Original Article

Risk factors for remnant gastric cancer after distal gastrectomy for gastric cancer: a retrospective database review

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Background: The number of patients with remnant gastric cancer (RGC) following gastrectomy for gastric cancer (GC) is increasing due to the increasing number of patients undergoing function-preserving gastrectomy and improved outcomes for patients with GC. A few studies involving a small number of cases reported male sex, old age, differentiated type, tumor depth and synchronous multiple GC were associated with RGC development. However, the risk factors for RGC development had not been fully understood. This study aimed to examine the clinicopathological features, followed up patients with GC after they underwent distal gastrectomy (DG), and evaluated the potential risk factors for RGC development.

Methods: A retrospective database review of 438 patients who underwent DG for GC at a single institution, from 2006 to 2017, was conducted. We investigated the relationship of clinicopathological features, operative findings, and postoperative course with RGC development was estimated using Cox proportional hazard analysis. The cumulative incidences of RGC were calculated using the Kaplan-Meier method.

Results: We retrospectively analyzed 405 cases. The median patient age was 69 years, and the patient cohort consisted of 263 men and 142 women. The Billroth-I reconstruction method was used in 204 cases, Billroth-II method was used in 3 cases, and Roux-en Y method was used in 198 cases. RGC was diagnosed in 11 of the 405 patients. The median follow-up period was 5 years. The cumulative incidences of RGC calculated by the Kaplan-Meier method were 3.0%, 4.1%, and 10.5% at 5, 10, and 15 years after DG, respectively. During the initial surgery, differentiated type was significantly associated with RGC development [hazard ratio (HR): 4.71, 95% confidence interval (CI): 1.02–21.80, P=0.05]. Male sex (HR: 2.97, 95% CI: 0.64–13.75, P=0.16), old age (≥70 years) (HR: 2.72, 95% CI: 0.78–9.47, P=0.11), and synchronous multiple GC (HR: 1.31, 95% CI: 0.28–6.08, P=0.73) were not associated with RGC development.

Conclusions: Patients who have undergone DG for differentiated type GC were statistically significantly associated with developing RGC. Intensive endoscopic surveillance would be needed for the patients who underwent DG for differentiated type GC.

Keywords: Distal gastrectomy; remnant gastric cancer (RGC); risk factors

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Introduction

Gastric cancer (GC) ranks fifth in terms of incidence and fourth in terms of mortality worldwide. In Eastern Asia, the incidence of GC is the highest among the other regions and is a serious health problem (1). The term remnant gastric cancer (RGC) has been used to define all cancers arising from the remnant stomach after partial gastrectomy, regardless of the initial disease or operation (2,3). RGC was commonly thought to develop near the gastric stump, more than 10 years following Billroth-II (B-2) reconstruction for benign disease (4). However, due to an increase in the number of patients undergoing function-preserving gastrectomy and improved outcomes for patients with GC, the number of patients with RGC following gastrectomy for GC is increasing (5). According to a nationwide Japanese survey, the incidence rate of RGC was 2.4% after distal gastrectomy (DG) for GC (6). Several reports on the cumulative incidence of RGC after DG have been published. The cumulative incidence rate of RGC was 2.6–6.1% (7-9) at 10 years, 3.2% (4) at 15 years, and 4.0–5.4% (7,9) at 20 years after DG for GC. As the incidence of RGC is high and increases over time, the nontumorous mucosa in primary GC could be the cancer-causing region of RGC. Male sex (7,10), old age (10), differentiated type GC (7,10), tumor depth (10), and synchronous multiple GC (9,11,12) have been reported to be associated with RGC development. However, these risk factors that have been previously identified were from studies that included only a small number of cases and had not been not fully understood.

Radical surgery remains the only curative treatment for RGC; however, because of intraabdominal adhesions and different lymphatic structures in RGC, surgical treatment is complex and remains to be associated with relatively high rates of morbidity and mortality (2,13). Moreover, the reported 5-year survival rates after gastrectomy were worse in cases of stage III RGC than in proximal primary GC cases (14). Moreover, endoscopic submucosal dissection (ESD) of the remnant stomach is technically difficult because of the limited working space, particularly for lesions that involve the suture line or anastomosis, which contains staples and may have severe fibrosis (15). However, the indications of ESD for primary GC can be applied to RGC (16). Compared with surgical treatment, ESD is considered a minimally invasive treatment even for early GC in the remnant stomach, based on the reported favorable long-term outcomes (15). Therefore, endoscopic surveillance of the gastric remnant for early detection of RGC that can be treated with ESD is extremely important.

