Diagnostic yield of flexible bronchoscopic procedures in lung cancer patients according to tumour location

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ABSTRACT

Introduction: This study aims to determine whether the diagnostic yield of flexible bronchoscopy sampling procedures in patients with lung cancer was dependent on tumour location.

Methods: A retrospective analysis was conducted on the diagnostic yield of bronchial washing (BW), endobronchial biopsy (EBB), bronchial brushing (BB), bronchoalveolar lavage (BAL), blind brushing (B) and transbronchial biopsy (TBB) specimens obtained at fibre-optic bronchoscopy for patients with lung cancer.

Results: Of 503 patients who underwent fibre-optic bronchoscopy examination, BW, EBB, BB, BAL, B and TBB were performed on 254, 325, 67, 155, 70 and 54 patients, respectively. For patients with bronchoscopically-visible tumours, BW, EBB and BB yielded diagnostic specimens for lung cancer in 28.3 percent, 77.5 percent and 53.7 percent of patients, respectively. For patients whose tumours were not visible bronchoscopically, BAL, B and TBB yielded diagnostic specimens for lung cancer in 35.5 percent, 22.9 percent and 31.5 percent of patients, respectively. EBB was less likely to be diagnostic in patients with tumours in the middle or lingular lobe bronchi. The diagnostic yields of all the other sampling techniques were not influenced by the location of the bronchoscopically-visible or non-visible tumours.

Conclusion: The diagnostic yields of bronchoscopic sampling procedures were dependent on tumour visibility during bronchoscopy and location of bronchoscopically-visible tumours.

Keywords: bronchial brushing, bronchoalveolar lavage, bronchoscopy, endobronchial biopsy, lung cancer, transbronchial biopsy

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INTRODUCTION

The use of flexible bronchoscopy in the investigation of patients suspected to have lung cancer is well established.[1,2] The main sampling techniques performed at flexible bronchoscopy examination for histopathological diagnosis of lung cancer include endobronchial forceps biopsy (EBB) and transbronchial forceps biopsy (TBB) for more peripheral tumours.[3,4] Bronchial washing (BW), bronchoalveolar lavage (BAL) and brushing specimens can also be obtained for cytopathological examination.[4-7] 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.[4,7-10]

We conducted this retrospective review of fibre-optic bronchoscopy performed in our centre for the diagnosis of lung cancer, to determine whether the yield of these bronchoscopic sampling techniques was dependent on the tumour location within the bronchial tree or lung lobe, apart from its visibility during bronchoscopy.

METHODS

A retrospective analysis was carried out from September 1994 to August 2002, on the diagnostic yield of BW, EBB, bronchial brushing (BB), BAL and TBB specimens obtained at fibre-optic bronchoscopy for patients with lung cancer. If the bronchoscopic results were negative, confirmation of the diagnosis depended on transthoracic fine-needle aspiration, or needle biopsy of the lung lesion under computed tomography (CT) guidance, open-lung biopsy, resected lung specimen, pleural fluid cytology, pleural biopsy, cervical lymph node aspiration cytology, sputum cytology, and/or other biopsies.

Fibre-optic bronchoscopy with the Olympus BF-10 flexible fibre-optic bronchoscope (Olympus, Tokyo, Japan) was performed by one of the authors, all of

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whom had at least three years experience in performing diagnostic flexible bronchoscopy. Premedication included 0.5 mg atropine injected intramuscularly 30 minutes before bronchoscopic examination. The upper airway was anaesthetised with 2 ml of 10% lignocaine solution. Additional small quantities of 1% lignocaine were instilled through the bronchoscope for topical bronchial anaesthesia, as needed. Patients were sedated with intravenous midazolam. The bronchoscope was inserted transnasally in about 85% of cases, while in the remaining cases, the transoral route was used. Fluoroscopy facility was not available in our unit.

