

Complications and predictors of diagnostic yield of endobronchial forceps biopsy in visible lesions

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Keywords: Bronchoscopy; forceps biopsy; exophytic growth; predictors



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Abstract

Background: Fiberoptic bronchoscopy is an important and relatively safe procedure for evaluation of various pulmonary diseases. Endobronchial forceps biopsy is commonly performed sampling technique for visible lesions in tracheobronchial tree. Diagnostic yield of biopsy depends upon lesion type and the number of biopsy samples taken. This study aimed to evaluate the complications and diagnostic yield of endobronchial forceps biopsy in visible lesions and correlate the number of biopsy samples taken with the yield.

Methods:

This was an observational study conducted at two tertiary care hospitals in Chitwan; Chitwan Medical College Teaching Hospital and B P Koirala Memorial Cancer Hospital. One hundred and forty patients who underwent endobronchial forceps biopsy of bronchoscopically visible lesions were included. Complications and diagnostic yield of the biopsy samples and its correlation with number of biopsies taken were evaluated.

Results:

The common complications observed were transient drop in saturation > 4% (22%) and mild bleeding (9.9%). The net diagnostic yield was 67.4% that significantly improved with an increase in the number of biopsies taken. The yield was better for exophytic growths compared to submucosal/mucosal lesions (83.7% vs. 57%, OR = 8.1 (2.2 – 29.9), P<0.001). The association of improved yield with increased number of biopsy was more pronounced in exophytic growths compared to submucosal/mucosal lesions.

Conclusion:

Endobronchial forceps biopsy is a safe procedure that gives a good diagnostic yield in bronchoscopically visible lesions, provided adequate number of biopsy sample are taken. The probability of getting a positive yield is high in exophytic growths.

Introduction

Fiberoptic bronchoscopy (FOB) has greatly revolutionized the field of pulmonary medicine and has been the procedure of choice for diagnosis of various pulmonary diseases.¹ It is a safe procedure that can be performed under local anaesthesia and provides maximal visualization of tracheobronchial tree in short time.² FOB is primarily used to obtain tissue samples for histologic

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examination. Various conventional bronchoscopic sampling techniques are bronchial wash and bronchoalveolar lavage, bronchial brushing, transbronchial and endobronchial needle aspiration, and transbronchial and endobronchial forceps biopsy. The practice of sampling technique depends upon skill and experience of the operator and resources available for sample acquisition.

Bronchoscopic samples collected by multiple sampling techniques give better diagnostic yield than any of the techniques alone.³⁻⁵ Endobronchial forceps biopsy (EBB) of bronchoscopically visible lesions is commonly utilized sampling technique. Visibility of the endobronchial lesions and the numbers of biopsy sample taken are regarded as good predictors of diagnostic yield. The visible lesions that can be biopsied generally are categorized as exophytic growth and submucosal/mucosal infiltrative lesion.⁶ Very few studies have attempted to correlate the yields of EBB in these two categories of visible lesions. The aims of this study were to find the complications associated with EBB and its diagnostic yield in visible lesions, and to correlate the number of biopsy samples with positive yield.

Methods:

After obtaining ethical clearance from Institutional Review Boards, this cross-sectional observational study was conducted over a period of 3 months (March 2018 – May 2018) at Chitwan Medical College Teaching Hospital (CMCTH), Chitwan and B P Koirala Memorial Cancer Hospital (BPKMCH), Chitwan. A total of 140 consecutive patients who underwent EBB (EBB rate: 56.9 %) were included. A written informed consent was taken from all the participants of the study.

A detailed clinical data including age, gender, symptoms, smoking status, comorbidities, clinical and radiological (based on CT scan chest) indications for bronchoscopy and routine investigations results were recorded in proforma at the time of enrolment in the study. At least 6 hours fasting prior to the procedure was made mandatory and an intravenous line was accessed in all the patients.

After thoroughly explaining the procedure to the patient, 10% lidocaine was sprayed onto oropharynx and 2% lidocaine jelly was put into the nostril. Briefly following topical anaesthesia, bronchoscopy was performed, mostly through trans-nasal route in supine position, using Fujinon EB-530T bronchoscope with working channel 2.8 mm in CMCTH or PENTAX 1000 series bronchoscope with working channel 2 mm in BPKMCH, whose distal ends were lubricated with 2% lidocaine jelly prior to insertion. Bronchoscopy was performed via trans-oral route with mouth guard in 5 patients (3.5%). All the patients received oxygen supplementation by nasal cannula, started 2 to 5 minutes prior to the procedure and were continuously monitored with cardiac monitor and pulse oximeter.

