Risk Factors of Postoperative Intra-Abdominal Infectious Complications after Robotic Gastrectomy for Gastric Cancer

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Keywords
Gastric cancer · Robotic gastrectomy · Complication · Risk factor

Abstract
Introduction: Robotic surgery is regarded as an evolved type of laparoscopic surgery. Few studies have undertaken detailed analysis of complications following robotic gastrectomy for gastric cancer. Methods: This is a single-center retrospective study of 149 consecutive patients with gastric cancer who underwent robotic gastrectomy. It examines in detail the postoperative complications in robotic gastrectomy for gastric cancer, focusing on intra-abdominal infectious complications including anastomotic leakage, pancreatic fistula, and intra-abdominal abscess. We also aim to identify the related risk factors. Results: The median operation time was 299 min and the median bleeding was 25 mL. The incidence of overall complications higher than grade II was 8.7%. Clinically serious complications higher than grade IIIa occurred in 6.7% of cases. The incidence of intra-abdominal infectious complications that were higher than grade II was 4.0%. Mortality in our consecutive series was zero. Multivariate logistic regression analysis indicated that postoperative intra-abdominal infectious complications were significantly associated with history of abdominal surgery ($p = 0.043$), with odds ratios of 17.890 (95% confidence interval 1.092–293.150) and with non-curative resection ($p = 0.025$), with odds ratios of 58.629 (95% confidence interval 1.687–2,037.450). Discussion/Conclusion: Robotic gastrectomy was shown to be a safe and effective treatment for gastric cancer when performed by experienced surgeons. Attention should be paid to the risk of developing postoperative complications when performing robotic gastrectomy in gastric cancer patients with a history of abdominal surgery and in patients with advanced gastric cancer in whom there is expected to be difficulty in curative resection.
the RG group has been shown to have a lower rate of complications than the laparoscopic gastrectomy (LG) group [1–4]. Conversely, other reports have argued that the technological benefits of robots do not necessarily lead to a reduction in postoperative complications [5–7].

Few studies have undertaken deep analysis of complications following RG, although one report highlighted that elderly patients and insufficient surgeon experience were risk factors for morbidity in robotic gastric cancer surgery [8]. The present study aimed to evaluate the postoperative complications in RG for GC, focusing on intra-abdominal infectious complications including anastomotic leakage, pancreatic fistula, and intra-abdominal abscess, and to identify the related risk factors.

Materials and Methods

Patients

This study was a single-center retrospective analysis of prospectively collected data. This study was approved by the Institutional Review Board at the Wakayama Medical University Hospital (W MUH). The committee that approved the research confirmed that all research was performed in accordance with relevant guidelines/regulations. Written informed consent was obtained from all participants and all research was performed in accordance with the Declaration of Helsinki.

Between May 1, 2017 and March 31, 2021, 486 patients underwent radical gastrectomy for GC at WMUH. Of these, 152 patients underwent RG, 311 patients underwent LG, and the remaining 23 patients underwent open gastrectomy. Patients with GC that underwent RG were included as part of a clinical trial (UMIN000027969/000031536) [9]. Among the 152 patients that underwent RG, we excluded 2 patients that required conversion to laparoscopic surgery due to machine trouble and 1 patient that required conversion to open surgery due to portal vein injury [9]. The remaining 149 consecutive patients were included in this retrospective study.

Tumor stage was classified by the International Union against Cancer TNM Criteria, Eighth Edition [10]. Operation time was defined as the time from the skin incision to skin closure, and console time was the overall surgery time at the console. All surgical and medical complications and mortality events were documented. Postoperative complications were analyzed according to the Clavien-Dindo classification [11]. Complications higher than grade II were considered to be clinically significant [11]. Surgical complications were confined to events that occurred within 90 days after surgery; these included anastomotic leakage, pancreatic fistula, intra-abdominal abscess, intra-abdominal bleeding, intraluminal bleeding, ileus, cholecystitis, anastomotic stenosis, and wound infection [9]. Medical complications included pulmonary, cardiovascular, liver, urinary, and thrombosis events [9]. Intra-abdominal infectious complications were defined as anastomotic leakage, pancreatic fistula, and intra-abdominal abscess [9]. Reoperation cases were defined as any reoperation connected with any surgery-related complications [9]. Mortality was defined as any death that occurred during the hospital stay [9].

