Original Research Article

Yield of different bronchoscopic techniques in diagnosis of lung cancer

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ABSTRACT

Background: Lung cancer is generally diagnosed during late stage of the disease so early diagnosis of lung cancer is very important to reduce lung cancer death rate. Flexible fibreoptic bronchoscopy revolutionized early diagnosis of lung cancer as it provides sufficient cytologic and histologic specimens in form of bronchial brushings, broncho-alveolar lavage and bronchial forceps biopsy. Cytologic techniques are safe, economical, and provide quick results. They not only complement tissue biopsies in the diagnosis of lung cancer but are also comparable in yield.
Methods: The present study analyzes cytology of Bronchoalveolar lavage, Bronchial Brushings and histology of bronchial biopsy in 45 patients diagnosed as lung cancer by fiber-optic bronchoscopy. Age, gender, smoking habits, various histological types of malignancies, and yield of various bronchoscopic diagnostic techniques in the diagnosis of lung cancer were evaluated.
Results: Of the 45 cases with confirmed diagnosis, 37 (82.22%) were males and 8 (17.17%) were females with male to female ratio of 4.6:1. The mean age in this study group was 54.71 years. Squamous cell carcinoma was the most common primary bronchogenic tumor (62.22%) followed by adeno carcinoma (26.66%). The overall diagnostic yield of fiber-optic bronchoscopy procedures was 100% (32/32 patients) in bronchoscopically visible tumors. Bronchial biopsy was most sensitive (100%) followed by Bronchial Brushings (88%) and BAL (81.25%). However, in non-visible tumors, biopsy, brush and BAL yielded diagnostic specimens for lung cancer in 84.61%, 76.92% and 46.15% of patients respectively.
Conclusions: Lung cancer is a common malignancy with male preponderance. Bronchial biopsy has a very high diagnostic yield. Cytopathological examination of bronchial brushings and broncho-alveolar lavage not only complement tissue biopsies in the diagnosis of lung cancer but have comparable diagnostic yield.

Keywords: Adenocarcinoma, Bronchial biopsy, Bronchial brushings, Broncho-alveolar lavage, Lung cancer, Squamous cell carcinoma

INTRODUCTION

Lung cancer is one of the most prevalent and lethal cancers which accounts for 17.8% of all cancer deaths. Five-year survival rate of lung cancer has remained unchanged at <15% since the last few decades.[1,2] It has been recognized that the prognosis of lung cancer is strongly related with the stage at which the disease is diagnosed. In India, lung cancer is the fifth most common cancer.[1,2] Squamous cell type is the most common cell type in smokers and adenocarcinoma in nonsmokers. A long-standing goal of cancer researchers has been to develop techniques that would facilitate earlier diagnosis and treatment of lung cancer and thereby decrease its mortality. The use of flexible bronchoscopy in the investigation of patients suspected to have lung cancer is

well established.[3] The main sampling techniques performed at flexible bronchoscopy include endobronchial forceps biopsy (EBB) for central tumors and transbronchial forceps biopsy (TBB) for more peripheral tumours.[4,5] Bronchoalveolar lavage (BAL), bronchial washing (BW) and bronchial Brushing (BB) specimens can also be obtained for cytopathological examination.[6] Cytologic techniques are safe, economical and provide quick results. Cytologic techniques not only complement tissue biopsies in the diagnosis of lung cancer but are also comparable. Bronchoscopic diagnostic techniques are one of the most common invasive diagnostic methods used by pulmonologists all over the world for early diagnosis and treatment of lung cancer.

METHODS

Fiber-optic bronchoscopy was performed under local anesthesia along with sedation with intravenous midazolam wherever required. When the tumor was visible bronchoscopically, BWs were obtained by aspiration of any secretion and instillation, followed by immediate aspiration of two aliquots of 20 ml of sterile isotonic 0.9% saline solution at room temperature. Following this, EBB was performed with alligator forceps with serrated jaws. The specimens were immediately fixed in 10% buffered formalin. Brushing specimens were taken from the surface of bronchoscopically-visible lesions using a reusable sheathed cytology brush, smeared on clean glass slides and immediately fixed in 95% ethanol for cytological examination.

When the tumor was not bronchoscopically visible, BAL was performed by instilling aliquots of 20 ml sterile isotonic 0.9% saline solution and then immediately aspirating by suction into a plastic specimen trap. Brushing specimens were taken blindly from anatomical segments suspected to be involved with tumor using a cytology brush and these were immediately fixed in 95% ethanol. Trans-Bronchial Biopsy with alligator forceps was performed in patients with bronchoscopically non-visible lesions. Usually, three to four specimens were obtained and were immediately fixed in 10% formalin. Broncho-alveolar Lavage was performed first then brushing followed by TBB.

