

## Original Research Article

# Real time endobronchial ultrasound guided transbronchial needle aspiration of intrathoracic lymphadenopathy: an initial experience

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## ABSTRACT

**Background:** Conventional TBNA has been used in the evaluation of intrathoracic lymphadenopathy with varied success rates depending upon size, site and aetiology of the node. Although mediastinoscopy has higher successes but it comes at the cost of general anaesthesia, more complications and limited access to the inferior and posterior mediastinum. Endobronchial ultrasound guided transbronchial needle aspiration has the advantage of real time nodal sampling with good success rates and minimal complications. The aim of our study was to assess the diagnostic yield and safety of EBUS TBNA in the evaluation of intrathoracic lymphadenopathy.

**Methods:** This prospective observational study was conducted at government chest diseases hospital Srinagar over a period of two years from January 2016-December 2018 on 100 consecutive patients who underwent EBUS TBNA procedure for evaluation mediastinal and hilar lymphadenopathy. The data was collected and analysed for diagnostic yield and safety profile.

**Results:** Out of the 100 subjects included in the study 52% were males and 48% were females. Mean age of the study population was 48.5±16.65 years. Most of the nodes sampled were subcarinal in location followed by paratracheal and hilar group. Granulomatous pathology (tuberculosis and sarcoidosis) was present in 41 patients followed by malignancy in 39 patients. Anthracosis was the cause of lymphadenopathy in 4 of the patients. There were no major complications in our study.

**Conclusions:** EBUS TBNA is an effective and safe procedure for evaluation of mediastinal and hilar lymphadenopathy.

**Keywords:** EBUS-TBNA, Intrathoracic adenopathy, Malignancy, Tuberculosis, Sarcoidosis

## INTRODUCTION

Diagnostic evaluation of enlarged mediastinal and hilar lymph nodes has always been difficult and of interest to

interventional pulmonologists. Because of different causes of mediastinal lymphadenopathy, which in turn affects the outcome it is very important to get samples from these nodes and subsequently subject them for

various diagnostic tests. Evaluation of mediastinal nodes is crucial for proper staging for lung cancer.<sup>1,2</sup> Various methods have been used for diagnostic evaluation of enlarged mediastinal structures. Mediastinoscopy has been considered as gold standard for evaluation of mediastinum however the procedure in itself has many limitations as requirement of surgical operating room, general anaesthesia and is associated with certain complications such as bleeding, recurrent nerve damage and more importantly needs well trained, experienced thoracic surgeons to do the job. Mediastinoscopy has a limited access to posterior and inferior mediastinum and required either extended cervical mediastinoscopy or thoracoscopy.<sup>3</sup>

Alternative minimally invasive bronchoscopic methods have been devised. Transbronchial needle aspiration (TBNA) as mentioned in literature has been used to sample the mediastinal and hilar lymph nodes with variable sensitivity ranging from 20-89% depending on various factors such as aetiology, size and location of lymph node and more importantly on the experience of the operator.<sup>4-9</sup> Since the development of convex probe endobronchial ultrasound which allows real time sampling of the intrathoracic lymphnodes, the diagnostic yield of transbronchial needle aspiration has improved significantly. EBUS TBNA has the advantage of being performed under conscious sedation although not always with excellent yields in the range of 80-86%.<sup>10-12</sup> The yield has significantly increased over the last decade. In this study, we report our initial experience with EBUS TBNA in patients of intrathoracic lymphadenopathy of both unknown aetiology and suspecting of having metastatic disease.

**METHODS**

A prospective observational study was conducted on 100 consecutive patients at government chest diseases hospital Srinagar over a period of two years from January 2016 to December 2018. Patients with intrathoracic lymphadenopathy of both unknown cause and suspected for malignancy on the basis of radiological findings were included in the study. As per the study design, all the patients underwent detailed history, physical examination and radiological study in the form x-ray and CT chest was done besides routine haematological investigations. Supportive investigations in the form of Mantoux test, serum ACE, serum calcium, urinary calcium and ophthalmological check-up were done as per requirement. A written informed consent was taken from all the subjects. This study was approved by the ethical committee.

