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Original Article

Postoperative Complications and Their Risk Factors of Completion Total Gastrectomy for Remnant Gastric Cancer Following an Initial Gastrectomy for Cancer

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ABSTRACT

Purpose: Completion total gastrectomy (CTG) for remnant gastric cancer (RGC) is a technically demanding procedure and associated with increased morbidity. The present study aimed to evaluate postoperative complications and their risk factors following surgery for RGC after initial partial gastrectomy due to gastric cancer excluding peptic ulcer.
Materials and Methods: We retrospectively reviewed the data of 107 patients who had previously undergone an initial gastric cancer surgery and subsequently underwent CTG for RGC between March 2002 and December 2020. The postoperative complications were graded using the Clavien-Dindo classification. Logistic regression analyses were used to determine the risk factors for complications.
Results: Postoperative complications occurred in 34.6% (37/107) of the patients. Intra-abdominal abscess was the most common complication. The significant risk factors for overall complications were multi-visceral resections, longer operation time, and high estimated blood loss in the univariate analysis. The independent risk factors were multi-visceral resection (odds ratio [OR], 2.832; 95% confidence interval [CI], 1.094–7.333; P=0.032) and longer operation time (OR, 1.005; 95% CI, 1.001–1.011; P=0.036) in the multivariate analysis. Previous reconstruction type, minimally invasive approach, and current stage were not associated with the overall complications.
Conclusions: Multi-visceral resection and long operation time were significant risk factors for the occurrence of complications following CTG rather than the RGC stage or surgical approach. When multi-visceral resection is required, a more meticulous surgical procedure is warranted to improve the postoperative complications during CTG for RGC after an initial gastric cancer surgery.

Keywords: Morbidity; Stomach neoplasm; Gastrectomy; Gastric stump

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
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INTRODUCTION

Patients who have undergone gastric resection for any cause have a higher risk of developing malignancy in the remnant stomach [1-3].. Previously, remnant gastric cancer (RGC) was commonly diagnosed in patients who underwent gastric resection for peptic ulcer disease. Recently, the surgical indications for peptic ulcer surgery are limited owing to the improved response to medical treatment; consequently, the incidence of RGC following peptic ulcer surgery has decreased. By contrast, the incidence of RGC is increasing among long-term survivors following gastric resection for early-stage gastric cancer (EGC) as detected during the national screening program [4-6].

Completion total gastrectomy (CTG) and lymph node dissection are the standard treatments for resectable RGC as well as primary disease [7]. CTG is correlated with a high risk of complications due to the formation of adhesions after surgery and altered gastrointestinal tract anatomy. In particular, lymph node dissection during initial gastric resection for cancer can cause profound adhesions between the remnant stomach and surrounding organs, such as the pancreas, spleen, liver, and transverse colon, with its mesentery [8,9].

Several risk factors for the occurrence of complications of CTG as treatment for RGC have been reported, regardless of the initial disease status [8]. However, as the indication for initial partial gastrectomy has changed from peptic ulcer disease to EGC, re-evaluation of the complications and their risk factors is warranted to identify new information. Moreover, the effect of minimally invasive surgery (MIS) for CTG should be evaluated as this procedure has become a popular surgical approach.

In this study, we aimed to analyze the postoperative complications and their risk factors following CTG for RGC after previous gastrectomy for cancer, excluding peptic ulcer, to improve the postoperative surgical outcomes.

MATERIALS AND METHODS

Study design and patients

Among 157 patients who underwent CTG between March 2002 and February 2021, 107 who had previously undergone distal gastrectomy as initial treatment for cancer were included. In the present study, RGC was defined as a newly detected cancer located in the remaining stomach, despite the time interval.

Data on the demographic features, details of the initial gastrectomy (approach and anastomosis type, extent of lymph node dissection, and stage), and the interval between the initial gastrectomy and CTG were collected. Comorbidity was calculated using the Charlson comorbidity index (CCI) scale, and the severity of comorbidity was categorized as low grade (CCI scores ≤2) or high grade (CCI scores >2).

