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Original Article

Laparoscopic D2 radical gastrectomy improves postoperative inflammation and gastric function in elderly patients with advanced gastric cancer

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Abstract: Objective: To investigate the effect of laparoscopic radical gastrectomy on the inflammation and recovery of gastrointestinal function in elderly patients with advanced gastric cancer (GC). Methods: Data of 80 elderly patients with advanced GC admitted to the Taizhou First people's Hospital from May 2014 to January 2019 were collected for this retrospective analysis. Among them, 34 patients underwent open D2 radical gastrectomy were regarded as control group. The other 46 patients underwent laparoscopic D2 radical gastrectomy were considered as observation group. Both groups underwent 2/3 or more mid-segment gastrectomy with D2 regional lymphatic dissection. The operative time, intraoperative bleeding, postoperative ventilation time, length of stay (LOS) and perioperative complication rates were compared between the two groups. Peripheral blood was drawn before and after surgery to detect the inflammatory factors C-reactive protein (CRP), calcitoninogen (PCT), tumor necrosis factor-α (TNF-α), gastric function gastrin 17 (G-17), and pepsinogen (PG) I and II. Subsequently, patients were followed up for 3-year prognosis to document the survival of patients. Results: The operative time and LOS were shorter and intraoperative bleeding was lower in the observation group than those in the control group ($P<0.05$). There was no statistical difference in treatment costs and incidence of perioperative complications between the two groups ($P>0.05$). After surgery, CRP, PCT and TNF-α were elevated in both groups but were lower in the observation group than that in the control group ($P<0.05$). PG I was dramatically higher ($P<0.05$), while PG II and G-17 were lower ($P<0.05$) in both groups after treatment. Also, the posttreatment PG I and G-17 were higher ($P<0.05$) and PG II was lower ($P<0.05$) in the observation group than those in the control group. Prognostic follow-up revealed no statistical difference between groups in terms of the 1-year and 3-year overall survival ($P>0.05$). Conclusion: Laparoscopic D2 radical surgery is more effective in the treatment of advanced GC in the elderly, because it can effectively suppress the postoperative inflammation and improve recovery of gastric function. Hence, it has a high clinical application value.

Keywords: Laparoscopic radical gastrectomy for gastric cancer, advanced gastric cancer, inflammatory factors, gastric function

Introduction

At present, population aging in China is characterized by a large elderly population base, rapid growth rate, obvious trend of advanced ageing, large regional differences in the degree of aging, and incompatibility between population aging and socioeconomic development level [1]. Gastric cancer (GC) is one of the most common diseases among the elderly, who are prone to various diseases due to the decline of their body functions [2]. GC is the fifth most common cancer and the third leading cause of cancer-related deaths worldwide [3, 4]. Various factors including smoking, alcohol consumption, high salt, oil and sugar intake, and H. pylori infection can increase the risk of GC [5-7]. Since the main symptom of this disease is abdominal pain, and there is often no obvious symptom in the early stage, by the time of diagnosis, the disease has often progressed to an advanced stage [8]. Advanced GC has rapid tumor progression, metastasis and spread of cancer cells, leading to high clinical mortality [9]. Therefore, for GC, early detection and treatment are of great importance.

Clinically, open surgical resection used to be the main method for treating GC, but it tends to cause more harm to patients [10]. Thus, the surgical approach to GC has been continuously improved with the aim of reducing surgical injuries to patients and promoting better recovery [11]. Among them, D2 radical gastrectomy is an effective procedure for advanced GC. It is performed according to the principle of tumor resection and can completely remove the tumor lesion, perigastric lymph nodes at stations 1 and 2, and extra-retinal capsular resection of the large and small omentum and stomach, which means lymph nodes and GC lesions are both removed [12]. Recently laparoscopic surgery has gradually become more common and has the advantage of less invasive, less postoperative pain and faster recovery compared to open surgical resection [13]. Postoperative gastrointestinal dysfunction is still one of the most common side effects in patients undergoing GC surgery. It not only increases the risk of early postoperative aspiration, but also exacerbates nutritional deficiencies and even leads to systemic dysfunction [14]. Gastrointestinal dysfunction is also not conducive to the postoperative recovery and long-term prognosis of elderly patients. Therefore, choosing an appropriate surgical method is crucial to promoting the recovery of postoperative gastrointestinal function in elderly patients [15].

