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Laparoscopic Total Gastrectomy for Remnant Gastric Cancer: A Single-institution Experience and Systematic Literature Review

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Abstract. *Background/Aim: The safety and efficacy of laparoscopic total gastrectomy (LTG) for remnant gastric cancer (RGC) remains unclear. The purpose of this study was to compare the clinical outcomes of LTG with open total gastrectomy (OTG) for RGC. Patients and Methods: Twenty-two patients who underwent total gastrectomy for RGC were enrolled in this study. Results: LTG was carried out in seven patients, and OTG was performed in the remaining 15 patients. The mean operation time in the LTG group was longer than that in the OTG group. The estimated blood loss in the LTG group was less than that in the OTG group. No cases in the LTG group required open conversion. Postoperatively, the first meal and defecation were earlier in the LTG group than in the OTG group. The overall survival rates of the two groups were comparable. Conclusion: Laparoscopic total gastrectomy is a feasible surgical option for RGC.*

Earlier detection of gastric cancer and improved medical treatment have led to an increased prevalence of remnant gastric cancer (RGC) after gastrectomy for previous gastric cancer (1). Although remnant gastric cancer was initially defined as gastric cancer in the residual stomach after gastrectomy for gastric cancer, it has recently been defined as gastric cancer in the remnant stomach after partial gastrectomy for benign disease and gastric cancer (2). Despite the recent progress in chemotherapy, gastrectomy combined with adequate lymphadenectomy remains the standard treatment option for resectable gastric cancer as well as RGC.

The guidelines in Japan recommend laparoscopic distal gastrectomy for clinical stage I gastric cancer (3). In some reports, it has been suggested that laparoscopic total gastrectomy for gastric cancer is also feasible (4, 5). The laparoscopic approach provides several advantages, including a magnified view and minimal invasiveness. Gradually it is considered that a history of abdominal surgery is no longer a contraindication for laparoscopic gastrectomy. However, even in this situation, hurdles remain for performing LTG for RGC due to issues of severe adhesion and the complexity of RGC. The difficulty in adopting a laparoscopic approach for RGC is due to the fact that the same surgical field and organ are targeted as in the previous surgery. The severity of adhesion depends on the previous approach used (open or laparoscopy), the history of lymphadenectomy (benign or malignancy) and the previous reconstruction methods used. The complexity of the surgical procedure, especially concerning the maintenance of a safety margin and reconstruction, is also affected by these factors.

The first case of laparoscopic total gastrectomy (LTG) for RGC was reported by Yamada *et al*. in 2005 (6). Since then, several other studies have reported similar LTG procedures for RGC. However, the number of cases reported per study has remained small because of the rarity of RGC, and the usefulness of laparoscopic approaches for the treatment of RGC remains unclear.

Thus, the aim of the current study was to investigate the safety and efficacy of LTG for RGC. For this purpose, we

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Key Words: Laparoscopic total gastrectomy, remnant gastric cancer.

Table I. *The clinical background of the patients who underwent gastrectomy for remnant gastric cancer according to surgical approach.*

Characteristics	LTG (n=7)	OTG (n=15)	*p*-Value
Age (years)	65, 59-85	63, 47-81	0.42
Gender			0.82
Male	2	5	
Female	5	10	
BMI (kg/m^2)	22.0, 17.9-29.0	29.6, 16.5-29.9	0.27
Previous disease			0.29
Benign	4	5	
Malignant	3	10	
Time interval (months)	444, 72-540	240, 13-540	0.16
Previous surgical approach			0.74
Open	6	12	
Laparoscopy	1	3	
Previous reconstruction			0.66
Billroth-I	4	10	
Billroth-II	3	5	

LTG: Laparoscopic total gastrectomy; OTG: open total gastrectomy; BMI: body mass index. Data are median and range, or number.

