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ORIGINAL ARTICLE

# Outcome of laparoscopic total gastrectomy for gastric carcinoma

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## Summary

***Purpose:*** *Minimally invasive gastrectomy for gastric carcinoma is gaining widespread acceptance. However, data are still lacking on the feasibility, long- and short-term outcomes of laparoscopic total gastrectomy. The purpose of the study was to evaluate the feasibility, safety and long-term results of laparoscopic total gastrectomy.*

***Methods:*** *Between January 2008 and January 2013, 74 patients with gastric carcinoma who had been subjected to laparoscopic total gastrectomy were evaluated. Each patient was matched to one patient undergoing open total gastrectomy for age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) grade and clinical TNM stage. Surgical and long-term survival outcomes were evaluated.*

***Results:*** *No differences in baseline data, pathological data and incidence of postoperative 30-day complications were found between the two groups. The blood loss and postoperative hospital stay for the laparoscopy group was significantly shorter than for the open group. In long-term results, no difference was found in overall survival rate (p=0.257) and disease-free survival rate (p=0.207) between the two groups. When patients were analyzed according to the pathological TNM stage, the 5-year overall survival rates and disease-free survival rates were not different.*

***Conclusion:*** *Laparoscopic total gastrectomy for gastric carcinoma is feasible and results in comparable oncologic outcomes as in open total gastrectomy.*

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

## Introduction

Gastric carcinoma is the second most common cancer in China. About 95% of gastric carcinoma patients have advanced-stage disease when diagnosed [1-3]. Radical gastrectomy with D2 lymphadenectomy is regarded as a standard treatment that offers a chance of cure for patients with operable gastric carcinoma [4-6]. Gastrectomy has been established as a safer operative procedure than before because of technical refinements, advances in diagnostic methods, and improvement in postoperative patient care [4-7].

The development of minimally invasive surgery during the past two decades has had a substantial effect on surgical practice around the world [8,9]. Laparoscopic distal gastrectomy has been widely accepted for early gastric carcinoma in Eastern Asia countries [10]. The advantages of laparoscopic gastric resection are those of minimally invasive surgery in general, such as early recovery, shorter hospital stay, and better cosmet-

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ic outcome [10]. The postoperative course after laparoscopic gastrectomy may also be improved because the abdominal wall is preserved.

Currently, the laparoscopic approach is used mainly for distal gastrectomy. Laparoscopic total gastrectomy is still a matter of debate because of the uncertain long-term results and the fear of compromising the oncologic resection. Available data about laparoscopic total gastrectomy for gastric carcinoma and published data from the follow-up evaluation in the literature are still limited.

The aim of the present study was to study the feasibility, safety, and long-term results of laparoscopic total gastrectomy.

## Methods

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

Seventy four patients who had undergone a laparoscopic total gastrectomy for gastric carcinoma were identified during the period from January 2008 to January 2013. Each patient was matched to one patient who had undergone open total gastrectomy according to age, sex, BMI, ASA score and clinical TNM stage. All resections were performed by a specialist general surgeon (X.L) at a University teaching centre.

Upon diagnosis of gastric carcinoma, all patients were staged with upper gastrointestinal endoscopy, endoscopic ultrasonography, computed tomographic scans of the brain, chest, and abdomen. If necessary, positron emission tomography-computerized tomography (PET-CT), staging laparoscopy and bone scanning were employed [11]. The stage of gastric cancer was based on the 7th edition of the TNM classification of gastric cancer, which was proposed by Union International Contre le Cancer, Japanese Gastric Cancer Association (JGCA) and American Joint Committee on Cancer (AJCC) [12]. For patients operated before 2010, their staging was recalculated to match the latest TNM edition by UICC, JGCA and AJCC.

The indication for laparoscopic total gastrectomy was tumor located in the upper or middle third of the stomach, clinical stage T1-3N0-1M0 disease without multivisceral resection. The technique employed for laparoscopic total gastrectomy has been described previously [13].

Patient demographics, including gender, age at resection, BMI, ASA score and clinical TNM stage were recorded. Short-term outcomes included operative time, blood loss, conversion rate, postoperative 30-day complication rate, severity of complications based on Clavien–Dindo classification and length of postoperative stay. Major complications were defined as grades 3, 4 and 5. Minor complications were classified as 1 and 2 [14-17]. Histological analysis of resected specimens was also assessed, including pathological stage, subtypes, harvested lymph nodes and surgical margin [18].

