Original Article

'Bronchoscopic Characterization of Lesions': Significant Impact on Lung Cancer Diagnosis with Use of Transbronchial Needle Aspiration (TBNA) in comparison to Conventional Diagnostic Techniques (CDTs)

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Abstract

Background: Lung Cancer is the leading cause of cancer deaths around the world. Lung cancer accounts for 13.8% of all cancer diagnosis in India. **Aims:** (1) To find the role of bronchoscopic characterization of lesions and its impact on outcome in yield in lung cancer with use of conventional diagnostic techniques. (2) To observe additional yield of transbronchial needle aspiration (TBNA) in comparison to other conventional diagnostic techniques (CDTs) such as bronchial wash (BW), bronchial brush (BB), and forcep biopsy. **Settings and Design:** This is a prospective muticentric study conducted during June 2013–December 2016 at bronchoscopy unit of Venkatesh Chest Hospital Latur and Pulmonary Medicine, MIMSR Medical College Latur India. **Materials and Methods:** The study included 210 patients on the basis of clinical and radiological features of malignancy after inclusion and exclusion criteria and institutional review board approval. Fiberoptic bronchoscopic abnormalities were categorized as Exophytic endobronchial lesions, submucosal lesions, peribronchial lesions, and no abnormality. TBNA and other CDTs such as forcep biopsy, BB, and BW were performed during bronchoscopy procedure. Histopathological and cytological examinations of specimens were performed at pathology department. **Statistical Analysis Used:** The statistical analysis was done using Chi-square test. **Results:** In exophytic endobronchial lesions, yield of TBNA, CDTs, and TBNA plus CDTs was 62.60%, 79.67%, and 84.55%, respectively ($P < 0.001$). TBNA was found complementary to CDTs. TBNA has an additive yield in aiding diagnosis by 4.87%. In submucosal lesions, TBNA has low yield, i.e., 38.88% as compared to forcep biopsy, i.e., 47.22% in diagnosing lung malignancies. The additional diagnostic yield of other CDTs such as BB and BW has nil effect on yield difference over forcep biopsy ($P > 0.8$). In peribronchial lesions, TBNA has significant yield, i.e., 63.41% individually as compared to forcep biopsy 26.82% and CDT 39.02% ($P < 0.001$). Overall diagnostic yield of fiberoptic bronchoscopy in confirming the diagnosis was 71.95%. **Conclusions:** Bronchoscopic characterization of lesions and use of technique accordingly during bronchoscopy has a significant outcome in the form of yield also it will decrease the need for repeat bronchoscopy.

Keywords: *Bronchoscopy, conventional diagnostic techniques, lung cancer, transbronchial needle aspiration*

Introduction

Lung cancer is the leading cause of cancer deaths around the world. Lung cancer has been the most common cancer worldwide since 1985 and is the largest contributor to new cancer diagnosis and death from cancer. Globally, lung cancer is the largest contributor to new cancer diagnosis (1,350,000 new cases and 12.4% of total new cancer cases) and to death from cancer (1,180,000 deaths and 17.6% of total cancer deaths).[1,2] Lung cancer accounts for 13.8% of all cancer diagnosis in India.[3]

Since its introduction, fiberoptic bronchoscope has become an increasingly important diagnostic and therapeutic tool in respiratory diseases including lung cancer. Various diagnostic techniques such as forcep biopsy, bronchial washing and bronchial brushing, and transbronchial needle aspiration (TBNA) cytology are employed during fiberoptic bronchoscopy to increase the diagnostic yield.[4] In 1983, Wang and Terry adapted the TBNA technique originally described by Schieppati in 1949 for use within the flexible bronchoscope.[5]

TBNA through flexible bronchoscopy is a well-established sampling tool for diagnosis of lung malignancies.[6] TBNA is superior to all other sampling modalities in

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peribronchial and submucosal lesions and is on par with bronchoscopic forcep biopsy in endobronchial tumour with an average diagnostic yield of 80%.[6,7] Dasgupta *et al*. used flexible bronchoscopy and TBNA to diagnose carcinoma of the bronchus in endobronchial lesions, which may manifest as exophytic masses. They concluded that the diagnostic yield appeared to be further enhanced when this technique was combined with other conventional methods.[6] These findings were also confirmed by Govert *et al*.[7] TBNA improves the yield of FOB when added to bronchial washing, brushing and forcep biopsy.[8,9] Despite all these positive aspects, however, TBNA is underutilized.[10] This has been ascribed to lack of formal training, difficulties with needle handling, poor success rate, and insufficient cytological laboratory support.[11] Although a combination of all these techniques has been shown to increase the diagnostic yield, it is not always possible to perform all these sampling techniques in the same patient.[11]

In the present study, we focused on the role of various bronchoscopy-guided procedures in diagnosing lung cancer with special emphasis on TBNA and comparing it with other conventional diagnostic techniques (CDT) such as forcep biopsy, bronchial brush (BB) cytology, and bronchial wash (BW) cytology.