Local anaesthesia was supplemented with aliquots of 1 to 2 millilitres of 1% lidocaine solution through the procedure port for topical bronchial anaesthesia as needed, not exceeding 300 mg of lidocaine in total. None of the patient received sedation during the procedure.

Thorough examination of tongue base, epiglottis, vallecula, aryepiglottic folds, pyriform fossa, vocal cords, upper airways and tracheobronchial tree was performed. Bronchoscopically visible endobronchial lesions were classified as exophytic growth, submucosal/mucosal infiltrative lesions and extrinsic compression. Exophytic growth included fleshy or friable

polypoidal, cauliflower, nodular or multilobular endobronchial growth. Submucosal/mucosal infiltrative lesions included loss of normal bronchial markings, mucosal irregularity, erythema or vascular flares, mucosal/submucosal thickening causing none to minimal luminal narrowing. Extrinsic compression consisted of luminal narrowing due to peribronchial lesions with or without abnormalities of overlying mucosa/submucosa. EBBs were obtained from both the types of lesion viz exophytic growth and infiltrative submucosal/mucosal lesions. EBB was not performed in normal appearing mucosa/submucosa overlying extrinsic compression. When both exophytic growth and infiltrative lesions were found in the same patient, EBBs were taken from exophytic growth only. All the biopsy samples were immediately transferred to Formaldehyde containing container.

The number of biopsies taken was decided by several factors like discomfort to the patient, probability of excessive bleeding and oxyhemoglobin desaturation during the procedure. In each case, biopsies were attempted till the operator/brochoscopist felt that the samples were adequate or the biopsy procedure had to be stopped prematurely due to complication.

Decline in oxyhemoglobin saturation during bronchoscopy was managed by increasing the oxygen supplementation, withdrawing bronchoscope into the trachea, jaw thrust and suctioning out secretions. Severity of bleeding was assessed as per BTS guidelines (2013)⁷ as no bleeding, mild bleeding, moderate bleeding and severe bleeding. Cold saline and diluted adrenaline solution were kept ready during the procedure. All the patients were kept under constant supervision for assessing post-bronchoscopy complication with advice of nil per oral for 2 hours. The bronchoscopic findings, number of biopsies taken from the lesion type and complications observed were mentioned in the bronchoscopy report, which were later recorded in the proforma.

The biopsy samples were sent for histologic examination at the earliest possible. All the samples were examined and interpreted by consultant pathologists of the respective hospitals. Histopathology reports that mentioned "sample inadequate for analysis" (n=5) were excluded from yield calculation and the report that mentioned "suspicious for malignancy" (n=3) were taken as positive yield and included in the yield calculation.

The data collected were entered and analyzed using IBM SPSS Statistics 20. The data were presented as mean (\pm SD), frequency (percentage). Multivariate logistic regression analysis was used to calculate the effect size of possible predictors of diagnostic yield of the bronchoscopic biopsy procedure.

Results

The baseline data of the patients is shown in Table 1

Variables	Variables
Age	61.72 \pm 12.38 years
Sex	
Male	69 (48.9 %)
Female	72 (51.1 %)
Comorbidities	
Yes	77 (54.6 %)
No	64 (45.4 %)

Chief complaints	
Cough	112 (79.4 %)
Hemoptysis	72 (51.1 %)
Dyspnea	54 (38.3 %)
Chest pain	41 (29.1 %)
Fever	12 (8.5 %)
Hoarseness of voice	11 (7.8 %)
Weight loss	11 (7.8 %)
Dysphagia	2 (1.4 %)
Smoking status	
Ex-smoker	64 (45.4 %)
Current smoker	66 (46.8 %)
Non-smoker	11 (7.8 %)
Radiological indication	
Mass	111 (78.7 %)
Collapse/consolidation	35 (24.8 %)
Nodule	16 (11.3 %)
Cavitating mass	9 (6.4 %)
Cavity	5 (3.5 %)
Parenchymal infiltration	1 (0.7 %)
Patchy opacity	1 (0.7 %)
Repeat bronchoscopy (for inconclusive previous bronchoscopy)	7 (5.0 %)
Extra-parenchymal manifestations	
Pleural effusion	15 (10.6 %)
SVC syndrome	9 (6.4 %)
Supraclavicular lymph node	6 (4.2 %)
	1 (0.7 %)

Out of 140 patients, 37.1 % (52/140) had biopsies taken from exophytic growths and the remaining 62.9 % from submucosal/mucosal infiltrative lesions.

