ORIGINAL ARTICLE

Short- and long-term outcomes after conversion of laparoscopic total gastrectomy for gastric cancer: a single-center study

Minfeng Ye, Ketao Jin, Guangen Xu, Fangqin Lin, Qiuli Zhou, Kelong Tao, Feng Tao

Department of Gastrointestinal Surgery, Shaoxing People's Hospital, Shaoxing Hospital of Zhejiang University, Shaoxing, Zhejiang Province, China

Summary

Purpose: *Conversion of laparoscopic surgery for colorectal cancer has been fully studied. However, no study has investigated conversion of laparoscopic total gastrectomy for gastric cancer. We evaluated the effect of conversion to open total gastrectomy on short- and long-term outcomes among patients who underwent laparoscopic total gastrectomy for gastric cancer and identified factors predictive of survival.*

Methods: *A prospective database of consecutive laparoscopic total gastrectomies for gastric cancer was reviewed. Patients who required conversion (converted group) were compared with those who had completed laparoscopic total gastrectomy (completed group). Kaplan–Meier method was used to compare and analyze survival. Univariate and multivariate analyses were performed to identify predictors of poor survival.*

Results: *The conversion rate was 17.4%, and the most common reason for conversion was a locally advanced tu-*

mor. Conversion was associated with significantly longer operative time and greater blood loss. No differences were observed in terms of postoperative morbidity or mortality between the converted and completed patients. The converted group had significantly worse 5-year overall survival (OS) and disease-free survival (DFS). Univariate analysis showed that conversion to open total gastrectomy, pathological (p) T4 disease, and pathological N2-N3 disease were significant risk factors for OS and DFS. In multivariate analysis, pT4 cancer was the only independent predictor of DFS and OS.

Conclusion: *Conversion to open total gastrectomy per se was not associated with worse short-term outcomes or worse long-term survival.*

Key words: *conversion, gastric carcinoma, laparoscopy-assisted surgery, minimally invasive surgery, total gastrectomy*

Introduction

Laparoscopic operations for malignant diseases must have proven equivalence to established conventional procedures in terms of surgical morbidity, practiced oncological surgical standards (free margins, adequate number of harvested nodes), and long-term survival outcome (OS and DFS rates) [1-7]. Several studies have suggested that laparoscopic total gastrectomy for gastric cancer is safe and gives oncological outcomes similar to those for open total gastrectomy [8-14]. Compared with open total gastrectomy, laparoscopic total gastrectomy has been associat-

ed with better short-term outcomes in terms of blood loss, hospital length of stay, return to normal bowel function, and better cosmesis results [8-23]. However, there is concern that patients with operations begun laparoscopically and then converted not only will have worse early perioperative outcomes but also worse long-term survival outcomes than will patients who undergo completed laparoscopic total gastrectomy.

Laparoscopic total gastrectomy is a challenging operation and has a slow learning curve. Consequently, conversion rates of ≤30% have been

reported in the literature [8-23], which shows that this group of patients is clinically relevant. If the results after converted laparoscopic total gastrectomy are indeed significantly worse than after the completed procedure, then surgeons must focus on reducing the conversion rate, either by more adequate patient selection or by improvement of the surgical technique.

To the best of our knowledge, no study has investigated outcomes after conversion of laparoscopic gastrectomy for gastric cancer. The current study compared the short- and long-term outcomes of patients requiring conversion with those patients who had completed laparoscopic total gastrectomy and identified factors predictive of OS and DFS.

Methods

This retrospective study complied with the Declaration of Helsinki rules and was approved by the local ethics committee. The need for informed consent from all patients was waived because of its retrospective nature.

This research was a retrospective analysis of a prospectively collected database. Consecutive patients with gastric cancer referred for surgical management at our institution between January 2009 and December 2015 and treated by laparoscopic total gastrectomy were identified. The exclusion criteria were preoperative diagnosis of liver or lung metastases or peritoneal carcinomatosis, invasion of adjacent organs evident preoperatively, acute perforation at diagnosis, and history of upper abdominal surgery.

All procedures were performed by two surgeons who had extensive experience in gastric and laparoscopic advanced surgery, and the same oncological principles were followed in all procedures.

