

Original Article

Laparoscopic versus open total gastrectomy for advanced proximal gastric carcinoma: a matched pair analysis

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Abstract: Laparoscopic total gastrectomy for advanced proximal gastric carcinoma is a complex and challenging laparoscopic procedure and is limited to a few expert centers. This study compared the short- and long-term outcomes of laparoscopic total gastrectomy for advanced proximal gastric carcinoma with open gastrectomy. From January 2008 to January 2015, 183 patients underwent laparoscopic total gastrectomy for advanced proximal gastric carcinoma. These patients were matched and compared with 183 patients who underwent conventional open surgery. Short-term operative and postoperative outcomes as well as long-term outcomes, including overall survival and disease-free survival rates, were assessed. The patients were matched for several preoperative factors. Overall postoperative 30-day complication rates were significantly higher for the open surgery group than for the laparoscopy group. No significant differences were observed in the 5-year overall and disease-free survival between the open surgery and laparoscopy groups. The same results were observed in the subgroup analyses of the TNM stage. In summary, this study shows the feasibility of laparoscopic total gastrectomy for advanced proximal gastric carcinoma compared with open resection with regard to both short- and long-term outcomes. Laparoscopic surgery offers many advantages and is well suited for treating proximal gastric carcinoma.

Keywords: Proximal gastric carcinoma, laparoscopic total gastrectomy, minimally invasive surgery, survival

Introduction

Radical gastrectomy with a D2 lymphadenectomy is one of the most challenging and complex procedures encountered by gastrointestinal surgeons, requiring considerable expertise and surgical skill [1-9]. Laparoscopic gastrectomy requires additional advanced skills [10-20]. Despite the technical difficulties of this technique, more centers have been using laparoscopy in gastric surgery throughout the last decade [10-23]. Significant advantages of laparoscopic distal gastrectomy versus the open procedure have been widely reported [24-32]. These advantages include decreased incision size, postoperative pain, blood loss, surgical complications, and length of hospital stay [24-32]. In contrast, the technical demands of laparoscopic total gastrectomy have limited the use of the procedure to only a few centers. Laparoscopic total gastrectomy is perceived as

the most complex of all laparoscopic procedures and is limited to surgical teams experienced in both laparoscopic and gastric surgery [33-41]. Laparoscopic total gastrectomy was first performed in the 2000s [42]. Previous studies on the short- and long-term outcomes of laparoscopic total gastrectomy for advanced proximal gastric carcinoma have the limitations of small sample size (< 100 cases) and relatively shorter survival outcomes (only 3-year survival outcomes) [33-41]. This study assessed the feasibility and results of laparoscopic total gastrectomy for advanced proximal gastric carcinoma, with regard to both short- and long-term outcomes via a concurrent case-matched comparison with open total gastrectomy.

Patients and methods

This study complied with the Declaration of Helsinki rules. This retrospective research was

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approved by local ethics committees. The need for informed consent from all patients was waived because this was retrospective study.

From January 2008 to January 2015, 183 patients underwent laparoscopic total gastrectomy for advanced proximal gastric carcinoma and were included in this retrospective study. A control group that underwent open total gastrectomy for advanced proximal gastric carcinoma was case-matched for age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and clinical TNM stage in a 1:1 manner. Medical records were retrospectively reviewed for demographics, clinical presentation, operative results, hospital course, postoperative 30-day complications and postoperative 30-day mortality, pathological findings, and long-term follow-up results. Postoperative 30-day complications were stratified according to the Clavien-Dindo classification [43-50], and complications of grade 3 or greater were considered major.

The routine preoperative evaluation included taking history; physical examination; routine biochemical examination; blood coagulation testing; tumor marker testing; upper gastrointestinal endoscopy; endoscopic ultrasonography; computed tomographic scans of the brain, chest, and abdomen; and ultrasonography of the abdomen [42, 51-60]. Positron emission tomography-computerized tomography and bone scanning were performed in selected cases when necessary. The clinical stage of gastric carcinoma was based on the seventh edition of the TNM classification of gastric carcinoma that was proposed by the Japanese Gastric Cancer Association, Union for International Cancer Control, and American Joint Committee on Cancer [42].

