A retrospective study about 140 mediastinal lymphadenectasis patients receiving video-assisted mediastinoscopy

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Received December 12, 2015; Accepted April 13, 2016; Epub July 15, 2016; Published July 30, 2016

Abstract: This study aimed to provide theoretical bases for choosing examination methods on patients with mediastinal lymphadenectasis. The clinical characteristics of 140 patients with unexplained mediastinal lymphadenectasis who received video-assisted mediastinoscopy (VAM) were reviewed retrospectively. The relationship between various factors and pathological results of mediastinal lymphadenectasis was analyzed. There were no severe complications or death in these patients. The average operation time was 75.00±33.22 min and average blood loss was 55.07±14.13 ml. Pathological results showed that there were 74 malignant cases and 66 benign cases. The accuracy, sensitivity and specificity of VAM were 97.9%, 98.6% and 100% in identifying causes of mediastinal lymphadenectasis, respectively. These findings demonstrated that: 1) VAM is minimally invasive, safe and effective for the diagnosis and treatment of mediastinal lymphadenectasis. 2) During the diagnosis and staging of lung cancer or unexplained mediastinal lymphadenectasis with pulmonary abnormalities, endobronchial ultrasound-guided transbronchial needle aspiration may be applied first, and VAMs indicative for further diagnosis if negative results are found. 3) If patients with mediastinal lymphadenectasis have no pulmonary abnormalities or mediastinal neoplasm, VAMs preferred for examination.

Keywords: Video-assisted mediastinoscopy, mediastinal lymphadenectasis, endobronchial ultrasound-guided transbronchial needle aspiration, diagnosis

Introduction

Mediastinum is a common site for both benign and malignant diseases. There are many different organs in the mediastinum and thus the anatomical structure of the mediastinum is very complicated. In addition to its location and structure, the mediastinum does not communicate with the environment outside. These make the diagnosis of mediastinal diseases difficult and exert adverse effects on their treatments that largely rely on the accuracy of diagnosis. The treatments are significantly different between mediastinal diseases, and thus delayed and inaccurate diagnosis usually delays the treatment of these diseases, which significantly threaten the health of these patients. In 1954, Harken et al. for the first time conducted the biopsy of mediastinal lymph nodes by using the laryngoscope [1]. In 1959, Carlens perfected and systemically introduced the mediastinoscopy [2]. The significance of video-assisted mediastinoscopy (VAM) has been confirmed in the diagnosis of mediastinal diseases. This study aimed to further investigate the clinical use of VAM in the clinical diagnosis of mediastinal disease.

Patients and methods

A total of 140 patients who received video-assisted mediastinoscopy (WOLF CH-15DXA GERMANY) due to unexplained mediastinal lymphadenectasis were recruited from the Department of Cardiothoracic Surgery, The First Affiliated Hospital of Anhui Medical University between November 2009 and October 2014. All these patients had or had no lung lesions.

Clinical characteristics

There were 81 males and 59 females with the mean age of 47.11±15.13 years (range: 18-70 years). Nineteen patients were diagnosed with mediastinal diseases by physical examination and had no symptoms, while 119 patients had
clinical symptoms such as cough, chest tightness, hoarseness, hemoptysis, fever, etc. Two patients showed head and facial swelling (superior venacava syndrome).

All the patients received sputum cytological examination, chest enhanced CT as well as fiberoptic bronchoscopy. Additionally, PET-CT, bronchoscopy biopsy (TBNA) or CT guided percutaneous biopsy was performed in several patients. Mediastinal lymphadenectomy was defined as at least one enlarged mediastinal lymph node which was more than 10 mm in short axis in CT and located around the trachea [3].

Preoperative diagnosis: mediastinal lymphadenectomy with lung lesions was found in 67 patients, and mediastinal lymphadenectomy without lung lesions or mediastinal neoplasm was noted in 73 patients. Video-assisted mediastinoscopy (VAM) was performed for confirmed diagnosis.

