Section: Pulmonology

Original Research Article

COMPARISON OF ENDOBRONCHIAL CRYOBIOPSY AND CONVENTIONAL FORCEPS BIOPSY IN SUSPECTED LUNG CARCINOMA: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE CENTRE

Davinder Kumar Kundra[1], Vikas Jaiswal[2], Sachin Baliyan[3]

[1]Unit Head, Department of Pulmonology (Respiratory and Sleep Medicine), Manipal Hospital Dwarka, Delhi, India
[2]HOD, Department of Pulmonology, Popular Group of Hospital, Varanasi, India
[3]Senior Consultant, Oncoplus Hospital, New Delhi

Received *: 12/01/2026*
Received in revised form *: 08/03/2026*
Accepted *: 25/03/2026*

Corresponding Author:
Dr. Davinder Kumar Kundra,
Unit Head, Department of Pulmonology (Respiratory and Sleep Medicine), Manipal Hospital Dwarka, Delhi, India.
Email: drkundra@gmail.com

DOI: 10.70034/ijmedph.2026.2.54

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (2); 325-331

ABSTRACT

Background: Accurate histopathological and molecular diagnosis is essential in the management of lung carcinoma, particularly in the era of targeted therapy and immunotherapy. Conventional endobronchial forceps biopsy, though widely used, often yields small and fragmented specimens with crush artifacts. Cryobiopsy has emerged as a promising alternative that may provide larger and better-preserved tissue samples. This study compared the diagnostic yield, specimen adequacy, and safety of cryobiopsy versus forceps biopsy in patients with suspected lung carcinoma presenting with visible endobronchial lesions.

Materials and Methods: This hospital-based cross-sectional study included 76 adult patients undergoing flexible bronchoscopy for suspected lung carcinoma with visible endobronchial growth. All patients underwent both forceps biopsy and cryobiopsy during the same procedure. Primary outcome was diagnostic yield. Secondary outcomes included specimen size, adequacy for immunohistochemistry (IHC) and molecular testing, crush artifact, and procedure-related complications. Statistical analysis was performed using paired tests, with $p < 0.05$ considered significant.

Results: Cryobiopsy demonstrated significantly higher diagnostic yield compared to forceps biopsy (88.2% vs 68.4%; $p = 0.002$). Mean specimen size was larger with cryobiopsy (6.8 ± 1.9 mm vs 3.2 ± 1.1 mm; $p < 0.001$), with significantly lower crush artifact (7.9% vs 42.1%; $p < 0.001$). Adequacy for IHC (85.5% vs 57.9%; $p < 0.001$) and molecular testing (81.6% vs 50.0%; $p < 0.001$) was superior with cryobiopsy. Bleeding was more frequent with cryobiopsy (39.5% vs 23.7%; $p = 0.041$), though predominantly mild and manageable. No major procedure-related morbidity or mortality was observed.

Conclusion: Endobronchial cryobiopsy provides significantly higher diagnostic yield and superior molecular adequacy compared to conventional forceps biopsy, with an acceptable safety profile. Incorporation of cryobiopsy into routine bronchoscopic practice may enhance diagnostic precision and reduce the need for repeat procedures in lung carcinoma evaluation.

Keywords: Cryobiopsy; Forceps biopsy; Lung carcinoma; Endobronchial lesion; Diagnostic yield.

INTRODUCTION

Lung cancer remains the leading cause of cancer-related mortality worldwide, accounting for approximately 2.2 million new cases and 1.8 million deaths annually, representing nearly 18% of all cancer deaths globally.[1] In India, lung carcinoma constitutes one of the most common malignancies among males and is increasingly observed among females, with late-stage presentation being frequent due to delayed diagnosis.[2] Early and accurate histopathological confirmation is crucial not only for

establishing the diagnosis but also for molecular profiling and therapeutic decision-making in the era of precision oncology.

