Endobronchial Ultrasound Guided Transbronchial Needle Aspiration (EBUS-TBNA) for Diagnosis of Mediastinal and Hilar Masses

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ABSTRACT
Objective: To determine the sensitivity, specificity, negative and positive predictive values, and diagnostic accuracy of Endobronchial Ultrasound Guided Transbronchial Needle Aspiration (EBUS-TBNA).
Study Design: A cross-sectional validation study.
Place and Duration of Study: Department of Histopathology, Army Medical College, in collaboration with Department of Pulmonology, Military Hospital Rawalpindi, from March 2014 to March 2015.
Methodology: Cases of EBUS-TBNA comprised of both TBNAs and cell block/biopsy of the same patients. Diagnosis was made on the TBNA slides and cell block/biopsy material. Taking biopsy/cell block as the gold standard, the data was analysed to calculate the sensitivity, specificity, negative and positive predictive values, and diagnostic accuracy of EBUS-TBNA.
Results: The sensitivity of EBUS-TBNA was found to be 96.5%; whereas, specificity and positive predictive values were 100%. The negative predictive value was calculated at 50%. Diagnostic accuracy of the procedure was found to be 96.67%.
Conclusion: EBUS-TBNA is a sensitive and a specific test and is accurate in diagnosing mediastinal and hilar pathologies.


INTRODUCTION
Fine-needle aspiration cytology (FNAC) is a method generally considered as a rapid, reliable, safe diagnostic tool for the diagnosis of various benign, malignant and infectious condition.1 It was first described and performed in 1930.2 It has now been augmented by USG and CT guided techniques. Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) is a sampling method for patients that have enlarged mediastinal or hilar lymph nodes/masses, detected on computed tomography.3 Bronchoscopy alone is unable to assess all the pathological processes both within and outside the airway wall. Endobronchial ultrasound (EBUS) and endobronchial ultrasound guided-transbronchial needle aspiration (EBUS-TBNA) are new diagnostic tools that have great potential for diagnosis of mediastinal processes in general and staging of lung cancers in particular.4 EBUS-TBNA was first introduced in the early 1990s.5 Several other techniques are available for the diagnosis of suspected lesions of the mediastinum, including standard flexible bronchoscopy and transthoracic needle aspiration. However, EBUS-TBNA is the least invasive, and provides good diagnostic yield and material for staging of lung cancers.6 The technology is available as radial EBUS probes and linear EBUS-TBNA bronchoscopes. Radial EBUS helps evaluate the airway walls, guide TBNA with diagnostic yield of 72 - 86%, and diagnose peripheral lung lesions with diagnostic yield of 61 - 80%. Linear EBUS-TBNA transducers produce real-time BNA.7 At present, EBUS-TBNA is being carried out only in one center in Pakistan (Pulmonology Department, Military Hospital, Rawalpindi. Hence, limited data and information is available regarding this procedure. Therefore, this study was conducted to determine the sensitivity, specificity, negative and positive predictive values, and diagnostic accuracy of EBUS-TBNA, in obtaining cytological and histological diagnosis of mediastinal and hilar masses.

