

Thoracoscopic Lung Biopsy by Cryomodality versus Electrocautery in Patients with Diffuse Parenchymal Lung Disease

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Abstract

Background: There are about 200 different pulmonary illnesses that can cause diffuse or patchy involvement of the lung parenchyma; these are collectively known as diffuse parenchymal lung disorders (DPLDs). The origin, clinical manifestations, treatment choices, and prognosis of DPLDs vary considerably.

Aim and objectives: To compare the safety and effectiveness of two thoracoscopic techniques for the identification of diffuse parenchymal lung disease: cryoprobe and electrocautery.

Patients and methods: Taking place between February 2023 and February 2025, this prospective study was carried out in the Endoscopy Unit of the Chest Department at Al-Azhar University Hospitals. Forty patients who underwent comprehensive clinical and investigative evaluation for unconfirmed diagnoses of diffuse pulmonary infiltrates as shown on high resolution computed tomography (HRCT) scans of the chest comprised the study.

Results: Hypersensitivity pneumonitis affected 25% of patients, idiopathic pulmonary fibrosis 17.5%, non-specific interstitial pneumonia 15%, sarcoidosis 10%, and adenocarcinoma 10%, according to pathological diagnosis. The study revealed statistically significant differences between the groups, showing that the time for full lung expansion and length of hospital stay were both notably longer in patients who underwent cryo-forceps biopsy. Additionally, the occurrence of air leak was significantly higher among these patients.

Conclusion: Medical thoracoscopic lung biopsy, in the hands of experienced interventional pulmonologists, is a practical, safe, effective, and feasible diagnostic procedure. Major complication and longer hospital stays are associated with cryobiopsy, despite the fact that it produces larger and more reliable biopsy samples. Electrocautery is preferable to cryomodality in terms of complications and hospital stay duration.

Keywords: Thoracoscopic Lung Biopsy; Cryomodality; Electrocautery; Parenchymal Lung Disease

1. Introduction

Even after a thorough clinical evaluation, laboratory testing (including serology for specific connective tissue diseases), chest x-rays, and HRCT, diagnosing DPLDs in immunocompetent patients remains a formidable challenge for the clinician.¹

To differentiate between typical interstitial pneumonia (UIP) and other ILDs, a lung biopsy is advised since chest HRCT alone may not be enough to detect the cause in around half of

DPLD patients.²

When performed by an experienced pulmonologist, medical thoracoscopy with forceps biopsy offers several benefits over surgical intervention in the diagnosis of DPLDs and is generally regarded as a safe maneuver.³ One of the most applicable modalities used for such a purpose is electrocautery.⁴

In order to diagnose diffuse parenchymal lung disease, this study aimed to compare the safety and effectiveness of two thoracoscopic modalities: cryoprobe and electrocautery.

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2. Patients and methods

Forty patients with unconfirmed DPLD on HRCT scans of the chest were a part of this prospective study that ran from February 2023 to February 2025 at Al-Azhar University Hospitals' Chest Department Endoscopy Unit. The patients underwent a comprehensive clinical and investigative evaluation.

Inclusion criteria:

Patients with undiagnosed diffuse parenchymal lung diseases are assessed by clinical, laboratory, and radiological assessment.

Exclusion criteria:

Patients requiring mechanical ventilation or experiencing respiratory failure, as well as those with coagulopathy, cystic lung disorders, a single lung, or severe pulmonary hypertension.

Enrolled patients were randomly distributed into two equal groups (electrocautery and cryoprobe) according to an alternating case by case approach. Following the provision of written consent, all patients included in the study were subjected to detailed history taking, physical examination, labs including (CBC, KFT, LFT ANA, anti-ds DNA, ANCA and coagulation profile), imaging (CXR, HRCT, echocardiography), physiological studies (ABG, spirometry, ECG, 6MWT), and Medical thoracoscopic lung biopsy using electrocautery for 20-patient and cryoprobe for another 20-patients

Pulmonary function tests (PFTs):

PFTs were done for all participants at the Pulmonary Function Tests Unit in Al-Hussein University Hospital, using computerized pulmonary function apparatus Blue Cherry Version 1.2.2.4 (Geratherm Respiratory GmbH, Bad Kissingen, Germany). Measured parameters were forced vital capacity (FVC) and FEV1/FVC ratio.