Flexible bronchoscopy plays a central role in the diagnostic evaluation of suspected lung carcinoma, particularly in patients with visible endobronchial lesions. Conventional endobronchial forceps biopsy has long been considered the standard diagnostic technique in such cases, with reported diagnostic yields ranging from 60–85% depending on lesion characteristics, size, and operator expertise.[3,4] However, forceps biopsy samples are often small, fragmented, and susceptible to crush artifacts, which may compromise histopathological interpretation and limit the adequacy of tissue for immunohistochemistry and molecular testing.[5] With the increasing need for molecular biomarkers such as EGFR mutations, ALK rearrangements, and PD-L1 expression to guide targeted therapy and immunotherapy, obtaining larger and better-preserved tissue samples has become imperative.[6]

Transbronchial cryobiopsy has emerged as a novel technique that utilizes rapid freezing to obtain tissue samples with minimal mechanical distortion. By adhering tissue to the cryoprobe tip through rapid cooling (typically using carbon dioxide or nitrous oxide), larger and more intact biopsy specimens can be retrieved compared to conventional forceps biopsy. Studies have demonstrated that cryobiopsy specimens may be three to five times larger in surface area than forceps samples and are associated with reduced crush artifact, thereby enhancing diagnostic accuracy.[6,7] Initially established in the evaluation of interstitial lung diseases, cryobiopsy has increasingly been applied in endobronchial tumors with promising diagnostic yields exceeding 85–95% in some series.[8]

Despite these advantages, concerns remain regarding the safety profile of cryobiopsy, particularly the risks of bleeding and airway complications. Although most bleeding episodes are mild to moderate and manageable endoscopically, standardized protocols and operator experience are essential to ensure safety.[9] Furthermore, there is limited data from developing countries comparing cryobiopsy and forceps biopsy specifically in patients with suspected lung carcinoma presenting with visible endobronchial growths.

Given the growing demand for high-quality tissue sampling for histopathological and molecular analysis, and the need to balance diagnostic yield with procedural safety, a direct comparison between cryobiopsy and conventional forceps biopsy in patients with suspected lung carcinoma and endobronchial lesions is warranted. The present cross-sectional study was therefore undertaken to compare the diagnostic adequacy, sample quality, and safety outcomes of cryobiopsy and forceps biopsy in this clinically significant population.

MATERIALS AND METHODS

Study Design and Setting: This hospital-based cross-sectional comparative study was conducted in the Department of Pulmonary Medicine in collaboration with the Department of Pathology at a tertiary care teaching hospital over a period of 18 months between October 2023 to October 2025. The study aimed to compare the diagnostic yield, specimen quality, and safety profile of transbronchial cryobiopsy and conventional forceps biopsy in patients with suspected lung carcinoma presenting with visible endobronchial lesions. The study protocol was approved by the Institutional Ethics Committee, and all procedures were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

Study Population: Patients aged ≥18 years with clinical and radiological suspicion of lung carcinoma who were scheduled for diagnostic flexible bronchoscopy and found to have visible endobronchial growth during the procedure were considered eligible. Suspicion of malignancy was based on clinical features (chronic cough, hemoptysis, unexplained weight loss, dyspnea), imaging findings on chest radiograph and/or contrast-enhanced computed tomography (CECT) thorax suggestive of an endobronchial mass, and multidisciplinary evaluation.

Patients were excluded if they had uncorrectable coagulopathy (platelet count <50,000/mm³, INR >1.5), severe hypoxemia (SpO_2 <88% on room air), hemodynamic instability, recent myocardial infarction, severe pulmonary hypertension, inability to tolerate bronchoscopy, pregnancy, or refusal to provide consent.

Sample Size: The sample size was calculated based on expected differences in diagnostic yield between cryobiopsy and forceps biopsy, assuming a diagnostic yield of approximately 85–90% for cryobiopsy and 65–75% for forceps biopsy, with 80% power and 5% level of significance. Using a two-sided test for comparison of paired proportions (as both procedures were performed in the same patient), the minimum required sample size was estimated to be 68 patients. Considering an anticipated 10–12% rate of inadequate samples, procedural dropouts, or exclusion due to unforeseen intra-procedural complications such as significant bleeding or poor patient tolerance—factors commonly encountered in routine bronchoscopic practice in Indian tertiary care settings—the sample size was inflated accordingly. Thus, a total of 76 patients were enrolled in the study to ensure adequate statistical power and reliability of the findings.

Bronchoscopic Procedure: All bronchoscopic procedures were performed in a dedicated bronchoscopy suite under standard monitoring, including continuous electrocardiography, pulse oximetry, and non-invasive blood pressure monitoring. Patients were kept fasting for at least 6 hours prior to the procedure. Flexible bronchoscopy

was performed using a standard adult video bronchoscope under local anesthesia with 2% lignocaine and conscious sedation using intravenous midazolam and/or fentanyl as per institutional protocol. Supplemental oxygen was administered throughout the procedure.

After systematic airway inspection, patients with visible endobronchial lesions underwent both conventional forceps biopsy and cryobiopsy during the same sitting. To minimize sampling bias, forceps biopsy was performed first, followed by cryobiopsy from the same lesion site or an adjacent representative area. A minimum of 3–5 forceps biopsy samples were obtained using standard endobronchial biopsy forceps.

