ORIGINAL ARTICLE

Pathological Characteristics of Fiberoptic Bronchoscopy Procedure in Ulin General Hospital, Banjarmasin

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ABSTRACT

Introduction: Fiberoptic bronchoscopy (FOB) has emerged as the method of choice for the detection of lung tumors due to its availability of adequate cytological and histological samples in the form of bronchoalveolar lavage (BAL), bronchial brushings, and bronchial forceps biopsy. This study aimed to identify characteristics of BAL, aspiration cytology, brushing cytology, and forceps cytology of patients suspected of malignancy at Ulin General Hospital, Banjarmasin.
Methods: A cross-sectional study was performed utilizing medical documentation of patients suspected of lung cancer from March 2018 to March 2020. Data were grouped by gender, age, type of procedure, and cytology and histopathology findings.
Results: The result showed that 67.5% of 117 patients who underwent bronchoscopy had positive results and common histological diagnosis. The frequent histopathological conclusion was adenocarcinoma (45.6%), tailed by squamous cell carcinoma (40.55%). Forceps bronchoscopy showed a greater positivity rate (75.0%) than without forceps (63.6%). By combining BAL and brushing and forceps biopsy, the detection rate of lung malignancy increased to 85.7%. Still, no correlation between the type of procedure and the likelihood of malignancy was discovered.
Conclusions: Forceps bronchoscopy showed a greater positivity rate than bronchoscopy without forceps, but no correlation between the type of procedure and the likelihood of malignancy was discovered in this study.

INTRODUCTION

After female breast cancer, lung cancer is the second most significant cause of cancer-related mortality worldwide. According to worldwide cancer statistics (Globocan), there are 2.2 million new cases of lung cancer (11.4 % of all cancer cases) and 1.79 million deaths (18.0 % of all cancer-related deaths) in 2020, which is higher than the number reported in 2018 (2.09 million new cases and 1.76 million deceased cases).[1] According to data from Globocan 2020, lung cancer fatalities in Indonesia surged to 30,843 people (13.2% of overall cancer deaths), with new cases reaching 34,783. (8.8% total cancer cases). This resulted in lung cancer being the most prevalent form of cancer and the primary reason for cancer-related fatalities among males and females.[2]

Using cytological approaches to diagnose malignant pulmonary lesions is widely regarded as one of the most successful applications. Since Shigeto Ikeda's invention in the late 1960s, flexible bronchoscopy has been and continues to be a useful

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diagnostic tool.[3,4] Flexible bronchoscopy has revolutionized how we evaluate the endoluminal extension of cancers, especially in segmental and subsegmental airways. This has led to a significant improvement in delineating the prospective resection lines for thoracic surgery.[5] For the objective of obtaining various types of biological products for diagnosis in pulmonary pathology, several methods and processes have been developed.[3,4]

The tumor's location and distribution determine the expected diagnostic outcomes of fiberoptic bronchoscopy (FOB). Small peripheral lesions are frequently more difficult to obtain unless more precise and time-consuming procedures are performed.[3,4] Locating the path to the lesion can be challenging since relying solely on an endoscopic view to approach it, based on the calculated location from an X-ray or computed tomography (CT) scan, has a low success rate.[5] Lesions located at the center of the endobronchial provide the most significant diagnostic output (90%), whereas central endobronchial lesions yield the best diagnostic yield (90%). Regarding presentation, endoluminal tumors have a positive biopsy rate of 70-95%, while submucosal and intramural lesions have a biopsy rate of 55-86%.[6] Whether the combination of cytologic and histological methods provides the best diagnostic results has yet to be answered. However, it may be determined by the center's expertise.[3,4]

Sputum collection, bronchoalveolar lavage (BAL) or bronchial washing, aspiration, brushing, and biopsy are the five basic procedures to retrieve cellular material for diagnosing lung pathology. A transbronchial technique is used to obtain the biopsy.[7,8] Cell retrieval techniques are chosen based on the physician's personal preferences, the patient's condition, the location of the lesion, and other considerations. The procedure's effectiveness in diagnosis and treatment depends on skill, accessibility, and compliance.[7,9]

