Bronchoscopy findings in 1074 lung cancer patients in a tertiary care center in Nepal.

Shashank Shrestha[1], Binay Thakur[1], Mukti Devkota[1], Nikesh Bhandari[1], Ashish Kharel[1], Asha Thapa[2]

[1]Thoracic Unit, Department of Surgical Oncology, BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal. [2]Bharatpur Hospital Nursing College, Bharatpur, Nepal.

Abstract

Background: Fiberoptic bronchoscopy is the most important diagnostic tool for lung cancer. Early tissue diagnosis and proper staging remains the key to the management of the lung cancer patient. Endobronchial forceps biopsy has high diagnostic yield from the visible lesions. The aim of the study was to evaluate diagnostic yield of endobronchial biopsy.

Methods: A retrospective cross-sectional study was conducted at B.P. Koirala Memorial Cancer Hospital, Bharatpur, Nepal. Bronchoscopy reports of 1074 patients from January 2000 to December 2009 were included. Endobronchial biopsy was the main procedure performed.

Results: A total of 1074 patients underwent bronchoscopy for suspected lung cancer. Majority of the patients (N=340) had lesion in lobar bronchus. Squamous cell carcinoma was the most common histological diagnosis. The diagnostic yield of endobronchial biopsy was 75%. The diagnostic yield for central tumor was 82.3% which was statistically significant ($p<0.001$) compared to peripheral tumor and extrinsic compression.

Conclusion: Endobronchial biopsy provides good diagnostic yield especially in central tumors. Fiberoptic bronchoscopy is a safe procedure.

Keywords: *Fiberoptic bronchoscopy, Lung cancer, Endobronchial biopsy*

Introduction

Lung cancer is the leading cause of cancer related mortality in the world.[1] Mortality remains high all across the world despite newer targeted therapies developed by the higher knowledge of the tumor biology.[1] Lung cancer is classified histologically into two types: Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC). NSCLC is subdivided into adenocarcinoma, squamous cell carcinoma and large cell carcinoma. Previously squamous cell carcinoma was the most common histological

Correspondence: Dr. Shashank Shrestha, Department of Surgical Oncology,BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal Email: shashank920@gmail.com Phone no: +977-9841811335

subtype of NSCLC reported by various studies including those from Nepal.[2,3] However adenocarcinoma is increasing globally and it is currently the most common histological subtype.[1,4] Early tissue diagnosis and proper staging remains the key to management of the lung cancer patients.[5]

Fiberoptic bronchoscopy has been a valuable tool in the diagnosis of pulmonary diseases since the introduction of the first flexible fiberoptic bronchoscope by Shigeto Ikeda in 1966.[6] It is the important diagnostic modality which allows direct visualization of the tumors and biopsy can be obtained for the histopathological diagnosis.[7] Bronchial wash and bronchoalveolar lavage, bronchial brushing, transbronchial and endobronchial needle aspiration, and transbronchial and endobronchial forceps biopsy are the various conventional bronchoscopic techniques with variable diagnostic sensitivity.[8] Endobronchial biopsy forceps is used for taking the biopsy from the visible lesions with high diagnostic yield of up to 85%.[9] The most common indication for performing endobronchial biopsy is to diagnose lung cancer.[10]

The aim of this study is to report the 10 years' experience in 1074 patients who underwent fiberoptic bronchoscopy with suspected lung cancer and analyze diagnostic yield and complications of endobronchial biopsy in B.P. Koirala Memorial Cancer Hospital, Bharatpur, Nepal.

Methods

A Cross Sectional Retrospective study of all patients with provisional diagnosis of lung cancer based on computed tomography (CT) scan of chest undergoing fiberoptic bronchoscopy was done at BP Koirala Memorial Cancer Hospital, Bharatpur from January 2000 to December 2009.

Ethical clearance was provided by Institutional Review Committee of BP Koirala Memorial Cancer Hospital and informed consent was waived off being retrospective study.

Procedure of bronchoscopy:

All fiberoptic bronchoscopy was done in endoscopy suite under local anesthesia. Patients were explained about the procedure thoroughly. Bronchoscopy was done in supine position using Pentax Bronchoscope (EB15-J10) with 5.2 mm diameter and 2 mm working channel. Continuous pulse oximetry, electrocardiography and sphygmomanometry were used for patient monitoring. Pre oxygenation was done via face mask with oxygen at 6 L/min. Local anesthesia was given transtracheal using 2% lignocaine and also in bilateral nostrils. Shaft of bronchoscope was lubricated with 2% lignocaine jelly before insertion through nasal pathway. Bronchoscope was inserted till the vocal cords and epiglottis were clearly visible, then 2 ml of 2% lignocaine was flushed. Bronchoscope was then inserted into the trachea where another 2 ml of 2% lignocaine was flushed.