For cryobiopsy, a flexible cryoprobe (1.9 mm or 2.4 mm diameter) connected to a cryotherapy unit using carbon dioxide or nitrous oxide as the cryogen was introduced through the working channel of the bronchoscope. The cryoprobe tip was placed in direct contact with the lesion, and freezing was applied for approximately 3–5 seconds. The bronchoscope and cryoprobe were then withdrawn en bloc with the frozen tissue attached to the probe tip. The specimen was immediately thawed in normal saline and transferred to formalin. A minimum of 1–3 cryobiopsy samples were obtained per patient.

Prophylactic measures to control bleeding, including the availability of cold saline, diluted adrenaline solution, and balloon tamponade catheter, were ensured prior to cryobiopsy. The severity of bleeding was graded as mild (self-limiting or requiring suction only), moderate (requiring topical vasoconstrictors), or severe (requiring advanced interventions such as balloon tamponade or procedure termination).

Histopathological Evaluation: All biopsy specimens were fixed in 10% neutral buffered formalin and processed according to standard histopathological protocols. Paraffin-embedded sections were stained with hematoxylin and eosin (H&E). Immunohistochemistry (IHC) was performed where required for tumor typing (e.g., TTF-1, p40, CK7) as per standard diagnostic algorithms.

Specimen adequacy was assessed by an experienced pulmonary pathologist who was blinded to the biopsy technique. Parameters evaluated included specimen size (maximum diameter in millimeters), presence of crush artifact, depth of tissue, preservation of architecture, and diagnostic adequacy. Diagnostic yield was defined as the proportion of biopsies that provided a definitive histopathological diagnosis of malignancy or a specific benign pathology.

Outcome Measures: The primary outcome measure was diagnostic yield of cryobiopsy versus forceps biopsy. Secondary outcome measures included specimen size, presence of crush artifact, need for additional procedures due to non-diagnostic samples, and procedure-related complications, particularly bleeding severity and hypoxemia.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0. Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and percentages. Comparisons between cryobiopsy and forceps biopsy were performed using paired statistical tests, as both techniques were applied to the same patient, thereby minimizing inter-individual variability. The McNemar test was used to compare paired categorical outcomes, including overall diagnostic yield, adequacy for histopathology, immunohistochemistry (IHC), molecular testing, presence of crush artifact, and procedure-related bleeding. Continuous variables such as specimen size, number of samples obtained, and procedure duration were assessed for normality using the Shapiro–Wilk test. Normally distributed variables were compared using the paired Student's t-test, while non-normally distributed variables were analyzed using the Wilcoxon signed-rank test. Multivariate logistic regression analysis was performed to identify independent predictors of diagnostic success, with results expressed as adjusted odds ratios (OR) and 95% confidence intervals (CI). A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

The mean age of the study population was 59.4 ± 9.8 years with the majority belonging to the 60–69-year age group (36.8%). There was a marked male predominance (80.3%). A high burden of tobacco exposure was observed, with 51.3% current smokers and 23.7% former smokers; the mean smoking index among smokers was 28.6 ± 11.2 pack-years. Among females, 60.0% reported biomass fuel exposure. The most common presenting symptoms were cough (82.9%), weight loss (60.5%), and dyspnea (53.9%), while hemoptysis was present in 44.7% of cases. Radiologically, mediastinal lymphadenopathy was observed in 57.9% and endobronchial mass with distal collapse in 38.2%. Bronchoscopically, lesions were more frequently located in the right bronchial tree (59.2%), with the right upper lobe bronchus being the most common site (25.0%) [Table 1].

Cryobiopsy yielded significantly larger specimens compared to forceps biopsy (6.8 ± 1.9 mm vs 3.2 ± 1.1 mm; $p < 0.001$), despite requiring fewer samples (2.2 ± 0.6 vs 4.1 ± 0.8; $p < 0.001$). Adequacy for histopathological diagnosis was significantly higher with cryobiopsy (89.5% vs 69.7%; $p = 0.003$). Similarly, adequacy for IHC (85.5% vs 57.9%; $p < 0.001$) and molecular testing (81.6% vs 50.0%; $p < 0.001$) was markedly superior with cryobiopsy. Crush artifact was significantly more frequent in forceps biopsy specimens (42.1% vs 7.9%; $p < 0.001$). Additionally, deep stromal tissue was obtained in 78.9% of cryobiopsy samples compared to 38.2% of forceps samples ($p < 0.001$), indicating improved tissue architecture preservation. The overall diagnostic yield was significantly higher with