All patients were diagnosed with gastric cancer by upper gastrointestinal endoscopy and biopsy. Furthermore, all patients were evaluated by endoscopic ultrasonography, brain, chest, and abdominal computed tomography (CT), and abdominal ultrasonography. Positron emission tomography-CT (PET-CT) and bone scanning were performed in selected cases. Clinical (c) stage T1-3N0-1M0 gastric carcinoma patients were selected as candidates for laparoscopic total gastrectomy. The tumor stage of gastric cancer was based on the seventh edition of the TNM classification of gastric carcinoma [24-26].

Conversion to open total surgery was defined as an unplanned incision or an incision made larger or earlier than planned. The short-term outcomes, including surgical outcomes, morbidity according to the Clavien–Dindo classification, overall and 30-day mortality, and length of postoperative hospital stay, were reviewed. Major complications were classified as grades 3, 4, and 5, whereas minor complications were classified as grades 1 and 2 [27-29].

Adjuvant chemotherapy was administered routinely to stage II and III gastric cancer patients with good performance status [30]. Patients were seen in the outpatient department every 3 months for the first postoperative year, every 4-5 months for the next 2 years, and then annually. Tumor recurrence was diagnosed by history, physical examination, endoscopic evaluation, radiological investigations, or pathological analysis when available. Recurrence was classified as locoregional recurrence, distant metastasis, and mixed. Locoregional disease was defined as recurrence with peritoneal seeding, or within the regional lymph nodes or the anastomosis. Distant disease included metastasis at distant organ sites (e.g., brain, lung, liver, bone, ovary, adrenal gland, distant lymph nodes, or other organs). The long-term oncological outcomes included the recurrence rate, OS, and DFS. The follow-up was closed in May 2016.

Statistics

All the statistical analyses were performed using SPSS, Version 14.0 (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 test, as appropriate. Survival rates were analyzed by the Kaplan–Meier method, and differences between the two groups were analyzed by the 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 ≤ 0.1 were included in the multivariate analysis. The results are reported as hazard ratios with 95% confidence intervals. A level of 5% was set as the criterion for statistical significance.

Results

Between January 2009 and December 2015, 219 patients with cT1-3N0-1M0 gastric cancer underwent laparoscopic total gastrectomy. Whereas 181 procedures (82.6%) were completed laparoscopically (complete group), 38 (17.4%) patients required conversion to open surgery.

The characteristics of the patients are listed in Table 1. No differences in age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and tumor site in gastric cancer patients were observed between the two groups.

Among the 38 conversions to open total gas-

Table 1. Baseline characteristics of the two groups

Characteristics	Completed group (N=181)	Converted group (N=38)	p value
Age, years, median (range)	58 (39-76)	62 (41-71)	0.199
Gender (N)			0.977
Male	110	23	
Female	71	15	
BMI, kg/m^2, median (range)	21 (19-26)	22 (18-29)	0.088
Clinical TNM stage (N)			0.367
IB	16	3	
IIA	71	12	
IIB	94	23	
Location of the primary tumor (N)			0.637
Upper	79	15	
Middle	102	23	
ASA score (N)			0.318
I	155	30	
II	21	7	
III	5	1	

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

Table 2. Surgical outcomes of the two groups

Outcomes	Completed group (N=181)	Converted group (N=38)	p value
Reasons for conversion	-		-
Tumor related, N		24	
Non–tumor related, N		14	
Adhesions, N		4	
Obesity, N		3	
Unclear anatomy, N		5	
Bleeding, N		2	
Operative time (min), median (range)	190 (160–260)	210 (180–280)	0.024
Estimated blood loss (ml), median (range)	240 (170–550)	320 (200–600)	0.010
Blood transfusion	6	5	0.034
Hospital stay after surgery (days), median (range)	10 (6-27)	14 (8-35)	0.014
Patients with complications, N	34	8	0.747
Patients with major complications, N	7	2	1.000
Highest grade of complications, N			
1	15	4	0.898
2	12	2	1.000
3	6	2	0.915
4	1	0	-
5	0	0	-

Table 3. Conversion and locally advanced tumor rates over time

Number of cases	1-60	61-120	121-180	181-219
Conversion (%)	19	16	17	20
Locally advanced tumor (%)	92	87	85	92

trectomy, 24 (63.2%) were because of locally advanced cancer, whereas 14 (36.8%) were because of non–tumor related reasons (Table 2). The conversion rate did not change significantly over time, as shown in Table 3.