According to the Japanese Gastric Cancer Association guidelines, endoscopy should be performed every 2 years after gastrectomy for up to 5 years, regardless of the cancer stage (17). However, an optimal surveillance program for the early detection of RGC more than 5 years after gastrectomy remains controversial. Hosokawa *et al.* reported that endoscopic examinations should be performed at intervals of 2–3 years (8); Ojima *et al.* and Ohashi *et al.* recommended that endoscopic surveillance should be conducted annually (5,18). Moreover, Nozaki *et al.* recommended endoscopic surveillance for an appropriate period according to the risk (11).

In summary, the risk factors for RGC had been understudied. Moreover, an endoscopic surveillance program for early detection of RGC has not yet been established. This study aimed to clarify the risk factors for RGC development after an initial DG. We examined the clinicopathological features, and followed up patients with GC after they underwent DG. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-545/rc).

Highlight box

Key findings

- Differentiated type gastric cancer (GC) is a risk factor for developing remnant GC (RGC).

What is known and what is new?

- The risk factors for developing RGC had not been fully understood.
- Patients who have undergone distal gastrectomy (DG) for differentiated type GC were statistically significantly associated with developing RGC.

What is the implication, and what should change now?

- Intensive endoscopic surveillance would be needed for the patients who underwent DG for differentiated type GC.

Methods

Study design and population

We conducted a retrospective database review of 438 patients who underwent DG for GC at Tokyo Metropolitan Bokutoh Hospital from June 2006 to March 2017. The study was conducted in accordance with the Declaration of Helsinki (as

revised in 2013). The study was approved by Institutional Review Board of Tokyo Metropolitan Bokutoh Hospital (No. 03-010). Informed consent was obtained in the form of an opt-out on the website of Tokyo Metropolitan Bokutoh Hospital. Patients who underwent radical surgery according to the Japanese Gastric Cancer Practical Guidelines 5th Edition were eligible for the study (17). We excluded patients who (I) had metastatic lesions detected in the preoperative examination; (II) had histologically proven peritoneal dissemination; (III) had positive ascites cytology; (IV) underwent palliative surgery without adequate lymph node dissection; (V) had macroscopic or microscopic residual cancer; or (VI) had non-common-type GC defined in the Japanese Classification of Gastric Carcinoma 15th Edition (19). A total of 405 patients who underwent R0 DG were retrospectively analyzed. No patients who underwent neoadjuvant chemotherapy were included in this study. The following data were obtained from electronic medical records: sex, age, diagnosis, adjuvant chemotherapy, drinking habit, smoking history, perioperative outcomes (surgical procedure and reconstruction method), and tumor characteristics (number of lesions, size, macroscopic type, histology, depth of lesion, node metastasis, and vascular or lymphatic invasion). All the patients included in this study were Japanese. In synchronous multiple GC, cancer invading the deepest area was considered the main lesion. If the depth of cancer infiltration was the same in two or more lesions, the one extending over the greatest area was considered the main lesion. For histological classification, differentiated types GC were well-differentiated adenocarcinoma (tub1), moderately-differentiated adenocarcinoma (tub2), and papillary adenocarcinoma (pap). Undifferentiated types GC were solid type poorly differentiated adenocarcinoma (por1), non-solid type poorly differentiated adenocarcinoma (por2), signet ring cell carcinoma (sig), and mucinous adenocarcinoma (muc).

RGC definition

RGC was defined as GC in the remnant stomach after 6 months from the initial gastrectomy, excluding recurrent cancers of the initial curative resection lesion. The diagnosis of RGC was based on a pathological diagnosis of an endoscopic biopsy from the remnant gastric lesion. The recurrence date was the date of the biopsy. The pathological classification of GC was based on the Japanese Classification of Gastric Carcinoma 15th Edition (19).

