Original Article

The Utility of Various Cytological Specimens in Relation with Bronchoscopic Biopsy Findings for Diagnosis of Lung Carcinoma: Clinicopathological Study

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Abstract

Background: Bronchoscopy and different modalities to obtain tissue samples form the cornerstone of lung cancer diagnostics. **Objectives:** To evaluate the efficacy of cytological samples in diagnosing or aiding the diagnosis of lung cancer and to compare its results with biopsy, as well as the utility of tiny lung biopsy in the diagnosis and staging of lung carcinoma, and its utility in applying immunohistochemical stains. **Materials and Methods:** One hundred and forty-nine patients with radiological and bronchoscopic data suggested lung malignancy. The bronchial wash (BW), transbronchial needle aspirate cytology, and lesion-directed biopsy specimens were obtained and underwent cytological, histological, and statistical analysis. **Results:** Regarding group 1 data (three samples, $n = 45$), the sensitivity of lesion-directed biopsy was 80.0% and the sensitivity of transbronchial needle aspirate was 80.6%. The sensitivity of BW was 25%. Regarding group 2 data (two samples, $n = 102$), it was found that the transbronchial needle aspirate was more sensitive than BW with a sensitivity of 50.0%, while the sensitivity of BW was 48.8%. Data from group 3 (one sample, $n = 2$) include two patients, both samples were positive transbronchial needle aspirate. Evaluation of efficacy of transbronchial needle aspirate in staging showed that the sensitivity of transbronchial needle aspirate was 61.5%. The diagnostic efficacy of endotracheal biopsy was better than transbronchial biopsy (P value = 0.028). **Conclusion:** Transbronchial needle aspirate is the most sensitive cytological procedure for establishing or yielding pathological diagnoses of lung carcinoma. The endobronchial ultrasound-guided core needle biopsy and aspirate cytology are useful for staging purposes. Endobronchial biopsy has better diagnostic efficacy than transbronchial biopsy.

Keywords: Bronchial wash, bronchoscopy, EBUS-TBLB, lung carcinoma, TBNA

Introduction

Lung cancer is one of the most significant prevalent plus lethal cancers, accounting for 4.08–5.60 per 100,000, most of whom are male; it has increased from 4.08% in 2000 to 5.60% in 2016.[1] Genomic examinations have recognized and initiated mutations in proto-oncogene B-Raf among patients with lung malignant growth.[2] There are two types of lung cancer: non-small cell (NSCLC) and small cell (SCLC). The incidence of NSCLC is about 80–85% of lung cancer patients, while about 15% have SCLC.[3] Basically, it has been documented that early diagnosis is associated with a better stage. The ratio of the five-year survival rate ranges from 5% for stage IV cancers to 80% for stage I cancers.[4] Bronchoscopy is one of the most invaluable instruments for the diagnosis of lung cancer. It is linked with high diagnostic accuracy in the detection of malignant central airway lesions. Moreover, several localization techniques can be used to improve diagnostic

Access this article online

Quick Response Code:

Website: https://journals.lww.com/mjby

DOI: 10.4103/MJBL.MJBL_986_24

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Submission: 24-Oct-2024 **Accepted:** 25-May-2025 **Published:** 23-Jul-2025

How to cite this article: Baiee FHA, Karbel HA, Baay AS, AI-Bakaa FK. The utility of various cytological specimens in relation with bronchoscopic biopsy findings for diagnosis of lung carcinoma: Clinicopathological study. Med J Babylon 2025;22:S61-8.

sensitivity, which includes radial probe endobronchial ultrasound (EBUS), CT-guided transthoracic needle aspiration (TTNA), and electromagnetic navigation bronchoscopy.[5]

