Effect of radical gastrectomy for stress and immune function in patients with cardiac cancer
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Objective: To investigate the effects of abdominal and transthoracic surgery on perioperative stress and immune function in patients with cardiac cancer. Methods: 60 patients with cardiac cancer treated in our hospital from May 2016 to October 2017 were collected. According to the different surgical methods, they were divided into the transthoracic group and the abdominal group, with 30 cases in each group. The changes of inflammatory factors, T-lymphocyte subsets, NK cells, immune globulin, and oxidative stress parameters were compared between the two groups before and 7 d after surgery. Result: There were no significant differences in preoperative inflammatory factors, T lymphocyte subsets, NK cells, immunoglobulins, and oxidative stress between the two groups. At 7 d after surgery, COR and CRP levels increased in both groups, but COR and CRP levels in abdominal group were (63.03±5.31) mg/L and (245.15±22.88) ng/L which were lower than those in transthoracic group. The levels of CD4+, CD4+/CD8+ and CD8+ and NK were significantly increased in both groups after operation, and CD4+ and CD4+/CD8+ were (34.23±3.42)% and (1.22±0.12), which were higher than those in the transabdominal group. While the number of CD8+ and NK cells in the group was (28.12±2.91)% and (19.11±1.92)% respectively, which were lower than those in the transthoracic group. The levels of IgA, IgG, and IgM were significantly reduced in both groups after operation, and IgA, IgG, and IgM were (2.84±0.27) g/L, (12.11±1.20) g/L, and (1.46±0.15) g/L respectively, which were lower than those in the transabdominal group. MDA levels in both groups were increased, while SOD levels in both groups were decreased. However, the MDA in the abdominal group was (5.27±0.53) mmol/mL which were lower than those in the transthoracic group. Conclusion: The radical gastrectomy can reduce inflammatory stress and oxidative stress in patients with cardiac cancer and protect immune function.

1. Introduction

Gastric cardia cancer is a common gastrointestinal tumor. It is located in the transitional zone between the stomach and the esophagus. In recent years, the incidence of cardiac cancer has increased year by year, and has become the world’s most frequent disease. Clinical studies have found that radiotherapy and chemotherapy are ineffective in the treatment of cardiac cancer, and surgery is the most effective treatment method at present. Simple transabdominal radical resection and simple transthoracic radical resection of cardiac cancer are common surgical methods in clinic. Because simple transabdominal radical resection of cardiac cancer has less wound, less respiratory function and cardiopulmonary function, its clinical application is more extensive than simple transthoracic radical resection of cardiac cancer. The purpose of this study was to investigate the effects of transabdominal and transthoracic surgery on perioperative stress and immune function in 60 patients with cardiac cancer treated in our hospital from May 2016 to October 2017.

2. Data and methods

2.1. Clinical data

Sixty patients with cardiac cancer admitted to our hospital from May 2016 to October 2017 were enrolled in the study. The criteria were as follows: 1) All patients were diagnosed by pathology...
and imaging; 2) None received radiotherapy, chemotherapy and immunotherapy; 3) Normal liver and kidney function. According to the different surgical methods, they were divided into 30 groups: Transthoracic group and transabdominal group. In the transabdominal group, there were 17 males and 13 females aged 46-76 years, 11 patients with stage I, 12 patients with stage II, 4 patients with stage III A and 3 patients with stage III B. In the transthoracic group, there were 16 males and 14 females aged 45-77 years, 10 patients with stage I, 11 patients with stage II, 5 patients with stage III A and 4 patients with stage III B. Exclusive criteria: 1) surgical contraindications such as intestinal obstruction or distant metastasis; 2) hypertension, diabetes, cardiovascular and cerebrovascular diseases; 3) preoperative infection. The study of all patients with gender, age and tumor staging were not statistically significant, comparable.

