Int J Clin Exp Med 2020;13(11):9033-9039
www.ijcem.com /ISSN:1940-5901/IJCEM0118692

Original Article

Curative effects and influence on patient's immune function of thoracoscopic esophagectomy

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Received July 22, 2020; Accepted August 15, 2020; Epub November 15, 2020; Published November 30, 2020

Abstract: Objective: To explore curative effects and influence on patient's immune function of thoracoscopic esophagectomy. Methods: Patients with esophageal cancer (EC, n=120) admitted in The First Affiliated Hospital of Soochow University from July 2018 to January 2020 were included in the study. These patients were assigned to the observation group and the control group through prospective analysis according to the digital random table, both with a sample size of 60. The control group and observation group received conventional open surgery and thoracoscopic esophagectomy, respectively. Then, clinical indexes of these two groups were compared. Immune function, lung function, quality of life and postoperative complications were also measured and compared between the two groups. Results: Comparing to the control group, intraoperative bleeding volume in the observation group was markedly reduced, intraoperative time and incision length were also dramatically shortened, and incidence of postoperative complications was substantially decreased, all with significant difference (P<0.001). Levels of $CD4^+$, $CD4^+/CD8^+$, IgA and IgG were all obviously decreased while the level of $CD8^+$ was significantly elevated in the two groups after operation (P<0.001), but significant difference existed between the two groups (P<0.001). FEV1, FVC and PRV in the two groups were all evidently declined through the operation (P<0.001), but these indexes of the observation group were still much higher than those of the control group with a significant difference (P<0.001). Moreover, EORTCQLQ-C30 scores of two groups were both sharply elevated after operation (P<0.001), but scores of the observation group was still much higher than that of the control group with a significant difference (P<0.001). Conclusion: Thoracoscopic esophagectomy effectively helps to improve the immune function and lung function of patients with esophageal cancer with low postoperative complications rate and high quality of life, which is worthy of clinical application.

Keywords: Thoracoscopic esophagectomy, esophageal cancer, immune function, lung function, curative effects

Introduction

Esophageal cancer (EC), a common clinical digestive tract cancer, has a high mortality rate in the whole world. According to clinical data, EC induces 300000 deaths annually in the world, among which China has a high incidence [1]. Although modern medicine has developed more advanced means and technology for the diagnosis and treatment of EC, the 5-year survival rate of EC is still less than 30% according to clinical reports [2]. At present, clinical treatment of EC mainly relies on surgery and open radical resection of EC can better remove the focus and lymph nodes. However, poor curative effects still appear in some patients due to large wound and obvious stress response [3]. Now, developing endoscopy technology has gained more and more attention of clinicians, which aims to provide new means for patients undergoing esophageal cancer radical surgery. According to a previous study, patients with EC were randomly classified into endoscopic group and open group, and the research showed that the incidence of postoperative pulmonary infection was significantly reduced and the length of hospital stay was significantly shortened in the endoscopic group compared with the control group, which was conducive to improving short-term quality of life [4]. However,

there are few reports about the clinical influence of thoracoscopic esophagectomy on the indexes such as immune function (including cellular immune function and humoral immune function), lung function, quality of life, postoperative complications and so on. Our present study aims to explore the therapeutic effect of thoracoscopic esophagectomy on esophageal cancer patients and its influence on immune function, lung function, quality of life and postoperative complications. Related results are reported as follows.

Materials and methods

General materials

Patients with esophageal cancer (EC, n=120) admitted in The First Affiliated Hospital of Soochow University from July 2018 to January 2020 were included in the study. The patients were assigned to the observation group and the control group through prospective analysis according to the digital random table, both with a sample size of 60. This study was approved by the medical Ethics Committee of The School of Biology & Basic Medical Sciences, Soochow University, and all the participants and their families signed the informed consent.

Inclusion criteria: (1) Confirmed by pathological biopsy. (2) No contraindication to the methods used in this study. (3) All patients underwent thoracoscopic esophagectomy alone. (4) With complete clinical data. (5) No cognitive impairment. (6) TNM clinical stage I-III [5]. (7) No abnormal coagulation.

Exclusion criteria: (1) Withdrawal from the study halfway. (2) Those who cannot follow the doctor's instructions and do not cooperate with the treatment. (3) Heart and lung function intolerant. (4) Those with other malignant tumors. (5) Immune system disorders. (6) Patients who have been treated with chemotherapy and radiotherapy before operation.

