



Uniportal video-assisted thoracic surgery in the diagnosis of mediastinal lymphadenopathy of unknown aetiology

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Background: Recently endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) has been widely reported to be useful for patients with lung cancer for lymph node staging, and this tool may be the first line procedure for patients with mediastinal and hilar lymphadenopathy of unknown aetiology. However, more invasive techniques as mediastinoscopy and video-assisted thoracic surgery (VATS) are useful in well-selected patients, and surgery has a significant role in the evaluation of some areas in the mediastinum. The purpose of the current study was to investigate the clinical utility of VATS with the uniportal approach in the diagnosis of mediastinal lymphadenopathies of unknown aetiology.

Methods: Retrospective chart review of our VATS database between 2003 and 2013 (10-year experience) was performed. All mediastinal lymphadenopathies of unknown origin were included in the study and were classified and designated according to the International Staging System. Pathological diagnosis was determined in all patients and was classified into two categories: malignant lymphadenopathy and benign lymphadenopathy.

Results: A total of 136 patients with mediastinal lymphadenopathy of unknown origin were identified, and the final diagnosis was available in all patients' means of VATS surgery with uniportal technique. We no consider mediastinoscopy cases. The final diagnosis was available in all patients and was 114 malignant lymphadenopathies and 22 benign lymphadenopathies. VATS was safe (without complications) and had a sensitivity and a specificity of 100%, and it permits to study all areas of the mediastinum. Additionally, VATS surgery is accurate in the diagnosis of EBUS-TBNA negative lymphadenopathy (26 patients, 19%).

Conclusions: VATS is a safe and reliable minimally invasive approach for a sampling of mediastinal and hilar lymphadenopathies, and it should be considered a second line procedure for a sampling of mediastinal tissue. However, in some areas of the mediastinum (anterior, posterior, left 5–6 lymph node stations) and in the cases where EBUS-TBNA fails, this is a winning tool for obtaining a pathological diagnosis of mediastinal disease. We also believe that for these patients are paramount a multidisciplinary approach.

Keywords: Mediastinal lymphadenopathy; endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA); video-assisted thoracic surgery (VATS); minimally invasive surgery

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Introduction

Patients with mediastinal lymphadenopathy require an accurate diagnosis to determine as soon as possible an optimal treatment. During the past decade, real-time endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) has become a safe technique for staging lung cancer (1-3).

EBUS-TBNA combines endoscopic visualisation with high-frequency ultrasound imaging, which is used to obtain tissue samples of mediastinal lesions adjacent to the tracheobronchial tree, under sedation in the outpatient setting (4). As many authors reported, EBUS-TBNA had a sensitivity of more than 90% (5,6) equivalent to or even superior to that of mediastinoscopy and had lower associated costs and fewer morbidities (7). Now EBUS-TBNA is the first line procedure for the diagnosis of benign and malignant lesions of the mediastinum (lymphoma, lung cancer, sarcoidosis, tuberculosis, etc.).

However, also EBUS-TBNA has its limitations, either because some areas in the mediastinum are inaccessible for this procedure or because of its false negative rate. The main aim of our study was to evaluate the reliability of video-assisted thoracic surgery (VATS) in obtaining a histological diagnosis of mediastinal lymph nodes (in all areas of mediastinum) and define its role in subsequent workup and treatment plan for these patients.

Methods

We retrospectively reviewed 136 patients who underwent to VATS biopsy of mediastinal lymphadenopathy from January 2003 to December 2013 at the Department of Thoracic Surgery of AUSL Romagna, and data were retrieved from individual medical records. Patients with mediastinal lymphadenopathy of unknown aetiology (also those with a previous history of lung cancer or others extrapulmonary malignancy) were identified and were considered eligible for VATS biopsy by traditional staging with chest radiography, bronchoscopy, thoracic/abdominal/brain CT. All 136 patients were investigated by CT scan, performed not later than 30 days from the surgery, and 92 patients were also evaluated by positron emission tomography (PET)/CT with fluorodeoxyglucose.

The lymph node stations of the mediastinum and hilar regions were designated according to the International Staging System (8).

