Risk factors for complications during surgical treatment of remnant gastric cancer

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Abstract

Background Surgical treatment for remnant gastric cancer is related to high mortality and morbidity. The aim of this study was to identify risk factors that predispose to postoperative complications after gastrectomy for remnant gastric cancer.

Methods A total of 210 patients who underwent a gastrectomy for remnant gastric cancer between January 1998 and December 2012 were retrospectively analyzed. Surgical complications were reviewed and graded using the Clavien–Dindo classification. Univariate and multivariate analysis was performed to identify the risk factors for development of complications.

Results The incidence of postoperative complications was 46 % (96/210), and major complications occurred in 14 % (30/210). The operation-related mortality rate was 1.0 %. Multivariate analysis revealed that only a BMI ≥ 25 ($P = 0.001$) and blood transfusion ($P < 0.001$) were significant independent risk factors for major complication. Indication for the initial gastrectomy and previous anastomosis type were not related to the development of surgical complications.

Conclusions Although surgery for remnant gastric cancer is a complex procedure because of the previous operation, factors related to the previous operation do not affect the development of postoperative complications.

Keywords Complication · Remnant gastric cancer · Gastrectomy · Risk factor

Introduction

Patients who have undergone a partial gastrectomy for any reason are considered at increased risk of malignant formation in the remnant gastric tissue, termed a remnant gastric cancer [1–3]. As a result of recently increased health screening in Korea and Japan, more than 50 % of newly diagnosed cases of gastric cancer are in an early stage [4, 5]. Moreover, advances in surgical procedures and adjuvant therapies have enabled long-term survival, even in patients with advanced gastric cancer [6]. Gastric resection for a benign ulcer was frequently performed two or three decades earlier when physicians did not commonly use H₂-receptor antagonists or proton pump inhibitors. However, the risk of remnant gastric cancer is linked to the length of time that has passed since the gastrectomy was performed [7, 8]. Therefore, we can anticipate an increasing occurrence of remnant gastric cancer in patients who have undergone a gastrectomy for any reason.

Favorable prognosis could be achieved when the tumor is removed completely from patients with remnant gastric cancer [9]. Although gastrectomy is currently the only curable treatment for remnant gastric cancer, this complex surgery remains associated with relatively high rates of morbidity and mortality [10, 11]. Anatomical alterations, intraabdominal adhesions, and the frequent combined resection of other organs make an operation for remnant gastric cancer difficult.

Most studies that have investigated this surgical treatment have enrolled only a few dozen patients and supplied only a brief descriptive analysis of their complications.

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Hence, the risk factors that predispose to those complications are yet to be fully understood. We aimed to analyze the early postoperative complications following gastrectomy for remnant gastric cancer and to achieve a better understanding of the risk factors involved.

Methods

Study design

Data of 210 patients who underwent a gastrectomy for remnant gastric cancer in the Yonsei University Health System between January 1998 and December 2012 were retrospectively collected. The definition of remnant gastric cancer used in this study was a newly diagnosed carcinoma located in remnant gastric tissue regardless of time interval and the type of initial disease.

We checked body weight, hemoglobin, and albumin as potential risk factors for evaluating nutritional status. Body mass index (BMI) status was divided into three groups, using the conventional World Health Organization BMI classification: $<18.5 \text{ kg/m}^2$ = underweight, ≥ 18.5 to $<25 \text{ kg/m}^2$ = normal, $\geq 25 \text{ kg/m}^2$ = overweight [12]. The 7th edition of the International Union for Cancer Control/American Joint Committee on Cancer (UICC/AJCC) was used for gastric cancer staging. Postoperative complications were defined as the occurrence of any adverse event up until 1 month post surgery and which were recorded by reviewing the patient data and graded according to the Clavien–Dindo classification [13]. Grade I or II complications were considered as minor, and grade IIIa or greater, which required additional interventional or surgical treatment, were considered as major complications.

