

Parallelism in the Diagnostic Performance of Bronchoscopic Sampling Techniques in Lung Carcinoma

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Abstract--- **Context:** Flexible bronchoscopy is the recommended procedure for diagnosis of all suspected lung carcinoma, having sensitivity of 88% for central airway lesion and 78% for peripheral. The diagnostic yield of bronchoscopy combining various sampling techniques for visible lesions was predicted to be at least 80%.

Aims: To compare the diagnostic yield of various sampling techniques of bronchoscopy in diagnosing lung carcinoma at a rural tertiary care centre.

Settings and Design: Retrospective observational study centre in respiratory medicine at tertiary care.

Methods and Material: 26 bronchoscopies done in radiologically suspected malignancy in previous two and a half years were included. Histopathological or cytological evidence of malignant cells was considered as final diagnosis of malignancy. Data of radiological and bronchoscopic findings and reports of sampling techniques were analysed.

Statistical analysis used: SPSS for windows.

Results: The overall diagnostic yield is 46.15%, while for central lesion it is higher than peripheral lesion, 42.30% and 7.69% respectively. EBLB gave highest diagnostic yield 69.2%. BAL cytology is the most common procedure performed. Central lesion on imaging and visible endobronchial abnormalities like narrowing, intraluminal growth, mucosal irregularity are predictors of higher diagnostic yield.

Conclusions: The overall diagnostic yield in radiologically suspected lesions to be 46.15% and highest diagnostic yield with endobronchial lung biopsy. Central lesion on radiology and endobronchial abnormalities are strong predictors of high diagnostic yield, with highest yield in biopsy amongst all techniques. Hence biopsy should be done in all such cases.

Keywords--- Lung Cancer, Survival Rate, Bronchoscopic.

Key Messages: Flexible unaided bronchoscopy is diagnostic in 46.15% of radiologically suspected malignancy cases. Endobronchial Lung Biopsy has highest diagnostic yield 69.2% Central lesion and endobronchial abnormality are predictors of higher yield.

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I. INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths worldwide with an overall five-year survival rate of 17% after diagnoses.^[1]

Flexible bronchoscopy has become the recommended procedure for all patients suspected of having lung cancer, showing sensitivity for central airway lesions of 88% and overall sensitivity for all modalities in the diagnosis of peripheral disease of 78%.^[1]

The major sampling techniques for tissue sampling in bronchial carcinoma remain as forceps endobronchial lung biopsy (EBLB) for centrally located lesions and transbronchial biopsy for peripherally located lesions at most centers. While Brushing and Bronchoalveolar Lavage (BAL) also provide a sample for cytology. Studies showed that a combination of all these techniques increases the diagnostic yield.^[2]

The diagnostic yield of bronchoscopy combining various sampling techniques for visible lesions was predicted to be at least 80%.^[3]

Many previous studies have determined different diagnostic yield with bronchoscopy, and higher diagnostic yield can be obtained with C-arm fluoroscopic guidance or virtual bronchoscopic guidance. Newer sampling techniques like endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), the cryo-probe endobronchial biopsy also yield better tissue sampling hence better yield. But these usually require the procedure to be carried under sedation or anaesthesia, with higher cost and increased risk of complications. Although new bronchoscopic procedural techniques have been developed to facilitate accuracy in locating a lesion, they are not used in routine practice, especially in developing countries, where even the fluoroscope is not available for routine bronchoscopy in the diagnosis of a localized lesion.^[4] We have designed this study to find out the diagnostic yield of flexible bronchoscopy without guidance in a resource-limited setting with basic sampling techniques like Endobronchial lung biopsy, brush biopsy and BAL cytology.

While Computed tomography (CT) is poor at differentiating the pattern of endobronchial abnormalities, it is more accurate in the detection of airway abnormalities compared with bronchoscopy. Thus, CT is considered to be a necessary investigation before the evaluation of pulmonary nodules or masses by bronchoscopy without guidance.^[5]

This study aimed to compare the diagnostic yield of various sampling techniques of bronchoscopy in diagnosing lung carcinoma at a rural tertiary care center.

The objectives of our study were, to find out overall diagnostic yield of bronchoscopy in radiologically suspected cases of lung malignancy, to compare the efficacy of bronchoscopic diagnostic tools (Bronchoalveolar Lavage, Brush Biopsy, Endobronchial Lung Biopsy, Post bronchoscopy sputum) in lung carcinoma, to compare the frequency of utilization of bronchoscopic diagnostic tools (Bronchoalveolar Lavage, Brush Biopsy, Endobronchial Lung Biopsy, Post bronchoscopy sputum), and to find out comparative diagnostic yield in central v/s peripheral lung lesions by bronchoscopy.

