Preservation of pulmonary branch of vagus nerve in three-dimensional thoracoscopic radical resection of lung cancer: a retrospective study

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Research Article

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Abstract

Background

Preservation of the pulmonary branch of the vagus nerve during systematic dissection of mediastinal lymph nodes in radical resection of lung cancer was studied to explore its role in reducing postoperative complications.

Methods

The clinical data of 80 patients who underwent three-dimensional thoracoscopic radical resection of lung cancer in the Department of Thoracic Surgery of Huizhou Municipal Central Hospital from 2020 to 2022 were analyzed. The patients were divided into two groups according to whether the pulmonary branch of the vagus nerve was retained during intraoperative carinal lymph node dissection: those in whom the pulmonary branch of the vagus nerve was retained and those in whom the pulmonary branch of the vagus nerve was not retained. The operative duration, first postoperative defecation time, chest tube duration, total chest drainage volume, average pain intensity during the first 5 days, incidence of postoperative pneumonia, and postoperative hospitalization duration were compared between the two groups.

Results

There was no significant difference in the first postoperative defecation time between the two groups (P > 0.05). However, there were statistically significant differences in the operative duration, chest tube duration, total chest drainage volume, average pain intensity during the first 5 days, white blood cell count and procalcitonin level on postoperative days 1 and 5, and postoperative hospitalization duration between the two groups (P < 0.05).

Conclusion

Preserving the pulmonary branch of the vagus nerve during carinal lymph node dissection in three-dimensional thoracoscopic radical resection of lung cancer can reduce postoperative complications.

Background

The vagus nerve is the tenth cranial nerve and contains mixed afferent (sensory), efferent (motor), and parasympathetic nerve fibers that innervate principal organs including the liver, lung, spleen, kidneys, and gut. The vagus nerve also plays an important role in regulating the heart rate [9, 10, 11]. The pulmonary branch of the vagus nerve is the parasympathetic nerve of the lung and is distributed in the bronchial smooth muscle, glands, and vascular wall. Inferior to the azygos arch, the main branches of the vagus nerve pass posteromedially to the main right bronchus and pulmonary hilum; they then branch off, forming the posterior pulmonary plexus, which contains 77% (62–100%) of the total nerve supply of the right lung [12, 14, 15]. Stimulation of the corresponding receptors leads to bronchial smooth muscle
contraction, glandular secretion, vascular congestion, and mucosal swelling, promoting timely sputum excretion and preventing postoperative lung infection \cite{1,2}. Perioperative pulmonary complications can be caused by many factors, including damage to the vagus nerve during thoracic surgery, severe pain caused by injury to the intercostal nerve, impaired postoperative lung function, and fear of coughing. Several studies in China and abroad have confirmed that preserving the vagus nerve during radical resection of upper gastrointestinal cancer can effectively reduce postoperative abdominal distention, constipation, vomiting, and other complications \cite{3,12,13}. However, few studies have focused on complications of radical resection of lung cancer with preservation of the vagus nerve. In this study, preservation of the pulmonary branch of the vagus nerve during systematic dissection of mediastinal lymph nodes in radical resection of lung cancer was studied to explore its role in reducing postoperative complications.

**Methods**

**Clinical data and grouping**

The clinical data of 80 patients who underwent three-dimensional (3D) thoracoscopic radical resection of lung cancer in the Department of Thoracic Surgery of Huizhou Municipal Central Hospital from 2020 to 2022 were analyzed. The patients were randomly divided into two groups by assignment of a single or double number. In Group A, the pulmonary branch of the vagus nerve was preserved during intraoperative carinal lymph node dissection; in Group B, the pulmonary branch was not preserved.

The inclusion criteria were (1) age of 18 to 65 years; (2) primary lung cancer requiring radical surgery; (3) performance of 3D thoracoscopic radical resection of the lung cancer; (4) no serious basic diseases of the heart, liver, kidney, or other organs that may affect postoperative recovery or prolong the hospital stay; and (5) an Eastern Cooperative Oncology Group (ECOG) score of 0 to 2.

The exclusion criteria were (1) benign pulmonary diseases not requiring lymph node dissection; (2) advanced lung cancer requiring only wedge resection; (3) serious basic diseases of the heart, liver, kidney, or other organs affecting postoperative recovery and prolonging the hospital stay; (4) preoperative pulmonary infection or long-term abdominal discomfort, such as abdominal distension and diarrhea; (5) an ECOG score of 3 or 4; (6) a requirement for intraoperative open surgery; and (7) injury or incision of the pulmonary branch of the vagus nerve during the operation.