Surgical procedures

Typically, patients in our study group received a completion total gastrectomy, in which case the bowel was reconstructed using a Roux-en-Y esophagojejunostomy. When a patient had sufficient remnant stomach to secure adequate resection margins, a subtotal gastrectomy was considered. In those cases, either a gastrojejunostomy or Roux-en-Y gastrojejunostomy was performed depending on the individual situation and the surgeon's preference. The extent of the lymph node dissection was determined by the Japanese guideline for the treatment of gastric carcinoma [14–17]. Lymph nodes that belonged to D1+ (nos. 1–4, 7, 8a, 9, and 11p) were dissected in early gastric cancer, as well as those associated with D2 (D1+ plus nos. 10, 11d, and 12a) in advanced gastric cancer, with the exception of the suprapyloric and infrapyloric lymph nodes

(nos. 5 and 6). A combined splenectomy was not typically performed, especially in early-stage cases.

Statistical analysis

Patients were divided into two groups; those who had a complication and those who did not. The independent *t* test for continuous variables and chi-square test or Fisher's exact test for categorical variables were used to find factors that predisposed patients to having a complication of any severity. Furthermore, logistic regression (univariate and multivariate) was performed to identify factors with an independent contribution to the outcome. The result of the logistic regression model was expressed as an odds ratio (OR) with 95 % confidence interval. Variables with a *P* value of <0.10 in the univariate analysis were applied to the multivariate regression test. A *P* value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 19.0 (IBM, New York, NY, USA).

Results

Among the 210 patients, 157 (74.8 %) underwent initial gastrectomy for gastric cancer and the remaining 53 (25.2 %) for benign disease (predominantly gastroduodenal ulcer). A total of 167 patients (79.5 %) received gastrojejunostomy reconstruction after the initial gastrectomy. A total of 124 patients (59.0 %) had a lesion with anastomosis involvement. A completion total gastrectomy was performed in 197 patients (93.8 %) and a subtotal gastrectomy was performed in 13 patients (6.2 %). D2 or more extensive lymph node dissection was performed in 118 patients (56.2 %). The spleen was the most common organ simultaneously resected, followed by the transverse colon. Splenectomy was more frequent in patients with gastrojejunostomy (71 of a total of 77 splenectomies) than in those with a gastroduodenostomy (5 of a total of 77 cases). Segmental resection of the transverse colon was similar in both sets of patients (33 cases in gastrojejunostomy and 2 cases in gastroduodenostomy patients among a total of 35 cases of transverse colon resection). Postoperative complications (including both minor and major issues) occurred in 96 patients (45.7 %), and 30 patients (14.3 %) suffered from major complications. As shown in Table 1, wound problems (13.8 %) and atelectasis (7.6 %) were the most common surgical and medical complications. Pleural effusion (5.7 %) was the most common major complication after operation for remnant gastric cancer.

Patient characteristics and clinical information were compared by the overall postoperative complications and major complications as shown in Table 2. Mean operation

Table 1 Postoperative complications

	Minor complications (Grade I or II)		Major complications (Grade ≥ 3 a)	
	Type	No. (%)	Type	No. (%)
Surgical	Wound	29 (13.8 %)	Pleural effusion	12 (5.7 %)
	Pancreatic injury	9 (4.3 %)	Anastomotic leakage	8 (3.8 %)
	Intestinal obstruction or ileus	6 (2.9 %)	Intraabdominal fluid collection/abscess	5 (2.4 %)
	Intraabdominal fluid collection/abscess	3 (1.4 %)	Pancreatic injury	4 (1.9 %)
	Pleural effusion	2 (1.0 %)	Intraabdominal bleeding	2 (1.0 %)
	Intraluminal bleeding	1 (0.5 %)	Intestinal obstruction	2 (1.0 %)
	Anastomotic leakage	1 (0.5 %)		
	Others ^a	2 (1.0 %)		
	Atelectasis	16 (7.6 %)	Pneumonia	5 (2.4 %)
	Neurological problem	5 (2.4 %)	Pulmonary edema	1 (0.5 %)
Medical	Liver enzyme elevation	4 (1.9 %)		
	UTI	2 (1.0 %)		
	Voiding difficulty	3 (1.4 %)		
	Others ^b	2 (1.0 %)		

UTI urinary tract infection

^a Bile leakage, remnant stomach infarction

^b Thrombophlebitis, fungemia

time was 227 min, and mean estimated blood loss was 286 ml. Previous operation-related factors (anastomosis type, the cause of the initial gastrectomy) and anastomosis involvement did not have an effect on the development of complications.

