Assessing the effectiveness and safety of transbronchial lung cryobiopsy utilizing a flexible bronchoscope with an endobronchial blocker in diffuse parenchymal lung lesions

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Abstract

Transbronchial lung cryobiopsy (TBLC) with flexible bronchoscope represents an encouraging modality to obtain a larger-sized specimen without crush artifact and a higher diagnostic yield in patients with diffuse parenchymal lung lesions/diseases as compared to conventional transbronchial lung biopsy, and fewer complications as opposed to surgical lung biopsy. An artificial airway is preferred as it provides better airway protection in cases of severe bleeding. Although various researchers have published data on different modalities, the data is not sufficient to standardize a single technique. This study describes the procedural technique, safety, and yield of TBLC using a flexible bronchoscope with an endobronchial blocker. We performed a retrospective analysis of 100 consecutive patients who underwent TBLC using flexible bronchoscopy from May 2018 to June 2022. TBLC samples were obtained under moderate sedation without the use of an artificial airway or fluoroscopy. Among the 100 patients, the majority were male (63%). The mean age of the enrolled patients was 44.43±15.92 years. The predominant diagnoses in our study were hypersensitivity pneumonitis (27%), followed by sarcoidosis (12%) and tuberculosis (10%). We obtained alveolated lung tissue in 90 out of 100 cases with a median biopsy size of 5 mm (in greatest dimension, interquartile range 5-4 mm), resulting in a specific histopathological diagnosis in 82 cases. The most frequent complications were bleeding and pneumothorax (13%). Mild bleeding occurred in 58% of the patients, and moderate bleeding occurred in 20%. There was no episode of severe/life-threatening bleeding. None of the patients required intensive care unit admission or endotracheal intubation. In conclusion, the use of TBLC through flexible bronchoscopy with an endobronchial blocker emerges as a minimally invasive, secure, time-efficient, and readily reproducible technique. Significantly, this procedure can be seamlessly executed in the bronchoscopy suite, eliminating the requirement for an artificial airway or general anesthesia.

Introduction

Diffuse parenchymal lung disease (DPLD) encompasses a diverse range of over 200 pulmonary disorders, classified into various subtypes according to their clinical, radiological, and histopathological characteristics. The diagnosis of DPLD poses a significant challenge. When the clinical evaluation, laboratory test-

ing, imaging, and lung function data do not suffice to reach a definitive diagnosis, lung biopsy with histopathological examination of the tissue is often necessary to obtain a conclusive diagnosis. A recent expert panel report has recommended that transbronchial lung cryobiopsy (TBLC) may be considered as an alternative to surgical lung biopsy (SLB) owing to fewer complications and acceptable diagnostic yield, by adopting precautionary measures such as fluoroscopy and endobronchial blocker [1]. Different operators have described various techniques to perform TBLC [1-9]. Due to the associated high morbidity and non-availability of SLB, computed tomography followed by transbronchial lung biopsy (TBLB) continues to remain the mainstay of diagnosis of DPLDs in the majority of the centers. The small size of the TBLB specimen makes it a "histopathologist's nightmare", leading to difficulty in categorization within the spectrum of DPLDs. Although rigid bronchoscopy with bronchial blocker is the preferred modality for TBLC, the requirements for general anesthesia and rigid bronchoscopy setup are the reasons for its limited utilization. Development of a safe and efficacious technique to perform TBLC with a flexible bronchoscope in the bronchoscopy room should address these practical issues. The present study was undertaken to evaluate the yield and safety of TBLC using a flexible bronchoscope with an Arndt endobronchial blocker.

Materials and Methods

Study design, population and settings

This retrospective analysis involved 100 consecutive cases of suspected DPLDs in whom TBLC was performed using a flexible bronchoscope under sedation at our tertiary care referral center from May 2018 to June 2022. Ethical clearance was obtained from the institutional ethical committee. Patients with diffuse parenchymal lung infiltrates for whom a definitive diagnosis could not be established following clinical, radiological, and laboratory assessments were included in this study. Patients with platelet count <70,000/mm³, an international normalized ratio >1.5, or an activated partial thromboplastin time >50 seconds were excluded from the study. Additionally, exclusion criteria included a forced expiratory capacity below 50%, forced expiratory volume in the first second below 0.8 L, diffuse bullous disease, or any major comorbidities like severe cardiac, renal, liver disease, or history of bleeding disorder. Patients with pulmonary hypertension and those requiring oxygen were high-risk candidates, and a detailed risk-benefit assessment was done prior to the procedure. Procedural complications, including bleeding, pneumothorax, and histopathological diagnosis, were analyzed.