Follow-up surveillance

At our institution, the patients were regularly screened for recurrences by monitoring the plasma levels of the carcinoembryonic antigen and carbohydrate antigen 19-9 performed every 3–6 months, enhanced computed tomography performed every 6–12 months, esophagogastroduodenoscopy was performed every year up to 5 years after surgery. However, in this study, the frequency was different because the schedule changed according to the patients' conditions. Six years after surgery, follow-ups were usually terminated, but the patients who visit our hospital due to their comorbidities or who request follow-up at our institution are followed up for >6 years.

Statistical analysis

We investigated the risk factors for RGC after DG. We assessed previously reported risk factors (7,10,12), including the depth of tumor, age, sex, and synchronous multiple GC. The relationship of clinicopathological features, operative findings, and postoperative course with RGC development was estimated using Cox proportional hazard analysis. Patient demographics and clinicopathological characteristics were compared using Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. The cumulative incidences of RGC were calculated using the Kaplan-Meier method. Data were analyzed using R software version 4.04 (R Foundation, Vienna, Austria) and EZR (20). All statistical tests were two-sided, and significance was set at $P<0.05$.

Results

Treatment flow and baseline characteristics

In total, 405 cases were retrospectively analyzed (*Figure 1*). The median patient age was 69 years and the patient cohort consisted of 263 men and 142 women. The Billroth-I (B-1) reconstruction method was used in 204 cases, the B-2 method was used in three cases, and the Roux-en Y (R-Y) method was used in 198 cases. The median endoscopic surveillance interval was 12 months, and no significant difference was observed between the RGC and no RGC groups (*Table 1*). Laparoscopic surgery was performed in 92 cases; 52 of those cases were reconstructed using the B-1 method, 1 using the B-2 method, and 39 using the R-Y method. The median follow-up period was 5 years.

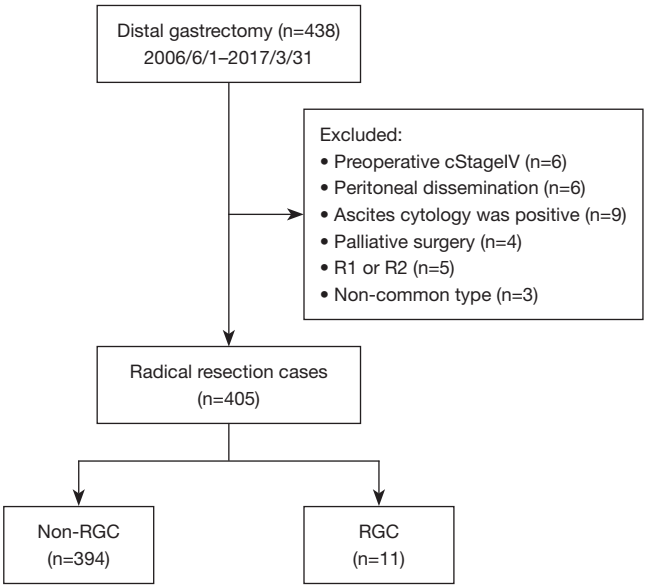

Figure 1 Selection criteria for patients in this study. A series of 438 consecutive gastrectomy procedures for pathologically confirmed gastric cancer from 2006 to 2017 was included. Non-radical resected cases and non-common-type gastric cancer were excluded. A total of 405 radical resected cases were retrospectively analyzed. cStageIV, clinical Stage IV; RGC, remnant gastric cancer.

Postoperative gastritis of the stomach remnant was detected in 215 cases (68.0%). Single lesions occurred in 351 cases and synchronous multiple lesions occurred in 54 cases. Two hundred and ten cases were differentiated type and 195 cases were undifferentiated GC. The surgical margin status was not significantly different between the RGC and no RGC group (*Table 2*).

Clinicopathological feature of RGC cases and cumulative incidences

Eleven cases (2.8%) developed RGC (*Table 3*). The median interval between endoscopy in which RGC was detected and the previous endoscopy was 13 months. Eight cases were treated by endoscopic resection, whereas one case did not meet the curable resection criteria and underwent surgery, followed by endoscopic resection. Two patients underwent surgical resection of the gastric remnant. One case of advanced GC with peritoneal dissemination was treated by chemotherapy, but the patient died 4 months after RGC was detected. One case was not treated owing to the presence of advanced lung cancer. All 11 RGC cases were detected by follow-up endoscopy. No RGC case was suspected for new recurrence based on increasing tumor marker levels. Differentiated GC occurred in the remnant stomach treated for differentiated type GC. Undifferentiated type GC occurred in the remnant stomach treated for undifferentiated type GC. Therefore, the histological type of the main lesion at the initial surgery was the same as that of the RGC. The cumulative incidences of RGC calculated by the Kaplan-Meier method were 3.0%, 4.1%, and 10.5% at 5, 10, and 15 years after DG, respectively (*Figure 2*).

