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ORIGINAL ARTICLE

Comparison of clinical efficacy between laparotomy and laparoscopic radical surgery for gastric cancer and their effects on CRP, CEA and insulin resistance

Xudong Wu*, Xingguang Wang*, Yong Wang, Weichun Cui, Pengfei Liu

Department of Gastroenterological Surgery, Dongying People's Hospital, Dongying 257091, P.R. China.

*Xudong Wu and Xingguang Wang contributed equally to this study.

Summary

Purpose: *This study aimed to compare between the clinical efficacy of laparotomy and laparoscopic radical resection of gastric cancer and their effects on C-reactive protein (CRP), carcinoembryonic antigen (CEA) and insulin resistance.*

Methods: *210 patients with gastric cancer admitted to Dongying People's Hospital from September 2013 to July 2015 were included in this study. The patients were divided according to surgery type into the laparotomy group (n=104) and the laparoscopy group (n=106). The operative time, intraoperative bleeding, lymph node dissection, postoperative exhaust time and postoperative complications were recorded. Peripheral blood CRP and CEA levels were measured by enzyme-linked immunosorbent assay (ELISA). Fasting blood glucose (FBG), AND fasting insulin (FINS) levels were measured before operation and 1, 3 and 7 days after operation. All patients were followed up by telephone and letters for 5 years. The patients in the two groups were investigated by a quality of life questionnaire.*

Results: *The intraoperative bleeding and postoperative exhaust time in THE laparoscopy group were significantly lower than those in the traditional laparotomy group, while the operative time and the number of lymph node dissections were higher. The CRP and CEA in the laparoscopy group were significantly lower than in the laparotomy group on the 1st, 2nd and 3rd day after operation ($p<0.05$). The FBG, FINS and HOMA-IR in the laparoscopy group were significantly lower than those in the laparotomy group on the 1st and 3rd day after operation ($p<0.05$). The scores of quality of life in the laparoscopy group were lower than those in the laparotomy group ($p<0.05$).*

Conclusion: *In conclusion, laparoscopic radical resection of gastric cancer can reduce the levels of CRP, CEA and insulin resistance, while the degree of inflammation and insulin resistance after laparoscopy is lower than that after laparotomy, which is beneficial to postoperative recovery.*

Key words: *carcinoembryonic antigen, C-reactive protein, gastric cancer, insulin resistance, laparoscopic radical surgery*

Introduction

Gastric cancer is one of a malignant tumor with high incidence being the fifth most common cancer in the world [1,2]. At present, laparotomy and laparoscopy are the main clinical treatments for gastric cancer [3]. The prognosis of patients with gastric cancer depends to a great extent on whether radical resection can be performed. In recent years, the laparoscopic technique has developed [4,5] and gradually became an important option. Compared with laparotomy, which causes a large wound and increases the risk of infection due to long-time exposure of the abdominal cavity during operation [6], laparoscopic radical resection of gastric cancer has the advantages of being

Corresponding author: Dr. Xudong Wu. Department of Gastroenterological Surgery, Dongying People's Hospital, No. 317 Nanyi Rd, Dongying District, Dongying 257091, P.R. China.
Tel: +86 0546 8901209, Email: xpth33@163.com
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minimally invasive, requiring short hospitalization and having low incidence of adverse reactions [7]. Laparoscopic surgery forms a pneumoperitoneum through the introduction of carbon dioxide (CO_2), but this may cause or aggravate the stress response [8]. Moreover, Hiki et al found that the incidence of pancreatic fistula in laparoscopic distal gastric resection was high [9]. The question whether the laparoscopic-assisted radical resection of gastric cancer leads to a strong inflammatory reaction and insulin resistance has become of interest.

