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Diagnostic Performance of Bronchoscopic Sampling Techniques in Suspected Bronchial Carcinoma

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ABSTRACT

Background: Lung cancer is the top cause of cancer deaths worldwide. Delayed diagnosis worsens outcomes. Flexible bronchoscopy is a key tool with several sampling techniques. Assessing their effectiveness helps improve early, accurate detection.

Objective: To study the yield of malignant or suspicious cells from bronchoalveolar lavage (BAL), endobronchial biopsy (BX), and endobronchial brushing (BR) specimens obtained at bronchoscopy.

Methodology: A prospective cross-sectional study was conducted on 142 patients suspected of having bronchial carcinoma. All patients underwent flexible bronchoscopy (a procedure using a thin, flexible tube to inspect the airways) with bronchoalveolar lavage (BAL: washing fluid through the airways). When feasible, endobronchial biopsy (BX: sampling of tissue from inside the bronchial tubes) and brushing (BR: collecting cells with a small brush) were also performed. Samples were examined for cytology (the study of cells) and histopathology (the study of tissue structure and disease). The diagnostic yield was then calculated for each method and compared across tumor types, locations, and stages.

Results: Among 142 patients, the overall diagnostic yield using combined bronchoscopic techniques was 85.9%. BAL had the highest individual yield (70.4%), followed by BX (57.7%) and BR (25.4%). Combining sampling methods significantly enhanced diagnostic accuracy compared to individual methods. Diagnostic yield was not significantly affected by tumor location or TNM stage. The highest yield was observed in adenocarcinoma and centrally located tumors.

Conclusion: The combined use of BAL, BX, and BR significantly increases diagnostic yield in suspected bronchial carcinoma. Endobronchial biopsy and BAL are still the most effective individual techniques. A multimodal bronchoscopic approach should be employed for optimal diagnostic accuracy.

Keywords: Bronchscopy; Carcinoma; Endobronchial Biopsy; Bronchoalveolar Lavage

Introduction

Bronchial carcinoma, a type of lung cancer, is the leading cause of cancer deaths worldwide. In 2020, lung cancer accounted for about 2.2 million new cases and 1.8 million deaths globally.[1] Non-small cell lung carcinoma (NSCLC) accounts for approximately 85% of cases, while small cell lung carcinoma (SCLC) comprises the remaining 15%.[2] Early and accurate diagnosis is crucial for patient management and guiding staging and treatment, particularly as targeted therapies and immunotherapy continue to advance.

Flexible fiberoptic bronchoscopy is a key diagnostic tool for assessing suspected bronchial carcinoma, particularly when the lesion is centrally located or visible during the exam. It enables direct visualization of the tracheobronchial tree and allows for tissue sampling through various methods, including bronchoalveolar lavage (BAL), endobronchial biopsy (EBX), and endobronchial brushing (EBR).[3] The procedure is minimally invasive, generally safe, and can be done under local anesthesia, making it suitable for patients with other health issues.

BAL uses saline to collect cells from lower airways, aiding cytological diagnosis, especially for non-visible or peripheral tumors. Endobronchial biopsy is the gold standard for histological confirmation of visible lesions.[4] Brushing collects cells for cytology by scraping lesion surfaces. Each method has specific advantages, limitations, and varying levels of effectiveness depending on the tumor factors.[5,6]

Studies have compared the diagnostic yields of these bronchoscopic techniques alone and in combination. Endobronchial biopsy can have a sensitivity of up to 80%. BAL and BR add value, especially for small or non-visible lesions. Combining biopsy and brushing increases yield, but clinical practice varies due to resource limitations.[7]

Several patient, tumor, and procedural factors influence bronchoscopy success, such as age, sex, lesion characteristics, endobronchial abnormalities, TNM staging, biopsy attempts, operator experience, and sample processing. There is growing interest in whether combining sampling techniques improves outcomes without increasing procedure time or complications.[8]

Although international studies have offered valuable insights, there is a lack of recent, local data from resource-limited settings on the effectiveness of these bronchoscopic sampling methods.[9,10] In Pakistan, where lung cancer often appears at advanced stages and diagnostic resources may be limited, optimizing bronchoscopy to achieve the best diagnostic results is crucial. Furthermore, no recent study from this region has thoroughly compared the yields of BAL, BX, and BR in a single group with standardized procedures.