Multivariate analysis identified two significant risk factors for developing overall complications: male gender [OR = 2.4 (1.1–5.2); $P = 0.030$] and high BMI (≥ 25 kg/m²) [OR = 9.2 (2.7–31.3); $P < 0.001$] (Table 3). High BMI (≥ 25 kg/m²) [OR = 8.4 (2.3–30.2); $P = 0.001$] and blood transfusion [OR = 6.0 (2.2–16.0) $P < 0.001$] was identified as independent risk factors for developing major complications after operation for remnant gastric cancer (Table 4).

Two patients died after surgery (1.0 %), one of anastomotic leakage combined with postoperative bleeding and the other of hospital-acquired pneumonia.

Discussion

Blood transfusion and obesity are known risk factors for the development of postoperative complications in general surgery as well as in gastric surgery [18–21]. Our study confirmed this, and further revealed that previous operation-related factors such as anastomosis type and the indication for initial gastrectomy have no impact on the risk of developing complications.

Although all patients with remnant gastric cancer have an identical history of gastric surgery, they are a very diverse population. The current intraabdominal state of patients is different, depending on whether the cause of previous gastrectomy was a benign or malignant disease.

Patients who have undergone a gastrectomy in the context of benign disease (typically a gastroduodenal ulcer perforation) might be characterized by diffuse intraabdominal adhesions. When those patients present with remnant gastric cancer, dissection of the lymph nodes around major blood vessels and an omentectomy are required. Conversely, patients who underwent their first gastrectomy in the context of malignant disease might be characterized by dense adhesions concentrated to the remnant stomach, liver, pancreas, and transverse colon. Nevertheless, we are able occasionally to omit dissection for already removed lymph nodes and omentum. Not only that, there are some differences according to previous anastomosis types. During a gastrojejunal anastomosis, the jejunum is pulled up across the transverse colon, which causes the jejunum or the anastomosis site to adhere with the transverse colon. When patients with a gastrojejunostomy present with a remnant gastric cancer, the dissection of a broader area is required for adhesiolysis. Severe adhesion may lead to frequent colon resection itself. Sometimes it is difficult to distinguish adhesion from tumor invasion. Our data have already shown more frequent colon resection in patients with a gastrojejunostomy compared with patients with a gastroduodenostomy. In contrast, gastroduodenostomy causes dense adhesions to liver and pancreas. However, we are not aware of any previous investigations into remnant gastric cancer that address risk factors related to anastomosis type, previous disease, or nutritional status. This is the first study to investigate risk factors for developing complications after remnant gastric cancer surgery.

Previous studies report an overall surgical complication rate for remnant gastric cancer of 19–47 %, with operation-related mortality rates of 2–13 % [9–11, 22–24]. In our

Table 2 Patient characteristics and statistical analysis of overall and major complications