### 2.2 Treatment

1) All patients underwent surgery under general anesthesia with tracheal intubation. 2) Transthoracic group: through the left chest 6-7 intercostal thoracotomy to explore the lower esophageal free, open the diaphragm to explore the tumor and surrounding organs, clear the lesion after the free proximal stomach, resection of the proximal stomach, the whole stomach and lower esophagus, the use of staplers for distal gastroesophageal anastomosis, complete clearance of regional lymph nodes after closure of the diaphragm, and then Place chest drainage tube and close chest. 3) Transabdominal group: The abdominal incision around the umbilical cord was used to explore the abdominal tumor, the involvement of surrounding organs and lymph node metastasis. After laparotomy, the proximal stomach and the lower esophagus were removed after ligation of the splenogastric ligament and the primary gastrocolic band, the regional lymph nodes were cleared, the gastric minor curvature was free, the lymph nodes adjacent to the left gastric artery and the celiac artery were cleared after ligation of the left gastric artery, the primary hepatogastric band was free and ligated, the paracardial celiac artery were cleared after ligation of the left gastric artery, the regional lymph nodes were cleared, the gastric minor curvature the splenogastric ligament and the primary gastrocolic band, the stomach and the lower esophagus were resected. The pancreatic capsule, omentum and mesentery of transverse colon were excised as a whole. The distal gastric or proximal jejunal-esophageal anatomosis was performed with stapler. The abdominal drainage tube was placed and the abdomen was closed. 4) All patients were given antibiotics to prevent infection within 2 h before operation. All patients were given intravenous or enteral nutrition intervention, anti-infection treatment and acid suppression treatment after operation.

#### 2.3 Observation indicators

1) Cortisol (COR) and C-reactive protein (CRP) levels measured:: Fasting venous blood (1 mL) was taken one day before operation and 7 d after operation respectively, and upper serum was taken 4 min after 3 500 r/min centrifugation. The levels of COR and CRP were detected by ELISA. COR and CRP ELISA kit are purchased from Shanghai enzyme linked Biotechnology Co., Ltd. 2) T lymphocyte subsets: fasting venous blood 3 mL was taken from 1 d before operation and 7 d after operation respectively, and detected by flow cytometry (purchased from BD China Branch); 3) Comparison of immunoglobulin between two groups: 1 mL of fasting venous blood was taken one day before operation and 7 d after operation respectively. After centrifugation, immunoglobulin A (IgA), immunoglobulin G (IgG) and immunoglobulin M (IgM) were determined by rate nephelometry. M, IgM level; 4) Detection of MDA and SOD levels: Fasting venous blood 1 mL was taken 1 d before operation and 7 d after operation respectively, and upper serum was taken 4 min after 3 500 r/min centrifugation. The levels of malondialdehyde (MDA) and superoxide dismutase (SOD) were measured by ELISA. MDA and SOD ELISA kit are purchased from Shanghai enzyme linked Biotechnology Co., Ltd.

#### 2.4 Statistical methods

The data of this study were analyzed by SPSS 21.0 statistical software. All the indexes in this study were in normal distribution, expressed as mean ± standard deviation (Mean ± SD). The comparison between the two groups was performed by independent t test. Paired t-test was used to compare with postoperatively. P<0.05 was considered statistically significant.

### Table 1.

Comparison of inflammatory factors before and after treatment in two groups of patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>CRP (mg/L)</th>
<th>COR (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transthoracic group</td>
<td>30</td>
<td>Preoperative</td>
<td>12.18±1.23</td>
<td>161.23±16.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postoperative</td>
<td>132.5±13.24</td>
<td>325.6±31.28</td>
</tr>
<tr>
<td>Transabdominal group</td>
<td>30</td>
<td>Preoperative</td>
<td>12.19±1.22</td>
<td>162.57±16.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postoperative</td>
<td>63.0±5.31</td>
<td>245.1±22.88</td>
</tr>
</tbody>
</table>

Note: compared with preoperative P<0.05, compared with the transthoracic group, P<0.05.

### Table 2.

Comparison of T lymphocyte subsets and NK cells in two groups before and after treatment (n=45).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>CD4+ (%)</th>
<th>CD8+ (%)</th>
<th>CD4+/CD8+ (%)</th>
<th>NK (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transthoracic group</td>
<td>30</td>
<td>Postoperative</td>
<td>36.1±3.61</td>
<td>27.1±2.68</td>
<td>1.3±0.13</td>
<td>17.1±1.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Preoperative</td>
<td>28.1±3.37</td>
<td>29.8±2.61</td>
<td>0.9±0.10</td>
<td>22.3±2.97</td>
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<tr>
<td>Transabdominal group</td>
<td>30</td>
<td>Postoperative</td>
<td>35.8±3.86</td>
<td>27.2±2.66</td>
<td>1.3±0.12</td>
<td>16.8±1.70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Preoperative</td>
<td>34.2±3.42</td>
<td>28.1±2.91</td>
<td>1.2±0.12</td>
<td>19.1±1.92</td>
</tr>
</tbody>
</table>

Note: compared with preoperative P<0.05, compared with the transabdominal group, P<0.05.
Table 3.
Comparison of immunoglobulin levels between two groups (n=45).