After resection, patients were followed every 3 months in the first 2 years and then at 4-month intervals for the next 3-5 years. Overall survival was calculated from the day of gastrectomy until the day of death or last contact. Disease-free survival of patients who recurred was defined as the time from the day of surgery to the day of imaging study that confirmed tumor recurrence. For patients who did not develop tumor recurrence, the day of gastrectomy by laparoscopy or open approach to the day of death or last contact was used. The patient follow-up ended in April 2015.

*Statistics*

All the statistical analyses were performed using SPSS software 14.0 (SPSS Inc., Chicago, Ill, USA). For variables following normal distribution, data were presented as mean and standard deviations and were analyzed by Student's t-test. For variables following non-normal distribution, data were expressed as median and range and were compared by Mann–Whitney U test. Differences of semiquantitative results were analyzed by Mann–Whitney *U* test. Differences of qualitative results were analyzed by chi-square test or Fisher's exact test where appropriate. Survival rates were analyzed using the Kaplan-Meier method and differences were analyzed with the log-rank test. Univariate analyses were performed to identify prognostic variables related to overall survival and disease-free survival. Univariate variables with probability values $<0.05$ were selected for inclusion in the multivariate Cox proportional hazard regression model. Adjusted hazard ratios (HR) along with the corresponding 95% confidence intervals (CI) were calculated. $p< 0.05$ was considered as statistically significant.

## Results

The two patient groups were comparable in terms of age, sex, BMI, ASA score, comorbidity and clinical TNM stage (Table 1).

Table 2 presents the characteristics of tumor in the two groups. There was no difference in the rate of R0 resection, harvested lymph nodes, pathological stage and histological subtypes between the two groups. There was one involved resection margin in each group; the difference was not statistically significant.

The surgical outcomes are shown in Table 3. Two patients were converted to open resection in the laparoscopy group. All of these two cases occurred in the first 2 years and there were no conversions later. These two cases were converted as a result of uncontrolled bleeding. There was no

**Table 1.** Patient characteristics

| *Characteristics* | *Laparoscopy (N=74) N (%)* | *Open (N=74) N (%)* | *p value* |
|---|---|---|---|
| Age (years), median (range) | 62 (38-76) | 60 (42-72) | 0.205 |
| Sex | | | 0.592 |
| Male | 53 (71.6) | 50 (67.6) | |
| Female | 21 (28.4) | 24 (32.4) | |
| BMI (kg/m²), median (range) | 19 (16-25) | 21 (18-29) | 0.410 |
| Clinical TNM stage (7th AJCC-UICC-JGCA) | | | 0.934 |
| IA | 2 (2.7) | 2 (2.7) | |
| IB | 12 (16.2) | 10 (13.5) | |
| IIA | 28 (37.8) | 32 (43.2) | |
| IIB | 32 (43.2) | 30 (40.5) | |
| ASA grade | | | 0.299 |
| I | 57 (77.0) | 62 (83.8) | |
| II | 11 (14.9) | 8 (10.8) | |
| III | 6 (8.1) | 4 (5.4) | |
| Comorbidities | | | 0.895 |
| Liver cirrhosis | 2 (2.7) | 1 (1.4) | |
| Hypertension | 7 (9.5) | 4 (5.4) | |
| Diabetes mellitus | 5 (6.8) | 4 (5.4) | |
| Renal failure | 1 (1.4) | 2 (2.7) | |
| Stable angina | 2 (2.7) | 1 (1.4) | |

**Table 2.** Tumor characteristics

| *Characteristics* | *Laparoscopy (N=74) N (%)* | *Open (N=74) N (%)* | *p value* |
|---|---|---|---|
| Histological type | | | 0.587 |
| Differentiated | 51 (68.9) | 54 (73.0) | |
| Undifferentiated | 23 (31.1) | 20 (27.0) | |
| Retrieved lymph nodes, median (range) | 18 (17-23) | 19 (16-29) | 0.140 |
| Pathological TNM stage (7th AJCC-UICC-JGCA) | | | 0.867 |
| IB | 6 (8.1) | 5 (6.8) | |
| IIA | 24 (32.4) | 23 (31.1) | |
| IIB | 29 (39.2) | 32 (43.2) | |
| IIIA | 6 (8.1) | 5 (6.8) | |
| IIIB | 4 (5.4) | 6 (8.1) | |
| IIIC | 5 (6.8) | 3 (4.1) | |
| Residual tumor (R0/R1/R2) | 71/3/0 | 72/2/0 | 0.650 |

30-day mortality in both groups. There was no difference in the postoperative 30-day complications and the severity of postoperative 30-day complications. The operation time was significantly longer, whereas the blood loss and postoperative hospital stay were significantly shorter in the laparoscopy group.

