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Original Article

Assessing the Safety and Efficacy of Thoracoscopic Lung Biopsy in Patients with Interstitial Lung Disease

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ABSTRACT

Background: Interstitial lung disease [ILD] is a difficult-to-treat disease. The patient continues treatment for his/her whole life. However, certain causes – when diagnosed - could change their treatment plan. Radiological investigations cannot elicit the underlying pathology 100%. Thus, transthoracic lung biopsy is of utmost importance, especially in undiagnosed patients. But, it is not free of risk, and thus, its use is still controversial.

Aim of the work: This work aims to evaluate the role of medical thoracoscopic lung biopsy [TLB] in diagnosing diffuse parenchymal lung diseases.

Patients and Methods: Fifty patients with diffuse lung infiltrate on high-resolution computed tomography [HCRT] of unconfirmed diagnosis were included. All patients have been submitted to detailed clinical examination and specific laboratory investigations. Furthermore, all had high resolution computed tomography, pulmonary function tests], echocardiography, arterial blood gas analysis, and bronchoalveolar lavage assessment. The thoracoscopic lung biopsy was performed under local anesthesia. The specimens were preserved in formalin containing cups till examination. Patients were followed up, and any complications were documented.

Results: The lung HCRT revealed ground-glass opacity [44%], reticulonodular interstitial pattern [38%], honeycombing [14%], crazy paving [10.0%], and consolidation [20.0%]. The histopathology revealed alveolar proteinosis [2.0%], alveolar hemosidrosis [2.0%], hypersensitivity pneumonitis [24.0%], sarcoidosis [8.0%], nonspecific interstitial pneumonia [20%], Idiopathic pulmonary fibrosis [12.0%], respiratory bronchiolitis ILD [18%], and desquamative ILD [14.0%]. All patients positive on HCRT had pathological change. Complications were [12%] bulla in partnehymea, [4%] plural disear, [2%] pneumothorax, and 2% died during follow up duration.

Conclusion: TLB is an effective and relatively safe, minimally invasive intervention for interstitial lung disease diagnosis. Accordingly, it must be considered a standard diagnostic tool for undiagnosed suspected cases.

Keywords: Interstitial Lung Disease; Transthoracic; Lung Biopsy; Efficacy; Safety.

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* Main subject and any subcategories have been classified according to the research topic

INTRODUCTION

Interstitial lung disease [ILD], also recognized as diffuse parenchymal lung disease, refers to a heterogeneous group of over 150 unconnected disorders. Each ILD form has its own distinct clinical, radiological, and pathological manifestations. Several key differences are due to variations in the anatomic distribution of the disease. ILD represented about 15% of the respiratory disease in general populations [1].

In 2020, ILD has been reported in 595,000 people all over the globe. With very high mortality rate [471,000 deaths]. The evolution in these disorders' classification has been driven by epidemiologic, clinical, radiologic, biochemical, genetic, and pathological investigation [2].

ILD in the non-immunocompromised subject is often a problematic challenge from clinical point of view, especially when specific diagnosis clues are found after thorough assessment, investigations and chest imaging. Traditionally, high resolution computed tomography [HRCT] broncho-alveolar lavage and Transbronchial biopsy [TBLB] the next steps [3].

Thoracoscopy has been performed by professional pulmonologists, with satisfactory safety and efficacy, for many decades [4].

The recent advances in video equipments and more sophisticated, fine instruments has expanded its indications. There are encouraging reports for lung biopsy by medical thoracoscopy in ILD in immune-compromised subjects. However, this procedure gained a little acceptance among pulmonologists [5].

Medical thoracoscopic lung biopsy in the diagnosis of interstitial lung disease [ILD] can be considered a second choice after the failure of bronchoalveolar lavage [BAL] and [TBLB] to provide the diagnosis, and this procedure has some advantages over surgical lung biopsy [SLB]. The possibility to obtain numerous biopsies under respectable visual guidance and lower complication rate are the most important advantages [6].

Others argued that treatment did not differ widely and mortality did not decrease with confirmation of diagnosis by biopsy [7].