Considering the significant impact of bronchial carcinoma and the importance of accurate diagnosis, this study was specifically designed to evaluate and directly compare the diagnostic performance of bronchoalveolar lavage, endobronchial biopsy, and endobronchial brushing in patients undergoing bronchoscopy for suspected bronchial carcinoma in a tertiary care setting. By examining the diagnostic yield of each method individually and in combination, and by analyzing how these yields relate to patient and tumor characteristics, we aim to identify which technique or combination offers the most reliable results. This should aid in developing more effective diagnostic strategies and procedural planning for suspected cases of bronchial carcinoma.

Objectives

To study the yield of malignant or suspicious cells from BAL, BX, and BR specimens at bronchoscopy.

Methodology

This prospective cross-sectional study took place at the Department of Pulmonology, Pakistan Institute of Medical Sciences (PIMS). A total of 142 patients were enrolled based on clinical and imaging suspicion of bronchial cancer. This suspicion arose from ongoing respiratory symptoms such as chronic cough, hemoptysis, unexplained weight loss, or dyspnea. These symptoms were combined with imaging findings that suggested a pulmonary mass, lung collapse, hilar lymphadenopathy, or infiltrate visible on chest X-rays or high-resolution computed tomography (HRCT). All participants were adults aged 18 or older. Written informed consent was obtained from each patient before the procedure.

Patients were excluded if they were hemodynamically unstable, had severe hypoxia or uncorrected bleeding issues, or had already received a histological or cytological diagnosis of bronchial carcinoma. Those who were unwilling or unable to undergo bronchoscopy or give informed consent were also excluded. Each patient underwent a baseline evaluation that included a thorough clinical examination, a chest X-ray, and an HRCT scan. Tumors were classified by their radiological location, including upper lobe, middle lobe (including lingula), lower lobe, hilar, or diffuse (involving more than two lobes). The disease was staged using the TNM classification from the 8th edition of the American Joint Committee on Cancer (AJCC), incorporating radiographic, clinical, and, when available, pathological findings.

Experienced pulmonologists performed flexible fiberoptic bronchoscopy under local anesthesia with 2% lidocaine. Conscious sedation was provided if necessary, using intravenous midazolam or fentanyl. Procedures were done in a standardized order to ensure consistency and reduce contamination. BAL was always performed first by wedging the bronchoscope into the bronchus closest to the radiographic lesion. Two aliquots of 50 mL of sterile

normal saline (total 100 mL) were instilled and then immediately aspirated for cytological analysis. If visible, an endobronchial biopsy (BX) followed. A minimum of four tissue samples were collected using flexible forceps and placed in 10% buffered formalin for histopathology. Finally, bronchial brushing (BR) was done from the same or nearby area using a cytology brush, with at least six smears prepared on glass slides and fixed in 95% alcohol for cytological examination.

BAL was successfully performed in all 142 patients. Biopsies were completed in 104 patients (73.2%), and brushing was done in 59 patients (41.5%). The lower number of biopsies and brushing procedures was due to technical challenges, significant bleeding after biopsy, or patient intolerance. For those who could expectorate, post-bronchoscopy sputum samples were collected within 24 hours and sent for cytology. Sputum samples were obtained from 114 patients (80.3%). All specimens were analyzed in the hospital's pathology department by experienced thoracic pathologists who remained unaware of clinical and imaging details. Cytological samples (BAL, BR, and sputum) were stained with Papanicolaou and Giemsa stains and classified as benign, atypical, suspicious, or malignant. Histological specimens from biopsies were processed using standard formalin-fixed paraffin embedding and reported according to the 2021 World Health Organization (WHO) classification of thoracic tumors.

For this study, only samples with confirmed malignant cells were considered positive. Atypical or suspicious results were noted but not deemed diagnostic unless further confirmed. The primary outcome measure was the diagnostic yield of each sampling technique, defined as the proportion of patients who received a definitive diagnosis of bronchial carcinoma. Secondary outcomes included the additional yield from performing a biopsy or brushing along with BAL, the correlation of yield with tumor site, histology, and TNM stage, and the agreement between cytological and histological findings.

Data were entered and analyzed using SPSS version 25. Continuous variables, such as age, were reported as mean ± standard deviation, while categorical variables were shown as frequencies and percentages. The diagnostic yields of BAL, BX, and BR were compared using the Chi-square test. The correlation between diagnostic yield and clinical factors, such as tumor location, staging, and histology, was assessed using Spearman's rank correlation. A p-value of less than 0.05 was considered statistically significant for all tests.