Tracheobronchial tree including bronchial segments B1-B10 were examined. Broncoscopically tumors were classified into central (lesions located up to the level of segmental bronchi), peripheral (located beyond segmental bronchi), extrinsic compression and normal. Endobronchial biopsy (EBB), brush

cytology and bronchoalveolar lavage (BAL) were taken (in indicated patients only). For endobronchial biopsy 3-4 pieces of samples were taken. Biopsy material obtained was transferred to a container containing 10% formalin and send for histopathological examination. All the patients were monitored for assessing post-bronchoscopy complications and advised to be nil per oral for 1 hour.

Retrospective review of consecutive bronchoscopy reports and medical records of patients was done. Therapeutic bronchoscopy and incomplete records were excluded from the study. Data entry and analysis was done in Statistical software Package for Social Sciences (SPSS version 25). Descriptive statistics was performed and results were interpreted in mean, frequency and percentage.

Results

A total of 1074 patients underwent bronchoscopy for suspected lung cancer during the period of 2000-2009. The mean age of the patients was 60 years with range of 15 to 84 years. Among them 698 (65%) were male and 376 (35%) were female. Majority of the patients, 966 (90%) were smoker with a mean pack year of 42.

The lesion was present more in right side (N=602) than the left side (N=472). Majority of the lesion was present in lobar bronchus followed by main bronchus. Bronchoscopy was normal in 93 patients (8.7%). 108 patients had lesion in multiple locations. Vocal cord palsy, congested mucosa and suppurative infections were the additional findings.

Table 1. Bronchoscopy findings

Bronchoscopy Findings		N	%
Visible tumor	Main bronchus	328	30.5
	Lobar bronchus	340	31.7
	Segmental bronchus	88	8.2
	Subsegmental bronchus	2	0.2
	Carina & main bronchus	75	7.0
	Trachea & main bronchus	10	0.9
	Trachea, carina, main bronchus	23	2.1
Extrinsic compression only		73	6.8
Normal		93	8.7
Vocal cord palsy		13	1.2
Congested mucosa		27	2.5
Suppurative Infection		2	0.2

Squamous cell carcinoma was the most common histological diagnosis seen in 365 cases. NSCLC accounted for 587 cases (79.86%) while SCLC was seen in 148 cases (20.14%). Normal bronchoscopic findings was present in 93 cases, so biopsy was not done in those cases.

The overall diagnostic yield was 68.4% which included all the patients undergoing bronchoscopy. The diagnostic yield while considering only the cases undergoing endobronchial biopsy was 75%. In 228 cases (21.2%), repeated biopsy (more than one procedure) had to be done to obtain positive histopathological diagnosis. The diagnostic yield for central tumor was 82.3%, peripheral tumor was 48.2% and extrinsic compression was 3.6%. The diagnostic yield was statistically significant

($p<0.001$) for central tumors compared to peripheral and extrinsic compression.

Table 2. Histopathological findings of Endobronchial biopsy

Histopathological diagnosis	N
Non-small cell lung cancer (NSCLC)	138
Squamous cell carcinoma (SCC)	365
Adenocarcinoma	56
Large cell carcinoma	5
Poorly differentiated carcinoma	23
Small cell lung cancer (SCLC)	148
Negative	246
Biopsy not done	93
Total	1074

Most common complication was temporary desaturation seen in 198 patients (18.4%). There were 3 mortalities (0.3%) due to massive hemorrhage. Minor bleeding was present in 43 patients (4%) which was managed conservatively. Eight percent of the patients (N=86) required admission due to respiratory distress or hemorrhage.

Table 3: Comparison between location and diagnostic yield (excluding normal bronchoscopy cases)

Location	+ve	-ve	Total	p-value
Central	692	149	841	<0.001
Peripheral	41	44	85	
Extrinsic compression	2	53	55	
Total	735	246	981	

Discussion

Internationally, lung cancer continues to be the leading cause of cancer-related deaths in men and women.[1] Lung cancer is more prevalent in older age group. The mean age of the patients in our study was 60 years which is similar to the most of the previous studies. The majority of the patients were male (65%) which is similar to the study by Devkota KC et al[11], Ghimire RH et al[12] and Pant P et al.[13] The preponderance of males probably was related to their smoking habits and greater exposure to environmental pollutants. The correlation between smoking and lung cancer has been established by several studies. In this study, most of the patients (90%) were smokers with significant mean pack year (42 pack years).