Associated factors of RGC development

According to the univariate Cox proportional hazards analyses, differentiated type GC at the time of the initial surgery was significantly associated with the development of RGC (*Table 4*). Male sex and older patients had higher incidences of RGC, but the relationships were not statistically significant. Synchronous multiple lesions, tumor type, tumor depth, venous or lymphatic invasion, lymph node metastasis, the reconstruction method, and postoperative gastritis were not associated with the development of RGC.

Discussion

This study aimed to evaluate the potential risk factors for RGC development after an initial DG. In this study, according to the univariate analysis, the differentiated type lesion was associated with the development of RGC. Therefore, we considered intensive endoscopic surveillance for patients who underwent DG for differentiated type GC.

RGC has been defined to encompass all cancers that arise from the remnant stomach after partial gastrectomy (2,3). This definition includes local recurrence in the gastric stump, synchronous GC that was not detected during preoperative endoscopic examination, and new GC arising from the gastric remnant. In the present study, we excluded patients with positive surgical margins during the primary operation in order to exclude local recurrence. Because the mechanism completely differs between local recurrence and newly developed cancer, inclusion of patients who developed local recurrence was not suitable for this investigation of the risk factors. Differentiating between missing synchronous GC and metachronous GC was difficult, although we thought that this was not clinically essential, because both lesions require similar treatment. Therefore, we defined RGC as GC in the remnant stomach,

Table 1 Clinical characteristics of the initial surgery

Patient	Non-RGC (n=394)	RGC (n=11)	P value[†]
Sex, n (%)			0.34
Male	254 (64.5)	9 (81.8)	
Female	140 (35.5)	2 (18.2)	
Age (years), median [range]	68 [36–89]	71 [43–74]	0.63[‡]
Cancer history other than GC, n (%)			0.23
Yes	72 (18.3)	0	
No	322 (81.7)	11 (100.0)	
Hypertension, n (%)			>0.99
Yes	175 (44.4)	5 (45.5)	
No	219 (55.6)	6 (54.5)	
Drinking habit[$], n (%)			0.89
Non-drinker	85 (32.2)	2 (25.0)	
Chance-drinker	41 (15.5)	1 (12.5)	
Habitual-drinker	138 (52.3)	5 (62.5)	
Smoking history[$$], n (%)			0.72
Never-smoker	95 (34.8)	2 (25.0)	
Current/former smoker	178 (65.2)	6 (75.0)	
Procedure, n (%)			>0.99
LADG/LDG	90 (22.8)	2 (18.2)	
ODG	304 (77.2)	9 (81.8)	
Reconstruction method, n (%)			0.89
Billroth-I	200 (50.8)	4 (36.4)	
Billroth-II	3 (0.8)	0	
Roux-en Y	191 (48.5)	7 (63.6)	
Adjuvant chemotherapy, n (%)			0.71
Yes	85 (21.6)	3 (27.3)	
No	309 (78.4)	8 (72.7)	
Post-operative gastritis[$$$], n (%)			0.34
Yes	209 (68.5)	6 (54.5)	
No	96 (31.5)	5 (45.5)	
Endoscopic interval (months), median [range]	12 [1–70]	12 [8–39]	0.11[‡]

[†], Fisher exact test, unless indicated otherwise; [‡], the Mann-Whitney *U* test; [§], reviewed in 272 cases; [§§], reviewed in 281 cases; [§§§], reviewed in 316 cases. RGC, remnant gastric cancer; GC, gastric cancer; LADG, laparoscopic assisted distal gastrectomy; LDG, laparoscopic distal gastrectomy; ODG, open distal gastrectomy.