Surgical technique

All patients were operated on under general anaesthesia with double-lumen endotracheal intubation. All were positioned in the lateral decubitus, and in all cases, only one incision (2–2.5 cm) is placed in the fifth intercostal space along the middle axillary line (9-11). Sometimes, for high lymph node stations as left 5–6 lymph node stations or 2–4 stations, the incision is placed in the fourth or third intercostal place along the middle axillary line. A 30° 5-mm video thoracoscope and 5-mm endoscopic instruments were used. The targeted nodal station is approached, and the mediastinal pleura is opened by endoscissors or terminal devices. The nodes are sampled with a biopsy forceps, in a fashion similar to the traditional mediastinoscopy procedure. If it is possible, the entire lymph node is excised, and an endoclip is fired at the base of the vascular pedicle. Adequate haemostasis is obtained with use of endoclips, coagulation, thermal devices. We used a singular 28 French thoracic tube to drain the mediastinum for 1–2 days. The uniportal-VATS biopsies were uneventful, and there were no complications for the patients.

Statistical analysis

Patient characteristics are reported as means \pm standard deviations or n (%), as appropriate. Overall survival (OS) was defined as the time from date of surgery to death due to any cause.

Results

One hundred thirty-six patients were identified from our database (85 men, and 51 women), mean age 57 ± 17 and underwent to VATS surgery and no complications were observed. The final diagnosis was obtained by final pathologic confirmation in all the patients.

All 136 patients underwent to definitive VATS biopsy, in all of these areas of mediastinum with a sensitivity and a specificity of 100%.

A malignant mediastinal process was diagnosed in 114 patients and a benign process in 21 patients.

Malignant lymphoma was the most frequently seen malignant mediastinal tumour (n=43) (Table 1). There were 25 cases of lung cancer, 28 cases of thymoma, 16 cases of lymph node metastases from epithelial tumours of extrathoracic origin, 2 cases of sarcoma.

The benign mediastinal lymphadenopathies consisted of sarcoidosis (n=6), and tuberculosis (n=16).

Table 1 Clinical Characteristics and final diagnosis of mediastinal lymphadenopathy of unknown origin

Parameter	No (%)
Number of patients	136 (100.0)
Sex	
Male	85 (62.0)
Female	51 (38.0)
Age (mean \pm SD)	57 \pm 17
Histology	
Malignant mediastinal	114
Malignant lymphoma	43 (32.0); 28 NHL, 15 HL
Thymoma	28 (21.0)
NSCLC/SCLC metastasis (lung cancer)	25 (18.0)
Nodal metastasis from extrathoracic epithelial tumours	16 (11.0)
Sarcoma	2 (1.5)
Benign mediastinal	22
Tuberculosis	16 (12.0)
Sarcoidosis	6 (4.4)
EBUS	
Yes	26 (19.0)
No	110 (81.0)

HL, hodgkin lymphoma; NHL, non-hodgkin lymphoma.

The pretracheal and subcarinal lymph node stations (3a-7) were the site of biopsy in 34 (25%) patients, paratracheal lymph node (R2-4/L2-4) were the site of biopsy in 16 (12%) patients. Para-aortic and subaortic nodes [5-6] were the site of biopsy in 35 (26%) patients, para-esophageal and pulmonary ligament nodes (R-L8-9) were the site of biopsy in 23 (17%) patients. Twenty-seven (20%) patients had only hilar lymph nodes (R-L10) sampled (*Table 2*).

After a mean follow-up of 38 months, 65 (45%) patients are alive. Twenty-six (19%) patients had previous negative EBUS-TBNA with a VATS diagnosis of malignant disease in 15 cases. Mean hospital stay was 2 \pm 1.8 days.

Discussion

EBUS-TBNA is an accurate and safe tool in the diagnosis of benign and malign mediastinal lymphadenopathies. It

Table 2 Lymph node stations

Lymph node stations	No (%)
3-7	34 (25.0)
R2-4/L2-4	16 (12.0)
L5-L6	35 (26.0)
R8-9/L8-9	23 (17.0)
R-L10	28 (20.0)

L, left; R, right.

can necessarily be the first-line procedure in these patients, but it cannot completely replace surgery.

EBUS-TBNA requires considerable training to acquire adequate competence [previously significant improvement in diagnostic performance was seen after the completion of 20 procedures and diagnostic accuracy did not peak until after 50 procedures (11)].

Besides, there is controversy regarding the role of small volume diagnostic specimens for the diagnosis of lymphoma, and cytological diagnosis of lymphoma is harder than that for epithelial tumours. For these reasons, today many authors prefer surgical biopsy for patients with suspicious of mediastinal lymphoma.