### Table 1. Patient demographics and tumor characteristics

| Variables | n = 149 |
|-----------|---------|
| Patients demographics | |
| Gender, male/female | 93/56 |
| Age, year, median (range) | 72 (34–90) |
| BMI, kg/m², median (range) | 21.9 (14.0–32.1) |
| ASA score, 1/2/3 | 49/93/7 |
| Comorbidity, n (%) | |
| Hypertension | 73 (49.0) |
| Diabetes | 28 (18.8) |
| Pulmonary | 12 (8.1) |
| Cardiovascular | 18 (12.1) |
| Renal | 4 (2.7) |
| Hepatic | 2 (1.3) |
| Cerebrovascular | 6 (4.0) |
| History of abdominal surgery, n (%) | 41 (27.5) |
| Laparoscopic or open cholecystectomy | 5 |
| Appendectomy | 20 |
| Colorectal surgery | 4 |
| Gynecological surgery | 11 |
| Hepatectomy | 1 |
| Nephrectomy | 1 |
| Smoking history, n (%) | 83 (55.7) |
| Daily drinker, n (%) | 62 (41.6) |
| Tumor characteristics | |
| Location, U/M/L/W | 42/39/65/3 |
| Size, mm, median (range) | 30 (4–150) |
| Histological type, differentiated (%) | 89 (59.7)/60 (40.3) |
| pStage, I/II/III/IV | 98/33/14/4 |

BMI, body mass index; ASA, American Society of Anesthesiologists; U, upper third of the stomach; M, middle third of the stomach; L, low third of the stomach; W, whole stomach. 1 Japanese Classification of Gastric Carcinoma. 2 UICC 8th edition.

Quality Control

The qualification of the surgeon for this study were as follow: (1) experience of more than 40 RG, (2) be qualified for surgery according to endoscopic surgical skill qualification system established by the Japan Society for Endoscopic Surgery, and (3) be a board-certified fellow of the Japanese Society of Gastroenterological Surgery.

Surgical Procedures

Details of the RG procedures performed at WMUH have been previously described [9, 12, 13]. All RG procedures were performed using da Vinci S, Si, or Xi Surgical System (Intuitive, Sunnyvale, CA, USA) with four articulating robotic arms; a central second arm for a 30° rigid endoscope, a first arm for fenestrated bipolar forceps, a third arm for monopolar scissors, and a fourth arm for Cadiere forceps [9]. One additional port for assisting forceps was placed at the right umbilical level. D1 or D1+ dissection was applied for clinical stage IA tumors, while D2 or D2+ para-aortic nodal dissection was performed for tumors higher than clinical stage IB [14]. We performed lymph node dissection using mo-
n bipolar scissors and a vessel sealer. Lymph node dissection was completed intracorporeally [9, 12, 13]. Intracorporeal anastomosis was performed using linear staplers, such as gastroduodenostomy, gastrojejunoanastomosis, or esophagojejunoanastomosis [15–18]. All operations were performed or overseen by one senior surgeon (T.O.) as a console surgeon or instructor.

Statistical Examinations
SPSS version 24.0 (SPSS, Chicago, IL, USA) was used for all statistical analyses. Quantitative results are expressed as medians and ranges. To identify risk factors for postoperative intra-abdominal infectious complications, we analyzed univariate and multivariate logistic regression. In the multivariate analysis, risk factors with a univariate $p < 0.20$ were included, and risk factors with a multivariate $p < 0.05$ were defined as independent risk factors.