C-reactive protein (CRP) is a cyclic pentameric protein found in plasma, which helps complement bind to foreign and damaged cells, enhances the phagocytosis of macrophages (modulin-mediated phagocytosis), and is a marker of inflammation. Elevation of CRP can reflect the trauma of laparoscopic radical resection of gastric cancer to a certain extent [10]. Carcinoembryonic antigen (CEA) is a highly related glycoprotein involved in cell adhesion it is mainly used as a tumor marker to monitor the treatment of colorectal cancer, identify recurrence after surgical resection, and locate cancer diffusion by staging or by measuring biological body fluids. Detection of free cancer cells in gastric cancer resection can explain the levels of free cancer cells in gastric cancer patients to a certain extent [11]. Insulin resistance occurs when the body produces insulin under insulin-resistant conditions, so cells develop resistance to insulin and cannot effectively use it, leading to hyperglycemia [12,13]. When the surgical trauma is severe, insulin resistance develops as a protection mechanism, which is characterized by metabolic disorder and changes in physiological function. Therefore, we measured CRP, CEA and the degree of insulin resistance, and compared the safety and efficacy of laparotomy or laparoscopy for gastric cancer resection.

The purpose of this study was to analyze a series of clinical indexes such as CRP, CEA and insulin resistance in patients with gastric cancer who underwent laparotomy or laparoscopy in order to provide references for clinical treatment.

Methods

General materials

210 patients with gastric cancer admitted to Dongying People's Hospital from September 2013 to July 2015 were included in this study. The patients were divided according to surgery type into the laparotomy group (104 cases) and the laparoscopy group (106 cases). This study was approved by the Ethics Committee of Dongying People's Hospital. All the subjects have signed informed consent forms.

Inclusion and exclusion criteria

Inclusion criteria: all patients diagnosed with gastric cancer according to diagnostic criteria; patients treated in Dongying People's Hospital; patients WHO were 18 to 70 years old; patients who could comply with the investigation; signed informed consent forms by the patients or their families; patients WHO had a complete medical record.

Exclusion criteria: patients with heart, liver, spleen, lung, kidney and other important major organ disease; patients with mental illness and speech dysfunction; patients with diabetes; pregnant and lactating women; patients with lymph node, organ and tissue metastasis; patients with surgical contraindication; patients with drug allergy.

Surgical method

Laparotomy group: The patients were treated with routine laparotomy. General anesthesia and routine endotracheal intubation were given before the operation. After routine disinfection, a 15-20 cm incision was made in the middle of the abdomen to check and determine the location of the tumors, remove the lesions and perform lymph node dissection.

Laparoscopy group: General anesthesia and routine endotracheal intubation were given. The patients were placed in horizontal position and 1 cm transverse incision was made under the umbilicus to construct artificial pneumoperitoneum. Pneumoperitoneum pressure was maintained between 12 and 15 mmHg. Laparoscopy was used to determine the volume and location of the tumor, and to determine whether there were as well as the presence of metastatic nodules in the surrounding organs and tissues. Depending on the patient's condition, the diseased tissue was removed and lymph node dissection was performed.

Observation indices

Comparison of short-term therapeutic effects between the two groups

The operation time, intraoperative bleeding, lymph node dissection, postoperative exhaust time and surgical complications were recorded and compared between the two groups.

Detection of CRP and CEA in serum

Blood samples were collected before the operation and on the 1st, 2nd, 3rd and 7th day after the operation. The levels of CRP (IBL International, LD51031) and CEA (IBL International, RE59101) were detected by enzyme-linked immunosorbent assay (ELISA), and the operative steps were carried out strictly according to the instructions of the kit.

Detection of insulin resistance index (HOMA-IR)

Blood samples were collected before the operation and on the 1st, 3rd and 7th day after the operation. The glucose oxidase method was used for detecting FBG. The chemiluminescence method was used for detecting fasting insulin (FINS). The steady-state mode evaluation

method was used for calculating the insulin resistance index (HOMA-IR).

Observation of quality of life and prognosis

All patients were followed up by telephone and letters for 5 years. The patients in the two groups were investigated using the EORTC QOQ-22 questionnaire on the quality of life of patients with gastric cancer before the operation, and 6 months, 1 year and 2 years after the operation [14]. The improvement of patients' quality of life before and after the operation was evaluated comprehensively. The final score was processed. The total score was 50 points, and the higher the score, the worse the quality of life.

