Int J Clin Exp Med 2016;9(7):12839-12845
www.ijcem.com /ISSN:1940-5901/IJCEM0021747

Original Article

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

Feng Zhu[1,2], Jian-Jun Ge[1]

[1]*Department of Cardiothoracic Surgery, The First Affiliated Hospital of Anhui Medical University, Hefei 230022, China;* [2]*Department of Thoracic Surgery, Anhui Provincial Chest Hospital, Hefei 230022, China*

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 onpatients 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 VAMis indicative for further diagnosis if negative results are found. 3) If patients with mediastinal lymphadenectasis have nopulmonary abnormalities or mediastinal neoplasm, VAMis preferred for examination.

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

Introduction

Mediastinum is acommon 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. Thesemake 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 alfor the first time conductedthe 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

Table 1. Univariate analysis of clinical parameters between patients with malignant and benign mediastinal lesions

	Malignant	Benign	x^2/t	*P*
Gender			0.165	0.684
Male	44	37		
Female	30	29		
Age	46.76±15.767	47.50±14.501	-0.289	0.773
Clinical symptoms			1.020	0.313
Yes	66	55		
No	8	11		
Pulmonary abnormality*			15.419	0.000
Yes	47	20		
No	27	46		

NOTES: Pulmonary abnormalities: lung placeholder, nodular shadows, patchy shadows and cavity lesions. *P<0.01: Significant differences were observed between patients with or without lung abnormalities.

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 lymphadenectasis 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 lymphadenectasis with lung lesions was found in 67 patients, and mediastinal lymphadenectasis 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 thelocation 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 separatetissues until theaorta 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; X^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-

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

Malignant diseases	Number	Benign diseases	Number
Adenocarcinoma	36	Sarcoidosis	22
Squamous cell carcinomas	12	Tuberculosis	28
Small cell carcinoma	19	Lymphadenitis*	5
Lymphoma	5	Thymoma	3
Sarcomatoid carcinoma	1	Paraganglioma	1
		Leiomyoma	1
		Lymphatic cyst	1
		Bronchial cyst	1
		Reactive hyperplasia	5

*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.

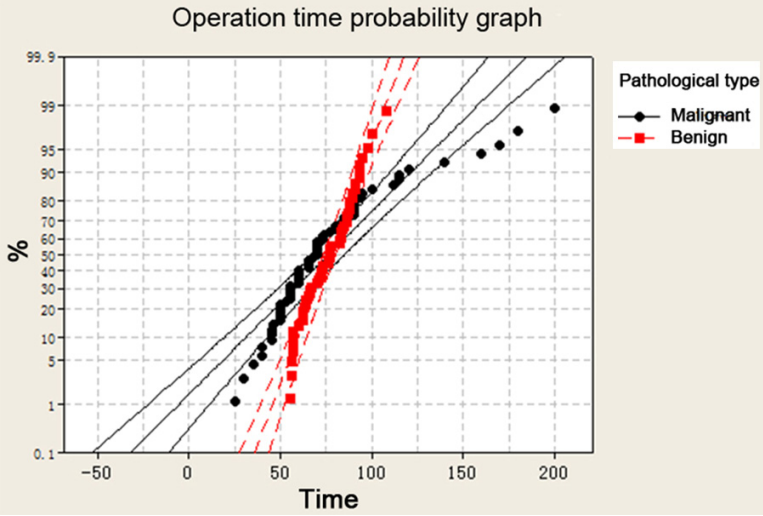

Figure 1. Operation time probability graph of 140 patients with mediastinal lymphadenectasis. The average operation time was 75.00±33.22 min.

ed superior vena cava syndrome, which was managedby endotracheal intubation and mechanical ventilation at 4 day 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 transparent jelly liquid was collected by mediastinoscopy and the cyst was then completely removed.

Another 41 year-old male pa tient was diagnosed with lymphatic cyst. Chest CT showed mediastinal cyst that 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.

Malignancies were found in 73 patients (adenocarcinoma: n=36, small-cell-carcinoma: n=19, squamous cell carcinoma: n=12, lymphoma: n=5 and sarcomatoid carcinoma: n=1) and benign diseases in 67 patients (tuberculosis: n=28, sarcoidosis: n=22, reactive hyperplasia: n=5, inflammatory lymph nodes: n=5, thymoma: n=3, paraganglioma: n=1, leiomyoma: n=1, lymphatic cyst: n=1 and bronchial cyst: n=1) (**Table 2**).

The operationtime and blood loss were also recorded in 140 patients with mediastinal lymphadenectasis (**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.

