Utility of conventional transbronchial needle aspiration with rapid on-site evaluation (c-TBNA-ROSE) at a tertiary care center with endobronchial ultrasound (EBUS) facility

ABSTRACT
Background: Conventional transbronchial needle aspiration (c-TBNA) is an underutilized bronchoscopic modality. Endobronchial ultrasound (EBUS) guided-TBNA though efficacious is an expensive modality, facilities of which are available at only limited centers. c-TBNA is cost-effective and has potential for wide utilization especially in resource-limited settings. Rapid on-site evaluation (ROSE) improves the yield of c-TBNA.

Materials and Methods: A retrospective review of the bronchoscopy records (May 2012 to July 2014) was performed. The patients who underwent c-TBNA with ROSE were included in the study and their clinical details were extracted. Convex probe EBUS-TBNA was being regularly performed during the study period by the operators performing c-TBNA.

Results: c-TBNA with ROSE was performed in 41 patients with mean age of 42.4 (16.2) years. The most frequently sampled node stations (>90% patients) were the subcarinal and lower right paratracheal. Representative samples could be obtained in 33 out of the 41 patients (80.4%). c-TBNA was diagnostic in 32 [tuberculosis (TB)-8, sarcoidosis-9, and malignancy-15] patients out of the 41 patients. The overall diagnostic yield (sensitivity) of c-TBNA with ROSE was 78%. Mean procedure duration was 18.4 (3.1) min and there were no procedural complications.

Conclusion: c-TBNA with ROSE is a safe, efficacious, and cost-effective bronchoscopic modality. When it was performed by operators routinely performing EBUS-TBNA, diagnostic yields similar to that of EBUS-TBNA can be obtained. Even at the centers where EBUS facilities are available, c-TBNA should be routinely performed.

Key words: Bronchoscopy; lung cancer; sarcoidosis; transbronchial needle aspiration

Introduction

Transbronchial needle aspiration (TBNA) refers to a technique wherein a needle catheter introduced through the working channel of the bronchoscope punctures the tracheobronchial wall in order to sample the peribronchial locations.[1] Till the introduction of endobronchial ultrasound guided (EBUS)-TBNA, conventional TBNA (c-TBNA or TBNA) was the globally accepted standard bronchoscopic modality for the evaluation of undiagnosed mediastinal lymphadenopathy. Multiple studies established the utility of c-TBNA in staging lung cancer and in diagnosis of tuberculosis. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

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hilar and mediastinal lymphadenopathy.\[1]\) The particular advantages of c-TBNA are as follows: Minimally invasive, highly specific, less time consuming, safe, and cost-effective flexible bronchoscopic modality. However, c-TBNA remains a grossly underutilized modality.\[3]\) It has been highlighted that c-TBNA should be performed routinely during the first diagnostic bronchoscopy in patients with radiological evidence of mediastinal involvement.\[3]\)

Due to the limited availability of EBUS-TBNA facilities in the developing countries and the lack of expertise of performing c-TBNA among bronchoscopists, many patients with mediastinal lymphadenopathy remain undiagnosed and often undergo unnecessary and invasive investigations. In the context of resource-limited settings, facilities of EBUS are available only at a few centers while flexible bronchoscopy is widely available. Therefore, there is need for evaluation and routine performance of c-TBNA at centers where flexible bronchoscopy is routinely performed. Rapid on-site evaluation (ROSE) is one of the modalities that improve the yield of c-TBNA.\[6]\) On performing a search of the PubMed and EMBASE database, only one previously published study on c-TBNA with ROSE from India was identified.\[5]\) We performed a retrospective review of our bronchoscopy records to evaluate the diagnostic utility c-TBNA with ROSE. The aim of our study was to evaluate the performance characteristics of c-TBNA with ROSE. The procedure was performed by operators regularly involved in performing EBUS-TBNA at a facility with an established endobronchial ultrasound program.