Endobronchial ultrasound was done using a dedicated EBUS bronchoscope (CP-EBUS, BF-UC 180F using the EU-ME2 Ultrasound system, EVIS EXERA III Series CV190 Video Processor, Olympus Medical Systems, Tokyo, Japan). The procedure was performed under conscious sedation using midazolam and fentanyl,

however, 21 patients underwent the procedure under general anaesthesia. EBUS TBNA was performed using a dedicated 21-gauge vizishot needle (NA-201SX-4021 Olympus Medical Systems Corp. Japan). Lymph nodes were classified using the International Association for the Study of Lung Cancer (IASLC) classification.<sup>13</sup> The lymph nodes were assessed systematically and most hypoechoic lymph node was targeted. In case of malignancy the higher and opposite side nodes were chosen for sampling. A minimum of 3-4 passes were done per lymph node. The first aspirate was done without suction; however subsequent aspirates were performed with suction depending upon the nature of lymph nodes.

On-site cytological evaluation was not performed due to non-availability. The aspirated material was analysed cytologically, microbiologically and histopathological evaluation if a core was aspirated from the target node. An aspirate was also sent for genexpert and TB culture in normal saline. A routine bronchoscopy was done in all patients before EBUS TBNA.

**RESULTS**

Out of the 100 subjects included in the study 52% were males and 48 and were females. Mean age of the study population was 48.5±16.65 years (Table 1). Maximum number of subjects were in the age group of 51-60 years followed by followed by 21 in the age group of 41-50 years, 15 in the age group of 31-40 years, 14 in age group of 21-30 years and 9 subjects in the age group of 71-80 years. The minimum numbers of subjects (4) belong to the age group of 11-20 years (Table 2). Most of the patients presented with cough followed by fever and shortness of breath, weight loss and haemoptysis.

**Table 1: Baseline characteristics of the patients.**

Characteristic	Findings
Age (Mean±SD)	48.5±16.65 years
Males	52
Females	48

**Table 2: Age wise distribution of the patients.**

Age	Frequency	Percentage (%)
11-20	4	4
21-30	14	14
31-40	15	15
41-50	21	21
51-60	25	25
61-70	12	12
71-80	9	9
Total	100	100

Out of the total lymphnodes sampled in the study population, 47% were Subcarinal (C7) in location followed by 28 paratracheal (4R and 4L) and 25% were hilar (Station10) (Table 3).

**Table 3: Frequency of various lymph nodes involved.**

Lymph node station	Frequency	Percentage (%)
Paratracheal	28	28
Subcarinal	47	47
Hilar	25	25
Total	100	100

**Table 4: Adequacy of samples.**

Lymph node station	Frequency	Percentage (%)
Adequate	89	89
Inadequate	11	11
Total	100	100

After receiving the results from the pathology department, 89% of the samples were found to be adequate while as 11% of the samples showed no define pathology due to inadequate material (Table 4). Out of the 89 adequate samples, granulomatous pathology was found in 41. Tuberculosis was found in 26 samples (29.21%) and sarcoidosis was found in 15 (16.85%). The diagnosis of tuberculosis was confirmed in 10 patients by microbiological tests (smear, CBNAAT and Culture). The remaining 16 patients were diagnosed on the basis of cytology findings. Diagnosis of sarcoidosis was mainly based on cytopathological findings of non-caseating granulomas supported by investigations such as mucosal biopsy and serum angiotensin-converting enzyme results. 43.82% (39) of the samples were positive of malignancy. 5 samples were reported as reactive lymphnodes and 4 samples as anthracosis (Table 5).

**Table 5: Frequency of diagnostic groups among the patients.**

Diagnosis	Frequency	Percentage (%)
Tuberculosis	26	29.21
Sarcoidosis	15	16.85
Malignancy	39	43.82
Anthracosis	4	4.49
Reactive	5	5.62
Total	89	

**Table 6: Mean age in diagnostic groups.**

Diagnosis	Frequency	Mean age (Years)	Standard deviation
Tuberculosis	26	37.58	13.38
Sarcoidosis	15	31.47	8.02
Malignancy	39	62.85	10.11
Anthracosis	4	59.5	4.20
Reactive	5	44.6	9.18
Inadequate	11	44	12.38

The mean age of patients in different diagnostic groups is shown in Table 6. Malignancy was diagnosed in 39 of the samples. The most common type was adenocarcinoma

(15), followed by squamous (8) and small cell carcinoma (6). Lymphoma was diagnosed in 4 patients and was differentiated by immunohistochemistry. Six of the 39 samples were positive for metastatic disease from other primaries (Table 7).