Results

Patient Demographics and Tumor Characteristics
The detailed characteristics of the 149 patients are listed in Table 1; there were 93 males and 56 females with a median age of 72 years. Forty-one patients had a history of abdominal surgery. The median tumor size was 30 mm. Eighty-nine (65.8%), 33 (22.1%), 14 (9.4%), and 4 (2.7%) patients had TNM Stages I, II, III, and IV, respectively.

Surgical Results and Postoperative Complications
The detailed surgical results of the patients are listed in Table 2. Ninety-three patients underwent distal gastrectomy, 43 patients underwent total gastrectomy, and 13 patients underwent proximal gastrectomy. One hundred forty-five patients underwent curative resection. Nineteen patients had simultaneous combined organ resection. The median operation time was 299 min and the median bleeding was 25 mL.

Postoperative complications are listed in Table 3. The incidence of overall complications was 8.7%. Clinically serious complications higher than grade IIIa occurred in 6.7%. The incidence of intra-abdominal infectious complications was 4.0%. Reoperations (grade IIIb) were required for 2 patients; 1 patient underwent laparoscopic ileus repair and the other required laparoscopic resection of the anastomotic site for refractory anastomotic ulcer. Mortality in our consecutive series was zero.

Univariable and Multivariable Analyses of Risk Factors Influencing Intra-Abdominal Infectious Complications
Univariable and multivariable analyses were performed to identify associative risk factors influencing the intra-abdominal infectious complications (higher than Clavien-Dindo grade II) in patients with GC who underwent RG. The 28 variables were univariately examined as potential associative risk factors for the six patients with complications compared with the 143 patients without complications (Table 4). In univariable analyses, seven of the 28 risk factors differed significantly between these groups and were selected as significant associative risk factors. Multivariate logistic regression analysis indicated

| Variables                                                                 | n = 149 |
|---------------------------------------------------------------------------|---------|
| Operative procedure, DG (%)/TG/PG                                          | 93 (62.4)/43 (28.9)/13 (8.7) |
| Lymph node dissection, D1/D1+/D2/D2+PAND                                   | 2/78/68/1 |
| Reconstruction, BI (%)/BI/RY/EG/DT                                        | 51/20/65/4/9 |
| Combined resection, yes (%)                                                | 19 (12.8) |
| Gall bladder/spleen/pancreas/colon/renal (partial)                        | 14/6/2/1/2 |
| Robot type, da Vinci Xi/da Vinci Si/da Vinci S                             | 100/29/20 |
| Operation time, min, median (range)                                       | 299 (179–654) |
| Console time, min, median (range)                                         | 252 (134–586) |
| Blood loss, mL, median (range)                                            | 25 (5–475) |
| Intraoperative transfusion, yes (%)                                        | 1 (0.7) |
| No. of retrieved lymph nodes, median (range)                              | 32 (10–103) |
| No. of involved lymph nodes, median (range)                               | 0 (0–46) |
| R classification R0,* n (%)                                                | 145 (97.3) |

DG, distal gastrectomy; TG, total gastrectomy; PG, proximal gastrectomy; PAND, para-aortic nodal dissection; BI, Billroth-I reconstruction; BII, Billroth-II reconstruction; RY, Roux-en-Y reconstruction; EG, esophagogastrostomy; DT, double-tract reconstruction. * Japanese Classification of Gastric Carcinoma.
Pancreatic fistula, and intra-abdominal abscess was 4%. Infectious complications including anastomotic leakage, higher than grade II was 8.7%, and the intra-abdominal scope resection of anastomotic ulcer.

