

ORIGINAL ARTICLE

Short- and long-term outcomes of conversion in laparoscopic gastrectomy for gastric cancer

Zhenhao Ding, Li Jiang, Ke Zhang, Ronghai Huang

Department of General Surgery, Beijing Ditan Hospital, Capital Medical University, Beijing, People's Republic of China

Summary

Purpose: In laparoscopic gastrectomy (LG) for gastric cancer, conversion to open gastrectomy may sometimes be unavoidable. This study aimed to investigate the short-term and long-term outcomes of conversion from LG to open gastrectomy in patients with gastric cancer.

Methods: Patients with gastric cancer who underwent LG from January 2010 to December 2016 were included in this study. Patients were divided into a laparoscopic group and a conversion group based on the occurrence of conversion to open gastrectomy during LG. We carried out a retrospective analysis of the clinical and follow-up data of patients. Univariate and multivariate analysis were carried out on factors affecting prognosis.

Results: In this study, the conversion rate of patients was 8%. The most common reason for conversion to open gastrectomy was bleeding, followed by adhesions. Compared with those in the laparoscopic group, the conversion group had longer operation time, greater intraoperative blood loss,

longer time to first flatus and longer hospitalization time. They also had higher incidence of postoperative complications, but the rates of major complications were similar in both groups. Patients in both groups had similar pathological results. During the follow-up period, the tumor recurrence rates in both groups were similar. There were no statistical differences in the 5-year overall survival (OS) and 5-year disease-free survival (DFS) in both groups. On multivariate analysis, tumor invasion depth and lymph node metastasis were independent predictors of OS. Tumor invasion depth, lymph node metastasis, and cancer differentiation were independent predictors of DFS.

Conclusion: The long-term outcomes of patients with gastric cancer who were converted to open gastrectomy during LG are similar to those who did not undergo conversion.

Key words: conversion, gastric carcinoma, laparoscopic gastrectomy, minimally invasive surgical oncology, prognosis

Introduction

Japanese surgeons reported the first use of laparoscopic gastrectomy (LG) for the treatment of gastric cancer in 1994 [1]. Since then, there have been increasing reports of LG for the treatment of gastric cancer [2-4]. Currently, randomized controlled trials [5-8] have found that when LG was used for the treatment of early gastric cancer, characteristics such as a smaller surgical incision site, reduced postoperative pain, faster postoperative recovery, and incidence of postoperative complications were equivalent or better than open gas-

trectomy; the long-term prognosis of LG was also similar to that of open gastrectomy. Therefore, LG has been recommended for the treatment of early gastric cancer. LG applications in locally advanced gastric cancer have also shown an increasing clinical trend [9-13]. Currently, there are many retrospective studies and meta-analyses indicating better short-term outcomes and similar long-term outcomes as open gastrectomy when LG was used to treat locally advanced gastric cancer [9-16]. Similar to other laparoscopic surgeries (such as laparo-

scopic colectomy and laparoscopic total mesorectal excision), during LG treatment of gastric cancer, conversion to open gastrectomy may sometimes be unavoidable. The causes of conversion to open gastrectomy can be divided into technical factors and tumor factors [17]. However, to the best of our knowledge, currently there is only one article in English reporting on the effects of conversion to open gastrectomy in patients with gastric cancer undergoing LG [17]. The article only included patients with gastric cancer who had undergone total gastrectomy, and did not involve distal gastrectomy, which is widely used clinically [17]. Therefore, this study aimed to investigate the short-term and long-term outcomes of conversion from LG to open gastrectomy in patients with gastric cancer.

Methods

This study complied with the Declaration of Helsinki rules. This retrospective research was approved by local ethics committees. The need for informed consent from all patients was waived because this was retrospective study.

Patients with gastric cancer who underwent LG from January 2010 to December 2016 and fulfilled the following criteria were included in this study: (1) undergoing radical resection, (2) complete clinical and follow-up data, (3) no tumor-related treatment prior to LG, such as endoscopic resection and neoadjuvant chemotherapy. Exclusion criteria were as follows: (1) discovery of tumor metastasis during surgery without the ability to perform radical resection, (2) emergency operations, and (3) resection of other organs. A total of 311 patients fulfilled the above criteria and were included in this study.