Results

A total of 142 patients with suspected bronchial carcinoma were enrolled. Among them, 97 were males (68.3%) and 45 were females (31.7%). The average age was 62.4 years, with a standard deviation of 11.9 years (ranging from 30 to 84 years). The diagnosis was confirmed by histology or cytology in 138 patients. Four patients were diagnosed based only on clinical and radiological findings. Macroscopic tumors were visible during bronchoscopy in 92 patients (64.8%). Additionally, 31 patients (21.8%) showed nonspecific mucosal changes, while 19 patients (13.4%) had normal findings (Table 1).

Bronchoalveolar lavage (BAL) was done in all 142 patients (100%). Endobronchial biopsy (BX) was done in 104 patients (73.2%), and bronchial brushing (BR) in 59 patients (41.5%). We could not completely use biopsy and brushing because of complications like bleeding, low oxygen levels, or patient discomfort. From the procedures performed, BAL found malignant cells in 100 patients (70.4%), BX in 82 of 104 patients (78.8%), and BR in 36 of 59 patients (61.0%). Overall, the diagnostic yield for BAL was 70.4%, for BX it was 57.7%, and for BR it was 25.4%. Additionally, suspicious or atypical cells were seen in another 18 BAL, 5 BR, and 0 BX specimens (Table 2).

Using BAL alone diagnosed 100 patients, which is 70.4%. A biopsy (BX) added 9 more cases, while a brushing (BR) contributed 2 unique cases. Post-bronchoscopy sputum, collected from 114 patients, or 80.3%, showed malignant

Table 1. Diagnostic Evidence Distribution Among Patients

Type of Diagnostic Evidence	Males (n=97)	Females (n=45)	Total (n=142)	Percentage (%)
Histological and Cytological	38	16	54	38.0
Histological only	20	8	28	19.7
Cytological only	31	21	52	36.6
None (clinical/imaging diagnosis)	4	0	4	2.8
Total	93	45	142	100.0

Table 2. Diagnostic Yield of Bronchoscopic Sampling Techniques

Sampling Method	No. Performed	Carcinoma Cells Detected	Suspicious Cells	Total Positive Diagnostic Yield (%)
Bronchoalveolar Lavage (BAL)	142	100 (70.4%)	18 (12.7%)	100 (70.4%)
Endobronchial Biopsy (BX)	104	82 (78.8%)	0	82 (57.7%)
Endobronchial Brushing (BR)	59	36 (61.0%)	5 (8.5%)	36 (25.4%)
Combined (any modality)	142	122	—	85.9%

cells in 47 patients, or 41.2%, and suspicious cells in 11 others, or 9.6%. The total diagnostic yield from combining all bronchoscopic methods reached 85.9%, or 122 out of 142 patients.

Figure 1 shows the comparative diagnostic yield of the three main sampling methods. BAL had the highest yield at 70.4%, followed by BX at 57.7% and BR at 25.4% when looking at the entire group. These results highlight BAL's better performance in routine bronchoscopic evaluation for suspected bronchial carcinoma.

There was no significant difference in diagnostic yield based on where the tumor was located. The BAL yield was 73.4% for upper lobe lesions, 68.8% for lower lobe lesions, and 76.9% for hilar lesions. Biopsy and brushing had similar yields across various lobar sites. For histology, BAL showed the highest positivity in adenocarcinoma at 76.9%, followed by small cell carcinoma at 70.0% and squamous cell carcinoma at 66.7% (Table 3).

TNM staging was available for 138 patients. Most of them had advanced disease: Stage IIIb (n=30) and Stage IV (n=84). BAL produced positive results in 83.3% of patients with Stage I–IIIa and 87.8% in those with Stage IIIb–IV. There was no statistically significant difference ($p > 0.05$). Similar trends were seen for BX and BR.