Intra-abdominal infectious complication, ≥ grade II, n (%) 6 (4.0)
Intra-abdominal infectious complication, ≥ grade IIIa, n (%) 5 (3.4)
Reoperation, ≥ grade IIIb, n (%) 2 (1.3)
Mortality 0

Surgical complication, n (%) 10 (6.7)

Overall complication, ≥ grade II, n (%) 13 (8.7)
Overall complication, ≥ grade IIIa, n (%) 10 (6.7)

Table 3. Postoperative complications

| Variables                                      | n = 149 |
|------------------------------------------------|---------|
| Overall complication, ≥ grade II, n (%)       | 13 (8.7)|
| Overall complication, ≥ grade IIIa, n (%)     | 10 (6.7)|
| Intra-abdominal infectious complication, ≥ grade II, n (%) | 6 (4.0)|
| Intra-abdominal infectious complication, ≥ grade IIIa, n (%) | 5 (3.4)|
| Reoperation, ≥ grade IIIb, n (%)              | 2 (1.3)|
| Mortality                                     | 0       |
| Surgical complication, n (%)                  | 10 (6.7)|
| Anastomotic leakage, ≥ grade II               | 4 (2.7)|
| Anastomotic leakage, ≥ grade IIIa             | 3 (2.0)|
| Pancreatic fistula, ≥ grade II                | 0       |
| Intra-abdominal abscess, ≥ grade IIIa         | 2 (1.3)|
| Intra-abdominal bleeding, ≥ grade II          | 2 (1.3)|
| Intra-abdominal bleeding, ≥ grade IIIa        | 1 (0.7)|
| Ileus, ≥ grade IIIa                           | 2 (1.3)|
| Cholecytitis, ≥ grade II                      | 0       |
| Stenosis, ≥ grade II                          | 0       |
| Wound infection, ≥ grade IIIa                 | 1 (0.7)|
| Medical complication, n (%)                   | 1 (0.7)|
| Pneumonia, ≥ grade II                         | 1 (0.7)|
| Pneumonia, ≥ grade IIIa                       | 0       |
| Cardiovascular system, ≥ grade II             | 0       |
| Liver system, ≥ grade II                      | 0       |
| Urinary system, ≥ grade II                    | 0       |
| Thrombosis, ≥ grade II                        | 0       |

1 Complications were classified into five categories according to the Clavien-Dindo classification. 2 Including anastomotic leakage, pancreatic fistula, and intra-abdominal abscess. 3 One patient underwent laparoscopic ileus repair and the other underwent laparoscopic resection of anastomotic ulcer.

that postoperative intra-abdominal infectious complications were significantly associated with a history of abdominal surgery, with odds ratios of 17.890, and with non-curative resection, with odds ratios of 58.629.

**Discussion/Conclusion**

The present study examined the surgical outcomes of RG for GC in a relatively large cohort of patients managed by a single surgeon. Robotic surgery for GC patients was a safe and feasible procedure with a low frequency of postoperative complications. Risk factors for the development of intra-abdominal infectious complications after RG were history of abdominal surgery and non-curative resection.

In this study of 149 patients, the overall morbidity with higher than grade II was 8.7%, and the intra-abdominal infectious complications including anastomotic leakage, pancreatic fistula, and intra-abdominal abscess was 4%.

Our postoperative complication rate was as low as that in high volume centers in Japan and East Asia [19–23]. Notably, no pancreatic fistulas were found in our surgical series. A nationwide Japanese registry database indicated that pancreatic fistulas tend to increase in LG [24]. Laparoscopic ultrasonically activated devices (USAD) and assisting forceps may cause thermal damage and pressure injury to the pancreas [1, 12, 19]. Our study showed that the RG procedure without the use of USAD, which avoids contact with the pancreas, could result in reduced incidences of pancreatic fistulas. In addition, robotic surgery is designed to overcome the drawbacks of laparoscopy in that forceps with articulated function can be used [1–8]. In RG using articulating forceps, it is possible to perform lymphadenectomy without contact with the pancreas.