Respiratory tract cytology is well established throughout the world as a diagnostic procedure in the evaluation of patients with suspected lung lesions.[6] Techniques, like bronchial wash (BW) and transbronchial needle aspiration (TBNA), have become popular tools for obtaining diagnostic cytological material from various sites of the tracheobronchial passage. Today, these cytological procedures constitute the most useful and least invasive tools available for the detection of pulmonary lesions.[7] Bronchoscopic biopsies are widely used in the histopathologic diagnosis of lung cancer. Common biopsy procedures include forceps biopsy, core needle biopsy, and cryoprobe (cryobiopsy).[8] To evaluate the efficacy of cytological samples (BW and transbronchial needle aspirate) in diagnosing or aiding the diagnosis of lung cancer and comparing their results with lesion-directed biopsy, as well as the utility of tiny lung biopsy in the diagnosis of lung carcinoma, staging, and its utility in applying immunohistochemical stains.

Materials and Methods

Study design and setting

This is a retrospective study carried out at the Department of Pathology. The samples for cytological and histological examination were collected from the private Teba Respiratory Center in Hilla City, Babylon province, from December 2017 to November 2021. The reports were retrieved from the digital archives of the Department of Pathology and the Department of Respiratory. The following data were extracted from the reports: age, gender, radiological findings, type of technique (conventional bronchoscopy or EBUS_bronchoscopy), type of lung malignancy, and immunohistochemical stain (TTF1, P40, and chromogranin). A total of 149 cases were included in this study. Socio-demographic information was recorded on a predesigned schedule.

Then, the blocks and H&E slides were retrieved and reexamined by an expert pathologist with a light microscope. The results of the immunohistochemistry (IHC) study were reassessed to reach the final pathological diagnosis in some cases.

Inclusion and exclusion criteria

The inclusion criteria included the bronchoscopic specimens of BW, TBNA (under endobronchial ultrasound guide, EBUS-TBNA), and endobronchial lung biopsy/transbronchial lung biopsy core needle biopsy under EBUS technique.

The exclusion criteria included patients with benign lung lesions, samples obtained by cryoprobe excluded because small number of cases at Teba Respiratory Center, and nonepithelial tumors.

Statistical analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 27.0 (SPSS, IBM Company, Chicago, IL 60606, USA). Categorical variables were presented as frequencies and percentages. Continuous variables were presented as means ± SD. Student *t*-test was used to compare means between the two groups. Pearson's chi-square test and Fisher's exact test were used to find the association between categorical variables. A P value of ≤ 0.05 was considered significant.

Results

The study groups consisted of 149. The majority of patients were male (n = 91, 61.1%), the mean age of patients was 64.42 ± 9.72 years, and the age range was 36–89. The distribution of patients according to radiological findings was found that the majority of patients showed mass lesions (n = 118), while others showed non-mass lesions either consolidation, LAP, collapse, effusion (n = 19), or both mass and non-mass lesions (N = 12)

The patients were distributed according to the bronchoscopic technique used by pulmonologists to obtain specimens into the conventional technique (n = 86) and those with endobronchial ultrasound guide EBUS technique (n = 63).

For all patients involved, they should have either one tiny biopsy (out of endobronchial, extrabronchial, or core biopsy) positive or cytology (TBNA or BW) positive. The final diagnosis was made based on abnormalities detected by tiny biopsy endobronchial biopsy (EBB)/TTB (core needle biopsy) that diagnosed 128 cases or cytology (TBNA diagnosed 20 cases and BW diagnosed only one case as squamous cell carcinoma [SCC]). All these modalities were not used simultaneously in all patients in this study. The number of samples depends on the patient's general condition, radiological findings, and accessibility to reach lesions, so patients were divided into three groups.