Statistics

SPSS24.0 statistical software (Shanghai Yuchuang Network Technology Co., Ltd.) was used to calculate all the results. Graphpad 8 (Shenzhen Tianruiqi Software Technology Co., Ltd.) software was used to plot all the graphics, and the results were checked twice. The counting data were represented in the form of rates. Chi-square (x^2) test was used for comparisons between groups. The measured data were expressed as mean ± standard deviation. T-test was used for comparisons between groups. Kaplan-Meier method was used for establishing the survival curve in the laparotomy and laparoscopy groups. Log-rank test was used to evaluate the differences in survival between the two groups. A p value < 0.05 was considered as statistically significant difference between the two groups.

Results

Comparison of general materials

There were no significant differences in age, sex, BMI, course of disease, tumor location, pathological classification, TNM stage, smoking, drinking and exercise between the control group and the study group (p>0.050), which proved that the two groups were comparable (Table 1).

Table 1. Comparison of clinical data

	Control group (n=104)	*Studied group (n=106)*	*x^2 or t*	*P*
Age (years)	49.42±9.68	48.77±10.24	0.473	0.637
Sex, n			<0.001	0.978
Male	62	63		
Female	42	43		
BMI (kg/m^2)	22.86±2.14	22.41±1.73	1.677	0.095
Course of disease (weeks)	5.74±1.04	5.72±1.36	0.119	0.905
Tumor location, n (%)			0.170	0.679
Sinuses Ventriculi	51 (49.04)	55 (51.89)		
Corpora Ventriculi	53 (50.96)	51 (48.11)		
Pathological classification, n (%)			0.389	0.943
Well-differentiated	17 (16.35)	14 (13.21)		
Moderately differentiated	42 (40.38)	45 (42.45)		
Poorly differentiated	25 (24.04)	28 (26.42)		
Undifferentiated	20 (19.23)	19 (17.92)		
TNM stage, n			0.176	0.916
I	31	29		
II	38	41		
III	35	36		
Smoking history, n (%)			0.318	0.573
Yes	58 (55.77)	55 (51.89)		
No	46 (44.23)	51 (48.11)		
Drinking history, n (%)			0.482	0.487
Yes	71(68.27)	77(72.64)		
No	33(31.73)	29(27.36)		
Exercise, n (%)			0.315	0.575
Yes	27 (25.96)	24 (22.64)		
No	77 (74.04)	82 (77.36)		

Comparison of operative indexes and postoperative complications

The intraoperative bleeding and postoperative exhaust time in the laparoscopy group were significantly lower than those in the traditional laparotomy group, while the operative time and the number of lymph node dissections were higher. There were significant differences in operative time, intraoperative bleeding, number of lymph node dissections and postoperative exhaust time between the laparoscopy group and the traditional laparotomy group (p<0.05).

Severe adverse reactions occurred in 6 cases (5.76% incidence of adverse reactions) in the traditional laparotomy group, including 2 cases of pulmonary infection, 1 case of urinary retention, 1 case of anastomotic fistula and 2 cases of gas-

Table 2. Comparison of surgical indexes between the two groups

Surgical Index	*Laparotomy group (n=104)*	*Laparoscopy group (n=106)*	*t*	*P*
Operative time (min)	204.26±19.39	238.39±21.52	12.072	<0.001
Intraoperative bleeding (mL)	195.42±54.48	157.19±21.38	6.717	<0.001
Number of lymph node dissections	13.21±2.23	18.37±3.85	11.863	<0.001
Postoperative exhaust time (h)	68.39±9.21	53.29±8.73	12.206	<0.001

Table 3. Comparison of complications

	Laparotomy group (n=104)	*Laparoscopy group (n=106)*	x^2	*P*
Pulmonary infection	2	1		
Urinary retention	1	1		
Anastomotic Fistula	1	1		
Gastrasthenia	2	0		
Complications (cases)	6	3	1.105	0.293