Overall, the median surgical time decreased significantly after the first 60 patients, from 210 min (range 180–280) to 180 min (range 160–270) (p=0.041). The median operative time was 220 min (range 200–280) in the converted group and

Table 4. Pathological outcomes of the two groups

| Outcomes	Completed group (N=181)	Converted group (N=38)	p value
Pathological T stage, N			
T_1	11	3	0.959
T_2	54	11	0.913
T_3	79	6	0.001
T_4	37	18	0.001
Pathological N stage, N			
N_0	68	13	0.697
N_1	66	17	0.339
N_2	39	6	0.425
N_3	8	2	1.000
Retrieved lymph nodes, N (range)	17 (16-25)	18 (17-29)	0.103
Pathological TNM stage, N			
I	13	6	0.163
II	132	14	0.016
III	36	18	0.000
Residual tumor, N			
R0	174	36	1.000
R1	7	2	1.000
R2	0	0	-

Table 5. Comparison of cancer recurrence data of the two groups

Outcomes	Completed group (N=181)	Converted group (N=38)	p value
Tumor recurrence, N	45	16	0.031
Locoregional recurrence	21	9	0.049
Distant metastasis	19	6	0.514
Mixed	5	1	1.000
Time to first recurrence, median, months (range)	20 (5-44)	18 (11-45)	0.254

190 min (range 160–260) in the completed group (p=0.024). The median estimated blood loss was 320 ml (range 200–600) in the converted group and 240 ml (range 170–550) in the completed group (p=0.010). A significantly higher rate of blood transfusions was observed in the converted group (13.2 vs 3.3%; p=0.034). No differences in the overall rate and severity of the postoperative 30-day morbidity were observed between the converted and completed groups (Table 2). The median postoperative hospital stay was longer in the converted group than in the completed group (14 vs 10 days; p=0.014).

The number of harvested lymph nodes and positive margin rates did not differ between the two groups (Table 4). R2 tumor was not detected at the specimens.

Significantly higher rates of pT4 (p=0.001) were reported in the converted group than in the completed group. Overall, stage III disease was more frequently observed among the converted patients (p=0.000). A total of 28 (73.7%) converted
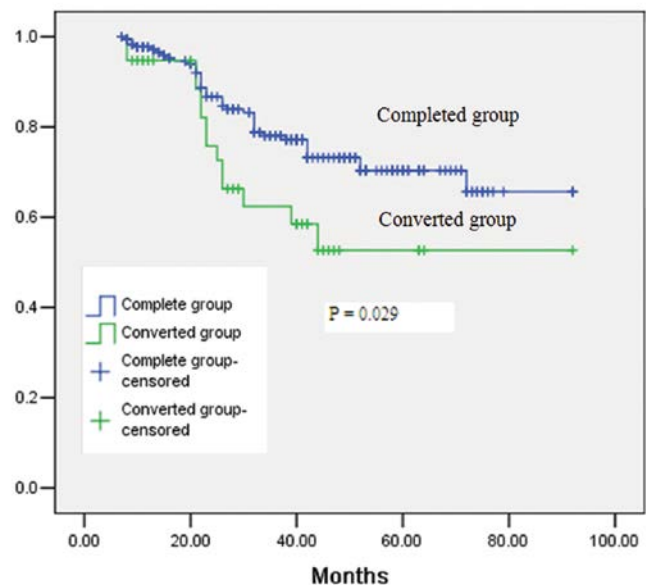
Figure 1. Overall survival of the two groups.