Forty-five cases were proved to be cases of bronchogenic carcinoma using bronchoscopic diagnostic techniques. These cases were studied with reference to the age, sex, smoking habits, various histological types of malignancy and the yield of various bronchoscopic diagnostic techniques in the diagnosis of lung cancer.

RESULTS

Forty-five patients with confirmed lung cancer were analyzed. The diagnosis of lung cancer was based on positive histology, cytology or both. Of the 45 cases with confirmed diagnosis, 37 (82.22%) were males and 8 (17.17%) were females with male to female ratio of 4.6:1. The mean age in present study group was 54.71years. The mean age of male and female patients was 54.89 years and 53.87 years respectively (Table 1).

Table 1: Age and sex distribution.

Age group (years)	Male	Female	Total number	Percentage
< than 40 years	3 (8.10%)	-	3	6.66%
40-49	10 (27.02%)	2 (25%)	12	26.66%
50-59	14 (37.83%)	3 (37.5%)	17	37.77%
60-69	5 (13.51%)	3 (37.5%)	8	17.77%
70-79	5 (13.51%)	-	5	11.11%
Total	37 (82.22%)	8 (17.77%)	45	(100%)

Table 2: Distribution of patients according to histopathological diagnosis.

Histological type	Male	Female	Total Number	Percentage
Squamous cell carcinoma	24 (64.86%)	4 (50%)	28	62.22%
Small cell carcinoma	1 (2.70%)	-	1	2.22%
Adenocarcinoma	8 (21.62%)	4 (50%)	12	26.66%
Carcinoma of unspecified histology	4 (10.81%)	-	4	8.88%
Total	37 (82.22%)	8 (17.77%)	45	(100%)

Squamous cell carcinoma was the most common primary bronchogenic tumor (62.22%) followed by adeno carcinoma (26.66%) in the study (Table 2). Squamous cell carcinoma was the predominant cell type in males whereas squamous cell carcinoma and adenocarcinoma occurred equally in females.

The prevalence of smoking was 66.66% in the study population. Most (90%) of the smokers were male. Squamous cell carcinoma (55.55%) was the predominant cell type in male smokers whereas adenocarcinoma (66.66%) occurred most frequently in female smokers. Among non-smokers, squamous cell carcinoma was the predominant cell types in both sexes (Table 3).

Table 3: Type of malignancy among smokers and non-smokers.

Histological type	Smokers			Non-smokers		
	Male	Female	Total number	Male	Female	Total number
Squamous cell carcinoma	15 (55.55%)	1 (33.33%)	16	9 (90%)	3 (60%)	12
Small cell carcinoma	1 (3.70%)	-	1	-	-	-
Adenocarcinoma	8 (29.62%)	2 (66.66%)	10	-	2 (40%)	2
Carcinoma of unspecified histology	3 (11.11%)	-	3	1 (10%)	-	1
Total	27 (90%)	3 (10%)	30	10 (66.66%)	5 (33.33%)	15

Thirty-Two i.e. 71.11% tumors were visible by bronchoscopy. Squamous cell carcinoma (71.87%) was most commonly associated with bronchoscopically visible tumors as compared to other cell types (Table 4).

Table 4: Proportion of lung cancer cell types among bronchoscopically visible and non-visible tumors.

Bronchoscopically visible tumors	No. of patients according to cell type (%)			
	Squamous cell carcinoma	Small Cell carcinoma	Adenocarcinoma	Carcinoma of unspecified histology
Yes (n=32)	23 (82.14%)	1 (100%)	7 (58.33%)	1 (25%)
No (n=13)	5 (17.85%)	-	5 (41.66%)	3 (75%)
Total (n=45)	28	1	12	4

Table 5: Bronchoscopic findings in endoscopically non-visible tumors.

Finding	No. of cases (n=13)	Percentage
Widening of carina	3	23.07%
Narrowed lumen	1	7.69%
Bronchial distortion	1	7.69%
Pale mucosa	6	46.15%
Normal study	2	15.3%

Paleness of mucosa (46.15%) and widening of carina (23.07%) were the main findings associated with endoscopically non-visible tumors (Table 5). Various bronchoscopic techniques were utilized in patients depending on tumor location. Table 6 shows the bronchoscopic procedures performed alone or in combination and the respective yields, in patients with bronchoscopically visible and non-visible tumors.

In visible tumors, the overall diagnostic yield of fiber-optic bronchoscopy procedures was 100% (32/32 patients). Bronchial biopsy was most sensitive (100%) followed by bronchial brushings (88%) and BAL (81.25%) in tumors which could be visualized on endoscopy.