The history of abdominal surgery has been traditionally considered to be a relative contraindication for LG, and with a high rate of conversion to open gastrectomy [25, 26]. With the improvement of minimally invasive surgery technology, recent studies have found no differences between patients with and those without a history of abdominal surgery in surgical outcomes following LG [27–29]. However, the feasibility of RG for patients with a history of abdominal surgery has not yet been demonstrated. RG is generally avoided for such patients because of the risk of injuring the gut during exfoliation of adhesions. In patients with a history of colorectal surgery, robotic exfoliation of ball-shaped jejuno-to-jejuno adhesions was especially difficult because the robotic system lacks tactile sensation. Patients after colorectal surgery who require robotic total gastrectomy and Roux-en-Y reconstruction might therefore have been at a high risk for intra-abdominal infectious complications. Indeed, in our series, patients with colorectal cancer or appendicitis who had a history of colectomy developed postoperative intra-abdominal complications after robotic gastrectomy in 3 of 7 patients. However, few postoperative complications were found in patients with a history of previous gynecological surgery or cholecystectomy.

We performed RG only on patients with GC undergoing curative-intent resection. However, 4 of the 149 patients underwent non-curative resection, and non-curative resection was an independent risk factor for complications. Of the 4 patients who underwent non-curative resection, 2 patients had peritoneal dissemination and the resected specimens of 2 patients had a positive proximal margin. The incidence of postoperative complications in patients with GC that underwent non-curative resection was shown in previous reports to be about 30%, which was higher than that in patients that underwent...
Table 4. Univariable and multivariable analyses of risk factors influencing intra-abdominal infectious complication with higher than grade II

| Risk factors               | Variables | Univariate analysis | Multivariate analysis |
|----------------------------|-----------|---------------------|-----------------------|
|                            |           | p value  | odds ratio (95% CI)  | p value  | odds ratio (95% CI)  |
| Gender                     | Female    | 0.827   | 1                    |           |                     |
|                            | Male      | 1        | 0.824 (0.146–4.652)  |           |                     |
| Age, years                 | <72       | 0.337   | 1                    |           |                     |
|                            | ≥72       | 0.429   | 0.076–2.415          |           |                     |
| BMI, kg/m²                 | 17.5–25   | 0.735   | 1                    |           |                     |
|                            | ≥25       | 0.681   | 0.074–6.293          |           |                     |
|                            | <17.5     | 0.392   | 2.722 (0.274–27.021) |           |                     |
| ASA                        | 1         | 0.997   | 1                    |           |                     |
|                            | 2/3       | NE      |                       |           |                     |
| Hypertension               | No        | 0.441   | 1                    |           |                     |
|                            | Yes       | 0.507   | 0.090–2.856          |           |                     |
| Diabetes                   | No        | 0.892   | 1                    |           |                     |
|                            | Yes       | 0.859   | 0.096–7.658          |           |                     |
| Pulmonary                  | No        | 0.442   | 1                    |           |                     |
|                            | Yes       | 2.400   | 0.257–22.396         |           |                     |
| Cardiovascular             | No        | 0.727   | 1                    |           |                     |
|                            | Yes       | 1.482   | 0.163–13.458         |           |                     |
| Renal                      | No        | 0.999   | 1                    |           |                     |
|                            | Yes       | NE      |                       |           |                     |
| Hepatic                    | No        | 0.999   | 1                    |           |                     |
|                            | Yes       | NE      |                       |           |                     |
| Cerebrovascular            | No        | 0.150   | 1                    | 0.070    | 1                    |
|                            | Yes       | 5.250   | 0.540–56.454         | 29.695   | 0.755–1,167.344     |
| Charlson Comorbidity Index | 0         | 0.420   | 1                    |           |                     |
|                            | ≥1        | 1.409   | 0.046–3.597          |           |                     |
| History of abdominal surgery | No   | 0.409   | 1                    |           |                     |
|                            | Yes       | 1.482   | 0.163–13.458         |           |                     |
| Smoking history            | No        | 0.774   | 1                    |           |                     |
|                            | Yes       | 1.788   | 0.154–4.035          |           |                     |
| Daily drinker              | No        | 0.676   | 1                    |           |                     |
|                            | Yes       | 0.692   | 0.123–3.900          |           |                     |
| Operative procedure        | DG        | 0.156   | 1                    |           |                     |
|                            | TG/PG     | 1        | 3.500 (0.620–19.767) | 0.982    | 1                    |
|                            |           |           | 0.304                | 1         | 0.154 (0.004–5.452) |
| Lymph node dissection      | D1/D1+    | 0.010    | 1                    | 1         | 0.968 (0.061–15.409) |
|                            | DG/D2/D2+PAND |           | 6.172 (0.703–54.173) | 0.982    | 1                    |
|                            | BI/BII    | 0.480   | 1                    |           |                     |
|                            | RY/EG/DT  | 1.865   | 0.331–10.506         |           |                     |
| Combined resection         | No        | 0.770   | 1                    |           |                     |
|                            | Yes       | 1.389   | 0.153–12.574         |           |                     |
| Robot type                 | da Vinci Xi | 0.981    | 1                    |           |                     |
|                            | da Vinci Si | 1        | 1.021 (0.181–5.777)  |           |                     |
| Operation time, min        | <300      | 0.130   | 1                    |           |                     |
|                            | ≥300      | 5.362   | 0.611–47.056         | 0.116    | 1                    |
|                            |           |           | 43.464 (0.392–4,824.197) |           |                     |
curative resection [30–32]. Robotic extended lymph node dissection and gastrectomy with multiple organ resections are controversial for patients with locally advanced GC.