The median number of biopsies taken was 5 (Range: 2 – 8). The diagnostic yield increased significantly with the increase in the number of biopsies taken (Table 2)

Number of biopsies taken	Diagnostic yield (%)
3 (n =18)	10.5 %
4 (n = 45)	40.0 %
5 (n = 65)	98.5 %
6 (n = 5)	100.0 %
8 (n = 2)	100.0 %

The most common complication observed was transient drop in saturation > 4% (22.0%). Mild bleeding occurred in 9.9%, which was significantly associated with presence of superior vena cava obstruction (SVCO) (incidence of mild bleeding: 60.0 % vs. 8.1 % in patients with and without SVCO respectively, P <0.001). Bradycardia and transient fever occurred in 1% each. Table 3 shows the distribution of histopathological diagnoses obtained. The net diagnostic yield was 67.4%. Diagnosis of

“suspicious for malignancy” was made in 3 patients (2.2%).

Diagnosis	N (%)
Lung malignancy	81 (60.0%)
SCLC*	22
NSCLC**	56
Squamous cell carcinoma	14
Adenocarcinoma	4
Morphologically unclassifiable NSCLC	38
Small round cell tumor	2 (1.5 %)
Typical carcinoid tumor	1 (0.7%)
Chronic inflammatory lesion	6 (4.4 %)
TB	1 (0.7 %)
Suspicious for malignancy	3 (2.2 %)
No diagnosis made	44 (32.6 %)

*SCLC: Small Cell lung cancer **NSCLC: Non-small cell lung cancer

Overall, the diagnostic yield increased significantly with increase in the number of biopsies taken. The yield was 98.5% (n=65) with 5 and 100% (n=6) with 6 biopsy samples. There was a significant difference in diagnostic yield between the patient group where <4 biopsies were taken and patient group where ≥ 4 biopsies were taken (10.5 % vs. 73.6 %, P <0.001).

On subgroup analysis, diagnostic yield of biopsies taken from exophytic growth was 83.7% (41/49) and that from submucosal/mucosal infiltrative lesion was 57.0% (49/86) (Table 4). The diagnostic yield was significantly higher in the patient group that had ≥ 4 biopsies (for both exophytic growth and submucosal/mucosal infiltrative lesion) compared to <4 biopsies [95.2 % vs. 14.3% for exophytic growth, 64.9 % vs. 8.3 % for infiltrative lesion, P<0.001).

Number of biopsies	Diagnostic yield from exophytic growth (%) (n=49)	Diagnostic yield from infiltrative lesions (%) (n=86)
3	14.3 %	8.3 %
4	77.8 %	30.5 %
5	100.0 %	97.1 %
6	100.0 %	100.0 %
8	-	100.0%
Overall diagnostic yield	83.7 %	57.0 %

After multivariate logistic regression, it was found that the number of biopsies taken and the type of bronchoscopically visible lesion significantly predicted diagnostic yield. The odds of getting positive diagnostic yield was 8.1 times higher when the sample was taken from exophytic growth compared to infiltrative lesion. Similarly, the diagnostic yield reduced by 98.5 % when <4 biopsies were taken from the samples compared to ≥ 4 biopsies. (Table 5)

	aOR (95 % CI)*	P-value
Bronchoscopic biopsy taken from		0.002
Infiltrative lesion	1	
Exophytic growth	8.104 (2.198 - 29.873)	
Number of biopsies		0.000
≥ 4 biopsies	1	
< 4 biopsies	0.015 (0.003 - 0.112)	

* adjusted for age and gender

Discussion:

Flexible bronchoscopy is the most commonly performed procedure to diagnose various pulmonary diseases including lung cancer. Endobronchial forceps biopsy (EBB) of bronchoscopically visible lesions (exophytic endobronchial growth and submucosal/mucosal bronchial infiltration) has variable diagnostic yields ranging from 48% to 97%.⁸⁻¹¹

In this study, lung mass was the most common radiological indication for bronchoscopy (78.7%), with majority of them presenting with cough. The most common histopathological diagnosis was lung malignancy (60%), the most common being non-small cell lung cancer (NSCLC). These findings are in close agreement with a recent study by Dhungana A et al.¹² This observation however is incongruent with the recent trend of rising adenocarcinoma incidence, both in men and women.¹³ This disparity could be because majority of NSCLC diagnosed in our study was morphologically undifferentiated and immunohistochemistry staining was not performed to differentiate NSCLC subtypes.