Aim of the study

The objective of this study was to assess the safety, diagnostic yield, and potential complications associated with TBLC in patients with diffuse parenchymal lung lesions.

Procedural technique

Equipment

Therapeutic flexible bronchoscope (instrument channel diameter 2.8 mm), Cryostation with gas (cryogen) cylinder, 1.9 mm outer diameter flexible cryoprobe (ERBE, Tubingen, Germany), 9.0 Fr Arndt endobronchial blocker set (Cook Inc., Bloomington, USA), bite block, and airway resuscitation equipment. The bronchoscopist

should be proficient in handling airway emergencies and performing endotracheal intubation if needed during the procedure.

Patient preparation and procedure

A comprehensive clinical history was obtained, encompassing details on smoking habits, occupational hazards, and drug and pet exposure. Additionally, a chest radiograph and high-resolution computed tomography (HRCT) scan of the thorax were performed along with blood tests comprising complete blood profile, liver function test, renal function test, and coagulation profile. All procedures were carried out in the bronchoscopy suite as a daycare procedure without the presence of an anesthetist. Subjects on anticoagulants and aspirin, we performed the procedure after discontinuing the drug for 2-5 days (depending on the drug the patient was taking) and ensuring that the international normalized ratio was less than 1.5. Patients were kept fasting (2 hours for liquids and 6 hours for solids before procedure) for the bronchoscopy, and a written informed consent was obtained before the procedure. No premedication was given. Topical anesthesia included 2 mL of 4% lignocaine and 2 mL of normal saline nebulization for 5 minutes to 10 minutes prior to the procedure. For pharyngeal anesthesia, 3-5 sprays of 10% lignocaine were used, and the loss of gag reflex was used as an indicator of adequate anesthesia. Intravenous midazolam and fentanyl were used for sedation. Starting with 1 mg of midazolam and 25 μg of fentanyl, an intermittent bolus of the same dose was repeated to achieve the desired level of sedation during the procedure. The average required dose of midazolam and fentanyl was 2 mg and 75 μg, respectively. Supplemental oxygen was provided through a nasal cannula, and patients had spontaneous breathing without any support of an artificial airway or assisted ventilation. After ensuring that the patient was sedated, a bite block was placed in the mouth. No CO2 monitor was used. The pulmonologist assessed sedation through clinical monitoring, utilizing indicators such as heart rate, blood pressure, level of consciousness, and pupil size. An adult therapeutic broncho-videoscope (Olympus BF-1TQ170, Olympus Corporation, Aomori, Japan; channel diameter: 2.8 mm, outer diameter: 6.0 mm) was utilized, and an adjustable guide loop of the Arndt blocker was coupled with the distal end of the bronchoscope (Figure 1A). A bronchoscope with an Arndt blocker was then simultaneously introduced through the mouth, and a method of applying a 1% lignocaine solution through a "spray-as-you-go" approach was employed to provide topical anesthesia to the vocal cords and tracheobronchial tree. Before the sampling procedure, a bronchoscopic examination of the bronchial tree was conducted, and the Arndt blocker was released into the target lobar bronchus by loosening the loop. An assistant held the blocker in place at the level of the bite block. The video bronchoscope was kept proximal to the Arndt blocker. The blocker balloon was inflated and deflated to ensure the patient's tolerance and adequacy of the balloon to block the target bronchus. The flexible bronchoscope was then advanced into the segment to be biopsied. Before biopsy, the cryoprobe was tested in room temperature saline to determine the optimal freezing time. A flexible cryoprobe of 1.9 mm (outer diameter) size and length of 900 mm (ERBE, Tubingen, Germany) was inserted through the bronchoscope instrument channel port and advanced till resistance was felt. Once resistance was encountered (up to pleura), the probe was retracted by 1.5 cm and activated for 3-6 seconds. No fluoroscopic guidance was used. The flexible bronchoscope and cryoprobe were then quickly removed en-block. Immediately, the second assistant inflated the Arndt blocker to block off the target segments (Figure 1B) and secured it in place at the bite block to prevent any displacement. The biopsy sample was taken off after thawing in room temperature

saline. The bronchoscope was quickly reintroduced to confirm the inflation and correct positioning of the Arndt blocker and to look for bleeding (Figure 1C). The balloon was deflated after 30-40 seconds, and airways were observed for bleeding (Figure 1D). Typically, only one biopsy was taken from the area of significant radiographical abnormality from the lower lobes, however, up to 3 biopsies were performed if the specimen was found inadequate on visual inspection. The Arndt blocker was removed after ensuring adequate hemostasis. Subsequently, the bronchoscope was removed after performing airway toileting.

