

## Endobronchial ultrasound-guided transbronchial needle aspiration of lesions in mediastinum

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### ABSTRACT

**Background** Lesions in mediastinum can represent malignancy and warrants further workup. Commonly a diagnosis is achieved by conventional bronchoscopy, transbronchial needle aspiration or CT guided fine needle aspiration, however a number of patients remain undiagnosed despite these common investigations

**Methods** During a period of 36 months 601 patients underwent EBUS at our institution. Two hundred ninety three patients had an established diagnosis of lung cancer and were referred to us for mediastinal staging. The remaining patients had a radiologically suspicious intrathoracic lesion of which 107 had an undiagnosed lesion in mediastinum. All patients had been investigated by previous chest CT and bronchoscopy including brush cytology but remained undiagnosed.

**Results** Of the 107 patients with undiagnosed lesions in the mediastinum 89 enlarged lymph nodes and 18 mediastinal tumours. Forty-eight of the 89 patients (54%) with enlarged mediastinal lymph nodes were diagnosed by EBUS of the remaining 41 patients 11 went on to more invasive methods.

In patients with undiagnosed tumours in mediastinum we achieved a final diagnosis by EBUS in 14 of the 18 patients (78%) and 3 went on to more invasive methods.

**Conclusion** EBUS provides a final diagnosis in 78% of patients with tumour in mediastinum and in more than half of patients with enlarged lymph nodes despite previous workup.

### Key Words:

lung cancer; tumour mediastinum; EBUS

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## Introduction

Lesions in mediastinum represent enlarged lymph nodes or tumour, and warrants further workup. Commonly a diagnosis is achieved by conventional bronchoscopy, transbronchial needle aspiration (TBNA) or CT guided fine needle aspiration (CT-FNA), however a number of patients remain undiagnosed despite these common investigations. A tissue diagnosis is often achieved by repeating the TBNA/ CT-FNA or performing a mediastinoscopy which is an invasive surgical procedure that poses a small but significant risk to the patient (1).

Endobronchial ultrasound-guided trans-bronchial needle aspiration (EBUS) is a well established method for mediastinal

staging of lung cancer (2-6). Previous investigations have demonstrated that EBUS may also be used in the diagnostic workup of patients with suspicious central masses (7,8). We recently demonstrated that the yield of EBUS for undiagnosed intra-thoracic lesions in general was 45%-55% (9,10). The yield of EBUS depends on previous diagnostic workup and the anatomical location of the intra-thoracic lesion (10).

Patients with undiagnosed lesion in mediastinum despite previous workup are a common challenge for the clinician. We conducted an analysis of our data to investigate if EBUS can provide a diagnosis of undiagnosed lesions in mediastinum despite previous workup.

## Material and methods

During a period of 36 months (January 2006 to December 2008) 601 patients underwent EBUS at our institution. Two hundred ninety three patients had an established diagnosis of lung cancer and were referred to us for mediastinal staging. The remaining 308 patients had a radiologically suspicious lesion but no diagnosis in mediastinum (n = 107) consisting of enlarged lymph nodes in the mediastinum (n = 89) and suspicious tumor in the mediastinum (n = 18), peripheral lung parenchyma (n =

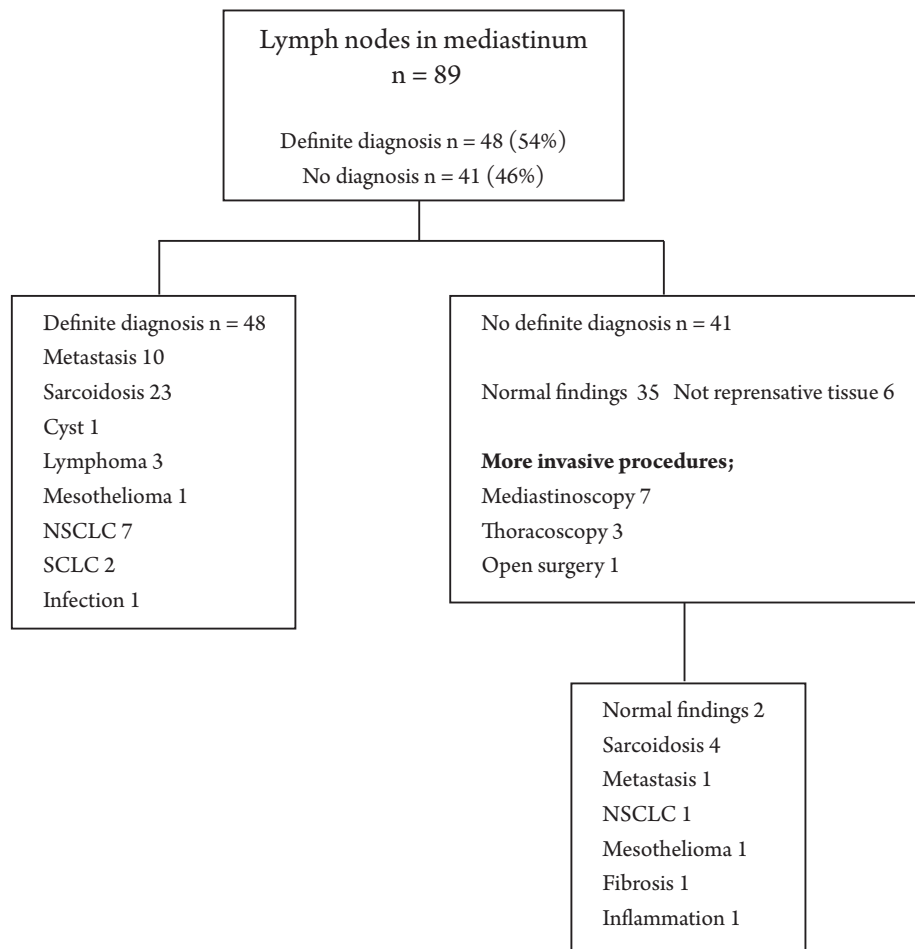
No potential conflict of interest.