patients and 126 completed patients (69.6%) received adjuvant chemotherapy (p=0.618).
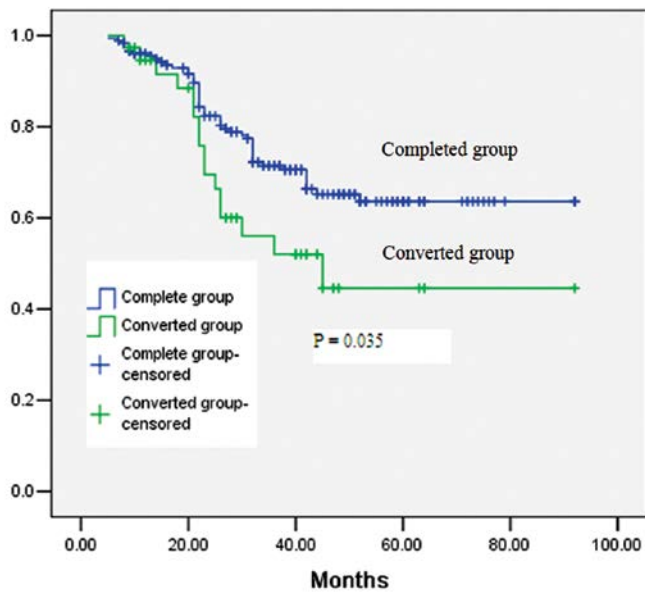
Figure 2. Disease-free survival of the two groups.

The median follow-up period was 37 months in the converted group and 42 months in the completed group. Tumor recurrence occurred more frequently in the converted group (42.1 vs 24.9%; p=0.031). The median time until the first disease recurrence did not differ between the two groups (p=0.254). Both the 5-year OS (p=0.029) and DFS (p=0.035) rates were significantly lower for the converted patients than in the completed patients (Figures 1 and 2). No significant differences were observed in a stage-by-stage comparison between the two groups (Table 6).

The univariate analysis showed that conversion to open total gastrectomy, p T4 cancer, and p N2-N3 disease were significant risk factors for OS and DFS (Tables 7 and 8). In the multivariate analysis, pT4 cancer was the only independent predictor of OS and DFS (Tables 5 and 6).

Discussion

The feasibility and safety of laparoscopic total gastrectomy for cancer has been demonstrated in several studies [8-15]. However, laparoscopic total gastrectomy is a technically demanding procedure [8-23]. Many factors associated with conversion to open total gastrectomy have been reported [8-23] and include patient-specific factors and disease-specific factors.

We observed a 17.4% conversion rate in this series of 219 patients who underwent laparoscopic total gastrectomy for gastric cancer, which was similar to previously reported rates [8-23]. We found that a locally advanced tumor was the most common reason for conversion to open total gastrectomy, followed by bleeding and adhesions, findings that were consistent with those previously reported in the literature [8-23].

Currently, we consider a preoperatively suspected T4 gastric cancer to be a contraindication to laparoscopic gastrectomy [31-34]. However, 55 patients in our series had a postoperative diagnosis of pT4 cancer, which reflected that CT scan sensitivity for the preoperative diagnosis of T4 gastric cancer was suboptimal.

Some studies have investigated the learning curve in laparoscopic total gastrectomy for gastric cancer and observed trends in operative times and conversion rates that depended on the surgeon's experience [9,10,35]. A study performed in Seoul National University Bundang Hospital showed a significantly lower conversion rate for general surgeons with experience of >75 laparoscopic resections than for surgeons who had performed <75 such procedures [9]. In contrast, other studies and the current series did not show significant differences in terms of conversion rate according to the surgeon's experience [10,35].

To the best of our knowledge, this is the first study with a focus on conversion of patients who underwent laparoscopic total gastrectomy for gastric cancer. We demonstrated a significant decrease in the operative time after the first 60 cases, but no significant differences in the conversion rates were observed over time. This may be relat-

Table 6. Five-year survival data of the two groups

Survival	Complete group (N=181)	Converted group (N=38)	p value
Overall survival			
Pathological stage			
I	86	81	0.210
II	59	54	0.194
III	40	37	0.540
Disease-free survival			
Pathological stage			
I	71	72	0.120
II	51	46	0.540
III	32	28	0.199

