

Outcomes of Laparoscopic Gastrectomy after Endoscopic Treatment for Gastric Cancer: A Comparison with Open Gastrectomy

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Purpose: Additional gastrectomy is needed after endoscopic resection for early gastric cancer when pathology confirms any possibility of lymph node metastasis or margin involvement. No studies depicted the optimal type of surgery to apply in these patients. We compared the short-term and long-term outcomes of laparoscopic gastrectomy with those of open gastrectomy after endoscopic resection to identify the optimal type of surgery.

Materials and Methods: From 2003 to 2010, 110 consecutive patients who underwent gastrectomy with lymphadenectomy either by laparoscopic (n=74) or by open (n=36) for gastric cancer after endoscopic resection were retrospectively analyzed. Postoperative and oncological outcomes were compared according to types of surgical approach.

Results: Clinicopathological characteristics were comparable between the two groups. Laparoscopic group showed significantly shorter time to gas passing and soft diet and hospital day than open group while operation time and rate of postoperative complications were comparable between the two groups. All specimens had negative margins regardless of types of approach. Mean number of retrieved lymph nodes did not differ significantly between the two groups. During the median follow-up of 47 months, there were no statistical differences in recurrence rate (1.4% for laparoscopic and 5.6% for open, P=0.25) and in overall (P=0.22) and disease-free survival (P=0.19) between the two groups. Type of approach was not an independent risk factor for recurrence and survival.

Conclusions: Laparoscopic gastrectomy after endoscopic resection showed comparable oncologic outcomes to open approach while maintaining benefits of minimally invasive surgery. Thus, laparoscopic gastrectomy can be a treatment of choice for patients previously treated by endoscopic resection.

Key Words: Gastric cancer; Endoscopic procedure; Gastrectomy; Laparoscopy

Introduction

With the help of widespread health screening and development of endoscopic technology, early detection of gastric cancer has been raised where gastric cancer is prevalent such as Korea and

Japan.^{1,2} Endoscopic resection, endoscopic submucosal resection or endoscopic submucosal dissection has been gaining acceptance as a useful method to treat early gastric cancer due to its minimal invasiveness and favorable results in maintaining good quality of life.³⁻⁶ However, additional gastrectomy is needed after endoscopic resection for early gastric cancer when pathology confirms any possibility of lymph node metastasis or margin involvement.^{7,8}

While there have been several reports regarding the necessity of additional surgery after endoscopic resection, no studies depicted the optimal type of surgery to apply in these patients. Some studies showed successful outcomes of laparoscopic gastrectomy after endoscopic resection. However, most of these studies only focused on

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short-term outcomes and not the long-term outcomes.⁹⁻¹¹ Whether the benefits of minimally invasive surgery can be maintained and oncological safety of laparoscopic approach in these specific patients is not investigated.

To the best of our knowledge, there has been no study evaluating oncologic feasibility as well as early postoperative outcomes of laparoscopic gastrectomy after endoscopic resection compared with open surgery. In this context, to identify the optimal type of gastrectomy we compared the long-term outcomes of surgery laparoscopic gastrectomy with those of open gastrectomy for patients previously treated by endoscopic resection. In addition we also assessed the short-term outcomes whether the benefits of laparoscopic approach are existed in these specific patients group.

Materials and Methods

1. Patients

From January 2003 to December 2010, 139 consecutive patients who underwent gastrectomy with lymph node dissection either by laparoscopic or by open for gastric cancer after endoscopic treatment, either by endoscopic mucosal resection or by endoscopic submucosal dissection, at Severance Hospital, Yonsei University Health System, Seoul, Korea were included in this study. Of these 139 patients, 29 patients underwent gastrectomy because of local tumor recurrences in the same stomach area during follow up after complete resection by endoscopically without any probability of lymph node metastasis. After excluding 29 recurred patients after complete endoscopic resection, 110 patients were included for the analyses.

Patient demographics, pathologic feature after endoscopic treatment, pathologic outcome after surgery, clinical outcomes including operation time, time to gas passing, time to soft diet, hospital day, complications and long term oncologic outcomes were compared between open and laparoscopic group. The written informed consent was received from all of the patients at the time of surgery.