Methods

The control group received conventional open radical resection as following: routine preoperative preparation was performed firstly. Patients were kept in right lateral position, and combined anesthesia was given adopting single lung ventilation mode of double lumen endotracheal intubation. Right side of the body was selected for thoracotomy with a large incision (the incision length was about 15-20 cm), the routine lymph node cleaning operation was carried out, and then the esophagogastrostomy on left thoracic arch was performed.

The observation group received thoracoscopic esophagectomy as following: routine preoperative preparation was performed firstly. Patients were kept in horizontal lateral decubitus position, and combined anesthesia was given adopting single lung ventilation mode of double lumen endotracheal intubation. Then, the stomach was dissociated under endoscopy. After the lymph nodes were cleaned thoroughly, the patient's position was changed and kept in left lateral position. Then the right chest was opened (the incision length was about 8 cm). The diaphragm was kept normal and the patient's stomach was lifted to the chest through the diaphragmatic hiatus to perform the right thoracic esophagogastrostomy [6].

Observation index and clinical effect evaluation

The clinical indexes (including amount of intraoperative bleeding, intraoperative time and incision length) were counted and compared between the two groups.

Fasting venous blood (5 mL) was collected from the patients in the two groups before and 2 days after operation. The supernatant was separated by centrifuge and stored at -20°C for further detection. Indexes of cellular immune function in two groups, including $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$, were measured by flow cytometry. Indexes of humoral immune function of the two groups, including immunoglobulin A (IGA) and immunoglobulin G (IgG), were detected by enzyme-linked immunosorbent assay.

The lung function indexes of the two groups, including forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and pulmonary residual volume (PRV), were measured and compared before and 7 days after operation.

Quality of life in the two groups was evaluated before and 1 month after operation by the European cancer patient's quality of life scale (EORTCQLQ-C30) [7]. There are 30 items in

Table 1. Comparison of clinical data (n, $\bar{x} \pm sd$)

Groups	Observation group (n=60)	Control group (n=60)	t/χ^2	P
Gender (n)			0.034	0.854
Male	34	35		
Female	26	25		
Age (year)	50.2±3.7	50.3±3.6	0.150	0.881
BMI (kg/m^2)	22.16±2.09	22.14±2.11	0.052	0.958
TNM clinical stage			0.160	0.923
I	20	22		
II	29	28		
III	11	10		
Tumor location			0.462	0.794
Upper segment	12	15		
Middle segment	29	28		
Lower segment	19	17		

Note: BMI: body mass index.

EORTCQLQ-C30, including 5 functional dimensions, 3 symptom dimensions and 1 overall quality of life dimension. Through linear transformation, the total score is standardized within 0-100. The higher the score is, the higher the quality of life is.

The postoperative complications of the two groups were analyzed. Total complication rate = total number of complications/total number of cases × 100%.

Statistical methods

SPSS 20.0 software was used for statistical analysis, and the measurement data conforming to normal distribution were expressed as mean ± standard deviation. Comparison before and after operation within the group was conducted using paired t test and comparison between the groups was done with independent t test. Enumeration data was expressed in the number of cases/percentage (n/%), and was analyzed by χ^2 test. P<0.05 means the difference was statistically significant.

Results

Comparison of clinical data

The two groups were comparable as there was no significant difference between them in clinical baseline data, including gender, age, body mass index (BMI), tumor node metastasis (TNM) clinical stage and tumor location (P>0.05). See **Table 1**.

Comparison of clinical indexes

Amount of intraoperative bleeding in the observation group was much less than that in the control group. Intraoperative time and incision length of the observation group were also sharply shorter than those of the control group, and these above differences between the two groups were all significant (P<0.001). See **Table 2**.

Comparison of cellular immune function before and after operation

No significant difference existed between the two groups in cellular immune function before operation (P>0.05). After operation, levels of $CD4^+$, $CD4^+/CD8^+$ of the two groups were obviously decreased and $CD8^+$ was both elevated than before operation, (P<0.001), but the difference between the two groups was still significant (P<0.001). See **Table 3**.

Comparison of humoral immune function before and after operation

No significant difference existed in humoral immune function between the two groups before operation (P>0.05). After operation, levels of IgA and IgG in the two groups were both strongly decreased than those before operation (P<0.001), and the difference between the two groups was significant (P<0.001). See **Table 4**.

Comparison of lung function before and after operation

No significant difference existed in lung function between the two groups before operation (P>0.05). After operation, FEV1, FVC and PRV in the two groups were all prominently decreased than those before operation (P< 0.001), and corresponding index in observation group was much higher than that in the control group with significant difference (P<0.001). See **Table 5**.