The inclusion criteria for laparoscopic total gastrectomy in this study were: histopathologically proven gastric carcinoma, no neoadjuvant chemotherapy or radiotherapy, and patients with clinical T2-3N0-1M0 disease preoperatively [42]. Exclusion criteria for this study were: palliative resection or cases requiring multivisceral resection.

All patients were placed in the supine position with legs apart, and were under general anesthesia. The surgeon stood on the right side of the patients, and the first assistant stood on

the left side. The camera assistant stood on the same side as the surgeon. Carbon dioxide pneumoperitoneum was established at 15 mmHg after a 12-mm trocar was introduced through an umbilical incision. Two 12-mm trocars were introduced in the left and right lower quadrants, and two 5-mm trocars were inserted in the left and right upper quadrants. Firstly, the operator harvested the lymph node located along the greater curvature of the stomach, and then performed a resection of the distal margin. Secondly, the operator harvested the lymph node located along the lesser curvature of the stomach and the suprapancreatic area. Thirdly, after the lymph node dissection was finished, the proximal margin was resected. Finally, Roux-en-Y reconstruction was performed for the gastrointestinal tract reconstruction. A detailed procedure of laparoscopic and open total gastrectomy has been described elsewhere [33].

Follow-up data were obtained through office visits or telephone interviews. The overall survival was assessed from the date of surgery until the last follow-up or death of any cause. The disease-free survival was calculated from the date of surgery until the date of cancer recurrence or death from any cause. Disease recurrence was defined as locoregional, peritoneal, distant lymph node, hematogenous recurrence, or mixed recurrence proven by radiology or pathology when available. Locoregional recurrence included instances that were proximal to the anastomotic site and gastric regional lymph nodes. Extraregional lymph nodes were defined as distal lymph nodes. Hematogenous recurrence included recurrences that occurred at remote sites, such as the brain, lung, and kidney [61-70]. The follow-up was closed in August 2015.

SPSS for Microsoft Windows version 14.0 (SPSS Inc.; Chicago, IL, USA) was used for statistical analysis. Data were presented as the mean \pm standard deviation for variables with a normal distribution, and were analyzed by *t*-test. For data with a non-normal distribution, results were expressed as the median and range, and were compared using nonparametric tests. Differences of semiquantitative results were analyzed by the Mann-Whitney *U*-test. Differences of qualitative results were analyzed by chi-square tests or Fisher's exact

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Table 1. Comparison of demographic data of the two groups

	Laparoscopy (n = 183)	Open (n = 183)	P value
Age (years)	59 (41-72)	57 (43-70)	0.351
Sex			0.709
Male	117	111	
Female	66	72	
BMI (kg/m ²)	19 (19-24)	22 (19-27)	0.520
Clinical TNM stage (7th AJCC-UICC-JGCA)			0.814
IB	54	54	
IIA	51	57	
IIB	78	72	
ASA grade			0.794
I	135	129	
II	33	45	
III	15	15	
Comorbidity			0.645
0	135	129	
1	24	18	
2	15	33	
3	9	3	

Table 2. Comparison of surgical outcomes of the two groups

	Laparoscopy (n = 183)	Open (n = 183)	P value
Operative time (min)	240 (220-320)	190 (170-260)	0.020
Estimated blood loss (ml)	250 (170-450)	330 (220-470)	0.015
Number of analgesic injections	3 (1-6)	5 (4-10)	0.018
Time to first flatus (days)	2 (1-5)	4 (2-7)	0.028
Hospital stay after surgery (days)	8 (5-18)	10 (7-32)	0.011

Table 3. Comparison of complications of the two groups

	Laparoscopy (n = 183)	Open (n = 183)	P value
Overall complications n	24	51	0.044
Major complications n	21	42	0.093
Minor complications n	3	9	0.611
Pneumonia	12	18	0.509
Anastomosis leakage	6	9	1.000
Wound infection	3	9	0.611
Ileus	3	3	1.000
Atelectasis	0	3	-
Intra-abdominal bleeding	0	3	-
Intra-abdominal abscess	0	3	-

test when appropriate. Survival rates were analyzed using the Kaplan-Meier method; differ-

ences between the two groups were analyzed with the log-rank test. $P < 0.05$ was considered statistically significant.

