



# Effect of laparoscopy on serum inflammatory factor, oxidative stress and immune function in patients with rectal cancer

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## ABSTRACT

**Objective:** To investigate the effect of laparoscopy on inflammatory factor, oxidative stress and immune function in patients with rectal cancer. **Methods:** According to random data table method, 80 cases of rectal cancer were randomly divided into the control group ( $n=40$ ) and observation group ( $n=40$ ), patients in the control group were given conventional open surgery and the observation group received laparoscopic surgery. The level of the serum inflammatory factor, oxidative stress and immune function before and after surgery were compared. **Results:** The levels of serum hs-CRP, IL-6, TNF- $\alpha$ , MDA, SOD, CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> in the two groups before treatment were not statistically significant. The level of serum hs-CRP, IL-6 and TNF- $\alpha$  in the two groups were increased firstly and then decreased, which at 1 d and 3 d after operation were significantly higher than those in the same group before operation and the observation group levels were significantly higher than those in the control group at same time point. The level of serum MDA increased first and then decreased in both groups, and the level of SOD decreased firstly and then increased in two groups; the level of MDA in the two groups after 1 d and 3 d of operation were significantly higher than those before operation, and the observation group was significantly lower than the control group at the same time; the levels of SOD in the two groups after operation of 1 d and 3 d were significantly lower than those before operation, and the observation group was significantly higher than the control group at the same time. The levels of T lymphocyte: serum CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> in the two groups were decreased at first and then increased, which at 1 d, 3 d after operation were significantly lower than those in the same group before operation; the observation group level were significantly higher than those in the control group after 1 d and 3 d, there was statistical significant difference. The levels of serum CD8<sup>+</sup> in the two groups were increased at first and decreased subsequently, which at 1 d and 3 d after operation were significantly higher than those in the same group before operation and the observation group levels were significantly lower than those in the control group at same time point, the difference was statistical significant. **Conclusion:** Compared with traditional open surgery, laparoscopic resection can reduce patient's inflammation, stress response and immune suppression, and the overall effect is better and with important clinical value.

## 1. Introduction

Rectal cancer was the most common malignant tumors in digestive

tract, its pathogenesis mainly related to social environment, diet habit. In recent, morbidity of rectal cancer was in increasing trend year by year, usually company with hematochezia, obstruction and other symptoms in patients, which severely affected life quality of patients[1]. Now treatment for rectal cancer chiefly was radical operation, laparoscopic surgery had many characteristics such as small wound, fast recovery and little complication after operation compared with conventional open surgery, which was widely used in treatment of rectal cancer[2]. At present research proved that: minimally invasive surgery could reduce inflammatory and

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oxidative reaction, protect immune function better[3]. This research explored effect of laparoscopy on inflammatory factor, oxidative stress and immune function in patients with rectal cancer.

## 2. Research subjects and method

### 2.1. Research subjects

A total of 80 cases of patients with rectal cancer who were admitted in our hospital from December 2015 to May 2017 were selected as research subject. All subjects were conformed to selection criteria of this research, inclusion criteria: (1) Accorded with WHO cancer diagnostic criteria established by "tumor pathology and genetics of digestive system"[4]; (2) Age were 30-65 years old; (3) Cardiac, pulmonary, liver, kidney function were normal before treatment; (4) without disturbance of water and electrolyte, acid-base imbalance; (5) All of patients signed informed consent and willing to participate. Exclusion criteria: (1) Juveniles, over 80 years old or female in pregnancy and breastfeeding; (2) Combined with other malignant tumors; (3) Accepted radio-chemotherapy recently; (4) Combined with severe hepatic and renal dysfunction; (5) Cannot complete treatment according to course of treatment and take off in the midway, moreover with incomplete clinical data. All patients was divided into control group ( $n=40$ ) and observation group ( $n=40$ ) according to random data table, in control group 25 males, 15 females, aged from 30-61 years old; in observation group 21 males, 19 females, aged from 32-65 years old. There was no difference in general data of both groups ( $P>0.05$ ). This research was conformed to standard of ethic committee of hospital; process met the specification and was approved to conduct.