Patients were divided into a laparoscopic group and a conversion group based on the occurrence of conversion to open gastrectomy during LG. Before surgery, patients underwent routine blood tests, serum biochemistry, electronic gastroscopy, endoscopic ultrasound, chest computed tomography (CT), abdominal ultrasound, and other relevant examinations to verify the clinical staging and presence of surgical contraindications [18]. When necessary, positron emission tomography-computed tomography (PET-CT) and bone scans were carried out to exclude tumor metastasis. The indications for LG were as follows: (1) clinical stage of cT1-3N0-1M0, (2) no prior upper abdominal surgery (such as cholecystectomy and splenectomy); (3) body mass index (BMI) <25 kg/m². Surgical details are described in previous reports [19,20]. Postoperative complications, morbidity occurring within 30 postoperative days or hospital stay were graded according to the Clavien-Dindo classification [21-23]. Major complications were defined as grades 3, 4, and 5. Minor complications were classified as 1 and 2.

Adjuvant chemotherapy

For patients with postoperative pathological stage Ib accompanied by lymph node metastasis or patients with pathological stage II and above, adjuvant chemo-

therapy was administered 4 weeks after surgery provided there were no chemotherapy contraindications [24]. The specific adjuvant chemotherapy regimen was decided by the oncologist [24].

Follow-up

Follow-up data were obtained through office visits and telephone interviews. The OS was assessed from the date of surgery until the last follow up or death from any cause. The DFS was calculated from the date of surgery until the date of cancer recurrence or death from any cause. Disease recurrence was defined as locoregional or distant metastasis proven by radiology or pathology.

Statistics

All the statistical analyses were performed using SPSS Version 14.0 software (SPSS Inc., Chicago, IL, USA). Normally distributed variables were analyzed by Student *t*-test and presented as means and standard deviations. Non-normally distributed variables were analyzed by Mann-Whitney *U* test and presented as medians and ranges. Differences between semiquantitative results were analyzed by Mann-Whitney *U* test. Differences between qualitative results were analyzed by chi-square or Fisher exact tests, as appropriate. Survival rates were analyzed by the Kaplan-Meier method, and differences between the two groups were analyzed by log-rank test. Multivariate Cox regression analysis was performed to identify factors predictive of poor DFS and OS by using both forward and backward stepwise selection. Explanatory variables with univariate *p* values ≤ 0.100 were included in the multivariate analysis. The results are reported as hazard ratios (HR) with 95% confidence intervals (CI). A level of 5% was set as the criterion for statistical significance.

Results

The conversion rate of patients was 8% (25/311). The reasons for conversion are presented according to their incidence from high to low and were as follows (Table 1): bleeding, adhesion, and bulky tumor. There were no significant differences in the preoperative data such as age, sex, BMI, ASA status and Charlson comorbidity index between two groups.

Table 1. Reasons for conversion during LG for gastric cancer

Reasons	n (%)
Bleeding	8 (32)
Adhesion	7 (28)
Bulky tumor	5 (20)
Unclear anatomy	3 (12)
Intraoperative T4 tumor	2 (8)

Table 2. Baseline clinicopathological characteristics of the two groups

Characteristics	Laparoscopic group (n=286) n (%)	Conversion group (n=25) n (%)	p value
Age, years, median (range)	61 (41-77)	63 (38-70)	0.251
Gender			0.889
Male	179 (62.6)	16 (64.0)	
Female	107 (37.4)	9 (36.0)	
BMI (kg/m ²), median (range)	21 (18-23)	22 (20-24)	0.179
Charlson comorbidity index			0.158
<2	247 (86.4)	19 (76.0)	
≥2	39 (13.6)	6 (24.0)	
Clinical T stage			0.517
T1	95 (33.2)	9 (36.0)	
T2	148 (51.7)	14 (56.0)	
T3	43 (15.1)	2 (8.0)	
Clinical N stage			0.521
N0	174 (60.9)	17 (68.0)	
N1	109 (38.1)	8 (32.0)	
Tumor location			0.508
Upper	56 (19.6)	5 (20.0)	
Middle	43 (15.0)	6 (24.0)	
Lower	187 (65.4)	14 (56.0)	
ASA score			0.064
I	189 (66.1)	21 (84.0)	
II	63 (22.0)	3 (12.0)	
III	34 (11.9)	1 (4.0)	