Materials and Methods

This is a prospective muticentric study conducted during June 2013–December 2016 at bronchoscopy unit of Venkatesh Chest Hospital Latur and pulmonary medicine, MIMSR Latur to find the role of bronchoscopic characterization of lesions and its impact on outcome in yield in lung cancer with use of CDTs. A total of 210 patients with suspected lung malignancy on clinical and radiological basis were included in the study after Hospital's Ethical committee approval and written informed consent of the patient.

Inclusion criteria

Unexplained paralysis of vocal cord (hoarseness of voice) or stridor, chest X-ray with radiological features of malignancy (coin lesions, mass lesions, mediastinal widening, unilateral high hemidiaphragm, segmental/complete lung collapse, and nonresolving pneumonia), normal chest X-ray with high clinical suspicion, localized monophonic wheeze, endobronchial disease or growth symptoms such as hemoptysis, persistent cough, cases with suspected recurrent post-obstructive pneumonia, suspicious sputum cytology, unexplained, and recurrent pleural effusion.

Exclusion criteria

Coagulopathy which cannot be corrected and platelets <50,000 per μL, pulmonary hypertension, uremia and serum creatinine >3, mechanical ventilation with high positive end-expiratory pressure, refractory hypoxemia, recent myocardial infarction or unstable angina, significant dysrhythmia and hemodynamic instability, and poor ability to cooperate with the procedure.

The Fiberoptic Video Bronchoscope FUJINON EPX-201H, fiberoptic video bronchoscope was used during procedures in all patients enrolled in the study by three operators. The upper airway was anaesthetized with 2 ml of 10% lignocaine solution. An additional small quantity of 1% lignocaine is instilled through the bronchoscope for topical bronchial anesthesia, as needed. Patients if he/she was apprehensive were sedated with intravenous midazolam.

Bronchoscope was inserted transnasally in about 85% of cases, while in the remaining cases, the transoral route is used. Fluoroscopy facility is also available in our unit.

During bronchoscopic procedure abnormalities were noted as[12,13] exophytic endobronchial, submucosal, peribronchial, and normal or no abnormality. Exophytic endobronchial lesions-predominant endoscopic findings are cauliflower, polypoidal-like or nodular or multinodular endobronchial growth. Submucosal lesions – predominant endoscopic findings are erythema, vascular flares and enhanced rugal pattern, loss of normal bronchial markings, or thickening of mucosa and narrowing of bronchus. Peribronchial lesions – predominant endoscopic findings are narrowing of airway due to extrinsic compression of airways by tumor or lymphadenopathy, or bulge seen in the lumen.

To avoid contamination TBNA was performed before other procedures such as BB, forcep biopsy, and BW. Endobronchial needle aspiration/TBNA was taken in all the cases except in no abnormality pattern. TBNA procedure was done first to avoid false positive, and then, other techniques were performed. TBNA and forcep biopsy performed in most of the cases and other CDTs such as BW and BB decision taken by operator doing bronchoscopy.

TBNA was performed using MW 522 needle catheters (Mill-Rose Laboratories). During bronchoscopy, the catheter was passed through the biopsy channel with the needle retracted. Under direct vision, the needle was advanced into the endobronchial lesion or 45° for submucosal lesions or 90° peribronchial lesions or bulge. In peribronchial lesions, needle was inserted into lesion according to pushing technique introduced by Wang. Once the needle was appropriately placed within the lesion, it was minimally advanced, so that the entire length of the needle will be in the tissue. Then, the inner 22-gauge needle was retracted and locked in position. The needle was moved to and fro, under applied suction from a 20-mL syringe. The pressure was released before the needle was taken out from the tissue, to avoid false-positive aspirates. The aspirated material was blown into four or five slides, smeared, fixed with 95% alcohol and sent for cytological examination at pathology department.