<table>
<thead>
<tr>
<th>Group</th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transabdominal</td>
<td>n</td>
<td>IgA</td>
</tr>
<tr>
<td>Group</td>
<td>30</td>
<td>2.97±0.30</td>
</tr>
<tr>
<td>Transabdominal</td>
<td>Postoperative</td>
<td>2.18±0.21</td>
</tr>
<tr>
<td>Transabdominal</td>
<td>Preoperative</td>
<td>3.01±0.31</td>
</tr>
<tr>
<td>Transabdominal</td>
<td>Preoperative</td>
<td>2.84±0.27</td>
</tr>
</tbody>
</table>

Note: compared with preoperative, *P<0.05, compared with the transabdominal group, *P<0.05.

Table 4.
Comparison of oxidative stress indexes between two groups before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transabdominal</td>
<td>n</td>
<td>MDA (mmol/mL)</td>
</tr>
<tr>
<td>Group</td>
<td>30</td>
<td>4.19±0.42</td>
</tr>
<tr>
<td>Transabdominal</td>
<td>Postoperative</td>
<td>6.34±0.52</td>
</tr>
<tr>
<td>Transabdominal</td>
<td>Preoperative</td>
<td>4.23±0.42</td>
</tr>
<tr>
<td>Transabdominal</td>
<td>Preoperative</td>
<td>5.27±0.53</td>
</tr>
</tbody>
</table>

Note: compared with preoperative, *P<0.05, compared with the transabdominal group, "P<0.05.

3. Results

3.1. Comparison of inflammatory factors in the two groups before and after treatment

Before treatment, there was no significant difference in the levels of COR and CRP between the two groups (P>0.05). Seven days after operation, the levels of COR and CRP in both groups increased (P<0.05), but the COR and CRP in transabdominal group were (63.03±5.31) mg/L and (245.15±22.88) ng/L lower than those in transthoracic group (P<0.05), respectively, as shown in Table 1.

3.2 Comparison of T lymphocyte subsets and NK cells in two groups before and after treatment

There was no significant difference in T lymphocyte subsets and NK cell levels between the two groups before operation (P>0.05). The levels of CD4+, CD4+/CD8+, CD8+ and NK in both groups were significantly decreased, and the levels of CD4+ and CD4+/CD8+ in transabdominal group were (34.23±3.42)% and (1.22±0.12), respectively, higher than those in transthoracic group (P<0.05). The numbers of CD8+ and NK cells in transabdominal group were (28.1±2.91)% and (19.1±1.92)% lower than those in transthoracic group (P<0.05).

3.3 Comparison of immunoglobulin in two groups of patients

There was no significant difference in the level of immunoglobulin between the two groups before operation (P>0.05). The levels of IgA, IgG and IgM were significantly lower in the two groups 7 d after operation, but the levels of IgA, IgG and IgM in the transabdominal group were (2.84±0.27), (12.11±1.20) g/L and (1.46±0.15) g/L respectively, higher than those in the transthoracic group, as shown in Table 3.

3.4 Comparison of oxidative stress indexes between two groups before and after treatment

Before treatment, there was no significant difference in the levels of MDA and SOD between the two groups (P>0.05). After 7 d, the MDA levels of the two groups increased (P<0.05) and SOD decreased. But the MDA of transabdominal group was (5.27±0.53) mmol/mL, lower than that of transthoracic group, and the SOD of transthoracic group was (80.26±8.06) U/mL, higher than that of transthoracic group (P<0.05).