METHODOLOGY
This validation study was carried out at the Department of Histopathology, in collaboration with Department of Pulmonology, Military Hospital Rawalpindi from March 2014 to March 2015. The study included 30 cases of EBUS-TBNA that comprised of both TBNAs and cell block/biopsy of the same patients. The EBUS-TBNAs and cell blocks/biopsies of the patients diagnosed on CT
scans with mediastinal or hilar masses were included in the study. Material collected for TBNAs was laid on cleaned slides. Some of the slides were air dried while others were placed in Coplin jars containing 90% ethanol, to be wet fixed. The slides were stained with Hemacolor and Hematoxylin and Eosin (H&E). On-spot adequacy and diagnosis was made by the principal investigator. EBUS-TBNA slides were examined under light microscope the very day of the procedure. The diagnosis on the TBNA was confirmed by the consultant histopathologist (supervisor). Biopsy/cell block samples preserved in 10% formal saline were received in the department of Histopathology, Pathology Laboratory, at Army Medical College, Rawalpindi from Pulmonology Department Military Hospital Rawalpindi. Independent unbiased diagnosis was made once the cell block/biopsy slides were prepared, which was not influenced by the TBNA report. The histopathological diagnosis established on TBNA was evaluated and correlated with that found on cell block/biopsy. The clinical and histopathological data was recorded in carefully structured proformas. Demographic data was recorded. Frequency was calculated for histopathological diagnosis. Statistical data was analyzed using SPSS version 20. Diagnostic accuracy, sensitivity, specificity along with positive and negative predictive values were calculated with the help of 2 x 2 table and formulas.

RESULTS

Thirty patients were included in the study. The mean age was 43.4 years ranging from 22-80 years. Most patients were in the age group of 31 to 40 years. Twenty-three (76.6%) were males while seven (23.3%) were females. The main lesions identified on EBUS-TBNA and cell block/biopsy included chronic granulomatous inflammation, squamous cell carcinoma, adenocarcinoma, small cell carcinoma, neuroendocrine tumor, and schwannoma. Chronic granulomatous inflammation was detected in 50% of EBUS-TBNAs and 53.3% of cell blocks. Squamous cell carcinoma was detected in 50% of EBUS-TBNAs and 53.3% of cell blocks. Small cell carcinoma, neuroendocrine tumor, and schwannoma was detected in 6.67% of EBUS-TBNAs and 10% of cell blocks. Table I:

<table>
<thead>
<tr>
<th>Mediastinal / hilar pathology</th>
<th>EBUS-TBNA % (n)</th>
<th>Cell block/biopsy % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic granulomatous inflammation</td>
<td>50% (15)</td>
<td>53.3% (16)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>16.67% (5)</td>
<td>16.67% (5)</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>10% (3)</td>
<td>10% (3)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>6.67% (2)</td>
<td>6.67% (2)</td>
</tr>
<tr>
<td>Neuroendocrine tumor</td>
<td>6.67% (2)</td>
<td>6.67% (2)</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>3.33% (1)</td>
<td>3.33% (1)</td>
</tr>
<tr>
<td>Mature lymphocytes seen (Reactive hyperplasia)</td>
<td>3.33% (1)</td>
<td>3.33% (1)</td>
</tr>
<tr>
<td>Endobronchial cell aspirate with reactive lymphocytes</td>
<td>3.33% (1)</td>
<td>-</td>
</tr>
</tbody>
</table>

In one case, chronic granulomatous inflammation was diagnosed on cell block but the TBNA slides showed endobronchial cells with lymphocytes in the background. This case was considered as the false negative one. One case showed reactive lymphocytes on the TBNA smears and cell block, which was labelled as the true negative case. The total number of true positive, false positive, true negative and false negative cases was 28, 0, 1 and 1, respectively. Using 2 x 2 table and the statistical formula, the sensitivity of EBUS-TBNA was calculated to be 96.5%, specificity and positive predictive value were 100%, negative predictive value was calculated at 50% and the diagnostic accuracy was calculated to be 96.67%.

Post-procedure hemoptysis was noted in two patients, who were conservatively managed.