Table 7. 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				
≥65	1.00	0.368		
<65	1.57 (0.45-1.98)			
Gender				
Male	1.00	0.510		
Female	1.20 (0.74-1.58)			
Location of the primary tumor				
Upper	1.00	0.697		
Middle	1.14 (0.44-1.36)			
ASA score				
I-II	1.00	0.448		
III	1.08 (0.55-1.25)			
Conversion to open total gastrectomy				
No				
Yes	1.00	0.041	1.00	0.540
	1.87 (1.06-2.32)		1.21 (1.09-1.58)	
Pathological T stage				
T1-T3	1.00	0.002	1.00	0.009
T4	3.55 (2.98-5.84)		3.99 (2.59-6.59)	
Pathological N stage				
N0-N1	1.00	0.041	1.00	0.302
N2-N3	1.88 (0.84-2.39)		1.25 (0.65-3.98)	
Adjuvant chemotherapy				
No	1.00	0.123		
Yes	1.65 (0.87-1.99)			

Table 8. 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				
≥65	1.00	0.159		
<65	1.25 (0.66-1.36)			
Gender				
Male	1.00	0.125		
Female	1.45 (0.54-1.88)			
Location of the primary tumor				
Upper	1.00	0.178		
Middle	1.12 (0.54-1.45)			
ASA score				
I-II	1.00	0.208		
III	1.11 (0.68-1.39)			
Conversion to open total gastrectomy				
No				
Yes	1.00	0.036	1.00	0.198
	1.98 (1.25-2.77)		1.44 (1.22-2.88)	
Pathological T stage				
T1-T3	1.00	0.008	1.00	0.000
T4	2.88 (1.80-3.44)		2.54 (2.01-3.76)	
Pathological N stage				
N0-N1	1.00	0.070	1.00	0.208
N2-N3	1.38 (0.70-2.59)		1.12 (0.54-2.09)	
Adjuvant chemotherapy				
No	1.00	0.400		
Yes	1.24 (0.73-1.48)			

ed to the fact that in our experience, the learning curve is reflected in the operative time required to complete the procedure, whereas the selection criteria for laparoscopic total gastrectomy did not change during the study period.

In our series, we observed a significantly

higher rate of blood transfusion in the converted group than in the completed group. However, there were no statistically significant differences in overall and severity of postoperative morbidity between the converted and completed groups. The hospital stay was prolonged in the converted group, a finding that was consistent with results reported in the literature.

We analyzed patients over a median follow-up period of 38 months after laparoscopic gastrectomy. The median time until first recurrence did not differ between the two groups. Both OS and DFS were significantly lower for the converted patients. However, in the multivariate analysis, pT4a cancer was the only independent predictor of DFS and OS. In particular, both the 5-year OS and 5-year DFS were significantly poorer for the pT4 patients than for the pT1–pT3 patients.

We believe that the good results obtained in our series of converted patients are associated with our attitude of considering early conversion for locally advanced gastric malignancies. This surgical strategy avoids excessive tumor handling or incorrect oncological dissection by the laparoscopic approach and thus reduces the risk of tumor cell spillage and potentially adverse oncological outcomes.

Recently, a retrospective study from Eulji General Hospital (Seoul, Korea) has specifically investigated the oncological outcomes in T4 gastric cancer patients after laparoscopic gastrectomy and concluded that, compared with the open approach, the laparoscopic approach to T4 gastric cancer was safe and did not adversely affect the oncological outcomes [36]. However, large-scale randomized controlled trials are needed to confirm the conclusions of these studies.

This study has limitations, including its non-randomized design, retrospective nature, and the small sample size of the conversion group, which may have led to an unpowered conclusion. However, the effect of conversion on short- and long-term outcomes has rarely been analyzed, and we believe that the study is valuable even though the sample size was not sufficiently large. At the least, the study demonstrated that conversion was not an independent risk factor of poor survival in our institution. Furthermore, we will continue to follow these patients and will enlarge the database over the next 5 years. Therefore, a large-scale, multicenter, randomized controlled trial should be conducted in the future.

In conclusion, despite the limitations of this retrospective study, the results showed that locally advanced cancer is the primary reason for conversion to open total gastrectomy and that pT4 cancer was independently associated with poor survival. Conversion *per se* did not adversely affect short- or long-term survival outcomes in patients with gastric cancer.

Acknowledgements

Conflict of interests

The authors declare no confict of interests.

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