4. Discussion

Early clinical symptoms of cardiac cancer are not obvious, leading to more patients who are already in the advanced stage when they visit the doctor. In addition, cardiac cancer is adjacent to peripheral organs and easily involved peripheral organs, so the resection rate of cardiac cancer is low and the prognosis is poor[6]. Studies have found that the lymph node metastasis of cardiac cancer is mainly abdominal metastasis, so the application of abdominal surgery is relatively extensive[7]. The patients with cardiac cancer are mostly elderly, and the elderly population has low immunity, weak immune function, and more postoperative complications. Choosing a reasonable surgical approach can not only improve the treatment effect of cardiac cancer, but also reduce postoperative complications and improve survival time through reasonable surgical incision[8]. In this study, the effects of abdominal and thoracic surgeries on stress and immune function of patients with cardiac cancer were compared, and the reasonable path of cardiac cancer radical resection was discussed.

Surgery itself is a kind of trauma that can lead to inflammatory stress while treating the disease[9]. Studies have shown that CRP levels are directly proportional to the degree of trauma[10,11]. COR is closely related to immune function and inflammatory stress. When the body is in inflammatory stress or immune function is impaired, COR level is significantly increased[12,13]. The results showed that there was no significant difference in COR and CRP levels between the two groups before treatment (P>0.05). At 7 d after surgery, the levels of COR and CRP increased in both groups (P<0.05), but the COR and CRP in the abdominal group were (63.03±5.31) mg/L and (245.15±22.88) ng/L, respectively, lower than the transthoracic group (P<0.05), suggesting that simple transabdominal cardiac cancer radical surgery has less effect on inflammatory stress response in patients with cardiac cancer. The possible cause is laparoscopic surgical incision length. Smaller, less invasive, less painful, and less damaging to surrounding organs, reducing the inflammatory stress response caused by injury.

Fine regulatory T lymphocytes play a key role in tumor immunity.
Surgery can significantly impair the body’s immune function, especially T lymphocyte-mediated cellular immune response, and the study found that the more severe the surgical trauma, the more serious the degree of immune function damage[14,15]. At 7 d after operation, CD4+, CD4+/CD8+ levels were significantly decreased, CD8+ and NK levels were significantly increased in the two groups, and CD4+ and CD4+/CD8+ in the transabdominal group were (34.23±3.42)% and (1.22±0.12), respectively. In the thoracic group, the number of CD8+ and NK cells was (28.12±2.91)% and (19.11±1.92)% lower than that of the thoracic group (both P<0.05), indicating that the trauma caused by surgery can inhibit the cellular immune function of patients with cardiac cancer. However, the effect of abdominal surgery on immune function of patients is lower than that of thoracic surgery, which is consistent with studies by Tang Qingying[16].

Immunoglobulin (Ig), as an immunoreactive factor, can remove viruses and toxins in the body, thus playing a role in protecting the body. Generally, the levels of gA, IgG and IgM in the body are in a stable state. If the body is injured, it will be significantly reduced, and the decline is related to the degree of surgical trauma[17,18]. The results showed that the levels of IgA, IgG and IgM were significantly lower in the two groups 7 d after operation, but the levels of IgA, IgG and IgM in the transabdominal group were lower than those in the thoracic group (2.84±0.27) g/L, (12.11±1.20) g/L and (1.46±0.15) g/L respectively, suggesting that the effects of IgM on complement activation and phagocytosis regulation were less than those in the control group, which were consistent with previous studies. MDA is one of the products of membrane lipid peroxidation. It can reflect the degree of lipid peroxidation and the degree of oxidative damage. Surgery results in body damage, resulting in the production of oxygen free radicals (ROS) in large quantities, resulting in the reduction of antioxidant substance SOD[19-21]. It was found that after 7 d, the MDA levels of the two groups increased (P<0.05) and SOD decreased. But the MDA of transabdominal group was lower than that of thoracic group, and the SOD of transabdominal group was lower than that of thoracic group (P<0.05), suggesting that transabdominal radical resection of cardiac cancer can reduce the oxidative stress and promote the recovery of patients. The possible reason is that laparoscopic surgery is less traumatic, less pain stimulation, less damage to the body, so a certain extent alleviate the oxidative stress response.

To sum up, transabdominal radical resection of cardiac cancer can relieve inflammation and oxidative stress and protect immune function in patients with cardiac cancer after surgery. Therefore, transabdominal radical resection of cardiac cancer is more suitable for patients with cardiac cancer than thoracic radical resection of cardiac cancer under the same clinical characteristics.

References