**Materials and Methods**

A retrospective review of the bronchoscopy records was undertaken for the period May 2012 to July 2014. The patients who have undergone c-TBNA with ROSE for undiagnosed mediastinal lymphadenopathy were included in the study. c-TBNA procedures were performed as part of the routine clinical protocol and ROSE was performed depending upon the availability of the cytopathologist. Informed and written consent for the procedure was obtained from the patients. Convex probe EBUS-TBNA with ROSE was being regularly performed at the department during the study period. A contrast-enhanced computed tomography (CT) scan of the thorax was done in all the patients. The patients underwent the procedure if the CT short axis diameter of the enlarged node/peribronchial abnormality was greater than 10 mm. Other ancillary investigations as appropriate for the clinical and radiological profile were obtained in all the patients.

**Patient preparation and premedication**

The patients were advised to report nil per oral (at least 8 h for solids and 4 h for liquids) on the day of the procedure. Prothrombin time, activated partial thromboplastin time (APTT), platelet counts, and hemoglobin values were available for all patients. After peripheral intravenous access had been secured, low flow oxygen was administered via nasal cannula. The procedures were performed without sedation in most cases. Sedation was administered if there was patient preference for the same or if during the course of the procedure, the operator felt that sedation was required to improve procedure tolerance. Sedation, if administered, comprised of intravenous midazolam with or without intravenous fentanyl. We routinely perform outpatient flexible bronchoscopy procedures without sedation at our department.

Local anesthesia was obtained using topical spray with 10% lignocaine spray on the posterior pharynx and spray as you go method (2% lignocaine solution) while the flexible bronchoscope was being advanced through the airways. Hemodynamic monitoring (heart rate, blood pressure, and pulse oximetry saturation) was performed during the procedure. The patients were discharged from the hospital on the same day.

**c-TBNA procedure**

Flexible bronchoscopy was performed using the Olympus BF-TE2 fiberoptic bronchoscope/Olympus BF-1T-180 Video bronchoscope/Pentax FB 18V flexible bronchoscope (Olympus Corporation, Japan/Pentax, Japan). Bronchoscopy was performed through the nasal/oral route after application of lubricating lignocaine jelly. TBNA was performed using a 21-gauge, 13-mm long cytology needle (Olympus, Japan). The bronchoscope was positioned at the target site and following that the TBNA needle was inserted into the working channel. After the sheath had been visualized to exit, the scope was positioned at the target site and the assistant pushed out the needle into vision. Puncture of the tracheobronchial wall was obtained usually via the Piggyback technique. The jabbing technique and hub against the wall method were also occasionally employed. Upon successful puncture (i.e. when the entire needle was seen to have penetrated the wall), the assistant applied suction to the TBNA syringe, either manually or using the Vaclok Negative Pressure syringe (Merit medical systems, USA). The suction pressure was kept at 15-20 cc, and the needle was agitated 15-20 times. The suction pressure was reduced/no application of suction was performed in case the ROSE assessment indicated hemorrhagic aspirates. The suction was stopped, and the needle was withdrawn into the sheath and was removed. Care was taken to ensure that the needle had been fully retracted into the sheath prior to the
removal from the working channel in order to prevent damage to the internal working channel. Other adjunctive procedures, such as endobronchial biopsy, transbronchial lung biopsy (TBLB), bronchoalveolar lavage, and bronchial brushings were performed wherever indicated based on the patient profile and flexible bronchoscopic examination findings.

**ROSE and sample processing**

Aspirates were expressed onto glass slides and smearing was performed by an on-site cytopathologist. Rapid staining was performed using the toluidine blue stain, and specimen adequacy/diagnostic aspirate were intimated to the operator after each needle puncture. Slides were also fixed in alcohol for further performance of the papanicolaou stain in the pathology laboratory. If on ROSE assessment, adequate material had been obtained, no further aspirates were obtained. A detailed review of the cytological specimens was performed by an experienced cytopathologist in the pathology laboratory. Blood clot, if obtained during sampling, was also sent for histopathological processing in a few patients. Routine cell block preparations/core tissue analysis were not performed. The presence of lymphoid tissue or the detection of malignant cells or granulomas was taken as an indicator of sample adequacy. The number of aspirates per node varied, according to the feedback obtained from ROSE.