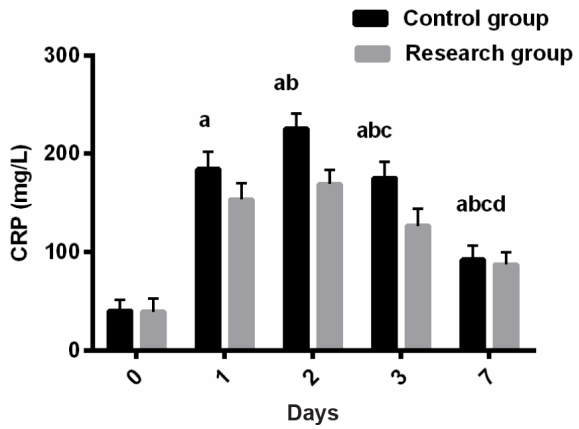

Figure 1. CRP levels in both groups before treatment and 1, 2, 3 and 7 days after treatment. CRP in the two groups increased on the 1st, 3rd and 7th day after operation (p<0.05), and reached the peak on the second day after the operation. The level of CRP in serum in the laparoscopy group (169.24 ± 14.34 mg/L) was significantly lower than that in the laparotomy group (225.62 ± 15.39 mg/L) on the second day after treatment, p<0.001. **a** indicates that compared with the same group of preoperative CRP, p<0.05. **b** indicates that compared with the level of CRP 1 day after treatment in the same group, p<0.05. **c** indicates that compared with the level of CRP 2 days after treatment in the same group, p<0.05. **d** indicates that compared with the level of CRP 3 days after treatment in the same group, p<0.05.

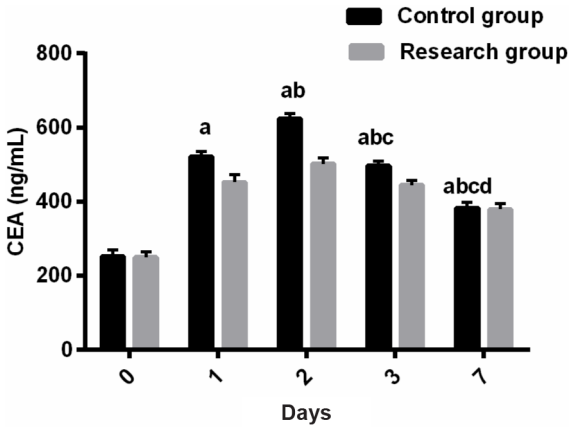

Figure 2. CEA levels in both groups before treatment and 1, 2, 3 and 7 days after treatment. CEA in the two groups increased on the 1st, 3rd and 7th day after operation (p<0.05) and reached the peak on the second day after the operation. The level of CEA in serum in the laparoscopy group (502.31 ±16.32 ng/mL) was significantly lower than that in the laparotomy group (623.42 ± 15.24 ng/mL) on the second day after treatment (p<0.001). **a** indicates that compared with the same group of preoperative CEA, p<0.05. **b** indicates that compared with the level of CEA 1 day after treatment in the same group, p<0.05. **c** indicates that compared with the level of CEA 2 days after treatment in the same group, p<0.05. **d** indicates that compared with the level of CEA 3 days after treatment in the same group, p<0.05.

trasthenia. Severe adverse reactions occurred in 3 cases (2.83% incidence of adverse reactions) in the laparoscopy group, including 1 case of pulmonary infection, 1 case of urinary retention and 1 case of anastomotic fistula (Tables 2 and 3).

Comparison of CRP and CEA levels in both groups before and after operation

CRP and CEA increased in the two groups on the 1st, 2nd, 3rd and 7th day after the operation ($p<0.05$), and reached the peak on the second day after the operation. The level of CRP in serum in the laparoscopy group (169.24 ±14.34 mg/L) was significantly lower than that in the laparotomy group (225.62 ±15.39 mg/L) on the second day after treatment ($p<0.001$).

The level of serum CEA in the laparoscopy group (502.31 ± 16.32 ng/mL) was significantly lower than that in the laparotomy group (623.42 ± 15.24 ng/mL) on the second day after treatment ($p<0.001$). CRP and CEA in the laparoscopy group were significantly lower than those in the control group on the 1st, 2nd, 3rd and 7th day after the operation ($p<0.05$) (Figures 1 and 2).