Results

Patient demographics and tumor features are listed in **Table 1**. The patients were matched for age, gender, BMI, ASA score, and clinical TNM stage. There was no significant difference in comorbidity between the groups (**Table 1**).

Table 2 summarizes the operative outcomes and postoperative courses of the two groups. The operative time was significantly longer in the laparoscopy group ($P = 0.020$). However, patients in the laparoscopy group enjoyed faster recovery, including less blood loss ($P = 0.015$), fewer analgesic injections ($P = 0.018$), earlier time to first flatus ($P = 0.028$), and earlier hospital discharge ($P = 0.011$) (**Table 2**).

The postoperative 30-day complication rates were significantly higher in the open surgery group than in the laparoscopy group ($P = 0.044$) (**Table 3**). However, the proportion of patients with Clavien-Dindo classification > 2 were 18.4% in the open group and 13.2% in the laparoscopy group, with no significant difference observed between the groups ($P = 0.093$). No postoperative 30-day deaths were recorded. The pathological data showed comparable results between the two groups (**Table 4**).

The overall survival and disease-free survival rates of the two groups are shown in **Figures 1** and **2**. With a median follow-up of 38 months, there were no significant differences between the 5-year overall survival and disease-free survival between the two

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Table 4. Comparison of pathological data (define what kind data?) of the two groups

	Laparoscopy (n = 183)	Open (n = 183)	P value
Histological type			0.703
Differentiated	66	60	
Undifferentiated	117	123	
Lauren classification			0.765
Intestinal	84	87	
Diffuse	63	69	
Mixed	36	27	
Retrieved lymph nodes	18 (17-23)	19 (16-24)	0.548
Pathological TNM stage (7th AJCC-UICC-JGCA)			0.616
IB	18	24	
IIA	45	48	
IIB	72	60	
IIIA	24	33	
IIIB	9	6	
IIIC	15	12	
Residual tumor (R0/R1/R2)	183/0/0	183/0/0	1.000

are shown in **Table 5**. There were no significant differences in the disease-free survival and overall survival between the open surgery and laparoscopy groups in terms of the pathological TNM stage.

The sites of recurrence and recurrence-free interval from surgery to the first cancer recurrence were not significantly different between the two groups (**Table 6**). There were no port-site recurrences in the patients who underwent laparoscopic total gastrectomy for advanced proximal gastric carcinoma.