II. METHODOLOGY

A retrospective study was designed at our tertiary care center in the Department of Respiratory Medicine. All

bronchoscopies which were done in the previous two and a half years from September 2017 to May 2019 were reviewed. All procedures where the indication for bronchoscopy was suspicion of malignancy were included, cases where procedure was abandoned due to unavoidable reasons, or samples were not sent for investigations were excluded from the study. Institutional Ethics Committee clearance was obtained before obtaining data. A total of 26 patients were included and cases where indication was other than malignancy or where procedure was abandoned or samples, were not processed were excluded.

Radiologically suspected cases of lung carcinoma were included and based on computed tomography scanning report the lesions were divided into central and peripheral types. Lesions with hilar mass or having intrabronchial mass or compressing bronchus were counted as central lesions.

The procedure was performed by pulmonologist consultants, using an Olympus BF Type 1T150 Bronchoscope. The biopsy was performed by using Olympus reusable round cup biopsy forceps FB19-C, Olympus Reusable Alligator Cup with Needle Biopsy Forceps FB-55CP1. Brush cytology was performed by Olympus cytology brush BC-202D-3010.

Commonly, a combination of multiple techniques was performed and the most common order was lavage followed by biopsy and then brushing. The biopsy was repeated two to three times at the same site depending on the size of the bit until adequate bit was obtained. It was followed by brushing two to three times at biopsy site and multiple smears were prepared immediately and fixed. Lavage was mostly before applying these procedures or in stable conditions was collected afterward also. Post flexible bronchoscopic sputum was collected immediately after the procedure.

Diagnosis of malignancy was defined as a positive histopathological report or cytological report for malignant cells.

Statistical methods used: SPSS for Windows (version 16.0).

III. RESULTS

The baseline characteristics are compared in Table no.1. The majority of the patients were males (76.92%) and the most common age group was 61- 65 years (30.43%). The centrally distributed lesion was more commonly indicated for bronchoscopy 18/26 (69.23%).

Table 1: Baseline Characteristics of 26 Cases

<i>Character</i>	<i>N</i>	<i>%</i>
Sex		
Males	20	76.92
Females	06	23.07
Age (years)		
<= 50	06	23.07
51 – 55	05	19.23
56 – 60	04	15.38
61 – 65	07	30.43
66 – 70	04	15.38
Lesion on CT		

Central	18	69.23
Peripheral	08	30.76

The overall diagnostic yield of bronchoscopy was 46.15% (12/26). Diagnostic yield of malignancy by bronchoscopy in the central lesion is much higher 66.67% compared to peripheral lesion 7.69%. While there were 23.07% cases where malignancy was not diagnosed in the central lesion.

Table 2: Comparative Diagnostic Yield in Central v/s Peripheral Lesions on CT

CT lesions	Final diagnosis – malignancy	Final diagnosis – not malignancy
Peripheral	02 (7.69%)	06 (23.07%)
Central	12 (66.67%)	06 (23.07%)

Table no. 3 presents the diagnostic yield of various sampling techniques. The sampling techniques performed were Endobronchial biopsy (13/26), Brush biopsy (16/26), BAL cytology (21/26) and Post FOB (Post - Fiberoptic Bronchoscopy) sputum cytology (10/26). BAL cytology was the most common procedure performed, followed by brush biopsy and then an endobronchial biopsy.

Endobronchial lung biopsy gave the highest diagnostic yield of 69.2%. Brush biopsy had a yield of 56.25% while BAL cytology had 19.04%. Post FOB sputum cytology was not diagnostic in any of the cases.

Table 3: Comparative Diagnostic Yield of various Sampling Methods

Sampling technique	Report positive for malignancy	Total no. of procedures	Diagnostic yield
Endobronchial Lung Biopsy	09	13	69.2%
Brush Biopsy	09	16	56.25%
BAL Cytology	04	21	19.04%
Post FOB Sputum Cytology	00	10	0

We compared different sampling techniques with factors affecting diagnosis like the position of lesion on CT thorax and Endobronchial visibility of growth or mucosal abnormality or extraluminal compression, depicted in Table no. 4. The central lesion group had higher yield in all techniques. Endobronchial lung biopsy showed the highest yield in both central (83.33%) and peripheral lesions (42.85%).