Surgical procedure

On the basis of the location of lesions, cervical mediastinoscopy was performed in 132 patients and left parasternal mediastinoscopy in 8. Only 2 patients received local and intravenous anesthesia, and general anesthesia was performed in remaining 138 patients.

Cervical mediastinoscopy

Patients were placed in a supine position with a pillow under the shoulder to allow the hyperextension of the neck. Then, a 3-cm transverse incision was made at about 1.5 cm above the sternal notch. The skin and subcutaneous tissues were opened, pretracheal muscles were separated longitudinally, and the pretracheal fascia was exposed. After separation of the trachea, the surgeon used their fingers to touch the lesions. Upon the lesion being localized, the mediastinoscope was gently inserted, followed by needle aspiration biopsy at several sites. After biopsy, gelatin sponge was applied for hemostasis, and percutaneous drainage and absorbable hemostatic gauze were used when necessary.

Left parasternal mediastinoscopy

Patients were placed in a supine position. A 2-4 cm transverse incision was made at cm away from the 2nd or 3rd intercostal parasternal. Similarly, the surrounding skin and subcutaneous tissue as well as intercostal muscles were opened (the second costal cartilage was occasionally cut during this procedure). During the surgery, attention should be paid for the protection of the internal thoracic artery. The surgeon placed his index finger into the anterior mediastinum to push the left mediastinal pleura aside, open the front fascia of the thymus, and separate tissues until the aorta bow was exposed. The mediastinoscope was then inserted to search the aortic and hilar lymph nodes. After localization of lymph nodes, biopsy was performed. Then, the mediastinoscope was withdrawn and focal hemostasis was performed. Chest drainage was not necessary if this procedure was used.

Statistical analysis

All the data are expressed as mean ± standard deviation. Statistical analysis was performed with SPSS version 19; $\chi^2$ test or t test was used for the comparisons of factors between malignant and benign mediastinal lesion groups. A value of $P<0.05$ was considered statistically significant (Table 1).

Results

All the operations were successful and none died during the study. After operation, 2 patients presented cervical incision infection, which resolved after therapy; 1 patient present-
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ed superior vena cava syndrome, which was managed by endotracheal intubation and mechanical ventilation at 4 days after surgery.

Among these patients, a 25-year-old male was diagnosed with bronchial cyst. Chest CT showed mediastinal cyst which located in the right lower part of the trachea and was about 2 cm in diameter. The cyst was also completely removed by mediastinoscopy after collection of pink turbid liquid in the cyst.

Another 41-year-old male patient was diagnosed with lymphatic cyst. Chest CT showed sarcoidosis had high incidences in patients with benign diseases.

Discussion

Applications of mediastinoscopy:

Mediastinoscopy can be employed for the diagnosis and staging of mediastinal lymph nodes, primary lung cancer, metastatic carcinoma, esophageal cancer, head and neck cancer, lymphoma, inflammatory and granulomatous diseases, sarcoidosis, tuberculosis, pneumoconiosis and other tumors.

Table 2. Mediastinal diseases diagnosed with VAM in 140 patients with unexplained mediastinal lymphadenectasis

<table>
<thead>
<tr>
<th>Malignant diseases</th>
<th>Number</th>
<th>Benign diseases</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>36</td>
<td>Sarcoïdosis</td>
<td>22</td>
</tr>
<tr>
<td>Squamous cell carcinomas</td>
<td>12</td>
<td>Tuberculosis</td>
<td>28</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>19</td>
<td>Lymphadenitis</td>
<td>5</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5</td>
<td>Thymoma</td>
<td>3</td>
</tr>
<tr>
<td>Sarcomatoid carcinoma</td>
<td>1</td>
<td>Paraganglioma</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Leiomyoma</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lymphatic cyst</td>
<td>1</td>
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<tr>
<td></td>
<td></td>
<td>Bronchial cyst</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reactive hyperplasia</td>
<td>5</td>
</tr>
</tbody>
</table>

Five patients presented lymphadenitis: one was diagnosed with pulmonary mass and managed by lobectomy and lymph node dissection, pathological examination of the subcarinal lymph nodes after operation showed metastatic carcinoma; 2 patients received the thoracoscopic biopsy of pulmonary hilar lymph nodes, and pathological examination showed sarcoidosis; the remaining 2 patients were followed up for more than 6 months, the clinical diagnosis showed no change during the follow-up.