Table 6: Bronchoscopic techniques utilized and their yield in visible and non-visible tumors

Bronchoscopic technique	Visible tumors			Non-visible tumors		
	Attempted	Positive	Yield	Attempted	Positive	Yield
Broncho-alveolar lavage	32	26	81.25%	13	6	46.15%
Bronchial brushings	25	22	88%	13	10	76.92%
Bronchial biopsy /trans-bronchial biopsy	32	32	100%	13	11	84.61%

In non-visible tumors, Trans bronchial biopsy had the highest yield (84.61%) followed by Bronchial Brushings (76.92%). In one case, Brushings and biopsy were negative but BAL was positive for malignancy. This is possible when sometimes the biopsy is taken from the necrotic part of the tumor. All three samples were found positive for malignancy in 28 out of 45 patients (62.22%). Bronchial biopsy contributed to the diagnosis in 43 out of 45 patients (95.55%) making it the highest yield procedure. Bronchial brushings were positive in 32 out of 38 patients in which it was done providing a sensitivity of 84.21%. Bronchoalveolar lavage examination helped in diagnosis of 32 patients out of 45 patients attempted yielding a sensitivity of 71.11%.

Table 7: Evaluation of the role of bronchoscopic techniques in diagnosis of lung cancer.

BAL, brushings and biopsy positivity	Total no of cases (n=45)	Percentage (%)
Negative by all three techniques	-	-
Positive by all three techniques	28	62.22%
Positive by biopsy but negative by BAL and brushings	10	22.22%
Positive by brushings but negative by BAL and biopsy	1	2.22%
Positive by BAL but negative by brushings and biopsy	-	-
Biopsy and brushings positive but BAL negative	2	4.44%
Biopsy and BAL positive but brushings negative	3	6.66%
BAL and brushings positive but biopsy negative	1	2.22%

DISCUSSION

In current study majority of the patients diagnosed to have bronchogenic carcinoma were in their sixth and seventh decades of life (50-70 years). The mean age in study group was 54.71 years. The mean age of male and female patients was 54.89 years and 53.87 years respectively. These observations are consistent with many Indian studies done in the past in which the mean age was between fifty and seventy years.[1,2]

The disease is known to be more common in males than in females. In current study, 82.22% patients were males and 17.17% were females with male to female ratio of 4.6:1. In another study of 638 patients diagnosed to have lung cancers, males and females were in a ratio of 6.7:1.[7] Other authors have also reported similar ratio in the previous studies.[1]

Tobacco smoking along with rising levels of environmental pollution has been implicated in causation of lung cancer. In the present study, 66.66% of the patients were smokers, once again suggesting a close link between this habit and the development of the disease. In a study by Gupta et al[8], 80% of men and 33% of women among the patients were ever-smokers as compared to 60% of men and 20% of women among controls.

The odds ratio (OR) for ever-smoking was 5.0 (95% CI=3.11-8.04) among men and 2.47 (95% CI=0.79-7.75) among women. Smoking of bidi and hooka as well as cigarettes had similar ORs for cumulative consumption. The risk increased with both the duration and quantity of all smoking products. In the present study, smoking has been the predominant contributory factor both in males and females. Due to the same reason, squamous cell carcinoma was the commonest malignancy (62.22%) detected in present study.

Adenocarcinoma was seen in 26.66% of patients. Some studies have suggested higher detection of adenocarcinoma (32%), even more than squamous cell carcinoma (29%).[9] But most of the studies in India suggest a higher prevalence of Squamous cell carcinoma. Gupta et al, detected 42.3% squamous cell carcinoma and 19.9% adenocarcinoma in their study.[10] Similarly, Thippanna et al, in their study done in 1998 found 67.5% patients of squamous cell carcinoma in contrast to 18.75% adenocarcinoma patients.[11] Kashyap et al, also found 58.3% squamous cell and 10.8% adenocarcinoma patients in their study group.[7]

In present study, thirty-two (32) i.e. 71.11% tumors were visualised by bronchoscopy. Squamous cell carcinoma (71.87%) was most commonly associated with bronchoscopically visible tumors as compared to other cell types. For patients with bronchoscopically-visible tumors, BAL, brush and biopsy yielded diagnostic specimens for lung cancer in 81.25%, 88% and 100% of patients respectively, in whom these samples were collected (Table 6). The overall diagnostic yield of fiber-optic bronchoscopy procedures was 100% (32/32 patients). However, in non-visible tumors, BAL, brush and biopsy yielded diagnostic specimens for lung cancer in 46.15%, 76.92% and 84.61% of patients respectively. Trans bronchial biopsy had the highest yield (84.61%) followed by bronchial brushings (76. 92%).The yield was higher in patients with endoscopically visible tumors than in those with tumors not visible endoscopically. Liam CK et al observed that for patients with bronchoscopically-visible tumors, bronchial wash, endobronchial biopsy and

bronchial brushings yielded diagnostic specimens for lung cancer in 28.3%, 77.5% and 53.7% of patients, respectively, upon whom these sampling techniques were performed.[12]