In view of this, our study aimed to verify the effectiveness of laparoscopic radical gastrectomy by observing its effect on inflammation, gastrointestinal function and the 1-year and 3-year survival rates.

Methods and materials

Patient data

Eighty patients with advanced GC admitted to the Taizhou First People's Hospital from May 2014 to January 2019 were selected for this retrospective analysis. Among them, 34 patients underwent open D2 radical gastrectomy were considered as control group, with 21 males, 13 females and a mean age of 68.12±3.91 years. The other 46 patients underwent laparoscopic D2 radical gastrectomy were regarded as observation group, with 32 males, 14 females and a mean age of 67.72±4.79 years. This research was conducted after approval by the Taizhou First People's Hospital medical ethics committee (Ethical lot number: 20140208).

Inclusion and exclusion criteria

Inclusion criteria: patients who were diagnosed with advanced GC by gastroscopy and biopsy, and staged according to the 7th edition of the AJCC Cancer Staging Manual 2010 [16]; patients who were 60 years old or older; patients without tumor metastasis to surrounding sites (checked by abdominal ultrasound examination, enhanced chest CT of the upper abdomen and other means); patients with complete clinical information.

Exclusion criteria: patients with other malignancies; patients who did not meet the indications for surgery or did not want to have surgery; patients who were unable to communicate properly or with severe mental disorders; patients with coagulation disorders; patients with anesthetic risks; patients with intraoperative tumor dissemination or distant metastases in the abdominal cavity; patients who were transferred from laparoscopic intraoperative to open surgery.

Treatment options

The control group underwent open D2 radical gastrectomy: general anesthesia was performed with tracheal intubation in a supine position. A 15-20 cm incision was made around the umbilical cord on the middle-left side of the abdomen. The abdominal skin and subcutaneous tissue were separated layer by layer. After the focus of the tumor was found, the tumor and the majority stomach (more than 2/3) were removed, and the D2 lymph nodes were also dissected. Then, we anastomosed the esophagojejunum, cleaned the abdominal cavity, and closed the incision.

In the observation group, laparoscopic radical gastrectomy was performed: general anesthesia with tracheal intubation was performed, and the surgical position was supine with head high and feet low. The puncture point was determined according to the preoperative CT images, and a 1 cm observation hole was made by puncturing 3 cm below the umbilicus in the patient's abdomen to establish an artificial pneumoperitoneum (12 mmHg). A 10 mm diameter Trocar needle and laparoscope were

placed, and the patient's intra-abdominal cavity was explored using laparoscopy to identify the gastric tumor lesion. A primary and a secondary operating hole, each 1 cm long, were made 5 cm to the left and 5 cm to the right of the umbilicus, into which the surgical instruments were placed. Then we dissected the anterior lobe of the colonic mesentery with ultrasonic knife, clamped the right vein of the gastric omentum, removed the tumor lesion and majority gastrectomy (more than 2/3), cleared the D2 lymph nodes, anastomosed the esophageal jejunum, withdrew the surgical instruments, and closed the incision.

Outcome measures

Primary outcome measures were surgical indicators (operative time, intraoperative bleeding, length of stay (LOS)) and perioperative complications.

Secondary outcome measures: (1) Altogether 4 mL of fasting peripheral elbow venous blood was collected from all patients before and 3 days after surgery and centrifuged at 3500 r/min for 10 min. Serum was collected, and enzyme-linked immunosorbent assay was conducted to assess inflammatory factors C-reactive protein (CRP), calcitoninogen (PCT), tumor necrosis factor-α (TNF-α), gastric function gastrin 17 (G-17), and pepsinogen (PG) I and II. The kits used for CRP, PCT, TNF-α, PG I and II were purchased from Thermo Fisher Scientific (KHA0031, EHPCT, KHC3011, EHPGI, EHPGC). The G-17 kit was purchased from Tianjin Bunsen Health Technology Co. Ltd. (BS-1626). (2) All patients were followed up for 3 years by telephones as well as by reviews, and their 1-year and 3-year survival rates were recorded.

Statistical methods

The collected data were statistically analyzed via SPSS 20.0 (SPSS Ltd., Chicago, USA). The counting data expressed as rate (%) were assessed using Chi-square test, marked as χ^2. The measurement data were all conformed to a normal distribution and were represented as the mean ± standard deviation (mean ± SD). Comparisons between two groups were conducted using independent sample t-test, and those within two groups using paired t-test, expressed as t. Patients' survival at 1 and 3 years was plotted using K-M survival curves and analyzed using Log-rank test. P<0.05 was considered statistically significant.