The patient was kept under observation for 2 hours; continuous monitoring was in place for electrocardiogram, heart rate, blood pressure, and oxygen saturation. Chest X-ray was done in all patients within 3 hours of the procedure to rule out pneumothorax. Post-biopsy bleeding was classified as per British Thoracic Society bronchoscopy guidelines [10]. Mild bleeding required broncho-

scopic aspiration, and bleeding halted on its own. Moderate bleeding required intubation with the bronchoscope in a wedge position, and use of adrenaline (1:10000) or cold saline to stop bleeding. Severe bleeding demanded interventions like bronchial blocker placement, resuscitation, blood transfusion, critical care unit admission, or death.

The study focused on primary endpoints, including the pathological diagnostic yield, the final multidisciplinary diagnosis, the sample size (in greatest dimension), and the complication rate (specifically, the occurrence of pneumothorax and bleeding). These endpoints collectively served as crucial measures to evaluate the effectiveness and safety of the procedures conducted in the study. Clinicians, radiologists, and pathologists subsequently reviewed clinical information, radiological characteristics, and biopsy findings obtained from TBLC. The final diagnosis was made by the institutional multidisciplinary diagnosis committee.
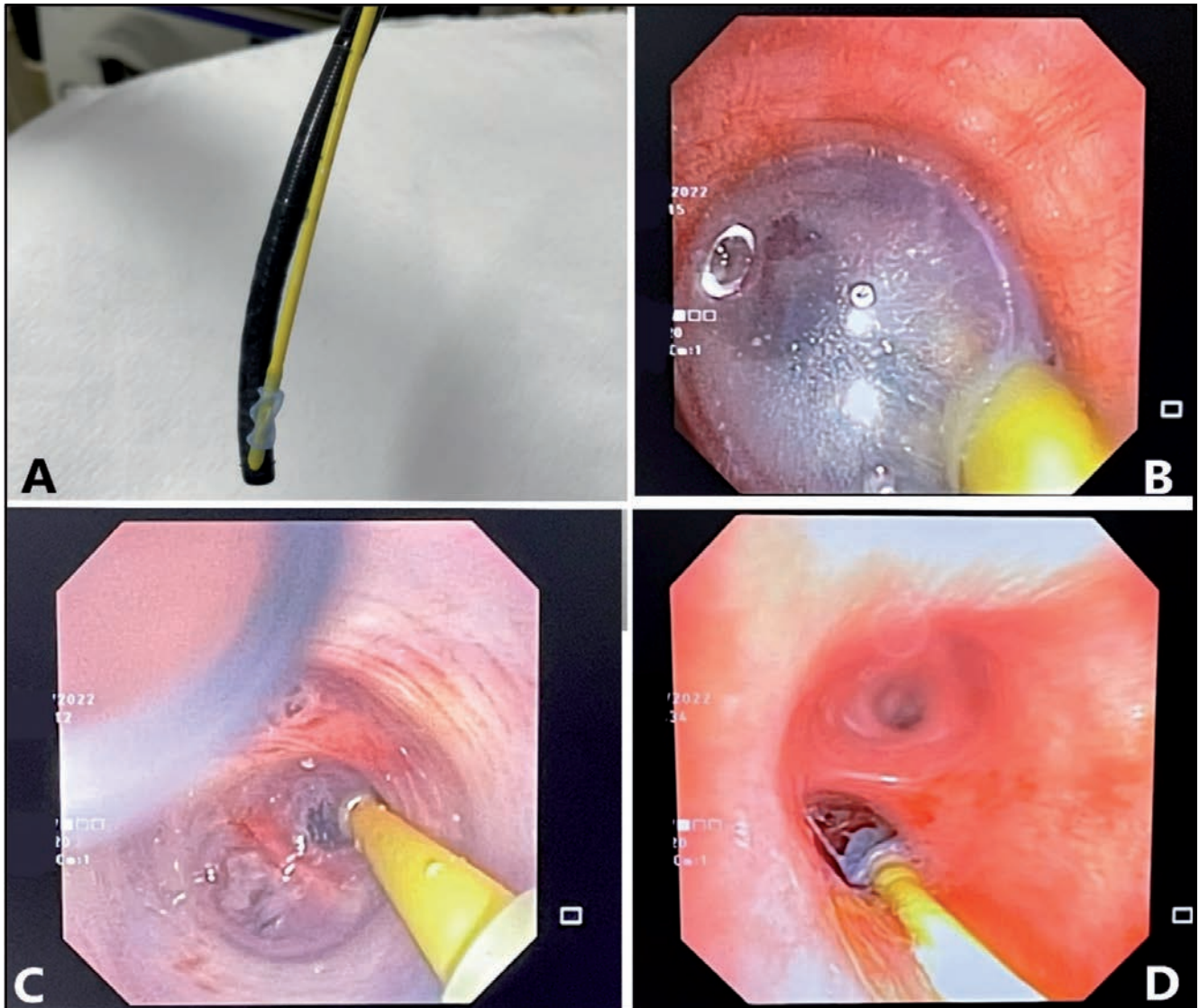
Figure 1. A) Securing the Arndt blocker to the bronchoscope before introducing the scope; B) bronchoscope view with the Arndt blocker inflated; C) bronchoscope view through the inflated balloon; D) bronchoscope view with the Arndt blocker deflated.

