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ORIGINAL ARTICLE

A propensity score-matching analysis comparing the oncological outcomes of laparoscopic and open gastrectomy in patients with gastric carcinoma

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Summary

Purpose: *To compare the oncological outcomes of patients with laparoscopy-assisted gastrectomy with those with open resection to remove nonmetastatic gastric cancer.*

Methods: *A total of 532 patients were initially enrolled. Propensity score matching was applied to assemble a study cohort. The primary objective was overall survival (OS). Cancer-specific survival (CSS) and disease-free survival (DFS) were secondary objectives.*

Results: *A total of 388 patients were matched for analysis. The morbidity, number of lymph nodes harvested and surgical margins were similar between the two groups. OS following laparoscopic gastrectomy was similar to open resection. Neither CSS nor DFS following laparoscopic gastrectomy was inferior compared with open resection*

Conclusion: *Laparoscopic gastrectomy for gastric cancer is feasible and safe with acceptable oncological outcomes. Further prospective multicenter trials are warranted before incorporating laparoscopic gastrectomy into routine surgical practice.*

Key words: *gastric carcinoma, laparoscopic gastrectomy, minimally invasive surgery, survival*

Introduction

Gastric cancer is one of the most common malignancies in Eastern Asian countries [1,2]. Radical gastrectomy allows for sufficient resection margins, and complete lymphadenectomy is the gold standard of surgical approach. Although gastric cancer is traditionally excised through large abdominal incisions [3-8], the first report of a laparoscopic gastrectomy was published in 1994 [9]. Since that publication, several studies have reported on the association of laparoscopic gastrectomy with improved convalescence and decreased morbidity compared to open gastrectomy [10-13]. Currently, the laparoscopic approach plays an important role in elective gastric operations. However, most of these reports involved observational studies without control groups, and the few prospective randomized clinical trials had only short-term follow-up periods or had relatively small sample sizes [14-16]. Furthermore, some disadvantages of laparoscopic gastrectomy have been described, including a high conversion rate and a trend toward lesser number of dissected lymph nodes [10-16].

The aim of the present study was to compare the oncological outcomes of laparoscopic gastrectomy with those of open resection for gastric

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carcinoma. In such retrospective studies, patient characteristics might significantly differ between two different cohorts because of the confounding of technique choices by observable factors. Therefore, the appropriate matching of patients to cohorts could lead to a better understanding of the true significance of the outcomes. Propensity score analysis can be used to control such confounding factors. This method was used here to compare the oncologic outcomes for a consecutive series of patients who underwent laparoscopic gastrectomy or open resection.

Methods

Patients

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

In this study, 532 patients with clinical stage T1-3N0M0 gastric cancer who underwent primary radical gastrectomy between January 2008 and January 2015 at the Department of General Surgery, Hainan Provincial People's Hospital, were initially enrolled. Hainan Provincial People's Hospital is a tertiary care center in the city of Haikou and covers an urban area of approximately 5,000,000 people. Patients who underwent conversion to open resection were excluded. Also, those who underwent multivisceral resection were not included. Finally, those undergoing laparoscopic and open gastrectomies were matched using a propensity score matching method.

Surgical techniques

Three senior surgeons with proven expertise in gastric cancer performed all laparoscopic and open gastrectomies. Patients received general anesthesia while in supine position with their legs apart. Carbon dioxide pneumoperitoneum was established at 15 mm Hg 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. The details of the laparoscopic gastrectomy (distal or total gastrectomies) and open resection have been described elsewhere [17,18].

Postoperative follow-up

The postoperative follow-up involved the use of computed tomography scans of the chest and abdomen (every 6 months), upper gastrointestinal endoscopy (every year), and routine outpatient visits. Recurrent disease was diagnosed based on clinical, laboratory, diagnostic imaging, or pathological findings when available. The last follow-up visit was in July 2015.

Data collection

Data included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, tumor location, comorbidities, and clinical TNM stage. In addition, operative procedures, surgical data, pathological findings, and perioperative complications were registered. Postoperative complications, morbidity occurring within 30 postoperative days or the hospital stay, were graded according to the Clavien–Dindo classification [19-21]. Major complications were defined as grades 3b, 4a, 4b, and 5. Minor complications were classified as 1, 2, and 3a. Gastric cancer staging was based on the 7th edition of the TNM classification of gastric cancer proposed by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) [22-25]. For those patients who underwent their operation before 2010, staging was recalculated to match the 7th TNM classification [22-25].

Endpoints

The primary outcome result was OS, while the secondary outcomes included CSS and DFS times. OS was assessed from the date of surgery until the date of the last follow up visit or death. DFS was calculated from the date of surgery until the date of disease recurrence. And CSS was assessed from the date of surgery until the date of death from gastric cancer.