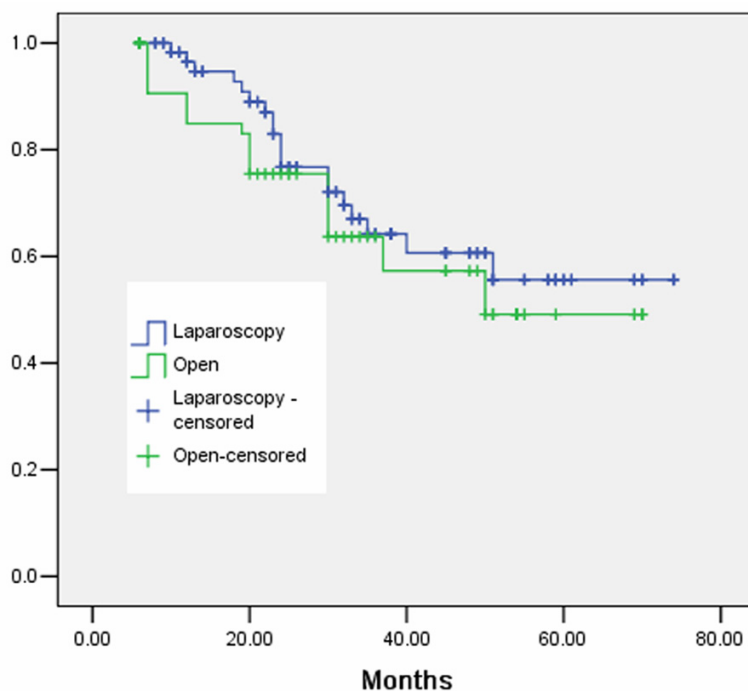


Figure 1. Comparison of overall survival rate between laparoscopy and open groups.

groups ($P = 0.444$ and 0.561 , respectively). Subset analyses by the pathological TNM stage for overall survival and disease-free survival

Of the 183 patients in the laparoscopy group, 18 required conversion to laparotomy (conversion group), and the procedure was completed in the remaining 165 with laparoscopy alone (complete group). The reasons for the conversions were as follows: severe adhesions in six patients, and uncontrollable bleeding in 12 patients. There were no differences between the conversion group and complete group in the postoperative 30-day morbidity, disease-free survival, and overall survival (**Table 7**).

Discussion

Although previous studies have suggested the feasibility of laparoscopic total gastrectomy [33-41], this procedure remains challenging and demands both laparoscopic and gastric surgery expertise. There is also insufficient evidence to determine whether laparoscopic total gastrec-

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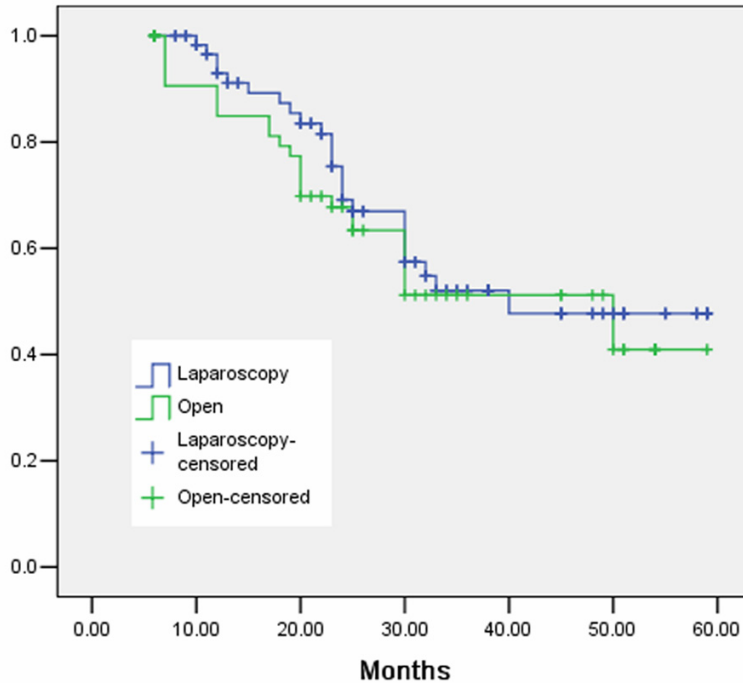


Figure 2. Comparison of disease-free survival rate between laparoscopy and open groups.

Table 5. Comparison of five-year overall survival and disease-free survival rate following laparoscopic and open gastrectomy with regard to pathological stage

Pathological stage	Laparoscopy (%)	Open (%)	<i>P</i>
Overall survival			0.550
I	87	88	
II	74	78	0.098
III	46	40	0.250
Disease-free survival			0.280
I	69	65	
II	59	64	0.189
III	29	20	0.190

tomy is more suitable than open resection for the treatment of advanced proximal gastric carcinoma without compromising oncologic efficacy.