1. Group 1: Patients with three samples (45 [30.2%])
2. Group 2: Patients with two samples (102 [68.5%])
3. Group 3: Patients with one sample (2 [1.3%])

Group 1 results (N = 45)

Bronchial biopsy was positive in 36 out of 45 patients, while negative in nine patients. Sensitivity of lesion-directed biopsy was 80.0%. TBNA was positive in 37 out of 45 patients, while negative in eight patients. True positive was in 29 cases, true negative was in one case, false positive was in eight cases, and false negative was in seven cases [Table 1]. The sensitivity of TBNA was

80.6%. Specificity was 11.1%. Positive predictive value (PPV) was 78.4%. Negative predictive value (NPV) was 12.5%. Overall accuracy was 66.7% [Table 2]. BW was positive in 14 out of 45 patients, while negative in 31. True positive was in nine cases. The true negative was in four cases. False positives were in five cases. False negatives were in 27 cases [Table 1]. The sensitivity of BW was 25.0%. Specificity was 44.4%. PPV was 64.3%. NPV was 12.9%. Overall accuracy was 28.9% [Table 2]. At the same time, bronchial biopsy and TBNA had high positivity rates of 80.0% and 82.2%, respectively.

Table 1: Results of cytological techniques including bronchial wash (BW) and TBNA compared to bronchial biopsy

Sample	Test result				Total
	True positive	True negative	False positive	False negative	
BW	9	4	5	27	45
Transbronchial needle aspirate	29	1	8	7	45

Table 2: Sensitivity, specificity, positive predictive value (PPV), negative predictive value, and overall accuracy of BW and TBNA compared to bronchial biopsy

Sample	Test result				
	Sensitivity	Specificity	PPV	NPV	Overall accuracy
BW	25.0%	44.4%	64.3%	12.9%	28.9%
Transbronchial needle aspirate	80.6%	11.1%	78.4%	12.5%	66.7%

Table 3: Distribution of patients with three modalities according to the results of bronchial biopsy, TBNA, and BW (*N* = 45)

Type of technique	Positive + %	Negative + %	Total + %
Bronchial biopsy	36 (80.0%)	9 (20.0%)	45 (100%)
TBNA	37 (82.2%)	8 (17.8%)	45 (100%)
BW	14 (31.1%)	31 (68.9%)	45 (100%)

In contrast, BW showed a much lower positivity rate of 31.1% [Table 3].

The distribution of patients with three modalities according to results is shown in Table 4, including positive by all modalities, negative by all modalities, (positive bronchial biopsy and BW, negative TBNA), (positive bronchial biopsy, negative BW and TBNA; positive bronchial biopsy and TBNA, negative BW), (negative bronchial biopsy, positive BW and TBNA), (negative bronchial biopsy and BW, positive TBNA), and (negative bronchial biopsy and TBNA, positive BW).

Group 2 results (*N* = 102)

In this group, patients were divided into:

- Patient with bronchial biopsy and BW (wash *N* = 86)

Biopsy positive was 80 out of 86, while negative was six out of 86.

- Patient with bronchial biopsy and TBNA (*N* = 16)

Biopsy positive was 12 out of 16, while negative was four out of 16.

Bronchial biopsy was positive in 92 out of 102 patients, while negative in 10 patients. Sensitivity of lesion-directed biopsy was 90.2%. TBNA cytology was positive in 10 out of 16 patients, while negative in six patients. True positive was found in six cases, true negative was in 0 cases, false positive was in four cases, and false negative was in six cases. The sensitivity of TBNA was 50.0%, and specificity was 00.0%. PPV was 60.0%. NPV was 0.0%. Overall accuracy was 38.0% [Table 5]. BW was positive in 45 out of 86 patients, while negative in 41. True positives were in 39 cases. True negatives were in zero cases. False positives were in six cases. False negatives were in 41 cases [Table 6]. The sensitivity of BW was 48.8%. Specificity was 0.0%. PPV was 86.7%. NPV was 0.0%. Overall accuracy was 45.3% [Table 5].