This method is most commonly used to diagnose lung cancer, followed by the diagnosis of infection. It reduces the amount of pain and number of complications experienced by the patient. Laryngeal spasms, hypoxia, bronchial spasm, disease, aspiration, hemorrhage, and cardiac arrhythmias are all uncommon complications. In the study by Vijay, *et al*. cited by Ojha, *et al*. (2019), about 0.5% of severe problems and 0.8% of minor complications were described.[7] Respiratory tract cytology is now well-established as a critical diagnostic tool in the evaluation of pulmonary pathology all over the world.[3,7]

There has been no study on the pathological characteristic of FOB procedures, such as BAL, aspiration cytology, and brush smear cytology with forceps cytology outcomes at Ulin General Hospital, Banjarmasin. Furthermore, as far as we know, it is the first study in Indonesia about the characteristics of BAL, aspiration cytology, brush smear cytology, and forceps cytology.

METHODS

This was a descriptive-analytic study. It was conducted using cytological and histopathological data from bronchoscopy procedures recapitulated from the Pathological Anatomy Laboratory of Ulin General Hospital, Banjarmasin. Bronchoscopy was performed from March 2018 to March 2020 and obtained as many as 117 samples. Data were grouped by gender, age, type of procedure, and cytology and histopathology findings. Patients were considered positive for malignancy if the cytology and histopathological results obtained from bronchoscopy showed malignant cells and were considered negative if inflammatory cells or atypical cells were obtained. Patients were categorized as other malignancies if the malignant cells obtained were not of pulmonary origin.

This study utilized statistical computer software to outline data and outcomes with descriptive statistics. The appropriate data were reported in mean values, while categorical variables were presented as counts and percentages. The correlation analytic test was performed using the chi-square test if the expected value of the number of sample observations in every factor category was no less than 5.5. Data that could not be tested using the chi-square method were tested using the Fisher extract method. Statistical significance was indicated by $p < 0.05$. This study was approved by the Research Ethics Board of Ulin General Hospital, Banjarmasin, bearing registration identification number 42/VI-Reg Research/RSUDU/21, on 28 June 2021.

RESULTS

This study found 117 patients who underwent bronchoscopy at Ulin General Hospital, Banjarmasin, from March 2018–March 2020 (Table 1). The number of patients in 2018 was 14 patients (12.0%), 2019 was 77 patients (65.8%), and 2020 was 26 patients (22.2%). A positive finding of malignancy was found in 79 patients (67.5%), while 38 patients (32.5%) had a negative result.

Table 1. Number of patients by year of bronchoscopy procedure was performed

	Year			Total
	2018	2019	2020	
Positive	13	54	12	79
Negative	1	23	14	38
Total	**14**	**77**	**26**	**117**

Table 2. Sample distribution of patients undergoing bronchoscopy at Ulin General Hospital, Banjarmasin

Characteristics	Positive (n = 79)		Negative (n = 38)		Total (n = 117)	
	n	%	n	%	n	%
Gender						
Male	63	79.7	29	76.3	92	78.6
Female	16	20.3	9	23.7	25	21.4
Age (years old) (mean = 55.97)						
21-30	1	1.3	1	2.6	2	1.7
31-40	3	3.8	6	15.8	9	7.7
41-50	15	19.0	7	18.4	22	18.8
51-60	28	35.4	14	36.8	42	35.9
61-70	23	29.1	5	13.2	28	23.9
71-80	9	11.4	5	13.2	14	12.0
Procedures						
No forceps	**49**	62.0	**28**	73.7	**77**	65.8
Forceps procedure	**30**	38.0	**10**	26.3	**40**	34.2
BAL + forceps	5	6.3	2	5.3	7	6.0
BAL + brushing + forceps	6	7.6	1	2.6	7	6.0
BAL + aspiration + forceps	6	7.6	3	7.9	9	7.7
BAL + brushing + aspiration + forceps	13	16.5	4	10.5	17	14.5
Total	**79**	**67.5**	**38**	**32.5**	**117**	**100.0**