Laparoscopic total gastrectomy was introduced in the 2000s, and more than 400 procedures have since been performed [33-41]. A previous report describing this novel conceptual technique showed that laparoscopic total gastrectomy is performed using essentially the same

steps and principles as those used in the open procedure. This setting is ideal and appropriate for a comparative study of open and laparoscopic total gastrectomy. The main findings of this study are: (1) the short-term outcomes of laparoscopic total gastrectomy for advanced proximal gastric carcinoma appeared to be superior to those of the open procedure; (2) the technical feasibility of laparoscopic total gastrectomy has been proven in expert centers; and (3) oncological outcomes, including overall and disease-free survival rates, after laparoscopic total gastrectomy were comparable with those after the open procedure for advanced proximal gastric carcinoma. To the best of our knowledge, only two reports have demonstrated the feasi-

bility and safety of laparoscopic total gastrectomy for proximal gastric carcinoma in comparison with open resection [33, 40].

With regard to the short-term outcome of overall complications, which is the most important outcome, laparoscopic total gastrectomy was superior to open resection. There was no difference between the two groups with regard to the severity of the complications, which were defined using the Clavien-Dindo classification. Clavien-Dindo classifications of > 2 were significantly less frequent in the laparoscopy group. Most common complications were pneumonia and anastomotic leakage, requiring treatment. These complications represent the significant disadvantages of the open procedure. The apparent benefit of laparoscopy may be explained by the lack of damage to the abdominal wall, which causes less inflammatory cytokine release and exposure of the abdominal viscera [71-76].

This study suggests comparable oncological outcomes between laparoscopic total gastrectomy and open resection. Overall, TNM staging was comparable between the two groups. Other pathological findings were also compara-

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Table 6. Comparison of cancer recurrence data of the two groups

Outcomes	Laparoscopy (n = 183)	Open (n = 183)	P
Tumor recurrence	63	72	0.573
Locoregional	21	24	0.783
Peritoneal	18	21	0.769
Distant lymph node	9	9	1.000
Hematogenous	9	6	1.000
Mixed	6	12	0.675
Time to recurrence (median, months)	17	13	0.102
Treatment for recurrence			
Metastasectomy	21	12	0.343
Chemotherapy	27	36	0.472
Supportive care	15	24	0.379

Table 7. Comparison of morbidity and prognosis data of the conversion and complete group

	Conversion group (n = 18)	Complete group (n = 165)	P
Postoperative 30-day morbidity	1	7	1.000
Five-year overall survival	54%	61%	0.820
Five-year disease-free survival	47%	53%	0.507

ble between the two groups, including histology, tumor-free margin, and the results of D2 lymphadenectomy, which could significantly influence disease-free and overall survival. Both groups were therefore well matched with regard to the tumor behavior, suggesting the reliability of the long-term outcomes analysis. The long-term outcomes were similar between the two groups. Furthermore, subgroup analyses by pathological TNM stage showed similar results, indicating that compared with open surgery, laparoscopic total gastrectomy is associated with similar oncological results.

This is an intention-to-treat analysis; thus, all 18 converted cases in the laparoscopy group were analyzed as laparoscopic cases. We have compared the complete cases (n = 165) and conversion cases (n = 18), and there were no significant differences between the two groups in postoperative 30-day morbidity and prognosis. The conversion rate for laparoscopic procedures was nearly 10%, which is similar to those of previous reports [33-41].

The reliability of the current study is limited because of the relatively small sample size and the limitations of the study design. Although

well-designed, randomized controlled trials with larger sample sizes would be preferred; when considering the difficulty in designing such a study, our conclusions will nonetheless be very useful in the future development of laparoscopic total gastrectomy for advanced proximal gastric carcinoma.

In conclusion, the present study compares the technical feasibility, superior short-term outcomes, and comparable oncological outcomes of laparoscopic total gastrectomy for advanced proximal gastric carcinoma with open resection. Although laparoscopic total gastrectomy offers many advantages commonly attributed to laparoscopy and is thus well suited to treat advanced proximal gastric carcinoma, given the relatively high incidence of

conversion, laparoscopic total gastrectomy should be regarded as a highly complicated procedure.

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Disclosure of conflict of interest

None.

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