When the tumour 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 over the tumour. The aspirate was collected in a plastic specimen trap in circuit. Following this, EBB was performed with FB-15C alligator forceps with serrated jaws (Olympus, Tokyo, Japan). Whenever possible, at least three biopsies were obtained from the centre of the most abnormal area and the specimens were immediately fixed in 10% buffered formalin. Using a reusable sheathed cytology brush, BC-5C (Olympus, Tokyo, Japan), brushing specimens were taken from the surface of bronchoscopically-visible lesions. Brushing samples were smeared on clean glass slides and immediately fixed in 95% ethanol for cytological examination. At least six smeared samples from the brushing were obtained from each patient. Rapid on-site cytopathology evaluation service was not available during the period of this study.

When the tumour 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 until a total of 100 ml were instilled. Using a cytology brush, BC-5C (Olympus, Tokyo, Japan), brushing specimens were taken blindly from anatomical segments suspected to be involved with tumour, as determined by chest CT. At least six smears from the brushing samples were made for each patient, and these were immediately fixed in 95% ethanol for cytological examination.

TBB using FB-15C alligator forceps with serrated edge (Olympus, Tokyo, Japan), guided by chest CT findings, was performed in patients without bronchoscopically-visible lesions. Usually, three to four specimens were obtained and were immediately fixed in 10% formalin. Whenever possible, BW, followed by EBB and then BB, were performed sequentially for patients with bronchscopically-visible tumours. For patients with tumours which were not visible bronchoscopically, BAL was performed first, then brushing followed by TBB, if necessary. Prior to 2004, transbronchial needle aspiration (TBNA) was not performed in our centre. Post-bronchoscopy sputum was not obtained from the patients for cytological examination.

The histological and cell typing from biopsy and cytology specimens were classified according to the World Health Organisation classification for lung cancer.[11] Histological typing was used whenever available. Biopsy or cytological specimens that showed atypical or suspicious cells were regarded as non-diagnostic. Cytological analysis was considered positive only when large numbers of definitely malignant cells were present.

The possible relationships between the tumour site/location and the diagnostic yields of the bronchoscopic techniques were examined by the chi-squared (χ^2) test (with Yate's correction) or Fisher's exact test, when appropriate. A p-value of less than 0.05 for a two-tailed test was considered statistically significant. All analyses were performed using Statistical Package for Social Sciences version 11.0 for Windows (SPSS Inc, Chicago, IL, USA). Hospital ethics committee approval and informed consent from the patients were not required for this retrospective study.

RESULTS

503 patients with confirmed lung cancer were analysed. The diagnosis of lung cancer was based on positive histology, cytology or both (Table I). Bronchoscopically-visible tumours were found in 340 (67.6%) patients (Table

Table I. Distribution of lung cancer cell types.

Histological or cytological confirmation	No. of patients according to cell type				
	Adenocarcinoma	Squamous cell carcinoma	Small cell lung cancer	Large cell carcinoma	Undifferentiated NSCLC
Histology alone (n = 280)	88	105	40	12	35
Cytology alone (n = 106)	63	12	4	–	27
Histology and cytology (n = 117)	55	36	21	2	3
Total (n = 503)	206	153	65	14	65

NSCLC: non-small cell lung cancer.

II). Squamous cell carcinoma and small cell lung cancer were more commonly associated with bronchoscopically-visible tumours compared to the other cell types (84.9% [185/218] versus 54.4% [155/285]; odds ratio [OR], 4.70; 95% confidence interval [CI], 3.04–7.28; $p < 0.001$).

BW, EBB, BB, BAL, blind brushing and TBB were performed on 254, 325, 67, 155, 70 and 54 patients, respectively (Table III). The diagnosis of lung cancer was confirmed in 358 patients by one or more of these bronchoscopic procedures, giving an overall diagnostic yield of fibre-optic bronchoscopy of 71.2%. Proximal airway sampling methods (i.e. EBB and BB of bronchoscopically-visible lesions) had a higher positive yield than sampling methods for the peripheral airways or lesions that were not visible bronchoscopically (i.e. BAL, brushing and TBB of peripheral lesions).