Thoracoscopic approach to a mediastinal lymphadenopathy requires a significant experience in VATS but is a safe and accurate procedure for these patients (12). It can necessarily be a second-line procedure for the majority of cases. Also, it can be essential for those patients with negative EBUS-TBNA but with high suspicion of mediastinal disease (EBUS false-negative) and for those with lymphadenopathies in not accessible areas of the mediastinum. Indeed, EBUS-TBNA has the inability to access some parts of the mediastinum and in particular the anterior and posterior mediastinum. The posterior mediastinum may be accessible by EUS-FNA, and some authors believe that by combining EBUS-TBNA and EUS-FNA the majority of the mediastinum is accessible (13,14). However, even with this combination, the anterior mediastinum is tough to access; in our experience stations, L5-6 are not manageable with this EBUS-TBNA.

VATS is feasible for all areas of the mediastinum, with a sensitivity of 100% and a specificity and overall accuracy of 100%. In our population of 26 (19%) cases of EBUS-TBNA negative, VATS permitted to obtain a particular diagnosis of disease (11 cases of benign disease and 15 cases of malignant lymphadenopathies).

In the competent hands, VATS is an accurate and

safe procedure in the diagnosis of mediastinal and hilar lymphadenopathy, and sometimes, it can necessarily be the first-line procedure. Also, it requires considerable training to acquire competence in different areas of the mediastinum, especially with uniportal technique. However, it should always be considered for evaluation of mediastinal lymphadenopathies in non-accessible areas and in all cases in which TBNA failed to obtain a diagnosis, but it is highly suspicious of disease. In our experience is crucial to offer patients with the mediastinal disease a multidisciplinary approach in which different experiences (pneumologist, surgeon, endoscopist) may compare and identify the best diagnostic procedure for the patient.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/vats.2018.09.04>). LB serves as an unpaid editorial board member of *Video-Assisted Thoracic Surgery* from Jul 2016 to May 2019. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was given by all patients. IRB for this retrospective analysis was waived.

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References

- Varela-Lema L, Fernández-Villar A, Ruano-Ravina A. Effectiveness and safety of endobronchial ultrasound-transbronchial needle aspiration: a systematic review. *Eur Respir J* 2009;33:1156-64.
- Trisolini R, Lazzari Agli L, Patelli M. Conventional vs endobronchial ultrasound-guided transbronchial needle aspiration of the mediastinum. *Chest* 2004;126:1005-6.
- Herth FJ, Eberhardt R, Vilmann P, et al. Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes. *Thorax* 2006;61:795-8.
- Yasufuku K, Chiyo M, Koh E, et al. Endobronchial ultrasound guided transbronchial needle aspiration for staging of lung cancer. *Lung Cancer* 2005;50:347-54.
- Medford AR, Bennett JA, Free CM, et al. Mediastinal staging procedures in lung cancer: EBUS, TBNA and mediastinoscopy. *Curr Opin Pulm Med* 2009;15:334-42.
- Yasufuku K, Chiyo M, Sekine Y, et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. *Chest* 2004;126:122-8.
- Lemaire A, Nikolic I, Petersen T, et al. Nine-year single center experience with cervical mediastinoscopy: complications and false negative rate. *Ann Thorac Surg* 2006;82:1185-9; discussion 1189-90.
- Mountain CF, Dresler CM. Regional lymph node classification for lung cancer staging. *Chest* 1997;111:1718-23.
- Solaini L, Prusciano F, Bagioni P, et al. Video-assisted thoracic surgery major pulmonary resections. Present experience. *Eur J Cardiothorac Surg* 2001;20:437-42.
- Solaini L, Prusciano F, Bagioni P, et al. Video-assisted thoracic surgery (VATS) of the lung: analysis of intraoperative and postoperative complications over 15 years and review of the literature. *Surg Endosc* 2008;22:298-310.
- Rocco G, Brunelli A, Jutley R, et al. Uniportal VATS for mediastinal nodal diagnosis and staging. *Interact Cardiovasc Thorac Surg* 2006;5:430-2.
- Steinfort DP, Hew MJ, Irving LB. Bronchoscopic evaluation of the mediastinum using endobronchial ultrasound: a description of the first 216 cases carried out at an Australian tertiary hospital. *Intern Med J* 2011;41:815-24.
- Solaini L, Bagioni P, Campanini A, et al. Diagnostic role of videothoracoscopy in mediastinal diseases. *Eur J Cardiothorac Surg* 1998;13:491-3.
- Vilmann P, Krasnik M, Larsen SS, et al. Transesophageal endoscopic ultrasound-guided fine-

needle aspiration (EUS-FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsy: a combined approach in

the evaluation of mediastinal lesions. *Endoscopy* 2005;37:833-9.

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