Original Article Laparoscopic versus open gastrectomy for gastric carcinoma in elderly patients: a pair-matched study

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Abstract: The safety of laparoscopic gastrectomy in elderly patients with gastric carcinoma has not been demonstrated. The aim of this study was to compare the outcomes of laparoscopic and open gastrectomy and estimate the feasibility of laparoscopic gastrectomy in gastric carcinoma patients aged \geq 70 years. We conducted a retrospective pair-matched study of gastric carcinoma patients aged \geq 70 years between January 2008 and January 2015. A total of 128 gastric carcinoma patients (64 pairs) underwent radical resection and were included in this analysis. The primary end point was 5-year overall survival. Secondary end points included disease-free survival and short-term outcomes. No significant differences were observed in baseline data between the laparoscopy group and open group. Overall survival and disease-free survival did not differ between the two groups (*P* = 0.335 and 0.239, respectively). Laparoscopic gastrectomy was associated with less blood loss, faster recovery and shorter hospital stay than was open gastrectomy. Laparoscopic gastrectomy was not found to be a significant predictor for overall survival and disease-free survival by univariate and multivariate analysis. In summary, laparoscopic gastrectomy is an acceptable alternative to open gastrectomy in elderly patients with operable gastric carcinoma.

Keywords: Gastric carcinoma, gastrectomy, laparoscopic gastrectomy, elderly patients

Introduction

Gastric carcinoma is one of the most common cancers in Eastern Asia countries, such as China, Korea and Japan, and it is the second leading cause of cancer-related deaths in China [1-5]. The incidence of gastric carcinomas that necessitate surgical intervention continues to increase because of the prolonged life expectancy in China [6-9]. Several studies have reported that in gastric carcinoma cases, laparoscopic resection shows comparable longterm survival results and improved short-term outcomes compared to open surgery [10-15]. However, postoperative morbidities and mortalities increase with age in older patients with gastric carcinoma. Therefore, resection with radical intent needs to be modified for geriatric patients. Thus far, it remains unclear whether elderly patients respond to laparoscopic gastrectomy as they do to laparoscopic gastrectomy. Because of this uncertainty, investigators have been unwilling to include frail patients in randomized controlled studies, and only little study has investigated the feasibility of laparoscopic gastrectomy in elderly patients with gastric carcinoma [16-18]. Hence, the important issue of whether the laparoscopic approach can serve as well as open gastrectomy in elderly patients with gastric carcinoma remains to be elucidated.

In this study, we compared the surgical outcomes between elderly patients with gastric carcinoma who underwent either laparoscopic gastrectomy or open gastrectomy and assessed whether laparoscopic gastrectomy is an acceptable alternative to open resection. Moreover, we evaluated the results to determine whether the survival data justify the implementation of laparoscopic techniques in geriatric oncology.

Patients and methods

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

Table 1. Baseline data

	Laparoscopy (n = 64)	Open (<i>n</i> = 64)	Р
Age (years)	75 (71-82)	75 (70-79)	0.541
Sex			0.585
Male	41 (64.1%)	38 (59.4%)	
Female	23 (35.9%)	26 (40.6%)	
Comorbidity			0.770
Liver cirrhosis	2 (3.1%)	1 (1.6%)	
Hypertension	8 (12.5%)	9 (14.1%)	
Diabetes Mellitus	6 (9.4%)	7 (10.9%)	
Stable angina	4 (6.3%)	2 (3.1%)	
Clinical TNM stage (7th AJCC-UICC)			0.937
IB	8 (12.5%)	10 (15.6%)	
IIA	33 (51.6%)	29 (45.3%)	
IIB	23 (35.9%)	25 (39.1%)	
Location of the primary tumor			0.706
Upper	13 (20.3%)	17 (26.6%)	
Middle	13 (20.3%)	12 (18.8%)	
Lower	38 (59.4%)	35 (54.7%)	
ASA score			0.815
I	44 (68.8%)	45 (70.3%)	
II	15 (23.4%)	15 (23.4%)	
III	5 (7.8%)	4 (6.3%)	
Type of gastrectomy			0.845
Distal gastrectomy	46 (71.9%)	45 (70.3%)	
Total gastrectomy	18 (28.1%)	19 (29.7%)	

Table 2. Postoperative results

	Laparoscopy (n = 64)	Open (<i>n</i> = 64)	Р
Operative time (min)	210 (170-240)	180 (150-210)	0.021
Estimated blood loss (ml)	250 (190-310)	290 (200-450)	0.014
Days to fluid diet (days)	3 (2-4)	4 (3-5)	0.010
Days to solid diet (days)	5 (3-6)	3 (4-8)	0.031
Postoperative hospital stay (days)	10 (8-19)	12 (9-25)	0.028

approved by the Ethics Committee of Guangdong General Hospital. The need for informed consent from all patients was waived because this was retrospective study, not prospective study.