	Total	Overall complication			Major complication		
	<i>n</i> = 210	Absence (<i>n</i> = 114)	Presence (<i>n</i> = 96)	<i>P</i>	Absence (<i>n</i> = 180)	Presence (<i>n</i> = 30)	<i>P</i>
Age	59.8 ± 11.1	59.0 ± 10.9	60.7 ± 11.3	0.270	59.1 ± 10.8	63.6 ± 12.4	0.039
Sex				0.019			0.008
Male	164	82 (50.0 %)	82 (50.0 %)		135 (82.3 %)	29 (17.7 %)	
Female	46	32 (69.6 %)	14 (30.4 %)		45 (97.8 %)	1 (2.2 %)	
Comorbidity				0.187			0.492
No	124	72 (58.1 %)	52 (41.9 %)		108 (87.1 %)	16 (12.9 %)	
Yes	86	42 (48.8 %)	44 (51.2 %)		72 (83.7 %)	14 (16.3 %)	
Diabetes	26	11 (42.3 %)	15 (57.7 %)	0.190	22 (84.6 %)	4 (15.4 %)	0.771
Cardiovascular	49	23 (46.9 %)	26 (53.01 %)	0.238	39 (79.6 %)	10 (20.4 %)	0.162
Pulmonary	26	14 (53.8 %)	12 (46.2 %)	0.962	24 (92.3 %)	2 (7.7 %)	0.386
Other	16	8 (50.0 %)	8 (50.0 %)	0.720	12 (75.0 %)	4 (25.0 %)	0.255
BMI (kg/m ²)	21.2 ± 3.1	20.7 ± 2.6	21.9 ± 3.4	0.004	21.0 ± 2.9	22.7 ± 3.7	0.019
Hemoglobin (g/dl)	12.2 ± 1.8	12.3 ± 1.7	12.2 ± 1.8	0.580	12.3 ± 1.7	12.1 ± 2.0	0.606
Albumin (g/dl)	4.2 ± 0.8	4.3 ± 1.0	4.1 ± 0.5	0.209	4.2 ± 0.8	4.1 ± 0.5	0.369
Previous anastomosis type				0.789			0.383
B-I	40	22 (55.0 %)	18 (45.0 %)		37 (92.5 %)	3 (7.5 %)	
B-II	167	91 (54.5 %)	76 (45.5 %)		140 (83.8 %)	27 (16.2 %)	
Other ^a	3	1 (33.3 %)	2 (66.7 %)		3 (100.0 %)	0 (0.0 %)	
Previous disease				0.942			0.795
Benign	53	29 (54.7 %)	24 (45.3 %)		46 (86.8 %)	7 (13.2 %)	
Cancer	157	85 (54.1 %)	72 (45.9 %)		134 (85.4 %)	23 (14.6 %)	
Lesion				0.299			0.136
Anastomosis involved	124	71 (57.3 %)	53 (42.7 %)		110 (88.7 %)	14 (11.3 %)	
Body	86	43 (50.0 %)	43 (50.0 %)		70 (81.4 %)	16 (18.6 %)	
Resection				0.588			0.222
Subtotal	13	8 (61.5 %)	5 (38.5 %)		13 (100.0 %)	0 (0.0 %)	
Completion total	197	106 (53.8 %)	91 (46.2 %)		167 (84.8 %)	30 (15.2 %)	
LN dissection				0.091			0.212
<D2	92	56 (60.9 %)	36 (39.1 %)		82 (89.1 %)	10 (10.9 %)	
≥D2	118	58 (49.2 %)	60 (50.8 %)		98 (83.1 %)	20 (16.9 %)	
Combined resection				0.030			0.310
No	109	67 (61.5 %)	42 (38.5 %)		96 (88.1 %)	13 (11.9 %)	
Yes	101	47 (46.5 %)	54 (53.5 %)		84 (83.2 %)	17 (16.8 %)	
Approach				0.270			0.727
Open	192	102 (53.1 %)	90 (46.9 %)		165 (85.9 %)	27 (14.1 %)	
MIS	18	12 (66.7 %)	6 (33.3 %)		15 (83.3 %)	3 (16.7 %)	
Transfusion				0.002			<0.001
No	149	91 (61.1 %)	58 (38.9 %)		139 (93.3 %)	10 (6.7 %)	
Yes	61	23 (37.7 %)	38 (62.3 %)		41 (67.2 %)	20 (32.8 %)	
Operation time (min)	227.1 ± 80.7	222.5 ± 84.2	232.5 ± 76.3	0.374	223.2 ± 80.0	250.4 ± 80.5	0.086
Estimated blood loss (ml)	286.4 ± 499.1	228.5 ± 501.0	355.4 ± 490.6	0.068	256.2 ± 483.0	466.1 ± 561.8	0.033
Retrieved LN	14.5 ± 14.5	13.7 ± 13.8	15.4 ± 15.2	0.419	14.4 ± 14.0	15.2 ± 17.5	0.767
T stage				0.055			0.940
T1, T2, T3	125	74 (59.2 %)	51 (40.8 %)		108 (86.4 %)	17 (13.6 %)	
T4a	45	25 (55.6 %)	20 (44.4 %)		38 (84.4 %)	7 (15.6 %)	
T4b	40	15 (37.5 %)	25 (62.5 %)		34 (85.0 %)	6 (15.0 %)	