The distribution of patients with two modalities according to results includes positive bronchial biopsy and positive

Table 4: Distribution of patients with three modalities according to results (*N* = 45)

Results of three modalities	Number	%
Positive by all modalities	9	20.0%
Negative by all modalities	0	0.0%
Positive by bronchial biopsy and BW, negative by TBNA	0	0.0%
Positive by bronchial biopsy, negative by BW and TBNA	7	15.6%
Positive by bronchial biopsy and TBNA, negative by BW	20	44.4%
Negative by bronchial biopsy, positive BW and TBNA	4	8.9%
Negative by bronchial biopsy and BW, positive by TBNA	4	8.9%
Negative by bronchial biopsy and TBNA positive by BW	1	2.2%
Total	45	100.0%

BW, positive bronchial biopsy and positive TBNA, negative bronchial biopsy and negative BW, negative bronchial biopsy and negative TBNA, positive bronchial biopsy and negative BW, positive bronchial biopsy and negative TBNA, negative bronchial biopsy and positive BW, and negative bronchial biopsy and positive TBNA [Table 7].

Group 3 results (*N* = 2, 1.3%)

Two samples of TBNA were positive. One was diagnosed as NSCLC NOS obtained from a lymph node, and the other as squamous cell carcinoma obtained from a mass diagnosed by conventional light microscopy.

EBUS – core needle biopsy and TBNA for staging NSCLC (*N* = 15). Bronchial biopsy (TBB)/core needle biopsy was positive in 13 out of 15 patients, while negative in two patients. TBNA cytology was positive in 10 out of 15 patients, while negative in five patients. True positive was in eight cases, true negative in zero cases, false positive in two cases, and false negative in five cases [Tables 8 and 9]. The sensitivity of TBNA was 61.5%. Specificity was 0.0%. PPV was 80.0%. NPV was 0.0%, and overall accuracy was 53.3% [Table 10].

The distribution of patients according to final pathological diagnosis includes small-cell carcinoma and non-small-cell carcinoma. Small-cell carcinoma represents (*N* = 46, 30.9%) of patients diagnosed by conventional light microscopy. Non-small-cell carcinoma of patients represents (*N* = 103, 69.1%) of patients, subtype of non-small-cell carcinoma that can be identified: squamous cell carcinoma (39), non-small-cell carcinoma NOS (39), and adenocarcinoma (25) [Table 11]. A total of 82 were diagnosed by conventional light microscopy, and 21 needed immunohistochemistry to be diagnosed as follows: 47.6% as adenocarcinoma, 42.9% as squamous cell carcinoma, and 9.5% as NSCLC NOS [Table 12].

Bronchoscopic biopsy is either an endobronchial biopsy or a transbronchial biopsy (core needle biopsy). In our study, we found that EBB is more significant than TBB [Table 13].

Table 5: Sensitivity, specificity, PPV, negative predictive value, and overall accuracy of BW and TBNA compared to bronchial biopsy

Sample	Test result				
	Sensitivity	Specificity	PPV	NPV	Overall accuracy
BW	48.8%	0.0%	86.7%	0.0%	45.3%
Transbronchial needle aspirate	50.0%	0.0%	60.0%	0.0%	38.0%

Table 6: Results of cytological techniques including BW and TBNA compared to bronchial biopsy

Sample	Test result				Total
	True positive	True negative	False positive	False negative	
BW	39	0	6	41	86
Transbronchial needle aspirate	6	0	4	6	16

Table 7: Distribution of patients with two modalities according to results (*N* = 102)

Results of two modalities	Number	%
Positive bronchial biopsy and positive BW	39	38.2%
Positive bronchial biopsy and positive TBNA	6	5.9%
Negative bronchial biopsy and negative BW	0	0.0%
Negative bronchial biopsy and negative TBNA	0	0.0%
Positive bronchial biopsy and negative TBNA	6	5.9%
Positive bronchial biopsy and negative BW	41	40.2%
Negative bronchial biopsy and positive BW	6	5.9%
Negative bronchial biopsy and positive TBNA	4	3.9%
Total	102	100.0%

Table 8: Distribution of patients according to the results of TBNA and biopsy of the lymph node

Investigations	No.	%
Results of LN TBNA		
Positive	10	66.7%
Negative	5	33.3%
Total	15	100.0%
Result of LN biopsy		
Positive	13	86.7%
Negative	2	13.3% positive by surgery
Total	15	100.0%