The clinicopathological features of RGC (tumor histologic type, tumor location, tumor size, and stage) and surgical details of CTG (approach, combined resected organs, extent of lymph node dissection, operation time, and estimated blood loss) were reviewed. The main location of RGC was classified into the gastrointestinal anastomosis and remnant stomach. The histologic type was classified into two groups: differentiated (papillary, well-differentiated, and moderately

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differentiated tubular adenocarcinoma) or undifferentiated (poorly differentiated, mucinous tubular adenocarcinoma, and signet ring cell carcinoma). Gastric cancer staging was based on the 8th edition of the International Union for Cancer Control/American Joint Committee on Cancer [10]. All study patients underwent CTG with Roux-en-Y esophagojejunostomy.

The postoperative complications were defined as any adverse outcome occurring within one month after surgery and graded using the Clavien-Dindo classification [11]. Pancreatic fistula was defined as a drain output with an amylase level of >3 times the upper limit of normal serum amylase level and was associated with clinical significance [12]. Grade IIIa or higher complications, requiring additional intervention or surgery, were regarded as major complications. The risk factors were analyzed by comparing patients with and without complications.

All study procedures were performed in accordance with the principles of the 1964 Declaration of Helsinki. This study was reviewed and approved by the Institutional Review Board of the National Cancer Center, Korea (NCC 2021-0310).

Statistical analysis

Categorical variables were expressed as frequencies with percentages. Continuous variables were expressed as means with standard deviations. To analyze the relevant factors between the groups with and without complications, significant differences in categorical data and continuous variables were examined using Pearson's χ^2 test and Student's t-test or Mann-Whitney U test, respectively. Logistic regression analyses were performed to determine the factors that independently contributed to the occurrence of complications, and the values of these variables were expressed as odds ratios (ORs) with their corresponding 95% confidence intervals (CIs). Only variables with a P-value of less than 0.10 in the univariate analysis were included in the multivariate analysis. A P-value of <0.05 was considered significant. Data were analyzed using Systat R version 13.0 (Systat Software Inc., San Jose, CA, USA).

Informed consent statement

The requirement for obtaining informed consent was waived because of the retrospective study design.

RESULTS

Patients' demographic characteristics

The patients' baseline characteristics are summarized in **Table 1**. Most patients had previously undergone open distal gastrectomy (82/107, 76.6%). Billroth II anastomosis (80/107, 74.8%) was more frequently performed compared with Billroth I (27/107, 25.2%), and Roux-en Y reconstruction was not identified. The mean time interval between the previous gastrectomy and the development of RGC was 101.4±96.7 months (range:6–488 months). The time intervals between previous gastrectomy and the development of RGC were within 5 years and after 5 years in 47.7% and 52.3% of the patients, respectively. The tumor was located more frequently in the remnant stomach (75/107, 70.8%) than in the anastomosis site (31/107, 29.2%). Undifferentiated tumors (56/107, 52.3%) were more common than differentiated tumors (51/107, 47.7%). Open CTG was performed in 95 patients (88.8%), and splenectomy frequently performed during CTG (30/107, 28.0%), followed by colon resection (14/107, 13.1%). 51.5% of the patients had pStage 1 disease (52/101). The mean operative time was 246.6 minutes, and the volume of estimated blood loss was 304.3 mL.

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Table 1. Patients' demographic data

Variables	Value (n=107)
Sex	
Male	87 (81.3)
Female	20 (18.7)
Age (yr)	64.1±10.7
BMI (kg/m²)	21.6±3.1
Comorbidity	
Low CCI	78 (72.9)
High CCI	29 (27.1)
Previous approach	
Laparoscopy	24 (22.4)
Open	82 (76.6)
Robot assisted	1 (0.9)
Previous anastomosis	
Billroth I	27 (25.2)
Billroth II	80 (74.8)
Previous LN dissection	
Unknown	33 (30.8)
D1+	17 (15.9)
≥D2	57 (53.3)
Previous T classification	
Unknown	22 (20.6)
T1	40 (37.4)
T2	12 (11.2)
T3	17 (15.9)
T4a	16 (15.0)
Previous N classification	
Unknown	22 (20.6)
N0	64 (59.8)
N1	8 (7.5)
N2	6 (5.6)
N3a	7 (6.5)
Previous TNM stage	
Unknown	22 (20.6)
Stage 1	48 (44.9)
Stage 2	23 (21.5)
Stage 3	14 (13.1)
Time interval (mon)	101.4±96.7
≤5 yr	51 (47.7)
>5 yr	56 (52.3)
Tumor location*	
Anastomotic site	31 (29.2)
Remnant stomach	75 (70.8)
Histology	
Differentiated	51 (47.7)
Undifferentiated	56 (52.3)
Current approach	
Laparoscopy	12 (11.2)
Open conversion from laparoscopy	3 (2.8)
Open	92 (86.0)
Current LN dissection	
Unknown	1 (0.9)
D1+	31 (29.0)
D2	75 (70.1)
Combined resection	
No	71 (66.4)
Yes	36 (33.6)
Spleen	30 (28.0)
Pancreas	12 (11.2)
Colon	14 (13.1)
Liver	5 (4.7)