BMI: body mass index, ASA: American Society of Anesthesiologists

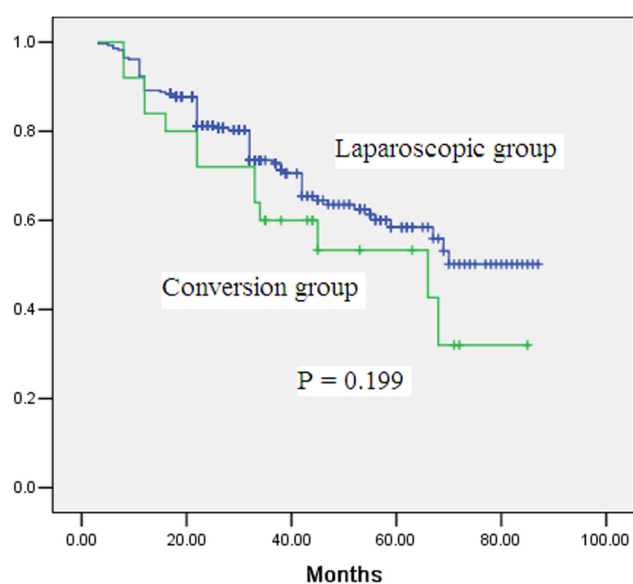


Figure 1. Overall survival of laparoscopic group vs the converted group (p=0.199).

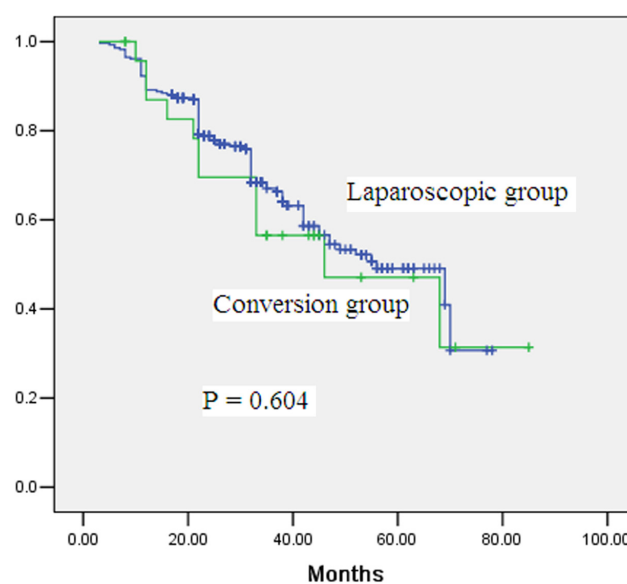


Figure 2. Disease-free survival of laparoscopic group vs the converted group (p=0.604).

Table 3. Surgical outcomes of the two groups

Outcomes	Laparoscopic group (n=286) n (%)	Conversion group (n=25) n (%)	p value
Type of surgery			
Total gastrectomy	89 (31.1)	7 (28.0)	
Distal gastrectomy	197 (68.9)	18 (72.0)	
Operative time (min), median (range)	150 (140–250)	190 (170–280)	
Estimated blood loss (ml), median (range)	210 (180–450)	260 (200–540)	
Hospital stay after surgery (d), median (range)	6 (4-21)	10 (7-24)	
Time to first flatus (d), mean±SD	2.8±0.5	3.5±1.2	
Patients with complications n	40 (14.0)	8 (32.0)	
Patients with minor complications			
Pneumonia	7 (2.4)	4 (16.0)	
Wound infection	6 (2.1)	3 (12.0)	
Anastomotic stricture	5 (1.7)	1 (4.0)	
Anastomotic leakage	4 (1.4)	1 (4.0)	
Pancreatic fistula	6 (2.1)	1 (4.0)	
Ileus	6 (2.1)	0 (0.0)	1.000
Lymphatic fistula	3 (1.0)	0 (0.0)	1.000
Intra-abdominal abscess	4 (1.4)	0 (0.0)	1.000
Patients with major complications			
Intra-abdominal bleeding	3 (1.0)	1 (4.0)	0.741
Heart failure	2 (0.7)	0 (0.0)	1.000
Mortality within 30 postoperative days or hospital stay	0	0	-

Table 4. Pathological outcomes of the two groups

Outcomes	Laparoscopic group (n=286) n (%)	Conversion group (n=25) n (%)	p value
Retrieved lymph nodes	19 (16-25)	18 (17-27)	0.251
Pathological T stage			0.580
T1	84 (29.4)	8 (32.0)	
T2	127 (44.4)	12 (48.0)	
T3	46 (16.1)	3 (12.0)	
T4	29 (10.1)	2 (8.0)	
N stage			0.666
N0	133 (46.5)	12 (48.0)	
N1	78 (27.3)	8 (32.0)	
N2	54 (18.9)	4 (16.0)	
N3	21 (7.3)	1 (4.0)	
Histological differentiation			0.927
Differentiated	197 (68.9)	17 (68.0)	
Undifferentiated	89 (31.1)	8 (32.0)	
Residual tumor			1.000
R0	286 (100.0)	25 (100.0)	
R1	0 (0.0)	0 (0.0)	

Tables 2 and 3 show the comparison of preoperative and postoperative information of both groups. Compared with those in the laparoscopic group, the conversion group had a longer operational time, greater intraoperative blood loss, longer time to first flatus, and longer hospitalization time. A total of 48 patients had postoperative complications and the incidence of postoperative complications in

the conversion group was higher. This was due to the higher incidence of surgical site infection and pneumonia in the conversion group. The incidence of major complications was similar in both groups when the severity of postoperative complications was compared.