### 2.2 Treatment method

Operations of both groups were conducted by same operation group, according to radical principles of tumor treatment. Patients of observation group were conducted laparoscopic radical surgery, process as following: firstly established CO<sub>2</sub> pneumoperitoneum, kept pressure at 13-15 mmHg, adopted routine four or five-hole operation. For example, the five-hole operation, openings at belly button or 10 mm of pubis upward, inserted laparoscopic lens (diameter was 3-10 mm) to abdominal cavity, got 12 mm to open hole at 5 cm of left umbilical region as the main operation hole, made 5 mm incision at left and right upper abdominal clavicular line and right lower quadrant. In processing of operation, strictly abide by "Chinese laparoscopic radical treatment guidance"[5]. Control group was conducted incision at midsection of abdomen or along with rectus abdominis. Conventional medication was same of both groups after operation.

**Table 1.**

Comparison of inflammatory factors level of both groups.

Group	<i>n</i>	Treatment time	hs-CRP (mg/L)	IL-6 (ng/L)	TNF- $\alpha$ (ng/L)
Control group	60	Before operation	6.15 $\pm$ 3.17	8.19 $\pm$ 4.35	37.95 $\pm$ 13.17
		1 d after operation	62.95 $\pm$ 16.78*	65.83 $\pm$ 21.52*	101.35 $\pm$ 32.11*
		3 d after operation	40.25 $\pm$ 16.57*	38.17 $\pm$ 12.93*	78.17 $\pm$ 23.39*
Observation group	60	Before operation	6.12 $\pm$ 3.08	8.21 $\pm$ 4.22	37.67 $\pm$ 11.89
		1 d after operation	37.35 $\pm$ 15.82* <sup>#</sup>	35.79 $\pm$ 10.98* <sup>#</sup>	76.28 $\pm$ 26.32* <sup>#</sup>
		3 d after operation	26.58 $\pm$ 12.13* <sup>#</sup>	15.59 $\pm$ 7.23* <sup>#</sup>	54.22 $\pm$ 15.73* <sup>#</sup>

Note: Compared with before operation in same group, \* $P<0.05$ ; compared with control group of same time point, <sup>#</sup> $P<0.05$ .

### 2.3 Observation index

Observed respectively inflammatory factors, oxidative stress and immune function level of both groups before operation and 1 d and 3 d of post-operation: extracted 10 mL of fasting periphery venous blood of patients, put common tube for standing a few minutes, following by centrifuge 10 min, 3 000 r/min, collected supernatant in EP tube, stocked at -20 °C freezer for detection. (1) Observation of inflammatory factors: tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) was measured by radioimmunoassay, kits were purchased from Shanghai Sangon bio-engineering Co. Ltd; ELISA was applied to detect interleukin-6 (IL-6), its corresponding kits were purchased from Shanghai Meilian biotechnology Co., Ltd. Hypersensitive C reaction protein (hs-CRP) level was detected by latex-enhanced immunoturbidimetric assay (Kits was provided by Shanghai Ruikang bio-technology Co., Ltd.). (2) Observation of oxidative stress level: serum malondialdehyde (MDA) (thiobarbituric acid method), superoxide dismutase (SOD) (Xanthine oxidase method). (3) Detection of immune function: flow cytometry was used to detect CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup>, operation was strict with kits introduction.

### 2.4. Statistical analysis

Statistical Software SPSS 17.0 was used for all data processing and analyzing, inflammatory factors, oxidative stress and immune function indexes were conformed to normal distribution and represented by Mean  $\pm$  SD, t-test was applied to comparison of intra-group before and after treatment and inter-block after treatment,  $P<0.05$  indicated the difference was statistical significant.

## 3. Results

### 3.1. Comparison of inflammatory factors level of both groups

Before treatment serum hs-CRP, IL-6, TNF- $\alpha$  in observation group and control group were no obvious difference ( $P>0.05$ ). After operation, hs-CRP, IL-6, TNF- $\alpha$  level of both groups was increased firstly and decreased subsequently, these level of 1 d, 3 d after operation were obviously higher than before operation, moreover hs-CRP, IL-6, TNF- $\alpha$  in observation group after 1 d, 3 d of operation were respectively (37.35 $\pm$ 15.82), (35.79 $\pm$ 10.98), (76.28 $\pm$ 26.32) and (26.58 $\pm$ 12.13) mg/L, (15.59 $\pm$ 7.23)  $\mu$ g/L, (54.22 $\pm$ 15.73)  $\mu$ g/L, which was significantly lower than control group at same time point, the difference was significant ( $P<0.05$ ). As shown in Table 1.

