

Original Article

The effect and safety of laparoscopic D2 radical gastrectomy for advanced gastric cancer

Hong Ji, Yafei Zhang, Yiming Li, Hongwei Lu

Department of General Surgery, Second Affiliated Hospital, School of Medicine, Xi'an Jiaotong University, Xi'an 710004, Shaanxi, China

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Abstract: Objectives: To compare the curative effect and safety of laparoscope and laparotomy in D2 radical gastrectomy of for advanced gastric cancer (AGC). Methods: 217 cases of patients with advanced gastric cancer treated in our hospital from March 2011 to March 2014 were selected and divided into laparoscopy group (LG) (103 cases) and open group (OG) (114 cases). Gastric cancer patients in LG were given laparoscopic D2 radical gastrectomy (LD2RG), and gastric cancer patients in OG were given D2 radical gastrectomy with laparotomy. The operation effect, safety, complication and operative cost in the two groups were compared. Results: In LG the lengths of incision were shorter, the blood loss during operation were less and the postoperative recovery were better than OG, the difference between 2 groups were statistically significant ($P < 0.05$). But the operation time, the tumor resection proximal (distal) margin length and the mean number of removal LN in laparoscopy and laparotomy group were not significantly ($P > 0.05$). Conclusions: Both of the two methods of treatment can obtain exactly equal clinical effect in AGC treatment. But compared with laparotomy, LD2RG can reduce surgical trauma and complications and improve postoperative recovery, so LD2RG is safe and reliable in treat AGC.

Keywords: Advanced gastric cancer, laparoscopic radical gastrectomy, open radical gastrectomy, postoperative recovery

Introduction

Gastric cancer is the fourth most common cancer and the second leading cause of cancer-related death worldwide. Surgical resection remains the only curative treatment option [1]. Although laparoscopic surgery is currently being regarded as the suitable alternative treatment of choice for early gastric cancer, the use of laparoscopic gastrectomy in AGC remains a controversial topic [2, 3]. Therefore, we conducted this study to verify the effect and safety of LD2RG for AGC.

Methods

Patient cohort

217 cases of patients with AGC treated in our hospital from March 2011 to March 2014 were selected as research objects (**Figure 1**). Inclusion criteria: 1. Tumors of all the cases had invaded muscularis and serosa confirmed by endoscopic ultrasonography and CT. 2. The pre-

operative examinations conformed to operation indications, excluded surgical contraindication; 3. Underwent D2 radical gastrectomy. Exclusion criteria: tumors up to ten centimeters in diameter, abdominal cavity adhesion, tumors invaded other organs, emergency operation, organ dysfunction and operation intolerance, etc. According to patients' and their relatives' choice for surgical methods, they were divided into LG (103 cases) and OG (114 cases). Gastric cancer patients in LG were given LD2RG, and gastric cancer patients in OG were given open D2 radical gastrectomy. Lymph nodes are grouped in accordance with the Provisions of the Statute of Gastric Cancer in Japan [4], The disease stage was classified according to the 7th International Union Against Cancer (UICC) TNM classification [5]. The clinical and pathological characteristics of patients are summarized in **Table 1**. No significant differences were observed in clinicopathologic parameters between the two groups such as age, gender, TNM stage, histologic grade of tumor, diameter of tumor, histological