For patients with bronchoscopically-visible tumours, BW, EBB and BB yielded diagnostic specimens for lung cancer in 28.3%, 77.5% and 53.7% of patients, respectively, upon whom these sampling techniques were performed (Table III). The overall diagnostic yield of fibreoptic bronchoscopy procedures was 83.2% (283/340 patients). Table IIIa shows the bronchoscopic procedures performed alone or in combination, and the respective yields, in patients with bronchoscopically-visible tumours. In 191 patients upon whom both EBB and BW were performed, 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. EBB and BB were performed in 13 patients, and the addition of BB to EBB did not increase the yield. BW and BB were performed on only seven patients, and BB was diagnostic in one patient whose BW was negative. A combination of all these three procedures was performed in 48 patients with a diagnostic yield of 68.8% (33/48 patients). Adding BW increased the diagnostic yield by 4.2% (2/48 patients) and adding BB increased the yield by 10.4% (5/48 patients).

For patients whose tumours were not visible bronchoscopically, BAL, brushing and TBB yielded diagnostic specimens for lung cancer in 35.5%, 22.9% and 31.5% of patients, respectively, in whom these sampling techniques were performed (Table III). The overall diagnostic yield of fibre-optic bronchoscopy procedures was 43.6% (71/163 patients). Table IIIb shows the number of patients with bronchoscopically non-visible tumours, in whom bronchoscopic procedures were performed alone or in combination, and the respective yields. In 46 patients in whom both BAL and brushings were performed, the positive yield was 30.4% (14/46 patients) and the addition of brushing to BAL added 6.5% (3/46 patients) to the yield. In 29 patients in whom both BAL and TBB were performed, the positive yield was 75.9% (22/29 patients) and the addition of TBB to BAL added 6.9% (2/29 patients) to the yield. A combination of all these three procedures was performed in 20 patients with a diagnostic yield of 50% (10/20 patients). The addition of brushing increased the diagnostic yield by 20% (4/20 patients) and the addition of TBB increased the yield by 15% (3/20

Table II. Proportions of lung cancer cell types with bronchoscopically-visible and non-visible tumours.

Bronchoscopically-visible tumour	No. of patients according to cell type (%)				
	Adenocarcinoma	Squamous cell carcinoma	Small cell lung cancer	Large cell carcinoma	Undifferentiated NSCLC
Yes (n = 340)	107 (51.9)	129 (84.3)	56 (86.2)	8 (57.1)	40 (61.5)
No (n = 163)	99 (48.1)	24 (15.7)	9 (13.8)	6 (42.9)	25 (38.5)
Total (n = 503)	206	153	65	14	65

NSCLC: non-small cell lung cancer.

Table III. Diagnostic yield of different bronchoscopic sampling techniques.

Technique	No. of patients (%)		
	Application No. (%)	Diagnostic yield No. (%)	Only technique with a diagnostic result No. (%)
Bronchoscopically-visible tumours (n = 340)			
Bronchial washing	254 (74.7)	72 (28.3)	21 (8.3)
Endobronchial biopsy	325 (95.6)	252 (77.5)	143 (44.0)
Bronchial brushing	67 (19.7)	36 (53.7)	6 (9.0)
Bronchoscopically non-visible tumours (n = 163)			
Bronchoalveolar lavage	155 (95.1)	55 (35.5)	38 (24.5)
Brushing	70 (42.9)	16 (22.9)	9 (12.9)
Transbronchial biopsy	54 (33.1)	17 (31.5)	7 (13.0)

Table IIIa. Bronchoscopic procedures and yields in patients with bronchoscopically-visible tumours.

Procedure(s) performed / Procedure(s) and yield	EBB only	BW only	BB only	EBB and BW	EBB and BB	BW and BB	EBB, BW and BB
EBB positive	62			71	1		9
EBB negative	11			–	–		4
BW positive		2	–	17		–	2
BW negative		6	–	–		–	4
BB positive					–	1	5
BB negative					–	–	–
EBB and BW positive				80			–
EBB and BW negative				23			–
EBB and BB positive					12		–
EBB and BB negative					–		–
BW and BB positive						4	–
BW and BB negative						2	–
EBB, BW and BB positive							17
EBB, BW and BB negative							7
Total	73	8	–	191	13	7	48

EBB: endobronchial biopsy; BW: bronchial washing; BB: bronchial brushing.
The figures represent the numbers of patients in whom the procedure(s) was/were performed which yielded positive or negative results.