Comparison of fasting plasma glucose (FBG), fasting insulin (FINS) and insulin resistance index (HOMA-IR) between the two groups before and after operation

The levels of FBG, FINS and HOMA-IR in the two groups were higher on the 1st, 3rd and 7th day after the operation than those before the operation ($P < 0.05$). The highest level of FBG in the

Table 4. Comparison of quality of life scores at different times before and after operation between the two groups

Group	*Preoperative*	*Half a year after operation*	*One year after operation*	*Two years after operation*
Laparotomy group	43.42±1.32	37.51±1.54*	32.52±1.63*	24.13±1.24*
Laparoscopy group	43.34±1.39	33.85±1.62*#	29.45±1.81*#	21.57±2.11*#
t	0.428	16.773	12.918	10.692
P	0.669	<0.001	<0.001	<0.001

* indicates that there was a significant difference between before operation and after operation ($p<0.005$). # indicates that there was a significant difference between the two groups ($p<0.005$).

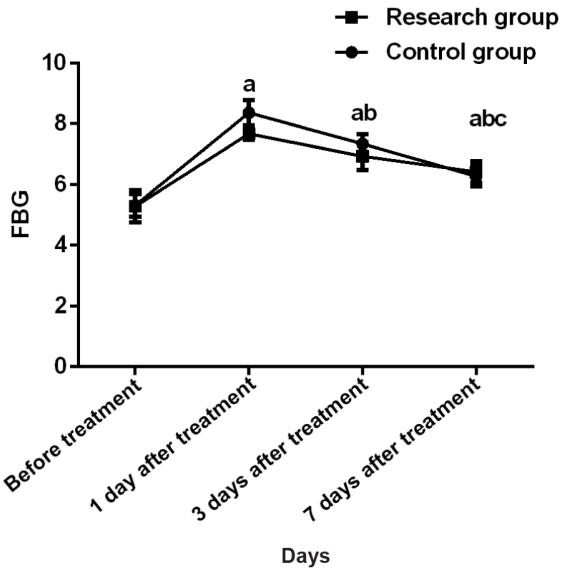

Figure 3. FBG levels in both groups before treatment and 1, 3 and 7 days after treatment. FBG in the two groups increased at 1, 3 and 7 days after operation ($p<0.05$). The highest level of FBG in the laparotomy group was (8.36 ±0.42) on the first day after operation, which was higher than that in the laparoscopy group (7.67 ±0.21), $p<0.05$. **a** indicates that compared with the same group of preoperative FBG, $p<0.05$. **b** indicates that compared with the level of FBG 1 day after treatment in the same group, $p<0.05$. **c** indicates that compared with the level of FBG 3 days after treatment in the same group, $p<0.05$.

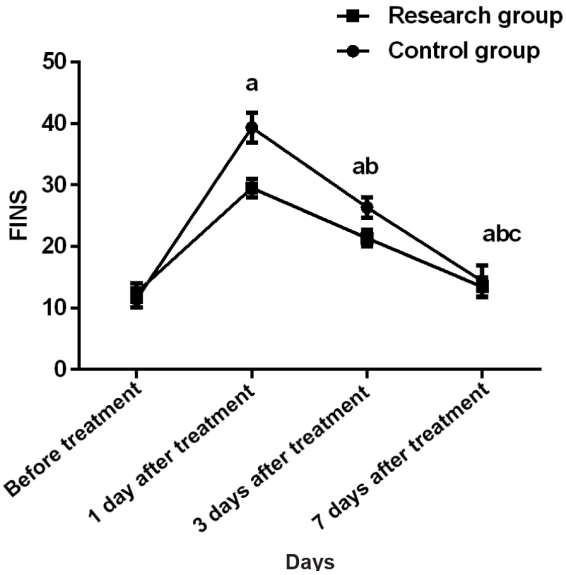

Figure 4. FINS levels in both groups before treatment and 1, 3 and 7 days after treatment. The levels of FBG and FINS in the two groups were higher on the 1st and 3rd day after operation than those before operation ($p<0.05$). The FINS level in the laparoscopy group reached the peak value of 29.54 ±1.50 on the first day after operation, which was lower than that in the laparotomy group (39.34 ±2.24), $p<0.05$. **a** indicates that compared with the same group of preoperative FINS, $p<0.05$. **b** indicates that compared with the level of FINS 1 day after treatment in the same group, $p<0.05$. **c** indicates that compared with the level of FINS 3 days after treatment in the same group, $p<0.05$.