Statistics

The collected data were transformed into variables, coded, and entered into Microsoft Excel (Redmond, WA, USA). The data were analyzed and statistically evaluated using Statistical Package for Social Studies (IBM, Chicago, IL, USA), Windows version 23.0. Continuous variables were expressed in mean ± standard deviation, while discrete variables were expressed in number and percentage.

Results

Among 100 patients, 63 were male and 37 were female. The mean age of the enrolled patients was 44.43±15.92 years.
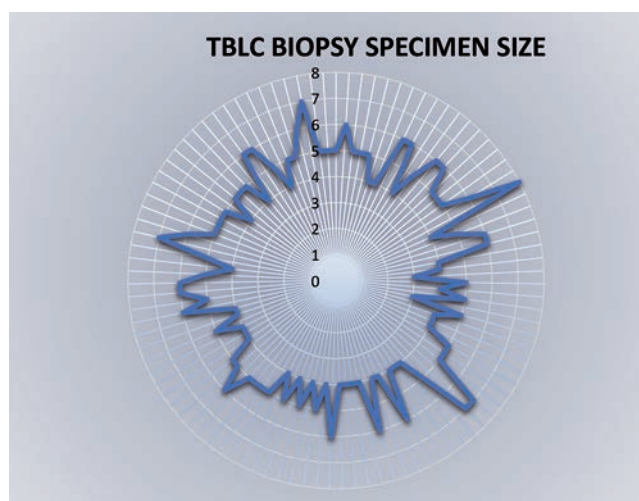
Figure 2. Radar graph depicting the tissue size obtained through transbronchial lung cryobiopsy (TBLC) (100 participants), ranging from 0 mm at the inner circle to 8 mm at the outer circle.

Alveolated lung tissue was obtained in 90 patients, and specimen size ranged between 4 mm to 8 mm, with a median size of 5 mm (in greatest dimension; interquartile range: 4-5 mm). The biopsy specimen size of the tissue is shown in Figure 2. The biopsy reports confirmed the existence of pleural tissue in 15 patients. No crush artifact was observed in any of the biopsy samples obtained.

Diagnostic yield

Definitive histopathological diagnosis was made in 82 patients, and for 8 patients, a confident diagnosis could not be ascertained based on histology. The remaining 10 samples were reported as inadequate bronchial mucosal tissue or non-specific inflammation. The most frequently identified diagnoses comprised hypersensitivity pneumonitis (n=27), followed by sarcoidosis (n=12), tuberculosis (n=10), adenocarcinoma (n=6), lymphangioleiomyomatosis (n=4), non-specific interstitial pneumonia (n=4), idiopathic pulmonary fibrosis (n=3), langerhans cell histiocytosis (n=3), organizing pneumonia (n=2), respiratory bronchiolitis associated interstitial lung disease (ILD) (n=2), and various less common conditions (such as lymphocytic interstitial pneumonia, follicular bronchiolitis, chronic bronchitis with emphysema, anthracosis, diffuse panbronchiolitis, anthrosilicotic fibrosis, obliterative bronchiolitis, lipoid pneumonia, and non-small cell carcinoma of the lung). Diagnosis with their histopathological findings obtained in the study is shown in Table 1.

Complications

In terms of safety, mild bleeding was observed in 58 patients, while 20 patients experienced moderate bleeding. Minimal or no bleeding was seen in 22 patients, and there were no mortalities or significant bleeding attributable to the procedure. Pneumothorax occurred in 13 patients, with 6 of them necessitating intercostal drainage tube placement, while the remaining cases were managed conservatively with high-flow oxygen therapy. Moreover, 8 out of 13 patients with pneumothorax (61.5%) had pleural tissue in the biopsy. Complications are detailed in Table 2.

Table 1. Different histological diagnoses obtained in the study.