The sample distribution of patients who underwent bronchoscopy at Ulin General Hospital, Banjarmasin, from March 2018–March 2020 is shown in Table 2. In this study, 92 were males, and 25 were females. Based on age, most patients were 51–60 years old (35.9%), with a mean age of 55.97 years old. The youngest was 24 years old, and the oldest was 77 years old. The age range of 51-60 years old was also the age with the highest positive malignant results, as much as 35.4%. According to the bronchoscopy procedures performed, most patients (65.8%) did not undergo forceps procedures, with BAL + brushing + aspiration + forceps (14.5%) being the most frequent. BAL + brushing + aspiration + forceps accounted for up to 16.5% of all positive findings, making it the forceps procedure that contributed the most positive results.

Table 3. Lung malignancy rate and demography characteristics

Characteristics	Positive (n = 79)		Negative (n = 38)		Total (n = 117)	p-value
	n	%	n	%		
Gender						0.672
Male	63	68.5	29	31.5	92	
Female	16	64.0	9	36.0	25	
Age (years old)						0.136
21-30	1	50.0	1	50.0	2	
31-40	3	33.3	6	66.7	9	
41-50	15	68.2	7	31.8	22	
51-60	28	66.7	14	33.3	42	
61-70	23	82.1	5	17.9	28	
71-80	9	64.3	5	35.7	14	

The positivity rate of pulmonary malignancy based on demography characteristics can be seen in Table 3. The positivity rates for males and females are not far off at 68.5% and 64.0%, respectively. Based on age, 61-70 years old had the highest positivity rate at 82.1%. However, there were no statistically significant findings in the correlation test regarding the association between demographic characteristics and pulmonary malignancy results.

Table 4. Lung malignancy rate based on bronchoscopy procedures

Procedures	Malignant Cells				Total (n = 117)	p-value
	Positive (n = 79)		Negative (n = 38)			
	n	%	n	%		
No forceps	**49**	**63.6**	**28**	**36.4**	**77**	**0.213**
Forceps procedure	**30**	**75.0**	**10**	**25.0**	**40**	
BAL + forceps	5	71.4	2	28.6	7	
BAL + brushing + forceps	6	85.7	1	14.3	7	
BAL + aspiration + forceps	6	66.7	3	33.3	9	
BAL + brushing + aspiration + forceps	13	76.5	4	23.5	17	

The positivity incidence of pulmonary malignancy based on bronchoscopy procedures can be seen in Table 4. Forceps were only performed in 34.2% of the patients who underwent bronchoscopy. The procedure with forceps obtained a higher positivity rate (75.0%) than without forceps (63.6%). The procedure with the highest positivity rate was BAL with brushing and forceps (85.7%). Meanwhile, the positivity rate for the BAL procedure with brushing, aspiration, and forceps was only 76.5%. The correlation test, however, revealed no statistically significant findings on the correlation between the type of bronchoscopy procedure and the pulmonary malignancy result.

Table 5. Cytology and histopathology findings from bronchoscopy based on gender

Malignant cells	Total (n = 117)		Gender			
			Male (n = 92)		Female (n = 25)	
	n	%	n	%	n	%
Positive	**79**	**67.5**	**63**	**68.5**	**16**	**64.0**
Adenocarcinoma	36	45.6	28	44.4	8	50.0
Squamous cell carcinoma	32	40.5	26	41.3	6	37.5
SCLC	6	7.6	4	6.3	2	12.5
NSCLC	1	1.3	1	1.6	0	0.0
Adenosquamous carcinoma	1	1.3	1	1.6	0	0.0
Other malignancy	3	3.8	3	4.8	0	0.0
Negative	**38**	**32.5**	**29**	**31.5**	**9**	**36.0**
Inflammatory cells	27	23.1	21	72.4	6	66.7
Atypical cells	11	9.4	8	27.6	3	33.3
Total	**117**	**100.0%**	**92**	**78.6%**	**25**	**21.4%**