The overall diagnostic yield of Fibreoptic bronchoscopy procedures was 83.2% (283/340 patients). For patients whose tumors were not visible bronchoscopically, BAL, Transbronchial Biopsy and brushing yielded diagnostic specimens for lung cancer in 35.5%, 31.5% and 22.9% of patients, respectively, in whom these sampling techniques were performed. The overall diagnostic yield of fibre-optic bronchoscopy procedures was 43.6% (71/163 patients). Similar findings have been observed by Schreiber G, Mc Crory DC and Mak VH, Johnston ID, Hetzel MR, Grubb C.[5,13]

BAL was positive for malignant cells in 81.25% and 46.15% cases of endoscopically visible and non-visible tumors respectively with overall sensitivity of 71.11% in present study. However, the sensitivity of BAL in various other studies from literature varies widely from 21% to 78%.[14,15] This wide range of sensitivity may be due to difference in case selection. Some investigators discard the first aliquot which is relatively enriched in the bronchial material. The adequacy of BAL samples depends on several crucial factors such as the degree of differentiation of malignant growth, preservation of the morphology of cytological material obtained and technical skill of the pulmonologist.

In general, less differentiated, anaplastic lesions have more loosely cohesive cells in comparison to well differentiated lesions. These lesions exfoliate larger number of cells into the bronchial cavity. Some of these exfoliated cells while lying in the bronchus develop degenerative changes and progressively lose their morphological details. Rennard SI suggested that yield can be improved by taking multiple samples.[6]

Bronchial brushing (BB) is a technique where surface of a suspected lesion, visualized through a bronchoscope, is scraped in order to collect the cytological sample. This technique manages to 'dislodge' the cells from the surface of those well differentiated malignant lesions too, which do not exfoliate cells readily. Thus, the chances of getting adequate diagnostic cytological sample by BB greatly increase in comparison to BAL samplings. BB was positive in 88% and 76.92% cases of endoscopically visible and non-visible tumors respectively with overall sensitivity of 84.21% in present study. There is a wide range of sensitivity of BB in different studies in literature ranging from 21% to 93%. The sensitivity of 84.21% for BB in this study agrees with various other workers like Chopra et al (86.3%) and Zavala et al (88.5%).[4,16] Shroff et al have reported the sensitivity of BB to be as high as 97.3% in their study.[17]

Endobronchial forceps biopsy (EBB) and transbronchial biopsy (TBB) yielded positive results in 100% and 84.61% cases of endoscopically visible and non-visible tumors respectively with overall sensitivity of 95.55% in present study. The diagnostic yield for EBBs in patients with endoscopically-visible central tumors is reported to be superior to the yield for BW and BB.[5,18]

For EBB and TBB, the diagnostic yields of our patients were consistent with the reported yields of 48%-97%, in a review of published studies.[5] Cataluna JJ et al evaluated the diagnostic accuracy of bronchial biopsy (BB) specimens in establishing the specific cell type in primary lung cancer.[19] They found that the probability of BB accuracy was 2.7, 7.7, and 25 times higher in well-differentiated, than in poorly differentiated, moderately differentiated, or undifferentiated carcinomas. In a study done by Liam CK et al, 191 patients underwent both EBB and BW and the positive yield was 79.1% (151/191 patients) and the addition of BW to EBB added 8.9% (17/191 patients) to the yield.[13] Endobronchial Biopsy and BB were performed in 13 patients and the addition of BB to EBB did not increase the yield. Bhat N evaluated 902 bronchial biopsy specimens in suspected cases of lung cancer and found that 760 (84.25%) cases were diagnosed by bronchial biopsy to be suffering from lung cancer, of which 647 were males and 113 were females.[20]

CONCLUSION

The present study emphasizes the fact that lung cancer is common among male smokers with squamous cell carcinoma as the most common histological type. The yield of different fiber-optic bronchoscopy specimens for diagnosis of lung cancer is very good. Cytologic examination of bronchial brushings and broncho-alveolar lavage not only complement tissue biopsies but have comparable diagnostic yield.

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