Being a tertiary cancer center, most of the patients with lung cancer are referred for the evaluation in our center from all over the country. Fiberoptic bronchoscopy is the most common procedure to diagnose lung cancer and endobronchial biopsy is performed in all the visible lesions. The diagnostic yield of the EBB varies from 48 to 93%.[8] The overall diagnostic yield was 68.4% which is similar to the study by Shrestha BK et al[14] and Rivera MP et al[15] but it is lower than the study by Zavala DC [16]and Popp W et al.[17] British Thoracic Society guidelines recommends diagnostic level of 85% should be attainable when definite endobronchial tumor is visible. In the current study, the diagnostic yield of EBB was 75% despite repeated biopsies were taken in 21.2% of cases, which is below the recommended level. This could be increased with the addition of bronchial brushing and bronchial washing along with the EBB.[15,18] Various factors

like the number of biopsy samples taken, necrotic tissue overlying the lesion, crushing artifact of biopsied tissue, size of the sample and experience of the operator may affect the diagnostic yield.[19–22] In the subgroup analysis, the diagnostic yield of EBB was 82.3% for the central tumor which was statistically significant ($p<0.001$). The diagnostic yield of central tumor is better for EBB has been shown in various studies in the past.[15]

In this study, SCC was seen in 62% of NSCLC and adenocarcinoma was seen in only 9.5% of NSCLC. This finding is concurrent with previous studies from Nepal.[2,3] However, 138 patients had the diagnosis of only NSCLC and this could have affected the ratio of SCC and adenocarcinoma. Despite this, SCC would be the most common histological subtype. Over the last two decades, the adenocarcinoma is increasing in number and has surpassed SCC being the most common subtype.[1,23] This changing trend was also reported in recent study in Nepal by Dhungana A et al.[4] Adenocarcinoma mostly present as a peripheral lesion while SCC as a central lesion. In our study the predominant lesion was central (841/981) so this may be the reason for high prevalence of SCC. SCLC accounts for 15% of the lung cancer[24] but in our study it was seen in 20% of the patients.

Fiberoptic bronchoscopy is relatively safe procedure.[9] However, we had three mortalities due to massive hemorrhage. The incidence of significant hemorrhage ranges from 0.2% to 5% reported in various studies,[25] which is similar to our study with 4% patients having mild bleeding. Shrestha BK et al[14] reported mild bleeding of 9.9% in recent study, which may be higher due to EBB. The transient hypoxemia was seen in 18.4% and most of them did not require any specific intervention as stated by Jones A.[26]

The studies on flexible bronchoscopy in the diagnosis of lung cancer in Nepal are lacking. Only few studies have been done on the diagnostic yield of EBB for diagnosis of lung cancer.[4,14] Although this study had a large sample size, limitations are retrospective study, lack of data on other modalities like bronchoalveolar lavage and brush biopsy, lack of description of visible lesion and number of biopsies taken, and lack of immunohistochemistry for subtyping the morphologically undifferentiated NSCLC.

Conclusion

Fiberoptic bronchoscopy is the important diagnostic tool for diagnosing lung cancer. Endobronchial biopsy provides histopathological diagnosis with high diagnostic yield in the central tumors. It is a safe procedure with minor complications.

References

1. Barta JA, Powell CA, Wisnivesky JP. Global epidemiology of lung cancer. Annals of global health. 2019;85(1).
2. Chandrashekhar TS, Binu VS, Vadivelu G, Mallik S, Kurien R, Joshi HS. Clinicopathological profile of primary bronchogenic carcinoma treated in a tertiary care hospital of western Nepal. Asia−Pacific Journal of Clinical Oncology. 2006 Jun;2(2):98-103.
3. Hashibe M, Siwakoti B, Wei M, Thakur BK, Pun CB, Shrestha BM, Burningham Z, Lee YC, Sapkota A, Bahadur C, Shrestha BM. Socioeconomic status and lung cancer risk in Nepal. Asian Pac J Cancer Prev. 2010;11:1083-8.

4. Dhungana A, Bhattarai D, Shrestha P, Acharya N. Lung cancer in a tertiary hospital in Nepal: clinical-radiological profile and histological subtypes. Journal of Nepal Health Research Council. 2019;17(4):463-7.

5. McLean AE, Barnes DJ, Troy LK. Diagnosing lung cancer: the complexities of obtaining a tissue diagnosis in the era of minimally invasive and personalised medicine. Journal of Clinical Medicine. 2018 Jun 29;7(7):163.

6. Ohata M. History and progress of bronchology in Japan. The Journal of the Japan Society for Respiratory Endoscopy. 1998 Sep 25;20(6):539-46.