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Table 1. (Continued) Patients' demographic data

Variables	Value (n=107)
Reason for combined resection	
LN dissection	27 (25.2)
Direct invasion	16 (15.0)
Adhesion	1 (0.9)
Tumor size (cm)†	4.2±2.4
Retrieved LN‡	11.4±11.3
T classification	
T0	2 (1.9)
T1	38 (35.5)
T2	19 (17.8)
T3	19 (17.8)
T4	29 (27.1)
N classification‡	
N0	79 (78.2)
N1	11 (10.9)
N2	9 (8.9)
N3	2 (2.0)
M classification	
M0	101 (94.4)
M1 (peritoneal metastasis)	6 (5.6)
pStage	
1	52 (51.5)
2	25 (24.8)
3	18 (17.8)
4	6 (5.9)
Operation time (min)	246.6±96.2
EBL (mL)	304.3±344.4
Postoperative hospital stay (day)	14.6±12.8

Values are presented as mean ± standard deviation or number (%).
BMI = body mass index; CCI = Charlson comorbidity index; LN = lymph node; T = tumor; N = node; M = metastasis; EBL = estimated blood loss.
*Tumor location was unknown in 1 patient; †No residual tumors were detected in 5 patients; ‡No lymph nodes were retrieved in 6 patients.

Table 2. Postoperative complications

Variables	Value (n=107)
Complication	
No	70 (65.4)
Yes	37 (34.6)
Intra-abdominal abscess	19 (17.8)
Anastomotic leakage	9 (8.4)
Anastomotic stricture	3 (2.8)
Postoperative bleeding	1 (0.9)
Pancreatic fistula	1 (0.9)
Colon fistula	1 (0.9)
Pneumonia	5 (4.7)
Stroke	1 (0.9)
Wound problem	3 (2.8)
Clavien-Dindo classification	
II	10 (9.3)
IIIA	22 (20.6)
IIIB	4 (3.7)
IVA	1 (0.9)

Values are presented as number (%).

Postoperative complications

The details of postoperative complications are listed in **Table 2**. The complications rate was 34.6% (37/107), of which intra-abdominal abscess was the most common complication (19/107, 17.8%).

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The major complications (Clavien–Dindo grade III or higher) occurred in 25.2% (27/107). There was no mortality case.

Comparison of the clinicopathological characteristics according to the presence of overall complication

The clinicopathological features were compared based on the patients' complication (**Table 3**). The presence of combined resected organs, longer operative time, and higher volume of blood loss were significantly related to the occurrence of complications. However, previous operation-related factors (previous approach, anastomosis type, extent of lymph node dissection, and stage), current approach for CTG, tumor location, tumor size, extent of lymph node dissection, and T and N classifications were not markedly different between the two groups.