2. Indications of surgery after endoscopic resection and surgical procedures

The indications of surgery after endoscopic resection are when pathology reports confirms any of following conditions lateral margin involvement of cancer, submucosal invasion with or without basal margin involvement, lymph vascular invasion, and local tumor recurrence after endoscopic resection.

According to the tumor location, we performed distal subtotal or total gastrectomy. The lymph node dissection was performed

according to the rules of the Japanese Research Society for Gastric Cancer as follows: D1+ α (dissection of group 1 and number 7 lymph node), D1+ β (dissection of group 1 and number 7, 8a, and 9 lymph nodes), or D2 lymphadenectomy (dissection of all group 1 and group 2 lymph nodes).^{12,13}

3. Follow-up, categorization of recurrence pattern, and survival

We followed up the patients every 3 months for 1 year after operation and every 6 months for the next 4 years with physical examination, laboratory tests including tumor markers (carcinoembryonic antigen, carbohydrate antigen, 19-9). The chest radiography, abdominal pelvic computed tomography and endoscopy were performed at least once a year. We classified the recurrence pattern as loco-regional, lymphatic, distant metastasis and we confirm the recurrence by the tissue biopsy if possible.

The last follow up date was September 11th, 2012.

4. Statistical analysis

Statistical analysis was performed using SPSS version 18.0 for Windows (IBM Co., Armonk, NY, USA). Categorical variables were compared using chi-square or Fisher's exact test, and continuous variables were compared with Mann-Whitney test. The risk factors associated with tumor recurrence and death were analyzed with univariate and multivariate logistic regression test. The Cox proportional hazard model was used for risk factors affecting disease free survival and overall survival.

Results

1. Comparison of clinicopathologic features

Table 1 shows the clinical characteristics and pathologic results of endoscopic resection of the 110 patients who received radical gastrectomy after endoscopic resection. Demographic features in terms of in age and gender between open and laparoscopic gastrectomy group. There were no significant differences between the two groups in pathologic findings of endoscopic resection, except location of the tumor. In laparoscopic gastrectomy group, tumor located more commonly in the lower third (P=0.02).

2. Comparison of indications of radical gastrectomy

The indications of radical gastrectomy are demonstrated in Fig. 1. Incomplete resection is defined to presence of carcinoma at lateral resection margin. Presence of lymph node metastasis is defined to

Table 1. Comparison of clinicopathologic features after endoscopic treatment

Characteristic		Open (n=36, %)	Laparoscopy (n=74, %)	P-value
Age (yr)		60.3±9.8 (43~76)	60.4±10.2 (40~78)	0.99 [‡]
Gender	Male	22 (61.1)	49 (66.2)	0.38 [‡]
	Female	14 (38.9)	25 (33.8)	
Location	Upper	9 (25.0)	9 (12.0)	0.02*
	Middle	9 (25.0)	8 (10.8)	
	Lower	18 (50.0)	57 (77.0)	
Size (mm)		12.8±5.0 (4~30)	16.8±5.0 (2~52)	0.53 [‡]
Depth of invasion	Mucosa	13 (36.1)	25 (33.8)	0.83 [‡]
	Submucosa	23 (63.9)	49 (66.2)	
Histology	Adenoca. well diff.	11 (30.6)	29 (39.2)	0.42*
	Adenoca. moderate diff.	5 (13.9)	16 (21.6)	
	Adenoca. poor diff.	10 (27.8)	12 (16.2)	
	Signet ring cell	1 (2.8)	0 (0.0)	
	Mucinous	8 (22.2)	15 (20.3)	
	Undifferentiated	1 (2.8)	2 (2.7)	
Margin	All free	17 (47.2)	32 (43.2)	0.98*
	LM positive	9 (25.0)	19 (25.7)	
	BM positive	7 (19.4)	16 (21.6)	
	LM+BM positive	3 (8.3)	7 (9.5)	
LVI	Negative	30 (83.3)	60 (81.1)	>0.99*
	Positive	6 (16.7)	14 (18.9)	

Values are presented as mean±standard deviation (range) or number (%). Adenoca. = adenocarcinoma; diff. = differentiated; LM = lateral margin; BM = basal margin; LVI = lymphovascular invasion. *Chi-square test. [‡]Fisher's exact test; [†]Mann-Whitney U tests.