**Table 7: Frequency of various types of malignancies.**

Malignancy - types	Frequency	Percentage (%)
Adenocarcinoma	15	38.46
Squamous cell carcinoma	8	20.51
Small cell carcinoma	6	15.38
Lymphoma	4	10.25
Metastasis	6	15.38

There were no major complications in the study subjects. Mild fever (15/100), mild haemoptysis in 6 patients, bronchospasm in 5 patients, mild cough in 7 patients and 4patients develop mild oxygen desaturation. All of these patients responded to symptomatic treatment. All the patients were discharged on the same day except six patients who underwent the procedure under GA were observed overnight in the hospital.

**DISCUSSION**

In the present study, we analysed the data of 100 EBUS TBNA samples. Out of the 100 patients 52 were males and 48 were females with a mean age (SD) of 48.5±16.65 years and a range of 11-80 years. The number, age and gender distribution in previous studies varies depending upon the indications for EBUS TBNA. In a study by Rintoul RC et al, only 20 patients underwent EBUS TBNA±EUS FNA with a median age of 65 years (range 45-86 years) for evaluation of intrathoracic lymphadenopathy.<sup>14</sup> In another study by Herth FJ et al, a total of 160 patients were enrolled in the study with 106 men and 54 women with a mean age of 53.2 years (SD 11.6) and a range of 33-76 years.<sup>15</sup> In a study by Gahlot T et al, the mean age of study population was 47 years with a range of 18-83 years.<sup>16</sup> In another Indian study by Dhamija A et al, 300 patients underwent EBUS TBNA with age ranges from 11-88 years. The wide range of age in this study as well as in similar India studies is because of high incidence of infective causes as compared to western literature. In the present study, subcarinal lymph nodes were the most common nodes targeted (47%), followed by paratracheal (28%), and hilar nodes in 25% of patients. Mediastinal lymphnodes (subcarinal and paratracheal) were the most commons nodes targeted as compared to hilar nodes in various studies around the globe.<sup>11,16-18</sup>

Over the last decade, EBUS TBNA have been extensively evaluated and used in the diagnosis of intrathoracic lymphadenopathy and for staging of lung cancer. The diagnostic yield of EBUS-TBNA has been reported to be as good as that of mediastinoscopy. CT

chest has a sensitivity and specificity of 55% and 81% in identification of malignant lesions. Although PET-CT has a higher sensitivity and specificity but still false positives may occur especially in inflammatory lymph nodes.<sup>19,20</sup> In the present study out of the total patients, EBUS-TBNA was adequate in 89% of the patients leading to diagnosis supported by other investigations depending upon the clinical scenario. In 11% of the subjects, EBUS-TBNA was non-diagnostic due to inadequate samples. The diagnostic yield of EBUS-TBNA is varied as mentioned in literature. Rintoul RC et al, has a diagnostic yield of 72.2% in a small sample study.<sup>14</sup> Heath FJ et al, in a large sample size of 502 patients reported a diagnostic yield of 93.5% with majority of them having malignant disease.<sup>21</sup> Yasufuku K et al, reported an adequacy of 96% in their study.<sup>18</sup> In studies from India, the diagnostic yield of EBUS TBNA varied from 62.9% to 92%.<sup>16,17,22</sup>

In the present study, granulomatous pathology was diagnosed in 41 of the 89 adequate samples. Tuberculosis was found in 26 samples (29.21%) and sarcoidosis was found in 15 (16.85%). The mean age of patients in tuberculosis was 37.58±13.38 years while as in sarcoidosis the mean age was 31.47±8.02 years. Microbiological confirmation of tuberculosis was obtained in 38.5% of patients due to paucibacillary nature of lymph node tuberculosis. Gahlot T et al, reported 71 out of 100 subjects as granulomatous lymphadenitis (tuberculosis 41 and sarcoidosis 30), with microbiological confirmation of tuberculosis in 30% of subjects.<sup>16</sup> In the study by Dhamija A et al, 53% of the cases were diagnosed as having granulomatous pathology (both tuberculosis and sarcoidosis) with 55% of the tuberculosis cases had positive microbiological evidence.<sup>17</sup> In a study by Nair A et al, tuberculosis was the most common aetiology (16/78) among non-malignant lesions followed by sarcoidosis (11/78). 25% of the patients diagnosed as tuberculosis had a positive microbiological evidence of tuberculosis.<sup>23</sup> However, in most studies from western world, malignancy is the most common diagnosis. The difference is mainly due to high burden of tuberculosis in this part of world.