**Surgical approach**

Radical surgery for lung cancer was performed with a 3D thoracoscope (Karl Storz SE & Co. KG, Tuttlingen, Germany). Double-cavity endotracheal intubation anesthesia was performed in both groups. Minimally invasive surgery was performed by two-hole thoracoscopy with the patient in the lateral decubitus position. The main operating incision was at the level of the third or fourth intercostal space in the midaxillary line and was about 3 to 4 cm in length. The exploration incision was at the level of the sixth or seventh intercostal space in the axillary line and was about 1 cm in length. The thoracoscope and
other instruments were inserted, and the pulmonary ligament and mediastinal pleura of the hilum were divided. The pulmonary artery, vein, bronchus, and fissure were fully dissociated and cut off with a stapler (Endo GIA; Medtronic, Minneapolis, MN, USA), and the hilar mediastinal lymph nodes were systematically dissected. The pulmonary branch of the vagus nerve was either preserved (Group A) or not preserved (Group B) according to the group assignment (Exposure of the pulmonary branch of the vagus nerve during mediastinal lymph node dissection are shown in Fig. 1 and Fig. 2). Two indwelling #16 chest tubes were placed for postoperative drainage. Extubation was performed when the chest radiographs showed that the lung had completely recovered, no air leakage was present, the drainage fluid was a light red or light yellow clear liquid, and the drainage volume was < 200 mL/day.

Clinical data

The following data were compared between the two groups: operative duration, first postoperative defecation time, chest tube duration, total chest drainage volume, average pain intensity during the first 5 days (postoperative pain was scored by visual simulation: 0 points, no pain; 2 points, slight pain; 4 points, mild pain; 6 points, obvious pain; 8 points, strong pain; 10 points, severe pain), incidence of postoperative pneumonia (radiographs suggested pulmonary exudation and peripheral blood showed an increased white blood cell [WBC] count and procalcitonin [PCT] level; the WBC count and PCT level were recorded on postoperative days 1 and 5, and postoperative hospitalization duration.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics Version 22 (IBM Corp., Armonk, NY, USA). Quantitative data with a normal distribution are expressed as mean ± standard deviation and were compared between the two groups using the t-test; otherwise, the rank sum test was used. Qualitative data are expressed as number and percentage and were compared between the two groups using the chi-square test. A P value of < 0.05 was considered statistically significant.

Results

The patients’ detailed clinical data are shown in Table 1. No significant differences were found in age, sex, weight, or first postoperative defecation time between the two groups (P > 0.05). However, there were statistically significant differences in the operative duration, chest tube duration, total chest drainage volume, average pain intensity during the first 5 days, WBC count and PCT level on postoperative days 1 and 5, and postoperative hospitalization time between the two groups (P < 0.05).
Table 1
Clinical data of Groups A and B

<table>
<thead>
<tr>
<th></th>
<th>All patients n = 80</th>
<th>Group A n = 40</th>
<th>Group B n = 40</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>59.58 ± 10.112</td>
<td>59.05 ± 11.204</td>
<td>60.1 ± 9.001</td>
<td>0.645</td>
</tr>
<tr>
<td>Sex (male, %)</td>
<td>36.45%</td>
<td>17.42.5%</td>
<td>19.47.5%</td>
<td>0.653</td>
</tr>
<tr>
<td>Mean weights, kg</td>
<td>59.12 ± 8.991</td>
<td>59.75 ± 7.801</td>
<td>58.49 ± 10.103</td>
<td>0.534</td>
</tr>
<tr>
<td>Operating time (mean hours ± SD)</td>
<td>3.47 ± 0.782</td>
<td>3.76 ± 0.745</td>
<td>3.19 ± 0.715</td>
<td>0.001</td>
</tr>
<tr>
<td>The first postoperative defecation time (mean day ± SD)</td>
<td>2.89 ± 2.365</td>
<td>2.88 ± 1.305</td>
<td>2.9 ± 3.103</td>
<td>0.237</td>
</tr>
<tr>
<td>Chest tube duration time(mean day ± SD)</td>
<td>4.7 ± 3.188</td>
<td>3.28 ± 1.502</td>
<td>6.13 ± 3.763</td>
<td>0.000</td>
</tr>
<tr>
<td>total chest drainage volume(ml ± SD)</td>
<td>979.88 ± 678.675</td>
<td>653 ± 289</td>
<td>1306 ± 794</td>
<td>0.000</td>
</tr>
<tr>
<td>average pain intensity of the first 5 days (mean intensity ± SD)</td>
<td>2.06 ± 0.789</td>
<td>1.76 ± 0.682</td>
<td>2.36 ± 0.78</td>
<td>0.000</td>
</tr>
<tr>
<td>1st day's WBC(10^9/L)</td>
<td>16.75 ± 4.146</td>
<td>15.59 ± 3.949</td>
<td>17.91 ± 4.058</td>
<td>0.01</td>
</tr>
<tr>
<td>1st day’s PCT</td>
<td>1.324 ± 3.065</td>
<td>0.502 ± 0.53</td>
<td>2.146 ± 4.167</td>
<td>0.000</td>
</tr>
<tr>
<td>5th day’s WBC(10^9/L)</td>
<td>11.33 ± 3.408</td>
<td>9.93 ± 3.176</td>
<td>12.74 ± 3.067</td>
<td>0.000</td>
</tr>
<tr>
<td>5th day’s PCT</td>
<td>0.500 ± 0.670</td>
<td>0.263 ± 0.230</td>
<td>0.737 ± 0.861</td>
<td>0.000</td>
</tr>
<tr>
<td>postoperative hospitalization time (mean day ± SD)</td>
<td>11.19 ± 4.198</td>
<td>11.7 ± 3.376</td>
<td>10.68 ± 4.875</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Discussion