Table II. *The surgical outcomes according to the surgical approach.*

Characteristics	LTG (n=7)	OTG (n=15)	*p*-Value
Operative time (min)	394, 262-567	271, 210-525	<0.01
Blood loss (g)	70, 26-200	245, 40-1200	<0.05
Retrieved lymph node	21, 5-59	8, 0-61	0.201
Residual tumor			0.202
R0	7	13	
R1, 2	0	2	
Intraoperative complication			0.37
None	7	14	
Present	0	1	
Postoperative complication			0.65
None	5	12	
Present	2	3	
Histrogical type			0.45
Differentiated	3	4	
Non differentiated	4	11	
pStage			<0.05
I	2	11	
II	5	2	
III	0	0	
IV	0	2	
First meal (day)	4, 3-5	6, 3-21	<0.01
Flatus passage (day)	3,1-5	3, 1-5	0.61
Defecation (day)	5, 2-6	6, 3-17	<0.05
Postoperative hospital stay (day)	20, 17-30	23, 15-64	0.149

LTG: Laparoscopic total gastrectomy; OTG: open total gastrectomy. Data indicated median and range, or number.

compared the clinical outcomes of patients treated in our hospital and reviewed all the pertinent articles published in the English language literature on LTG for RGC.

Patients and Methods

Patients. Forty-one patients underwent gastrectomy for remnant gastric cancer in the National Hospital Organization Kyushu Cancer Center from January 1, 2005 to December 31, 2018. Twenty-two of these patients who underwent gastrectomy without combined resection were enrolled in this study. The other 19 patients underwent total gastrectomy with combined resection [gallbladder 13 cases, spleen 4, liver 2, colon 2 and pancreatic tail 1 (duplicate cases)]. The clinical stage was classified according to the Japanese classification of gastric carcinoma (7). The severity of the postoperative complications was classified according to the Clavien-Dindo classification system (8).

Surgical procedure. Under general anesthesia, the patient was placed in a modified lithotomy position in a reverse Trendelenburg fashion. The first port was inserted transumblically by the open method. CO_2 insufflation was maintained at 10 mmHg and four working ports were placed. Once a camera port and one or two ports were inserted, adhesiolysis was carried out laparoscopically if needed for the other trocars. The extent of the lymphadenectomy was determined using the Japanese gastric cancer treatment guidelines 2014 (version 4) (3). After the resected specimen was removed, intracorporeal reconstruction was performed with the Roux-en-Y method.

Literature search. A literature search was performed using the PubMed database to identify English-language reports describing clinical research on laparoscopic gastrectomy for remnant gastric cancer published before October 2019. The following search terms were applied: gastrectomy AND laparoscopy AND (remnant gastric cancer OR gastric remnant cancer OR gastric stump cancer). Related citations in all relevant articles were assessed to identify other related reports.

Statistical analyses. All statistical analyses were performed using the JMP11 software program (SAS Institute Japan Ltd. Tokyo Japan). Categorical variables were assessed using Fisher's exact test. Continuous variables were evaluated using Wilcoxon's rank-sum test, Student's *t*-test or Welch's *t*-test, according to the data distribution. Patient survival was calculated using the Kaplan-Meier methods. *p*-Values of <0.05 were considered to indicate statistical significance.

Results

Patient characteristics. Table I shows the clinical characteristics of the patients in the laparoscopic total gastrectomy (LTG) group and open total gastrectomy (OTG) group. LTG was carried out in 7 patients, and OTG was performed in the remaining 15 patients. The demographic features of the patients in the LTG and OTG groups were similar. Previous disease, previous surgical approach and previous type of reconstruction were likewise similar in both

Table III. *The surgical outcomes according to the surgical approach.*

Characteristics	Number	Operation time (minute, median, range)	*p*-Value	Blood loss (g, median, range)	*p*-Value
Previous stomach disease					
Benign	9	298, 210-439	0.71	73, 26-1200	0.74
Malignant	13	273, 213-567		210, 40-860	
Previous surgical approach					
Open	18	282.5, 210-567	0.67	135, 26-1200	0.54
Laparoscopy	4	299, 271-394		197.5, 80-300	
Previous reconstruction					
Billroth-I	14	282.5, 243-567	0.59	175, 26-860	0.70
Billroth-II	8	283, 210-439		76.5, 30-1200	
Current surgical approach					
Open	15	271, 262-567	<0.01	245, 40-1200	<0.05
Laparoscopy	7	394, 262-567		70, 26-200	

groups, and all patients had been undergone distal gastrectomy in the prior operation. The time interval between the operations was similar in both groups.