There were no significant differences in postoperative information between both groups, such

Table 5. Follow-up data of the two groups

Data	Laparoscopic group (n=286) n (%)	Conversion group (n=25) n (%)	p value
Tumor recurrence n	114 (40.0)	13 (52.0)	0.236
Locoregional	57 (19.9)	7 (28.0)	
Distant	36 (12.6)	4 (16.0)	
Mixed	21 (7.3)	2 (8.0)	
Mortality	84 (29.4)	11 (44.0)	0.128
Died of cancer	77 (26.9)	10 (40.0)	
Died of non-cancer-related diseases	7 (2.4)	1 (4.0)	

Table 6. Univariate and multivariate analysis for predictive factors of overall survival

Factors	Univariate analysis		Multivariate analysis	
	Hazard ratio (95 % CI)	p value	Hazard ratio (95 % CI)	p value
Age, years		0.049		0.097
≥65	1.00		1.00	
<65	1.57 (1.12-1.98)		1.28 (0.58-1.45)	
Gender		0.257		
Male	1.00			
Female	1.14 (0.54-1.21)			
Charlson Comorbidity Index		0.458		
≥2	1.00			
<2	1.24 (0.50-1.48)			
ASA score		0.203		
I-II	1.00			
III	1.18 (0.84-1.59)			
Conversion to open surgery		0.189		
No	1.00			
Yes	1.19 (0.46-1.45)			
Histological differentiation		0.026		0.178
Differentiated	1.00		1.00	
Undifferentiated	2.69 (1.36-4.51)		1.69 (0.78-2.87)	
Pathological T stage		0.015		0.0020
T1-T2	1.00		1.00	
T3-T4	3.05 (1.59-4.06)		3.28 (2.01-5.05)	
Pathological N stage		0.020		0.031
N0-N1	1.00		1.00	
N2-N3	2.98 (1.58-4.08)		2.48 (1.47-3.98)	
Adjuvant chemotherapy		0.250		
No	1.00			
Yes	1.47 (0.69-1.78)			

Table 7. Univariate and multivariate analysis for predictive factors of disease-free survival

Factors	Univariate analysis		Multivariate analysis	
	Hazard ratio (95 % CI)	p value	Hazard ratio (95 % CI)	p value
Age, years		0.108		
≥65	1.00			
<65	1.38 (0.40-1.88)			
Gender		0.230		
Male	1.00			
Female	1.20 (0.68-1.44)			0.200
Charlson Comorbidity Index		0.042	1.00	
≥2	1.00		1.31 (0.85-1.69)	
<2	1.54 (1.28-2.02)			
ASA score		0.351		
I-II	1.00			
III	1.21 (0.48-1.60)			
Conversion to open surgery		0.189		
No	1.00			
Yes	1.36 (0.54-1.68)			
Histological differentiation		0.039		0.021
Differentiated	1.00		1.00	
Undifferentiated	1.77 (1.29-3.69)		1.59 (1.38-3.19)	
Pathological T stage		0.008		0.000
T1-T3	1.00		1.00	
T4	2.88 (1.80-3.44)		2.54 (2.01-3.76)	
Pathological N stage		0.003		0.015
N0-N1	1.00		1.00	
N2-N3	2.01 (1.65-4.20)		2.36 (1.89-4.00)	
Adjuvant chemotherapy		0.153		
No	1.00			
Yes	1.54 (0.70-1.90)			

as TNM staging, tumor differentiation status, and lymph node cleansing results (Table 4).

The median follow-up time was 44 and 39 months in the laparoscopic and conversion groups, respectively. During the follow-up period, the tumor recurrence rate in the conversion group was similar to that in the laparoscopic group; the mortality rates of both groups of patients were also similar (Table 5). The cause of death in most patients was due to tumor recurrence; only a few patients died due to non-tumor-related causes.

There were no statistical differences in the 5-year OS (Figure 1; $p=0.199$) and 5-year DFS (Figure 2; $p=0.604$) between the groups. On univariate analysis, depth of tumor invasion, lymph node metastasis, tumor differentiation and age were related to OS. On multivariate analysis, depth of tumor invasion and lymph node metastasis were independent predictors of OS (Table 6). On univariate analysis, depth of tumor invasion, lymph node

metastasis, tumor differentiation, and Charlson Comorbidity Index were related to DFS. On multivariate analysis, depth of tumor invasion, lymph node metastasis and differentiation were independent predictors of DFS (Table 7).