### 3.2 Comparison of serum MDA, SOD level of both groups

Before operation, there was no obvious difference in serum MDA, SOD level of both groups ( $P>0.05$ ). The level of serum MDA increased first and then decreased and level of SOD decreased firstly and then increased in both groups after operation; level of MDA in the two groups after 1 d and 3 d of operation were significantly higher than those before operation, and the observation group was significantly lower than the control group at the same time ( $P<0.05$ ); the levels of SOD in the two groups after operation of 1 d and 3 d were significantly lower than those before operation, and the observation group was significantly higher than control group at same tie point, there was significant difference ( $P<0.05$ ). As shown in Table 2.

**Table 2.**

Comparison of serum MDA, SOD level of both groups.

Group	n	Treatment time	MDA (mmol/L)	SOD (U/mL)
Control group	60	Before operation	4.92±1.17	94.16±12.23
		1 d after operation	11.06±3.45 <sup>*</sup>	42.54±9.33 <sup>*</sup>
		3 d after operation	7.58±2.11 <sup>*</sup>	67.69±11.96 <sup>*</sup>
Observation group	60	Before operation	4.87±1.21	93.95±12.16
		1 d after operation	7.02±1.73 <sup>*#</sup>	67.56±10.27 <sup>*#</sup>
		3 d after operation	5.77±1.19 <sup>*#</sup>	84.35±11.82 <sup>*#</sup>

Note: Compared with before operation in same group, <sup>\*</sup> $P<0.05$ ; compared with control group of same time point, <sup>#</sup> $P<0.05$ .

### 3.3 Comparison of immune function level of both groups

CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> level in observation group and control group was no difference ( $P>0.05$ ). CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> level of both groups was decreased firstly and increased subsequently after operation, these level at 1 d, 3 d after operation was significantly lower than before operation, moreover CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> level in observation group at 1 d, 3 d after operation were (44.57±6.21), (28.89±3.72), (1.25±0.19) and (57.65±8.22), (35.53±6.19), (1.38±0.15) which was dramatically higher than control group at same time point, there was significant difference ( $P<0.05$ ). moreover, CD8<sup>+</sup> level of both groups was increased firstly and decreased subsequently after operation, the level at 1 d, 3 d after operation was significantly higher than before operation, CD8<sup>+</sup> level in observation group at 1 d, 3 d after operation was significantly lower than control group at same time point, the difference was significant ( $P<0.05$ ). As shown in Table 3.

**Table 3.**

Comparison of immune function of both groups.

Group	n	Treatment time	CD3 <sup>+</sup> (%)	CD4 <sup>+</sup> (%)	CD8 <sup>+</sup> (%)	CD4 <sup>+</sup> /CD8 <sup>+</sup>
Control group	60	Before operation	61.36±10.57	40.57±6.63	26.76±3.32	1.36±0.58
		1 d after operation	40.63±6.37 <sup>*</sup>	25.63±3.35 <sup>*</sup>	38.49±4.56 <sup>*</sup>	1.02±0.13 <sup>*</sup>
		3 d after operation	52.48±8.31 <sup>*</sup>	31.09±5.76 <sup>*</sup>	33.03±3.06 <sup>*</sup>	1.11±0.16 <sup>*</sup>
Observation group	60	Before operation	60.97±10.43	41.78±6.35	27.58±3.21	1.35±0.61
		1 d after operation	44.57±6.21 <sup>*#</sup>	28.89±3.72 <sup>*#</sup>	35.36±4.67 <sup>*#</sup>	1.25±0.19 <sup>*#</sup>
		3 d after operation	57.65±8.22 <sup>*#</sup>	35.53±6.19 <sup>*#</sup>	30.37±3.59 <sup>*#</sup>	1.38±0.15 <sup>*#</sup>

Note: Compared with before operation in same group, <sup>\*</sup> $P<0.05$ ; compared with control group of same time point, <sup>#</sup> $P<0.05$ .