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, ruberculosis, penumoconiosis and other tumors.

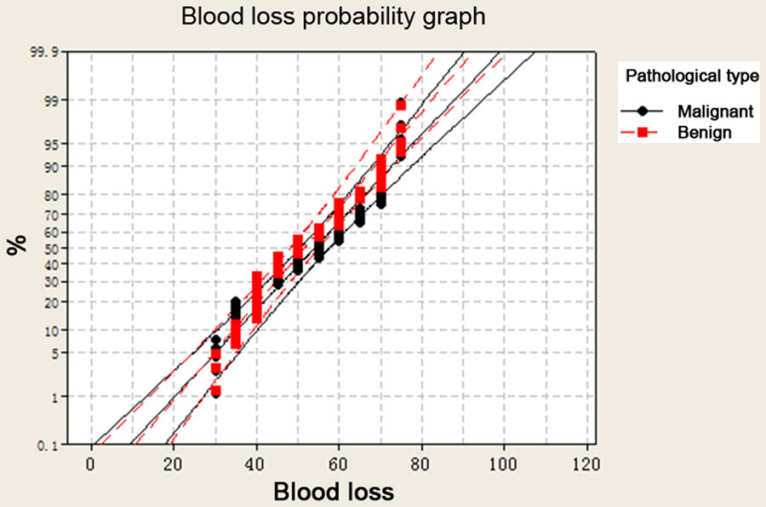

Figure 2. Blood loss probability graph of 140 patients with mediastinal lymphadenectasis. The average blood loss was 55.07±14.13 ml.

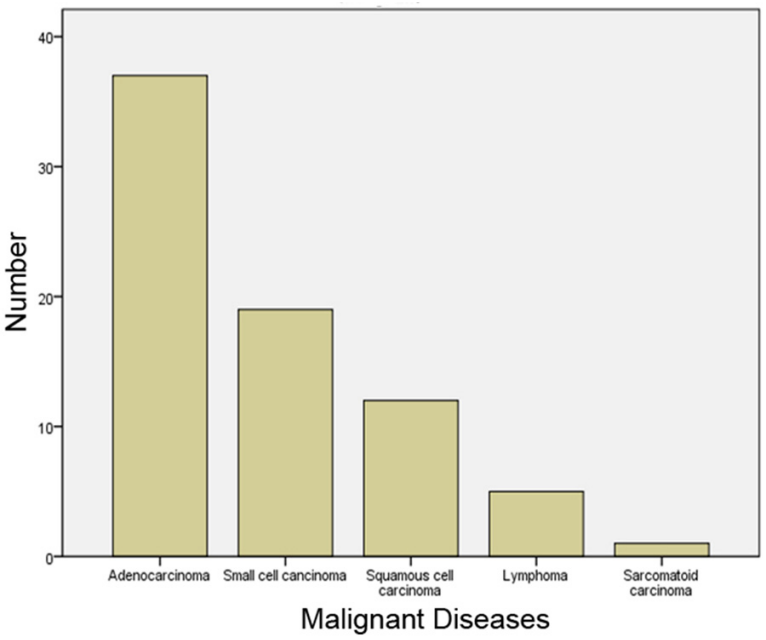

Figure 3. Prevalence of comorbidities associated with malignant mediastinal lymphadenectasis in 140 patients.

Mediastinoscopy can beused for the diagnosis of thymomas, bronchogenic cyst, teratoma, dermoid cyst, embryonic cell tumor, cervical space-occupying diseases, parathyroid diseaseas well as struma endothoracia.

The cervical mediastinoscopy can be used for the biopsy of enlarged lymph nodes and lesions that are located around the trachea, below the protuberantia, as well as in the main bronchus. However, this technique is difficult to detectlesions around aortic pulmonic window, around aortaand in theanterior mediastinum. Left para mediastinal endoscopy is preferred if lesions are found in these areas.

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 lymphadenectasis. 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 lymphadenectasis. 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 operationtime was 75.00±33.22 min and the average blood loss was 55.07±14.13 ml.

