ORIGINAL ARTICLE

Efficacy of On-Site Evaluation in EBUS-Guided Transbronchial Needle Aspiration Versus Cell Block

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ABSTRACT

Objective: To determine Rapid onsite evaluation (ROSE) effectiveness, sensitivity and specificity during Endoscopic ultrasound guided Transbronchial needle aspiration (EBUS TBNA) and compare it with cell blocks prepared during same process.

Study Design: Diagnostic Accuracy Study

Place and Duration of Study: Pathology department of Akhtar Saeed Medical College and Watim Medical and Dental College, from June 15, 2023, to June 15, 2024.

Materials and Methods: After getting approval from ERB, a written informed consent was taken from all the enrolled 110 patients who went through EBUS-TBNA in Farooq Hospital and Watim general Hospital depending upon inclusion and exclusion criteria. The age limit was more than 20 years and less than 65 years, including both genders. ROSE, EBUS TBNA and cell blocks of the patients diagnosed on CT scan with mediastinal or hilar masses were analyzed.

Results: Diagnostic parameters were calculated using ROC Curve analysis in SPSS version 23. Sensitivity of EBUS-TBNA with ROSE was discovered to be 95%, specificity was 60%, positive predictive value and negative predictive value were calculated to be 98.1% and 96 % respectively. Procedure's diagnostic accuracy of process with ROSE was 98%.

Conclusion: This study concludes that ROSE performed during EBUS TBNA has high sensitivity, moderately effective specificity and high concordance rate with cell block examination. It serves as a valuable adjunct to limit procedure time, enrich sample collection and benefit patient's well-being.

Key Words: *Cell Block, EBUS TBNA, Mediastinal, ROSE.*

Introduction

Pakistan is one of countries facing high prevalence of infectious lung diseases including tuberculosis as well as neoplastic diseases presenting as mediastinal or pulmonary pathologies. In the past various diagnostic modalities had been used to diagnose these diseases with variable outcome.[1] However very few studies have been done in relation to efficacy of diagnostic modalities of these commonly encountered mediastinal pathologies.

Transbronchial needle aspiration guided by endobronchial ultrasound is the sampling method that uses ultrasound combined with bronchoscopy to visualize air ways and various key nodal stations which are difficult to access on bronchoscopy alone.[2] It has served as excellent tool that is not only minimally invasive but also has excellent sample yield in cases of mediastinal masses/ lymphadenopathy detected on computed tomography scan.[3] It has been used more successfully for staging in known cancer patients as well as in benign and infectious pulmonary and mediastinal diseases as compare to other diagnostic modalities including standard flexible bronchoscopy and transthoracic needle aspiration.[4]

In addition, it allows access to a wider range of lymph nodes in the mediastinum than conventional mediastinoscopy.[5] Bronchoscopy alone is unable to assess all lesions lying within and outside the upper air way. In past bronchoscopist and clinicians were not sure of adequacy of material sampled during

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EBUS TBNA and that if lesion under question is approached or not.[6]

During recent years, introduction of rapid onset evaluation (ROSE) during EBUS TBNA by a cytopathologist not only addressed these difficulties but also reduced number of non-diagnostic samples and reduced additional biopsies by providing instant feedback of obtained material without altering the diagnostic efficacy of the procedure.[7]

Rapid onset evaluation is a procedure based on morphological examination of the cells that permits on-site evaluation of the site in a matter of minutes to determine whether the material acquired during the bronchoscopy is adequate and a preliminary diagnosis in most cases, however it is more costly and less available.[8] Several factors may influence diagnosis including reactive mesothelial cells, germinal center cells, may be misdiagnosed as malignant and neuroendocrine tumor, and metastatic cells of signet ring cell carcinoma mimics benign cells on rapid on site evaluation.[9] The cytopathologist also need to be careful of normal endobronchial cells mimicking epithelioid histiocytes and metaplastic cells lining air ways resembling malignant cells as such cells may lead to false positive results on rapid on site evaluation.[10]

The rationale of our study was to assess the efficacy of ROSE in EBUS TBNA cases which provide insight into its role in improving diagnostic outcomes, patient care and healthcare efficacy. Such research could validate ROSE as a standard adjunct in EBUS-TBNA procedures especially, in high stake diagnoses such as lung cancer.