LN: lymph node

Table 9: Results of TBNA of lymph node compared to lymph node biopsy (TBB)

Sample	Test result				Total
	True positive	True negative	False positive	False negative	
Transbronchial needle aspirate	8	0	2	5	15

Table 10: Sensitivity, specificity, PPV, negative predictive value, and overall accuracy of TBNA of lymph node compared to lymph node biopsy (TBB)

Sample	Test result				
	Sensitivity	Specificity	PPV	NPV	Overall accuracy
Transbronchial needle aspirate	61.5%	0.0%	80.0%	0.0%	53.3%

Table 11: Distribution of patients according to final diagnosis and methods of diagnosis

Study variables	Number	%
Final diagnosis		
Small-cell carcinoma	46	30.9%
Non-small-cell carcinoma	103	69.1%
Total	149	100.0%
Subtype of non-small-cell carcinoma that can be proved		
Squamous cell carcinoma	39	37.9%
Adenocarcinoma	25	24.2%
Non-small-cell carcinoma NOS	39	37.9%
Total	103	100.0%
Method of diagnosis of lung carcinoma		
Conventional	128	86.0%
Immunohistochemistry	21	14.0%
Total	149	100.0%

Table 12: Distribution of patients according to the result of immunohistochemical stain TTF1, P40 (n = 21)

Subtype of NSCLC diagnosed by IHC	Number	%
Adenocarcinoma	10	47.6%
Squamous cell carcinoma	9	42.9%
NSCLC NOS	2	9.5%
Total	21	100.0%

IHC: Immunohistochemistry

Table 13: Distribution of patients according to the results of EBB, TBB, and both EBB and TBB

Biopsy type	Biopsy results		Total	*P* value
	Positive	Negative		
EBB	67 (52.3)	6 (31.6)	73 (49.7)	0.028*
TBB	48 (37.5)	13 (68.4)	61 (41.5)	
TBB + EBB	13 (10.2)	0 (0.0)	13 (8.8)	
Total	128 (100.0)	19 (100.0)	147 (100.0)	

EBB: endobronchial biopsy.

*P value ≤ 0.05 was significant

Discussion

Fiber-optic bronchoscopy has been accepted by clinicians as a relatively safe technique for diagnosing bronchogenic carcinoma. However, there is a lot of conflicting data on the diagnostic yield of various bronchoscopic procedures, as BW and TBNA, in correlation to lesion-directed biopsies.

The study was composed of 149 patients. Regarding socio-demographic characteristics, the mean age of patients was 64.42 years (standard deviation [SD]: ±9.72). Age ranged from 36 to 89. Most patients were male, 91 (61.1%). This is near the result of a Binesh *et al*. study on 388 patients in Iran that showed a mean age of 61.3 ± 13.7 years; age ranged from 19 to 89 years, including 333 males (85.8%) and 55(14.2%) females.[9]

Sareen *et al*., in their study of 504 patients in India found that the mean age was 58.00 ± 10.175 with a male predominance (88.1%).[10]

Radiological findings in the present study demonstrated that the majority of lesions were mass (79.2%), while Sareen *et al*. showed that mass lesion (26.67%) was the most common radiological finding in their study.[10]

Regarding group 1 data (n = 45), it was revealed that the diagnostic yield of EBUS-TBNA was comparable to the diagnostic yield of lesion-directed biopsy, while BW had a low diagnostic yield. The sensitivity of lesion-directed biopsy was 80.0%, the sensitivity of EBUS-TBNA was 80.6%, the PPV was 78.4, the NPV was 12.5%, and the diagnostic accuracy was 66.7%. The sensitivity of BW was (25%), PPV was 64.3%, NPV was 12.9%, and overall accuracy was 28.9%. This result was compatible with Nazan Kacar *et al*. study on 95 patients presenting with visible tumors detected during a bronchoscopic procedure done in Turkey. Rates of positive results were 75.8% for needle aspiration, 71.6% for forceps biopsy, 61.1% for brushing, and 32.6% for washing.[11]