The statistical analysis was done using Chi-square test. Significant values of Chi-square were seen from probability

table for different degree of freedom required. *P* value was considered statistically significant if it was <0.05 and highly significant in case <0.001.

Figure 1a and b shows exophytic endobronchial growth.

Figure 2a and b shows submucosal growth.

Figure 3a and b shows peribronchial growth (bulge).

Histopathology with histopathological subtypes

Histology showing a papillary adenocarcinoma [Figure 4].

Sections reveal bronchial mucosal tissue lined by columnar epithelium showing squamous metaplasia. Dysplasia affecting full thickness is present. There is associated necrotic tissue with a few highly suspicious squamous cells entrapped within it. These cells appear malignant [Figure 5].

Sections show an undifferentiated carcinoma, a non-small cell type, infiltrating the bronchus [Figure 6].

Histology reveals small cell carcinoma bronchus [Figure 7].

Moderately differentiated squamous cell carcinoma [Figure 8].

Poorly differentiated squamous cell carcinoma [Figure 9].

Transbronchial needle aspiration cytology

TBNA cytology showing dysplastic cells [Figure 10].

Cytology Smears showing atypical, dysplastic, and suspicious cells [Figure 11].

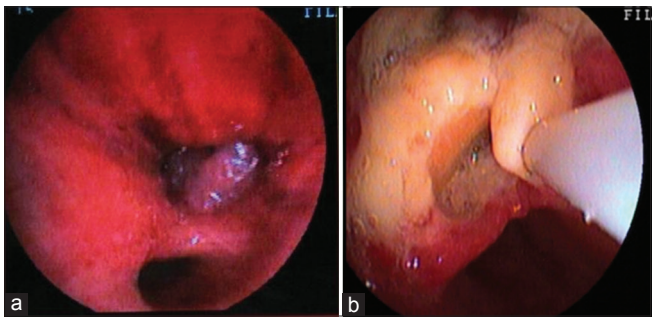

Figure 1: Fleshy exophytic growth blocking the lumen (a) with procedures TBNA (b)

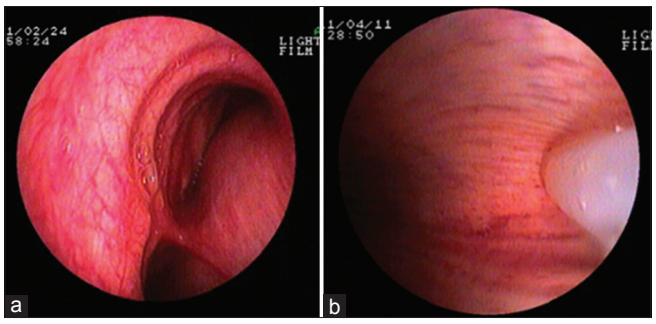

Figure 3: Intraluminal bulge (peribronchial lesions) (a) with bronchoscopic procedure TBNA (b)

TBNA cytology showing nonsmall cell carcinoma [Figure 12].

Malignant cytology from nonsmall cell type but exact typing not possible.

TBNA cytology showing squamous cell carcinoma [Figure 13].

Cytology showing malignant cells from squamous cell origin.

TBNA cytology showing Small cell carcinoma [Figure 14].

Cytology showing malignant cells of small cell origin.

TBNA cytology showing malignant cells [Figure 15].

Cytology showing malignant cells but differentiation is not possible.

Results

Totally 210 patients between age group 31–85 years, with mean age 59.93 years, male population constitutes 87.14% of total. About 77.14% cases were smoker with 59.87% cases having a history of >40 pack years. Most frequent observed symptoms are cough (79.52%), hemoptysis (32.85%), shortness of breath (27.61%), and hoarseness of

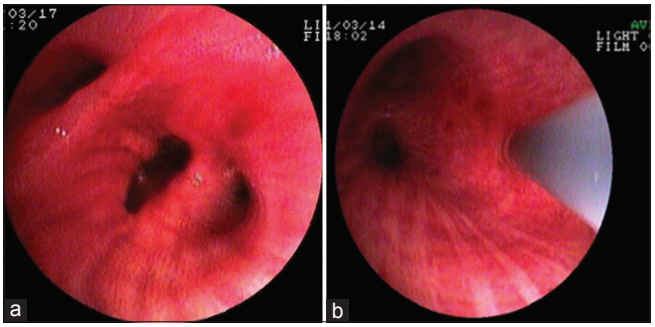

Figure 2: Submucosal abnormality (a) with bronchoscopic procedure like TBNA (b)