laparotomy group (8.36 ± 0.42) on the first day after the operation was higher than that in the laparoscopy group (7.67 ± 0.21), p<0.05. FINS in the laparoscopy group reached the peak value of 29.54 ± 1.50 on the first day after the operation, which was lower than that in the laparotomy group (39.34 ± 2.24), p<0.05. FBG, FINS and HOMA-IR in the laparoscopy group were significantly lower than those in the laparotomy group on the 1st and 3rd day after the operation (p<0.05) Figures 3, 4 and 5).

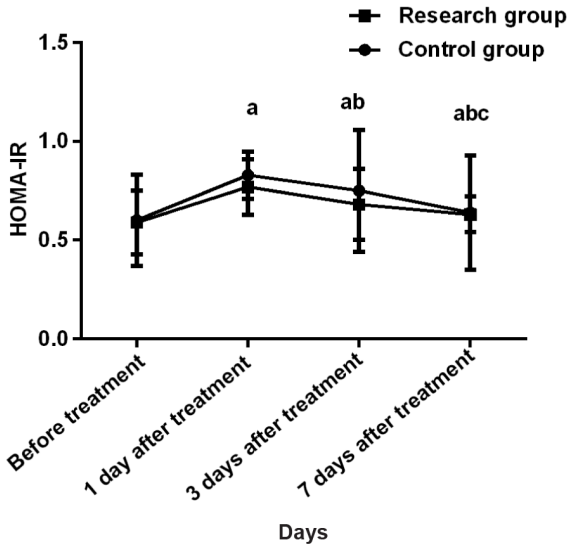

Figure 5. HOMA-IR levels in both groups before treatment and 1, 3 and 7 days after treatment. The levels of HOMA-IR in the two groups were higher on the 1st and 3rd day after operation than those before the operation (p<0.05). HOMA-IR in the laparoscopy group was lower than that in the laparotomy group (p<0.05). **a** indicates that compared with the same group of preoperative HOMA-IR, p<0.05. **b** indicates that compared with the level of HOMA-IR 1 day after treatment in the same group, p<0.05. **c** indicates that compared with the level of HOMA-IR 3 days after treatment in the same group, p<0.05.

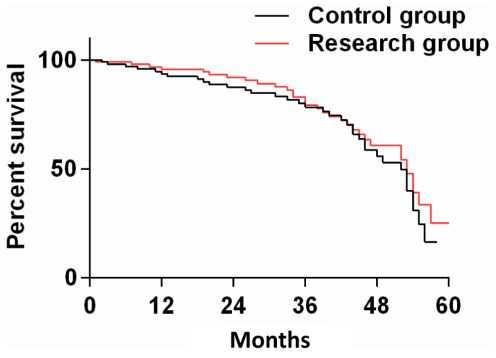

Figure 6. Survival curves in the two groups of patients. The 5-year survival rate was 65.38% (68/104) in the laparotomy group and 68.86% (73/106) in the laparoscopy group. There was no significant difference in the 5-year survival rate between the two groups (p>0.05).

Quality of life score

There was no significant difference in quality of life score between the two groups before the operation (p>0.005). The scores of quality of life decreased in the two groups after the operation. The score of quality of life in the laparoscopy group was lower than that in the laparotomy group (p<0.005) (Table 4).

Survival

The patients were followed up for 5 years by telephone, reexamination, letters and so on. The follow-up success rate was 83.31%. The 5-year survival rate was 65.38% (68/104) in the laparotomy group and 68.86% (73/106) in the laparoscopy group. There was no significant difference in the 5-year survival rate between the two groups (p>0.05) (Figure 6).