In the present study, 39 of the 89 adequate samples were positive for malignancy with mean age of 62.85±10.11 years. The most common type was adenocarcinoma (15), followed by squamous (8) and small cell carcinoma (6). Lymphoma was diagnosed in 4 patients and was differentiated by immunohistochemistry. Six of the 39 samples were positive for metastatic disease from other primary sites. The percentage of malignancy was higher as compared to other studies from India.<sup>16,17</sup> These studies were conducted mostly on intrathoracic lymphadenopathy of unknown aetiology. In present study authors take case both with unknown aetiology, high suspicion of malignancy and for evaluation of mediastinal nodes with known primaries. This difference may also be due to different patient profile in our study. However, a study by Nair A et al, from south India,

reported malignancy as most common finding (33/78), with non-small cell carcinoma as most common (18), followed by small cell carcinoma (6) similar to our results.<sup>23</sup> Most of the western literature regarding EBUS TBNA in intrathoracic lymphadenopathy mentioned malignancy as the most common findings.<sup>18,21</sup>

Authors had 5.62% patients (n=5) of reactive lymphadenitis. Two of them underwent further invasive investigations in the form of mediastinoscopy with diagnosis of sarcoidosis and lymphoma (Hodgkin's) one each. Another uncommon finding which we had in 4.49% (n=4) of patients is anthracofibrosis, where the pathology report reads as dense collection of anthracotic pigment laden macrophages with surrounding fibrosis. This finding was also evident to naked eye while performing EBUS-TBNA as necrotic black material was seen on the slides during their preparation. Dhamija et al, reported similar data regarding lymph node enlargement due to anthracosis.<sup>17</sup>

All the patients were observed for 2-3 hours after the procedure with 6 of them kept overnight in the hospital for observation. There were no major complications in the study subjects. Mainly in our study we had mild self-limiting complications in the form of fever (15/100), mild haemoptysis in 6 patients, bronchospasm in 5 patients, mild cough in 7 patients and 4 patients develop mild oxygen desaturation. There were no major complications in the study subjects. Our reported complication rate was similar to as reported by Gahlot T et al.<sup>16</sup> Most of the studies in literature do not report major complications of this procedure. However, few studies do mention mediastinal infection and lung abscess as a rare complication of EBUS TBNA procedure.<sup>24</sup>

Endobronchial Inflammatory polyp has also been reported as a rare complication of EBUS TBNA by Gupta et al.<sup>25</sup> In a systematic review by Varela-Lema L et al, on effectiveness and safety of endobronchial ultrasound-transbronchial needle aspiration, the authors reported that the procedure is a safe and highly accurate for the examination and staging of mediastinal and hilar lymph nodes in patients with known or suspected lung malignancy.<sup>26</sup>

Present study was not without limitations in the form of sample size as compared to larger studies, without any comparison and follow-up.

## CONCLUSION

Endobronchial ultrasound guided transbronchial needle aspiration is an effective and safe procedure in the evaluation of intrathoracic lymphadenopathy.