Tyagi *et al*. study on 200 patients in India with 62 neoplastic cases and 109 non-neoplastic cases show that TBNA is superior to all other sampling modalities and is on par with bronchoscopic biopsy in endobronchial tumors with an average diagnostic yield of 80%, while the diagnostic yield of BW was 26%. The sensitivity of TBNA in neoplastic cases was 52.6%. The PPV of TBNA was 98.9%, and NPV was 25.7%.[7] The reason for the high sensitivity in our study probably belongs to the use of the endobronchial ultrasound (EBUS) technique that was not used in the Gauray study.

The advantage of the study of three sample groups is that in a single visit, all the procedures are done, thereby improving patient compliance and inconvenience. But it can increase the time of the procedure, the chance of trauma, and the cost (which was not significant).

The disadvantage of multiple sampling methods includes time, complications (such as hemorrhage and pneumothorax), trauma to the fiber-optic bronchoscope, and cost.

Regarding group 2 data (n = 102), the results found that the bronchial biopsy was positive in 90.2% of patients. The result of TBNA was positive in 62.5%. The results of BW were positive in 52.3%. Despite differences in the number of samples, as the biopsy with TBNA was 16 and the biopsy with BW was 86, TBNA was more sensitive than BW, with a sensitivity of 50.0%, while the sensitivity of BW was 48.8%.

The results of lesion-directed biopsy and TBNA in the two sample groups (n = 16) were biopsy positive in 75%, TBNA was positive in 62.5%, lesion-directed biopsy and TBNA were positive in six cases, the sensitivity of

TBNA was 50.0%, PPV was 60.0%, and overall accuracy was 38.0%, by comparison to other studies. This study differs from that of Eftekhar-Javadi *et al*. study on 105 cases with intrathoracic lesions in Iran were divided into 73 (69.5%) malignant lesions and 32 (30.5%) benign lesions. Transthoracic fine needle aspiration (FNA) and core needle biopsy findings were in complete agreement in 63 cases (96.0%). The accuracy of FNA for malignant tumors was 86.3%.[12]

Nakajima *et al*. study on 35 patients with pulmonary masses in Japan showed that the sensitivity of EBUS-TBNA was 94.1%, the PPV was 100%, and NPV was 33.3%. The diagnostic accuracy of TBNA was 94.3.[13]

The difference was attributed to the small number of patients in the group as well as the presence of more false negatives and false positives resulting from the use of only tiny specimens, as well as non-malignant lesions were excluded.

By comparison with other studies, the results of lesion-directed biopsy and BW in two sample groups ($N = 86$) were biopsy positive in 93.0%, BW was positive in 52.3%, lesion-directed biopsy and BW were positive in 39 cases, the sensitivity of BW was 48.8%, PPV was 86.7%, and overall accuracy was 45.3%

This study differs from that of Raiza *et al*. study, which involved 38 cases with visible endobronchial lesions in Iran showed that biopsy was positive in 23 cases. BW was positive in 12 cases, biopsy and BW were positive in 16 cases, BW sensitivity was 80.5%, and accuracy was 80.5%[14]; our study differs because we deal with endobronchial and extrabronchial lesions and have more false negative results (41 cases) than Raiza *et al*. who had only six false negative cases. The reasons for false negative results in BW could be due to superadded inflammation and mucous material, no representative material, and hypocellular aspirate.