cryobiopsy compared to forceps biopsy (88.2% vs 68.4%; p = 0.002). In exophytic polypoidal lesions (n = 41), cryobiopsy demonstrated a yield of 92.7% compared to 75.6% with forceps biopsy (p = 0.031). Among infiltrative lesions (n = 35), diagnostic yield remained significantly superior with cryobiopsy (82.9% vs 60.0%; p = 0.021). Stratification by lesion size revealed that for lesions >2 cm (n = 49), cryobiopsy achieved a yield of 91.8% compared to 75.5% with forceps biopsy (p = 0.039). Even in smaller lesions (≤2 cm, n = 27), cryobiopsy maintained higher diagnostic success (81.5% vs 55.6%; p = 0.018), underscoring its consistent advantage across morphological subgroups [Table 2].

Table 1: Baseline Demographic, Clinical and Radiological Characteristics of Patients with Suspected Lung Carcinoma (n = 76).

Variable	Frequency (%)/mean ± SD
Age (years)	59.4 ± 9.8
Age Group (years)	
40–49	11 (14.5%)
50–59	24 (31.6%)
60–69	28 (36.8%)
≥70	13 (17.1%)
Gender	
Male	61 (80.3%)
Female	15 (19.7%)
Smoking Status	
Current smoker	39 (51.3%)
Former smoker	18 (23.7%)
Never smoker	19 (25.0%)
Pack-years (smokers)	28.6 ± 11.2
Biomass exposure (among females)	9/15 (60.0%)
Common Symptoms	
Cough	63 (82.9%)
Hemoptysis	34 (44.7%)
Dyspnea	41 (53.9%)
Chest pain	27 (35.5%)
Weight loss	46 (60.5%)
Radiological Findings (CECT)	
Endobronchial mass with collapse	29 (38.2%)
Hilar mass	21 (27.6%)
Central cavitary lesion	8 (10.5%)
Mediastinal lymphadenopathy	44 (57.9%)
Lesion Location (Bronchoscopy)	
Right upper lobe bronchus	19 (25.0%)
Right main bronchus	16 (21.1%)
Left main bronchus	14 (18.4%)
Left upper lobe bronchus	12 (15.8%)
Lower lobe bronchi	15 (19.7%)

(CECT: Contrast-Enhanced Computed Tomography)

Table 2: Detailed Comparison of Specimen Characteristics and Diagnostic Yield of Forceps Biopsy and Cryobiopsy (n = 76).

Parameter	Forceps Biopsy	Cryobiopsy	p-value
	Frequency (%)/mean ± SD		
Mean specimen size (mm)	3.2 ± 1.1	6.8 ± 1.9	<0.001
Mean number of samples taken	4.1 ± 0.8	2.2 ± 0.6	<0.001
Adequate for histopathology	53 (69.7%)	68 (89.5%)	0.003
Adequate for IHC	44 (57.9%)	65 (85.5%)	<0.001
Adequate for molecular testing	38 (50.0%)	62 (81.6%)	<0.001
Crush artifact present	32 (42.1%)	6 (7.9%)	<0.001
Deep stromal tissue obtained	29 (38.2%)	60 (78.9%)	<0.001
Overall diagnostic yield	52 (68.4%)	67 (88.2%)	0.002
Exophytic polypoidal lesion (n=41)	31 (75.6%)	38 (92.7%)	0.031
Infiltrative lesion (n=35)	21 (60.0%)	29 (82.9%)	0.021
Lesion >2 cm (n=49)	37 (75.5%)	45 (91.8%)	0.039
Lesion ≤2 cm (n=27)	15 (55.6%)	22 (81.5%)	0.018

(IHC: Immunohistochemistry)

Among the 67 cases with definitive diagnosis, squamous cell carcinoma was the most common histological subtype (47.8%), followed by adenocarcinoma (31.3%) and small cell carcinoma (11.9%). Less common diagnoses included large cell carcinoma (4.5%), carcinoid tumor (3.0%), and poorly differentiated NSCLC (1.5%). In adenocarcinoma cases (n = 21), cryobiopsy specimens demonstrated significantly higher adequacy for molecular testing compared to forceps biopsy. EGFR mutation testing was feasible in 85.7% of cryobiopsy samples versus 52.4% of forceps

samples (p = 0.02). Similarly, adequacy for ALK rearrangement testing was 81.0% versus 42.9% (p = 0.01), and for PD-L1 expression assessment was 90.5% versus 47.6% (p = 0.004), highlighting the superior molecular diagnostic capability of cryobiopsy [Table 3].