Between January 2008 and January 2015, there were 387 patients older than 70 years who underwent gastrectomy with radical intent for gastric carcinoma in our institution, including 96 who received laparoscopic gastrectomy and 291 who received open gastrectomy. Patients with the presence of distant metastases, multiple primary tumors, needed other organ(s) resection, or concurrent malignant tumors were excluded from this analysis. Using the remaining cohort, a retrospective pair-matched study was performed to compare 128 patients (gastrectomy pairs) who underwent either open surgery or laparoscopic gastrectomy. Patients were matched by age, sex, medical comorbidity, American Society of Anesthesiologists (ASA) score, tumor location, clinical TNM stage, and extent of gastrectomy. All patients were diagnosed with gastric carcinoma by upper gastrointestinal endoscopy and biopsy. All patients were evaluated with endoscopic ultrasonography, computed tomographic scans of brain, chest, and abdomen, and ultrasonography of abdomen. Positron emission tomography-computerized tomography (PET-CT), staging laparoscopy and bone scanning were performed in selected cases [19-23]. Pu-Imonary function tests were routinely obtained and cardiac stress testing if risk factors were present.

Clinical stage T1-3NO-1MO gastric carcinoma patients were selected as candidates for laparoscopic gastrecto-

my. The tumor stage of gastric carcinoma was based on the 7th edition of the TNM classification of gastric carcinoma, which was proposed by Union for International Cancer Control (UICC), Japanese Gastric Cancer Association (JGCA) and American Joint Committee on Cancer (AJCC) [10-12]. The lymph nodes staging was based on the 3rd English edition of Japanese classification of gastric carcinoma proposed by JGCA [24]. For those of the patients operated before 2010, their staging was recalculated to match the latest TNM edition by UICC, JGCA and AJCC.

Table 3. Short-term oncological data

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	Laparoscopy	Open	Ρ
	(<i>n</i> = 64)	(n = 64)	value
Retrieved lymph nodes	17 (16-20)	17 (16-23)	0.550
Residual tumor (R0/R1/R2)	62/2/0	63/1/0	0.561
Histological subtype			0.715
Differentiated	39 (60.9%)	41 (64.1%)	
Undifferentiated	25 (39.1%)	23 (35.9%)	
Pathological TNM stage (7th AJCC-UICC)			0.800
IB	4 (6.3%)	3 (4.7%)	
IIA	19 (29.7%)	20 (31.2%)	
IIB	22 (3.1%)	25 (39.1%)	
IIIA	7 (10.9%)	6 (9.4%)	
IIIB	6 (9.4%)	5 (7.8%)	
IIIC	6 (9.4%)	5 (7.8%)	

Table 4. Morbidity and mortality data

	Laparoscopy (n = 64)	Open (<i>n</i> = 64)	Р
Postoperative 30-day morbidity	13 (20.3%)	16 (25.0%)	0.526
Anastomosis leakage	4 (6.3%)	5 (7.8%)	
Intra-abdominal bleeding	2 (3.1%)	3 (4.7%)	
Intra-abdominal abscess	1 (1.6%)	2 (3.1%)	
Pancreatic fistula	2 (3.1%)	1 (1.6%)	
Heart failure	1 (1.6%)	2 (3.1%)	
Pneumonia	1 (1.6%)	2 (3.1%)	
Acute coronary syndrome	1 (1.6%)	1 (1.6%)	
Ischemic stroke	1 (1.6%)	0 (0.0%)	
Major complications	3 (4.7%)	4 (6.3%)	0.904
Minor complications	10 (15.6%)	12 (18.8%)	
Mortality	0 (0.0%)	0 (0.0%)	-

The operative technique of laparoscopic gastrectomy with radical intent for gastric carcinoma has been described elsewhere in detail [25]. The procedure of open surgery was performed in a manner similar to laparoscopic gastrectomy. Morbidity, postoperative complications occurring within 30 postoperative days, was classified using Clavien-Dindo classification [26, 27]. The definition of Clavien-Dindo system was as follows: Grade 1: oral medication or bedside medical care required; Grade 2: intravenous medical therapy required; Grade 3: radiologic, endoscopic, or operative intervention required: Grade 4: chronic deficit or disability associated with the event; and Grade 5: death related to surgical complication. Major complications were classified as grades 3, 4 and 5. Minor complications were defined as 1 and 2. Mortality was defined as death of any cause occurring within 30 postoperative days.