The clinical outcomes of our series. The mean operation time in the LTG group was longer than that in the OTG group (394±30.8 *vs*. 271±21.1 min, respectively; $p<0.001$) (Table II). The estimated blood loss in the LTG group was less than that in the OTG group (70±109.3 *vs*. 245±74.7 g, respectively; $p<0.05$). The surgical approach (LTG or OTG) was the only factor that affected the operation time and blood loss (Table III). No cases in the LTG group required open conversion. Similar numbers of lymph nodes were retrieved in the two groups. Although R0 resection was achieved in almost all cases, there were two R1 cases in the OTG group because of Intraoperative peritoneal lavage cytology (CY) positivity. For this reason, the pStage distribution differed between the two groups ($p<0.05$).

The first meal and defecation were earlier in the LTG group than in the OTG group ($p<0.01$ and $p<0.05$, respectively). The two groups showed a similar duration of postoperative hospital stay and similar postoperative complication rate. There were two cases of abdominal abscess (Grade 3) in the LTG group. However, there was one case of abdominal bleeding (Grade 3), one case of anastomotic stenosis (Grade 3) and one case of pancreatic fistula (Grade 2) in the OTG group.

The mean follow-up time after total gastrectomy was 1.96±0.59 years in the LTG group and 3.84±0.40 years in the OTG group. All 7 patients in the LTG group were alive at the time of writing. Two of the 15 patients in the OTG group died of recurrent disease due to CY positivity at the time of the operation. Another patient died of other cancer. The overall survival rates of the two groups were comparable ($p=0.23$) (Figure 1).

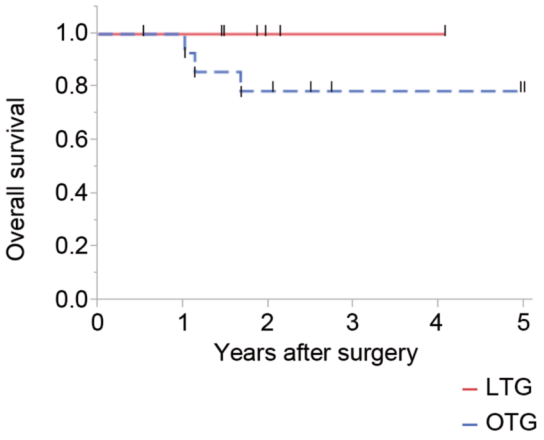

Figure 1. *Overall survival in the LTG (solid line) and OTG (broken line) groups. The survival of the two groups was not statistically significantly different.*

Literature review. Our search of the relevant literature yielded 3 case reports (6, 9, 10), 9 case series (9-17) and 8 case-control studies (18-25) on laparoscopic gastrectomy for remnant gastric cancer (Table IV). One institution reported two initial cases as a case report, and later published a case-control study. Thus, the former study was excluded from the analysis to avoid including duplicate cases.

A total of 179 patients were reported in the 21 studies, including our series. Six studies reported that the conversion rate to open gastrectomy was 5.6-47.1%; the other 15 studies reported no cases of conversion to open gastrectomy. In all studies, the mean operation time ranged from 197 to 487 min, the mean blood loss was up to 425 g, the mean number of retrieved lymph nodes ranged from 7 to 26 and the mean duration of postoperative hospital stay

Table IV. *Summary of the latest case series of laparoscopic total gastrectomy for remnant gastric cancer.*