In Table 5, we can see cytology and histopathology findings from bronchoscopy based on patients' gender. Adenocarcinoma was the most common type of malignancy in males (44.4%) and females (50.0%), followed by squamous cell carcinoma, 41.3% in males, and 37.5% in females. One patient had non-small cell lung carcinoma (NSCLC) with no further subtype classification due to histopathological inconclusiveness.

DISCUSSION

The advent of flexible FOB brought about a revolution in respiratory cytology, allowing the collection of various respiratory tract samples, such as bronchial washings, brushings, lavage, and needle aspirations. As a result, a significant amount of cytological material became available, changing focus from identifying malignancy in operable patients and confirming metastases to utilizing.[8]

In this study, 67.5% of 117 patients who underwent bronchoscopy had positive results. Błach, *et al*. (2021) revealed that from 5,279 patients diagnosed due to various respiratory symptoms, lung cancer was confirmed in 36.42% of patients who performed bronchoscopy.[10] Based on demographic characteristics in this study, 79.7% of patients were males, and 20.3% were females, with male to female ratio of 4:1. Men also have a slightly higher positivity rate for pulmonary malignancy than women. Tayal, *et al*. (2018) showed similar results, a minor dominance of males was observed, with a ratio of 1.29 males to every female.[11] Other studies by Reddy, *et al*. (2.64:1), Bhat, *et al*. (6.3:1), and Sareen, *et al*. (8.4:1) that were cited by Tayal, *et al.* (2018) were more similar to this study for the men and women ratio.[11] Błach, *et al*. (2021) also found that more men than women had lung cancer for a positive result of a bronchoscopy procedure.[10] A global cancer statistic from 2020 also revealed that the incidence of lung cancer was higher among men (14.3%) than women. The same was discovered in the mortality rate, with men (21.5%) outnumbering women (13.7%).[1]

The 61-70 age group has the highest positivity rate compared to other age groups. These findings are similar to those of a Norwegian cohort study, which found that the age groups 61-70 had the highest lung cancer rates. Tayal, *et al*. (2018) discovered that the average age of the cancer was 57.57 years old, with the most frequent age category being the fifth decade.[11] In

the study by Patel, *et al*. (2022), the average age in the study group was 58.15 years old.[12] The average age of male and female patients was 54.89 years old and 53.87 years old, respectively. However, statistical analysis revealed no significant relationship between lung malignancy rate and demography characteristics in sex and age, with p-values of 0.672 and 0.136, respectively.[1,11]

In this study, 77 patients (65.8%) underwent bronchoscopy without endobronchial forceps biopsy procedure, with a 63.6% positive malignancy result. Meanwhile, 40 patients (34.2%) had bronchoscopy with endobronchial forceps biopsy procedure, with a higher positivity rate of 75.0%. Although statistical analysis showed no significant relationship between lung malignancy rate and type of bronchoscopy procedures with a p-value of 0.213, these results imply that bronchoscopy with endobronchial forceps biopsy is superior at identifying lung cancer. An endobronchial biopsy is critical for investigating lung cancer and has a high diagnostic accuracy if enough samples are collected for histopathology.[13]

