Effects of laparoscopic minimally invasive surgery on coagulation, antioxidant function, angiogenesis, IGF-1 and IFN-γ levels in rectal cancer patients

Chun-Guang Zhang¹, Qing-Ya Tan², Yuan-Li Kuang¹, Zhi-Ming Tan¹✉

¹ Department of General Surgery, Chongqing Kaizhou District People’s Hospital, Chongqing 405400, China
² Respiratory Medicine, Chongqing Kaizhou District People’s Hospital, Chongqing 405400, China

ARTICLE INFO

Article history:
Received 12 Oct 2018
Received in revised form 1 Nov 2018
Accepted 9 Nov 2018
Available online 14 Nov 2018

Keywords:
Laparoscopy
Rectal cancer
Coagulation
Anti-oxidation
Angiogenesis
IGF-1
IFN-γ

ABSTRACT

Objective: To investigate the effects of laparoscopic minimally invasive surgery on coagulation, antioxidant function, angiogenesis, IGF-1 and IFN-γ levels in rectal cancer patients. Methods: A total of 90 patients with rectal cancer admitted to general surgery in our hospital from March 2016 to December 2017 were randomly divided into control group (n=45) and observation group (n=45), the control group underwent conventional open surgery and the observation group underwent laparoscopic radical resection. The blood coagulation function, antioxidant capacity, angiogenesis, IGF-1 and IFN-γ levels were compared between the two groups. Results: Before treatment, there was no significant difference in coagulation function, antioxidant capacity, angiogenesis, IGF-1 and IFN-γ levels between the two groups. After treatment, there was no significant difference in PT and APTT between the two groups, while FIB and DD were significantly increased compared with before treatment, and the FIB and DD of the observation group increased significantly compared with the control group; the SOD and GSH of the two groups were significantly lower than those before treatment, while the MDA was significantly increased compared with that before treatment, the decrease of SOD, GSH and the increase of MDA in the observation group was significantly greater than that of the control group; the levels of VEGF and MMP-9 in the two groups were significantly lower than those before treatment, and the VEGF and MMP-9 in the observation group were significantly lower than those in the control group; the IFN-γ levels in the two groups were significantly higher than those before treatment, and the IFN-γ was significantly increased in the observation group compared with the control group. Conclusions: Laparoscopic surgery for patients with rectal cancer can easily cause hypercoagulable state of the patient’s blood, but it can effectively avoid tumor metastasis and less stress damage, and further promote the rehabilitation of the patients, which is worthy of clinical promotion.

1. Introduction

Rectal cancer is a common malignant tumor disease of the digestive tract. With the rise of people’s quality of life, changes in eating habits and social environment, the incidence of rectal cancer has increased year by year. Patients with rectal cancer often have symptoms such as blood in the stool and obstruction, which seriously endanger the physical and mental health of patients[1,2]. Studies have confirmed that postoperative coagulation disorders, stress damage and disorders of related factors occur in patients with rectal cancer[3–5]. In recent years, laparoscopic surgery has been widely used in the clinical practice of rectal cancer treatment because of its minimal trauma, low pain, recurrence rate and less complications[6–7]. In order to understand the specific mechanism of laparoscopic surgery for rectal cancer patients, this study used...
laparoscopic minimally invasive surgery for patients with rectal cancer to explore the treatment of coagulation, anti-oxidation, angiogenesis, IGF-1 and IFN-γ. The effect of the level. It is reported as follows.

2. Data and methods

2.1 General information

A total of 90 patients with rectal cancer admitted to the General Hospital of Kaizhou District People’s Hospital of Chongqing from March 2016 to December 2017 were randomly divided into the control group (n=45) and the observation group (n=45). In the control group, 29 patients, 16 females, aged 40-76 years old, with a course of 2 to 5 years, tumor diameter 2 to 6 cm; In the observation group, 18 females, aged 41-75 years old, with a disease duration of 1 to 5 years, tumor diameter 2-5 cm; the general data of the two groups were not significantly different (P>0.05), which was comparable, and the patients and their families have signed informed consent of the study.

2.2 Inclusion and exclusion criteria

Inclusion criteria: All subjects were diagnosed by clinical examination and imaging diagnosis, all of which met the diagnostic criteria related to rectal cancer; the first onset; no recent abdominal surgery; no electrolytes and acid-base imbalance. Exclusion criteria: those with other malignant tumors; those with multiple key organ dysfunctions; those with immune diseases, chronic infections and blood diseases.

2.3 Treatment method

Before the operation, patients of both groups were selected for appropriate body position, and they were given general anesthesia, sterile disinfection, and surgery according to the principle of rectal cancer. Patients in the control group underwent open laparotomy, and a 12-14 cm incision was made in the middle of the abdomen. The laparotomy was performed layer by layer to fully expose the mesenteric vessels, clear the surrounding lymph nodes, cut and close abdomen. Patients in the observation group were treated with laparoscopic surgery, establish a CO2 pneumoperitoneum with a pressure of 12-15 mmHg, Observed holes and two operating holes were established under the umbilicus and at both sides of the Mcmaster. Two operation holes were established on both sides of the umbilical level and 20 mm on the outer edge. The rectal cancer lesions and metastases were examined and evaluated by laparoscopic surgery. The mesendy was opened in turn, the vascular roots and surrounding lymph nodes were removed, dissociate the colon after open peritoneum, the tumor lesions were completely removed, and the intestinal fracture was anastomosed, and the later operation procedure was same as the control group.