Overall tumor recurrence after primary surgery occurred at a median of 20 months in the laparoscopy group and 16 months in the open group (p=0.332) (Table 4). The pattern of tumor recurrence was similar. The 5-year disease-free survival was not different between the groups (Figure 1, p=0.207). When patients were analyzed according to the disease stage, the 5-year disease-free survival rates were not different (Table 5).

The 5-year overall survival was not different between the groups (Figure 2, p=0.257). When patients were analyzed according to the disease stage, the 5-year overall survival rates were not different (Table 6).

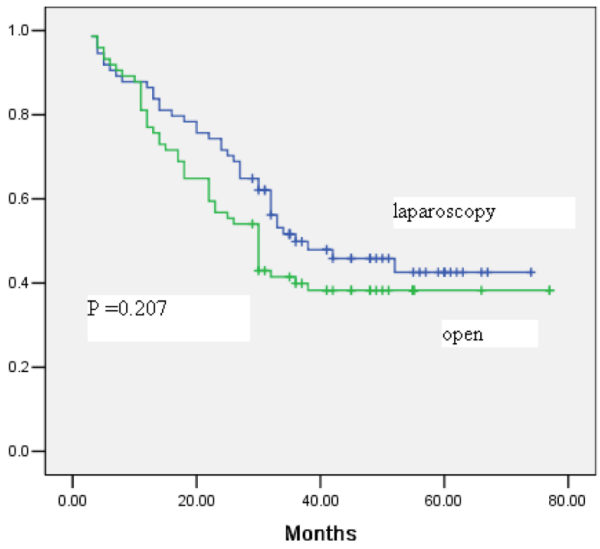


**Figure 1.** Comparison of disease-free survival rate between laparoscopy and open groups.

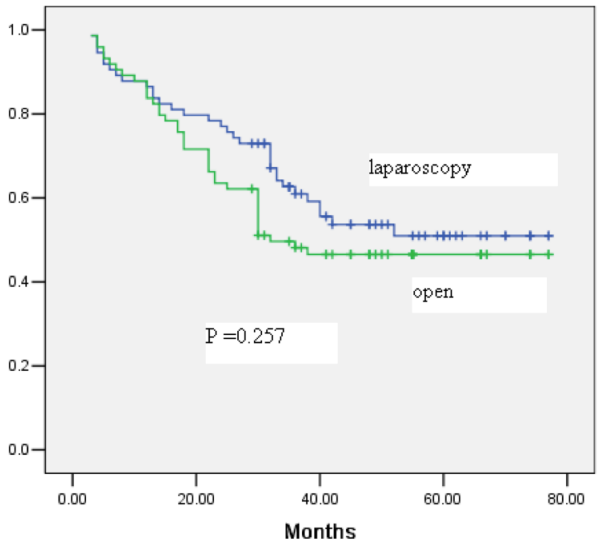


**Figure 2.** Comparison of overall survival rate between laparoscopy and open groups.

**Table 3.** Surgical outcomes

| *Outcomes* | *Laparoscopy (N=74) N (%)* | *Open (N=74) N (%)* | *p value* |
|---|---|---|---|
| Postoperative 30-day morbidity | 10 (13.5) | 14 (19.0) | 0.372 |
| Anastomosis leakage | 3 (4.1) | 5 (6.8) | |
| Intra-abdominal bleeding | 2 (2.7) | 2 (2.7) | |
| Intra-abdominal abscess | 1 (1.4) | 2 (2.7) | |
| Pancreatic fistula | 2 (2.7) | 3 (4.1) | |
| Ileus | 1 (1.4) | 1 (1.4) | |
| Pneumonia | 1 (1.4) | 1 (1.4) | |
| Atelectasis | 1 (1.4) | 1 (1.4) | |
| Major complications | 2 (2.7) | 3 (4.1) | 1.000 |
| Minor complications | 8 (10.8) | 11 (14.9) | 0.020 |
| Operative time (min), median (range) | 230 (200-300) | 180 (160-250) | |
| Estimated blood loss (ml), median (range) | 260 (180-400) | 310 (200-550) | 0.002 |
| Hospital stay (days), median (range) | 7 (4-20) | 11 (8-25) | 0.020 |