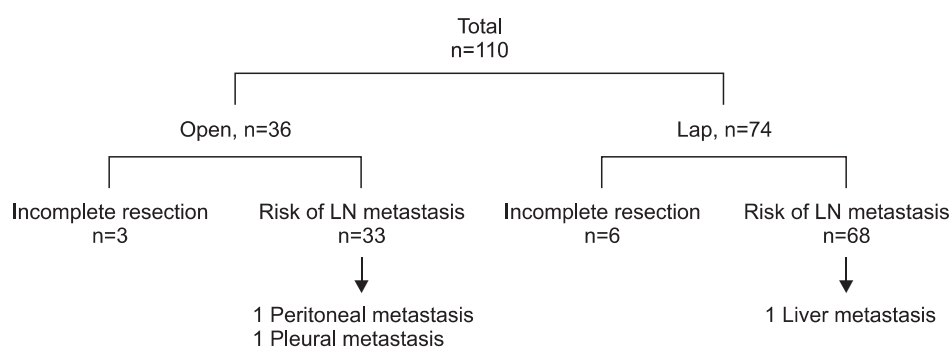


Fig. 1. Surgical indications and results of follow up according to types of surgery. Open = open gastrectomy; Lap = laparoscopic gastrectomy; LN = lymph node.

submucosal invasion, histologic undifferentiation or had lymphovascular invasion. There were no differences in indications of additional gastrectomy after endoscopic resection between open and laparoscopic resection group.

3. Short-term postoperative outcomes

Postoperative outcomes are summarized in Table 2. Type of operation (subtotal gastrectomy vs. total gastrectomy) and extent

of systemic lymph node dissection were similar between open and laparoscopic gastrectomy group. Mean operation time also showed no significant difference between the open and laparoscopic group (161.8 min vs. 155.1 min, $P=0.80$). Laparoscopic group showed significantly shorter time to gas passing (2.7 days vs. 3.5 days, $P<0.01$) and soft diet (4.2 days vs. 5.4 days, $P<0.01$) and hospital (8.6 days vs. 10.6 days, $P<0.01$) compared to open group. Rate of postoperative complications was comparable between the two groups. There

Table 2. Comparison of short-term outcomes and pathologic results after gastrectomy

Variable		Open (n=36)	Laparoscopy (n=74)	P-value	
Extent of resection	Distal subtotal	25 (69.4)	60 (81.1)	0.23 [†]	
	Total	11 (30.6)	14 (18.9)		
Extent of LN dissection	≤D1+β	30 (83.3)	55 (74.3)	0.34 [†]	
	D2	6 (16.7)	19 (25.7)		
Operation time (min)		161.8±66.3	155.1±50.3	0.80 [‡]	
Gas passing, mean (d)		3.5±1.0	2.7±0.7	<0.01 [‡]	
Soft diet, mean (d)		5.4±1.7	4.2±1.7	<0.01 [‡]	
Hospital stay, mean (d)		10.6±6.3	8.6±18.9	<0.01 [‡]	
Surgical complication	Absent	31 (86.1)	63 (85.1)	>0.99 [†]	
	Present	5 (13.9)	11 (14.9)		
Residual tumor	Absent	16 (44.4)	23 (31.1)	0.20 [†]	
	Present	20 (55.6)	51 (68.9)		
Depth of residual tumor	No residual	16 (44.4)	23 (31.1)	0.06*	
	Mucosa	7 (19.4)	22 (29.7)		
	Submucosa	9 (25.0)	26 (35.1)		
	Proper muscle	1 (2.8)	3 (4.1)		
	Subserosa	3 (8.3)	0 (0.0)		
Nodal stage	0	31 (86.1)	67 (90.5)	0.80*	
	1	2 (5.6)	4 (5.4)		
	2	2 (5.6)	2 (2.7)		
	3	1 (2.8)	1 (1.4)		
Number of retrieved LNs stage		31.6±10.9	35.1±14.1	0.16 [‡]	
	IA	30 (83.3)	65 (87.8)		0.47*
	IB	2 (5.6)	5 (6.8)		
	IIA	1 (2.8)	3 (4.1)		
	IIB	1 (2.8)	1 (1.4)		
	IIIA	1 (2.8)	0 (0.0)		
	IIIB	1 (2.8)	0 (0.0)		

Values are presented as number (%) or mean±standard deviation. LN = lymph node; *Chi-square test; [†]Fisher's exact test; [‡]Mann-Whitney U test.

was no mortality caused by surgical complication.