7. Rafanan AL, Mehta AC. Role of bronchoscopy in lung cancer. InSeminars in respiratory and critical care medicine 2000 (Vol. 21, No. 05, pp. 405-420). Copyright© 2000 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel.:+ 1 (212) 584-4662.

8. Rivera MP, Mehta AC. Initial diagnosis of lung cancer: ACCP evidence-based clinical practice guidelines. Chest. 2007 Sep 1;132(3):131S-48S.

9. du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, Mandal S, Martin J, Mills J, Navani N, Rahman NM. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. Thorax. 2013 Aug 1;68(Suppl 1):i1-44.

10. Mohan A, Madan K, Hadda V, Tiwari P, Mittal S, Guleria R, Khilnani GC, Luhadia SK, Solanki RN, Gupta KB, Swarnakar R. Guidelines for diagnostic flexible bronchoscopy in adults: Joint Indian Chest Society/National College of chest physicians (I)/Indian association for bronchology recommendations. Lung India: Official Organ of Indian Chest Society. 2019 Jul;36(Suppl 2):S37.

11. Devkota KC, Pathak R, Khanal A, Chokhani R. Fiber-optic bronchoscopy: seven-year experience at Nepal Medical College Teaching Hospital. Nepal Med Coll J. 2010 Dec 1;12(4):260-3.

12. Ghimire RH, Bhatta N, Koirala P, Bista B, Misra DR, Shah B. Outcomes bronchoscopic evaluation in a university hospital. JNMA J Nepal Med Assoc. 2016 Oct 1;55(204):51-4.

13. Pant P, Joshi A, Bam N. Diagnostic Fibreoptic Bronchoscopy at Tribhuvan University Teaching Hospital. Journal of Nepal Health Research Council. 2019;17(4):512-5.

14. Shrestha BK, Adhikari S, Thakur BK, Kadaria D, Tamrakar KK, Devkota M. Complications and predictors of diagnostic yield of endobronchial forceps biopsy in visible lesions. Journal of Advances in Internal Medicine. 2019 Dec 31;8(2):21-5.

15. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May 1;143(5):e142S-65S.

16. Zavala DC. Diagnostic fiberoptic bronchoscopy: techniques and results of biopsy in 600 patients. Chest. 1975;68(1):12–9

17. Popp W, Rauscher H, Ritschka L, Redtenbacher S, Zwick H, Dutz W. Diagnostic sensitivity of different techniques in the diagnosis of lung tumors with the flexible fiberoptic bronchoscope. Comparison of brush biopsy, imprint cytology of forceps biopsy, and histology of forceps biopsy. Cancer. 1991 Jan 1;67(1): 72-5.

18. Liam CK, Pang YK, Poosparajah S. Diagnostic yield of flexible bronchoscopic procedures in lung cancer patients according to tumour location. Singapore medical journal. 2007 Jul 1;48(7):625.

19. Gellert AR, Rudd RM, Sinha GA, Geddes DM. Fibreoptic bronchoscopy: effect of multiple bronchial biopsies on diagnostic yield in bronchial carcinoma. Thorax. 1982 Sep 1;37(9):684-7.

20. Roth K, Hardie JA, Andreassen AH, Leh F, Eagan TM. Predictors of diagnostic yield in bronchoscopy: a retrospective cohort study comparing different combinations of sampling techniques. BMC Pulmonary Medicine. 2008 Dec;8(1):1-8.

21. Coghlin CL, Smith LJ, Bakar S, Stewart KN, Devereux GS, Nicolson MC, Kerr KM. Quantitative analysis of tumor in bronchial biopsy specimens. Journal of Thoracic Oncology. 2010 Apr 1;5(4): 448-52.

22. Karahalli E, Yilmaz A, Türker H, Özvaran K. Usefulness of various diagnostic techniques during fiberoptic bronchoscopy for endoscopically visible lung cancer: should cytologic examinations be performed routinely?. Respiration. 2001;68(6):611-4.

23. de Groot PM, Wu CC, Carter BW, Munden RF. The epidemiology of lung cancer. Translational lung cancer research. 2018 Jun;7(3):220.

24. Rudin CM, Brambilla E, Faivre-Finn C, Sage J. Small-cell lung cancer. Nature Reviews Disease Primers. 2021 Jan 14;7(1):1-20.

25. Gao Y, Moua T, Midthun DE, Mullon JJ, Decker PA, Ryu JH. Diagnostic yield and bleeding complications associated with bronchoscopic biopsy of endobronchial carcinoid tumors. Journal of Bronchology & Interventional Pulmonology. 2020 Jul 17;27(3):184-9.

26. Jones AM, O'Driscoll R. Do all patients require supplemental oxygen during flexible bronchoscopy?. Chest. 2001 Jun 1;119(6):1906-9.