Diagnosis	Histopathological findings	Number (n=100)
Hypersensitivity pneumonitis	Thickened interstitium with mononuclear cell infiltrates and fibrosis, ill-defined histiocytic cells	27
Sarcoidosis	Non-necrotizing granuloma with multinucleated giant cells	12
Tuberculosis	Necrotizing granulomatous inflammation with a central necrotic zone and mononuclear cells	10
Adenocarcinoma	Malignant epithelial cells forming a glandular and tubular pattern	6
Lymphangioleiomyomatosis (LAM)	Lung cysts, abnormal smooth muscle cell (LAM cell) clusters surrounding the cysts	4
Non-specific interstitial pneumonia	Interstitial and chronic inflammation with varying degrees of mononuclear cell inflammation	4
Idiopathic pulmonary fibrosis	Clusters of fibroblasts and myofibroblasts, loss of alveolar architecture with patchy subpleural distribution	3
Langerhans cell histiocytosis	Cysts and variably aggregates of Langerhans cells	3
Organizing pneumonia	Buds of granulation tissue within alveoli with mild chronic inflammation	2
Respiratory bronchiolitis-associated interstitial lung disease	Pigmented macrophages in the bronchiolar lumens with chronic inflammation and fibrosis	2
Diagnosis not made based on histology alone	Unclassifiable fibrosis, airway-centered interstitial inflammation	8
Others	-	9
Inadequate tissue/ bronchial mucosal tissue/non-specific inflammation	Hyperplastic epithelium of bronchial mucosa, squamous metaplasia, infiltrates in lamina propria, atypical cells, and normal lung parenchyma	10

Table 2. Complications observed in the study.

Complications	Number
Bleeding	n=100
No or minimal bleeding	22
Mild	58
Moderate	20
Severe	0
Pneumothorax	n=13
Required indwelling chest drain	6
Managed conservatively	7

Discussion

Timely diagnosis holds significant importance in effectively managing patients with DPLDs. Presently, the diagnosis of DPLD typically involves the use of HRCT and bronchoalveolar lavage, with the option of performing a lung biopsy and subsequent histopathological examination when deemed necessary. While SLB remains the most efficacious sampling method, it is associated with an elevated risk of infection, acute exacerbation, and a reported 3-4% mortality rate within 30 days [11,12]. The indications for TBLC in the diagnosis of DPLD/lesions are currently being assessed within the framework of a multidisciplinary discussion. Additionally, the comparison of its risks and benefits with those of SLB is under examination. However, the recent European Respiratory Society guidelines recommend performing TBLC for unclassifiable ILD when histopathological diagnosis is needed. For undiagnosed ILD patients with inconclusive TBLC results, the Task Force suggests proceeding to step-up SLB if histopathological data is required [13]. The reported diagnostic yields of TBLC in the literature range from 60% to 100% [6,7,9,14-18], and observed complications, such as pneumothorax (0–30%) and bleeding, exhibit considerable variability across different studies [6,7,9,14,19]. The standardization of the technique is currently under consideration.

In our study, TBLC was performed as a day-care procedure in a specialized bronchoscopy suite. The most prevalent diagnoses included hypersensitivity pneumonitis (27%), followed by sarcoidosis (12%), and tuberculosis (10%). This observation could be attributed to the contrast between India and the developed Western world. While 65% of ILD cases in Western countries are categorized as idiopathic interstitial pneumonia, the predominant ILD diagnosis in India is hypersensitivity pneumonitis, constituting approximately 47.3% of cases [20]. In our study, 10% of patients received a tuberculosis diagnosis following a biopsy indicating necrotizing granuloma. In a tuberculosis-endemic country such as India, it is crucial to consider infectious causes when faced with patients exhibiting radiological features suggestive of ILD, as pulmonary tuberculosis can closely resemble ILD [21]. In inadequately treated pulmonary tuberculosis cases, diagnosing becomes challenging due to subtle clinical features and misleading radiological signs like fibrosis or lymphadenopathy, often leading physicians to consider ILD.