Comparison of quality of life before and after operation

No significant difference existed in EORTCQLQ-C30 score between the two groups before operation (P>0.05). After operation, the

Table 2. Comparison of clinical indexes ($\bar{x} \pm sd$)

Groups	Amount of intraoperative bleeding (mL)	Intraoperative time (min)	Incision length (cm)
Observation group (n=60)	130.33±20.68	69.55±14.37	4.49±1.32
Control group (n=60)	146.71±21.67	80.05±15.41	13.47±2.56
t	4.236	3.860	24.150
P	0.000	0.000	0.000

Table 3. Comparison of cellular immune function before and after operation ($\bar{x} \pm sd$)

Groups	Observation group (n=60)	Control group (n=60)	t	P
$CD4^+$ (%)				
Before operation	41.55±4.47	41.54±4.39	0.012	0.990
After operation	32.09±3.88###	28.55±3.64###	5.514	<0.001
$CD8^+$ (%)				
Before operation	24.11±2.69	24.13±2.70	0.041	0.968
After operation	29.05±2.87###	33.59±2.89###	8.634	<0.001
$CD4^+/CD8^+$				
Before operation	1.72±0.20	1.73±0.19	0.281	0.779
After operation	1.10±0.12###	0.85±0.11###	11.896	<0.001

Note: ###P<0.001 vs index of the same group before operation.

Table 4. Comparison of humoral immune function before and after operation ($\bar{x} \pm sd$, g/L)

Groups	Observation group (n=60)	Control group (n=60)	t	P
IgA				
Before operation	3.20±0.26	3.21±0.27	0.207	0.837
After operation	2.51±0.24###	1.79±0.30###	14.517	<0.001
IgG				
Before operation	12.48±1.75	12.47±1.68	0.032	0.975
After operation	11.03±1.32###	9.41±1.59###	6.072	<0.001

Note: ###P<0.001 vs index of the same group before operation.

EORTCQLQ-C30 scores of the two groups were both significantly higher than those before operation (P<0.001), and score of the observation group was much higher than that of the control group with significant difference (P<0.05). See **Table 6** and **Figure 1**.

Comparison of postoperative complications between the two groups

The incidence of postoperative complications in the observation group was markedly lower than that in the control group with significance difference (P<0.001). See **Table 7**.

Discussion

As a malignant disease occurring in the epithelium of esophageal mucosa, esophageal cancer is mainly caused by biological factors such as flavatin, insufficient intake of trace elements (such as iron and zinc), genetic predisposition or long-term bad eating habits [8, 9]. Clinical research found that, the incidence of esophageal cancer was increasing day by day due to the deterioration of the environment and irregular work and rest. However, most patients have reached the middle and late stage at the time of treatment because early clinical symptoms are very difficult to be found [10]. At present, main clinical treatments of esophageal cancer are surgical operation, radiotherapy and chemotherapy, among which surgical operation is usually considered as the first choice for patients in line with the surgical treatment [11, 12]. Although it had relatively good curative effect, open radical esophagectomy had higher risk coefficient due to the large incision in the operation and great adverse effects induced in later stage on the body. Thus, the application of open radical esophagectomy in the clinical is largely limited. It has been reported that thoracoscopic esophagectomy is a minimally invasive therapy, which has a better field of vision and can avoid further trauma to the tissues around the operation area as much as possible, so that patients can recover faster after operation [13].

In this study, patients in the control group and the observation group were treated with two

Table 5. Comparison of lung function between two groups before and after operation ($\bar{x} \pm sd$)

Groups	Observation group (n=60)	Control group (n=60)	t	P
FEV1 (L)				
Before operation	2.59±0.79	2.60±0.75	0.071	0.943
After operation	2.08±0.36###	1.30±0.28###	13.248	<0.001
FVC (L)				
Before operation	3.60±0.82	3.61±0.79	0.068	0.946
After operation	3.07±0.55###	2.51±0.47###	5.996	<0.001
PRV (L/s)				
Before operation	4.72±1.09	4.71±1.08	0.050	0.960
After operation	4.10±0.76###	3.59±0.77###	3.651	<0.001

Note: ###P<0.001 vs index of the same group before operation. FEV1: forced expiratory volume in one second; FVC: forced vital capacity; PRV: pulmonary residual volume.

Table 6. Comparison of quality of life between the two groups before and after operation ($\bar{x} \pm sd$)

Groups	Observation group (n=60)	Control group (n=60)	t	P
EORTCQLQ-C30 (score)				
Before operation	69.98±15.33	70.04±15.37	0.021	0.983
After operation	88.04±18.64###	80.78±15.76###	2.304	0.023

Note: ###P<0.001 vs index of the same group before operation.