Table 3: Final Histopathological Spectrum and Molecular Testing Feasibility (n = 67 Diagnosed Cases).

Diagnosis	Frequency (%)
Squamous cell carcinoma	32 (47.8%)
Adenocarcinoma	21 (31.3%)
Small cell carcinoma	8 (11.9%)
Large cell carcinoma	3 (4.5%)
Carcinoid tumor	2 (3.0%)
Poorly differentiated NSCLC	1 (1.5%)
Forceps adequate	
EGFR mutation testing	11 (52.4%)
ALK rearrangement	9 (42.9%)
PD-L1 expression	10 (47.6%)
Cryobiopsy Adequate	
EGFR mutation testing	18 (85.7%)
ALK rearrangement	17 (81.0%)
PD-L1 expression	19 (90.5%)

(NSCLC: Non-Small Cell Lung Carcinoma; EGFR: Epidermal Growth Factor Receptor; ALK: Anaplastic Lymphoma Kinase; PD-L1: Programmed Death Ligand-1).

Cryobiopsy was associated with a significantly longer mean procedural duration compared to forceps biopsy (24.8 ± 5.6 minutes vs 18.6 ± 4.3 minutes; p < 0.001). Bleeding occurred more frequently following cryobiopsy (39.5%) compared to forceps biopsy (23.7%; p = 0.041), although the majority of episodes were mild and self-limiting. Moderate bleeding was observed in 10.5% of cryobiopsy cases versus 3.9% in forceps cases, while severe bleeding was rare (1.3%) and successfully managed without escalation of care. The requirement for topical adrenaline was higher in the cryobiopsy group (11.8% vs 3.9%; p = 0.048). Transient hypoxemia occurred in 11.8% of cryobiopsy procedures and 6.6% of forceps procedures (p = 0.26). No pneumothorax, ICU admissions, or procedure-related mortality were recorded [Table 4].

Table 4: Procedure Duration and Complication Profile of Forceps Biopsy and Cryobiopsy (n = 76).

Parameter	Forceps Biopsy	Cryobiopsy	p-value
	Frequency (%)/mean ± SD		
Mean procedure time (minutes)	18.6 ± 4.3	24.8 ± 5.6	<0.001
Any bleeding	18 (23.7%)	30 (39.5%)	0.041
Mild bleeding	15 (19.7%)	21 (27.6%)	—
Moderate bleeding	3 (3.9%)	8 (10.5%)	—
Severe bleeding	0 (0.0%)	1 (1.3%)	—
Adrenaline required	3 (3.9%)	9 (11.8%)	0.048
Balloon tamponade used	0 (0.0%)	2 (2.6%)	—
Transient hypoxemia (<90%)	5 (6.6%)	9 (11.8%)	0.26
Pneumothorax	0 (0.0%)	0 (0.0%)	—
ICU admission	0 (0.0%)	0 (0.0%)	—

On multivariate analysis, the use of cryobiopsy independently predicted diagnostic success (adjusted OR 3.42; 95% CI: 1.48–7.89; p = 0.004). Lesion size greater than 2 cm was also significantly associated with higher diagnostic yield (adjusted OR 2.11; 95% CI: 1.01–4.42; p = 0.047). Exophytic morphology showed a positive but non-significant association (p = 0.08). Smoking history greater than 20 pack-years did not independently predict diagnostic success (p = 0.45) [Table 5].

Table 5: Multivariate Logistic Regression Analysis of Factors Associated with Diagnostic Success.

Variable	Adjusted OR	95% CI	p-value
Cryobiopsy technique	3.42	1.48–7.89	0.004
Lesion size >2 cm	2.11	1.01–4.42	0.047
Exophytic morphology	1.86	0.91–3.78	0.08
Smoking history (>20 pack-years)	1.34	0.62–2.91	0.45

(OR: Odds Ratio; CI: Confidence Interval)

DISCUSSION

The present cross-sectional study demonstrates that endobronchial cryobiopsy provides significantly higher diagnostic yield and superior tissue adequacy compared to conventional forceps biopsy in patients with suspected lung carcinoma presenting with visible endobronchial lesions. Cryobiopsy achieved an overall diagnostic yield of 88.2% compared to 68.4% with forceps biopsy (p = 0.002), while also producing larger specimens with substantially

reduced crush artifact and improved suitability for immunohistochemistry (IHC) and molecular testing.