Results

No difference in baseline data between the two groups

There was no statistical difference between the two groups in terms of age, sex, tumor site, degree of differentiation, pathological type, TNM stage, tumor diameter, ASA grade and history of abdominal surgery (P>0.05), as shown in **Table 1**.

Comparison of surgical indicators between the two groups

The observation group had dramatically shorter operative time and LOS, as well as less intraoperative bleeding than the control group, and the differences were statistically significant (P<0.05). However, there was no statistical difference in the cost of treatment between the two groups (P>0.05), as shown in **Table 2**.

Comparison of perioperative complications between the two groups

The total complication rate in the observation group was slightly lower than that in the control group, but the difference was not statistically significant (P>0.05), as shown in **Table 3**.

Comparison of inflammation levels between the two groups

There was no statistically significant difference in CRP, PCT and TNF-α between the two groups before surgery (P>0.05), and the postoperative CRP, PCT and TNF-α in the two groups were higher than those before surgery (P<0.05). Also, the postoperative CRP, PCT and TNF-α in the observation group were lower than those in the control group (P<0.05). See **Figure 1**.

Comparison of gastrointestinal function between the two groups

There was no statistically significant difference of PG I, PG II and G-17 between the two groups before surgery (P>0.05). Postoperatively, the PG I increased (P<0.05), while PG II and G-17 decreased (P<0.05) in both groups. The postoperative PG I and G-17 were higher (P<0.05)

Table 1. Baseline data

	Observation group (n=46)	Control group (n=34)	χ^2/t	P
Age	67.7±4.8	68.1±3.9	0.398	0.692
Sex			0.532	0.466
Male	32 (69.57)	21 (61.76)		
Female	14 (30.43)	13 (38.24)		
Tumor site			1.578	0.664
Cardia	13 (28.26)	10 (29.41)		
Fundus	6 (13.04)	3 (8.82)		
Corpus	9 (19.57)	4 (11.76)		
Antrum	18 (39.13)	17 (50.00)		
Degree of differentiation			0.371	0.831
Highly differentiated	34 (73.91)	27 (79.41)		
Moderately differentiated	8 (17.39)	5 (14.71)		
Poorly differentiated	4 (8.70)	2 (5.88)		
Pathological type			1.861	0.394
Adenocarcinoma	30 (65.22)	26 (76.47)		
Indocellular carcinoma	9 (19.57)	3 (8.82)		
Mixed type	7 (15.22)	5 (14.71)		
TNM stage			0.351	0.839
Stage I	5 (10.87)	3 (8.82)		
Stage II	20 (43.48)	17 (50.00)		
Stage III	21 (45.65)	14 (41.18)		
Tumor diameter (cm)	5.80±1.03	5.66±1.02	0.604	0.548
ASA grade			0.635	0.728
Grade I	14 (30.43)	8 (23.53)		
Grade II	18 (39.13)	16 (47.06)		
Grade III	14 (30.43)	10 (29.41)		
History of abdominal surgery			0.242	0.623
Yes	10 (21.74)	8 (26.47)		
No	36 (78.26)	26 (73.53)		

TNM stage: tumor node metastasis stage; ASA: American Society of Anesthesiologists.

and PG II was lower (P<0.05) in the observation group than those in the control group. See **Figure 2**.

No significant difference in prognostic survival between the two groups

We conducted a 3-year follow-up in both groups and counted the survival rates at 1 year and 3 years. In the observation group, there were 40 cases surviving at 1 year and 34 at 3 years, with 1- and 3-year survival rates of 86.96% and 73.91%, respectively. In the control group, there were 28 cases surviving at 1 year and 24 at 3 years, with 1- and 3-year survival rates of 82.35% and 70.59%, respectively. The K-M curves at 1 year and 3 years showed that there was no statistical difference between the two groups in terms of 1-year and 3-year survival (P>0.05), as shown in **Figure 3**.

Discussion

The early symptoms of GC onset are not obvious, resulting in the progressive stage of GC at the time of clinical diagnosis [17]. If advanced GC is not treated in time, it will seriously affect the quality of life of the patients, so effective treatment is of great importance [18]. Laparoscopic D2 radical gastrectomy, with a non-contact principle, provides adequate resection of the primary site and surrounding involved tissues and organs, and also removes perigastric lymph nodes [19].