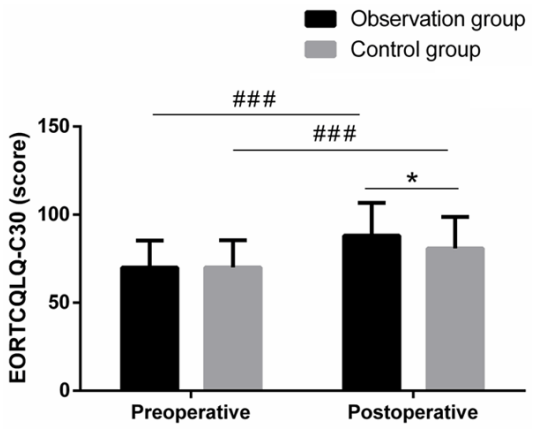

Figure 1. Comparison of quality of life before and after operation. *P<0.05 vs the control group after operation. ###P<0.001 vs the same group before operation.

different kinds of operation. Compared with the control group, amount of intraoperative bleeding in the observation group was much decreased, intraoperative time and incision length were sharply shortened, and the incidence of postoperative complications was also largely reduced, all with significant difference. It suggests that thoracoscopic esophagectomy has less damage to the body and lower incidence of postoperative complications. Scholars believe that through fully exposing the esophagus and surrounding tissues, thoracoscopic esophagectomy is conducive to the precise operation of the operator, and can better protect the integrity of the body contour, further reducing the impact on the traction of surrounding tissues and abdominal breathing [14, 15]. All operations can induce stress reaction. Although it belongs to the self-protection of the body, the stress response will still cause immunosuppression of the body, and ultimately bring great impact on the postoperative rehabilitation [16]. Immune function of the body includes cellular immunity and humoral immunity. Change of $CD4^+$ and $CD8^+$ T lymphocytes levels directly reflects the cellular immune state of the body and decrease of $CD4^+/CD8^+$ indicates the inhibition of cellular immune function. Humoral immunity can be expressed by the level of IgA and IgG, and the higher the level of indicators is, the stronger the humoral immune function of the body is [17, 18]. The results of this study showed that $CD4^+$, $CD4^+/CD8^+$, IgA and IgG in the two groups were all largely decreased and $CD8^+$ was strongly elevated through operation, and the difference between the two groups was significant with statistical significance. It suggests that thoracoscopic esophagectomy has less damage to the immune system, which is helpful for the postoperative recovery of patients. Many clinical results show that, open radical resection of esophageal cancer has great damage to the body. At the same time, lung function will also be greatly affected because of long time exposure of the thoracic cavity during the operation and the compression of hilar and lateral lung suffered during the reconstruction of digestive tract [19, 20]. It has been reported that quality

Table 7. Comparison of postoperative complications

Groups	Observation group (n=60)	Control group (n=60)	χ^2	P
Lung diseases (n)	2	10		
Acute respiratory distress (n)	1	4		
Arrhythmia (n)	1	6		
Others (n)	5	8		
Total incidence rate (n, %)	9 (15.00)	28 (46.67)	14.106	0.000

of lung function is closely related to the integrity of diaphragm during operation, and the integrity of diaphragm directly determines the performance and state of lung function after operation [21]. The results of this study showed that FEV1, FVC and PRV in the two groups were all obviously weakened through operation, but the levels of FEV1, FVC and PRV in the observation group was still evidently higher than those in the control group. In addition, the EORTCQLQ-C30 scores in the two groups were all highly elevated through the operation and the score of the observation group was significantly higher than that of the control group. The results indicate that thoracoscopic esophagectomy is of great significance for the recovery of pulmonary function to the best state, and is more conducive to the further improvement of the quality of life. The reason may be that thoracoscopic esophagectomy has weaker degree of thoracic adhesion and less limitation on diaphragm movement, so it has little effect on lung function and is beneficial to the improvement of patients' quality of life. However, the number of samples included in this study is small, and the effects of thoracoscopic esophagectomy on different stages of esophageal cancer have not been compared, which still needs to be studied in large-scale and multi center research.

In conclusion, thoracoscopic esophagectomy is helpful to improve the immune function and lung function of patients with esophageal cancer with low postoperative complications rate, high postoperative quality of life and good curative effect, which is worth popularizing.

Acknowledgements

This work was supported by the National Natural Science Foundation of China for Application of methylation of promoter gene of tumor suppressor gene ZNF132 in early diagnosis of esophageal carcinoma and its regulatory mechanism (81972800) and Natural Science Foundation of Jiangsu Province for The role and clinical significance of tumor suppressor gene ZNF132 regulated by methylation in esophageal cancer (BK20181175).

Disclosure of conflict of interest

None.

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