Out of the 100 patients, alveolated lung tissue was successfully obtained in 90 cases. The tissue diagnosis, along with the clinico-radiological information, was integrated to establish a final multidisciplinary diagnosis for comprehensive patient management. A definitive histopathological diagnosis was provided for 82 patients. The diagnostic and clinical yields in our study stood at 82% and 90%, respectively. Notably, these values align closely with those reported by Ravaglia *et al.* (87.8% and 90.1%) [14]. In a study by O'Mahony *et al.*, utilizing the same modality, a diagnostic yield of 67.1% and a clinical yield of 93.3% were documented [6]. Bango-Alvarez *et al.* reported an 86% yield in their study employing two bronchoscopes in a sequential manner for TBLC [9]. Approximately 10% of cryobiopsies were deemed non-diagnostic, primarily due to limited alveolar tissue, bronchial mucosal tissue, and non-specific inflammation. The ideal biopsy size that allows for effective pattern recognition remains undetermined. In our study, biopsy specimen sizes varied between 4 mm and 8 mm, with a median size of 5 mm. Pathologists generally regard a specimen size of at least 5 mm (in greatest dimension) as appropriate for histological evaluation [22], and a greater diagnostic yield is typically associated with larger biopsy samples containing more alveolated lung tissue [15,23]. Recent research conducted by Loor *et al.* revealed the efficacy of TBLC in diagnosing acute rejection and assessing its severity among mechanically ventilated lung allograft patients. The study showed that utilizing a cryoprobe enabled the retrieval of more alveolar tissue and samples containing increased blood vessels. The researchers concluded that employing cryoprobes, whether 1.9 mm or 2.4 mm, significantly improved diagnostic accuracy compared to forceps. Furthermore, the diagnostic performance was notably enhanced when specifically using the 2.4 mm cryoprobe [24].

Pneumothorax occurred in 13% of our patients, representing a relatively common adverse event associated with TBLC. Among the 13 cases, 7 were managed conservatively, while 6 required chest tube drainage. The indwelling chest drain was removed within 1-5 days after achieving complete lung expansion in all patients. The incidence of pneumothorax in our study was higher than that reported by Bango *et al.* (4.7%) [9] and lower than the reported incidence (17%) observed in the study by O'Mahony *et al.* [6], both of which had a similar sample size to ours. Notably, the incidence of pneumothorax in TBLC varies widely across studies [6,7,9,14,19]. In a study by Dhooria *et al.*, a lower occurrence of pneumothorax was noted in patients undergoing TBLC under fluoroscopic guidance (5.9%) compared to those without fluoroscopy (20.9%) [25]. However, this trend is not consistently observed in all studies [23,26], suggesting the involvement of other factors, including patient characteristics, procedural factors, and the operator's level of skill. The presence of pleural tissue in histopathological examinations is recognized as a correlated risk factor for pneumothorax [23].

Bleeding represents a prevalent and apprehension-inducing complication associated with lung cryobiopsy, yet it is generally manageable through bronchoscopic intervention employing endobronchial blockers, ice-cold saline, and topical epinephrine instillation [6,9,23,25]. The literature describes bleeding rates ranging from 0% to 56% [6,9,14,18,27], although there exists considerable variation in the definition of bleeding severity across different studies. In our study, 58% of patients had mild bleeding, and 20% experienced moderate post-biopsy bleeding necessitating interventions such as iced saline and/or topical epinephrine, along with prolonged inflation of the Arndt blocker. None of these cases required endotracheal intubation or intensive care unit admission. In our study, echocardiography was not included in the pre-procedural assessment. We hypothesize that the absence of a diagnosis for pulmonary hypertension in certain patients may have contributed to the comparatively elevated incidence of bleeding observed in our study. All bleeding incidents were effectively managed within the confines of the bronchoscopy room, and no procedure-related fatalities occurred. A study by Hetzel *et al.* reported a significantly higher

incidence of moderate or severe bleeding following TBLC compared to TBLB (16.2% *vs*. 4.2%) [27]. In their meta-analysis [28], Johannson *et al*. identified substantial heterogeneity across studies reporting bleeding following TBLC, with a mean incidence of 26.6% and a range of 0% to 78%. They proposed that the diverse rates of bleeding could be attributed to variations in procedural techniques, such as the duration of freeze time and probe positioning. A recent meta-analysis also underscored a higher risk of moderate to severe bleeding in patients undergoing cryobiopsy compared to those undergoing forceps biopsy [29]. Notably, the majority of severe bleeding episodes reported in the literature were successfully controlled through the placement of a bronchial blocker or catheter [30]. The routine use of an endobronchial blocker has demonstrated a significant reduction in the occurrence of moderate to severe bleeding in recent studies [6,25,31].

The procedures were conducted in a dedicated bronchoscopy suite with an experienced team of bronchoscopists and nursing staff with standard monitoring equipment, intubation tools, and access to the intensive care unit if deemed necessary. The approach to conducting TBLC varies, encompassing factors such as the setting (bronchoscopy room *vs*. operating theater), the method of bronchoscopy (flexible *vs*. rigid), sedation (moderate sedation with a conscious patient *vs*. general anesthesia), and strategies for managing complications, such as bleeding. While this study did not specifically address these issues, it employed a straightforward and standard bronchoscopic approach utilizing an Arndt endobronchial blocker, which is easily replicable. Conducting flexible bronchoscopy in a bronchoscopy room with moderate sedation is a more cost-effective alternative than performing it in an operating room under general anesthesia. Depending on the institution, this approach may prove advantageous in countries with a high disease burden, where scheduling constraints in the operating room and economic considerations are prominent. Drawbacks associated with this approach primarily center around the potential for complications, particularly severe bleeding. While rigid bronchoscopy is the preferred option, its availability is limited in many centers. Our approach involved incorporating TBLC as a standard bronchoscopic procedure, implementing thorough precautionary measures.