Table 3. Comparison of the clinicopathological characteristics according to the presence of overall complication

Variables	Without complication (n=70)	With complications (n=37)	P-value
Sex			0.828
Male	56 (80.0)	31 (83.8)	
Female	14 (20.0)	6 (16.2)	
Age	64.1±11.0	64.2±10.2	0.952
BMI	21.5±3.2	21.8±2.9	0.653
Comorbidity			0.112
Low CCI	55 (78.6)	23 (62.2)	
High CCI	15 (21.4)	14 (37.8)	
Previous approach			0.654
Laparoscopy	14 (20.0)	10 (27.0)	
Open	55 (78.6)	27 (73.0)	
Robot assisted	1 (1.4)	0 (0.0)	
Previous anastomosis			0.939
Billroth I	17 (24.3)	10 (27.0)	
Billroth II	53 (75.7)	27 (73.0)	
Previous LN dissection*			0.897
D1+	11 (21.6)	6 (26.1)	
≥D2	40 (78.4)	17 (73.9)	
Previous T classification†			0.971
T1	27 (45.8)	13 (50.0)	
T2	8 (13.6)	4 (15.4)	
T3	12 (20.3)	5 (19.2)	
T4a	12 (20.3)	4 (15.4)	
Previous N classification†			0.074
N0	45 (76.3)	19 (73.1)	
N1	3 (5.1)	5 (19.2)	
N2	4 (6.8)	2 (7.7)	
N3	7 (11.9)	0 (0.0)	
Time interval (mon)	93.2±91.5	116.9±100.2	0.229
Tumor location‡			0.204
Anastomosis	23 (32.9)	8 (22.2)	
Remnant stomach	47 (67.1)	28 (77.8)	
Histology			0.956
Differentiated	34 (48.6)	17 (45.9)	
Undifferentiated	36 (51.4)	20 (54.1)	
Current approach			0.748
Laparoscopy	7 (10.0)	5 (13.5)	
Open	63 (90.0)	32 (86.5)	
Current LN dissection			0.299
D1+	23 (33.3)	8 (21.6)	
D2	46 (66.7)	29 (78.4)	
Retrieved LN	11.2±11.0	11.8±11.4	0.777
Combined resection			0.002
No	54 (77.1)	17 (45.9)	
Yes	16 (22.9)	20 (54.1)	

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Table 3. (Continued) Comparison of the clinicopathological characteristics according to the presence of overall complication

Variables	Without complication (n=70)	With complications (n=37)	P-value
Tumor size	4.1±2.5	4.3±2.3	0.734
T classification			0.088
T0	1 (1.4)	1 (2.7)	
T1	25 (35.7)	13 (35.1)	
T2	14 (20.0)	5 (13.5)	
T3	16 (22.9)	3 (8.1)	
T4	14 (20.0)	15 (40.5)	
N classification			0.124
N0	54 (83.1)	25 (69.4)	
N1	7 (10.8)	4 (11.1)	
N2	4 (6.2)	5 (13.9)	
N3	0 (0.0)	2 (5.6)	
M classification			1.000
M0	66 (94.3)	35 (94.6)	
M1	4 (5.7)	2 (5.4)	
Operation time (min)	222.9±96.2	291.2±79.9	<0.001
EBL (mL)	247.7±241.3	411.5±406.1	0.042
Postoperative hospital stay (day)	9.5±3.8	24.2±17.6	<0.001

Values are presented as mean ± standard deviation or number (%).
BMI = body mass index; CCI = Charlson comorbidity index; LN = lymph node; T = tumor; N = node; M = metastasis; EBL = estimated blood loss.
*Unknown cases excluded (n=33); †Unknown cases excluded (n=22); ‡Excluded unknown case (n=1).

Risk factors for overall complication

In the multivariable Cox regression analysis, presence of combined resected organs (OR, 2.832; 95% CI, 1.094–7.333; P=0.032) and longer operation time (OR, 1.005; 95% CI, 1.001–1.011; P=0.036) were the significant factors for overall complications (**Table 4**).

DISCUSSION

In this study, we evaluated the incidence of postoperative morbidity and its risk factors following CTG for RGC. The overall complication rate was 34.6%. Multi-visceral resection and longer operation time were the significant factors for postoperative complications.