In the absence of significant differences in age, sex, and weight between the two groups, the significantly longer average operation time in Group A than B suggests that preserving the pulmonary branch of the vagus nerve during intraoperative dissection of the carinal lymph nodes increased the difficulty of the operation and prolonged the operation time.

The vagus nerve releases acetylcholine (ACh) and promotes gastrointestinal smooth muscle contraction, resulting in defecation symptoms. Therefore, preserving the vagus nerve during radical resection of a
malignant upper gastrointestinal tumor can effectively reduce postoperative abdominal distention and constipation [3]. In the present study, however, we found no difference in the first postoperative defecation time between the two groups. We consider that this lack of a difference occurred because the patients’ digestive tract symptoms were mainly controlled by the abdominal branch of the vagus nerve; thus, intraoperative resection of the pulmonary branch of the vagus nerve did not have a significant impact.

Some studies have confirmed that vagal amputation can lower the threshold of reflex of mechanical retraction, indicating that release of ACh by the vagus nerve can protect against postoperative pain [8]. In this study, the average pain intensity was lower in Group A than B during the first 5 days after surgery, consistent with these previous findings.

The WBC count and PCT level were lower in Group A than in Group B on postoperative days 1 and 5, indicating that the vagus nerve plays a crucial role in the regulation of systemic and local inflammatory responses and can reduce the occurrence of inflammation [4]. It has been hypothesized that vagal receptors are activated by local proinflammatory factors that transmit signals into the central nervous system through afferent nerves and reflexively release ACh through efferent nerves, which are known to produce ACh [5]. ACh inhibits immune cells from producing proinflammatory factors by activating α7 nicotinic ACh receptors (α7nAChR) on immune cells [7]. When vagal circuits are intact, activation of α7nAChR can promote phosphorylation of AKT1 in splenic α7nAChR-expressing CD11b + granulocytes and confine these cells in the spleen. In previous research, disruption of vagal circuits reduced phosphorylation of AKT1 in splenic α7nAChR + CD11b + granulocytes and facilitated egress of these cells from the spleen to the lung. Without functional vagal circuits or α7nAChR agonist stimulation, α7nAChR + CD11b + cells accumulated in lungs challenged by lipopolysaccharides or *Escherichia coli*, failed to clear bacteria, and propagated inflammatory responses [6]. ACh also acts on the trachea and bronchial glands, which can result in bronchial smooth muscle contraction, promote the secretion of mucus by the glands, promote timely discharge of sputum, and prevent postoperative sputum accumulation, thus reducing the risk of lung infection [1,2].

The chest tube duration and total chest drainage volume were lower in Group A than in Group B. We consider that this occurred because the local inflammation of the lungs and pleura was reduced after preserving the vagus nerve. Preservation of the nerve can reduce the permeability of pleural capillaries and reduce the infiltration of cells, proteins, and fluids from capillaries to the pleural cavity, thus shortening the postoperative chest tube duration and reducing the risk of pleural cavity infection.

**Conclusion**

Preserving the pulmonary branch of the vagus nerve during carinal lymph node dissection in 3D thoracoscopic radical resection of lung cancer can reduce postoperative complications.

**Abbreviations**
Declarations

Ethics approval and consent to participate: This study was approved by the ethics committee of Huizhou Municipal Central Hospital. All patients and their family members provided written informed consent before surgery.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors’ contributions: Wencong Huang conducted the study and drafted the manuscript. Jiantian Yang and Huiwen Chen collected the data and performed the statistical analysis. Wei Wei completed the operation and supervised the study. Peijian Li participated in the operation. All authors read and approved the final manuscript. All authors read and approved the final manuscript.

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References


Figures
Figure 1

Exposure of the left pulmonary branch of the vagus nerve during mediastinal lymph node dissection
**Figure 2**

Exposure of the right pulmonary branch of the vagus nerve during mediastinal lymph node dissection