Technique of medical thoracoscopy:

As a part of the patient's preparation, the physician confirmed the procedure's indication and went over the procedure's objectives, potential complications, and risks with each patient.

Diathermy forceps of Karl-Storz Endoscopy in Germany® and cryoprobe biopsies from Erbokryo CA, Tübingen, Germany, with a diameter of 2.4 mm, were used.

Steps of Medical Thoracoscopy:

Premedication:

Pethidine 100 mg and midazolam 5 mg were injected intravenously for adequate analgesia and conscious sedation with spontaneous ventilation during the procedure. General anesthesia was also used in some patients who were unable to tolerate local anesthesia due to severe anxiety, hypersensitivity to pain, or underlying comorbid conditions such as cardiac disorders.

Position of the patient:

With the armpits elevated and the side

to be operated upon facing up, the patient was put in the lateral decubitus posture. An iodol-povidone antiseptic solution was used to sterilize the lateral chest walls at the site of entry, which is located at the fifth or fourth intercostal space midaxillary line. After that, the patient was covered with a sterile drape, with just a tiny opening left to carry out the treatment. The patient's oxygen saturation was kept above 90% by administering supplemental oxygen.

Local anesthesia (in some patients):

Ten to twenty milliliters of 0.5-1% lidocaine were injected into every layer of the chest wall at the point of entry. To avoid toxicity, the total amount never exceeded 3mg/kg body weight.

Incision:

At the chosen entrance spot, a transverse incision is made through the skin and subcutaneous tissue using the scalpel. The size of the incision was kept to correspond to the trocar size, which was typically around 10 mm. The incision was parallel to and in the center of the chosen intercostal space. The pleural cavity was meticulously entered with a blunt dissection using a needle holder.

Trocar insertion:

A corkscrew motion was applied to insert the trocar, with the trocar handled firmly in the palm as the operator inserted it. After passing the costal pleura, a sudden release was felt. With the trocar still in the pleural cavity, the assistant removed it and positioned the cannula, such that it lied 1-3 cm inside the cavity.

Visualization of the Pleural Space:

One group was passed through the trocar port by Karl-Storz Endoscopy of Germany®. As part of the examination, the parietal, visceral pleura, and lung were studied using electro-coagulating biopsy forceps attached to diathermy coagulation (Olympus DSD 20). The forceps were inserted into the lung surface in an open position and subsequently closed. Short pulses of diathermy, adjusted to 60 watts for coagulation, were used to take lung samples. Typically, three to five biopsies were taken from different areas and kept in an isolated container.

In the second group, cryoprobe biopsies were collected through the Erbokryo CA facility, Tübingen, Germany. Using the Joule-Thompson effect, which involves a quickly releasing gas at a fast flow rate to bring the temperature down to -77 °C, the cryo-technique was able to freeze the specimen and caused it to adhere for a duration of 7-15 seconds. Eventually, the adhered tissue was removed along with the cryoprobe. The exact quantity of biopsies was then determined and stored in an isolated bottle.

Chest drain insertion:

Finally, the thoracoscope entry port was used to implant a chest tube. Sutures were used to bind

the chest tube to the patient's skin after the cannula was removed. The chest tube was thereafter covered with a sterile covering and a gauze pad.

Post-thoracoscopy care and follow-up:

During their stay in the inpatient unit, patients were closely monitored for vital signs, oxygen saturation using pulse oximetry, and chest tube drainage. They were also received broad-spectrum antibiotics and powerful analgesics, e.g., NSAIDs or pethidine, if needed. To confirm complete lung expansion, a plain chest x-ray was taken. If neither pneumothorax, nor air leakage observed, the tube was subsequently withdrawn.

Statistical Analysis:

SPSS version 28 (IBM corp., Armonk, NY, USA) was used to analyze data. Absolute frequencies and percentages showed categorical variables. Chi square or Fisher's exact tests were used to compare them.

The Shapiro-Wilk test verified the parametric test assumptions. Dependent on data type, quantitative variables were expressed as means $\pm$ standard deviations or median and interquartile range. The independent sample t-test or the Mann-Whitney test was utilized to compare quantitative data between two groups. P-value <0.05 indicated significance, while $p \leq 0.001$ was rated highly significant.

3. Results

Table 1. Distribution of patients according to socio-demographic data.