**Table 4.** Disease recurrences

| *Recurrences* | *Laparoscopy (N=74) N (%)* | *Open (N=74) N (%)* | *p value* |
|---|---|---|---|
| Overall recurrence | 37 (50.0) | 43 (58.1) | 0.322 |
| Locoregional | 23 (31.1) | 26 (35.1) | 0.600 |
| Peritoneal seeding | 12 (16.2) | 11 (14.9) | |
| Anastomosis | 8 (10.8) | 10 (13.5) | |
| Lymph nodes | 3 (4.1) | 5 (6.8) | |
| Metastasis | 14 (19.0) | 15 (20.2) | 0.836 |
| Adrenals | 3 (4.1) | 3 (4.1) | |
| Liver | 5 (6.8) | 7 (9.5) | |
| Lung | 3 (4.1) | 1 (1.4) | |
| Bone | 2 (2.7) | 2 (2.7) | |
| Ovary | 1 (1.4) | 2 (2.7) | |
| Time to recurrence, months (median) | 20 | 16 | 0.399 |

**Table 5.** Five-year disease-free survival following laparoscopic and open gastrectomy with regard to pathological stage

| Pathological stage | Laparoscopy (%) | Open (%) | *p* value |
|---|---|---|---|
| I | 66 | 65 | 0.562 |
| II | 54 | 49 | 0.650 |
| III | 31 | 25 | 0.189 |

**Table 6.** Five-year overall survival following laparoscopic and open gastrectomy with regard to pathological stage

| Pathological stage | Laparoscopy (%) | Open (%) | *p* value |
|---|---|---|---|
| I | 75 | 74 | 0.856 |
| II | 68 | 70 | 0.200 |
| III | 42 | 38 | 0.132 |

## Discussion

The aim of this study was to compare the short- and long-term outcomes of patients who underwent laparoscopic total gastrectomy to those who underwent total gastrectomy for gastric carcinoma. In two well-matched groups of patients, laparoscopic total gastrectomy for gastric carcinoma was associated with oncological outcomes similar to those of open total gastrectomy at follow-up. The short-term benefits of laparoscopic surgery in terms of less blood loss and faster recovery are well recognized [19], and this study demonstrated that laparoscopic total gastrectomy was associated with better surgical outcomes and in keeping with the reported data.

The completeness of D2 lymphadenectomy has been shown to be associated with long-term oncologic outcomes [20]. Nevertheless, laparoscopic total gastrectomy with D2 lymphadenectomy is still considered a technically demanding procedure. Laparoscopic total gastrectomy requires more time for training and has a steeper learning curve compared with distal gastrectomy. Our study had low conversion rate in the laparoscopy group and this may be explained by the lower BMI in our series [21].

Positive surgical margin, which has been reported to be associated with local recurrence [20], can be used as an indicator of the completeness of gastrectomy. The rate of R1 or R2 resection in the laparoscopic resection group have been reported to range from 0 to 3% due to sample size [22-24], similar to the rates reported in the open resection. In our series, the rate of positive surgical margin did not differ between the two groups. Furthermore, when analyzed separately, no differences in terms of distance to the resection margin were found (data not shown).

With respect to the number of harvested lymph nodes, there was no difference between the two groups. Our results indicated extensive resection in both groups, with the number of lymph

nodes harvested equaling or exceeding the numbers reported in previous studies [22-24]. The postoperative 30-day complications were not different between the open and laparoscopy groups in our study.

Currently, long-term survival analysis of laparoscopic total gastrectomy for gastric carcinoma is lacking. Overall, the 5-year survival rate ranges between 40 and 60% in previous reports [22-25]. No published study stratified the gastric carcinoma into actual TNM stages. To the best of our knowledge, this study is the first report to comment on the long-term survival of patients with gastric carcinoma in reference to the TNM stage of disease. In this report, no overall survival or disease-free survival difference was found between patients with TNM stage, and the two treatment approaches (open and laparoscopic) resulted in similar survival results.

The major drawback of this study is that the patients were not randomized into the treatment arms. Although matched pair analysis is a useful method for decreasing selection bias between groups, there are still inevitable selection biases from unmatched variables. In addition, our population had longer duration of hospital stay than those reported in other series [26-28]. The longer stay may be related to the different socioeconomic health systems.

In summary, laparoscopic total gastrectomy for gastric carcinoma resulted in a better short-term outcome than open total gastrectomy. Furthermore, the long-term outcome in the laparoscopic total gastrectomy group was similar to that in the open total gastrectomy group. Therefore, laparoscopic total gastrectomy can be considered a new alternative for treating patients with gastric cancer.

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## Conflict of interests

The authors declare no confict of interests.

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