Follow-up data were collected from outpatient follow-up database. Adjuvant chemotherapy was delivered to those who had advanced tumor stage or pathological R1 resection with generally good performance. 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, radiologic investigations, or pathology when available. Recurrence was classified as locoregional recurrence, distant metastasis and mixed. Locoregional disease was defined as recurrence within peritoneal seeding, the regional lymph nodes, the remnant stomach or the anastomosis. Distant disease included metastasis at distant organ sites (brain, lung, liver, bone, ovary, adrenal gland, distant lymph

nodes or other organs). The overall survival was calculated from the date of radical resection to the last follow up or death of any cause. The disease-free survival was assessed from the date of radical resection until the date of cancer recurrence or death of any cause. The follow-up was closed in May 2015.

All the statistical analyses were performed using SPSS 14.0 (SPSS Inc., Chicago, IL, USA). For variables following normal distribution, data were presented as mean and standard deviations and were analyzed by student *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



Figure 1. Overall survival curve in different procedure groups for elderly patients with gastric carcinoma. The overall survival did not differ between laparoscopy and open group (P = 0.335).

of qualitative results were analyzed by chisquare test or Fisher exact test where appropriate. Survival rates were analyzed using the Kaplan-Meier method; differences between the two groups 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 less than 0.05 were selected for inclusion in the multivariate Cox proportional hazard regression model. Adjusted hazard ratio (HR) along with the corresponding 95% confidence intervals (CI) were calculated. P < 0.05 was considered statistically significant.

Results

All baseline variables, including age, sex, medical comorbidity, American Society of Anesthesiologists (ASA) score, tumor location, clinical TNM stage, and extent of gastrectomy were well balanced in both groups (**Table 1**).

With regard to postoperative results, the operative times were significantly longer in the laparoscopy group than in the open group (**Table 2**). However, blood loss was lower in the laparoscopy group than in the open group, and patients undergoing laparoscopic resection showed a faster return of postoperative bowel function and a shorter hospital stay than those undergoing open surgery (**Table 2**).



Figure 2. Disease-free survival curve in different procedure groups for elderly patients with gastric carcinoma. The disease-free survival did not differ between laparoscopy and open group (P = 0.239).

The short-term oncological data were summarized in **Table 3**. There were no significant differences in pathological stage, residual tumor, number of harvested lymph nodes and histological subtype (**Table 3**). The number of harvested lymph nodes was greater than 15 in each resection specimen.

The overall morbidity rates were 20.3% (13/64) and 25.0% (16/64) in the laparoscopy and open group, respectively; however, this difference was not significant (*P* = 0.526). The severity of complications, classified by Clavien-Dindo classification, was comparable between the two groups (**Table 4**). There was no in-hospital or postoperative 30-day mortality in either group.

The median follow-up period was 40 months (range: 3-85 months) and 42 months (range: 4-86 months) for the laparoscopy and open groups, respectively (P = 0.586). The overall survival and disease-free survival did not significantly differ between laparoscopy and open patients (P = 0.335 and 0.239, respectively), and the 5-year overall survival for the laparoscopy and open groups were 54% and 50%, respectively (**Figure 1**). The 5-year disease-free survival for the laparoscopy and open groups were 41% and 38%, respectively (**Figure 2**). The location of the recurrence and the time to recurrence were not significantly different between the two groups (**Table 5**). In addition, overall

Outcomes	Laparoscopy (<i>n</i> = 64)	Open (<i>n</i> = 64)	Ρ
Tumor recurrence	26 (40.6%)	34 (53.1%)	0.156
Locoregional	12 (18.8%)	16 (25.0%)	
Peritoneal seeding	4 (6.3%)	4 (6.3%)	
Remnant stomach	3 (4.7%)	5 (7.8%)	
Distant lymph nodes	1 (1.6%)	2 (3.1%)	
Anastomosis	4 (6.3%)	5 (7.8%)	
Distant	12 (18.8%)	14 (21.9%)	
Brain	2 (3.1%)	3 (4.7%)	
Liver	4 (6.3%)	5 (7.8%)	
Lung	3 (4.7%)	2 (3.1%)	
Adrenal	1 (1.6%)	2 (3.1%)	
Ovary	2 (3.1%)	2 (3.1%)	
Mixed	2 (3.1%)	4 (6.3%)	
Time to recurrence (median, months)	19 (4-42)	13 (3-42)	0.259

Table 5. Tumor recurrence data

Table 6. The 5-year	overall survival and	disease-free surviva	al
data			

Pathological stage	Laparoscopy (%)	Open (%)	Р
Five-year overall survival			
I	74	73	0.581
II	61	59	0.349
111	34	28	0.214
Five-year disease-free survival			
I	68	70	0.741
II	54	50	0.484
	29	21	0.090

survival and disease-free survival analyses showed no significant differences between the laparoscopy and open groups when patients were classified by TNM stage (**Table 6**).