Currently, CT scan and PET are widely used for the noninvasive staging of the mediastinal lymph nodes. However, CT often presents a low accuracy and PET shows a high false-positive rate. Thus, for patients with mediastinal lymphadenectasis, invasive examinations are usually recommended if CT and/PET fails to confirm the diagnosis. In a study of Feng et al [7], the authors recommended both mediastinoscopy and endobronchial ultrasound-guided trans-

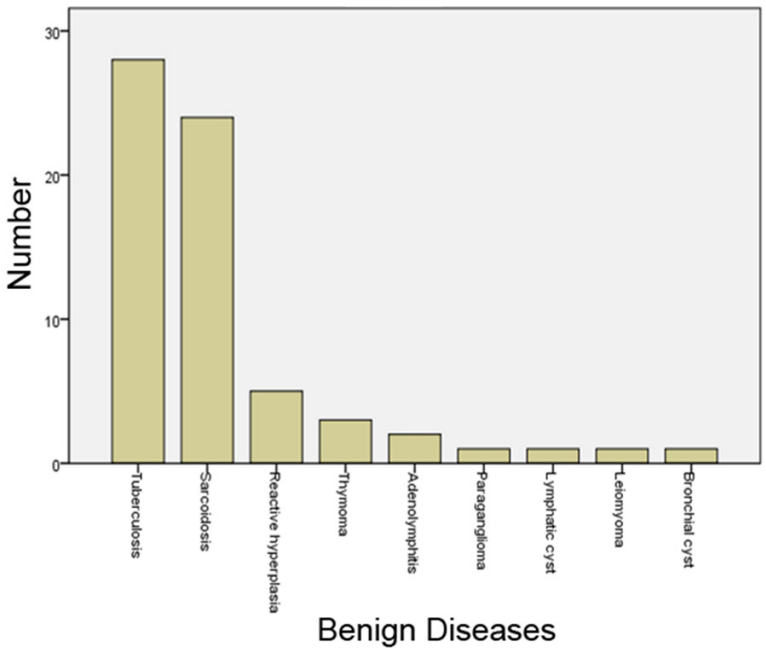

Figure 4. Prevalence of comorbidities associated with benign mediastinal lymphadenectasis in 140 patients.

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 asabest strategyfor the staging of mediastinal lymph nodes prior to surgery in lung cancer patients [8]. It has been widely accepted 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-TBNAin 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 diagnosisof mediastinal benign lesions was 97% (64/66). In conclusion, we speculate that VAM ismore 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 andother diseases share clinical symptoms as well as laboratory detections, which make theconfirmed 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 anti-tuberculosis 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 tofollow-up with a follow-up rate of 96.3%. 18 patients with small cell lung cancers all received chemotherapies and radiation therapies witha 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 inchest CTand gradually declined serum tumor markers after two cycles of neoadjuvant chemotherapies, and then received surgical interventions; one case gave up treatments; and the rest 44 cases were treated with chemotherapies and/or radiation therapies. Five cases with lymphoma are 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 todifferent 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 lymphadenectasis 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 lymphadenectasis 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 lymphadenectasis, 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 lymphadenectasis, 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.

Address correspondence to: Dr. Jian-Jun Ge, Department of Cardiothoracic Surgery, The First Affiliated Hospital of Anhui Medical University, Jixi Rd 218, Hefei 230022, China. Fax: 86-551-63633507; E-mail: gejianjundoc@163.com

References

[1] Harken DE, Black H, Clauss R and Farrand RE. A simple cervicomediastinal exploration for tissue diagnosis of intrathoracic disease; with comments on the recognition of inoperable carcinoma of the lung. N Engl J Med 1954; 251: 1041-1044.