The residual tumor was founded 55.6% in open group, and 68.9% in laparoscopic group (P=0.20). Depth of residual tumor was not different between two groups (P=0.06). The metastatic lymph nodes were founded in 13.9% of open gastrectomy and 9.5% of laparoscopic group (P=0.80). The number of lymph nodes retrieved in the laparoscopic group did not differ from those dissected during the conventional open group (P=0.46).

4. Long-term oncologic outcomes

There were 3 recurrences. All of the recurrences were distant metastases. Six patients died during the median follow-up period

of 47 months. Among 6 patients, three patients died of recurrent gastric cancer (1 in laparoscopic and 2 in open gastrectomy group) while but the other three patients died due to other malignancies of malignant lymphoma, renal pelvis cancer and breast cancer. There were no statistical difference in recurrence rate (1.4% for laparoscopic and 5.6% for open, P=0.25) and in overall (P=0.22) and disease-free survival (P=0.19) between the two groups (Fig. 2). In the univariate and multivariate logistic analysis, type of approach was not an independent risk factor for recurrence (Table 3). In the Cox regression hazard model, T stage and N stage were the significant prognostic factors associated with disease free survival (Table 4). However, type of approach was not an independent risk

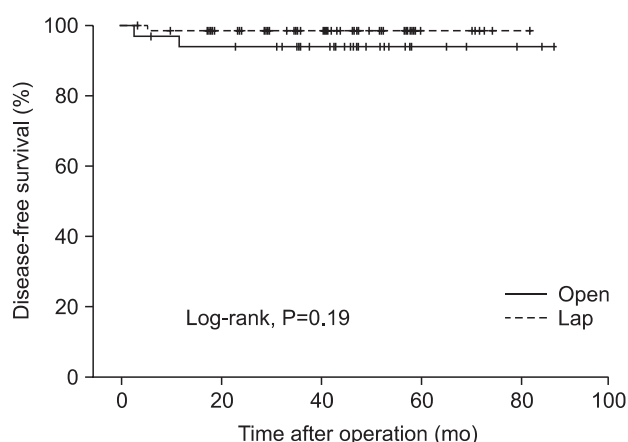


Fig. 2. Comparison of disease free survival open gastrectomy. Open = open gastrectomy; Lap = laparoscopic gastrectomy.

factor for disease free survival of the patients underwent additional gastrectomy after endoscopic resection.

Discussion

In this study, we compared the short-term postoperative outcomes and long-term oncologic outcomes between conventional open and laparoscopic gastrectomy in the patients who previously resected with endoscopy for clinically early gastric cancer. We found that the short-term outcomes, such as hospital day, time to gas passing and time to soft diet showed favorable results in laparoscopic gastrectomy group. The oncologic outcomes of laparoscopic gastrectomy were comparable to those of conventional open gastrectomy. The adequate lymph node dissection and favorable long-

Table 3. Uni- and multivariate analyses of risk factors for recurrence after gastrectomy

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (≤ 65 year vs. > 65 year)	3.60 (0.32~41.40)	0.30	3.60 (0.20~62.48)	0.38
Sex (Male vs. female)	3.78 (0.30~43.10)	0.28	2.90 (0.18~49.75)	0.45
Type of surgery (Open vs. laparoscopy)	0.23 (0.02~2.66)	0.24		
Extent of resection (Subtotal vs. total)	1.73 (0.15~19.90)	0.67		
Lymphovascular invasion (Absent vs. present)	2.32 (0.20~26.87)	0.50		
T stage (1 vs. 2, 3)	33.67 (2.67~425.95)	< 0.01	11.14 (0.57~218.95)	0.11
N stage (0 vs. 1, 2, 3)	19.40 (1.61~233.32)	0.02	8.90 (0.43~188.44)	0.16

Values are presented as mean (range). HR = hazard ratio; CI = confidential interval.