Statistics

Propensity score matching was used to assemble two comparable groups. Each patient undergoing laparoscopic gastrectomy was matched to a patient undergoing open resection according to age, sex, tumor location, and clinical TNM stage.

Variables are presented as means and standard deviations for variables following normal distribution and were analyzed using the Student's *t*-test. For variables following non-normal distribution, data were expressed as medians and ranges and were compared using non-parametric tests. Differences in semi-quantitative results were analyzed using the Mann–Whitney *U* test, while those in qualitative results were analyzed using the chi-square or Fisher's exact tests. Survival rates were analyzed using the Kaplan–Meier method, and differences between the two groups were analyzed using the log-rank test. Analysis was performed using SPSS 14.0 software (SPSS Inc., Chicago, IL, USA). All statistical tests were two-sided, with the threshold of significance set at $p<0.05$.

Results

Population study

In total, 388 patients were selected for this

analysis (Table 1), with a median follow-up period of 36 months. The two groups were similar in relation to age, sex, BMI, clinical TNM stage (7th AJCC-UICC), primary tumor location, ASA score, and preoperative comorbidities (Table 1).

Short-term outcomes

The median duration of the operation was significantly longer, with a lesser estimated blood loss, number of analgesic injections, and length of postoperative hospital stay, in the laparoscopy group (Table 2). No hospital stay or 30-day deaths occurred. Although the postoperative morbidity was less frequently noted in the laparoscopy

Table 1. Demographic data for patients undergoing laparoscopic or open gastrectomy

Demographic data	*Laparoscopy (N=194) N (%)*	*Open (N=194) N (%)*	*p value*
Age, years, median (range)	59.0 (42-73)	57.5 (40-75)	0.322
Sex			0.406
Male	121 (62.4)	113 (58.2)	
Female	73 (37.6)	81 (41.8)	
BMI, kg/m^2, median (range)	20.5 (16-26)	21.0 (20-27)	0.231
Clinical TNM stage (7th AJCC-UICC)			0.924
IA	3 (1.5)	2 (1.0)	
IB	38 (19.6)	40 (20.6)	
IIA	153 (78.9)	152 (78.4)	
Location of the primary tumor			0.945
Upper	36 (18.6)	41 (21.1)	
Middle	55 (28.4)	48 (51.1)	
Lower	103 (53.1)	105 (54.1)	
ASA score			0.858
I	98 (50.5)	94 (48.5)	
II	64 (33.0)	71 (36.3)	
III	32 (34.0)	29 (14.9)	
Comorbidity			0.727
Liver cirrhosis	8 (4.1)	10 (5.2)	
Hypertension	32 (16.5)	38 (19.6)	
Diabetes mellitus	13 (6.7)	10 (5.0)	
Stable angina	9 (4.6)	7 (3.6)	

Table 2. Short-term outcomes of patients undergoing laparoscopic or open surgery

Outcome	*Laparoscopy (N=194)*	*Open (N=194)*	*p value*
Postoperative morbidity, N (%)	17 (8.7)	25 (12.8%)	0.191
Major complications, N (%)	4 (2.1)	7 (3.6)	0.749
Minor complications, N (%)	13 (6.7)	18 (9.3)	
Operative time (min), median (range)	210 (195-265)	185 (170-210)	0.000
Estimated blood loss (ml), median (range)	215 (150-230)	280 (230-430)	0.000
Number of analgesic injections, median (range)	2.0 (1-3)	4.0 (2-5)	0.000
Postoperative hospital stay (days), median (range)	9.0 (5-16)	12.0 (7-19)	0.000

Table 3. Pathological data of patients undergoing laparoscopic or open gastrectomy

Pathological data	*Laparoscopy (N=194) N (%)*	*Open (N=194) N (%)*	*p value*
Lymph nodes removed, median (range)	18.0 (16-20)	17.0 (16-22)	0.810
Margins			0.563
R0	192 (99.0)	193 (99.5)	
R1	2 (1.0)	1 (5.1)	
Pathological TNM stage (7th AJCC-UICC)			0.572
IB	21 (10.8)	23 (11.9)	
IIA	94 (48.5)	98 (50.5)	
IIB	29 (14.9)	24 (12.4)	
IIIA	16 (8.2)	18 (9.3)	
IIIB	24 (12.4)	22 (11.3)	
IIIC	10 (5.0)	9 (4.6)	