Materials and Methods

This diagnostic accuracy study was conducted at Pathology department of Akhtar Saeed Medical College and Watim Medical and Dental College, from June 15, 2023, to June 15, 2024

The study included 110 cases of EBUS TBNA , collected through convenient sampling technique after approval from ERB, that comprises ROSE findings along with EBUS TBNA smears and cell block of the same patient diagnosed on CT scan with pulmonary, mediastinal or hilar masses while patients with severe hypoxemia, poorly managed heart failure and newly developed myocardial infarction were excluded. The analysis included slides with adequate tissue, good preservation and accurate staining while slides with poor quality, ambiguous morphology, contamination or irrelevant diagnosis were excluded.

Sample collected for EBUS TBNAs was laid on dry cleaned slides. Some of the slides were air dried while others were placed in Coplin jars containing 90% ethanol, to be wet fixed. The sections were stained using Hemacolor and Hematoxylin Eosin (H&E). Rapid onsite analysis of all cases was carried out by principal investigator. EBUS TBNA slides were examined under a light microscope the very day of the procedure. The diagnosis on the TBNA was confirmed by the consultant histopathologist. Biopsy/cell block samples preserved in 10% formal saline were received in the departments of Histopathology, Akhtar Saeed Medical College and Watim Medical and Dental College. Final diagnosis was made after examination of the cell block/biopsy after viewing the slides separately by consultant histopathologists at low power (4x, 10x objective), medium power (20x objective) and high power (40x objective), which was not influenced by the expression made on rapid onsite evaluation of the same case. The clinical and histopathological data was carefully recorded.

On ROSE the preliminary diagnosis was categorized as follows:

a). Non-diagnostic/inadequate, if the material on smears under examination do not include any diagnostic cells (cancer cells or inflammatory cells).

b). Diagnostic/adequate, when the examined smears contained diagnostic tumor cells or inflammatory cells.

On Cell block following Diagnostic categories were obtained:

a). Non diagnostic, if the material on slides do not reveal diagnostic cells of any specific pathologic process

b). Diagnostic, if the material on slides shows diagnostic neoplastic or inflammatory cells

If the ratio of lymphocytes to all nucleated components was greater than 30%, the case was considered as characteristic of lymph node tissue. Malignant elements, inflammatory smears and non-diagnostic or inconclusive, when no diagnosis could be made, were the criteria for final on-site analysis. Frequencies were calculated for benign and

malignant cases. Statistical data was analyzed using SPSS version 23. Sensitivity and specificity were calculated using ROC Curve analysis in SPSS.

Results

We studied 110 consecutive cases of EBUS-TBNA with Rapid on-site evaluation (ROSE) and cell block preparation retrieved from various nodal stations and corresponding mediastinal masses. Patients ranged in age from 20 - 65 years, with a mean age of 42.5 years. Out of total, 75 patients (69.1%), were male.

ROSE has been carried out in all cases by a skilled cytopathologist. Specimen smears and histopathological examination along with immunohistochemistry (IHC) for malignant and suspicious to be malignant cases, followed in our laboratory and results were interpreted by consultant histopathologist. The results of rapid onsite analysis revealed cancerous cells in 38 (34.5%) cases and for 69(62.7%) the ROSE observation revealed non neoplastic cells. For 107 cases, we were able to diagnose right away and were given a positive designation on analysis, were labeled positive and 03 samples were non diagnostic at ROSE and noted as negative as shown in Table I.

Table I: Summary of ROSE Results (n=110)

ROSE Results	Number of Cases (%)
Neoplastic	38 (34.5%)
Non neoplastic	69 (62.7%)
Non-diagnostic / negative	03 (2.7%)

Final pathological diagnosis made after cell block examination revealed malignancy in 37 (33.6%) cases, non-neoplastic in 68 (61.8%) cases and 5 (4.5%) were non diagnostic as shown in table II. For 105 cases the material obtained from procedure with ROSE was diagnostic and 5 cases were non diagnostic. Hence the sample adequacy of combined procedure was 95.5%.

Table II : Summary of Pathological Records on Cell Block (n=110)

Results of Histopathological Examination	Number of Cases (%)
Neoplastic	37 (33.6%)
Non neoplastic	68 (61.8%)
Non-diagnostic /negative	5 (4.5)

Using histological analysis as the gold standard, we assessed ROSE's ability to diagnose malignant tumors.