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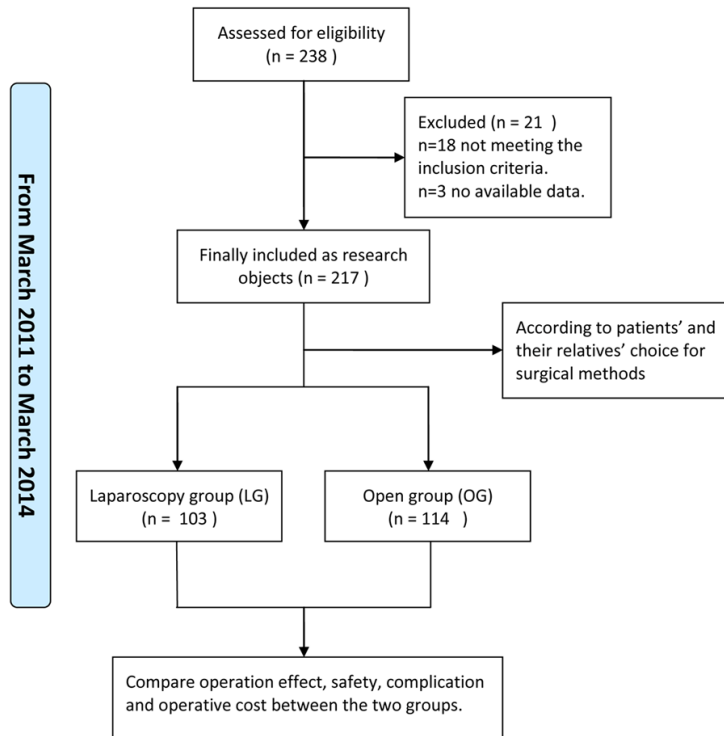


Figure 1. Flow chart for patients recruitment.

type, operation method, combined disease and history of abdominal operation ($P>0.05$). All the study was approved by the Ethical Committee.

Surgical procedure

Laparoscopy group: Patients were placed in the supine position and the operator stood on the left side of the patient. After general anesthesia, a 10 mm trocar was inserted at the infra-umbilical area and pneumoperitoneum was formed by insufflations of carbon dioxide. The patient was placed in the reverse trendelenburg position and four additional trocars were inserted. The laparoscopic radical gastrectomy was implemented according to Yu's reports in 2006 [6].

Open group: The procedure is carried out under general anesthesia with endotracheal intubation and epidural analgesia. The patient lies in the supine position. The excision region, extent of lymph nodes dissection and the strategies of digestive tract reconstruction were the same as LG.

Investigation index

The operation time, blood loss, proximal margin, distal margin, dissected lymph nodes,

length of incision, time to first flatus, time to resumed oral intake, analgesics given, time to ambulation, post-operative hospital stay, postoperative complications, operative cost, total treatment cost, mortality of gastric cancer and recurrence or metastasis were selected as investigation index between 2 groups.

Statistical analysis

We performed all statistical analyses using the Statistical Package for Social Science (SPSS) version 18.0 for Microsoft Windows (SPSS Inc. Chicago, IL, USA). Values are presented as mean \pm standard deviation ($\bar{x}\pm s$) or median (M). Z-test or rank-sum test was used to analyze the differences between the groups. Chi-square test or Fisher exact probability method was used to compare enumeration data. All P -values less than 0.05 were regarded as statistically significant.

Results

Intra-operative outcomes

No significant differences were observed regarding the operation time, proximal margin, distal margin, dissected lymph nodes between the two groups ($P>0.05$). Blood loss was significantly less in the LG ($P<0.05$). The length of incision was shorter in LG than OG ($P<0.05$) (Table 2).

Post-operative outcomes

The time to first flatus, time to resumed oral intake, analgesics given, time to ambulation, post-operative hospital stay and postoperative complications was significantly shorter in the LG ($P<0.05$). The operating cost in LG was more than that in OG ($P<0.05$), while the total hospitalization expense was no remarkable difference ($P>0.05$). The main complications were wound infection, reflux gastritis, bronchopneumonia, ileus, etc. No significant differences were observed regarding the post-operative complications between the two groups. There

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Table 1. Comparison of the clinicopathological features in the patients of 2 groups