Table 4. Tumor recurrence rates following laparoscopic and open gastrectomy

Recurrence	*Laparoscopy N (%)*	*Open N (%)*	*p value*
Tumor recurrence	32 (16.5)	39 (20.1)	0.358
Recurrence site			0.960
Brain	2 (1.0)	3 (1.5)	
Liver	10 (5.0)	12 (6.2)	
Lung	3 (1.5)	4 (2.1)	
Peritoneal seeding	5 (25.8)	6 (3.1)	
Remnant stomach	3 (1.5)	6 (3.1)	
Distant lymph nodes	6 (3.1)	4 (2.1)	
Anastomosis	3 (1.5)	4 (2.1)	
Time to recurrence, median, months (range)	16 (2-67)	14 (3-70)	0.180
Treatment of recurrence			0.998
Metastasectomy	5 (25.8)	6 (3.1)	
Chemotherapy	17 (8.8)	21 (10.9)	
Supportive care	10 (5.0)	12 (6.2)	

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

Pathological stage	*Laparoscopy (%)*	*Open (%)*	*p value*
IB	86	84	0.203
IIA	80	76	0.125
IIB	69	64	0.324
IIIA	46	48	0.253
IIIB	39	37	0.700
IIIC	21	23	0.289

group, the difference did not reach statistical significance. Pathological data did not differ between the two groups with respect to the excised lymph nodes, surgical margins, and pathological TNM stage (7th AJCC-UICC) (Table 3).

Long-term outcomes

Recurrent tumors developed in 16.5% of the patients in the laparoscopy group and in 20.1% of the patients in the open group. There were no significant differences with respect to the sites of recurrence (Table 4).

There was no difference in OS between the laparoscopy and open groups (Figure 1, p=0.206). The 5-year OS was 60% in the laparoscopy group and 55% in the open group. There were no significant differences in OS with regard to the pathological TNM stage between the laparoscopy and open groups (Table 5). The OS results were stratified according to the pathological TNM stage and were comparable to historical data (Table 6).

The CSS (Figure 2, p=0.374) and DFS (Figure 3, p=0.093) were almost identical in both groups.

Discussion

This study was designed to compare the long-term outcomes after laparoscopic and open gastrectomy in patients with gastric cancer and showed that for any stage of cancer, the 5-year outcomes were similar in the laparoscopy and open groups. Consistent with previous series [28-31], laparoscopic gastrectomy was associated with less morbidity and blood loss as well as a more rapid convalescence.

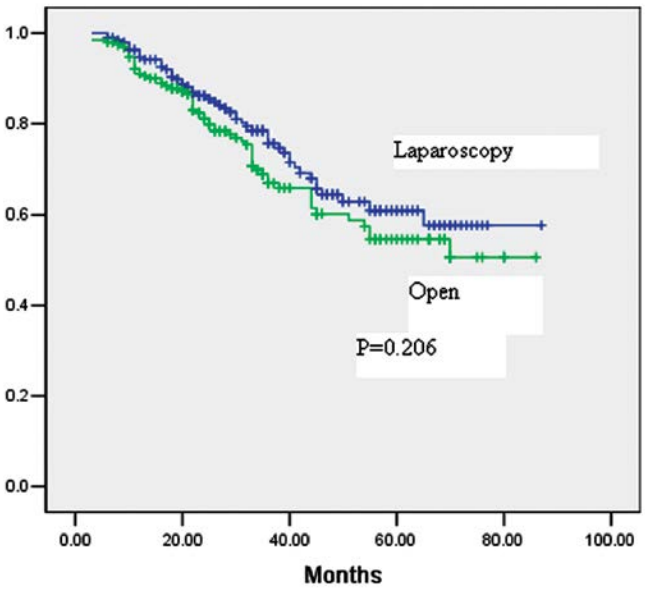

Figure 1. Overall survival of all patients treated by laparoscopic or open gastrectomy.

Table 6. 5-year overall survival rates after laparoscopic gastrectomy compared to historical data

Pathological stage	Present study (%)	SNUH (%) [26]	FAHCMU (%) [27]
IB	86	88.4	85.0
IIA	80	84.0	73.9
IIB	69	71.7	59.3
IIIA	46	58.4	46.2
IIIB	39	41.3	33.9
IIIC	21	26.1	18.5

SNUH: Seoul National University Hospital, Seoul, Korea;
FAHCMU: First Affiliated Hospital of China Medical University, Shenyang, China