Table 2. Comparison of surgical indexes between the two groups

	Operative time (min)	Intraoperative bleeding (mL)	Length of stay (days)	Treatment cost (million yuan)
Observation group (n=46)	141.20±24.83	94.22±21.95	10.83±2.05	5.13±0.92
Control group (n=34)	167.68±24.69	232.87±36.21	17.32±2.70	4.86±1.14
t	4.427	21.240	12.230	1.172
P	<0.001	<0.001	<0.001	0.245

Table 3. Complications

	Observation group (n=46)	Control group (n=34)	χ^2	P
Intestinal obstruction	1 (2.17)	2 (5.88)		
Gastroparesis	1 (2.17)	1 (2.94)		
Incision infection	1 (2.17)	2 (5.88)		
Anastomotic leakage	0 (0.00)	1 (2.94)		
Hemorrhage	1 (2.17)	1 (2.94)		
Total complications	4 (8.70)	7 (20.59)	2.332	0.127

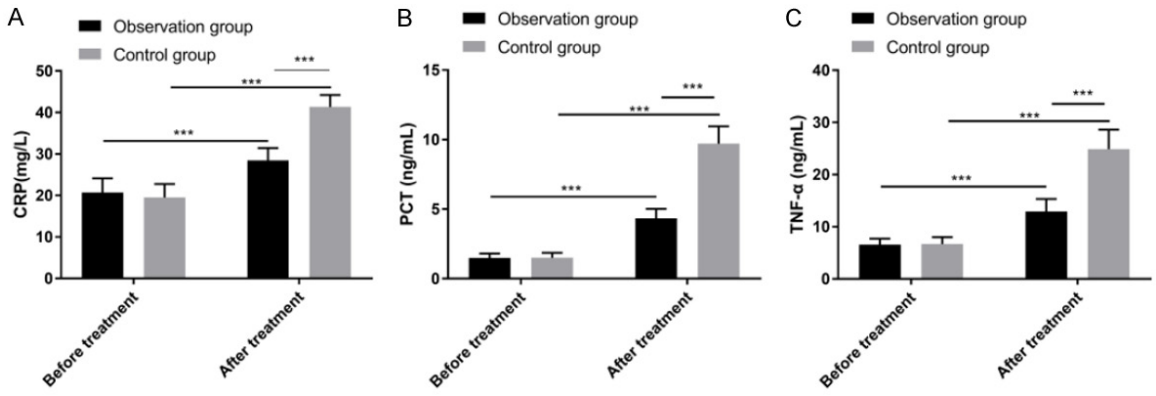

Figure 1. Comparison of inflammatory indicators. A. CRP levels before and after treatment in the two groups; B. PCT levels before and after treatment in the two groups; C. TNF-α levels before and after treatment in the two groups. CRP: C-reactive protein; PCT: calcitoninogen; TNF-α: tumor necrosis factor-α; ***P<0.001.

By comparing the surgical indexes of the two groups, we found that the operative time and LOS were shorter and intraoperative bleeding was less in the observation group than in the control group. This indicates that laparoscopic D2 radical gastrectomy is less invasive, and able to remarkably shorten the LOS and promote patients' postoperative recovery. Laparoscopy can magnify the field of view, and the tiny blood vessels and neuroanatomical structures can be clearly displayed, which improves the accuracy of operation [20], avoids damage to blood vessels and normal tissues, reduces intraoperative bleeding, decreases the postoperative pain, facilitates patients' early bedtime activities, and promotes recovery. In terms of inflammatory factors, patients' postoperative TNF-α, CRP and PCT levels were elevated compared to preoperative levels, but the changes were smaller in the observation group, which suggests that laparoscopic D2 radical gastrectomy produces less inflammation in the body.

PG I and PG II levels can accurately evaluate the secretory function of the gastric mucosa and are more sensitive to the condition of gastric mucosal lesions [21]. With GC, the patients have a rapid decrease in PG I level and a rapid increase in PG II level [22]. G-17 is secreted in gastric sinusoidal cells, which stimulates the division and differentiation of gastric mucosal cells and promotes gastric acid secretion, allowing accurate evaluation of gastric sinusoidal atrophy and its secretory function [23]. In