**Data analysis**

c-TBNA was considered diagnostic if a definite diagnosis was obtained with the analysis of the aspirates. In patients with a nondiagnostic c-TBNA, EBUS-TBNA was advised. In case a definitive pathological diagnosis was not obtained by other procedures, the patients were managed according to the clinicoradiological features and other supportive investigations [tuberculin skin test, serum angiotensin-converting enzyme (ACE) levels etc.] and treatment response was noted. Mediastinoscopy was not performed. Statistical analysis was performed using *Stata* statistical analysis software (Stata Corp, USA). A descriptive analysis was performed. Categorical variables were expressed as frequency (percentages) and quantitative variables were expressed as mean [standard deviation (SD)] or median [interquartile range (IQR)].

**Results**

During the study period, c-TBNA with ROSE was performed in 41 patients. The mean age of the study group was 42.4 (16.2) years and ranging from 16 years to 74 years. There were 25 males (61%) and 16 females (39%). Overall, 55 lymph node stations were sampled in 41 patients with a median of two stations sampled per patient. The median number of needle punctures per patient was three and ranged from one to six punctures per patient. The most frequently sampled lymph node stations were the subcarinal (station 7) and the lower right paratracheal (4R) and these constituted >90% of the sampled stations overall. These findings are summarized in Table 1.

Adequate/representative samples could be obtained in 33 out of the 41 patients (80.4%). c-TBNA was diagnostic in 32 out of the 41 patients (78%). The pathological diagnoses in patients with a diagnostic c-TBNA included granulomatous lymphadenopathy in 15 (6 TB and 9 sarcoidosis) patients and malignancy in the remaining 15 patients. In the remaining two patients, a diagnosis of TB was made based on the cytopathological examination of the aspirates demonstrating necrosis and positive staining for acid-fast bacilli only without any demonstrable granulomas. In two patients, blood clot obtained during TBNA was subjected to histopathological examination. In both cases, pathological examination of the blood clot yielded a diagnosis (granulomas-1 patient and non-small cell lung cancer-1 patient). The details of the various diagnoses obtained are summarized in Table 2.

In five out of nine patients for whom c-TBNA was nondiagnostic, EBUS-TBNA was performed. Four patients chose not to undergo EBUS-TBNA and opted for treatment based on the clinicoradiological profile. EBUS-TBNA was diagnostic in three of these five patients [sarcoidosis-2 patients and tuberculosis...
(TB)-1 patient] for whom a diagnosis of Granulomatous lymphadenopathy was established. A final pathological diagnosis could not be achieved in six patients and the final diagnosis was judged based on the response to the treatment initiated on the basis of the clinical and radiological profiles along with other ancillary investigations such as serum ACE levels and the tuberculin skin test.

The overall diagnostic yield (sensitivity) of c-TBNA with ROSE was 78%. Disease specific diagnostic yield was 64.3%, 72.7%, and 93.7% for sarcoidosis, TB, and malignancy, respectively. The mean procedure duration was 18.4 (3.1) min. There were no procedural complications.

**Discussion**

Common underlying etiologies for mediastinal lymphadenopathy/masses include granulomatous lymphadenopathy, lung cancer, lymphoma, etc. Bronchoscopic approaches to sampling of peribronchial lesions/mediastinal lymphadenopathy include c-TBNA and endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA). c-TBNA differs from EBUS-TBNA as there is no real time needle visualization and it is dependent upon the operator skill to perform an accurate puncture based on the anatomical landmarks. c-TBNA has high specificity (>95%) with variable sensitivity reported ranging from 37% to 89% depending upon the study population.[7,8] c-TBNA can be performed using the conventional flexible bronchoscope/video bronchoscope, and other procedures, such as bronchial biopsy and TBLC, can be performed in the same sitting using the single bronchoscope. In some studies, diagnostic yields similar to EBUS-TBNA have also been reported.[9] The utility of c-TBNA in diagnosis of lung cancer in high TB prevalence settings has also been previously described.[10] It is also a useful modality in the diagnosis of sarcoidosis and adds to the yield of concurrently performed TBLC in that context.[11,12]

Since the introduction and adoption of EBUS-TBNA, utilization of c-TBNA has declined further. In many centers, EBUS-TBNA has become the only applied method for transbronchial aspiration. Training of pulmonary fellows in c-TBNA has also showed a steady decline.[1,2] Lack of performance of c-TBNA is a missed opportunity for quick diagnosis of a patient with mediastinal involvement presenting for flexible bronchoscopy examination.