Discussion

Gastric cancer is the malignant tumor of the digestive system with the highest incidence, and the incidence of gastric cancer which has been increasing in recent years [15,16]. Traditional radical resection of gastric cancer can lead to serious secondary infection and dysfunction, and has high postoperative complications and mortality. Therefore, laparoscopic radical resection of gastric cancer is gradually accepted by the patient's family. At present, most studies suggest that laparoscopic radical resection of gastric cancer can achieve the same therapeutic effect as laparotomy [17]. However, there is no clear conclusion to whether laparoscopy radical resection of gastric cancer this surgical procedure aggravates stress, leads to serious immunosuppression and promotes micrometastasis. In this study, a series of clinical parameters such as CRP, CEA and insulin resistance were analyzed in order to provide a basis for the safety and feasibility of laparoscopic radical resection of gastric cancer.

The intraoperative bleeding and postoperative exhaust time in the laparoscopy group were significantly lower than those in the traditional laparotomy group, while the operative time and the number of lymph node dissections were higher. This is because laparoscopic radical resection of gastric cancer is more difficult for multi-level and multi-directional anatomical separation around the gastric cancer [18]. Under laparoscopy the patient vessels, nerves and tendons, can be observed more clearly, which is beneficial to the complete resection of lymph nodes and causes less damage to blood vessels, the effects being relatively similar

with those of laparotomy. These results fully reflect the minimally invasive advantages of laparoscopy [19]. When Wang et al studied laparoscopic and open gastrectomy in the treatment of elderly patients [20] and Furuta et al. studied the laparoscopic resection of gastric cancer combined with new chemotherapy [21], the results were consistent with our study, which proves the excellent effect of laparoscopic surgery in the treatment of tumors.

CRP and CEA reached the peak value on the 2nd day after the operation in both groups. On the 1st, 2nd and 3rd day after the operation, CRP and CEA in the laparoscopy group were significantly lower than those in the laparotomy group, while the CRP level in the laparoscopy group was lower than that in the laparotomy group. These results suggest that the stress response of laparoscopic surgery is mild, which may be related to the small incision, good visual field, less sharp cutting and damage to the surrounding tissues [22,23]. The CEA level in the laparoscopy group was lower than that in the laparotomy group, which indicates that the detection rate of free cancer cells in the laparoscopy group was lower than that in laparotomy group. HOMA-IR increased on the 1st and 3rd day after the operation in both groups. On the 1st and 3rd day after the operation, FBG, FINS and HOMA-IR in the laparoscopy group were significantly lower than those in the laparotomy group, suggesting that laparoscopic radical resection of gastric cancer led to mild postoperative insulin resistance.

In order to prevent or lower postoperative insulin resistance in patients after surgery, anesthesia and analgesia were performed epidurally on middle chest, the release of catecholamines and cortisol was reduced and minimally invasive laparoscopic surgery was performed; the guideline of preoperative fasting was breached and patients eat carbohydrates before surgery [24-27].

There was no significant difference in the 5-year survival rate between the two groups, suggesting that there was no difference in prognosis. The quality of life is an important reflection of the factors influencing cancer patients. More and more clinicians are committed to the improvement of the quality of life of cancer patients which has become an important standard for the evaluation of the therapeutic effect of treatment [28]. We followed up our patients for 2 years and showed that the quality of life in the laparoscopy group was higher, which may be related to the reduced psychological and physical effects of minimally invasive surgery.

Although difference between surgical indexes and complications during operation was observed, factors influencing the quality of life were not observed, the recurrence influencing factors of tumors was not analyzed, and the postoperative effect of laparoscopic surgery on patients undergoing chemotherapy was not taken into account. Therefore, this study has certain limitations. Future research should thoroughly analyze the factors influencing postoperative patients' quality of life, expand the sample, and give a deeper evidence providing further evidence to support the results of this study.

To sum up, laparoscopic laparoscopic radical resection of gastric cancer is safe, reliable, minimally invasive, and can remove a high number of lymph nodes, thus resulting in mild insulin resistance, which is beneficial to postoperative recovery.

Conflict of interests

The authors declare no conflict of interests.

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