SOCIO-DEMOGRAPHIC DATA			N=40	%
		Mean $\pm$ SD	Range	
AGE (YEARS)		47.4 $\pm$ 9.63	20-67	
SEX		25	62.5%	
FEMALE		15	37.5%	
MALE				
SMOKING				
NON-SMOKER		31	77.5%	
SMOKER		9	22.5%	
ENVIRONMENT EXPOSURE				
YES		3	7.5%	
NO		37	92.5%	

SD:standard deviation.

The age of studied patients ranged between 20-67 years, with a mean of 47.4 years. Females represented 62.5% of the cohort, 22.5% of patients were smokers and 92.5% had no environmental exposure to allergen or toxins (Table 1).

Table 2. Distribution of patients according to HRCT findings and lesion predominance.

HIGH-RESOLUTION COMPUTED TOMOGRAPHY			N=40	%
FINDINGS	Ground-glass opacity	12	30%	
	Reticulation	8	20%	
	Reticulonodular	9	22.5%	
	Nodular	3	7.5%	
	Consolidation	5	12.5%	
	Crazy paving	3	7.5%	
	Homogenously diffuse	28	70%	
	Lower lobe predominant	8	20%	
	Upper lobe predominant	2	5%	
	Upper and middle lobe predominant	2	5%	
LESION PREDOMINANCE				

HRCT findings revealed that 30% of patients had ground-glass opacities (GGO), 22.5% exhibited reticulonodular infiltrations, 20% showed reticulation, 12.5% had consolidation and 7.5% show nodulations and crazy paving pattern. Twenty-eight patients (70%) had homogenously diffuse infiltrations (Table 2).

Table 3. Distribution of patients according to final histopathological diagnosis.

FINAL DIAGNOSIS	N=40	%
HYPERSENSITIVITY PNEUMONITIS	10	25%
NON-SPECIFIC INTERSTITIAL PNEUMONIA	6	15%
IDIOPATHIC PULMONARY FIBROSIS	7	17.5%
SARCOIDOSIS	4	10%
ADENOCARCINOMA	4	10%
CRYPTOGENIC ORGANIZING PNEUMONIA	3	7.5%
ALVEOLAR PROTEINOSIS	3	7.5%
AMYLOIDOSIS	2	5%
TUBERCULOSIS	1	2.5%

Final diagnosis by histopathological examination revealed that 25% of patients had hypersensitivity pneumonitis (HP), 17.5% exhibited idiopathic pulmonary fibrosis (IPF), 15% showed non-specific interstitial pneumonia (NSIP), 10% displayed sarcoidosis and another 10% diagnosed as adenocarcinoma (Table 3).

Table 4. Comparison between method of biopsy collection and outcome

VARIABLE	CRYO-FORCEPS N=20	ELECTROCAUTERY N= 20	STATISTICAL TEST	P
	Median (IQR)	Median (IQR)		
SIZE OF BIOPSY(MM)	10(9-12.75)	7(6-8.5)	Z= 4.165	<0.001**
TIME OF FULL LUNG EXPANSION (DAYS)	5(1.25-7)	2(1-3)	Z=2.109	0.034*
LENGTH OF HOSPITAL STAY (DAYS)	9(5-12)	5(4-6)	Z=2.298	0.023*
COMPLICATIONS	N(%)	N(%)		
WOUND	1(5%)	0(0%)	Fisher's test	>0.999
INFECTION				
AIR LEAK	5(25%)	0(0%)	Fisher's test	0.047*
POSTOPERATIVE PAIN	1(5%)	2(10%)	Fisher's test	>0.999
SURGICAL EMPHYSEMA	2(10%)	1(5%)	Fisher's test	>0.999
BLEEDING	1(5%)	0(0%)	Fisher's test	>0.999
EXACERBATION OF UNDERLYING ILD	1(5%)	0(0%)	Fisher's test	>0.999

ILD:Interstitial lung disease, Z:Mann Whitney test, IQR:Interquartile range

*:Statistically significant.

There were statistically significant differences between studied groups regarding size of biopsy (significantly larger among patients underwent cryo-forceps biopsy), time of full lung expansion and length of hospital stay (both were significantly prolonged in cryo-forceps group). Moreover, the incidence of air leak was significantly higher among patients underwent cryo-forceps biopsy (Table 4).

Table 5. Correlation between pathological result and radiological infiltration.