Table 2 Pathological characteristics of the initial gastric cancer

Patient	Non-RGC (n=394)	RGC (n=11)	P value[†]
Number of lesion, n (%)			0.41
Single	342 (86.8)	9 (81.8)	
Double	37 (9.4)	1 (9.1)	
Triple	10 (2.5)	1 (9.1)	
Quadruple	4 (1.0)	0	
Quintuple	1 (0.3)	0	
Type, n (%)			0.5
Type 0	221 (56.1)	8 (72.7)	
Type 1	14 (3.6)	1 (9.1)	
Type 2	69 (17.5)	2 (18.2)	
Type 3	64 (16.2)	0	
Type 4	9 (2.3)	0	
Type 5	17 (4.3)	0	
Tumor size of main lesion (mm), median [range]	40 [5–190]	40 [10–65]	0.92[‡]
Histology, n (%)			0.06
Differentiated type	193 (49.0)	2 (18.2)	
Undifferentiated type	201 (51.0)	9 (81.8)	
Depth of invasion, n (%)			0.28
M	91 (23.1)	2 (18.2)	
SM	122 (31.0)	4 (36.4)	
MP	55 (14.0)	4 (36.4)	
SS	79 (20.1)	1 (9.1)	
SE/SI	47 (11.9)	0	
Node metastasis, n (%)			0.07
N0	268 (68.0)	6 (54.5)	
N1	57 (14.5)	5 (45.5)	
N2	38 (9.6)	0	
N3	31 (7.9)	0	
Vascular invasion, n (%)			0.54
+	152 (38.6)	3 (27.3)	
–	242 (61.4)	8 (72.7)	
Lymphatic invasion, n (%)			0.76
+	157 (39.8)	5 (45.5)	
–	237 (60.2)	6 (54.5)	
Proximal margin (mm), median [range]	38 [0.2–245]	30 [0.6–90]	0.26[‡]
Distal margin (mm), median [range]	45 [1–195]	47 [13–170]	0.76[‡]

[†], Fisher exact test, unless indicated otherwise; [‡], the Mann-Whitney *U* test. RGC, remnant gastric cancer; M, mucosa; SM, submucosa; MP, muscularis propria; SS, subserosa; SE, tumor invasion is contiguous to the serosa or penetrates the serosa and is exposed to the peritoneal cavity; SI, tumor invades adjacent structures.

Table 3 Summary of 11 patients with remnant GC

Case	Age[†] (years)	Sex	Pathology of initial GC	Reconstruction	Durations[§] (years)	Intervals[§§] (months)	Treatment for RGC	Pathology of RGC	TNM of RGC[‡]
1	84	M	Dif	R-Y	11	13	ESD	Dif	T1aN0M0
2	76	M	Dif	B-I	1	13	ESD	Dif	T1bN0M0
3	77	M	Dif	R-Y	4	12	ESD	Dif	T1aN0M0
4	68	M	Dif	B-I	1	12	ESD	Dif	T1aN0M0
5	73	M	Und	B-I	2	13	Gastrectomy	Und	T1aN0M0
6	72	M	Dif	B-I	4	13	Chemotherapy	Dif	T3N0M1(P)
7	49	F	Dif	R-Y	6	7	ESD	Dif	T1aN0M0
8	79	F	Dif	R-Y	5	19	ESD → gastrectomy	Dif	T1bN0M0
9	76	M	Dif	R-Y	3	40	Follow-up	Dif	T1aN0M0
10	68	M	Dif	R-Y	1	17	ESD	Dif	T1aN0M0
11	71	M	Und	R-Y	1	13	ESD	Und	T1bN0M0

[†], age at RGC documented; [§], durations mean duration from initial operation for gastric cancer to diagnosis for RGC; [§§], intervals mean intervals of endoscopic examination between detection of RGC and previous examination; [‡], according to the Japanese Classification of Gastric Carcinoma 15th Edition. GC, gastric cancer; M, male; F, female; Dif, differentiated type; Und, undifferentiated type; R-Y, Roux-en Y; B-I, Billroth-I; RGC, remnant gastric cancer; ESD, endoscopic submucosal dissection; TNM, tumor, node, metastasis.