Table IIIb. Bronchoscopic procedures and yields in patients with bronchoscopically non-visible tumours.

Procedure(s) performed / Procedure(s) and yield	BAL only	BB only	TBB only	BAL and B	BAL and TBB	B and TBB	BAL, B and TBB
BAL positive	21			4	10		3
BAL negative	39			–	–		1
B positive		2		3		–	4
B negative		1		–		–	3
TBB positive			2		2	–	3
TBB negative			2		–	–	3
BAL and B positive				7			–
BAL and B negative				32			–
BAL and TBB positive					10		–
BAL and TBB negative					7		–
B and TBB positive						–	–
B and TBB negative						1	–
BAL, B and TBB positive							–
BAL, B and TBB negative							3
Total	60	3	4	46	29	1	20

BAL: bronchoalveolar lavage; B: brushing; TBB: transbronchial biopsy
The figures represent the numbers of patients in whom the procedure(s) was/were performed which yielded positive or negative results.

patients). The yield of BAL in patients with tumours larger than 3 cm in diameter (22.1% [30/136 patients]) was not significantly higher than the yield of BAL in patients with tumours 3 cm or less in diameter (15.8% [3/19 patients]) ($p = 0.766$). The yield of blind brushing in patients with tumours larger than 3 cm in diameter (28.1% [18/64 patients]) and that in patients with smaller tumours ([33.3% [2/6 patients]) were not significantly different ($p = 1.000$). Similarly, there was no significant difference in the yield of TBB in patients with tumours larger than

Table IV. Other diagnostic procedures with positive yield.

Procedure	No. of patients
CT-guided transthoracic fine-needle aspiration of lung lesion	48
Cervical lymph node biopsy or fine-needle aspiration	40
Pleural fluid cytology	42
Pleural biopsy	28
Lobectomy	9
Bone biopsy	5
CT-guided transthoracic mediastinal lymph node fine-needle aspiration	3
Skin nodule biopsy	3
Open lung biopsy	2
Sputum cytology	1

3 cm in diameter (33.3% [16/48 patients]) and that in patients with smaller tumours (16.7% [1/6 patients]) (p = 0.652). Table IV shows the other diagnostic procedures which yielded results in patients whose diagnosis of lung cancer could not be confirmed by fibre-optic bronchoscopic procedures.

Table V shows the location of the lung cancer lesions based on chest CT and bronchoscopy findings according to the cell type. The lung cancer lesions were most frequently located in the upper lobes (47.5% [239/503 patients]). Analysis of diagnostic yield as a function of location of the lesion is shown in Table VI. In patients with bronchoscopically-visible tumours, EBB was more likely to be diagnostic in patients with tumours at sites other than the middle or lingular lobe bronchi (79.9% [243/304 patients] versus 57.1% [12/21 patients], respectively; OR, 2.99; 95% CI, 1.20–7.4; p = 0.014). The diagnostic yield of BW was 35.6% (31/87) in patients with tumours in the intermediate and lower lobe bronchi, compared to a diagnostic yield of 24.6% (41/167) in patients with tumours at other sites (OR, 1.70; 95% CI, 0.97–2.99; p = 0.063). The diagnostic yield of BB in patients with tumours situated in the main or intermediate bronchi was 78.6% (11/14) compared to a yield of 49.1% (26/53) for those with tumours located at other sites (OR, 3.81; 95% CI, 0.95–15.22; p = 0.070).

In patients with tumours not visible bronchoscopically, the diagnostic yield of blind brushing was not significantly affected by the tumour location. The yield in patients with tumours in the right middle, lingular and lower lobe bronchi was 39.4% (13/33 patients), compared to a yield of 18.9% (7/37) in patients with tumours in the upper lobe bronchi (OR, 2.79; 95% CI, 0.95–8.20; p = 0.058). Similarly, the diagnostic yields of BAL and TBB were not related to the tumour location.

