



# Effect of thoracoscopic esophagus cancer surgery on postoperative incision pain as well as non-specific and specific immune response

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## ARTICLE INFO

### Article history:

Received 7 Jul 2016

Received in revised form 17 Jul 2016

Accepted 12 Jul 2016

Available online 24 Jul 2016

### Keywords:

Esophagus cancer

Thoracoscope

Pain mediators

Immune response

## ABSTRACT

**Objective:** To explore the effect of thoracoscopic esophagus cancer surgery on postoperative incision pain as well as non-specific and specific immune response. **Methods:** 56 patients with esophageal cancer who accepted surgical treatment in our hospital between March 2011 and February 2016 were collected, the operation methods and related laboratory tests were reviewed, and then they were divided into the thoracoscope group ( $n=27$ ) who accepted thoracoscopic surgery and the open surgery group ( $n=29$ ) who accepted traditional thoracotomy. Before operation and 1 d after operation, immune scatter turbidimetry was used to detect serum levels of pain mediators, and flow cytometer was used to detect the levels of nonspecific immune indexes and specific immune indexes. **Results:** Before operation, the differences in serum pain mediators as well as nonspecific immune response and specific immune response indexes were not statistically significant between two groups of patients ( $P>0.05$ ). 1 d after operation, serum pain mediators 5-HT,  $K^+$  and NE levels of thoracoscope group were lower than those of open surgery group ( $P<0.05$ ); nonspecific immune response indexes NK cell as well as C3 and C4 levels in peripheral blood of thoracoscope group were significantly higher than those of open surgery group ( $P<0.05$ ); specific immune response indexes  $CD4^+$ ,  $CD4^+/CD8^+$ , IgA and IgG levels in peripheral blood of thoracoscope group were significantly higher than those of open surgery group ( $P<0.05$ ). **Conclusion:** Thoracoscopic esophagus cancer surgery causes less damage, has lighter inhibition on the immune response system, and is an ideal operation method for patients with early middle esophagus cancer.

## 1. Introduction

The clinical incidence of esophagus cancer is not low, about 150 000 people die of the disease in our country each year, and early diagnosis and tumor resection is the best way to optimize the treatment outcome[1,2]. Patients with early middle cancer are without distant metastasis of malignant tumor cells, so surgical tumor resection and lymph node dissection can effectively cure the disease, but the choice of specific operation methods is open to question. Traditional thoracotomy has been successfully applied in clinical patients with esophagus cancer, the surgery under direct vision ensures the completeness of the tumor resection, but huge chest

incision causes huge impact on patients' normal defense system, and patients are with acute postoperative pain, difficulty in wound healing and increased incidence of infectious events. With the popularity of endoscope in the clinical application, thoracoscopic surgery is also introduced in the treatment of esophagus cancer, three endoscopic operation and observation holes are built, the vision is amplified dozens of times under endoscope, it ensures the accuracy of the operation and reduces the damage to normal tissues and organs in the chest, chest incision is also small, and patients' postoperative recovery is relatively easy[3,4]. Overall superiority of thoracoscopic esophagus cancer surgery has been clinically proved, but there is not much comparative study about the pain and immune function between it and open surgery. In the following study, the effect of thoracoscopic esophagus cancer surgery on postoperative incision pain as well as non-specific and specific immune response was analyzed.

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Fund Project: National Science Funds for Young Scholars (No: 31600760).

## 2. Materials and methods

### 2.1. Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with esophagus cancer through pathological examination; (2) with tumor Ia–IIb stage; (3) without surgery history within 1 year prior to admission; (4) not associated with autoimmune diseases. Exclusion criteria: (1) with malignant tumor diseases of other tissues and organs; (2) with severe heart, liver and kidney dysfunction; (3) associated with coagulation dysfunction; (4) associated with systemic infectious diseases; (5) dropping out of the treatment, and with clinical data missing.

### 2.2. Clinical information

56 patients with esophageal cancer who accepted surgical treatment in our hospital between March 2011 and February 2016 were included, their operation methods and related laboratory tests were reviewed, and then they were divided into the thoracoscope group ( $n=27$ ) who accepted thoracoscopic surgery and the open surgery group ( $n=29$ ) who accepted traditional thoracotomy. Thoracoscope group included 14 male cases and 13 female cases, they were 49–72 years old, and the body weight was 48–80 kg and  $(65.38\pm 8.77)$  kg in average; open surgery group included 14 male cases and 15 female cases, they were 48–76 years old, and the body weight was 47–82 kg and  $(67.12\pm 9.54)$  kg in average. The two groups of patients were not significantly different in distribution of age, gender and body weight ( $P>0.05$ ). The included patients themselves understood the research process and signed the informed consent, and the study was approved by the hospital ethics committee.