Our findings are consistent with multiple international studies by Nakai et al., Giri et al., and Hetzel et al., that have reported superior diagnostic performance of cryobiopsy in endobronchial malignancies. Hetzel et al., reported diagnostic yields exceeding 90% with cryobiopsy compared to approximately 65–75% with forceps biopsy, attributing the difference to larger specimen size and preserved tissue architecture.[11] Similarly, Giri et al. demonstrated significantly improved diagnostic accuracy and reduced crush artifacts with cryobiopsy.[11] The present study reinforces these findings within the Yong et al., Kumar et al., and Shinagawa et al., where the diagnostic yield of conventional forceps biopsy in routine practice often ranges between 60–75%, particularly in infiltrative lesions.[12-14]

The mean specimen size in our study was more than double with cryobiopsy (6.8 ± 1.9 mm vs 3.2 ± 1.1 mm; $p < 0.001$), with deep stromal tissue obtained in nearly 79% of cases. This directly translates into higher histopathological adequacy (89.5% vs 69.7%; $p = 0.003$) and significantly lower crush artifact (7.9% vs 42.1%; $p < 0.001$). Mechanistically, unlike forceps biopsy—which relies on mechanical cutting and compression—cryobiopsy freezes tissue at the probe tip, allowing en bloc extraction with minimal distortion.[15,16] This preservation of tissue architecture is particularly valuable in poorly differentiated tumors where morphological assessment is critical.[17,18]

An important observation in our study was the consistent superiority of cryobiopsy across both exophytic and infiltrative lesions. Even in smaller lesions (≤2 cm), cryobiopsy maintained a significantly higher diagnostic yield (81.5% vs 55.6%; $p = 0.018$). This is clinically relevant, as smaller central lesions frequently pose diagnostic challenges with forceps due to limited tissue capture and fragmentation.[18,19]

Our multivariate analysis further confirmed cryobiopsy as an independent predictor of diagnostic success (adjusted OR 3.42; $p = 0.004$), even after adjusting for lesion size and morphology. This strengthens the argument that the technique itself contributes significantly to improved outcomes rather than lesion characteristics alone.[20,21]

With the increasing reliance on molecular profiling for non-small cell lung carcinoma (NSCLC), tissue adequacy has become a critical determinant of clinical decision-making.[22] In our cohort, cryobiopsy samples demonstrated markedly superior adequacy for EGFR mutation analysis (85.7% vs 52.4%; $p = 0.02$), ALK rearrangement testing (81.0% vs 42.9%; $p = 0.01$), and PD-L1 expression assessment (90.5% vs 47.6%; $p = 0.004$).

These findings align with contemporary global data emphasizing the need for larger and intact specimens for biomarker testing. Studies by Tanaka et al., Hetzel et al., and Sharma et al., repeat showed that bronchoscopic procedures due to inadequate tissue impose additional economic burden and delay treatment initiation.[23-25] Thus, cryobiopsy may have substantial cost-effectiveness implications by reducing repeat diagnostic interventions.[26]

The predominance of squamous cell carcinoma (47.8%) in our study reflects the central endobronchial location of lesions and the high smoking burden in Indian males in study by Sharma et al.[25] This distribution is comparable to several tertiary-care studies by where squamous histology remains common in centrally visible tumors, although adenocarcinoma incidence is rising overall.[23,24] The relatively high rate of mediastinal lymphadenopathy (57.9%) also indicates late-stage presentation, a well-recognized challenge in India.[26]

Bleeding was more frequent with cryobiopsy (39.5% vs 23.7%; $p = 0.041$), although most episodes were mild to moderate and manageable with topical measures. Only one patient (1.3%) experienced severe bleeding requiring additional intervention, and no pneumothorax or mortality occurred. Ehab et al., similarly reports higher bleeding rates with cryobiopsy but without significant increases in serious adverse events when performed by experienced operators.[27]

The slightly longer procedural duration (24.8 ± 5.6 vs 18.6 ± 4.3 minutes; $p < 0.001$) is expected due to equipment preparation and bleeding control measures. However, the trade-off between modestly increased procedure time and substantially improved diagnostic yield appears clinically justified.[28-30]

Clinical and Practical Implications

The results of this study have meaningful implications for bronchoscopy practice in India and other developing countries. The significantly higher diagnostic yield, improved molecular adequacy, and acceptable safety profile suggest that cryobiopsy may serve as a superior first-line endobronchial sampling technique in suspected lung carcinoma. This is particularly relevant in the current therapeutic landscape where timely molecular characterization directly influences targeted therapy and immunotherapy eligibility.