DISCUSSION

The overall sensitivity of flexible bronchoscopy in the diagnosis of lung cancer is reported to be 82%.[12] The yield is higher in patients with endoscopically-visible tumours than in those with tumours not visible endoscopically.[4,13-16] The overall diagnostic yield in our patients was 71.2%. While a higher overall yield of 83.2% was seen in our patients with bronchoscopically-visible tumours, a lower overall yield of 43.6% was obtained in our patients with tumours not visible bronchoscopically. These rates

Table V. Location of tumour based on chest computed tomography and bronchoscopy findings according to cell type.

Location of tumour	No. of patients according to cell type					Total
	Adenocarcinoma	Squamous cell carcinoma	Small cell lung cancer	Large cell carcinoma	Undifferentiated NSCLC	
Right upper lobe	55*	35	17	3	19	129
Left upper lobe	40**	35	11$^{\Psi,\Sigma}$	7	17	110
Right lower lobe	44$^{\phi}$	19$^{\infty}$	7	–	6	76
Left lower lobe	29**	19	7$^{\Psi}$	3	7	65
Left main bronchus	11	20	9	–	3	43
Right intermediate bronchus	9	12	7	–	4	32
Right middle lobe	11*$^{,\phi}$	5$^{\infty}$	5$^{\Sigma}$	1	4	26
Right main bronchus	6	7	3	–	3	19
Lingular	4	3	1	–	2	10
Total	206	153	65	14	65	

NSCLC: non-small cell lung cancer.

* One patient had adenocarcinoma in the right upper and middle lobes; ** One patient had adenocarcinoma in the left upper and left lower lobes; $^{\phi}$ One patient had adenocarcinoma in the right middle and lower lobes; $^{\infty}$ Two patients had squamous cell carcinoma in the right middle and lower lobes; $^{\Psi}$ One patient had small cell lung cancer in the left upper and left lower lobes; $^{\Sigma}$ One patient had small cell lung cancer in the left upper and right middle lobes.

Table VI. Effect of location of tumour on diagnostic yield of bronchoscopic sampling procedures.

Tumour location	No. of cases with diagnostic specimens/total no. of cases (%)					
	Bronchial washing	Endobronchial biopsy	Bronchial brushing in patients with BVT	Broncho-alveolar lavage	Bronchial brushing in patients with no BVT	Transbronchial biopsy
Main bronchus	10/40 (25.0)	52/59 (88.1)	7/9 (77.8)	–	–	–
Upper lobe	29/116 (25.0)	114/151 (75.5)	17/34 (50.0)	19/78 (24.4)	7/37 (18.9)	7/26 (26.9)
Intermediate bronchus	11/28 (39.3)	26/30 (86.7)	4/5 (80)	–	–	–
Middle/ lingular lobe	3/16 (18.8)	12/21 (57.1)	1/2 (50.0)	2/13 (15.4)	3/8 (37.5)	0/4 (0)
Lower lobe	20/59 (33.9)	53/70 (75.7)	8/18 (44.4)	12/65 (18.5)	10/25 (40.0)	10/24 (41.7)
Total	73/259* (28.2)	257/331*** (77.6)	37/68** (54.4)	33/156** (21.2)	20/70 (28.6)	17/54 (31.5)

BVT: bronchoscopically-visible tumour
* Five patients had tumours in two different lobes; ** One patient had tumours in two different lobes; *** Six patients had tumour in two different lobes.

are consistent with those reported in the literature.[4] The average reported sensitivity of bronchoscopy for peripheral lesions which are not endobronchially visible is 70% when fluoroscopy is routinely used, and 38% (range 28%–56%) when bronchoscopy is performed without fluoroscopy guidance.[12] The overall diagnostic yield of flexible bronchoscopy procedures in our patients could have been higher if TBNA had been performed, because this procedure has been shown to increase the diagnostic yield.[4,17,18]