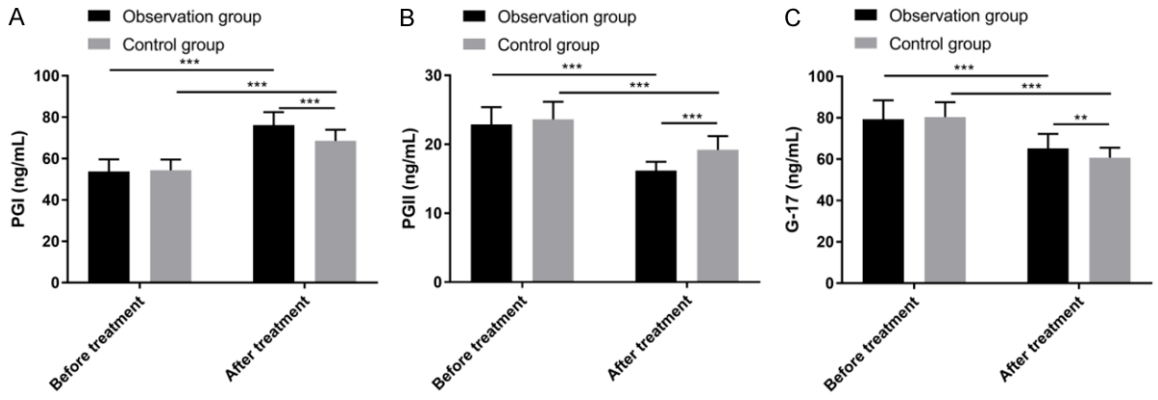

Figure 2. Comparison of gastrointestinal function. A. PG I levels of the two groups of patients before and after treatment; B. PG II levels before and after treatment in the two groups of patients; C. G-17 levels before and after treatment in the two groups of patients. G-17: gastric function gastrin 17; PG I: pepsinogen I; PG II: pepsinogen I; **P<0.01, ***P<0.001.

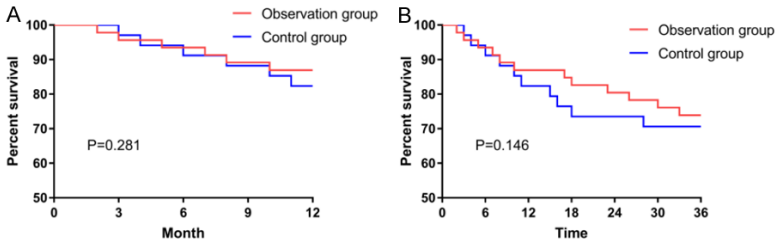

Figure 3. K-M curves of 1-year and 3-year survival of patients. A. K-M curves of 1-year survival in the two groups; B. K-M curves of 3-year survival in the two groups.

this study, the observation group had a more marked decrease in postoperative PG II level and a more marked increase in postoperative PG I level. The postoperative G-17 decreased in both groups due to surgery, but the decrease was less in the observation group, indicating that laparoscopic D2 radical gastrectomy was more efficacious in preserving gastrointestinal function. This study also found that there was no statistically significant difference in the 1- and 3-year survival rates between the two groups. This suggests that laparoscopic D2 radical gastrectomy can achieve a long-term outcome comparable to that of open gastrectomy.

Zhang et al. [24] found that patients received laparoscopic gastrectomy had shorter LOS, less blood loss and intraoperative transfusions, smaller trauma and faster recovery compared to those received open gastrectomy, which findings are similar to our study results. Nevertheless, their study also mentioned better survival rates at 3 and 5 years after laparoscopy, which differs from ours, perhaps due to differences in the procedure and the number of enrolled patients. Trastulli et al. [25] also conducted gastrectomy combined with D2 lymph node dissection, while they found no statistical difference in 5-year survival between the laparoscopic and open surgery groups. They discovered that although laparoscopic surgery did not increase the 5-year survival rate of patients, it can accelerate their postoperative recovery and reduce postoperative complications, which is also similar to our result.

The current study still has some shortcomings. First, this is a retrospective study, so the risk of unmeasurable bias in the analysis remains. Second, patients included in this study are the elderly over 60 years old, so the results cannot be extrapolated to all GC patients. Third, the statistical efficacy was lower in the laparoscopic group due to very low mortality and recurrence events, which may have contributed to the small difference in outcomes between the two groups.

To summarize, laparoscopic radical gastrectomy is more effective in elderly patients with advanced GC. This surgery can effectively suppress the postoperative inflammation and

improve the recovery of gastric function. Hence, it has high clinical application value.

Disclosure of conflict of interest

None.

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