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**Fig 1.** demonstrate diagnosis for patients with enlarged lymph nodes

95), a central lesion in lung parenchyma (n = 82), bilaterally lung lesions (n = 18) or rare causes (n = 6). All 308 patients had been investigated by previous chest CT and bronchoscopy including brush cytology but remained undiagnosed.

All patient charts were reviewed and the following data collected for analysis: age, sex, indication for diagnostic work-up, surgical notes, surgical procedures, complications, cytology report, histology reports after further investigations and outpatient notes. All EBUS examinations were performed in general anesthesia with a linear scanner (BF-UC160F, Olympus). Masses in the mediastinum, lung parenchyma or enlarged paratracheal or hilar lymph node stations 2, 3, 4, 7, 10 and 11 according to Mountain et al. (11) were systematically identified and punctured. Fine needle aspiration was performed with a 22G needle (NA-201SX-4022, Olympus) during real-time EBUS. Two aspirations were performed from each lesion to ensure that the biopsy contained sufficient material. Aspirated material was expelled onto glass slides and smeared for cytological examination or expelled into saline for preparation of cell blocks for histological examination. Rapid on-site evaluation was not performed. Instead, all biopsies were reviewed the following day by an experienced pathologist, and classified

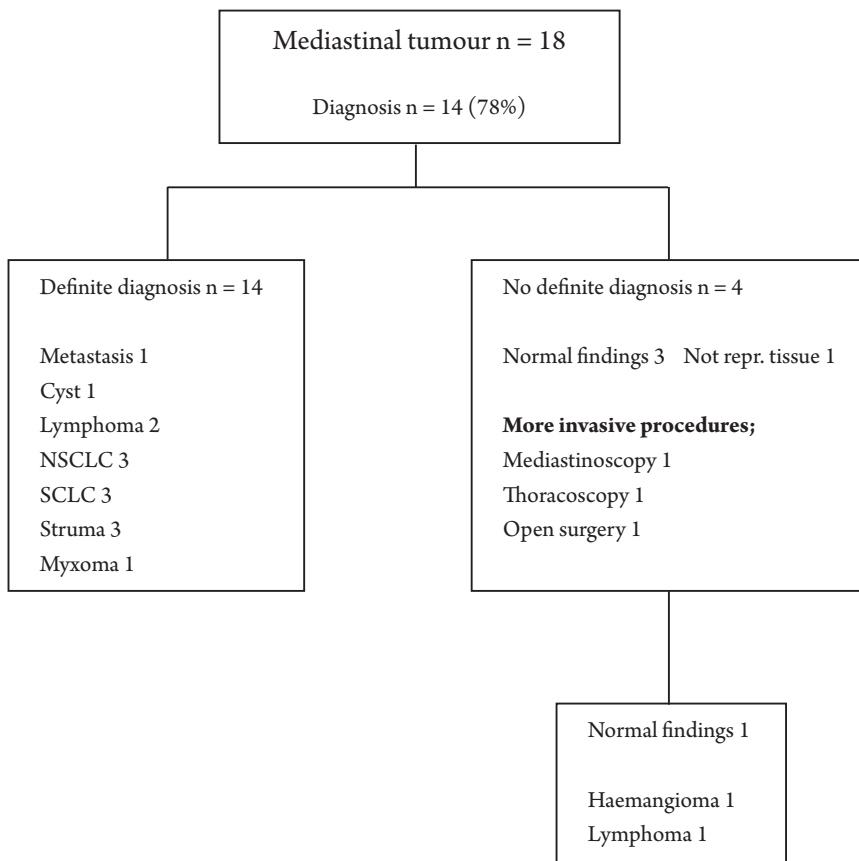
as “malignant”, “benign” or “non-diagnostic”. The latter group was further subdivided into biopsies with adequate cell sample (presence of lymphocytes) or inadequate cell sample without lymphatic tissue. Diagnostic yield was defined as samples which provided a final malignant or benign diagnosis.