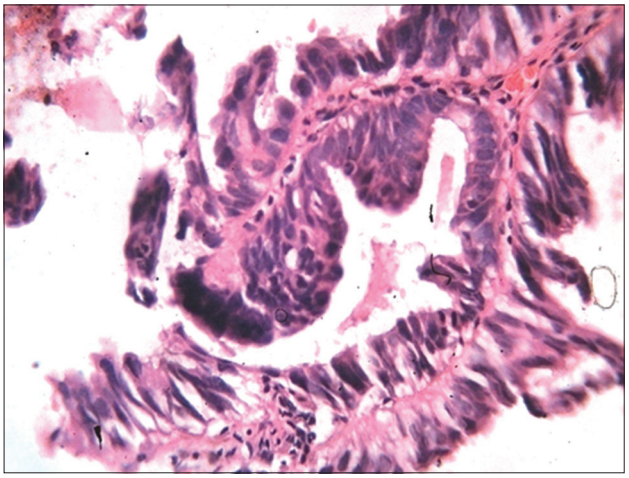

Figure 4: Histopathology section showing a papillary adenocarcinom

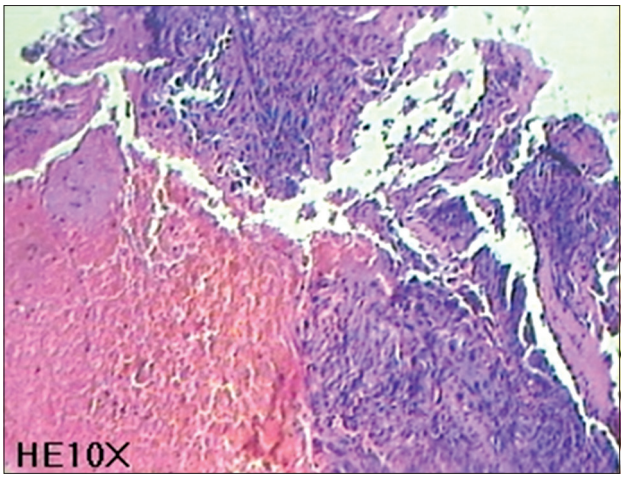

Figure 5: Histopathology sections reveal bronchial mucosal tissue lined by columnar epithelium showing squamous metaplasia. Dysplasia affecting full thickness is present. There is associated necrotic tissue with a few highly suspicious squamous cells entrapped within it. These cells appear malignant

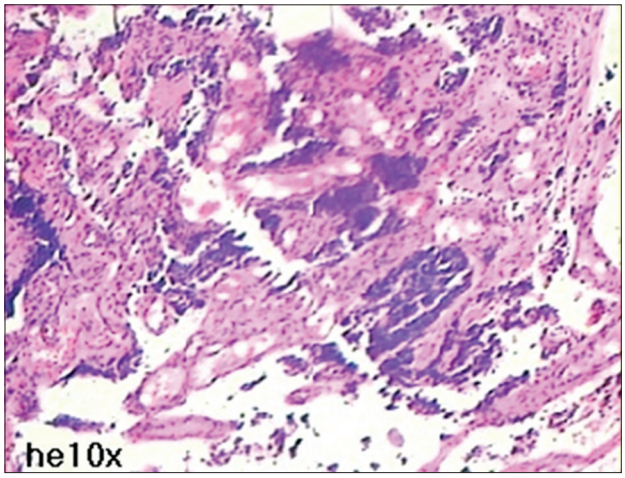

Figure 6: Histopathology sections shows an undifferentiated carcinoma, a non-small cell type, infiltrating the bronchus