As shown in Figure 2, the diagnostic yield of BAL stayed high across both early and advanced TNM stages, with 83.3% in Stage I–IIIa and 87.8% in Stage IIIb–IV disease. Yields for BX and BR showed a slight decline in late-stage disease, but the differences were not statistically significant ($p > 0.05$). This shows BAL's strength as a

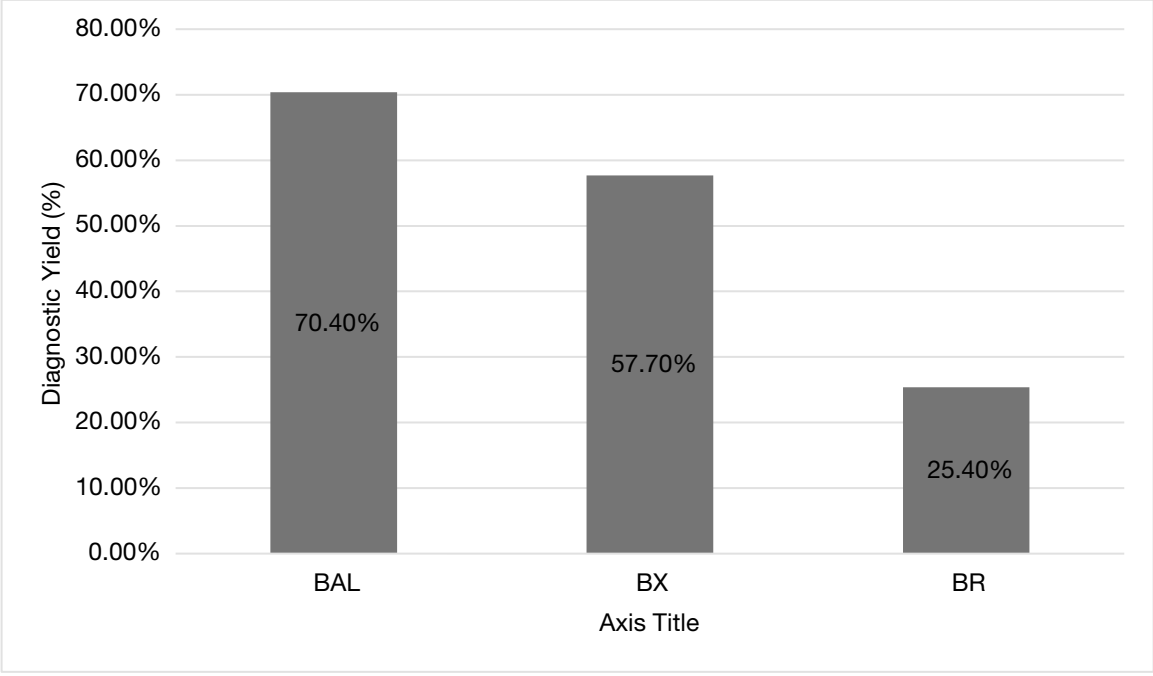

Figure 1. Bar Graph Showing Diagnostic Yield of BAL, BX, BR (n = 142)

Table 3. Diagnostic Yield by Tumor Location and Histological Type

Tumor Category	BAL Yield (%)	BX Yield (%)	BR Yield (%)
Tumor Location			
Upper lobe (n=62)	73.4	80.6	66.7
Lower lobe (n=51)	68.8	79.2	53.3
Hilar (n=22)	76.9	85.7	62.5
Diffuse (n=7)	57.1	60.0	—
Histology			
Adenocarcinoma (n=61)	76.9	75.0	63.6
Squamous cell (n=33)	66.7	78.9	50.0
Small cell (n=10)	70.0	100.0	66.7
NSCLC (unspecified) (n=25)	68.0	76.0	56.0

diagnostic tool, regardless of the disease stage.

Among 52 patients with both BAL cytology and BX histology results, there was full agreement in tumor typing in 34 cases, or 65.4%, and partial agreement in 16 cases, or 30.8%. No case had a significant error like misclassifying small cell and non-small cell carcinoma.

Discussion

In this study of 142 patients with suspected bronchial carcinoma, we evaluated the diagnostic performance of three commonly used bronchoscopic sampling techniques: bronchoalveolar lavage (BAL), endobronchial biopsy (EBX), and endobronchial brushing (EBR). The combined diagnostic yield from all methods was 85.9%. The individual yields were 70.4% for BAL, 57.7% for BX, and 25.4% for BR. We also examined the relationship between yield and tumor location, histological type, TNM staging, and the agreement between cytology and histology.

The diagnostic yield of BAL alone in our study was 70.4%. This result is comparable to that of Biciu c et al., whose 204-patient study in Romania yielded a 66.4% success rate, demonstrating the utility of BAL in moderate-resource settings.[2] Similarly, Zhang et al. recently found a yield of over 68% particularly when molecular markers accompany cytology which highlights BAL's value in personalized lung cancer diagnostics.10 In contrast, Fantin et al. reported a lower yield of about 61%, but noted improved accuracy when BAL is paired with image-guided tools for peripheral lesions.[7] These findings collectively underscore that BAL is a reliable front-line technique, especially when performed early during bronchoscopy.