The operation time and blood loss were also recorded in 140 patients with mediastinal lymphadenectomy (Figures 1 and 2). The average operation time was 75.00±33.22 min, and the average blood loss was 55.07±14.13 ml.

Prevalence of comorbidities associated with unexplained mediastinal lymphadenectasis was calculated in the present study (Figures 3 and 4). Malignancy was confirmed in 74 patients and benign diseases in 66. Tuberculosis and sarcoidosis had high incidences in patients with benign diseases.
Video-assisted mediastinoscopy has been proven to be an easy and reliable procedure in addition to its safety and minimal invasiveness. Currently, surgery is performed under the combination of local anesthesia and intravenous anesthesia in many medical centers [4-6]. Video-assisted mediastinoscopy shows high accuracy during the diagnosis of suspected thoracic diseases with mediastinal lymphadenectomy. Our study showed the accuracy, sensitivity and specificity of mediastinoscopy were 97.9%, 98.6% and 100%, respectively, in the identification of causes of mediastinal lymphadenectomy. Additionally, none died after mediastinoscopy and serious surgical complications were not observed in the present study. Two patients presented cervical incision infection after operation, which resolved after symptomatic treatment. The average operation time was 75.00±33.22 min and the average blood loss was 55.07±14.13 ml.
bronchial needle aspiration (EBUS-TBNA) for lung cancer patients with mediastinal lymph node enlargement alone. If EBUS-TBNA shows negative results, additional mediastinoscopy is required for the confirmed diagnosis. Currently, mediastinoscopy is still considered as the best strategy for the staging of mediastinal lymph nodes prior to surgery in lung cancer patients [8]. It has been widely accepted as the gold standard for the staging of lung cancer [9, 10].

EBUS-TBNA is a relatively new technique. In recent years, many studies have shown that the role of EBUS-TBNA in the staging of mediastinal diseases is similar to that of VAM in the sensitivity, specificity, and accuracy. However, the sensitivity, specificity, and accuracy of VAM are slightly higher than those of EBUS-TBNA in mediastinal diseases [11-14]. In addition, there is still controversy on the role of EBUS-TBNA in the diagnosis of other mediastinal masses [15], as it is debatable whether EBUS-TBNA may completely replace mediastinoscopy [16]. Currently, few studies have been conducted to investigate the mediastinal benign lesions and simple mediastinal lesions without lung abnormality. In a Chinese study [17], EBUS-TBNA was performed in 164 patients presenting mediastinal lesions alone, confirmed diagnosis was made in 139 patients, in whom malignant diseases were identified in 68 patients and benign diseases in 71. Pathological examination showed benign diseases in 90 patients. This suggests that the sensitivity of EBUS-TBNA in the diagnosis of benign mediastinal lesions is only 78.89% (71/90). Zhang et al [18] reported that the sensitivity of EBUS-TBNA in the diagnosing mediastinal masses other than lung cancer was 77.42%. Our study showed that the sensitivity of VAM in the diagnosis of mediastinal benign lesions was 97% (64/66). In conclusion, we speculate that VAM is more sensitive and accurate as compared to EBUS-TBNA in the diagnosis of mediastinal lesions and thus VAM is preferred under the similar circumstances.

Sarcoidosis, tuberculosis, lymphoma and other diseases share clinical symptoms as well as laboratory detections, which make the confirmed diagnosis difficult. Different diseases usually present distinct prognoses. In this study, 24 patients with sarcoidosis were treated with steroids after mediastinoscopy; 28 patients were diagnosed with tuberculosis, and antituberculosis treatments were applied for 12-18 months after surgery; 5 patients were diagnosed with malignant lymphoma, and chemotherapy was employed accordingly. Mediastinoscopy is a golden standard in the diagnosis of above diseases [19].