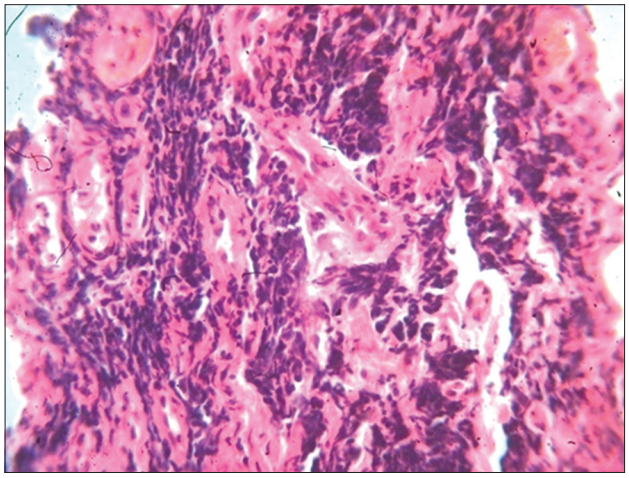

Figure 7: Histopathology section reveals small cell carcinoma bronchus

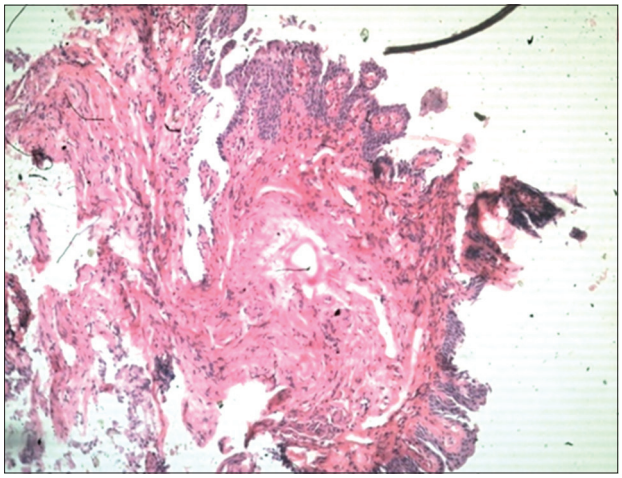

Figure 8: Histopathology section reveals moderately differentiated squamous cell carcinoma mall cell carcinoma bronchus

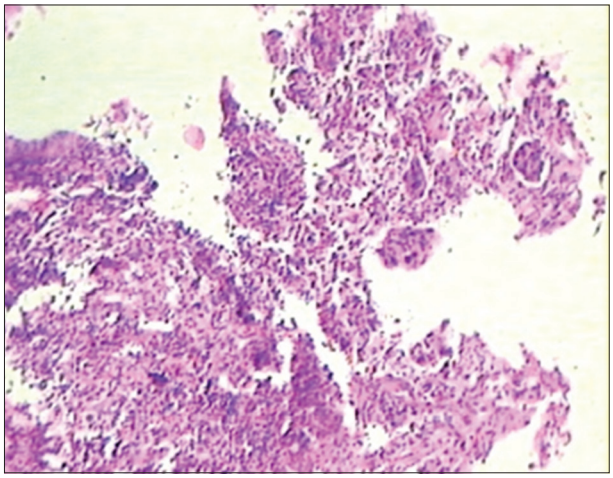

Figure 9: Histopathology section reveals poorly differentiated squamous cell carcinoma

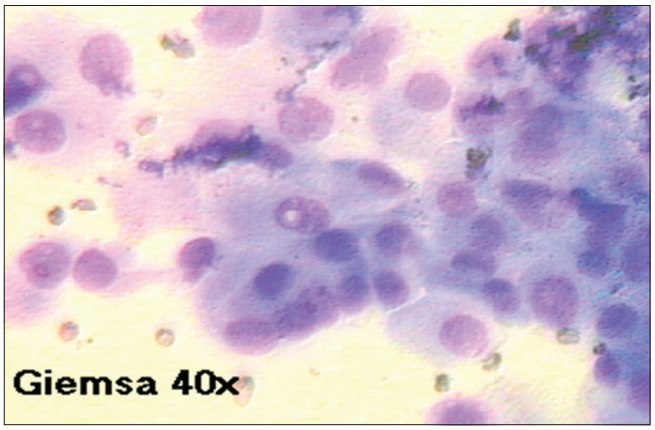

Figure 10: TBNA cytology image showing dysplastic cells

voice (16.66%). The most common observed general physical sign was clubbing (39.04%). Other signs such as superior vena cava syndrome and lymphadenopathy were seen in 3.8% and 5.23%, respectively. Radiological patterns of abnormalities documented in study are mass lesion (29.04%), hilar opacity (27.14%), collapse (segmental/lobar) (20.95%), and pleural effusion (12.38%).

