46:67	587:128:132:195	0.711	0.05	208:36:46:64	213:36:39:66	0.882	0.03
pN <sup>1</sup> (0:1:2:3)	249:47:24:39	700:127:113:102	0.145	0.05	246:46:24:38	244:48:18:44	0.72	0.01
pStage <sup>1</sup> (I:II:III)	221:80:58	635:200:207	0.200	0.01	219:78:57	224:71:59	0.823	0.03
No. of metastatic LNs	0 (0–43)	0 (0–63)	0.385	0.03	0 (0–43)	0 (0–37)	0.819	0.02
Use of preoperative chemotherapy, n (%)	19 (5.3)	101 (9.7)	0.011	0.17	19 (5.4)	18 (5.1)	> 0.999	0.01
Type of resection (DG:PG:IG)	250:42:67	743:47:252	< 0.001	0.13	248:39:67	252:33:69	0.778	0.01
Extent of lymphadenectomy (D1+:D2)	178:181	589:453	0.023	0.14	175:179	175:179	> 0.999	0
Splenectomy, n (%)	6 (1.7)	34 (3.3)	0.142	0.11	6 (1.7)	7 (2.0)	> 0.999	0.02

<sup>1</sup>Japanese Classification of Gastric Carcinoma, 15<sup>th</sup> edition. Data are shown as median with range unless otherwise specified. The  $\chi^2$  test was used for between-group comparison of gender, American Society of Anesthesiologist grade, history of laparotomy, cT, cN, cStage, pT, pN, pStage, use of preoperative chemotherapy, type of resection, extent of lymphadenectomy, and splenectomy. The Mann-Whitney *U* test was applied for between-group comparison of age, body mass index, tumor size, and number of metastatic lymph nodes. RG: Robotic gastrectomy; LG: Laparoscopic gastrectomy; SD: Standardized difference; ASA: American Society of Anesthesiologist; LNs: Lymph nodes.

this issue, future studies comparing RG and LG performed by experts and non-qualified surgeons would be necessary. Third, the advantages of RG on oncological outcomes remained inconclusive give that long-term surveillance is still underway. However, we had previously reported that RG had long-term oncological outcomes comparable to those for LG<sup>[41]</sup>. In addition, some reports demonstrated that intra-abdominal infectious complications after gastrectomy had a negative impact on long-term oncological outcomes<sup>[42,43]</sup>. Further investigations are nonetheless warranted to determine whether RG's effect in reducing intra-abdominal infectious complications can lead to improvement in oncological outcomes after RG in the present cohort. Fourth, robotic and technological advances may influence surgical outcomes. During this study period, three DVSS systems, *i.e.*, S, Si, and Xi, had been used for RG. Although no differences in complication rates had been observed between these three systems (data not shown), further investigation on how differences in the version of the robotic system affect surgical outcomes is imperative. In addition, multivariate analysis involving the PSM cohort identified the male gender as an independent risk factor for intra-abdominal infectious complications. However, factors primarily affected have remained unclear. Hence, further investigation regarding differences in clinical and anatomical characteristics between males and females is necessary.

In conclusion, the present study shown that robotic surgery might improve short-term outcomes following minimally invasive radical gastrectomy by reducing intra-abdominal infectious complications.

**Table 4 Surgical outcomes and short-term postoperative courses**

	Entire cohort (n = 1401)		P value	Propensity-score matched cohort (n = 708)		P value
	RG (n = 359)	LG (n = 1042)		RG (n = 354)	LG (n = 354)	
No. of operators (qualified surgeon)	8 (8)	33 (14)	NA	8 (8)	33 (14)	NA
Qualified:non-qualified surgeons	359:0	572:475	< 0.001	354:0	186:149	< 0.001
Total operative time (min)	360 (174–942)	342 (147–937)	< 0.001	360 (174–942)	347 (149–937)	0.001
Console time (min)	306 (136–860)	NA	NA	307 (136–860)	NA	NA
Estimated blood loss (mL)	36 (0–935)	29 (0–2150)	0.007	37 (0–935)	28 (0–2150)	0.005
No. of dissected LNs	37 (7–100)	35 (6–114)	0.058	37 (7–100)	36 (6–108)	0.807
Conversion to open procedure, n (%)	0 (0)	1 (0.1)	> 0.999	0	0	> 0.999
Reoperation rate, n (%)	4 (1.1)	11 (1.1)	> 0.999	4 (1.1)	6 (1.7)	0.750
Hospital stay following surgery (d)	12 (2–195)	13 (3–177)	< 0.001	12 (2–195)	13 (3–131)	0.001
In-hospital mortality, n (%)	2 (0.6)	2 (0.3)	0.578	2 (0.6)	1 (0.3)	> 0.999

Data are presented as median with range unless otherwise stated. The  $\chi^2$  test was used for between group comparison of comparison of proportion of qualified and non-qualified surgeons, splenectomy, conversion to open procedure, reoperation rate, and in-hospital mortality. The Mann-Whitney *U* test was applied for between-group comparison of total operative time, estimated blood loss, number of dissected lymph nodes, and hospital stay following surgery. RG: Robotic gastrectomy; LG: Laparoscopic gastrectomy; LNs: Lymph nodes.