### 2.3. Surgical methods

Thoracoscope group received thoracoscope surgery, which was as follows: after tracheal intubation under general anesthesia, patients took the left lateral position, a main operating hole was made in the right 6th anterior intercostal line (about 1.5 cm in diameter) to insert trocar (10 mm), a traction hole was made in the 3rd anterior intercostal line (about 1.5 cm in diameter) to insert trocar (5 mm), an observation hole was made in the 7th intercostal midaxillary line (about 1.0 cm in diameter) to insert trocar (10 mm), and parallel operation hole was made in infrascapular front and the fifth intercostal line to insert trocar (5 mm). The chest was inspected, then the pleura mediastinalis was opened along the anterior spine, separate the azygos vein and ligature it, and separate the esophagus from top to bottom to the cupula pleurae. The lymph nodes around inferior pulmonary ligament, esophagus and recurrent laryngeal nerve were dissected, the incision was carefully stanch and washed to prevent leakage, closed drainage of pleural cavity was embedded and then the incision was sutured. Laparoscopic gastric mobilization and neck operation were the same as those mentioned in the literature of Liang *et al*[5]. Open surgery group received traditional

thoracotomy, and the methods were the same as those mentioned by Cheng *et al*[6].

### 2.4. Incision pain

Before operation and 1d after operation, cubital venous blood was extracted from two groups of patients at the same time point and centrifuged at low speed to get serum, immune scatter turbidimetry was used to detect the levels of pain mediators 5-hydroxytryptamine (5-HT), potassium ( $K^+$ ) and norepinephrine (NE) in it, and the objective pain perception of two groups of patients was assessed.

### 2.5. Nonspecific and specific immune response indexes

Before operation and 1 d after operation, 2 mL of peripheral venous blood was extracted from two groups of patients, and flow cytometer (Bidi Medical Equipment Co., LTD., model BD FACSCanto II) was used to detect nonspecific immune index levels, including natural killer cells (NK), complement C3 and complement C4. Cellular immunity and humoral immunity index levels were determined, including  $CD4^+$  T lymphocytes,  $CD4^+$  T/ $CD8^+$  T, immunoglobulin A (IgA) and immunoglobulin G (IgG).

### 2.6. Statistical analysis

Data was input in software SPSS20.0 by specially-assigned person, measurement data was in terms of mean  $\pm$  standard deviation ( $\bar{x}\pm s$ ), respective comparison before operation and after operation was by group *t* test, comparison before and after operation was by paired *t* test and  $P<0.05$  meant statistical significance in differences.

## 3. Results

### 3.1. Serum pain mediator levels

Comparison of serum pain mediators 5-HT,  $K^+$  and NE levels between two groups of patients before and after operation was as follows: before operation, the differences in serum pain mediators 5-HT,  $K^+$  and NE levels were not statistically significant between two groups of patients ( $P>0.05$ ); 1 d after operation, serum pain mediators 5-HT,  $K^+$  and NE levels of both groups were significantly higher than those before operation, and differences within same group were statistically significant before and after operation ( $P<0.05$ ). 1 d after operation, serum pain mediators 5-HT,  $K^+$  and NE levels of thoracoscope group were significantly lower than those of open surgery group, and differences between groups were statistically significant after operation ( $P<0.05$ ), shown in Table 1.

### 3.2. Nonspecific immune response

Comparison of nonspecific immune response indexes NK cell as well as C3 and C4 levels in peripheral blood between two groups of

**Table 1**Comparison of objective pain extent before and after operation ( $\bar{x}\pm s$ ).

Groups	n	5-HT (nmol/L)		K <sup>+</sup> (mmol/L)		NE (ng/L)	
		Before operation	1 d after operation	Before operation	1 d after operation	Before operation	1 d after operation
Thoracoscope group	27	0.21±0.03	0.36±0.05	28.31±3.42	33.57±3.89	1.27±0.15	2.53±0.34
Open surgery group	29	0.23±0.03	0.67±0.07	28.54±3.09	38.61±4.52	1.25±0.16	5.61±0.68
t		0.162	6.492	0.135	8.293	0.129	6.482
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

patients before and after operation was as follows: before operation, differences in nonspecific immune response indexes NK cell, C3 and C4 levels in peripheral blood were not statistically significant between two groups of patients ( $P>0.05$ ); 1 d after operation, nonspecific immune response indexes NK cell, C3 and C4 levels in peripheral blood of both groups were significantly lower than those before operation, and differences within same group were statistically significant before and after operation ( $P<0.05$ ). 1 d after operation, nonspecific immune response indexes NK cell, C3 and C4 levels in peripheral blood of thoracoscope group were significantly higher than those of open surgery group, and differences between groups were statistically significant after operation ( $P<0.05$ ), shown in Table 2.

### 3.3. Specific immune response

Comparison of specific immune response indexes CD4<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup>, IgA and IgG levels in peripheral blood between two groups of patients before and after operation was as follows: before operation, differences in specific immune response indexes CD4<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup>, IgA and IgG levels in peripheral blood were not statistically significant between two groups of patients ( $P>0.05$ ); 1 d after operation, specific immune response indexes CD4<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup>, IgA and IgG levels in peripheral blood of both groups were significantly lower than those before operation, and differences within same group were statistically significant before and after operation ( $P<0.05$ ). 1d after operation, specific immune response indexes CD4<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup>, IgA and IgG levels in peripheral blood of thoracoscope

group were significantly higher than those of open surgery group, and differences between groups were statistically significant after operation ( $P<0.05$ ), shown in Table 3.