Endobronchial abnormality like narrowing, intraluminal growth mucosal irregularity are predictors of higher diagnostic yield. When the endobronchial biopsy was done in these suspected lesions all turned out to be a malignancy, while in Brush biopsy 81.81% turned out to be malignant.

Table 4: Predictors of Diagnostic Yield

Factors	Sampling technique	Endobronchial Lung biopsy	Brush biopsy	BAL cytology
CT Lesion	Peripheral	3/7 (42.85%)	1/3 (33.33%)	0/4 (0%)
	Central	5/6 (83.33%)	9/11 (81.81%)	3/11 (27.27%)
Endobronchial lesion	Present	9/9 (100%)	9/11 (81.81%)	3/11 (27.27%)
	Absent	0/1 (0%)	0/1 (0%)	0/1 (0%)

Table 5: Diagnostic Yield in different Types of Carcinoma

	Endobronchial Lung biopsy	Brush biopsy	BAL cytology
Adenocarcinoma	4/26 (15.38%)	1/26 (3.8%)	1/26 (3.8%)
Squamous cell carcinoma	4/26 (15.38%)	5/26 (19.23%)	1/26 (3.8%)
Small cell carcinoma	1/26 (3.8%)	1/26 (3.8%)	0/26 (0%)
Metastatic carcinoma	0/26 (0%)	2/26 (7.6%)	0/26 (0%)
Undifferentiated	0/26 (0%)	0/26 (0%)	1/26 (3.8%)

The above table depicts diagnostic yield as per different types of carcinoma, adenocarcinoma had 15.38% yield

in the endobronchial biopsy, 3.8% in brush biopsy and 3.8% in BAL cytology.

Squamous cell carcinoma also had the same yield of 15.38% in the endobronchial biopsy, but it had a higher brush biopsy yield of 19.23%. Small cell carcinoma had significantly lower diagnostic yield in all sampling procedures as compared to other variety.

IV. DISCUSSION

Flexible bronchoscopy with its attendant procedures is a valuable diagnostic procedure in the workup of a patient suspected of having lung cancer.^[6] Endobronchial lung biopsy had the highest diagnostic yield of 69.2% amongst all procedures, emphasizing the importance of performing this procedure in all suspected cases. Even then it is performed less commonly than brush biopsy and BAL cytology. This might be due to a higher risk of bleeding, hypoxia or other complications associated with it, especially in debilitated older individuals. It gave higher yields in both central as well as peripheral lesions when compared to other sampling tools and gave 100% yield of diagnosis when it was performed at the site of the endobronchial lesion. Hence, this underscores the importance of performing more endobronchial biopsies especially with mucosal abnormalities or intraluminal growth. Complications such as bleeding can be managed in most cases with local injection of adrenaline, cold saline or intravenous tranexamic acid administration. Training of more people and the availability of adequate equipment will help in increasing the use of this tool. American College of Chest Physicians (ACCP) has recommended direct forceps biopsy of visible central lesions and its sensitivity is 74%. At least three forceps biopsies of the visible lesion are recommended.^[6]

The comparative diagnostic yields of various sampling techniques were analogous to Roth et al^[6] where they also reported the highest yield with biopsy 60.7%, followed by Brush biopsy and BAL cytology. A contrasting finding was reported by Lam et al^[7] in yield of BAL cytology, which they reported to be higher than a biopsy and brushing 69%, whilst our study and Roth et al reported 19.04% and 8.1% respectively. This might be because most cases had advanced TNM staging and they used larger than usual volume (100ml) of saline for obtaining sample. Also due to the same reason they did not find any difference in the diagnostic yield of BAL in the central and peripheral lesion. Our study reported a much higher yield of BAL in central lesions 27.7% compared to none diagnosed in the peripheral lesion. This discrepancy of BAL cytology hints us towards an alternative approach of performing BAL with larger volumes of saline if other methods are unavailable or are unsuitable in that scenario and hence obtain yield comparable to biopsy or brushing.

Raymond et al^[8] described no difference in diagnostic yield relative to the timing of washings for central tumors. In peripheral non-visible tumors, however, the yield for bronchial washing after biopsy and brushing was significantly higher than the yield for washing before biopsy and brushing (45% and 25%, respectively).