Table 4. Uni- and multivariate analysis of prognostic factors for disease free survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (≤ 65 year vs. > 65 year)	3.90 (0.36~43.37)	0.26	15.52 (0.52~465.40)	0.11
Sex (Male vs. female)	3.60 (0.33~39.78)	0.30	1.06 (0.06~17.60)	0.96
Type of surgery (Open vs. laparoscopy)	0.23 (0.02~2.54)	0.23		
Extent of resection (Subtotal vs. total)	1.65 (0.15~18.20)	0.68		
Extent of LN dissection (D1+ β vs. D2)	0.03 (0.00~3,561.80)	0.57		
Histology (Diff. vs. undiff.)	79.20 (0.00~908,347)	0.36	11.14 (0.57~218.95)	0.11
Submucosal invasion (Absent vs. present)	40.17 (0.00~797,543)	0.47	8.90 (0.43~188.44)	0.16
Lymphovascular invasion (Absent vs. present)	2.16 (0.20~23.84)	0.53		
Size (< 25 mm vs. ≥ 25 mm)	0.03 (0.00~1,813.67)	0.53		
T stage (1 vs. 2, 3)	31.15 (2.82~343.89)	< 0.01	17.17 (1.17~251.93)	0.04
N stage (0 vs. 1, 2, 3)	18.28 (1.66~201.63)	0.02	24.78 (0.97~633.74)	0.04

Values are presented as mean (range). HR = hazard ratio; CI = confidential interval.

term outcomes, measured by disease free survival and recurrence were achieved by laparoscopic surgery for patients previously treated by endoscopic resection.

Endoscopic resection has been established as one of treatment options for early gastric cancer. Endoscopic resection provides a survival rate of 90% comparable to that of surgery if it is applied with appropriate indications.¹⁴⁻¹⁶ It also can avoid morbidity and mortality associated with surgery and maintain the patients' quality of life after treatment. However, additional gastrectomy is needed after endoscopic resection for early gastric cancer when pathology confirmed any possibility of lymph node metastasis or margin involvement.⁷⁻¹¹ While there have been several reports regarding the necessity of additional surgery after endoscopic resection, no studies depicted the optimal type of surgery to apply in these patients.

Laparoscopic gastrectomy for gastric cancers has been widely used for early gastric cancer. This approach increased because of its low invasiveness, good cosmesis and recovery.¹⁷⁻¹⁹ Although there are some unresolved oncologic problems for advanced gastric cancer, in early gastric cancer, laparoscopic gastrectomy is considered to be safe, and the rate of local failure after laparoscopic gastrectomy is comparable to that of open surgery.²⁰⁻²² Applications of laparoscopic gastrectomy for patients previously received endoscopic resection in early gastric cancer have been reported. But, these studies were focused on that laparoscopic surgery might be beneficial in regard to short term clinical outcome after surgery.

According to our results, oncologic outcomes of laparoscopic gastrectomy were comparable with those of conventional open gastrectomy in the patients who previously received endoscopic resection for gastric cancer. The favorable long-term outcomes, measured by disease free survival and recurrence were achieved by laparoscopic surgery. Also, D2 lymph node dissection was performed in laparoscopic gastrectomy similar to open surgery. The all of recurrences were distant metastases, which means that adequate local control was achieved by laparoscopic gastrectomy. The complication rates were also acceptable compared to open surgery and there was no mortality.

There are some important concerns of the long-term oncologic outcomes of laparoscopic gastrectomy. The first issue is the potential peritoneal recurrence or port site metastasis due to insufflated gas for a pneumoperitoneum. In our study, there were neither port-site metastases nor recurrence at surgical wound. The peritoneal recurrence occurred only in one patient of laparoscopic group. The second is the possible loco-regional recurrence because of inadequate lymph node dissection. However, our study revealed

that D2 dissection was performed similarly in two groups and the number of retrieved lymph nodes in laparoscopic surgery was comparable to that of open surgery. However, the study is limited by the retrospective nature of analyses and possibility of selection bias of applying laparoscopic surgery. Despite these limitations, we analyzed 110 gastric cancer patients who received endoscopic resection before radical gastrectomy and compared the long term oncologic outcome between laparoscopic and open surgery.

In conclusion, our study demonstrated that laparoscopic approach can be safely applied for gastric cancer patients previously treated by endoscopic resection. Laparoscopic gastrectomy after endoscopic resection showed comparable oncologic outcomes to open approach while maintaining benefits of minimally invasive surgery. Thus, laparoscopic gastrectomy can be a treatment of choice for patients previously treated by endoscopic resection.

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