Table III provides an overview of the descriptive features of the quick on-site inspection. ROSE had a 95% sensitivity, 60% specificity, 96% negative predictive value and a very high positive predictive value of 98.1%.

Table III: Descriptive Parameters of ROSE

Sensitivity (%)	95%
Specificity (%)	60%
False positive (%)	1.8%
False negative (%)	1.8%
Negative predictive value (%)	96%
Positive predictive value (%)	98.1%
Diagnostic Accuracy value (%)	98 %

Discussion

As EBUS-TBNA is less intrusive and causes less side effects than surgical lymph node sampling, it is becoming increasing popular for diagnosing mediastinal and hilar nodal lesions.[11] It is the best initial step in the diagnosis of pathology in mediastinal and hilar lymph nodes because of its high accuracy.[12]

Among the most frequently asked questions in this field is the ROSE conducted for EBUS-TBNA.[13] A pathologist or cytopathologist present during the aspiration operation reduces the risk of complication while increasing the possibility of getting sufficient diagnostic material through optimal collection and accurate pre-evaluation.[14]

Nakajima et al observed that ROSE had a 5.7% false negative rate owing to findings from a subsequent histological assessment, but no false positive outcomes.[4] In this study we found 1.8 % false positive and 1.8% false negative results on ROSE.

It had been suggested that number of non-diagnostic samples can be reduced if ROSE is done during EBUS TBNA.[5] Oki et al showed diagnostic yields of 94% while Madan NK in 2016 reported it to be 78%.[15,16] In our study number of non-diagnostic samples ware 5 and obtained sample adequacy of 95.5% which is in concurrence with studies of Vasugi et al having sample adequacy of 96.8% while Mallya et al studied the utility of ROSE in EBUS TBNA and reported sample adequacy of 96.3%.[9,17] Variation in hospital case load, operator ability with the size and quantity of lymph nodes sampled can all account for variation in yield across studies.

Vasugi and coworkers also found that EBUS TBNA conducted with ROSE produced a diagnostic yield of

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97.7%, sensitivity 94%, specificity 100%, positive predictive value 100%, and negative predictive value 12%, compared to a reported diagnostic yield of roughly 45% to 55% in traditional TBNA with mediastinoscopy.[9] Few researchers however also reported opposite results such as Murakami et al In 2014 concluded that ROSE has no additional benefits on diagnostic yield.[18]

Mallya V in 2015 according to reports, EBUS-TBNA's overall diagnostic sensitivity and specificity were 85.4% and 89.6%, respectively.[17] Yuan M in 2021 stated sensitivity and specificity for assessing specimen adequacy were 97.5% and 85.7%, respectively.[19] EBUS-TBNA has a sensitivity of 93.75% for detection of chronic granulomatous inflammation while Murthi M, found EBUS TBNA 81.2% accurate for overall pathologies.[20,21]

Dildar B and colleagues discovered that ROSE hag a 96% effectiveness rate in diagnosing small cell cancer when compared to EBUS TBNA.[13] Sentruk A et al showed that in 85.9% cases final diagnosis was compatible with rapid on site evaluation.[22] The sensitivity of ROSE was 77.78%, specificity was 91.23%, the negative predictive value was 72.22% and markedly high positive predictive value 93.33%, according to Simon M. in 2017.[23] Our study concluded ROSE has 100% sensitivity and 60% specificity. According to Rosso et all, sensitivity, specificity, diagnostic accuracy were 95%, 100%, and 96%, whereas the negative and positive predictive values were 90% and 100%, respectively.[7] The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of EBUS-TBNA in differentiating between malignant and benign lesions were determined to be 93.4%, 100%, 100%, 81.0% and 95.1% respectively, in analysis conducted in china.[24] Lin CK et al, tested ROSE and found that it has 96.9% sensitivity, 68.2% specificity, 89.9% positive predictive value (PPV), 88.2% negative predictive value (NPV), and 89.5% diagnostic accuracy.[14] In present study sensitivity, specificity, positive predictive value and negative predictive values are 95%, 60, 98.1% and 96% respectively.

Conclusion

This study concludes that ROSE performed during EBUS TBNA has high sensitivity, moderately effective specificity and high concordance rate with cell block examination. It serves as a valuable adjunct to limit procedure time, enrich sample collection and benefit patient's wellbeing.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.