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## REFERENCES

1. Sihoe AD, Yim AP. Lung cancer staging. *J Surg Res.* 2004;117:92-106.
2. Spira A, Ettinger DS. Multidisciplinary management of lung cancer. *N Engl J Med.* 2004;350:379-92.
3. Hoffmann H. Invasive staging of lung cancer by mediastinoscopy and videoassisted thoracoscopy. *Lung Cancer.* 2001;34:3-5.
4. Dasgupta A, Mehta AC. Transbronchial needle aspiration. An underused diagnostic technique. *Clin Chest Med.* 1999;20:39-51.
5. Harrow EM, Oldenburg FA, Smith AM. Transbronchial needle aspiration in clinical practice. *Thorax.* 1985;40:756-9.
6. Schenk DA, Bower JH, Bryan CL, Currie RB, Spence TH, Duncan CA, et al. Transbronchial needle aspiration staging of bronchogenic carcinoma. *Am Rev Respir Dis.* 1986;134:146-8.
7. Harrow EM, Oldenburg FA, Jr., Lingenfelter MS, Smith AM, Jr. Transbronchial needle aspiration in clinical practice. A five year experience. *Chest.* 1989;96:1268-72.
8. Gay PC, Brutinel WM. Transbronchial needle aspiration in the practice of bronchoscopy. *Mayo Clin Proc.* 1989;2 64:158-62.
9. Haponik EF, Shure D. Underutilization of transbronchial needle aspiration: experiences of current pulmonary fellows. *Chest.* 1997;112:251-3.
10. Herth F, Becker HD, Ernst A. Conventional vs endobronchial ultrasound guided transbronchial needle aspiration: a randomized trial. *Chest.* 2004;125:322-5.
11. Herth FJ, Becker HD, Ernst A. Ultrasound-guided transbronchial needle aspiration: an experience in 242 patients. *Chest.* 2003;123:604-7.
12. Okamoto H, Watanabe K, Nagatomo A, Kunikane H, Aono H, Yamagata T, Kase M. Endobronchial ultrasonography for mediastinal and hilar lymph node metastases of lung cancer. *Chest.* 2002;121:1498-506.
13. Rusch VW, Asamura H, Watanabe H, Giroux DJ, Rami-Porta R, et al. The IASLC [6] lung cancer staging project: a proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. *J Thorac Oncol.* 2009;4:568-77.
14. Rintoul RC, Skwarski KM, Murchison JT, Wallace WA, Walker WS, Penman ID. Endobronchial and endoscopic ultrasound-guided real-time fine-needle aspiration for mediastinal staging. *Eur Respir J.* 2005;25:416-21.
15. Herth FJ, Lunn W, Eberhardt R, Becker HD, Ernst A. Transbronchial versus transesophageal ultrasound-guided aspiration of enlarged mediastinal lymph nodes. *Am J Resp Crit Care Med.* 2005;171(10):1164-7.
16. Gahlot T, Parakh U, Verma K, Jain N. Endobronchial ultrasound guided transbronchial needle aspiration in diagnosing mediastinal lymphadenopathy. *Lung India.* 2017;34:241-6.
17. Dhamija A, Basu A, Sharma V. Mediastinal adenopathy in India: Through the eyes of endobronchial ultrasound. *J Assoc Physicians India.* 2015;63:15-8.
18. Yasufuku K, Chiyo M, Sekine Y, Chhajed PN, Shibuya K, Iizasa T, et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. *Chest.* 2004;126:122-8.
19. Plat G, Pierard P, Haller A, Hutsebaut J, Faber J, Dusart M, et al. Endobronchial ultrasound and positron emission tomography positive mediastinal lymph nodes. *Eur Respir J.* 2006;27:276-81.
20. Hwangbo B, Kim SK, Lee HS, Lee HS, Kim MS, Lee JM, et al. Application of endobronchial ultrasound-guided transbronchial needle aspiration following integrated PET/CT in mediastinal staging of potentially operable non-small cell lung cancer. *Chest.* 2009;135:1280-7.
21. Herth FJ, Eberhardt R, Vilmann P, Krasnik M, Ernst A. Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes. *Thorax.* 2006;61:795-8.
22. Srinivasan A, Agarwal R, Gupta N, Aggarwal AN, Gupta D. Initial experience with real time endobronchial ultrasound guided transbronchial needle aspiration from a tertiary care hospital in north India. *Indian J Med Res.* 2013;137:803-7.
23. Nair A, Haridas N, Ahmed S, Borkar PV. EBUS-TBNA-Initial Experience from a Tertiary Care Center in Southern India. *J Clin Diag Res.* 2018;12(9).
24. Huang CT, Chen CY, Ho CC, Yu CJ. A rare constellation of empyema, lung abscess, and mediastinal abscess as a complication of endobronchial ultrasound-guided transbronchial needle aspiration. *Eur J Cardiothorac Surg.* 2011;40:264-5.
25. Gupta R, Park HY, Kim H, Um SW. Endobronchial inflammatory polyp as a rare complication of endobronchial ultrasound-transbronchial needle aspiration. *Interact Cardiovasc Thorac Surg.* 2010;11:340-1.
26. 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.

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