## 4. Discussion

As a special trauma, operation could cause body inflammatory reaction, hs-CRP, IL-6, TNF- $\alpha$  were thought as important indexes of inflammatory reaction in acute stage, usually indicated the size of operative trauma[6,7]. hs-CRP was a kind of acute stage protein generated by liver cell, it could reflect post-traumatic acute stage reaction as an independent index and related to degree of trauma[8]. IL-6 was a multifunctional inflammatory factor, it could promote coagulation, activate liver cell produce acute stage protein and participate in inflammatory reaction; TNF- $\alpha$  was main pro-inflammatory factor in body, operative stimuli could result in macrophage activity increasing in general body especially in abdomen cavity locally, promote secretion of IL-6, TNF- $\alpha$  [9,10]. This research showed that hs-CRP, IL-6, TNF- $\alpha$  level of both groups was increased at 1 d after operation and decreased obviously at 3 d after operation, moreover these level in observation group were significantly lower than control group at same time point. All of these revealed that both open surgery and laparoscopic surgery could lead to inflammatory reaction, whereas due to small trauma of laparoscopic surgery, therefore its inflammatory reaction was milder than open surgery.

Operative trauma also was able to activate stress reaction. MDA was ultimate metabolite released when oxygen free radical reacted with multivalent unsaturated fatty acid of intramembrane, it was important marker that measured degree of oxidative stress and tissue injury[13]. SOD was a antioxidase and a critical member of oxidative defense system, maintained balance of oxidation and anti-oxidation through eliminating free radical in body, prevented cells from injury[14,15]. This research revealed that level of serum MDA increased first and then decreased in both groups, and level of SOD decreased firstly and then increased in two groups; and level of MDA in the two groups after 1 d and 3 d of operation were significantly higher than those before operation, moreover observation group was significantly lower than the control group at the same time ( $P<0.05$ ); the level of SOD in the two groups after operation of 1 d and 3 d were significantly lower than those before operation, the observation group was significantly higher than control group at same time point. This result indicated that both open surgery and laparoscopic surgery were able to cause oxidative stress, compared with laparoscopic surgery, oxidative stress resulted from open surgery was stronger, the reason was that open surgery lead to large trauma, free radical increased produced by stress reaction which made lipid per-oxidation, thereby generated more MDA, meanwhile consumption of SOD was increased subsequently.

T lymphocytes was multipotential stem cells from bone marrow, played critical role in cellular immune function and immunoregulation[16,17]. CD3<sup>+</sup> T cell was the general terms of mature T cell with common T cell function [18]; human mature T cell could be divided into CD4<sup>+</sup> and CD8<sup>+</sup> T cell according to different phenotype, CD8<sup>+</sup> T cell was named as toxic T cell, with eliminating virus and adhesive function[19]; CD4<sup>+</sup> T cell as adjuvant T cell could release a large number of cytokines and enhance anti-tumor effect[20]; CD4<sup>+</sup>/CD8<sup>+</sup> reflected immune state of host, ratio was 1.2-2.0, immune dysfunction would cause this ratio decreased which was critical indexes of measuring severe degree and prognosis of disease[21]. This research showed that serum CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> level of both groups was decreased firstly and increased subsequently after operation, at 1 d, 3 d after operation this level was significantly lower than before operation, moreover CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> level in observation group at 1 d, 3 d after operation were dramatically higher than control group at same time point; CD8<sup>+</sup> level of both groups was increased firstly and decreased subsequently after operation, the level at 1 d, 3 d after operation was significantly higher than before operation, CD8<sup>+</sup> level in observation group at 1 d, 3 d after operation was significantly lower than control group at same time point. This result revealed that both open surgery and laparoscopic surgery were able to inhibit cellular immune function, compared with open surgery, inhibition from laparoscopic surgery was slight. This result was identical to report of Pan Hongshu et al[22], whereas its mechanism was still further to explore. In conclusion, both rectal cancer radical surgeries could affect inflammatory reaction, oxidative stress and inhibition of cellular immune function. Compared with conventional open surgery, inflammation, oxidative stress, inhibition of cellular immune function, body injury of laparoscopic surgery were mild, the general recovery was better, with important clinical significance.

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