The findings from our study highlight that the availability of EBUS-TBNA should not deter “EBUS bronchoscopists” from routinely performing c-TBNA. In high volume tertiary care centers, especially in resource-limited settings, due to high patient load there is often a waiting period for EBUS-TBNA. It is common that patients who are referred for EBUS-TBNA have previously undergone flexible bronchoscopy examination in whom no endobronchial lesions were detected. In such situations and particularly in patients with large subcarinal or lower right paratracheal station nodal enlargement on CT, routine performance of c-TBNA can avoid the need for EBUS-TBNA in a substantial number of patients. Therefore, the need for repeated bronchoscopy procedures often with requirement of deep sedation/anesthesia can be avoided.

One of the most important factors determining C-TBNA yield is the operator skill and experience. The findings of our study demonstrate that when C-TBNA with ROSE is performed by operators well-versed with the performance of EBUS-TBNA and facilities of ROSE are available, comparable diagnostic yields of c-TBNA and EBUS-TBNA can be obtained. The diagnostic yield of 78% with C-TBNA in our study was marginally superior to the initial reported yield (76%) of EBUS-TBNA from our facility.[6] Compared to the previously published data from our center, the diagnostic yield of c-TBNA

| Patients with a diagnostic c-TBNA | 32/41 |
|----------------------------------|------|
| c-TBNA aspirate diagnostic of malignancy, n | 15 |
| Small cell carcinoma | 5 |
| Adenocarcinoma | 4 |
| NSCLC-NOS | 3 |
| Squamous cell carcinoma | 1 |
| Mucoepidermoid carcinoma, low grade | 1 |
| Hodgkin’s lymphoma | 1 |
| c-TBNA aspirate diagnostic of granulomatous pathology, N | 15 |
| Sarcoidosis | 9 |
| Tuberculosis (TB) | 6 |
| c-TBNA aspirate–necrosis, AFB positive, No granulomas (Diagnosis TB) | 2 |
| Patients with nondiagnostic c-TBNA with ROSE | 9/41 |
| Definitive pathological diagnosis with EBUS-TBNA in case c-TBNA with ROSE negative | 3 |
| Sarcoidosis | 2 |
| TB | 1 |
| Patients with no definitive pathological diagnosis available | 6/41 |
| Final clinicoradiological diagnosis in remaining with patients with no definite pathological diagnosis | 3 |
| Sarcoidosis | 2 |
| TB | 1 |
| Malignancy | 1 |
| Diagnostic yield (Sensitivity) of c-TBNA with ROSE | 32/41 (78%) |
| Sarcoidosis | 9/14 (64.3%) |
| TB | 8/11 (72.7%) |
| Malignancy | 15/16 (93.7%) |

NSCLC: Nonsmall cell lung cancer, NOS: Not otherwise specified, AFB: Acid-fast bacilli
with ROSE in the present study was markedly better than the TBNA without ROSE.[10]

The utilization of ROSE in TBNA has been a matter of debate for a long duration. We believe that ROSE facilities if available are useful in the context of interventional pulmonology training. Studies have demonstrated that ROSE can allow reduction in the procedure duration, the number of needle punctures, decrease complication rates, reduce procedure time and costs, improve diagnostic yield.[13,14] ROSE may also enable the operator to improve the TBNA technique.[3] If facilities of ROSE are available with TBNA, then other risky and invasive bronchoscopy procedures, such as TBLB, can be avoided.[15] Even if a trained cytopathologist is not available to perform ROSE, an alternative strategy has been described. Bonifazi et al. reported an 81% overall agreement between pulmonologist and cytopathologist in the evaluation of ROSE (when ROSE), was performed by a pulmonologist after a 3-month training in cytopathology.[14]

There is a need for a global revival of c-TBNA. The procedure has potential for widespread utilization. Especially in resource-limited settings where the facilities of EBUS-TBNA have limited availability, the potential benefits are enormous. Flexible bronchoscopy is performed by a considerably larger number of pulmonologists than endobronchial ultrasound. All pulmonologists who might have received training in EBUS may be unable to routinely perform EBUS subsequently due to limited availability of equipment especially in resource-constrained settings. The results of our study reinforce that training in EBUS-TBNA also leads to efficacious procedural performance of c-TBNA.

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Conflicts of interest
There are no conflicts of interest.

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