All studies showed a very low yield in peripheral lesion when unaided bronchoscopy was performed. Roth et al could diagnose only 4.8% cases while we could diagnose only 7.69% cases. Thus, malignancy cannot be ruled out confidently in peripheral lesions and they can be candidates for repeat bronchoscopic procedures with more advanced techniques.

The overall diagnostic yield of bronchoscopy in malignancy was 46.15% in our study and 85% in Lam et al.^[7]

They did a stepwise performance of BAL, biopsy and brush biopsy in all cases, which was similar to our technique also. Another study by Mohamed et al.^[9] diagnosed 1204 (70%) cases of malignancy out of 1720 suspected cases. The nature of the etiology (benign or malignant disease) also affects the diagnostic yield; hence, high diagnostic yields will be obtained if only malignant proven nodules or masses are enrolled when evaluating the diagnostic procedure. As we had included all suspected cases of malignancy rather than proven malignancy cases, we obtained a lower overall diagnostic yield. Also, we had performed bronchoscopy without any fluoroscopic or virtual guidance, or there was no rapid onsite examination of biopsy and brushing specimens. So, under such circumstances, one should be cautious in interpreting results and this study would help as guidance.

In centrally located lesions our yield was 42.30%, and respective to techniques it was 83.33% in the endobronchial biopsy, 81.81% in brush biopsy and 27.27% in BAL cytology. A comprehensive literature study from 1970 to 2001 revealed the sensitivity of all bronchoscopic methods in diagnosing central bronchogenic carcinoma by 88%, and individually 74, 61 and 47% for endobronchial biopsy, brushing and washing.^[6]

Studies conducted by Roth et al^[10] in 2008 and Boonsarnsuk V et al^[5] in 2010 reported diagnostic yield to be 76.6% and 80.6% in endobronchial lesions. Van der Drift et al^[11] diagnosed 94% cases from visible tumors. Similarly, on comparing various sampling techniques in visible endobronchial abnormalities, we have obtained a diagnostic yield of 100% in endobronchial biopsy and 81.81% in brush biopsy and 27.27% in BAL cytology. So, any endobronchial abnormality is a strong predictor of diagnostic yield and hence any abnormality should always be sampled with a combination of high yielding sampling techniques like endobronchial biopsy or brush biopsy.

Upon comparing various types of carcinomas and respective diagnostic yield adenocarcinoma and squamous cell carcinoma were diagnosed more frequently than small cell carcinoma and other varieties like undifferentiated and metastatic carcinoma were diagnosed very infrequently. Hence, if small cell carcinoma is suspected diagnosis based on radiologic and clinical findings one should plan bronchoscopic sampling accordingly. Adenocarcinoma was diagnosed much more on biopsy 15.38% rather than brushing or BAL cytology 3.8% each, while squamous variety was most frequently seen in brushing sample 19.38% closely followed by biopsy 15.38%. Pirozynsk^[12] studied the diagnostic yield of only BAL samples with different malignancies where adenocarcinoma had the highest 59.1% yield. In remaining correct type was identified in <50% cases.

Study Limitations: As this is a retrospective study, the data and information available were limited. Only basic sampling techniques have been compared, others like transbronchial lung biopsy (TBLB), transbronchial needle aspiration (TBNA), EBUS-TBNA, cryobiopsy were not available at our setup. Also, the procedures were performed without fluoroscopic guidance or virtual bronchoscopic guidance. In diagnosing malignancy histopathology is used for obtaining the type of carcinoma, while further immunohistochemical typing was not done, hence few cases were undifferentiated carcinoma. Repeat bronchoscopy was not performed.

Further Research: This study included small sample size and further larger prospective studies can be designed for determining the yield of all available procedures. Also, combined utility of various tools and the effect of change in technique can be studied if it affects the diagnostic yield. The technique and skill of pathological processing of samples also affect the yield which was not considered in this study.

In conclusion, this study has demonstrated the overall diagnostic yield in radiologically suspected lesions to be 46.15% and the highest diagnostic yield with an endobronchial lung biopsy. Central lesions on radiology and endobronchial abnormalities are strong predictors of high diagnostic yield, with the highest yield in biopsy amongst all techniques. Hence biopsy should be done in all such cases. BAL cytology is the most frequently done sampling technique for diagnosing malignancy. Small cell carcinoma was difficult to diagnose by all the sampling techniques and had a much lower diagnostic yield of 3.8%. While Post FOB sputum cytology proved to be inefficacious in providing a diagnosis.

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