Given the burden of lung cancer in India and the need to optimize diagnostic pathways, integration of cryobiopsy into standard bronchoscopic practice may enhance diagnostic efficiency, reduce repeat procedures, and potentially improve patient outcomes.

Limitations: This study was conducted at a single tertiary-care center with a relatively modest sample size, which may limit generalizability. Although both techniques were performed in the same sitting to reduce inter-patient variability, operator experience could have influenced outcomes. Long-term follow-up and cost-effectiveness analysis were not evaluated. Additionally, advanced airway support such as rigid bronchoscopy backup was not routinely utilized, which may influence the safety profile in different institutional settings.

CONCLUSION

In patients with suspected lung carcinoma presenting with visible endobronchial lesions, cryobiopsy demonstrated significantly higher diagnostic yield, superior specimen quality, and markedly improved adequacy for immunohistochemical and molecular testing compared to conventional forceps biopsy. Despite a modest increase in procedure duration and manageable bleeding risk, cryobiopsy proved to be a safe and effective technique in a tertiary-care Indian setting. Given the growing importance of molecular profiling in guiding targeted therapy and immunotherapy, cryobiopsy offers a substantial advantage in optimizing diagnostic pathways. Incorporating cryobiopsy into routine bronchoscopic practice may reduce repeat procedures, enhance diagnostic precision, and ultimately improve clinical outcomes in lung cancer management.