China has a high incidence of tuberculosis, and mediastinal tuberculosis without pulmonary involvement is very common in these patients (~50% in this study). However, the confirmed diagnosis of this disease is difficult. Some studies [20] have shown that, in the diagnosis of mediastinal tuberculosis in patients presenting tuberculosis symptoms, the accuracy is 79% for EBUS-TBNA, 84% for cellular morphological examination and 63% for microbiological examination. Our study showed the accuracy of VAM was as high as 96.15% (50/52) in the diagnosis.
of mediastinal tuberculosis and sarcoidosis, which was consistent with previously reported (96%) [21].

Additionally, our study (Table 1) showed the sex, age and clinical symptoms were comparable between patients with benign and malignant mediastinal diseases (P>0.05). However, significant difference was observed in the lung involvement between patients with benign and malignant mediastinal diseases (P<0.01). This suggests that the presence of malignancy increases the incidences of mediastinal lymph nodes enlargement and lung abnormalities. It also suggests that benign disease is highly suspected in patients who have mediastinal lymph node enlargement without lung involvement.

Follow-up and prognosis: 135 cases were followed up for one to five years postoperatively, among which five cases were lost to follow-up with a follow-up rate of 96.3%. 18 patients with small cell lung cancers all received chemotherapies and radiation therapies with median survival time (MST) of 2.2 years. 48 patients with non-small cell lung cancers had a MST of 2.7 years. Among them, three cases showed significantly narrowed mediastinal lymph nodes in chest CT and gradually declined serum tumor markers after two cycles of neoadjuvant chemotherapies and/or radiation therapies. Five cases with lymphoma were treated with chemotherapies and/or radiation therapies with a MST of 3.2 years. One case with sarcomatoid carcinoma received surgical treatment and had a survival time of 17 months. All thymoma patients underwent surgery interventions (thoracoscope surgeries or open thoracic surgeries), but no recurrences occurred during follow-ups. Tubercle patients were treated with hormone, and all symptoms were relieved to different degrees, without worsening during the follow-ups. Lymphatic tuberculosis patients underwent regular anti-tuberculosis treatments for 12 to 18 months, and symptoms were relieved to different degrees. Only one case had a recurrence at 11 months after drug withdrawal.

In summary, VAM is a highly reliable and minimally invasive technique in the diagnosis of mediastinal diseases characterized by mediastinal lymphadenectasis. Not only confirmed diagnosis can be made, but patients may rapidly recover from this procedure. In clinical practice, it is necessary to select optimal, direct and minimally invasive procedure achieving the best efficacy. In our opinion, in the diagnosis and staging of lung cancer or mediastinal lymphadenectomy with pulmonary involvement, EBUS-TBNA may be applied first, and then VAM is recommended for further diagnosis if negative results are shown in EBUS-TBNA. For patients presenting with mediastinal lymphadenectomy without pulmonary involvement or mediastinal neoplasm, mediastinoscopy is preferred in which enough tissues can be collected for pathological examination, which avoids a second mediastinoscopy when other procedures fail to identify the diseases, reduces the waste of medical resource and decrease the injury to patients and the medical cost.

Endoscopic ultrasound guided biopsy is an alternative method for the identification of causes of mediastinal lymphadenectomy, but it may not entirely replace mediastinoscopy in clinical practice [22, 23]. Thus, mediastinoscopy is irreplaceable under our current medical technology.

The present study had some limitations. This was a retrospective study and other methods were not used in the present study for the diagnosis of mediastinal lymphadenectomy, and thus it failed to compare the sensitivity, specificity and accuracy of VAM with other techniques. Moreover, the sample size was small. Thus, more studies with large sample size are required to confirm our findings.

Disclosure of conflict of interest

None.

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