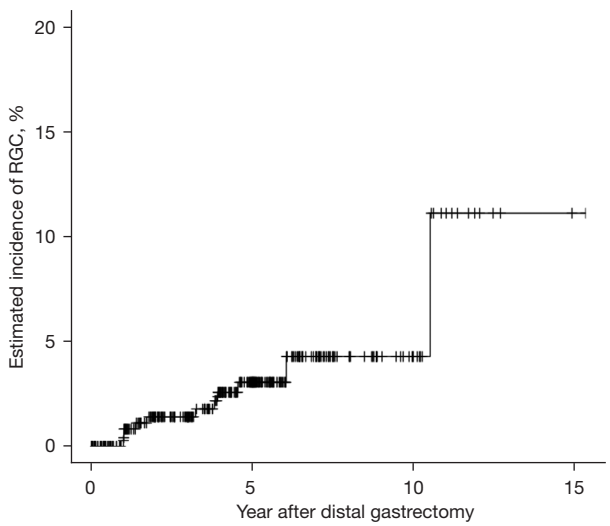

Figure 2 Kaplan-Meier estimates of the cumulative prevalence of RGC after distal gastrectomy for early gastric cancer. The cumulative incidence of RGC was estimated as 3.0% at 5 years, 4.1% at 10 years, and 10.5% at 15 years. RGC, remnant gastric cancer.

excluding recurrent cancer lesions after the initial curative resection. In the present study, surgical margin status was not significantly different between the RGC and no RGC groups. Therefore, short surgical margin was not associated with the development of RGC.

The incidence rate of metachronous cancer after ESD for differentiated type GC was significantly higher than undifferentiated type GC; moreover, differentiated type GC was reported as a significant risk factor for the development of metachronous GC in the preserved stomach after ESD (21). This explained the differences in the mechanism of GC development. Differentiated type GC primarily develops from severe atrophic gastritis and intestinal metaplasia. In contrast, undifferentiated type GC generally develops during the progression of atrophic gastritis (22). Therefore, the remnant stomach after DG for differentiated type GC more frequently has severe atrophic gastritis and intestinal metaplasia. As GC mainly develops from chronic active gastritis and results in gastric atrophy (23,24), differentiated type RGC may develop more frequently in the remnant stomach after gastrectomy for differentiated type GC than that for undifferentiated type GC. In the present study, the histological types of the main lesions of RGC were similar to those of the initial main lesions. We suspect that RGC developed in the remnant stomach from the already formed carcinogenic tissue. Synchronous multiple GC was reported to be associated with RGC development in previous reports (9,11,12); however, in this study, these factors showed no association with RGC

Table 4 The univariate Cox proportional hazard analyses of risk factors for the development of RGC in 405 patients with GC who underwent distal gastrectomy

Variables	Patient (n=405)	RGC (n=11)	HR (95% CI)	P value[†]
Sex				
Female	142	2	1	
Male	263	9	2.97 (0.64–13.75)	0.16
Age (years)				
<69	216	7	1	
≥70	189	4	2.72 (0.78–9.47)	0.11
Hypertension				
Negative	225	5	1	
Positive	180	6	1.07 (0.33–3.51)	0.91
Drinking habit[$]				
Negative	129	3	1	
Positive	143	5	1.56 (0.37–6.55)	0.54
Smoking history[$$]				
Negative	97	2	1	
Positive	184	6	2.09 (0.41–10.53)	0.37
Synchronous multiple GCs				
Negative	351	9	1	
Positive	54	2	1.31 (0.28–6.08)	0.73
Tumor type				
Type 0	229	8	1	
Type 1–5	176	3	0.52 (0.13–1.96)	0.33
Tumor size of main lesion, mm				
<49	253	7	1	
≥50	152	4	0.98 (0.29–3.36)	0.98
Histology				
Undifferentiated type	195	2	1	
Differentiated type	210	9	4.71 (1.02–21.80)	0.05
Depth of invasion				
M/SM	219	6	1	
MP/SS/SE/SI	186	5	1.07 (0.33–3.51)	0.91
Node metastasis				
Negative	274	6	1	
Positive	131	5	1.87 (0.57–6.15)	0.30

Table 4 (*continued*)

Table 4 (*continued*)