Biopsy showed the highest individual diagnostic accuracy in our cohort, with a 78.8% yield among those who underwent it. However, it was technically possible in only 73.2% of patients due to risks of bleeding or poor visibility. This yield closely matches Duma et al.'s reported 80% for endobronchial biopsy in patients with visible lesions.[2] Ramayanam and Puchalski reviewed various bronchoscopic biopsy tools, finding yields between 70% and 85%, with visibility and tool type affecting rates, comparable to our results.[8] Fantin et al. emphasized biopsy's diagnostic value, especially when combined with cryoprobes or navigation systems for deeper lesions.[7] Overall, these studies support that biopsy is the most reliable tool when feasible, but is sometimes limited by safety concerns.

The diagnostic performance of endobronchial brushing in our study was modest, with a success rate of 61.0% among those who underwent the procedure and 25.4% across the entire group. These results are lower than those of Wongsurakiat et al., who reported yields of about 66.7% in peripheral lung lesions using brushing cytology alone.[9] Similarly, Biciu c et al. observed that brushing can provide valuable results when combined with biopsy or BAL, especially in cases of squamous cell carcinoma.5

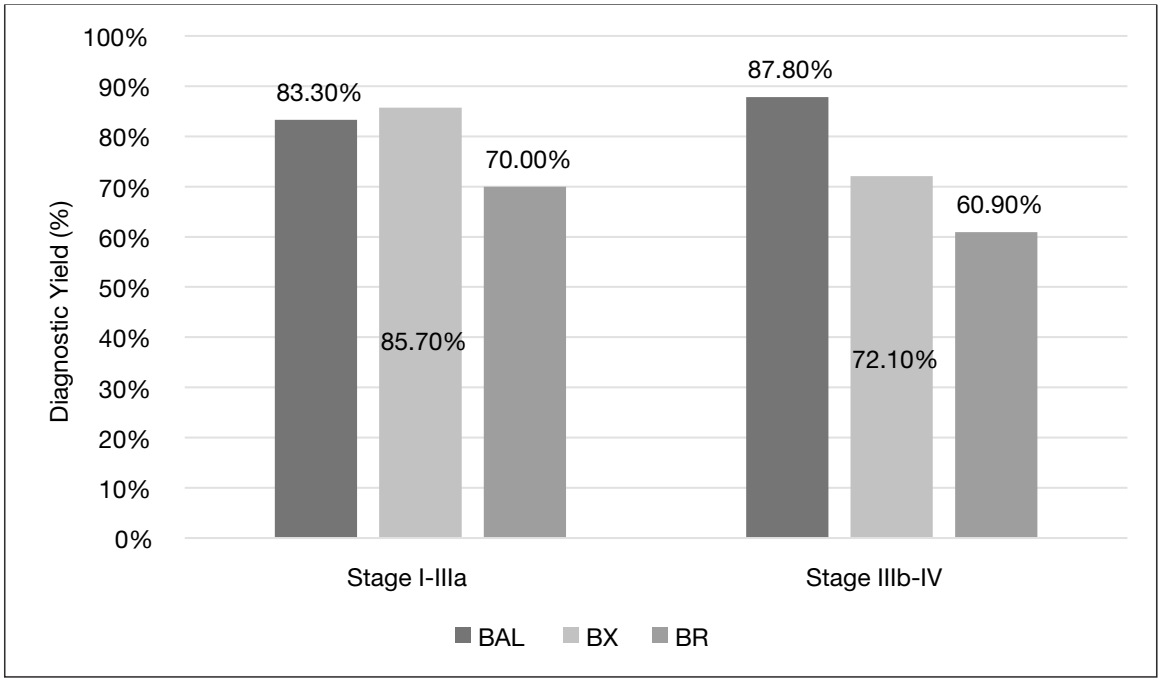

Figure 2. Diagnostic Yield by TNM Stage Across Sampling Methods

More recently, Fantin et al. suggested that the yield from brushing might improve by using robotic-assisted bronchoscopy or radial endobronchial ultrasound (r-EBUS); however, we did not use these technologies in our study.[7] Our results support the complementary role of brushing, especially in situations where a biopsy may be unsafe or technically difficult.