Clinicopathological feature	Laparoscopy group n=103	Laparotomy group n=114	Statistic	P value
Age (year, x±s)	56.73±9.84	60.45±10.93	t=-1.60	0.11
Gender (case)				
Male	72	85	$\chi^2=0.59$	0.44
Female	31	29		
TNM staging (case)				
I	22	24	$\chi^2=0.02$	0.99
II	53	58		
III	28	32		
Histologic grade of tumor (case)				
Poorly differentiated	18	20	$\chi^2=0.00$	1.00
Moderately differentiated	59	65		
Well differentiated	26	29		
Diameter of tumor (cm)				
<4	46	58	$\chi^2=2.95$	0.23
4~8	39	45		
>8	18	11		
Histological type (case)				
Adenocarcinoma	79	88	$\chi^2=1.69$	0.79
Tubular adenocarcinoma	9	11		
Papillary adenocarcinoma	2	1		
Mucinous adenocarcinoma	3	6		
Signet ring ceu carcinoma	10	8		
Operation method (case)				
Proximal gastrectomy	28	33	$\chi^2=0.08$	0.96
Distal gastrectomy	64	69		
Total gastrectomy	11	12		
Combined disease (case)				
Hypertension	18	28	-	0.41
Diabetes mellitus	1	4		
Hypertension and diabetes mellitus	4	2		
Heart disease	3	3		
No	77	77		
History of abdominal operation (case)				
Yes	15	9	$\chi^2=2.45$	0.12
No	88	105		

was no significant difference in mortality of gastric cancer and recurrence or metastasis between the two groups ($P>0.05$) (Table 2).

Discussion

The use of laparoscopic surgery has been widely used in various abdominal surgeries for its minimal invasiveness, making it a suitable alternative method to an open procedure. Not only is the standard surgery for cholecystectomy, laparoscopic surgery has been written into

the NCCN Guidelines [7] in radical resection of colon cancer. Since the first performance by Kitano et al. [8], the use of laparoscopic radical gastrectomy for early gastric cancer has exploded because of the high prevalence of early gastric cancer and the merits of laparoscopic radical gastrectomy, including less post-operative pain, earlier recovery and better cosmetic outcomes than open gastrectomy [9-13].

Laparoscopic gastrectomy has been widely accepted especially in patients with early-stage

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Table 2. Comparison of operative effect-related indicators between the 2 groups

Indicator	Laparoscopy group n=103	Laparotomy group n=114	Statistic	P value
Intra-operative indicators				
Operation time (min, x±s)	216.57±76.48	205.68±52.13	Z=-0.04	0.97
Blood loss (ml, M)	100.00	400.00	Z=-75.52	0.00
Proximal margin (cm, x±s)	6.24±0.82	6.40±0.76	Z=-0.16	0.87
Distal margin (cm, x±s)	5.58±0.98	5.44±0.64	Z=0.85	0.40
Dissected lymph nodes (case, x±s)	26.01±4.88	24.95±4.34	Z=1.08	0.28
Length of incision (cm, x±s)	5.33±1.00	18.39±1.91	Z=-20.94	0.00
Post-operative indicators				
Time to first flatus (d, M)	2.00	5.00	Z=-10.60	0.00
Time to resumed oral intake (d, M)	2.00	5.00	Z=-11.09	0.00
Analgesics given (time, M)	2.00	4.00	Z=-5.11	0.00
Time to ambulation (d, M)	2.00	4.00	Z=-10.60	0.00
Post-operative hospital stay (d, x±s)	7.43±2.13	14.85±7.63	Z=-22.32	0.00
Postoperative complications [case (%)]	5 (4.9)	21 (18.4)	χ ² =9.44	0.00
Wound infection	0 (0)	8 (7.0)	-	-
Reflux gastritis	2 (1.9)	2 (1.8)	-	-
Bronchopneumonia	1 (1.0)	8 (7.0)	-	-
Ileus	2 (1.9)	3 (2.6)	-	-
Operative cost (yuan, x±s)	5,166.30±571.77	4,452.10±1,091.35	Z=3.39	0.00
Total hospitalization expense (yuan, x±s)	44,632.59±6,963.01	43,377.78±7,391.24	Z=0.80	0.43
Mortality of gastric cancer [(%)]	0 (0)	2 (1.8)	χ ² =1.82	0.18
Recurrence or metastasis [case (%)]	2 (1.9)	3 (2.6)	χ ² =0.11	0.74
Peritoneal recurrence	1 (1.0)	1 (0.9)	-	-
Liver metastasis	0 (0)	1 (0.9)	-	-
Regional lymph node metastasis	0 (0)	1 (0.9)	-	-
Implantation metastasis	1 (1.0)	0 (0)	-	-