RAD. INFILT.	MALIG.	PAP	AMYL.	COP	HP	IPF	NSIP	SARC.	TB
GGO	0(0%)	0(0%)	0(0%)	0(0%)	9(90%)	0(0%)	3(50%)	0(0%)	0(0%)
CONS.	1(25%)	0(0%)	0(0%)	3(100%)	0(0%)	0(0%)	0(0%)	1(25%)	0(0%)
RN	3(75%)	0(0%)	2(100%)	0(0%)	0(0%)	2(28.6%)	1(16.7%)	1(25%)	0(0%)
RETIC.	0(0%)	0(0%)	0(0%)	0(0%)	1(10%)	5(71.4%)	2(33.3%)	0(0%)	0(0%)
NODULAR	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	2(25%)	1(100%)
CP	0(0%)	3(100%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)

Rad. infiltr.:Radiological infiltration, GGO:Ground-glass opacity, Cons.:Consolidation, RN:Reticulonodular, Retic.:Reticulation, CP:Crazy paving, Malig.:Malignancy, PAP:Pulmonary alveolar proteinosis, Amyl.:Amyloidosis, COP:Cryptogenic organizing pneumonia, HP:Hypersensitivity pneumonitis, IPF:Idiopathic pulmonary fibrosis, NSIP:non-specific interstitial pneumonia, Sarc.:Sarcoidosis, TB:Tuberculosis.

GGO was the overall most common radiological finding, particularly in HP (90%), while consolidation was more frequent in cryptogenic organizing pneumonia (COP) (100%). Reticulonodular pattern was seen in 100% of patients with amyloidosis, 28.6% of IPF cases and 25% of those suffering from sarcoidosis. Reticulation was the most prevalent pattern in IPF (71.4%), while nodular pattern was observed in 100% of TB patients and 25% of sarcoidosis cases. Crazy paving was a characteristic pattern for pulmonary alveolar proteinosis (PAP) (100%) (Table 5).

4. Discussion

With a thoracoscopic lung biopsy, more areas can be biopsied because the pleura and lung are better seen. As a less-invasive alternative to surgical intervention in the diagnosis of DPLDs, medical thoracoscopy with forceps biopsy is a safe technique when performed by an experienced pulmonologist.³

Patients' ages varied from twenty to sixty-seven years, with a mean of forty-seven years, according to the socio-demographic data collected for this study. The following statistics were offered from the cohort: 62.5% were female, 22.5% were smokers, and 92.5% reported no exposure to environmental toxins or allergens. Concerning age, sex, smoking, and environmental exposure, no statistically significant differences were found among the groups that were under study, enhancing the reliability of our results due to similar baseline characteristics.

Our study aligns with that of Ahmed et al.,⁵ which included 55 DPLD patients at an average age of 39.96 years, where 58.2% of the cohort were females and 25.5% were smokers. Likewise, Omar et al.,⁶ reported a mean age of 47 years, with an 80% female predominance among their studied 15 DPLD patients.

In the current study, HRCT findings elucidated that 30% of patients had GGO, 22.5% exhibited reticulonodular infiltrations, 20% showed reticulations, and 12.5% had consolidation. Crazy paving and nodulations were the least frequent findings detected among only 7.5% of

patients.

Coinciding with our results, Mohamed et al.,⁷ identified a reticulonodular pattern in 27.5% of cases. Moreover, Abdel-Ati et al.,⁴ reported a neighboring frequency of GGO (35%), but a higher prevalence of reticulonodular pattern (65%).

On the opposing side, Bondok et al.,⁸ reported GGO in 70% of cases, which by far exceeds our figure. Additionally, Akl et al.,⁹ observed an approximately double-fold prevalence of diffuse reticulation pattern (36.7%) and an extremely lower incidence of GGO (6.7%). These discrepancies in HRCT findings across different studies emphasize the heterogeneity of DPLDs at the radiological level, and may also be attributed to differences in patients' characteristics or disease stages.

In our study, a definitive diagnosis was obtained in all studied patients (100%). Final diagnoses distribution was as follows; 25% of patients had HP, 17.5% exhibited idiopathic IPF, 15% showed NSIP, 10% displayed sarcoidosis and another 10% diagnosed as adenocarcinoma. COP, pulmonary alveolar proteinosis (PAP), amyloidosis and TB were detected in lower frequencies (7.5%, 7.5%, 5% and 2.5%, respectively).