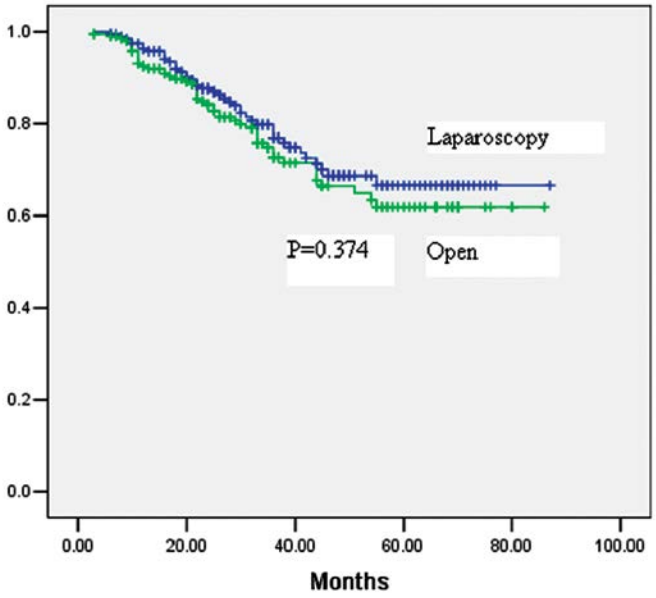

Figure 2. Cancer-specific survival of all patients treated by laparoscopic or open gastrectomy.

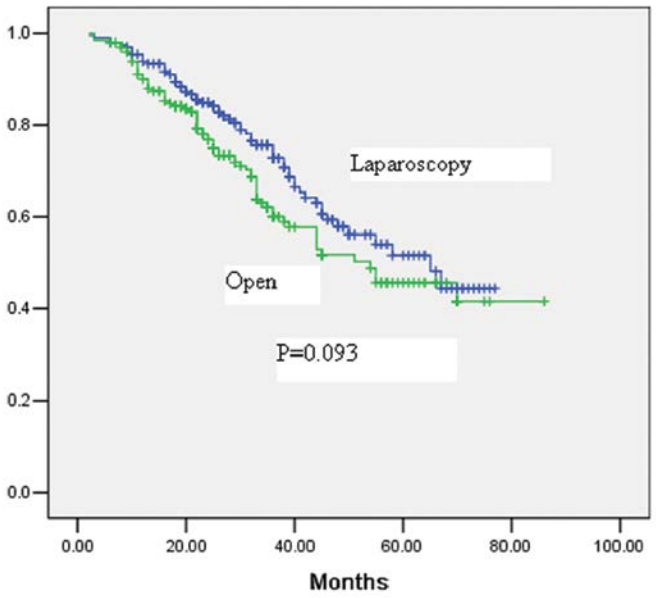

Figure 3. Disease-free survival of all patients treated by laparoscopic or open gastrectomy.

During this study period, the choice of intervention was at the discretion of the treating physician and patient. Therefore, from an analytical standpoint, our findings are subject to selection bias and confounding with respect to the relative preoperative characteristics between patients who underwent laparoscopic gastrectomy and those who underwent open surgery. To minimize these biases, a propensity score matching was used. A previous study has suggested that matching according to the propensity score eliminates a greater proportion of baseline differences between any two treatments compared to stratification or covariate adjustment. This 1-to-1 propensity score matching provides a robust evaluation of complete laparoscopic surgery for gastric cancer. The two groups were well matched for baseline clinical features and tumor characteristics affecting technical difficulties during gastrectomy.

There has been a consensus that the short-term outcomes are similar between laparoscopic gastrectomy and open surgery [28-31]. Our data also showed that the blood loss was lower in patients undergoing laparoscopic gastrectomy than in those undergoing open resection, while the operation time was longer for those undergoing laparoscopic gastrectomy. Previous studies have demonstrated that the incidence of postoperative complications associated with laparoscopic gastrectomy is comparable to that encountered during open surgery when performed by surgeons who have been trained in minimally invasive techniques [28-31]. We also confirmed that laparoscopic gastrectomy is not associated with a significant increase in overall complications. Our findings showed that oncological qualities, represented by the number of harvested lymph nodes and surgical margins, were not significantly different between the two methods.

Additionally, some reports have shown that the long-term outcomes of patients were better in the laparoscopy group than in the open surgery group [28,29]. The mechanism by which laparoscopic surgery is associated with outcomes that are more favorable remains unclear. Because im-

munity plays a crucial role in tumor progression and metastatic spread, this effect may be explained by the fact that surgical stress, which impairs immunity, is more intense following open resection than laparoscopic surgery [32-34]. Furthermore, laparoscopic surgery usually gives surgeons a better, magnified view of internal organs than that can be achieved by the unaided eye during traditional open resection.

The small sample size is a major limitation in this study. The exclusion of patients who underwent conversion to open resection is another major limitation. This study was designed to compare the outcomes between patients who underwent completed laparoscopic gastrectomy with those who underwent open resection. Therefore, the interpretation of this study is different from an intention-to-treat analysis.

In summary, we found that in matched cohorts of patients with gastric cancer, laparoscopic gastrectomy is feasible and safe with acceptable oncological outcomes. However, long-term outcomes of large-scale, randomized, multicenter trials are necessary to make a definitive statement on the efficacy of laparoscopic resection in gastric cancer therapy.

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Conflict of interests

The authors declare no confict of interests.

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