Author, Year of publication (references)	Approach	n	Operative time (min)	Blood loss (g)	Conversion to open	Retrieved lymph node	Postoperative hospital stay (day)	Complication
Yamada *et al*. 2005 (4)	LTG	1	274	30	None	NA	NA	None
Corcione *et al*. 2008 (9)	LTG	3	210	Minimal	None	18	11	1 (33.3%)
Cho *et al*. 2009 (10)	LTG	2	487.5	425	None	15.5	NA	None
Qian *et al*. 2010 (11)	LTG	15	205	110	1 (7%)	18	NA	1 (7%)
Shinohara *et al*. 2013 (12)	LTG	5	370.8	63.6	None	18.2	8.8	None
Pan *et al*. 2014 (13)	LTG	3	251.7	76.7	None	16.7	8	None
Nagai *et al*. 2014 (16)	LTG	12	362.3	65.8	None	23.7	11.3	None
	OTG	10	270.5	746.3	NA	15.9	24.9	2 (20%)
Kwon *et al*. 2014 (17)	LTG	18	266.2	182.2	1 (5.6%)	8	6	6 (33.3%)
	OTG	58	203.3	193.1	NA	7	9	26 (44.8%)
Kim *et al*. 2014 (18)	LTG	17	197.2	NA	None	NA	11.1	4 (23.5%)
	OTG	50	149.3	NA	NA	NA	13.8	15 (30%)
Kim & Kim, 2015 (7)	LTG	1	200	100	None	24	13	None
Yamamoto *et al*. 2015 (14)	LTG	3	356.7	41.7	None	26	20.3	None
Korehisa *et al*. 2015 (15)	LTG	4	413.3	270.3	None	NA	18	1 (25%)
Son *et al*. 2015 (19)	LTG	17	234.4	227.6	8 (47.1%)	18.8	9.3	6 (35.2%)
	OTG	17	170	184.1	NA	22.3	9.3	5 (29.4%)
Luo *et al*. 2015 (20)	LTG	9	221.1	105.6	None	16.2	NA	1 (11.1%)
	OTG	9	212.9	147.8	NA	16.7	NA	2 (22.2%)
Kim & Kim, 2016 (8)	LTG	1	295	200	None	20	7	None
Tsunoda *et al*. 2016 (21)	LTG	10	324.5	55.4	None	22.4	12.5	1 (10%)
	OTG	6	289	893	NA	7	24	2 (33.3%)
Otsuka *et al*. 2019 (22)	LTG	7	364	70	None	22	13	2 (28.6%)
	OTG	20	309	1066	NA	12	27	10 (50%)
Booka *et al*. 2019 (23)	LTG	8	307.5	135.5	2 (25%)	8.8	10.3	3 (37.5%)
	OTG	23	295.8	568.3	NA	6	21.3	6 (26.1%)
Kaihara *et al*. 2019 (24)	LTG	6	310.5	50	1 (17%)	7	9	3 (50%)
	OTG	15	263	465	NA	3	9	5 (33.3%)
Alhossaini *et al*. 2019 (25)	LTG	30	225	166	4 (13%)	NA	9.5	11 (37%)
	RTG	25	292	202	None	NA	8.9	10 (40%)
Current Study	LTG	7	394	70	None	21	20	2 (28.5%)
	OTG	15	271	245	NA	8	23	3 (20%)

LTG: Laparoscopic total gastrectomy; OTG: open total gastrectomy; RTG: robotic total gastrecetomy; NA: not appricable.

ranged from 6-24 days. Although 8 studies reported no complications, the other 12 studies reported postoperative complication rates of 7-50%.

Eight out of 21 studies, including our report, conducted a statistical comparison between laparoscopic gastrectomy and open gastrectomy for remnant gastric cancer (18-24). Among these 8 studies, 6 studies showed that LTG was associated with less blood loss, 4 studies showed that LTG was associated with a longer operation time, and 1 study showed that LTG was associated with a greater number of retrieved lymph nodes and shorter postoperative hospital stay in comparison to the OTG group.