The diagnostic yield for EBBs in patients with endoscopically-visible central tumours is reported to be superior to the yield for BW and BB,[4,13-16] with some authors reporting similar yields for BB and BW,[14-16] and other series reporting the lowest yield for BW.[10,13,17,19] In our patients with visible endobronchial tumours, the diagnostic yields for EBB, BB and BW were 77.5%, 53.7% and 28.3%, respectively. For EBB and BB, the diagnostic yields of our patients were consistent with the reported yields of 48%–97% and 23%–93%, respectively, for these two procedures in a review of published studies.[4] However, the yield of BW in our patients was lower than that of 29%–78% reported.[4] This could have been related to the timing of washings before biopsy and brushing in our patients. While studies by van der Drift et al[20] and Raymond et al[21] showed no difference in diagnostic yield relative to the timing of washings for bronchoscopically-visible tumours, Scriven et al[22] showed a higher yield for washings after biopsy and brushing.

Kvale et al[13] found no additional advantage in performing BW when EBB and BB were performed simultaneously. Dasgupta et al[17] found BW to provide the least diagnostic information and was never positive when the results of any of the other sampling techniques were negative. In contrast to these findings, this was the only procedure with a diagnostic yield in 7.3% of our patients with bronchoscopically-visible tumours. Some studies have reported that adding BW to EBB and BB increases the diagnostic yield,[10,14,15] whereas others have reported no additional value of BW.[13,18,23,24] The additional value of BW as the only test providing a diagnosis varies from 1.5%–5%.

The diagnostic yield of BAL in patients with endoscopically non-visible peripheral tumours is reported to be similar to the yield for brushings and for TBB.[13-16] Schreiber and McCrory has noted that brushing has the highest diagnostic yield, followed by TBB and BAL.[4] Our yields from BAL, brushing and TBB (35.5%, 22.9% and 31.5%, respectively), were low but consistent with the published results of 12%–65%, 21%–84% and 17%–80%, respectively, by others.[4] According to some reports,[25] the use of toothed versus non-toothed biopsy forceps has no bearing on the size of the TBB, while Wang et al reported that serrated forceps yielded larger transbronchial lung biopsy specimens, but the size of the biopsy specimen did not significantly alter the diagnosis.[26] Still other reports found that larger biopsy specimens were more likely to contain diagnostic tissue.[27] The same reports also found that cup forceps yielded smaller pieces of specimen compared to toothed forceps, and were less likely to obtain diagnostic tissue, and thus recommended using toothed rather than cup-shaped forceps for TBB.[27]

TBB and brushing have been reported to offer a higher diagnostic yield in lung cancer, not visible bronchoscopically, when performed under fluoroscopic guidance.[28,29] However, fluoroscopy during bronchoscopy is not routinely available in many respiratory units, including ours. Studies have also shown that diagnostic yield of specimens obtained at bronchoscopy is greater

when on-site cytopathology assessment is utilised.[30,31] However, the on-site cytopathology service was not available in our centre during the period of this study. We did not find that the size of the lesions (based on the CT scan findings) had a significant effect on the yield of bronchoscopic procedures in patients with bronchoscopically non-visible tumours, although others have reported poorer yields for peripheral lesions less than 2 cm in diameter.[4]

Although lesions in the upper lobes are often technically difficult to access because of the acute angulation of the bronchoscope needed to reach them, no difference in the yield of BW, EBB and BB, with respect to the location of the endobronchial lesion in the upper lobes, were reported by other authors.[17] For reasons which are unclear, in our patients with visible endobronchial tumours, the yield for EBB was lowest for lesions in the middle and lingular lobe bronchi, while the yields of BW and BB were not significantly affected by the location of the tumour. Similarly, the diagnostic yields of BAL, blind brushing and TBB were not affected by the location of the tumours not visible on bronchoscopy. In conclusion, the diagnostic yield of the different bronchoscopic sampling procedures for patients with lung cancer is dependent on whether the tumours were visible bronchoscopically and the location of bronchoscopically-visible tumours, but not dependent on the lobar distribution for tumours not visible on bronchoscopy.

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