Discussion

Previous large-sample studies have found that the conversion rate of LG ranges between 0 and 17.4% [17,19,20,25-28]. The reasons for conversion can be divided into tumor factors (such as bulky tumors and T4 tumors) and technical factors (such as bleeding and adhesions). According to an extensive database search of MEDLINE, Embase, Chemical Abstracts, and Web of Science, there is currently only one article in English reporting the short- and long-term outcomes of conversion to open gastrectomy in patients with gastric cancer who underwent LG [17]. In that study, the conver-

sion rate was 17.4%, and the most common reason for conversion to open gastrectomy were tumor factors [17]. However, in our study, the conversion rate was 8%, which was far below that reported in the aforementioned study, which only included patients who had laparoscopic total gastrectomy [17], while, in our study, about 70% of patients had laparoscopic distal gastrectomy and the technical difficulty of this type of surgery is lower than that of laparoscopic total gastrectomy. Therefore, the conversion rate of our study is lower than that reported. In our study, the most common reason for conversion to open gastrectomy were technical factors (such as bleeding and adhesions) and tumor factors accounted for only 28% of conversions. The reason for this was that every patient in this study underwent endoscopic ultrasound and other examinations to confirm T staging. The accuracy of T staging results from preoperative endoscopic ultrasound and postoperative pathology was very high [29]. Therefore, conversion to open gastrectomy due to tumor factors was lower.

This study showed that the short-term outcomes of the conversion group were worse than the laparoscopic group. This was expressed with the longer surgery time, greater intraoperative blood loss, longer time to first flatus, and longer hospitalization stay in the conversion group. The results of this study agree with this previous study [17]. This is because conversion to open gastrectomy is generally more complex, with unclear anatomical layers and greater manipulation difficulty, resulting in greater trauma to the body and worse short-term outcomes [17]. It is also because of a decrease in non-specific immunity caused by increased bodily stress from the greater blood loss and longer surgery time.

Obesity is a risk factor for conversion to open gastrectomy during LG [30,31]. Previous studies have found that the BMI of patients in the conversion group was higher than that in the laparoscopic group [30,31]. In this study, the surgery indications for LG treatment of gastric cancer were restricted to those with a BMI <25 kg/m². Therefore, there were no patients who were converted due to obesity. In recent years, as a result of the increased detection rate of early stage gastric cancer in East Asia and the Westernization of lifestyles, there have been increasing numbers of patients with gastric cancer who are obese. There is controversy over whether an increased rate of conversion in patients with gastric cancer with comorbid obesity who undergo LG exists. Recently, a study found that the conversion rate of patients with gastric cancer with comorbid obesity during LG was similar to that of non-obese patients [30]. However, avoiding conver-

sion in these cases requires skillful manipulations and extensive accumulation of experience by the surgeon.

In this study, there were no statistical differences in long-term outcomes between both groups. This was shown by the similar tumor recurrence rates, 5-year OS and 5-year DFS. In addition, on multivariate analysis, the T, N, and differentiation grade of tumors were independent predictors of prognosis and conversion to open gastrectomy did not affect the patient prognosis. A previous study had found that the prognosis of patients undergoing conversion were lower than in those undergoing LG because conversion to open gastrectomy was due to tumor factors [17]. In comparing the TNM staging of both groups of patients in previous studies, the proportion of patients with stages II and III in the conversion group was higher than that of the laparoscopic group. As TNM staging is an independent predictor for prognosis [32-37], it is expected that the patients in the conversion group would have a poorer prognosis than those in the laparoscopic group in those studies.

Our study has several limitations. First, it was a nonrandomized study subject to selection bias. The decision for LG was made at the discretion of the surgeon based on experience. Second, our relatively small number of converted cases may not be sufficient to demonstrate all significant differences in clinical outcomes between the two groups. Furthermore, our study compared the long-term outcomes in patients with laparoscopic surgery and conversion, but did not compare those who were subjected to open surgery for gastric cancer. It is uncertain if the survival outcome in patients with conversion would be worse than in those who had open surgery. A further prospective trial comparing groups undergoing these three treatments is needed to elucidate these differences.

In summary, this study showed that technical factors are the main reason for conversion to open gastrectomy during LG treatment of gastric cancer. The short-term outcomes of patients undergoing conversion were poorer than those who did not undergo conversion and both groups of patients had similar long-term outcomes.

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Conflict of interests

The authors declare no conflict of interests.

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