Short- and Long-term Outcomes of Surgical Treatment for Remnant Gastric Cancer After Distal Gastrectomy

YU NAKAJI¹, HIROSHI SAEKI¹, KENSUKE KUDOU¹, RYOTA NAKANISHI¹, MASAHIKO SUGIYAMA¹,
YUICHIRO NAKASHIMA¹, KOJI ANDO¹, YOSHINAO ODA², EIJI OKI¹ and YOSHIHIKO MAEHARA¹

¹*Department of Surgery and Science, Graduate School of Medical Sciences,
Kyushu University, Fukuoka, Japan;*

²*Department of Anatomic Pathology, Pathological Sciences,
Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*

Abstract. *Background/Aim:* Remnant gastric cancer (RGC) after distal gastrectomy occurs in 1-2% of patients, while the biological features of RGC are unknown. *Patients and Methods:* A total of 22 consecutive patients with RGC who underwent total gastrectomy were analyzed. Their disease history included either gastric cancer (n=16) or peptic ulcer (n=6). Overall, 18 underwent open total gastrectomy (OTG) and 4 underwent laparoscopic total gastrectomy (LTG). *Results:* The mean number of lymph nodes dissected and metastatic lymph nodes was larger in the Ulcer group than in the Carcinoma group ($p<0.005$). The mean operation time was longer in the LTG than OTG ($p<0.005$). The median blood loss tended to be smaller in the LTG ($p=0.090$). Five-year overall and recurrence-free survival rates were 94% and 81%, respectively. *Conclusion:* The status of lymph node metastasis after surgery for RGC should be cautiously considered in the context of disease history. Both LTG and OTG can be treatment options for RGC.

Incidence of remnant gastric cancer (RGC) is increasing due to previous improvements in the detection of gastric cancer and improved medical care (1). RGC after distal gastrectomy has been reported to occur in 2-3% of patients who have undergone gastrectomy for carcinoma or benign disease and was reported to account for 1-2% of all gastric cancers in Japan (2). RGC is caused by the continuous bathing of the gastric remnant with bile acids or duodenal

juice, resulting in repeated mucosal inflammation and regeneration (3). RGC is commonly detected at an advanced stage, resulting in low rates of curative resection (38-40%), and prognosis is reported to be worse than that of patients with primary cancers in the proximal third of the stomach at the same stage (1). However, the clinical features of and surgical results for RGC have not been fully elucidated.

Laparoscopic surgery for gastric cancer is widely used. Surgical treatment for RGC is more difficult than for primary gastric cancer due to adhesions to adjacent organs, displacement of anatomical structures, and changes in lymphatic flow. Laparoscopic gastrectomy for remnant gastric cancer has also been reported sporadically in association with the increased use of minimally-invasive techniques. However, because of the rarity of remnant gastric cancer, the number of cases reported per study has been small. Here, we report the short-term results of laparoscopic surgery for RGC in our institute (4).

The aim of this study was to clarify the clinico-pathological features and results of surgical treatment of RGC following distal gastrectomy with regard to previous gastric disease and surgical approach used.

Patients and Methods

Patients. RGC was defined as gastric cancer in the remnant stomach arising more than five years after distal gastrectomy for benign disease or gastric cancer (3). Between 2004 and 2014, 22 patients underwent surgery for remnant gastric cancer after distal gastrectomy in our institute. A total of 18 men and 4 women enrolled in the study, and the mean age was 73.9 years. Previous disease was gastric cancer in 16 patients (72.7%) and peptic ulcer in 6 patients (27.3%). Eighteen patients underwent open total gastrectomy (OTG) and 4 patients underwent laparoscopic total gastrectomy (LTG). The indication of a laparoscopic approach toward RGC was the same as that toward primary gastric cancer from 2013 (4).

Correspondence to: Hiroshi Saeki, MD, Ph.D., FACS, Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. Tel: +81 926425466, Fax: +81 926425482, e-mail: h-saeki@surg2.med.kyushu-u.ac.jp

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Methods. Clinical stage was classified according to the TNM classification (5). Postoperative complications occurring within 30 days after operation were classified according to the Clavien-Dindo classification (6). Clinicopathological features and surgical results were analyzed in terms of previous disease (Ulcer *vs.* Carcinoma) and surgical procedures (OTG *vs.* LTG).