2.4 Observation indicators

Venous blood of all patients before and 1 d after surgery were collected, and the level of coagulation index: prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (FIB) and D-dimer (DD) were detected by a fully automatic coagulation analyzer (purchased from Shenzhen Leidu Life Science Co., Ltd.); superoxide dismutase (SOD) and malondialdehyde (MDA), were detected by thiobarbituric acid colorimetry and xanthine oxidase colorimetric method, respectively, glutathione (GSH) detection by radioimmunoassay; vascular endothelial growth factor (VEGF), matrix metalloproteinase-9 (MMP-9), insulin-like growth factor 1 (IGF-1) and interferon-γ (IFN-γ), by ELISA, the above kits are all produced by Wuhan Merck Biotechnology Co., Ltd. All experimental procedures are strictly in accordance with the instructions of the instrument and kit.

2.5 Statistical processing

The data of this study were analyzed by SPSS 22.0. The count data were analyzed by chi-square test. The coagulation function, antioxidant index, angiogenesis, IGF-1 and IFN-γ were compared by t test and indicated by Mean ± SD. P<0.05 was considered statistically significant.

3. Results

3.1 Comparison of coagulation function between the two groups before and after operation

Before treatment, the levels of PT, APTT, FIB and DD were similar in the two groups (P>0.05). After treatment, there was no significant difference in PT and APTT levels between the two groups (P>0.05). Whereas the FIB and DD were significantly increased than before

### Table 1. Comparison of coagulation function between the two groups before and after surgery (n=45).

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment time</th>
<th>PT (s)</th>
<th>APTT (s)</th>
<th>FIB (g/L)</th>
<th>DD (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>10.86±1.06</td>
<td>29.86±3.22</td>
<td>2.91±0.60</td>
<td>0.17±0.08</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>10.75±1.25</td>
<td>30.07±3.59</td>
<td>4.01±0.70</td>
<td>0.68±0.19*</td>
</tr>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>10.93±1.18</td>
<td>30.05±3.59</td>
<td>2.93±0.58</td>
<td>0.19±0.07</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>11.06±1.37</td>
<td>30.16±3.73</td>
<td>3.62±0.69*</td>
<td>0.35±0.13*</td>
</tr>
</tbody>
</table>

Note: Compared with before treatment, *P<0.05; compared with the control group after treatment, †P<0.05.

### Table 2. Comparison of anti-oxidation indexes between the two groups before and after surgery (n=45).

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment time</th>
<th>SOD (U/L)</th>
<th>MDA (mol/L)</th>
<th>GSH (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>99.56±16.79</td>
<td>8.59±1.25</td>
<td>430.69±40.90</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>78.29±10.39*</td>
<td>13.87±2.07*</td>
<td>361.47±36.12*</td>
</tr>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>100.08±18.82</td>
<td>8.64±1.39</td>
<td>431.72±42.13</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>57.19±9.56*</td>
<td>20.16±2.30*</td>
<td>258.06±30.88*</td>
</tr>
</tbody>
</table>

Note: Compared with before treatment, *P<0.05; compared with the control group after treatment, †P<0.05.
were significantly lower than those in the control group (P<0.05), and MMP-9 were obviously decreased than before treatment (P<0.05), and decreased to (10.29±3.56) ng/L. IFN-\(\gamma\) in the observation group was significantly lower than that in the control group (P<0.05), and decreased to (129.16±16.30) ng/mL, respectively. See Table 2.

3.3 Comparison of angiogenesis indexes between both groups before and after operation

Before treatment, there was no significant difference in VEGF and MMP-9 between the two groups (P>0.05). After treatment, VEGF and MMP-9 were significantly decreased than before treatment (P<0.05), and the VEGF and MMP-9 in the observation group were significantly lower than those in the control group (P<0.05), and decreased to (238.19±49.56) ng/L and (160.87±72.07) ng/mL, respectively. See Table 3.

3.4 Comparison of IGF-1 and IFN-\(\gamma\) indexes between the two groups before and after operation

Before treatment, there was no significant difference in the difference of IGF-1 and IFN-\(\gamma\) between the two groups (P>0.05). After treatment, IGF-1 level in two groups were significantly decreased than before treatment (P<0.05), moreover the IGF-1 in the observation group was significantly lower than that in the control group (P<0.05), and decreased to (10.29±3.56) ng/L. IFN-\(\gamma\) in both groups was significantly increased compared with that before treatment (P<0.05), and the IFN-\(\gamma\) in the observation group increased significantly (P<0.05), increased to (142.57±18.62) μg/mL. See Table 4.