**Table 5 Postoperative complications with a Clavien–Dindo grade of IIIa or higher, n (%)**

	Entire cohort (n = 1401)		P value	Propensity-score matched cohort (n = 708)		P value
	RG (n = 359)	LG (n = 1042)		RG (n = 354)	LG (n = 354)	
Morbidity	13 (3.6)	92 (8.8)	0.002	13 (3.7)	27 (7.6)	0.033
Intra-abdominal infection	9 (2.5)	66 (6.3)	0.005	9 (2.5)	21 (5.9)	0.038
Anastomotic leakage	6 (1.7)	22 (2.1)	0.670	6 (1.7)	7 (2.0)	> 0.999
Pancreatic fistula	3 (0.8)	28 (2.7)	0.058	3 (0.8)	9 (2.5)	0.143
Intraperitoneal abscess	0 (0)	16 (1.5)	0.017	0 (0)	5 (1.4)	0.062
Other local complications	3 (0.8)	14 (1.3)	0.632	2 (0.6)	4 (1.1)	0.682
Intra-abdominal bleeding	2 (0.6)	4 (0.4)	> 0.999	1 (0.3)	2 (0.6)	> 0.999
Bowel obstruction	0 (0)	7 (0.6)	0.150	0 (0)	0 (0)	> 0.999
Anastomotic stenosis	1 (0.3)	3 (0.3)	> 0.999	1 (0.3)	2 (0.6)	> 0.999
Systemic complications	1 (0.3)	17 (1.6)	0.091	1 (0.3)	4 (1.1)	0.369
Pneumonia	0 (0)	9 (0.9)	0.256	0 (0)	2 (0.6)	0.499
Pulmonary embolism	1 (0.3)	2 (0.2)	0.726	1 (0.3)	0 (0)	> 0.999
Renal dysfunction	0 (0)	1 (0.1)	0.573	0 (0)	0 (0)	> 0.999
Cardiovascular disease	0 (0)	5 (0.5)	0.337	0 (0)	2 (0.6)	0.499

The  $\chi^2$  test was used for between-group comparison. RG: Robotic gastrectomy; LG: Laparoscopic gastrectomy.

**Table 6 Risk factors for intra-abdominal infectious complications (propensity score-matched cohort, *n* = 708)**

Factors	Univariate analysis, OR (95%CI)	P value	Multivariate analysis, OR (95%CI)	P value
Non-robotic minimally invasive surgery	2.333 (1.084–5.024)	0.038	2.463 (1.070–5.682)	0.034
Age ≥ 70 yr	1.141 (0.546–2.388)	0.849		
Male	4.852 (1.487–15.834)	0.003	3.937 (1.157–13.333)	0.028
Body mass index ≥ 23 kg/m <sup>2</sup>	1.064 (0.511–2.214)	> 0.999		
ASA score 2 or higher	1.135 (0.538–2.393)	0.851		
cStage II <sup>1</sup> or more	1.394 (0.651–2.982)	0.416		
Proximal or total gastrectomy	2.513 (1.205–5.240)	0.014	1.694 (0.722–3.974)	0.226
D2 dissection	1.023 (0.508–2.061)	> 0.999		
Splenectomy	1.579 (0.467–5.339)	0.668		
Operative time ≥ 360 min	4.863 (1.963–12.048)	< 0.001	2.779 (1.003–7.701)	0.049
Estimated blood loss ≥ 50 mL	3.596 (1.682–7.687)	0.001	2.204 (0.967–5.023)	0.060
Tumor size ≥ 30 mm	1.057 (0.508–2.201)	> 0.999		
pStage II <sup>1</sup> or more	1.120 (0.531–2.363)	0.848		
Use of neoadjuvant chemotherapy	1.599 (0.224–11.419)	0.729		
Non-qualified surgeons	2.047 (1.018–4.118)	0.045	1.852 (0.810–4.237)	0.145

<sup>1</sup>Japanese Classification of Gastric Carcinoma, 15<sup>th</sup> edition. The  $\chi^2$  test was used for univariate analysis. Multivariate logistic regression was used for multivariate analyses of factors having a *P* value of < 0.05 during univariate analysis. ASA: American Society of Anesthesiologist; OR: Odds ratio; CI: Confidence interval.

## ARTICLE HIGHLIGHTS

### Research background

Minimally invasive surgery for gastric cancer (GC) has gained widespread use as a safe curative procedure especially for early GC. However, several recent studies using the nationwide web-based database of Japan have revealed that laparoscopic gastrectomy (LG) promoted higher postoperative local complications compared with open gastrectomy.

### Research motivation

We launched robotic gastrectomy (RG) for GC in 2009. Our previous studies have consistently suggested that use of the surgical robot in LG might reduce postoperative complications, although use of the surgical robot was determined in a non-randomized manner. Actually, only experienced surgeons have performed RG, and RG was used for patients who hoped for uninsured use of the robot between 2009 and 2017.

### Research objectives

This study aimed to determine risk factors for postoperative complications after minimally invasive gastrectomy for GC using our prospectively maintained database between January 2009 and June 2019.

### Research methods

This study enrolled 1401 patients who underwent radical robotic gastrectomy (RG) or LG for clinical and pathological Stage III or lower GC. Retrospective chart review and multivariate analysis were performed for identifying risk factors for postoperative morbidity.

### Research results

Multivariate analyses demonstrated that non-robotic minimally invasive surgery, male gender, and an operative time of ≥ 360 min were significant independent risk factors for morbidity. Therefore, morbidity was compared between RG and LG using propensity score matched analysis. As a result, RG induced significantly fewer intra-abdominal infectious complications than the LG (2.5% *vs* 5.9%, respectively; *P* = 0.038). Multivariate analyses of the propensity-matched cohort revealed that non-robotic minimally invasive surgery [OR = 2.463 (1.070–5.682); *P* = 0.034] was a significant independent risk factor for intra-abdominal infectious complications.

### Research conclusions

RG might improve short-term outcomes following minimally invasive radical gastrectomy by reducing intra-abdominal infectious complications.

### Research perspectives

We will conduct an RCT on this topic in the near future. Impact of RG on long-term outcomes should also be examined at least in this cohort.

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