The incidence of major complications like cardiac arrest and death is extremely low for bronchoscopy, which is also observed in this study.^{14,15} Majority of the complications observed were minor and self-resolving, the most frequent being transient drop in oxygen saturation > 4%, which occurred in 22% of the patients. Gibson et al.¹⁶ and Grendelmeier P et al.¹⁷ also observed closely similar incidences of transient hypoxemia.

Mild bleeding was observed in 9.9% of the patients that stopped spontaneously after minimal suctioning. This is slightly higher than that reported in other study.¹⁸ The probable reason for this could be our study included only those patients who underwent EBB. EBB is associated with more incidences of bleeding than when bronchoscopy was performed without it.^{19,20} In our study, bleeding incidence was significantly higher in patients with superior vena cava obstruction, which is consistent with finding of other investigators.²¹

Our result (net diagnostic yield of 67.4%) is comparable with the study by Rivera MP et al.¹⁰ but is lower than the studies that reported yields over 85%.^{22,23} The reason for lower yield in our study could be attributed to higher number of patients with submucosal/mucosal infiltrative lesions that have proven lower diagnostic yield than exophytic growths.^{5,6,24} Besides, the yield of EBB is also affected by several other factors like necrotic tissue overlying the biopsy-site, crushing artifact of biopsied tissue in the

bronchoscope channel, size of the biopsied tissue, experience of the operator (bronchoscopist) and the number of biopsy samples taken.^{5,25-28}

The diagnostic yield for patients with exophytic growth was higher compared to patients with submucosal/mucosal infiltrative lesion (83.7% vs. 57%). This is in agreement with study by Kacar et al.²⁵ that reported similar yields for exophytic growth (86.4%) and infiltrative/peribronchial lesions (47.2%).

EBB specimens generally are small and contain small number of malignant cells.²⁹ Coghlin et al.³⁰ reported that not every biopsy sample contained tumour cells, with the mean percentage area of tumour in an endobronchial biopsy sample being 33% and fewer than half the cases contained tumour in all biopsy samples. In our study, the net diagnostic yield improved significantly with increase in the number of EBB taken and reached almost 100% when 5 or more EBB samples were taken. This is consistent with the study by Gellert AR et al.⁴ which reported the frequency of at least one specimen with evidence of carcinoma increased to 96% with 5 and 100% with 6 biopsy specimens. In our study, the difference in net diagnostic yield was significantly higher in patient group where ≥ 4 biopsies were taken (73.6 vs. 10.5%, p < 0.001). This observation is supported by other studies that reported higher diagnostic yield with increased number of biopsy specimens.^{5,24,26}

Several studies suggested bronchoscopic visibility, tumour-size and location as significant predictors of higher diagnostic yields.³¹⁻³³ We found that the odds of obtaining diagnostic yield was 8.1 times higher when EBB were taken from exophytic growth compared to infiltrative lesions. The probable reason for this finding could be that the tumour cell burden of exophytic growth and infiltrative lesion vary; the burden being higher in the exophytic growth increasing the probability of picking up sample with tumour cells.

This is an observational study and sample size is relatively small and may fall short to validate these findings in general. But it highlights the need of sufficiently powered larger study to confirm our findings, i.e., to ensure satisfactory yield, what minimum number of EBB is required from these two different categories of the visible lesions in different disease states.

Conclusion:

Endobronchial forceps biopsy is a safe procedure with few minor complications. The yield of EBB increased as the number of biopsy samples increased and satisfactory yield was obtained with minimum of five biopsy samples both in exophytic growths and submucosal/mucosal infiltrative lesions. However, the odd of getting positive diagnosis with EBB was high in exophytic growth.

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