4. Discussion

With the development of surgery and the increasing requirements for surgery, minimally invasive surgery has been widely used in clinical practice[9]. Laparoscopic surgery for rectal cancer has attracted much attention because of its advantages of small trauma, low pain, rapid recovery and high safety. In recent years, most studies about laparoscopic surgery for rectal cancer has focused on the basic conditions during operation, postoperative recovery, improvement of clinical symptoms and prognosis[10,11], research on coagulation function, oxidative stress, angiogenesis and other biochemical serological indicators of patients are not sufficient. In order to further clarify the advantages of laparoscopic surgery for patients with rectal cancer, this study will analyze the changes of multiple biochemical indicators, as detailed below.

Patients with rectal cancer often have hypercoagulable state after surgery, which is easy to form deep vein thrombosis. Rectal cancer is considered as a high risk factor for deep vein thrombosis[12]. PT and APTT are sensitive screening indicators often used in exogenous and endogenous coagulation systems[13]; FIB is the highest content of clotting factor in plasma. As a substrate for thrombin, the higher the value, the more obvious hypercoagulable state in the body. DD is the product of cross-linked fibrin through fibrinolytic enzyme, which can be used as the most sensitive indicator of intravascular coagulation status, and its content can reflect the strength of coagulation and fibrinolysis function[14]. The results of this study showed that after treatment, FIB and DD in both groups increased significantly compared with before treatment, and the FIB and DD in the observation group increased significantly compared with the control group. It is suggested that laparoscopic surgery has a greater influence on postoperative blood coagulation mechanism in patients with rectal cancer. The reason may be that laparoscopic surgery can induce the formation of deep vein thrombosis of lower extremity, which leads to hypercoagulability of blood, and the establishment of CO2 pneumoperitoneum is a significant difference from open surgery, laparoscopic surgery may be due to the establishment of CO2 pneumoperitoneum, which promotes the increase of abdominal pressure to compress the iliac vein, leading to obstruction of blood flow in the lower extremities, in long time causing increased venous pressure in the lower extremities, decreased flow rate, and damaged endothelial cells. And then the blood coagulation system is activated, which in turn makes it easier to induce blood to be hypercoagulable state.

Surgical trauma often leads to the formation of a large amount of reactive oxygen species, which activates the body’s oxidative...
stress response, and the stress response can inhibit the immune function, promote postoperative complications and tumor metastasis, and seriously endanger the patient’s life safety[15]. SOD is an antioxidant enzyme that can remove free radicals from the body and achieve antioxidant effects. The higher the content, the stronger the body’s antioxidant capacity[16]. MDA is the final metabolite of the body’s peroxidation reaction, the higher the level, The more severe the oxidative stress in the body, the more serious the tissue damage[17]; GSH is an antioxidant that can combine with free radicals to form acid substances that are more easily metabolized by the body, accelerate the elimination of free radicals, protect liver, and effectively avoid tissue damaged[18]. The results of this study showed that after treatment, the SOD and GSH in the two groups were significantly lower than before treatment, while the MDA was obviously increased compared with that before treatment, and the decrease range of SOD, GSH and the increase range of MDA in the observation group was significantly lower than that of the control group, suggesting that the surgery treatment can cause stress damage in the body, and the degree of oxidative stress damage caused by laparoscopic surgery is lower, which may be related to the minimally invasive trauma of laparoscopic surgery.

VEGF and MMP-9 are widely used in clinical trials to determine the severity of malignant tumors[19]. The former is a typical vascular growth factor that promotes tumor vasculature activity, and its level can reflect the ability of tumor cell metastasis; The later can reflect the extent that malignant tumors spread to surrounding cells. In addition, MMP-9 can also participate in angiogenesis by producing VEGF. The results of this study showed that after treatment, VEGF and MMP-9 in both groups were significantly lower than those before treatment, and the VEGF and MMP-9 in the observation group were significantly lower than those in the control group, suggesting that laparoscopic surgery can effectively transfer tumor cells and postoperative recovery, may be related to tumor removal and stress damage.

IGF-1 is regulated by phosphatidylinositol 3 kinase and other pathways, inhibits apoptosis, promotes cell proliferation, and plays an important role in tumor cell proliferation and metastasis[20]; IFN-γ can activate macrophages and regulate cellular immunity, participate in cellular immune responses, strengthen antiviral and anti-tumor effects[21]. The results of this study showed that after treatment, IGF-1 in both groups were significantly lower than before treatment, and IGF-1 in the observation group was significantly lower than that in the control group; IFN-γ was significantly increased in both groups compared with before treatment, and IFN-γ in the observation group increased more obviously compared with the control group, which further demonstrated the superiority of laparoscopic surgery in terms of tumor removal ability and stress damage.

In summary, laparoscopic surgery compared with open surgery for rectal cancer patients, it is easy to induce hypercoagulable state of the patient's blood, but can effectively avoid the body tumor metastasis, resulting in less stress damage, and thus better promote the rehabilitation of patients, it is worthy of clinical promotion.

References