Statistics. JMP (SAS, USA) was used for statistical analyses. The chi-square test and Student's *t*-test were applied for assessment of various factors. The Kaplan–Meier method was used to present the survival data. A value of $p < 0.05$ was assumed to indicate statistical significance.

Results

Comparisons between the Ulcer group and the Carcinoma group. The clinicopathological features of RGC according to previous disease (Ulcer group *vs.* Carcinoma group) are shown in Table I. There were no significant differences in various factors between the two groups.

Surgical results and pathological findings according to the two groups are shown in Table II. The mean number of lymph node dissection and lymph node metastasis were 12.4 (25 in the Ulcer group *vs.* 8 in the Carcinoma group; $p < 0.005$) and 0.95 (3 in the Ulcer group *vs.* 0.3 in the Carcinoma group; $p < 0.05$), respectively. The mean tumor diameter was 3.6 cm (5.6 cm in the Ulcer group, 2.9 cm in the Carcinoma group; $p < 0.05$). The mean interval between the first and the second operation was 19.1 years (35 years in the Ulcer group *vs.* 12 years in the Carcinoma group; $p < 0.0001$). The mean operation time was 347 min (260 min in the Ulcer group, *vs.* 380 min in the Carcinoma group; $p = 0.079$).

Comparisons between the OTG group and the LTG group. Clinicopathological features of RGC according to surgical procedure are shown in Table III. There were no significant differences in various factors between the two groups.

Surgical results and pathological findings according to surgical procedure are shown in Table IV. The mean number of lymph node dissections was 11 in the OTG group *vs.* 15 in the LTG group; there was no significant difference. The mean operation time was longer in the LTG group than in the OTG group (455 min *vs.* 293 min; $p = 0.005$). The mean intraoperative blood loss tended to be larger in the OTG group than in the LTG group (625 g *vs.* 158 g; $p = 0.09$).

There were two cases that experienced postoperative complications in the LTG group (pneumonia: 1, bleeding: 1) and five cases in the OTG group (minor leakage: 1, bile leakage: 1, bleeding: 1, surgical site infection: 2) There were no cases with in-hospital death in either group.

The mean time to postoperative resumption of food intake was not significantly different between the two groups (OTG 8 days *vs.* LTG 6 days; $p = 0.168$). The length of postoperative hospital stay was similar between the two groups (OTG 16 days *vs.* LTG 15 days; $p = 0.655$).

Table I. Clinicopathological characteristics of remnant gastric cancer according to previous disease (Ulcer group *vs.* Carcinoma group).

Factor	Previous disease		Total	p-Value
	Ulcer (n=6)	Carcinoma (n=16)		
Gender				
Male	6 (100)	12 (75.0)	18 (81.8)	0.176
Female	0 (0)	4 (25.0)	4 (18.2)	
Age (mean)				
<65	1 (16.7)	2 (12.5)	3 (13.6)	0.799
>65	5 (83.3)	14 (87.5)	19 (86.4)	
Depth of tumor				
T1/2	3 (50)	10 (62.5)	13 (59.0)	0.595
T3/4	3 (50)	6 (37.5)	9 (41.0)	
Lymph node metastasis				
N0	3 (50)	13 (81.3)	16 (72.7)	0.143
N1	3 (50)	3 (19.7)	6 (27.3)	
Differentiation of adenocarcinoma				
Well/moderate	5 (83.3)	8 (50)	13 (59.0)	0.157
Poorly	1 (16.7)	8 (50)	9 (41.0)	
Lymphatic invasion				
Ly (-)	3 (50)	7 (43.8)	10 (45.4)	0.793
Ly (+)	3 (50)	9 (56.2)	12 (54.6)	
Vascular invasion				
V (-)	5 (83.3)	11 (68.8)	16 (72.7)	0.494
V (+)	1 (16.7)	5 (31.2)	6 (27.3)	
Pathological stage				
I	3 (50)	9 (56.3)	12 (54.5)	0.180
II	1 (16.7)	7 (43.7)	8 (36.3)	
III	2 (33.4)	0 (0)	2 (9.2)	

(%)

Overall survival and relapse free survival. Five cases received adjuvant chemotherapy after operation for RGC (pStage II: 3 cases, pStage III: 2 cases). There were two postoperative recurrences. One case had para-aortic lymph node recurrence and died ten months after surgical operation (Carcinoma group, pT4a N0 M0 pStage IIB, ly3, v2). Another case had intraabdominal lymph node recurrence and died eleven months after surgical operation (Carcinoma group, pT3 N1 M0 pStage IIB, ly3, v0). The five-year overall survival and recurrence-free survival rate was 94% and 81%, respectively (range of observation period=11-194 months) (Figure 1).