Endobronchial biopsy (EBB) is suggested to identify visible endobronchial lesions. The correct placement of forceps is crucial concerning the intended area. Once positioned, the forceps should be opened beyond the end of the operating channel and pressed onto the affected region. After gathering the sample, the forceps' end should be sealed, removed from the bronchoscope's operating channel, and submerged in a formalin solution. Though forceps with different characteristics may be suitable for specific settings/lesions, the diagnostic yield of various forceps biopsy types was not significantly different. EBB is frequently used to identify suspected bronchogenic carcinoma and exhibits a sensitivity of 74%. Conducting at least three biopsies is recommended for proper diagnosis, while at least six biopsies are suggested for conducting immunohistochemical and molecular tests. According to several studies, the combination of EBB and endobronchial needle aspiration can achieve the best diagnostic performance.[14]

Endobronchial needle aspiration (EBNA) is a reliable and secure technique to diagnose endobronchial lesions, specifically lung tumors. When used in conjunction with endobronchial forceps biopsy, it significantly improves the accuracy of bronchoscopy in identifying central lung tumors. It has an average sensitivity rate of 56% and a complication rate of less than 1%, primarily involving minor bleeding. EBNA is particularly beneficial in obtaining samples from submucosal/peribronchial and necrotic lesions, allowing the needle to penetrate the mucosa and extract neoplasms extending into deeper layers.[15]

Numerous studies have evaluated various bronchoscopic methods for the detection of lung cancer. When Mrudula, *et al* (2019). compared BAL, bronchial brush cytology, and bronchial biopsy in patients with lung cancer, the bronchial biopsy discovered more cases of lung malignancy (58.8%) than BAL (11.8%) or bronchial brushing (28.9%).[15]

Lesions visible in the airway epithelium can be sampled for cytological assessment using a conical bristle brush. This method involves agitating the brush against the mucosal surface of the airway under direct visualization, pushing cells into the spaces between the bristles. Compared to biopsies, larger areas can be sampled using the strands of cytology brushes. However, brushing results can vary widely from as low as 28% to 81%, with an overall lower yield than biopsies, typically ranging from 50% to 70%. Notably, brushing is less effective for submucosal and intramural lesions than exophytic endoluminal lesions, especially those that are irregular or partially necrotic and not covered by an intact surface.[6,16]

Compared with well-differentiated cancerous growths, malignant tumors with inadequate differentiation exhibit more loosely bound cells. Compared to well-differentiated carcinoma, malignant lesions with poor differentiation feature more loosely cohesive cells. Compared to well-differentiated carcinoma, these lesions exfoliate a more significant number of cells.[17] Bronchoscopy techniques such as bronchial brushing and washing are crucial to obtain cytology samples from suspected malignant lesions. The cytological technique of bronchial brushing is more convenient than BAL, with a reliable sensitivity of 87.3% and an accuracy rate of 93.9%. It makes it helpful in screening doubtful cases and early lung cancer diagnosis while saving time for biopsy specimen processing. BAL is beneficial as a supplementary technique for diagnosing peripheral lesions, particularly primary epithelial lung tumors. The diagnostic yield is significantly higher in diffuse disease processes that spread through lymphatic or lepidic growth, such as bronchoalveolar cell carcinoma (BAC) and adenocarcinoma.[6,18]

Rao, *et al*. as cited by Błach, *et al*. (2021), evaluated the efficiency of bronchial wash cytology in diagnosing bronchopulmonary lesions and classifying dysplastic/malignant lesions. The technique of bronchial wash cytology showed high specificity and cytohistopathology correlation, revealing a concordance rate of 62.06%. The study indicated that, even though bronchial wash cytology has limited ability to identify pulmonary lesions, it can still be of value in patients with biopsy contraindication.[10]

Another study by Dinesh, *et al*. as cited by Błach, *et al*. (2021), investigated 50 patients who underwent BAL, brush cytology, and biopsy, disclosing that bronchoscopic biopsy yielded affirmative results for malignancy in 46 (92%) individuals. In contrast, bronchial brush and bronchoscopic BAL were positive in 44 (88%) and 15 (30%) individuals, respectively.[10]

A combination of brushing, washing, and biopsy approaches is expected to boost the overall diagnostic yield of diagnostic bronchoscopy more than biopsy results.[6,19] This study also found that by combining BAL and brushing and forceps biopsy, the detection rate of lung malignancy increased to 85.7%. However, no statistically significant findings were found between the types of bronchoscopy procedures.