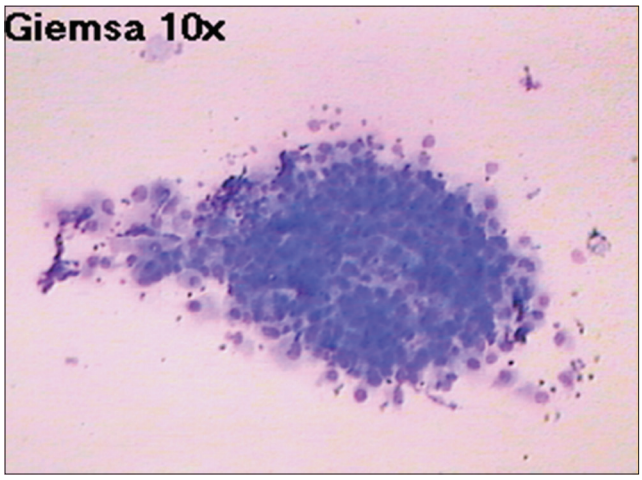

Figure 11: TBNA cytology image showing atypical, dysplastic and suspicious cells

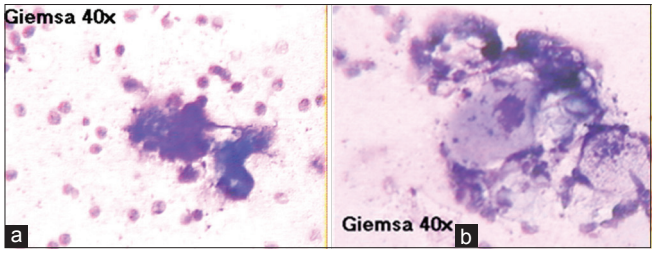

Figure 13: TBNA cytology showing squamous cell carcinoma (a) TBNA cytology showing malignant cells from squamous cell origin (b)

All suspected patients of lung malignancy underwent fiberoptic bronchoscopy in our Bronchoscopy suit and out of 210 enrolled cases abnormality was documented in 200 cases with normal study in remaining 10. Abnormalities were categorized as exophytic endobronchial lesions in 123 cases (58.57%), submucosal abnormalities in 36 cases (17.14%) and peribronchial lesions in 41 cases (19.52%) and no abnormality in 10 cases (4.76%).

In our study, bronchoscopic site of abnormality was noted on the right side of lung in 47.61% and on the left side of lung in 41.90% cases. Lin GAO *et al*.[14] reported lung cancer was more commonly found in the Right Lung in 51.58% and on left side in 42.82%.

Yield of TBNA, CDT, and TBNA plus CDT in exophytic lesions are 62.60%, 79.67%, and 84.55%, respectively, in diagnosis of lung malignancies. Yield difference of all these techniques is highly significant ($P < 0.001$) [Table 1].

TBNA has low yield, i.e., 38.88% as compared to forcep biopsy, i.e., 47.22% in diagnosis in submucosal lesions. The additional diagnostic yield of other CDTs such as BB and BW has nil effect on yield difference over forcep biopsy ($P > 0.8$) [Table 2].

TBNA has significant yield, i.e., 63.41% individually as compared to forcep biopsy 26.82% and CDT 39.02%. Additional CDTs such as BB cytology and BW has

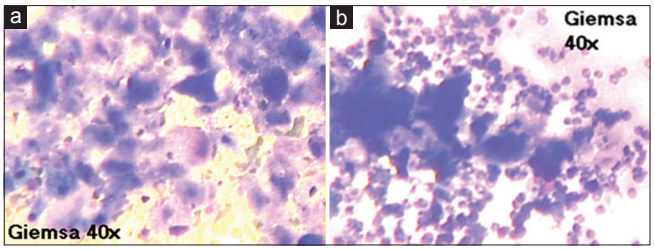

Figure 12: TBNA cytology showing non small cell carcinoma (a) TBNA cytology definitely shown malignant cytology in non small cell type but exact typing not possible (b)

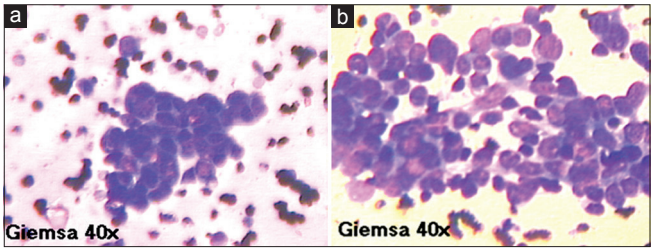

Figure 14: TBNA cytology showing small cell carcinoma (a) TBNA cytology showing malignant cells of small cell origin (b)

additive yield to forcep biopsy from 26.82% to 39.02% in peribronchial lesions ($P < 0.001$) [Table 3].