When looked at together, the total diagnostic yield of BAL, BX, and BR was 85.9%. This aligns with several large studies that support the use of multiple sampling methods. For instance, Popp et al. found that combining brushing, biopsy, and lavage increased diagnostic accuracy from 68% (using just one method) to over 88%.[11] Likewise, Rivera et al. pointed out the added benefit of using multiple methods in the American College of Chest Physicians guidelines.[3] A 2023 study by Fantin et al. also noted a combined diagnostic yield of 90% when all available methods were used on visible tumors.[7] These findings reinforce the idea that a structured step-by-step approach, starting with BAL and progressing to BR and BX, should be standard practice when possible.

Regarding tumor location, our results showed no significant difference in diagnostic yield across upper, middle, lower lobe, or hilar locations. This finding aligns with the results of Wongsurakiat et al. and Radke et al., who also observed site-independent yields in most cases.[9,12] This may be due to the fact that most tumors in our group were centrally located or at an advanced stage, which allowed easier access by bronchoscopy. In contrast, peripheral lesions often require guided tools, such as electromagnetic navigation or radial EBUS, to improve yield; these methods were not used in our setting.

In terms of histological subtype, BAL was most effective for adenocarcinoma, with a 76.9% success rate. It followed with small cell carcinoma at 70% and squamous cell carcinoma at 66.7%. These findings are consistent with those reported by Linder et al., who noted that BAL was particularly useful in identifying adenocarcinoma because of its exfoliative pattern.[13] Zhang et al. also highlighted the strong diagnostic and molecular value of BAL for adenocarcinoma subtypes.[10] They suggested including it in precision oncology practices. Therefore, the histological context should guide the choice and ranking of sampling methods.

No significant difference was found in diagnostic yield based on TNM staging. Both early-stage (Stage I-IIIa) and advanced-stage (Stage IIIb-IV) cancers showed similar results. This is slightly different from what Baaklini et al. reported, as they noted better yield in larger, more advanced tumors.14 However, it aligns with Rabahi et al., who found that performance was similar across stages.15 The consistent results in our study further support the use of BAL and BX, even in early-stage disease, as long as adequate sampling is done.

Finally, our study found a 65.4% complete agreement between BAL cytology and BX histology, along with a partial agreement of 30.8%. These results align with the findings of Gracia et al., who reported similar concordance between cytology and histology, thereby

Table 5. Cardiovascular assessment results of study cases

Parameter	Frequency, n (%)
Abnormal ECG (non-specific changes)	68 (28.9%)
Left ventricular dysfunction (EF < 50%)	32 (13.6%)
Myocardial fibrosis (on MRI)	21 of 42 scanned (50.0%)
Elevated NT-proBNP (>125 pg/mL)	56 (23.8%)
Elevated hs-Troponin I	19 (8.1%)
Pericardial effusion (mild/moderate)	14 (6.0%)

supporting the reliability of cytological sampling.16 Werpachowska et al. also highlighted the significance of the correlation between cytology and histology in assessing biopsy adequacy and planning follow-up procedures.17

Our study highlights the practical value of combining bronchoscopic sampling techniques, particularly BAL and BX, to improve the diagnostic yield in suspected bronchial carcinoma. Their consistent performance across different histological subtypes, anatomical sites, and disease stages demonstrates that these tools are reliable even in routine clinical practice, without the need for advanced navigational technologies. Although there are limitations, such as sample size and the lack of guided bronchoscopy methods, the strength of our results lies in their real-world applicability and connection to existing international evidence. These findings provide a basis for improving diagnostic protocols and support the use of multiple sampling techniques in standardized bronchoscopic workflows for the diagnosis of lung cancer.

Conclusion

Combining bronchoalveolar lavage, endobronchial biopsy, and endobronchial brushing significantly improves diagnostic yield for suspected bronchial carcinoma. Endobronchial biopsy offers the highest accuracy, especially for visible lesions. Bronchoalveolar lavage is effective when biopsy is not possible or for adenocarcinoma subtypes. Although endobronchial brushing is less sensitive on its own, it adds value when combined with other methods. Diagnostic yield remains consistent regardless of tumor location or stage, highlighting the robustness of these techniques. These findings support the adoption of a multimodal bronchoscopic strategy as standard practice, particularly in settings where advanced tools are limited.

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