Discussion

In previous studies, it has been suggested that RGC is commonly detected at an advanced stage, thereby resulting in low rates of curative resection (38-40%) and a poor prognosis (1). The exact reasons for this poorer survival are not clear, but the disruption of lymphatic channels during the

Table II. *Surgical results and pathological findings according to previous disease (Ulcer group vs. Carcinoma group).*

	Previous disease		<i>p</i> -Value
	Ulcer group (n=6)	Carcinoma group (n=16)	
Number of lymph node dissections (mean)	25	8	<0.005
Number of lymph node metastasis (mean)	3	0.3	<0.05
Tumor size (cm, mean)	5.6	2.9	<0.05
Interval between 1st and 2nd operations (years, mean)	35	12	<0.0001
Operation time (min, mean)	260	380	0.079
Blood loss (ml, mean)	422	599	0.460
Complication	0	6	0.350
Minor leakage	0	1	
Bile leakage	0	1	
Bleeding	0	1	
Surgical site infection	0	2	
Pneumonia	0	1	
Postoperative resumption of food intake (day, median)	6	8	0.082
Postoperative hospital stay (day, median)	15	16	0.528

first operation may lead to substantial changes in lymphatic flow from the remnant stomach, making surgical control of RGC with nodal disease difficult (7). The clinicopathological features of RGC have been analyzed in some reports, as summarized in Table V. Our study showed that the number of dissected and metastatic lymph nodes was larger in the Ulcer group than in the Carcinoma group. In the Ulcer group, right cardiac (No.1) and lesser curvature (No.3) lymph nodes were dissected during surgery for RGC. Meanwhile, in the Carcinoma group, these lymph nodes were already dissected during the initial surgery. Therefore, the number of metastatic lymph nodes might not always reflect the severity of disease for the Carcinoma group. Instead, it has been suggested that other factors, such as histological type, lymphatic invasion, and vascular invasion, could be indicators of malignant potential of RGC.

We previously reported four cases with RGC who underwent LPG at our hospital and demonstrated the favorable short-term results (4). Another previous study reported that operation time was longer in LTG than in OTG (7). Meanwhile, blood loss, complications, and postoperative hospital stay were reported to be less in LTG than in OTG (3). In our study, the results were consistent with those of previous reports. There was also no significant difference in the number of lymph node dissections between patients undergoing LTG of OTG. Surgical resection is more difficult in patients undergoing RGC than in patients with primary gastric cancer because of the severity of adhesions. In particular, LTG is more technically difficult than OTG. Although the oncological feasibility remains to be fully established, laparoscopy provides a magnified view of minute structures, such as tiny vessels and nerves (8), which

Table III. *Clinicopathological characteristics of remnant gastric cancer according to surgical procedure (OTG group vs. LTG group).*

Factor	Surgical procedure		Total	<i>p</i> -Value
	OTG (n=18)	LTG (n=4) (n=22)		
Gender				
Male	15 (83.3)	3 (75.0)	18 (81.8)	0.69
Female	3 (16.7)	1 (25.0)	4 (18.2)	
Age (mean)				
<65	3 (16.7)	0 (0)	3 (13.6)	0.70
>65	15 (83.3)	4 (100)	19 (86.4)	
Depth of tumor				
T1/2	11 (61.1)	2 (50)	13 (59.1)	0.68
T3/4	7 (38.9)	2 (50)	9 (41.0)	
Lymph node metastasis				
N0	13 (72.2)	3 (75.0)	16 (72.7)	0.91
N1	5 (27.8)	1 (25.0)	6 (27.3)	
Differentiation of adenocarcinoma				
Well/moderate	11 (61.1)	2 (50)	13 (59.1)	0.68
Poorly	7 (38.9)	2 (50)	10 (45.5)	
Lymphatic invasion				
Ly (-)	8 (44.4)	2 (50)	10 (45.5)	0.84
Ly (+)	10 (45.6)	2 (50)	12 (54.5)	
Vascular invasion				
V (-)	13 (72.2)	3 (75.0)	16 (72.7)	0.91
V (+)	5 (27.8)	1 (25.0)	6 (27.3)	
Pathological stage				
I	10 (55.4)	2 (50.0)	12 (54.5)	0.32
II	6 (33.4)	2 (50.0)	8 (36.4)	
III	2 (11.2)	0 (0)	2 (10)	