Table 2 continued

	Total <i>n</i> = 210	Overall complication			Major complication		
		Absence (<i>n</i> = 114)	Presence (<i>n</i> = 96)	<i>P</i>	Absence (<i>n</i> = 180)	Presence (<i>n</i> = 30)	<i>P</i>
N stage				0.030			0.006
N0	149	88 (59.1 %)	61 (40.9 %)		134 (89.9 %)	15 (10.1 %)	
≥N1	61	26 (42.6 %)	35 (57.4 %)		46 (75.4 %)	15 (24.6 %)	

P value <0.05 was expressed with bold characters

BMI body mass index, *B-I* gastroduodenostomy, *B-II* gastrojejunostomy, *MIS* minimally invasive surgery, *LN* lymph node

^a Roux-en-Y gastrojejunostomy and proximal gastrectomy

Table 3 Univariate and multivariate analysis for overall complications

	<i>n</i>	Univariate		Multivariate	
		Odds ratio (95 % CI)	<i>P</i>	Odds ratio (95 % CI)	<i>P</i>
Sex					
Male	164	2.286 (1.137–4.597)	0.020	2.375 (1.086–5.193)	0.030
Female	46	1		1	
BMI (kg/m ²)			0.007		0.001
<18.5	38	0.772 (0.371–1.607)	0.489	0.640 (0.280–1.461)	0.289
18.5–24.9	151	1		1	
≥25	21	5.623 (1.806–17.509)	0.003	9.178 (2.692–31.297)	<0.001
LN dissection					
<D2	92	1		1	
≥D2	118	1.609 (0.926–2.797)	0.092	1.754 (0.811–3.794)	0.154
Combined resection					
No	109	1		1	
Yes	101	1.833 (1.058–3.174)	0.031	1.124 (0.516–2.447)	0.769
Transfusion					
No	149	1		1	
Yes	61	2.592 (1.403–4.788)	0.002	1.962 (0.966–3.984)	0.062
T stage			0.061		0.467
T1, T2, T3	125	1		1	
T4a	45	1.161 (0.584–2.309)	0.671	0.869 (0.370–2.040)	0.746
T4b	40	2.418 (1.162–5.032)	0.018	1.218 (0.540–2.748)	0.635
N stage					
N0	149	1		1	
≥N1	61	1.942 (1.062–3.551)	0.031	1.218 (0.540–2.748)	0.635

CI confidence interval, *BMI* body mass index, *LN* lymph node

study, the overall complication rate was relatively high at 46 %, which might be partially explained by the fact that our study applied the Clavien–Dindo classification system strictly, and thus includes minor problems that could be resolved with just simple supportive care. The mortality rate in our research group was 1 %, which is relatively low not only when compared to other studies investigating surgery for remnant gastric cancer, but also when compared to primary gastric cancer treatment in general. In fact, it is impractical to compare the incidence of complications directly between studies because most studies apply different definitions or criteria for complications.