Overall diagnostic yield of fiberoptic bronchoscopy in diagnosis of lung malignancies in the study population is 71.95% [Table 4].

Discussion

Diagnostic Yield of fiberoptic bronchoscopy-guided procedures in lung malignancies

In exophytic endobronchial lesions

Overall diagnostic yield for exophytic endobronchial lesions (EEL) was 84.55% in our study by means of all techniques during bronchoscopy. Comparable with those of Bollinger *et al*.[15] 88% yield in endoscopically visible lesions in review of 30 studies, Roth *et al*.[16] 83.7% yield, Joos *et al*.[17] 92%, comparable to the data of Popovich *et al*. and BTS recommendations on bronchoscopy[18] mentioned the diagnostic yield for visible endobronchial lesions should be at least 80%.

Yield of TBNA, CDT, and TBNA plus CDT in EEL was 62.60%, 79.67%, and 84.55%, respectively, in diagnosis of lung malignancies in EEL ($P < 0.001$). A study conducted by Salathe *et al*.[18] reported a combination of TBNA with CDT increase yield from 65% to 79%. Gullón *et al*.[19] concluded addition of TBNA to CDT increase diagnostic yield of exophytic endobronchial lesions. Caglayan *et al*.[20] reported increase in yield from 79% to 91% after addition of TBNA to CDTs ($P < 0.001$). Contradictory to mentioned inference, Karahalli *et al*.[21] reported no significant improvement in yield by adding TBNA to CDT.

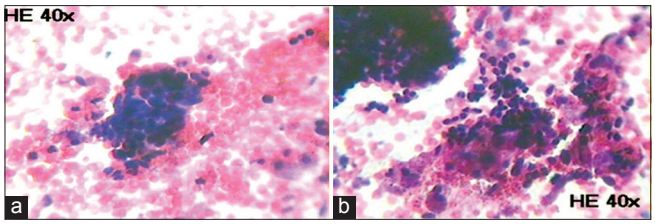

Figure 15: TBNA cytology showing malignant cells (a) TBNA cytology showing malignant cells but differentiation is not possible (b)

Table 1: Yield of transbronchial needle aspiration, conventional diagnostic techniques, and transbronchial needle aspiration plus conventional diagnostic techniques in exophytic lesions

Results	TBNA	CDT	TBNA plus CDT
Positive (%)	77 (62.60)	98 (79.67)	104 (84.55)
Negative	46	25	19
Total	123	123	123

TBNA: Transbronchial needle aspiration, CDT: Conventional diagnostic techniques

Table 2: Yield of transbronchial needle aspiration, forcep biopsy, and transbronchial needle aspiration plus conventional diagnostic techniques in submucosal lesions

Results	TBNA	Forcep biopsy	TBNA plus CDT
Positive (%)	14 (38.88)	17 (47.22)	17 (47.22)
Negative	22	19	19
Total	36	36	36

TBNA: Transbronchial needle aspiration, CDT: Conventional diagnostic techniques

Table 3: Yield of transbronchial needle aspiration, forcep biopsy, and conventional diagnostic techniques in peribronchial lesions

Results	TBNA	Forcep biopsy	CDT
Positive (%)	26 (63.41)	11 (26.82)	16 (39.02)
Negative	15	30	25
Total	41	41	41

TBNA: Transbronchial needle aspiration, CDT: Conventional diagnostic techniques

Table 4: Summarization of diagnostic yield of all bronchoscopy-guided procedures as per type of abnormality during procedure in the study

Type of abnormality	Total number	Positive	Yield (%)
Exophytic	123	104	84.55
Submucosal	36	17	47.22
Peribronchial	41	27	65.85
No abnormality	10	2	20.00
Total	210	150	71.95

TBNA was the only positive test in 6 cases out of 123, i.e., additional yield of technique was 4.87%. Similar studies from authors Roth *et al*.[16] reported 8.04%, Gullón *et al*.[19] reported 9.5%, Karahalli *et al*.[19] reported that additional yield of TBNA was 1% in their study. Rudd *et al*.[22] and Haponick *et al*.[11] concluded that addition of TBNA to routine diagnostic technique improves the diagnostic yield. Kaçar *et al*.[23] reported that additional yield is not satisfactory by TBNA over FB and other CDTs. Dasgupta *et al*.[6] and Guidelines from the American College of Chest Physicians[24] stated that in endobronchial lesions that are either necrotic in appearance or highly vascular, TBNA may be used to obtain a sample by altering the technique to directly place the needle into the endobronchial lesion.