Analyzing risk factors influencing the postoperative intra-abdominal infectious complications in patients with GC who underwent R0 curative resection is important. Therefore, additional analyses were performed. As shown in online supplementary Table 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000526920), even in patients who have undergone curative resection, multivariate logistic regression analysis indicated that postoperative intra-abdominal infectious complications were significantly associated with a history of abdominal surgery (online suppl. Table 1) with odds ratios of 10.700.

This study has several limitations; it was a retrospective study and conducted in a single institution. The small sample size and small number of determinants would decrease statistical power. The practical clinical applicability in the statistical analysis of this study is low. We have launched a multicenter retrospective study to identify risk factors for complications of robotic gastric cancer surgery. In contrast with Western countries, the number of obese patients in our Japanese hospital was extremely small, which may have led to the frequency of postoperative intra-abdominal infectious complications being lower than reported in previous studies. In addition, we did not show the long-term oncological outcomes of patients who underwent RG, which might confirm the final impact of RG. A multi-center prospective study is required that would evaluate the benefits including consideration of postoperative complications, quality of life, or more long-term oncological outcomes in patients with GC treated with RG.

In conclusion, this retrospective study suggests that RG is a safe and effective treatment for GC when performed by experienced surgeons. Special attention should be paid to the risk of developing postoperative complications when performing RG on GC patients with a history of abdominal surgery and on patients with advanced GC who are expected to have difficulty in curative resection.
Complications after RG

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Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board at the Wakayama Medical University Hospital, approval number 2283. All procedures were undertaken in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. All patients gave written informed consent in accordance with its guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Toshiyasu Ojima designed the study and wrote the initial draft of the manuscript. Toshiyasu Ojima and Keiji Hayata contributed to data interpretation and critical revision of the manuscript. All the other authors (Junya Kitadani, Akihiro Takeuchi, and Hiroki Yamaue) contributed to data collection and interpretation and critical review of the manuscript. All the authors have read and approved the final version of the manuscript and have agreed to be accountable for all aspects of the study, ensuring that any queries related to the accuracy or integrity of any part of the work are answerable.

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Data Availability Statement

The datasets generated and/or analyzed during the current study are not publicly available due to hospital regulations but are available from the corresponding author on reasonable request.
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