It has been reported that the overall complication rate of CTG for RGC was 10%–44.8% [13-15], while the mortality rate was 0%–13.7% [16-18]. In the present study, the mortality rate was 0%, but the complication rate was relatively high at 34.6%. The higher complication

Table 4. Univariate and multivariate analyses of the risk factors of the overall complication

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Combined resection			0.002			0.032
No	1.000			1.000		
Yes	3.973	1.691–9.327		2.832	1.094–7.333	
T classification			0.567			
T0–2	1.000					
T3–4	1.258	0.572–2.814				
N classification			0.116			
N0	1.000					
N1–3	2.162	0.829–5.651				
Operation time	1.010	1.001–1.013	0.001	1.005	1.001–1.011	0.036
EBL	1.003	1.001–1.008	0.032	1.000	0.999–1.002	0.808

OR = odds ratio; CI = confidence interval; T = tumor; N = node; EBL = estimated blood loss.

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rate reported in this study is due to the fact that only patients who underwent partial gastric surgery for gastric cancer were included, excluding those with peptic ulcer disease [19,20]. Our results indicate that the surgical approach used after initial gastric cancer surgery is more difficult than that used after initial peptic ulcer surgery.

As the indication of partial gastrectomy changed from peptic ulcer disease to gastric cancer due to the improvement in treatment response among peptic ulcer disease patients and the well-organized screening program for gastric cancer, re-evaluation of the complications and their risk factors of CTG is warranted to improve the surgical outcomes [21]. To the best of our knowledge, our study was the first report dealing RGC patients who underwent initial cancer surgery, excluding those with peptic ulcer disease.

Initial gastric cancer surgery is quite different from peptic ulcer surgery. Simple partial gastrectomy and gastrojejunostomy without lymph node dissection are performed in most patients with peptic ulcer disease. However, perigastric and extragastric lymph node dissection are indispensable in the initial cancer surgery. Moreover, several options for the reconstruction of the remnant stomach to the duodenum and jejunum are more sophisticated. Therefore, adhesion to the surrounding organs, such as the liver, pancreas, and transverse colon, was profound after the initial gastric cancer surgery. Adhesiolysis and removal of the remaining stomach and lymph nodes are technically demanding [15,20]. These differences were supposed to be the main reason for the high rate of postoperative complications in this study after initial gastric cancer surgery compared with peptic ulcer gastrectomy [19].

In this study, the risk factors for the occurrence of complications were determined as combined organ resection and longer operation time rather than RGC stage or surgical approach, which were comparable to the reports of previous studies [8,9,22]. Since most of the patients were diagnosed with RGC at an early stage through postoperative surveillance or screening endoscopy, the risk factors of CTG were related to reoperation itself rather than the current tumor stage and surgical approach, which was similar to the results of another study [8].

Previous studies reported that the rates of anastomotic leakage (3.8%–10.9%) and pulmonary complication (4%–8.6%) were relatively high in patients who underwent CTG [14,23,24]. On the contrary, intra-abdominal abscess was the most common (17.8%, 19/107), followed by anastomotic leakage (8.4%, 9/107) among complications in the present study. Compared with other studies, it was difficult to determine why intra-abdominal abscess is more common than anastomotic leakage.

Initial laparoscopic surgery might be related to a lower rate of open conversion for CTG owing to less adhesions [25,26]. However, Son et al. [20] reported that previous laparoscopic surgery did not reduce adhesions to the operative bed or anastomotic site. This study showed that the previous surgical approach did not affect the incidence of CTG complications.

Owing to the advances in laparoscopic instruments and the accumulated experience of surgeons, the rate of MIS for RGC is increasing. Several studies reported that MIS for RGC showed similar volume of blood loss, complication rate, number of retrieved lymph nodes, and pathologic findings and favorable overall survival compared with open surgery [14,20,26]. However, the open conversion rate from laparoscopy was also relatively high (25%–47%) due to the formation of adhesions from previous surgery. As MIS remains technically challenging, the selection of a surgical approach for CTG should be carefully considered.

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This study has some limitations, including its small, retrospective, single-center design. Only a few patients underwent initial and laparoscopic CTG for RGC after partial gastric cancer surgery. In the era of MIS, the role of this type of surgery should be evaluated to determine whether it can improve the surgical outcomes compared with conventional open surgery.

In conclusion, the complication rate of CTG for RGC after partial gastric cancer surgery is relatively high. The primary risk factors were multi-visceral resection and longer operative time rather than tumor stage and surgical approach. Hence, surgical strategies considering these factors are warranted to improve the outcomes of CTG for RGC.

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