[2] Carlens E. Mediastinoscopy: a method for inspection and tissue biopsy in the superior mediastinum. Dis Chest 1959; 36: 343-352.
[3] Evison M, Crosbie PA, Morris J, Martin J, Barber PV and Booton R. A study of patients with isolated mediastinal and hilar lymphadenopathy undergoing EBUS-TBNA. BMJ Open Respir Res 2014; 1: e000040.
[4] Rendina EA, Venuta F, De Giacomo T, Ciccone AM, Moretti MS, Ibrahim M and Coloni GF. Biopsy of anterior mediastinal masses under local anesthesia. Ann Thorac Surg 2002; 74: 1720-1722; discussion 1722-1723.
[5] Shao F, Su YJ, Xu DS, Yang RS and Wsng KP. Video-mediastinoscopy in the Diagnosis and Treatment of Chest Diseases in 36 Cases. Chin J Clin Thorac Cardiovasc Surg 2009; 16: 76-78.
[6] Wei B, Bryant AS, Minnich DJ and Cerfolio RJ. The safety and efficacy of mediastinoscopy when performed by general thoracic surgeons. Ann Thorac Surg 2014; 97: 1878-1883; discussion 1883-1874.
[7] Feng HX, Zhang ZR and Liu DR. The Value of endobronchial ultrasound-guide transbronchial needle aspiration versus mediastinoscopy in preoperative staging of lung cancer. J Chi-Japan Friendsh Hosp 2013; 27: 142-145.
[8] Bauwens O, Dusart M, Pierard P, Faber J, Prigogine T, Duysinx B, Nguyen B, Paesmans M, Sculier JP and Ninane V. Endobronchial ultrasound and value of PET for prediction of pathological results of mediastinal hot spots in lung cancer patients. Lung Cancer 2008; 61: 356-361.
[9] Guerra M. Video-mediastinoscopy is still the gold standard. Rev Port Pneumol 2014; 20: 52.
[10] Nalladaru ZM and Wessels A. The role of mediastinoscopy for diagnosis of isolated mediastinal lymphadenopathy. Indian J Surg 2011; 73: 284-286.
[11] Annema JT, van Meerbeeck JP, Rintoul RC, Dooms C, Deschepper E, Dekkers OM, De Leyn P, Braun J, Carroll NR, Praet M, de Ryck F, Vansteenkiste J, Vermassen F, Versteegh MI, Veselic M, Nicholson AG, Rabe KF and Tournoy KG. Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial. JAMA 2010; 304: 2245-2252.
[12] Tian Q, Chen LA, Wang HS, Zhu BH, Tian L, Yang Z and An Y. Endobronchial ultrasound-guided transbronchial needle aspiration of undiagnosed mediastinal lymphadenopathy. Chin Med J (Engl) 2010; 123: 2211-2214.
[13] Garcia-Olive I, Valverde Forcada EX, Andreo Garcia F, Sanz-Santos J, Castella E, Llatjos M, Astudillo J and Monso E. [Linear endobronchial ultrasound as the initial diagnostic tool in patients with indications of mediastinal disease]. Arch Bronconeumol 2009; 45: 266-270.
[14] Gu P, Zhao YZ, Jiang LY, Zhang W, Xin Y and Han BH. Endobronchial ultrasound-guided transbronchial needle aspiration for staging of lung cancer: a systematic review and meta-analysis. Eur J Cancer 2009; 45: 1389-1396.
[15] Zhang R, Mietchen C, Kruger M, Wiegmann B, Golpon H, Dettmer S, Haverich A and Zardo P. Endobronchial ultrasound guided fine needle aspiration versus transcervical mediastinoscopy in nodal staging of non small cell lung cancer: a prospective comparison study. J Cardiothorac Surg 2012; 7: 51.
[16] Medford AR, Bennett JA, Free CM and Agrawal S. Mediastinal staging procedures in lung cancer: EBUS, TBNA and mediastinoscopy. Curr Opin Pulm Med 2009; 15: 334-342.
[17] Zhen X, Zhao H, Zhou ZL, Sui XZ and Wang J. Endobronchial Ultrasound-guided Transbronchial Needle Aspiration for Diagnosis and Differential Diagnosis of Mediastinal Lesions. Chin J Min Inv Surg 2013; 13: 295-299.
[18] Zhang L, Mao F, Cai MH and Shen TY. A Comparative Study on the Diagnosis and Staging of Lung Cancer between Mediastinoscopy and EBUS-TBNA. Chin J Lung Cancer 2013; 16: 289-293.
[19] Li X, Xu S, Liu HX and Yang CL. Retrospective analysis of the diagnostic and therapeutic value of video-mediastinoscopy for disease of mediastinum. Chin J Cancer Prev Treat 2012; 19: 702-703.
[20] Hassan T, McLaughlin AM, O'Connell F, Gibbons N, Nicholson S and Keane J. EBUS-TBNA performs well in the diagnosis of isolated thoracic tuberculous lymphadenopathy. Am J Respir Crit Care Med 2011; 183: 136-137.
[21] Liu X, Zhang D, Lin D, Zhao J and Wang L. [The role of mediastinoscopy for the diagnosis of mediastinal tuberculous lymphadenopathy and sarcoidosis]. Zhonghua Jie He He Hu Xi Za Zhi 1999; 22: 156-158.
[22] Witte B, Neumeister W and Huertgen M. Does endoesophageal ultrasound-guided fine-needle aspiration replace mediastinoscopy in mediastinal staging of thoracic malignancies? Eur J Cardiothorac Surg 2008; 33: 1124-1128.
[23] Inzirillo F, Giorgetta C, Ravalli E, Tiberi S and Pona CD. Videomediastinoscopy: a ten year experience on lung cancer stadiation and non-diagnosed mediastinal lymphoadenopathy. Chirurgia (Bucur) 2014; 109: 451-454.