REFERENCES

1. Li C, Lei S, Ding L, et al. Global burden and trends of lung cancer incidence and mortality. Chin Med J (Engl). 2023;136(13):1583-90.
2. Iyer H, Ghosh T, Garg A, et al. Lung cancer in Asian Indian females: Identification of disease-specific characteristics and outcome measures over a 12-year period. Lung India. 2023;40(1):4-11.
3. Roșu SM, Mitroi DM, Catană OM, et al. Flexible Bronchoscopy and Non-Small-Cell Lung Cancer Staging: A Narrative Review of Modern Techniques for Optimized Clinical Decision-Making. J Clin Med. 2025;14(16):5773.
4. Andolfi M, Potenza R, Capozzi R, Liparulo V, Puma F, Yasufuku K. The role of bronchoscopy in the diagnosis of early lung cancer: a review. J Thorac Dis. 2016;8(11):3329-37.
5. Wetcho T, Rattanaburi A, Kanjanapradit K. Quality of tissue from punch biopsy forceps vs. round loop electrode in colposcopically directed biopsy: a randomized controlled trial. J Gynecol Oncol. 2018;29(4):e52.
6. Dalurzo ML, Avilés-Salas A, Soares FA, et al. Testing for EGFR Mutations and ALK Rearrangements in Advanced Non-Small-Cell Lung Cancer: Considerations for Countries in Emerging Markets. Onco Targets Ther. 2021;14:4671-92.
7. Lentz RJ, Argento AC, Colby TV, Rickman OB, Maldonado F. Transbronchial cryobiopsy for diffuse parenchymal lung disease: a state-of-the-art review of procedural techniques, current evidence, and future challenges. J Thorac Dis. 2017;9(7):2186-203.
8. Ankudavicius V, Miliauskas S, Poskiene L, Vajauskas D, Zemaitis M. Diagnostic Yield of Transbronchial Cryobiopsy Guided by Radial Endobronchial Ultrasound and Fluoroscopy in the Radiologically Suspected Lung Cancer: A Single Institution Prospective Study. Cancers (Basel). 2022;14(6):1563.
9. Nakai T, Watanabe T, Kaimi Y, et al. Safety profile and risk factors for bleeding in transbronchial cryobiopsy using a two-scope technique for peripheral pulmonary lesions. BMC Pulm Med. 2022;22(1):20.
10. Giri M, Huang G, Puri A, Zhuang R, Li Y, Guo S. Efficacy and Safety of Cryobiopsy vs. Forceps Biopsy for Interstitial Lung Diseases, Lung Tumors, and Peripheral Pulmonary Lesions: An Updated Systematic Review and Meta-Analysis. Front Med (Lausanne). 2022;9:840702.
11. Hetzel J, Eberhardt R, Herth FJ, et al. Cryobiopsy increases the diagnostic yield of endobronchial biopsy: a multicentre trial. Eur Respir J. 2012;39(3):685-90.
12. Yong SS, Kapp CM. The rising role of cryobiopsy in diagnosis of pulmonary disorders: a narrative review. Curr Chall Thorac Surg. 2024;6:17.
13. Kumar V, Gupta KB, Aggarwal R. Yield of different bronchoscopic techniques in diagnosis of lung cancer. Int J Res Med Sci. 2017;5:4098–103.
14. Shinagawa N. A review of existing and new methods of bronchoscopic diagnosis of lung cancer. Respir. Investig. 2019;57:3–8.
15. Madkour, A.M., Osman, N.M., Hewedi, I. et al. Diagnostic utility and safety profile of bronchoscopic cryobiopsy versus forceps biopsy in endobronchial and parenchymal lung lesions: a comparative study. Egypt J Bronchol. 2025;19:141.
16. Husnain SMN, Sarkar A, Huseini T. Utility and Safety of Bronchoscopic Cryotechniques—A Comprehensive Review. Diagnostics. 2023;13(18):2886.
17. Aktas Z, Gunay E, Hoca NT, et al. Endobronchial cryobiopsy or forceps biopsy for lung cancer diagnosis. Ann Thorac Med. 2010;5(4):242-6.
18. Cheng TL, Huang ZS, Zhang J, et al. Comparison of cryobiopsy and forceps biopsy for the diagnosis of mediastinal lesions: A randomised clinical trial. Pulmonology. 2024;30(5):466-74.
19. Nishimatsu K, Matsumoto Y, Kashima J, et al. Concordance between cryobiopsy and forceps biopsy specimens in assessment of immunohistochemistry staining for non-small cell lung carcinoma. Transl Lung Cancer Res 2023;12(6):1245-55.
20. Misra S, Bandyopadhyay A, Patra A, Mitra R, Sengupta A, Kundu S. A single-centre, randomised trial to compare diagnostic yield and safety between endobronchial cryobiopsy and endobronchial forceps biopsy procedure in patients with endobronchial lesions. Lung India. 2025;42(3):204-10.
21. Häntschel M, Eberhardt R, Petermann C, et al. Diagnostic Yield of Transbronchial Lung Cryobiopsy Compared to Transbronchial Forceps Biopsy in Patients with Sarcoidosis in a Prospective, Randomized, Multicentre Cross-Over Trial. J Clin Med. 2021;10(23):5686.
22. Arıcı MÖ, Demirkan B, Taştekin E, Kıvrak Salim D. Molecular Profiling in Non-Small-Cell Lung Cancer: A Single-Center Study on Prevalence and Prognosis. Curr Oncol. 2025;32(5):274.
23. Tanaka M, Matsumoto Y, Imabayashi T, et al. Diagnostic value of a new cryoprobe for peripheral pulmonary lesions: a prospective study. BMC Pulm Med. 2022;22:226.
24. Hetzel J, Linzenbold W, Boesmueller H, et al. Evaluation of Efficacy of a New Cryoprobe for Transbronchial Cryobiopsy: A Randomized, Controlled in vivo Animal Study. Respiration. 2020;99:248-56.
25. Sharma D, V V, Saini JK, Sethi P, Jain S, Puskar K. Elucidating diagnostic efficacy and safety of the procedure: cryobiopsy of endobronchial lesions with a flexible bronchoscope. Monaldi Arch Chest Dis. 2024;94(4).
26. Nasu S, Okamoto N, Suzuki H, et al. Comparison of the Utilities of Cryobiopsy and Forceps Biopsy for Peripheral Lung Cancer. Anticancer Res. 2019;39(10):5683-8.
27. Ehab A, Khairy El-Badrawy M, Abdelhamed Moawad A, El-Dosouky Abo-Shehata M. Cryobiopsy versus forceps biopsy in endobronchial lesions, diagnostic yield and safety. Adv Respir Med. 2017;85(6):301-6.
28. Moghazy MA, Elgazzar AG, Mohammad OI, Mohammed NA, Moussa HH. Comparison between endobronchial forceps-biopsy and cryo-biopsy by flexible bronchoscopy in the diagnosis of lung cancer. Benha J Appl Sci. 2021;6(5):27-30.
29. Zhang J, Guo JR, Huang ZS, et al. Transbronchial mediastinal cryobiopsy in the diagnosis of mediastinal lesions: a randomised trial. Eur Respir J. 2021;58(6):2100055.
30. Kho SS, Chan SK, Yong MC, Tie ST. Performance of transbronchial cryobiopsy in eccentrically and adjacently orientated radial endobronchial ultrasound lesions. ERJ Open Res. 2019;5(4):00135-2019.