False negatives imply that the cytological specimen does not contain malignant cells. The absence of malignant cells could be attributed to the inability of malignant cells to dislodge from the epithelial surface, causing lavage fluid to be low in malignant cells.[14]

Binesh *et al*. study showed that transbronchial lung biopsy (TBLB) identified malignancy in 183 of the 388 cases. The sensitivity of BW was 46.9%, a PPV of 83.4%, and the overall accuracy of bronchoalveolar lavage was 70.5%.[9]

Rao *et al*. study on 58 cases in India showed that biopsy and BW were positive in 20 cases, the sensitivity of BW was 52.63%, the PPV was 83.33%, and the NPV was 47.05% with an accuracy of 62.06%.[15]

The sensitivity of BW in other studies from literature varies from 21% to 93%[7,10]. This results from both groups fall within this range. Variation in sensitivity belonged to several reasons, like site of the lesion, the size of the lesion, the expertise of the pulmonologist, sampling, handling, processing, the number of attempts made, and the use of radiological modalities along with procedure.[7,16,17]

Data from group 3 included two patients. Both samples were TBNA. The reason for taking one sample is related to the patient's general condition and the accessibility to reach lesions. All lesions may not be amenable to biopsy, and some may not be stable enough to get a biopsy. In those cases, TBNA is a very useful diagnostic test.[7] No similar study was found to compare with.

This study also evaluates the efficacy of TBNA in patients with lymphadenopathy ($N = 15$) for staging. The core needle biopsy was positive in 86.7%, EBUS-TBNA was positive in 66.7%, the sensitivity of TBNA was 61.5%, PPV was 80.0%, and overall accuracy was 53.3%. This differs from David *et al*. study on 131 cases of lymph node sampling done in America, which showed that 45 cases (34.6%) were diagnosed as malignant, 73 cases (55.7%) as benign process, and 88 cases (65.2%) had corresponding core biopsies or follow-up surgery. When histology was taken as the gold standard, the sensitivity of EBUS-TBNA was 85.0%, PPVs was 100%, and NPV was 67–97%.[18]

The study of Herth *et al*. in Germany on 50 patients with enlarged or PET-positive lymphadenopathy showed that the sensitivity of TBNA was 88%, PPV was 100%, and overall accuracy was 88%.[19]

Similarly, Lee *et al*. in South Korea on 102 patients with mediastinal lymph nodes showed that the sensitivity was 93.8%, PPV was 100%, and the accuracy of EBUS-TBNA in predicting mediastinal metastasis was 96.9%.[20]

The difference from previous studies is probably due to the small number of patients with lymph node metastasis ($N = 15$), and the presence of false negative and false positive cases, compared to the large number and few or no cases with false positive results in previous studies.

The false positives in cytology can be reported due to misinterpretation of smears due to cellular changes in chronic inflammatory disorders such as pneumonia (atypical histiocytes), TB, bronchiectasis (misinterpretation of cuboidal epithelial cells as small-cell carcinoma), squamous metaplasia, and alveolar cell polymorphism in lung fibrosis. In addition, a false positive result could be due to insufficient tissue biopsy to interpret as carcinoma, so we get positive cytology and negative biopsy results. The comparison of cytology results with other patient parameters like bronchoscopic findings and radiological findings to reach the final pathological diagnosis and do not rely only on the result of biopsy as the gold standard, and repeating biopsy could be advised. False positive has very unfortunate consequences for patients; therefore, some advice "underreporting" instead of "overreporting" of suspicious cases.[10]

The presence of false negative cases is due to it is not always possible to obtain sufficient material for cytological assessment, especially when lesions are located in the left upper lobe. It is possible that this location affects the ability to aspirate enough cellular material.[21] Furthermore, with the presence of high-grade cancers, there is more necrosis which reduced the yield of viable tissue, as there was more necrotic material which resulted in false negative cases.

The final pathological diagnosis in this study includes 37.9% squamous cell carcinoma, 37.9% NSCLC NOS, 30.9% small-cell carcinoma, and 24.2% adenocarcinoma (ADC). IHC was used in 14.0% of cases (TTF1, P40).