Although there were no rigid criteria for blood transfusion, we chose blood transfusion for multivariate analysis rather than estimated blood loss for several reasons. First, blood transfusion had a stronger statistical power for developing complications than estimated blood loss in our study. Estimated blood loss had a higher *P* value than blood transfusion in spite of the application of various cutoff values. Second, a continuous variable could make different results in univariate and multivariate analysis according to cutoff value setting. However, the data for transfusion or not are concrete and unchangeable. Third, blood transfusion itself could affect a patient's condition

Table 4 Univariate and multivariate analysis for major complications

	<i>n</i>	Univariate		Multivariate	
		Odds ratio (95 % CI)	<i>P</i>	Odds ratio (95 % CI)	<i>P</i>
Age (years)					
<65	129	1		1	
≥65	81	2.370 (1.082–5.191)	0.031	2.125 (0.822–5.492)	0.120
Sex					
Male	164	9.667 (1.280–73.003)	0.028	7.280 (0.870–60.896)	0.067
Female	46	1		1	
BMI (kg/m ²)			0.009		0.004
<18.5	38	0.869 (0.276–2.737)	0.811	0.821 (0.223–3.028)	0.768
18.5–24.9	151	1		1	
≥25	21	4.547 (1.658–12.471)	0.003	8.400 (2.340–30.155)	0.001
Transfusion					
No	149	1		1	
Yes	61	6.780 (2.941–15.631)	<0.001	5.958 (2.219–16.001)	<0.001
Operation time					
<240 min	141	1		1	
≥240 min	69	2.739 (1.248–6.008)	0.012	1.699 (0.663–4.356)	0.270
N stage					
N0	149	1		1	
≥N1	61	2.913 (1.322–6.420)	0.008	2.119 (0.818–5.487)	0.122

CI confidence interval, BMI body mass index

immunologically or hemodynamically. The influence on the patient from the blood transfusion may be greater than from the amount of blood loss. Fourth, the blood transfusion reflects not only the amount of blood loss during an operation but also preoperative hemoglobin status or general condition. Patients with low hemoglobin levels in the preoperative evaluation could have received a blood transfusion easily even though there was relatively a small amount of blood loss during operation. Also, patients who have undergone gastrectomy are susceptible to developing chronic anemia. Additionally, we tried to analyze the development of complications with estimated blood loss instead of blood transfusion. When we set a cutoff value of estimated blood loss as 180 ml, which make the lowest *P* value, odds ratios for overall complication were 2.081 (1.189–3.644); *P* = 0.010 and 1.506 (0.795–2.852); *P* = 0.209 in univariate and multivariate analysis, respectively. For major complications, odds ratios were 4.229 (1.829–9.781); *P* = 0.001 and 3.695 (1.371–9.960); *P* = 0.010 in univariate and multivariate analysis, respectively. Odds ratios of other variables were largely identical with minor changes in multivariate analysis compared to using blood transfusion.

Thirteen patients (6.4 %) in our study group underwent a subtotal gastrectomy rather than a total gastrectomy as treatment of their remnant gastric cancer. A gastrectomy, whether indicated for a benign or malignant process, alters

the environment of the remnant stomach in such a way that novel neoplastic processes are more likely to arise [25, 26]. In addition, genetic factors such as p53 have also been suggested as etiological factors for carcinogenesis in the context of a gastrectomy for carcinoma [27, 28]. Because the remnant stomach might have been in the process of carcinogenesis already for a long period of time, total gastrectomy is considered preferable as a treatment for remnant gastric cancer, rather than subtotal gastrectomy.

This study was limited by the retrospective nature of its data collection, as well as the fact that the data were derived from a single institution. However, reports detailing several hundred cases collected from multiple centers are usually limited, displaying only the analysis of clinical and pathological characteristics or long-term survival [29, 30]. To our knowledge, our institution hosts the largest number of surgical cases of remnant gastric cancer in the world, which provides a highly consistent standard of treatment, resulting in the high quality and consistency of our surgical database.

Only high BMI and blood transfusion were found to be independent risk factors predisposing to complications during the surgical treatment of remnant gastric cancer. Previous operation-related factors such as anastomosis type and the indication for the initial gastrectomy have no impact on the risk of developing complications.

Conflict of interest All authors have no conflict of interest.

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