DISCUSSION

Isolated mediastinal lymphadenopathy is a common finding encountered by the pulmonologists; and establishing an accurate diagnosis in such patients has always been a perplexing task, especially in the developing countries.8 Endobronchial ultrasound guided TBNA has emerged as the first line of investigation for sampling of mediastinal/hilar lymphadenopathy in almost all the healthcare providing centres around the world.9 In Pakistan, EBUS-TBNA has recently been introduced as a diagnostic modality. This study is the first of its kind from Pakistan. It highlights the merits and demerits, for establishing the diagnostic accuracy of EBUS-TBNA. In the current study for chronic granulomatous inflammatory lesions, the sensitivity was 93.75%; whereas, in a study of Navani and coworkers,10 the sensitivity of EBUS-TBNA for detection of non-caseating granulomas was 85%, compared with a sensitivity of 35% for standard bronchoscopic techniques (p < 0.001). The diagnostic yield of combined EBUS-TBNA and bronchoscopy was 93% (p < 0.001). The aforementioned study concluded that EBUS-TBNA in combination with standard bronchosscopic techniques is not only safe and practical, but it also improves the diagnostic yield and so may be considered as a first-line investigation in patients with suspected sarcoidosis and enlarged intrathoracic lymphadenopathy. Navani and coworkers conducted another study to determine the role of EBUS-TBNA in diagnosing tuberculosis, in which they concluded that the technique had a sensitivity of 94% and was a practical alternative to procedures like mediastinoscopy that are more invasive, require general anesthesia and cannot access subcarinal and hilar lymph nodes.11

Despite the tremendous advances in preventive, diagnostic and treatment modalities, lung cancer still remains to be the leading cause of death worldwide.12 In
the present study, the sensitivity of EBUS to diagnose squamous cell carcinoma, adenocarcinoma, neuro-endocrine lesions, and small cell carcinoma was 100%. In another study regarding EBUS-TBNA following PET/CT scan positive cases, diagnosis and staging of non-small cell lung cancers were analysed. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of EBUS-TBNA in the detection of mediastinal metastasis was 90.0%, 100%, 100%, 96.7%, and 97.4%, respectively; whereas, for PET/CT scans, the values were 70.0%, 59.8%, 37.5%, 85.2%, and 62.4%, respectively. The author also suggested that EBUS-TBNA can be equally helpful in confirming mediastinal metastasis in PET/CT negative cases, specially adenocarcinomas. Another study by Felix and coworkers calculated the sensitivity, specificity, and negative predictive value of EBUS-TBNA for detecting malignancy at 92.3%, 100%, and 96.3%, respectively. These results prove that EBUS-TBNA is an excellent tool for diagnosing mediastinal metastasis, and is much more accurate than PET/CT. In a study carried out in China, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of EBUS-TBNA in distinguishing malignant from benign lesions were calculated to be 93.4% (60/64), 100% (17/17), 100% (60/60), 81.0% (17/21), and 95.1% (77/81), respectively.

In the present study, EBUS-TBNA costs almost 50,000 Pakistani rupees per patient. Navani and his colleagues conducted a study in 2012 in which they mentioned the cost effectiveness of EBUS-TBNA. According to this study, EBUS-TBNA procedure per patient on the average costs £1,892 ($2,998). On the other hand, mediastinoscopy was considerably more costly at £3,228 ($5,115) per patient. Hence, EBUS-TBNA was found to be statistically and significantly cost effective.

The complications associated with TBNA are hemorrhage, the most common one; while other rare complications are mediastinitis, pneumonia, sepsis, pericarditis, pneumoemothorax, arrhythmias, and hypotension. In the present study, however, during the TBNA procedure minimal complications were observed. In only two patients, mild post-procedure hemoptysis was witnessed. These patients were kept under observation overnight, and were discharged the next day.

In Pakistan, EBUS-TBNA has yet not been incorporated into routine practice and very few pulmonologists are as yet trained to perform it. It is not accessible to a majority of the country’s population because of its limited availability. This procedure can serve to make timely diagnosis of various pathologies of the mediastinum, helping improve both the quality and quantity of life.

**CONCLUSION**

EBUS-TBNA is a very reliable and minimally invasive procedure that can be used for the diagnosis of mediastinal and hilar lymphadenopathies. It has the same diagnostic accuracy as biopsy or cell block and is not associated with any major complications.

**Disclosure:** It is a thesis-based article for my Ph.D programme.

**REFERENCES**