These results are compatible with Abdel-Ati et al.,⁴ who showed the exact percentages of HP and sarcoidosis, close frequencies of TB, COP and adenocarcinoma (5%, 5% and 15%, respectively), but a higher IPF prevalence (35%), with a single case (5%) remained undiagnosed till the end of the study.

Likewise, in the study done by Omar et al.,⁶ 40% of patients were diagnosed as extrinsic allergic alveolitis, 33.3% were proved to have malignancy, 13.3% had idiopathic interstitial pneumonias, 6.7% showed sarcoidosis and 6.7% exhibited the pathology of TB granuloma. Distinct geographical and environmental factors, as well as substantial variations in sample size, account for the contradictory findings observed in the literature.

In the current work, the mean size of biopsy was significantly larger in the cryo-forceps group (median= 10 mm), compared with the electrocautery group (median= 7 mm). In accordance with this outcome, Romagnoli et al.,¹⁰

enlightened that trans-bronchial lung cryobiopsy (TBLC) provides larger biopsy samples, with a maximum diameter of 7–10 mm. Likewise, Bondok et al.,⁸ registered an adjacent electrocautery biopsy size (6.2 ± 1.4 mm) to ours.

There were statistically significant increased incidence of air leak among those underwent cryo-forceps biopsy. This higher frequency of air leak within cryomodality patients could be attributed to the larger biopsy size, more wound depth related to this procedure and technical challenges associated with the maneuver. However, it is not obvious if the sample size justifies this risk. On the other hand, there were statistically non-significant differences between the studied groups regarding other complications.

These findings are defended by the study of Mohamed et al.,⁷ where 5% of patients developed surgical emphysema and 2.5% developed empyema following electrocautery thoracoscopic lung biopsy. Similarly, Akl et al.,⁹ observed no major complications after electrocautery but reported prolonged air leaks in five patients.

In contrast, Bondok et al.,⁸ underscored surgical emphysema to be the most common complication, occurring in 40% of the medical thoracoscopy group and 60% of the mini-thoracoscopy group. Our results affirm the importance of vigilant monitoring and management of postoperative complications in electrocautery procedures.

In the current work, the electrocautery group showed a quicker median lung expansion time (2 days, IQR: 1–3 days) and a shorter median hospital stay (5 days, IQR: 4–6 days), compared to the cryo-forceps group.

These findings are corroborated with Omar et al.,⁶ who observed variable durations for intercostal tube (ICT) removal, ranging between 2–6 days. On the same bath, Mohamed et al.,⁷ discovered that patients required ICT for an average of 3.67 days following their procedures, with a range of 3–10 days.

Although Bondok et al.,⁸ reported an apparently longer mean hospital stay (13.3 ± 6.2 days) in patients managed through the medical thoracoscopy approach, they recorded a comparable mean full lung expansion time (3.3 ± 1.42 days) in the same group. Overall, our results suggest that electrocautery may lead to shorter hospital stays and speedy recovery, emphasizing its potential advantages over other possible modalities.

In terms of investigating the relation between final diagnoses and HRCT, our study showed that GGO was the overall most common radiological finding, particularly in HP (90%), while consolidation was more frequent in COP (100%). Reticulonodular pattern was seen in

100% of patients with amyloidosis, 28.6% of IPF cases, and 25% of those suffering from sarcoidosis. Reticulation was the most prevalent pattern in IPF (71.4%), while the nodular pattern was observed in 100% of TB patients and 25% of sarcoidosis cases. Crazy paving is a characteristic pattern for PAP. These findings harmonize with Akl et al.,⁹ who illustrated a compatibility of clinical and radiological findings in the diagnosis of DPLD.

Besides, Abdel-Ati et al.,⁴ found that certain radiological patterns were significantly correlated with various forms of DPLD. This provides more evidence that these imaging modalities are useful for diagnosing and distinguishing between different types of DPLDs.

Ultimately, our study is limited by being a single-center study and owing a relatively small sample size which may affect validity of results till larger multi-centric studies are available. Furthermore, lacking of presenting all subtypes of DPLD is another limiting factor.

4. Conclusion

Medical thoracoscopic lung biopsy is an effective, safe, feasible, and applicable procedure. Although cryomodality lung biopsy provides larger and highly valid biopsy samples, it is associated with more major complications and longer hospital stays. Electrocautery is preferable to cryomodality in terms of complications and hospital stay duration.

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