Submucosal lesions

Total yield of all fiberoptic bronchoscopy-guided procedures in submucosal lesions is 47.22%. Roth *et al*.[16] reported diagnostic yield in submucosal lesions 34.4% in their study.

TBNA has low yield, i.e., 38.88% as compared to forcep biopsy, i.e., 47.22% in diagnosis in submucosal lesions. Additional diagnostic yield of other CDTs such as BB and BW has nil effect on yield difference over forcep biopsy ($P > 0.8$). Lundgren *et al*.[25] and Karahalli *et al*.[21] reported that TBNA had lower diagnostic yield than forcep biopsy in submucosal lesions. Roth *et al*.[16] concluded no additional yield of BB and Small volume lavage over TBNA and forcep biopsy in submucosal lesions. Caglayan *et al*.[20] reported TBNA combined with CDTs has no additional yield over CDT in submucosal lesions.

Peribronchial lesions (bulge)

Total yield of all fiberoptic bronchoscopy-guided procedures in peribronchial lesions is 65.85%. TBNA has significant yield, i.e., 63.41% individually as compared to forcep biopsy 26.82% and CDT 39.02% ($P < 0.001$). Joos *et al*.[26] and Harrow *et al*.[27] reported yield of TBNA was 43.6% and 80% for peribronchial disease, respectively. Dasgupta *et al*.,[6] Govert *et al*.[7] found the combination of higher yield of TBNA over CDT and have increased yield CDT over forcep biopsy alone in their studies. Caglayan *et al*.[20] in peribronchial disease reported diagnostic rate was 52% by CDT, 87% by TBNA plus CDT and superiority of combination over CDT was significant ($P < 0.001$).

Sole yield of TBNA in our study is 24.39% which is significantly higher than any Individual CDTs. Caglayan *et al*.[20] reported 34.3% yield of TBNA as a sole in their study in peribronchial lesions.

Yield of fiberoptic bronchoscopy when no abnormality detected during procedure

In our study, total yield of all fiberoptic bronchoscopy-guided procedures when no documented abnormality was 20% noted with BW. Roth *et al*.[16] reported 16.7% yield in nonvisible lesions and Scottish Multicenter study[28] was 9%. van der Drift *et al*.[29] *et al*. reported diagnostic yield of washings in patients with endoscopically nonvisible (peripheral) tumors varies from 35% to 52%.

Histological types of lung cancer in our study

The most common histological type was squamous cell carcinoma observed in 54% cases followed by adenocarcinoma in 20%, small cell carcinoma in 12.66%, and undifferentiated non-small cell carcinoma in 11.33%. Rawat *et al*.[30] reported similar prevalence being squamous cell carcinoma in 44.83% and adenocarcinoma in 19.70%. Behra[31] reported collective evidence for Squamous cell carcinoma is the commonest histological type in India though the prevalence of Adenocarcinoma is on rising trends as like western countries. Verma *et al*.[32] reported squamous cell carcinoma in 60.00% and adenocarcinoma in 5.71%.

Conclusion

In exophytic endobronchial lesions, the use of conventional TBNA has a significant additive yield over other CDTs like forcep biopsy and BW. Use of conventional TBNA would decrease the need for repeat bronchoscopy, especially in the presence of necrosis or clot over endobronchial growth. In fleshy vascular endobronchial growth where risk of significant bleeding is high, TBNA is best technique.

As submucosal lesions, may be nonspecific abnormality ranging from inflammatory, malignant or changes secondary to infectious etiology, use of CDTs have comparable yield with TBNA. In submucosal lesions bronchoscopist would define either of techniques to be used in confirming the diagnosis.

As peribronchial lesions, intraluminal bulge with or without abnormality in mucosa secondary to extrinsic compression, TBNA is superior to all techniques used in CDTs and TBNA is most sensitive diagnostic tool in this category.

Bronchoscopic characterization of lesions and use of technique accordingly during bronchoscopy has a significant outcome in the form of yield also decrease need for repeat bronchoscopy.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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