(%)

OTG: Open total gastrectomy; LTG: laparoscopic total gastrectomy.

Figure 1. 5-year overall survival (a) and recurrence-free survival (b) in remnant gastric cancer after surgical treatment. 5-Year overall and recurrence-free survival was 94% and 81%, respectively.

Table IV. Surgical results and pathological findings according to previous disease (OTG group vs. LTG group).

	Surgical procedure		p-Value
	OTG group (n=18)	LTG group (n=4)	
Number of lymph node dissections (mean)	11	15	0.674
Number of lymph node metastasis (mean)	1.1	0.3	0.533
Tumor size (cm, mean)	3.4	4.5	0.478
Interval between 1st and 2nd operations (years, mean)	18	26	0.345
Operation time (min, mean)	293	455	<0.005
Blood loss (ml, mean)	625	158	0.090
Complication	5	2	0.388
Minor leakage	1	0	
Bile leakage	1	0	
Bleeding	1	1	
Surgical site infection	2	0	
Pneumonia	0	1	
Postoperative resumption of food intake (day, median)	8	6	0.168
Postoperative hospital stay (day, median)	16	15	0.655

OTG: Open total gastrectomy; LTG: laparoscopic total gastrectomy.

Table V. Summary of published series for interval between previous operation.

Author/Year of publication	Previous disease (benign/malignancy)	Interval (Mo) (median)	Interval (Mo) (benign/malignancy)	Lymph node metastasis (negative/positive)	Overall survival (%)
Kaneko K <i>et al.</i> /1998	21/22	180	288/118	-	84
Takano S <i>et al.</i> /2006	11/21	-	360/63	20/12	-
Ahn HS <i>et al.</i> /2008	13/45	150	384/83	25/19	63.4
Ojima T <i>et al.</i> /2010	17/21	180	264/108	-	-
Komatsu S <i>et al.</i> /2012	19/14	240	360/144	13/14	-
Current Study	6/16	150	420/144	16/6	94

Mo: Months.

allows lymphadenectomy to be more precisely performed, potentially leading to less intraoperative blood loss and fewer postoperative complications (9-11). However, further studies are required because the number of cases in our study was too small to draw any conclusion about the significance of LTG for RGC.

We previously reported the short-term surgical results of four cases with RGC who underwent laparoscopic gastrectomy (4). The long-term results of these four cases were additionally reported in the current study. It has been reported that there were no significant differences in terms of long-term results between OTG and LTG (1, 3, 8, 12-14). In our study, 5 of the 22 patients received adjuvant chemotherapy. Eighteen of the 22 cases survived without recurrence, including these 5 cases. The 5-year overall and recurrence free survival rates were 94% and 81%, respectively. It has been reported that the prognosis of RGC is unfavorable compared to that of primary gastric cancer, which may result from the more advanced stage of disease at the time of diagnosis (12-14). Surgery for RGC is an uncommonly performed procedure. Although our current results were based on a retrospective analysis of a small number of patients, these findings suggest that the surgical outcomes for RGC might be as poor as has been reported until now. Therefore, since prospective trials in this field are currently difficult or impractical, additional retrospective studies can provide useful information regarding the biological features of and appropriate treatment for RGC.

Conclusion

The results from our study demonstrated that surgical treatment for RGC was feasible and effective in terms of short- and long-term outcomes. Since the number of lymph node dissections and lymph node metastases was quite different according to disease history, the status of lymph node metastasis after surgery for RGC should be cautiously interpreted. Both LTG and OTG can be treatment options for RGC.

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