Discussion

The purpose of the current study was to investigate the safety and efficacy of LTG for RGC. In our data, LTG for RGC was associated with a significantly longer operation time, less blood loss, and earlier defecation and first meal in comparison to OTG. These data were consistent with the 8 previous studies that compared LTG to OTG for RGC.

A longer operation time, less blood loss and earlier recovery are consistent features of laparoscopic surgery in comparison to open surgery. At the beginning of the surgery for RGC, entering the abdominal cavity with adhesiolysis is one of the difficult parts of performing a repeated operation, regardless of its approach. In laparoscopic surgery, once a camera port and one or two working ports are inserted, exquisite adhesiolysis can be performed under the pneumoperitoneum with a magnified view.

After recent technical advances, several studies have shown that the performance of laparoscopic gastrectomy after previous laparotomy is safe and feasible (26, 27); however, a history of lower abdominal surgery and the need

for total gastrectomy were associated with conversion to open surgery (28). It is apparent that operations for the treatment of RGC are generally more difficult than those for primary gastric cancer because of adhesion. Although no cases in our series required conversion to open surgery, our systematic analysis of the relevant literature revealed that previous open surgery, previous Billroth I reconstruction (in comparison to Billroth II or Roux-en Y), and the surgeon's experience are associated with the risk for conversion to open during LTG for RGC (29). Thus, previous gastric cancer, previous open gastrectomy and previous Billroth I reconstruction potentially cause more adhesion in the surgical field; however, these factors did not affect the surgical difficulty (as reflected by operation time or blood loss) in our series. The current laparoscopic approach was only associated with a longer operation time and less blood loss. This means that laparoscopic surgery takes longer to perform, but also that even under severe adhesion, laparoscopic surgery with a magnified view and technical advances may contribute to the performance of a safe and secure operation for RGC.

Only 4 reports including our own have described long term clinical outcomes, and all of these studies indicated comparable survival rates between LTG and OTG groups (18, 19, 24). However, conclusions have not been reached because of the short follow-up time periods (median 21-39.1 months). Thus, further comparative case studies with longer follow-up periods are required to establish LTG as a standard treatment option for RGC.

The frequency of RGC has been reported to be 1-3% (30-32). In a recent report, the cumulative incidence of RGC after distal gastrectomy with Billroth I reconstruction for gastric cancer was 5.4% at 20 years (33). Because of the low incidence and complexity associated with previous surgical factors (approach, lymphadenectomy, reconstruction methods and previous postoperative complications), it is not feasible to plan a randomized trial to estimate the safety and feasibility of LTG for RGC. The accumulation of small case series may provide some suggestions on the application of LTG in the treatment of RGC. As the surgical difficulty of RGC can vary greatly depending on the surgical history, the current tumor status and surgeon-related factors, it is important to decide laparoscopic applications on an individual basis.

In summary, our analysis indicated that laparoscopic total gastrectomy for remnant gastric cancer was associated with a significantly longer operation time, significantly less blood loss, significantly earlier defecation and a significantly earlier first meal in comparison to open gastrectomy. The overall survival rates of the two groups were comparable. Thus, a laparoscopic approach may be a safe and feasible treatment option for remnant gastric cancer as it is for primary gastric cancer.

Conflicts of Interest

The Authors declare no conflicts of interest associated with this manuscript.

Authors' Contributions

Conception and design of study: M.O, M.I, M.K, T.N; Acquisition of data: M.O, Y.S, Y.M, Y.N, H.U, M.S, T.I, K.S; Analysis and/or interpretation of data: M.O, M.Y, M.M, Y.T; Drafting the manuscript: M.O; Revising the manuscript critically for important intellectual content: M.I, Y.S, M.K, Y.M, T.N, Y.N, H.U, M.S, T.I, K.S, M.Y, M.M, Y.T; Approval of the version of the manuscript to be published: M.O, M.I, Y.S, M.K, Y.M, T.N, Y.N, H.U, M.S, T.I, K.S, M.Y, M.M, Y.T.

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