## 4. Discussion

The selection of early middle esophagus cancer operation methods has been a clinical difficulty, malignant tumor itself has inhibitory effect on the body's defense function, and surgical trauma can further affect the body's immune function and cause postoperative inflammatory stress response[7]. Choosing effective and minimally invasive surgical method is one of the bases to radically cure malignant tumors, and along with the development of endoscopic techniques, thoracoscopic surgery becomes one of the reliable ways to radically cure esophagus cancer. In order to further clarify the advantages and disadvantages of thoracoscopic surgery and thoracotomy in the treatment of esophagus cancer, the incision pain and immune response were selected in the study to evaluate postoperative status of patients.

Surgical trauma is a kind of noxious stimulation that is transmitted to the central nervous system through sensory neurons, leads to the abnormality of a series of pain mediators, is finally transmitted out of the nerve centre and produces specific perception of pain[8,9]. Pain is a comprehensive feeling produced after a series of factor levels change, and its essence is the change of 5-HT, K<sup>+</sup>, NE and other pain mediator levels. K<sup>+</sup> is pain factor that can produce physical stimulation to the body and can also induce neurotransmitter 5-HT

**Table 2**Comparison of nonspecific immune response index levels before and after operation ( $\bar{x}\pm s$ ).

Groups	n	NK cell		C3 (g/L)		C4 (g/L)	
		Before operation	1 d after operation	Before operation	1 d after operation	Before operation	1 d after operation
Thoracoscope group	27	0.16±0.02	0.12±0.02	1.54±0.18	1.31±0.15	0.43±0.05	0.28±0.03
Open surgery group	29	0.15±0.02	0.06±0.01	1.57±0.19	1.08±0.13	0.42±0.05	0.17±0.02
t		0.162	6.482	0.217	6.392	0.155	6.498
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

**Table 3**Comparison of specific immune response index levels before and after operation ( $\bar{x}\pm s$ ).

Groups	n	CD4 <sup>+</sup>		CD4 <sup>+</sup> /CD8 <sup>+</sup>		IgA		IgG	
		Before operation	1 d after operation	Before operation	1 d after operation	Before operation	1 d after operation	Before operation	1 d after operation
Thoracoscope group	27	29.37±3.12	27.85±3.01	1.67±0.18	1.51±0.18	2.37±0.28	2.12±0.24	11.84±1.53	9.73±1.82
Open surgery group	29	29.54±3.09	24.69±2.74	1.69±0.19	1.27±0.16	2.41±0.27	1.76±0.23	11.75±1.69	6.94±0.75
t		0.162	6.993	0.109	6.283	0.217	7.342	0.142	9.834
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

secretion, act on the local area through the second messenger and stimulate sensory nerve endings to produce perception of pain[10,12]. NE is one of the important pain mediators, it has been found in rat models with a variety of acute or chronic pain that NE content increases, and it can reduce the pain threshold to increase the perception of pain[13]. In the study, postoperative pain mediator levels were compared between two groups of patients, and it was found that compared with open surgery group, the thoracoscope group were with lower serum 5-HT, K<sup>+</sup> and NE levels, which is consistent with the VAS score of the group in the study, and further illustrates that patients' incision pain is lighter after thoracoscope surgery.

Both surgical trauma itself and postoperative pain can inhibit the body's immune function and lead to the frequent occurrence of incision infection and the increased probability of residual tumor cell recurrence[14]. The immune response is the most important defense barrier of the body that includes two categories: nonspecific immunity and specific immunity. Nonspecific immunity, also called the innate immunity, can rapidly respond to the invaded pathogenic microorganisms, and also plays an important role in the specific immune start and effect process[15]. NK cells, complements and so on all belong to nonspecific immune system, and their levels directly reflect the nonspecific immune intensity[16,17]. In this study, thoracoscope group were with higher NK cell as well as C3 and C4 levels, showing that the thoracoscopic surgery inhibition on nonspecific immune system is lighter. Cellular immunity and humoral immunity form the specific immune system together, many studies have confirmed that surgical trauma can inhibit cellular immunity and humoral immunity function at the same time and weaken the killing effect of the body on pathogenic bacteria, and therefore, the more severe the surgical trauma, the higher the incidence of postoperative infection. In the study, early postoperative specific immune function was compared between two groups of patients, and it was found that compared with open surgery group, the thoracoscope group were with higher CD4<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup>, IgA and IgG levels 1d after operation, confirming that the thoracoscopic surgery inhibition on specific immune response system is lighter, and it indirectly confirms the minimal invasion of thoracoscopic surgery. To sum up, it is concluded that thoracoscopic esophagus cancer surgery causes less damage, has lighter inhibition on the immune response system, is an ideal operation method for patients with early middle esophagus cancer, and has positive application value in clinical practice.

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