Our study is subject to certain limitations, including retrospective study design and single-center experience. Notably, a significant portion of our cases involved hypersensitivity pneumonitis, sarcoidosis, and tuberculosis, which can be diagnosed with a small lung tissue sample. However, this stands in contrast to DPLDs with usual interstitial pneumonia (UIP) and other idiopathic interstitial pneumonias, where disease characterization necessitates both peripheral and larger lung tissue. Consequently, the use of a single biopsy sample may restrict the generalizability of our findings to other causes of DPLDs. It is important to note that we did not employ fluoroscopy due to its unavailability at our institute. The incorporation of fluoroscopy could potentially enhance patient safety. Additionally, the absence of an artificial airway/conduit influenced our decision to limit the number of biopsies to mitigate the risk of bleeding. However, it is crucial to highlight that this technique is not suitable for cases suspected to have UIP and other idiopathic interstitial pneumonias, where more lung tissue and peripheral sampling are required for disease characterization. The increased complexity of these cases raises the risk of potential complications, necessitating the use of general anesthesia with an airway conduit in such situations.

Ongoing studies aim to address the limitation of insufficient lung tissue for histopathological diagnosis in many cases. These investigations seek to enhance the efficacy and safety of TBLC through initiatives such as incorporating rapid on-site examination of the acquired tissue [32] and employing a sheathed cryoprobe with a 1.1 mm diameter [33].

Conclusions

Our study demonstrates that TBLC using flexible bronchoscopy with the Arndt blocker is a complex but high-yielding and safe procedure with a low prevalence of complications. To facilitate a successful execution, seamless collaboration among team members is essential during the procedure. Predefined roles should be assigned in advance, and a stepwise review of the process is recommended to enhance communication. Nevertheless, our current recommendation is that operators proficient in handling airway complications, preferably with prior experience in TBLC, should exclusively perform this procedural modality. It is advisable that such procedures take place in an institution equipped to manage respiratory emergencies.

References

1. Maldonado F, Danoff SK, Wells AU, et al. Transbronchial cryobiopsy for the diagnosis of interstitial lung diseases: CHEST guideline and expert panel report. Chest 2020;157:1030-42.
2. Hetzel J, Maldonado F, Ravaglia C, et al. Transbronchial cryobiopsies for the diagnosis of diffuse parenchymal lung diseases: expert statement from the cryobiopsy working group on safety and utility and a call for standardization of the procedure. Respiration 2018;95:188-200.
3. Dhooria S, Bal A, Sehgal IS, et al. Transbronchial lung biopsy with a flexible cryoprobe: first case report from India. Lung India 2016;33:64-8.
4. Madan K, Mittal S, Hadda V, Mohan A. Cryoprobe transbronchial lung biopsy with flexible bronchoscope using Arndt endobronchial blocker. Lung India 2019;36:241-3.
5. Madan K, Mittal S, Gupta N, et al. Cryoprobe transbronchial lung biopsy: how we do it? Lung India 2018;35:520-2.
6. O'Mahony AM, Burke L, Cavazza A, et al. Transbronchial lung cryobiopsy (TBLC) in the diagnosis of interstitial lung disease: experience of first 100 cases performed under conscious sedation with flexible bronchoscope. Ir J Med Sci 2021;190:1509-17.
7. Ramaswamy A, Homer R, Killam J, et al. Comparison of transbronchial and cryobiopsies in evaluation of diffuse parenchymal lung disease. J Bronchology Interv Pulmonol 2016;23:14-21.
8. Dhooria S, Sehgal IS, Bal A, et al. Transbronchial lung biopsy with a flexible cryoprobe during rigid bronchoscopy: standardizing the procedure. Lung India 2016;33:248-9.
9. Bango-Álvarez A, Ariza-Prota M, Torres-Rivas H, et al. Transbronchial cryobiopsy in interstitial lung disease: experience in 106 cases - how to do it. ERJ Open Res 2017;3:00148-2016.
10. Du Rand IA, Blaikley J, Booton R, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. Thorax 2013;68:i1-44.
11. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med 2011;183:788-824.