gastric cancer [14]. However, the safety and oncologic validity of laparoscopic gastrectomy for AGC remains a controversial topic due to its technical difficulties and the lack of long-term results. 2-3 the focus is mainly on that if the extent of lymph node dissection could meet the demand of radical gastrectomy for AGC. In 1997, LD2RG was used firstly by Goh [15] for the treatment of AGC, achieved good short-term effects and confirmed its technical feasibility and safety. Lee [16] found that there was no significant difference in the number of dissected lymph nodes between LD2RG and OG. With the development of technology of LD2G, reports related LD2G for AGC is increasing, which has made a great progress [17-20]. So far, more evidence-based large prospective clinical trials would be required to validate the use of LD2RG for AGC.

Through the comparison between 2 groups, the aims of our study were to verify the effect and

safety of LD2RG for AGC. The clinical and pathological characteristics of patients, such as age, gender, TNM stage, histologic grade of tumor, diameter of tumor, histological type, operation method, combined disease and history of abdominal operation have no significant differences between 2 groups, so differences caused by these conditions has been excluded. The results showed significant differences between the two groups in blood loss and the length of incision ($P<0.05$), which reflects the obvious advantage of minimal invasiveness in LG. Moreover, no significant differences were observed regarding the operation time, proximal margin, distal margin, dissected lymph nodes between 2 groups ($P>0.05$).

The widely accepted principle [21] of radical resection of gastric cancer is: En bloc resection of the lesion; margin ≥ 5 cm from tumor; complete removal of lymph node; non contact principle and destroy the intraperitoneal remaining

cancer cells. The key problem of laparoscopic radical gastrectomy for AGC is abdominal lymph node dissection, while, with better amplification effect, clearer anatomical plane, lesion location and the vessels, Laparoscopic operation is good for completely excising the lesion and radical dissecting lymph node [22, 23]. Our study shows no significant differences in the operation time, proximal margin, distal margin, dissected lymph nodes between 2 groups ($P>0.05$), demonstrated that the extent of lymph node dissection by laparoscope could come up to the requirements of radical gastrectomy for AGC, even better than laparotomy for the clear view under the laparoscope.

In our study, the time to first flatus and resumed oral intake, analgesics given, time to ambulation, post-operative hospital stay and postoperative complications was significantly shorter in the LG ($P<0.05$). It has been clearly shown that LD2RG has considerable benefits in minimal invasiveness, and speedy recovery over laparotomy. The operative cost was significantly different between the two groups ($P<0.05$), while the total hospitalization expense was indifference ($P>0.05$), which demonstrated that LD2RG for advanced gastric cancer is feasible and easily accepted by patients for its shorter hospital stay and less drug use.

Results from a postoperative show that the postoperative mortality and morbidity of LG was 0 and 1.8% respectively, which was no significant difference to OG (1.9% and 2.6%). The study suggested that LD2RG for AGC will not increase mortality of gastric cancer and recurrence or metastasis. While, for the time of our follow-up is limited, Long-time follow-up would be required to validate the effect and safety of LD2RG for AGC.

Above all, our research shows that LD2RG for AGC is safe and feasible in short term, characterized by such advantages as less pain, fewer postoperative complications and rapid recovery. Moreover, our results suggest that the application of LD2RG to this group results in adequate lymphadenectomy and similar recurrence and survival rates as laparotomy. However, there were several limitations in this research, a long-term prospective study of double-blind and randomized controlled trial is needed for further evaluation.

Disclosure of conflict of interest

None.

Address correspondence to: Yiming Li, Department of General Surgery, Second Affiliated Hospital, School of Medicine, Xi'an Jiaotong University, 157 Xiwu Road, Xi'an 710004, Shaanxi, China. E-mail: liyimingdoc@163.com

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