Binesh *et al*. study showed that malignancy in 183 out of the 388 cases, including 26.2% cases with adenocarcinoma, 2.1% with bronchoalveolar carcinoma, 25.6% with squamous cell carcinoma, 18.5% with well-differentiated neuroendocrine carcinoma, 19.1% with small-cell carcinoma, 7.6% with non-small-cell carcinoma, and 0.54% with large cell carcinoma.[9]

Sareen *et al*. study showed that the final histopathology diagnosis of 300 malignant cases included 51.33% cases of squamous cell carcinoma. The second malignancy to follow was small-cell carcinoma (27%) cases, followed by adenocarcinoma (5.67% of cases).[10]

The study has more NSCLC NOS cases than previous studies due to loss of contact with patients because they are referred from other centers. Bronchial biopsy was the most common type of specimen (147), followed by BW (131 specimens) and TBNA (63 specimens).

The distribution of patients according to the result of immunohistochemical stains ($n = 21$) includes ADC in 47.6%, squamous cell carcinoma at 42.9%, and NSCLC NOS in 9.5% (Table 3.22). No similar study was found for comparison.

Transbronchial needle aspirate yielded a diagnosis in 49 patients out of 63 and recognized types of lung carcinoma as follows: SCLC was 30.6%, NSCLS NOS was 44.9%, SCC was 16.3%, and ADC was 8.2%. While BW yielded a diagnosis in 59 patients out of 131 and recognized types of lung carcinoma as follows: SCLC was 33.9%, NSCLC NOS was 39.0%, SCC was 25.4%, and ADC was 1.7%.

Sareen *et al*. showed that CT_FNA (transthoracic) recognizes types of lung carcinoma as follows: NSCLC was 15.38%, metastatic carcinoma was 1.92%, small-cell carcinoma was 7.69%, poorly differentiated carcinoma was 3.85%, squamous cell carcinoma was 25.0%, and ADC was 11.53%. While BW recognizes types of lung carcinoma as following squamous cell carcinoma (20.97%), non-small-cell carcinoma (9.93%), small-cell carcinoma (6.62%), poorly differentiated carcinoma (1.32%), and adenocarcinoma (0.22%).[10]

The TBNA results in this study were comparable to lesion-directed biopsy, so there was no significance between the two procedures (P value = 0.431). This result was compatible with Nazan Kacar *et al*. who showed that biopsy yielded the highest diagnostic rate for an endobronchial lesion (86.4%); however, when compared with needle aspiration (77.9%), no significant difference was observed between these two procedures (P value = 0.302).[11]

The BW result is less consistent with lesion-directed biopsy; thus, there is significance between the two procedures (P value < 0.05). This was compatible with Rao *et al*. who showed that BW cytology has low sensitivity, and cytohistopathology correlation was statistically significant (P value < 0.05).[15] EBB biopsy is more diagnostic than TBB, with EBB positive at 52.3%, while TBB was positive in 37.5%, P value < 0.001.

In the study of Ghazarian *et al*. on 68 cases, the diagnostic accuracy of blind TBB in all lesions was 22.6%, while the diagnostic yield of EBB in all lesions was 81.1%, which was statistically significant (Pearson chi-square = 23.272 and $P < 0.001$).[22]

The diagnostic yield from various techniques of tissue sampling has been discussed by several authors, and the general conclusion is that those methods which obtain specimens directly from the tumor (biopsy, TBNA) are superior to indirect techniques (washings).[23-25]

Conclusion

Transbronchial needle aspirate is the most sensitive cytological procedure for establishing and yielding pathological diagnoses of lung carcinoma. TBNA result was comparable to lesion-directed biopsy result. Combination TBNA with lesion-directed biopsy increases sensitivity. TBNA is not associated with complications clinically or any difficulty during the processing of aspirate. BW cytology is a low-sensitive test for yielding a diagnosis of lung carcinoma. BW is a safe, inexpensive, and simple procedure that can be used routinely without complication. EBUS_core needle biopsy and TBNA cytology are useful for staging purposes. TBNA cytology is a useful diagnostic test when it is positive. Endobronchial biopsy has better diagnostic efficacy than transbronchial biopsy with the application of immunohistochemical stains in tiny biopsies.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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