12. Kaarteenaho R. The current position of surgical lung biopsy in the diagnosis of idiopathic pulmonary fibrosis. Respir Res 2013;14:43.

13. Korevaar DA, Colella S, Fally M, et al. European Respiratory Society guidelines on transbronchial lung cryobiopsy in the diagnosis of interstitial lung diseases. Eur Respir J 2022;60:2200425.

14. Ravaglia C, Wells AU, Tomassetti S, et al. Diagnostic yield and risk/benefit analysis of trans-bronchial lung cryobiopsy in diffuse parenchymal lung diseases: a large cohort of 699 patients. BMC Pulm Med 2019;19:16.

15. Babiak A, Hetzel J, Krishna G, et al. Transbronchial cryobiopsy: a new tool for lung biopsies. Respiration 2009;78:203-8.

16. Griff S, Ammenwerth W, Schönfeld N, et al. Morphometrical analysis of transbronchial cryobiopsies. Diagn Pathol 2011;6:53.

17. Chou CL, Wang CW, Lin SM, et al. Role of flexible bronchoscopic cryotechnology in diagnosing endobronchial masses. Ann Thorac Surg 2013;95:982-6.

18. Pajares V, Puzo C, Castillo D, et al. Diagnostic yield of transbronchial cryobiopsy in interstitial lung disease: a randomized trial. Respirology 2014;19:900-6.

19. Fruchter O, Fridel L, El Raouf BA, et al. Histological diagnosis of interstitial lung diseases by cryo-transbronchial biopsy. Respirology 2014;19:683-8.

20. Khot MS, Chakraborti A, Saini JK, et al. Comparison of the diagnostic yield of transbronchial lung biopsies by forceps and cryoprobe in diffuse parenchymal lung disease. Afr J Thorac Crit Care Med 2023;29:10.7196/AJTCCM.2023.v29i3.799.

21. Vinay V, Abdullah Y, Garg A, et al. The master impersonator: pulmonary tuberculosis mimicking diffuse cystic lung disease – a mini case series of a rare presentation. J Family Med Prim Care 2022;11:6590-2.

22. Colby T V., Tomassetti S, Cavazza A, et al. Transbronchial cryobiopsy in diffuse lung disease update for the pathologist. Arch Pathol Lab Med 2017;141:891-900.

23. Casoni GL, Tomassetti S, Cavazza A, et al. Transbronchial lung cryobiopsy in the diagnosis of fibrotic interstitial lung diseases. PLoS One 2014;9:e86716.

24. Loor K, Culebras M, Sansano I, et al. Lung allograft transbronchial cryobiopsy for critical ventilated patients: a randomised trial. Eur Respir J 2023;61:2102354.

25. Dhooria S, Mehta RM, Srinivasan A, et al. The safety and efficacy of different methods for obtaining transbronchial lung cryobiopsy in diffuse lung diseases. Clin Respir J 2018;12:1711-20.

26. Tomassetti S, Wells AU, Costabel U, et al. Bronchoscopic lung cryobiopsy increases diagnostic confidence in the multidisciplinary diagnosis of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2016;193:745-52.

27. Hetzel J, Eberhardt R, Petermann C, et al. Bleeding risk of transbronchial cryobiopsy compared to transbronchial forceps biopsy in interstitial lung disease - a prospective, randomized, multicentre cross-over trial. Respir Res 2019;20:140.

28. Johannson KA, Marcoux VS, Ronksley PE, Ryerson CJ. Diagnostic yield and complications of transbronchial lung cryobiopsy for interstitial lung disease: a systematic review and metaanalysis. Ann Am Thorac Soc 2016;13:1828-38.

29. Giri M, Huang G, Puri A, et al. 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.

30. Hagmeyer L, Theegarten D, Treml M, et al. Validation of transbronchial cryobiopsy in interstitial lung disease - Interim analysis of a prospective trial and critical review of the literature. Sarcoidosis Vasc Diffuse Lung Dis 2016;33:2-9.

31. Deasy KF, Walsh LJ, Kennedy MP, Henry MT. Endobronchial balloon blockers: a retrospective analysis of their implementation for use in transbronchial cryobiopsy under conscious sedation. Lung 2021;199:187-93.

32. Chen X, Luo J, Yang L, et al. The diagnostic value of transbronchial lung cryobiopsy combined with rapid on-site evaluation in diffuse lung diseases: a prospective and self-controlled study. BMC Pulm Med 2022;22:124.

33. Safety of a sheath cryoprobe bronchoscopic transbronchial biopsy technique (FROSTBITE). 2022. Available from: https://clinicaltrials.gov/ct2/show/study/NCT04486560