Variables	Patient (n=405)	RGC (n=11)	HR (95% CI)	P value[†]
Vascular invasion				
Negative	250	8	1	
Positive	155	3	0.71 (0.19–2.66)	0.61
Lymphatic invasion				
Negative	243	6	1	
Positive	162	5	1.32 (0.40–4.33)	0.65
Reconstruction method				
R-Y	198	7	1	
B-1/B-2	207	4	0.59 (0.17–2.02)	0.40
Adjuvant chemotherapy				
Negative	317	8	1	
Positive	88	3	1.14 (0.30–4.30)	0.85
Post-operative gastritis[§§§]				
Negative	101	5	1	
Positive	215	6	0.45 (0.13–1.52)	0.20

[†], the Cox proportional hazard analyses; [§], reviewed in 272 cases; [§§], Reviewed in 281 cases; [§§§], reviewed in 316 cases. RGC, remnant gastric cancer; GC, gastric cancer; M, mucosa; SM, submucosa; MP, muscularis propria; SS, subserosa; SE, tumor invasion is contiguous to the serosa or penetrates the serosa and is exposed to the peritoneal cavity; SI, tumor invades adjacent structures; R-Y; Roux-en Y, B-I; Billroth-I, B-2; Billroth-II; HR, hazard ratio; CI, confidence interval.

development. The presence of synchronous multiple GC, like the presence of differentiated type GC, appears to show already formed carcinogenic tissue. However, the antrum and lesser curvature of the stomach, which is the most common site of GC occurrence (25), are resected after DG; synchronous multiple GC had less effect than the histological type of GC.

More than 10 years following B-2 reconstruction, RGC was commonly developed near the gastric stump (4). RGC had been thought to develop secondary to duodenal fluid regurgitation (26). The relationship between duodenal fluid regurgitation and carcinogenesis has been demonstrated in rats (26). However, B-1 or B-2 reconstruction, which does not prevent duodenal fluid reflux (27), was not associated with RGC development in the current study. In addition, postoperative gastritis, which may be related to bile reflux (27), was not associated with RGC development in the present study. Therefore, the changing of the mucosa of remnant stomach resulting from bile reflex cannot explain the pathogenesis of RGC development. Similar to the pathophysiology of primary GC, we speculated that after gastrectomy for GC, RGC developed from an atrophic gastric mucosa (i.e., carcinogenic tissue) in the remnant stomach.

Endoscopic surveillance of the gastric remnant is extremely important for the early detection and curative treatment of RGC. The incidence of RGC development is high and increases over time; it is considerably high after ≥10 years following gastrectomy. Moreover, the detection of RGC after 5 years of follow-up was reported to be associated with a poor prognosis (28). Therefore, we recommend endoscopic surveillance, even after more than 5 years of the curative resection. However, an optimal endoscopic surveillance program remains unclear. In the present study, the median interval between endoscopy in which RGC was found and the previous endoscopy was 13 months. Furthermore, endoscopic resection was not indicated in only two cases; moreover, endoscopically treatable lesions accounted for 81% of the RGC cases. Thus, the annual surveillance seems appropriate. The usefulness of annual endoscopic surveillance has been reported for the detection of metachronous gastric GC after

ESD, wherein the incidence was much higher than that after gastrectomy (29). It is sometimes difficult to establish the diagnosis through endoscopic examination after gastrectomy because of residual food and mucosal changes due to bile reflux (30). Therefore, intense endoscopic surveillance, as that after ESD, might be acceptable for high-risk patients who have undergone gastrectomy.

Our study has several limitations. First, this study was a single-center study, and the number of RGC cases was low. Second, because this was a retrospective study, the follow-up periods and methods were not unified, especially after more than 5 years. Third, *Helicobacter pylori* (*H. pylori*) infection is associated with GC development (31), and the eradication of *H. pylori* prevents the development of metachronous GC in patients who underwent endoscopic resection for early GC (32); however, a survival benefit from *H. pylori* eradication in patients who underwent gastrectomy for GC has not been shown (33). As we did not examine and eradicate *H. pylori* infection at our institution, we could not investigate the effects of *H. pylori* infection on the development of RGC. Finally, we omitted matching analysis due to the small number of cases.

Conclusions

RGC development was statistically associated with patients who had undergone DG for differentiated type GC. For patients who underwent a DG for differentiated type GC, we recommended intensive endoscopic surveillance.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-545/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-545/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-545/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Review Board of Tokyo Metropolitan Bokutoh Hospital (No. 03-010). Informed consent was obtained in the form of an opt-out on the website of Tokyo Metropolitan Bokutoh Hospital.

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