## Results

The median age of the 308 patients with an undiagnosed radiologically suspicious lesion in the chest was 67 years (range 29 to 86 years) and 172 were men (56%). There was no operative mortality or any surgical complications. All patients were discharged from the hospital on the day of surgery. Diagnostic yield for all patients was 55%.

Forty-eight of the 89 patients (54%) with enlarged mediastinal lymph nodes were diagnosed by EBUS of the remaining 41 patients 11 went on to more invasive methods of which 3 patients were diagnosed with malignancy, 6 had a benign diagnosis and two had normal tissue (Fig 1).

In the group with undiagnosed tumours in mediastinum we achieved a final diagnosis by EBUS in 14 of the 18 patients (78%). In the remaining 4 patients, 1 patient was later diagnosed



**Fig 2.** demonstrate diagnosis for patients with tumour in mediastinum

with malignancy, 1 with benign disease, 1 with normal findings and 1 was followed in outpatient clinic (Fig 2).

Inadequate tissue samples were obtained in 6 patients (7%) with enlarged lymph nodes and in 1 patient (5%) with tumour in mediastinum.

EBUS did not provide an immediate malignant or benign diagnosis in 45 patients, where 7 patients (7%) had inadequate tissue samples and 38 patients (35%) had adequate tissue samples. Four-teen patients were referred for more invasive methods including mediastinoscopy ( $n = 8$ ), thoracoscopy ( $n = 4$ ) and thoracotomy ( $n = 2$ ). Five patients with inadequate diagnostic material and twenty-six patients with adequate cell samples were followed in the outpatient clinic because a new chest-CT demonstrated regression of the lesion in mediastinum.

## Discussion

Patients with radiologically suspicious lesion in mediastinum who remain undiagnosed despite conventional workup are a common challenge in the clinics. We have previously demonstrated that EBUS is a valuable diagnostic tool in approximately 55% of patients with undiagnosed intra-thoracic lesions (10).

One third of the patients with enlarged mediastinal lymph

nodes were found with malignancy ( $n=26$ ) and yield was 54% which was also found in other studies (12,13). Yield is lower than most physicians would expect since it is generally believed that EBUS is primarily used to stage mediastinal lymph nodes in lung cancer patients. However, it is important to distinguish the two patient populations: those with an established lung cancer diagnosis and those who are referred solely with enlarged lymph nodes which may simply be secondary to previous inflammation. Despite previous diagnostic work up sarcoidosis is still the most likely benign diagnosis in patients with enlarged lymph nodes (14,15), which were also found in one third of the patients in our study ( $n = 27$ ).

In patients with tumour in mediastinum yield was 78%. Two thirds of these patients were found with malignancy ( $n = 11$ ) and 4 patients were diagnosed with thyroid disease, which has been demonstrated previously (13).

Lymphoma was diagnosed in 5 patients with EBUS and 1 patient after mediastinoscopy which confirm that lymphomas can be diagnosed with EBUS but surgical biopsies are required to diagnose specific lymphoma subtypes not readily amenable to diagnosis with low volume specimens (14).

As demonstrated in a previous study (10) yield is different in the two groups as the frequency of malignancy is higher for patients with mediastinal tumor than enlarged lymph nodes

which can be explained by adenopathy secondary to previous inflammation or infection.

In the present study our patients are highly selected and thus biased because they were only referred to us if conventional methods failed to give a diagnosis. Diagnostic yield would increase if all patients with undiagnosed lesions in mediastinum were referred directly to EBUS.

We have not encountered any complications in 601 consecutive cases. As demonstrated in many other studies EBUS is a safe, minimally invasive and cost-effective tool because it allows investigation in an outpatient setting (16).

In patients who remain undiagnosed after conventional workup EBUS represents a fine alternative to more invasive diagnostic procedures and could be the first choice. However, even though EBUS provides a diagnosis in the majority of the patients, some will remain undiagnosed and need further more invasive procedures.

In conclusion this minimally invasive diagnostic modality provides a final diagnosis in 78% of patients with tumour in mediastinum and in more than half of patients with enlarged lymph nodes without exposing the patient to the risk of complications with more invasive procedures.

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