In current study, cytology and histopathology findings from bronchoscopy revealed adenocarcinoma as the most common type of malignancy in both male and female. Adenocarcinoma was the prevalent form of lung cancer, succeeded by squamous cell carcinoma, indicating a shift in smoking patterns and the preference for low-tar, high-nitrate content filter cigarettes. A previous study suggested that the increase in adenocarcinoma incidence was limited to smokers.[10] The World Health Organization (WHO) classifies lung cancer into two types: non-small cell lung carcinoma (NSCLC) and small cell lung carcinoma (SCLC). NSCLC represents around 85% of all lung cancer cases and can be categorized into three distinct subtypes: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[20,21] Guo, *et al*. (2021) found the most common type of lung cancer is adenocarcinoma, which accounts up to 40% of all cases.[22] Tayal, *et al*. (2018) from India and Błach, *et al*. (2021) from Poland have different results, where squamous cell carcinoma dominates the pathological findings.[10,11]

Błach, *et al*. (2021), Biciuşcă, *et al*. (2022), and Shrestha, *et al*. (2022) found the most common types of lung cancer were squamous cell carcinoma, followed by adenocarcinoma, SCLC, and NSCLC-not otherwise specified (NOS).[10,23,24] Women were more likely to have SCLC and adenocarcinoma, whereas men were more likely to have squamous cell carcinoma. Squamous cell carcinoma was more frequent in men and in patients older than 65 years old. Endobronchial biopsies were more successful in diagnosing lung cancer than endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) procedures, and different biopsy methods had varying success rates in diagnosing lung cancer. These differences in biopsy methods were statistically significant.[10,23,24]

Recent advances in bronchoscopy have improved its diagnostic accuracy for lung cancer detection. A study conducted by Ishiwata, *et al*. (2022) assessed the diagnostic accuracy of endobronchial ultrasonography with a guiding sheath (EBUS-GS) for detecting peripheral pulmonary lesions and found that EBUS-GS had a diagnostic yield of 86.4% and a sensitivity of 80.0%.[25] Similarly, a study by Zhang, *et al*. (2020) compared the diagnostic accuracy of virtual bronchoscopic navigation (VBN) and radial probe endobronchial ultrasound (RP-EBUS) for the diagnosis of peripheral pulmonary lesions and found that VBN had a higher diagnostic yield (92.1%) than RP-EBUS (81.6%).[18] These findings suggest that new bronchoscopic technologies may improve the diagnostic accuracy and yield for lung cancer detection.

The limitation of this study was the retrospective data collection, inadequacy of details on the quantity of biopsies, and absence of radiology data.

CONCLUSION

Bronchoscopy is an important instrument for identifying and discovering lung cancer. An endobronchial biopsy is crucial in examining lung cancer and can provide an accurate diagnosis if enough samples are gathered for histopathological analysis. Forceps bronchoscopy showed a greater positivity rate than bronchoscopy without forceps, but no correlation between the type of procedure and the likelihood of malignancy was discovered in this study.

Further study is needed with a larger sample size to determine the correlation between the type of bronchoscopy procedure and the pulmonary malignancy result and to determine the most dominant procedure in the diagnosis of lung malignancy. Early detection and diagnosis of lung cancer are crucial for improving patient outcomes, especially in high-risk populations. Therefore, bronchoscopy should be considered in diagnosing patients with suspected lung cancer.

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Conflict of Interest
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Authors' Contributions
Conceiving and designing the research protocol, collecting data, conducting research, providing research materials, organizing: IN, MAN, and IKO. Interpretating data and analyzing: IN, DR, and TAW. Writing initial and final draft of the article and providing logistic

support: IN, MAN, IKO, DR, and TAW. All authors critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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