Multivariate analysis identified pathological N stage (HR: 3.08, 95% CI: 1.22-4.70, P = 0.010) and pathological T stage (HR: 4.22, 95% CI: 1.22-4.70, P = 0.019) as the factors with independent effects on overall survival (**Table 7**). The type of operative approach did not influence the overall survival. In multivariate analysis, the pathological N stage (HR: 2.88, 95% CI: 2.00-3.80, P = 0.024) and pathological venous invasion (HR: 3.29, 95% CI: 2.87 -5.02, P = 0.029) had independent effects on disease-free survival (**Table 8**). The type of operative approach was not important in the multivariate analysis for disease-free survival.

Discussion

In our study, no statistically significant differences in long-term survival outcomes were found in elderly gastric carcinoma patients who underwent laparoscopic gastrectomy and open gastrectomy. To the best of knowledge, this is the first cohort study involving elderly patients (median age of 75 years in both laparoscopy and open groups) that studied the clinical feasibility and efficacy of laparoscopic gastrectomy for gastric carcinoma in China.

Radical gastrectomy plays an important role in the treatment of gastric carcinoma. However, elderly patients are associated with higher rate of medical comorbidities and reduced functional reserve compared with younger patients, and increasing age itself is an independent risk factor for postoperative morbidity and mortality and long-term survival. Previous studies found elderly patients who underwent open gastrectomy were associated with a relatively high mortality and morbidity [28-30].

Laparoscopic gastrectomy with radical intent is an emerging therapeutic option for gastric carcinoma patients. Randomized clinical trials have demonstrated laparoscopic gastrectomy is associated with less blood loss, more rapid postoperative recovery, shorter length of hospital stay, and better cosmetic outcomes, but equally short-term and long-term oncologic outcomes compared with open gastrectomy for early gastric carcinoma [11]. Retrospective series have also showed the similar results for locally advanced gastric carcinoma [13-15].

Although randomized clinical trials would be ideal for confirming the feasibility of laparoscopic gastrectomy in elderly patients, the increase in the incidence of postoperative morbidities and mortalities with advancing age may lead to investigators avoiding the inclusion of frail patients in prospective randomized trials.

survival			
Regression variables	Adjusted hazard ratio	95% CI	P value
Pathological T stage			
T ₂	1.00		
Τ ₃	1.36	0.25-1.89	0.064
T _{4a}	4.22	1.22-4.70	0.019
Pathological N stage			
N _o	1.00		
N ₁	1.24	0.65-1.25	0.095
N_2/N_3	3.08	2.51-5.78	0.010

 Table 7. Multivariate Cox regression analyses of overall survival

 Table 8. Multivariate Cox regression analyses of diseasefree survival

Regression variables	Adjusted hazard ratio	95% CI	P value
Pathological N stage			
N _o	1.00		
N ₁	1.23	0.28-1.45	0.165
N_{2}/N_{3}	2.88	2.00-3.80	0.024
Pathological venous invasion			
No	1.00		
Yes	3.29	2.87 -5.02	0.029

To circumvent the impracticability of randomized clinical trials, we conducted a retrospective pair-matched study.

In this study, we retrospectively evaluated the short-term and long-term outcomes of laparoscopic and open gastrectomy in patients with gastric carcinoma aged ≥70 years. The patients in laparoscopy and open groups were matched in terms of age, sex, medical comorbidity, ASA score, tumor location, clinical TNM stage, and extent of gastrectomy. We found that laparo-scopic gastrectomy could be safely performed in elderly patients with acceptable perioperative morbidity and mortality. Moreover, laparo-scopic gastrectomy lead to better short-term outcomes when compared with open gastrectomy, such as less blood loss and shorter post-operative hospital stay.

In our study, we demonstrated that laparoscopic technique was as effective as traditional open approach for early and locally advanced gastric carcinoma with regard to oncological outcomes. We showed that lymph nodes harvested and positive margin rate were similar between laparoscopy and open groups. Furthermore, recurrence rates and survival rates were not significantly different between the two groups. Our results showed that shortterm and long-term oncologic outcomes were similar between laparoscopy and open group in elderly patients with gastric carcinoma [11, 13-19].

Our study has certain limitations. First, this data analyses were affected by selection bias though pair-matched analysis was applied. Another limitation was the small sample of patients used in this study. One recommendation for future studies is to increase the sample size, which will also increase the power of the study.

In summary, our pair-matched study suggested that the laparoscopic approach is not inferior to the open approach and that laparoscopic gastrectomy can be an acceptable alternative to open gastrectomy in elderly patients with gastric carcinoma.

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Discourse of conflict of interest

None.

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