This view would be acceptable if empirical management always leads to an improvement, but when the reverse is the case, the next step in treatment is difficult and becomes worse if drug-induced unwanted side effects have settled [especially side effects related to high dose of steroids]. A definite diagnosis by the biopsy permits clinicians and their patients to build up a clear plan of management, based on weighing benefit-risk ratio [7].

AIM OF THE WORK

This work aims to assess the role of the medical thoracoscopic lung biopsy in diagnosis of diffuse parenchymal lung diseases.

PATIENTS AND METHODS

This study included 50 patients with diffuse lung infiltrates on high-resolution CT [HRCT] chest of un-confirmed diagnosis. The study was conducted between April 2019 and December 2020 at the chest department, Al-Azhar University hospital [Damietta].

Ethical consideration:

The study protocol was approved by our institution's research and ethics committee [IRB number: 00012367-19-04-002]. All patients signed informed consents, and all study procedures were completed according to local ethical codes that coincide with Helsinki declaration codes.

Patients with diffuse lung infiltrate on high-resolution CT chest with the unconfirmed diagnosis were included in the study. Otherwise, patients with one or more of the procedure contraindications were excluded from the study.

Contraindications include coagulation abnormalities [prothrombin level less than 50% or platelet count<70,000 cells/cc], severe respiratory failure [$PaCO_2$ >60 mmHg], mechanical ventilation, radiographic findings suggestive of significant pleural adhesions or major bullous degeneration of the lung, severe pulmonary hypertension, cardiac disorders, heart failure, renal failure or liver cell failure.

All patients gave the full medical history. Besides, they have been submitted to systematic clinical examination and specific laboratory investigations directed to markers of connective tissue diseases.

Furthermore, all patients have undergone high resolution computed tomography, pulmonary function tests [PFTs], echocardiography, arterial blood gas analysis, and bronchoalveolar lavage [BAL] assessment.

The thoracoscopic lung biopsy was performed under local anesthesia as described previously [8].

Figure [1]: Administration of local anesthesia

Figure [2]: Incision

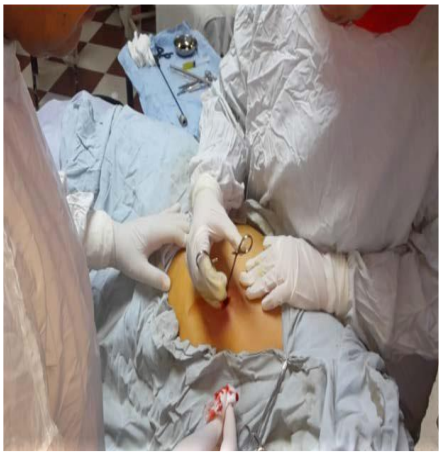

Figure [3]: Dissection

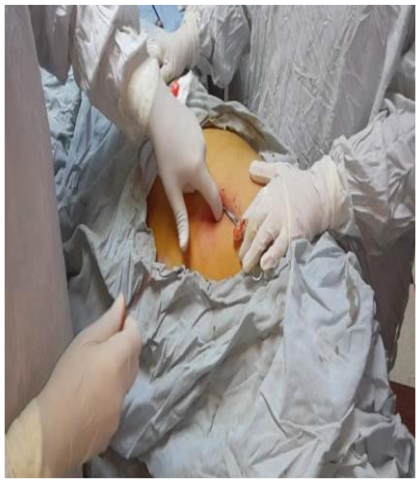

Figure [4]: Palpation by the index finger

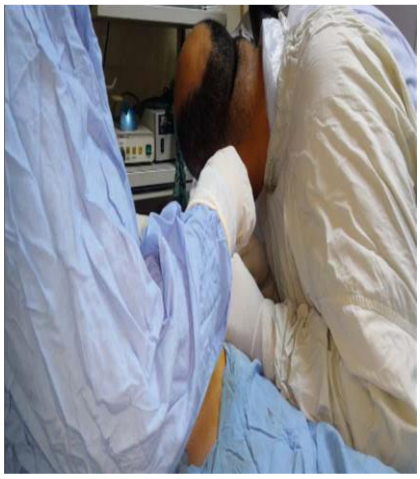

Figure [5]: Hearing air entry

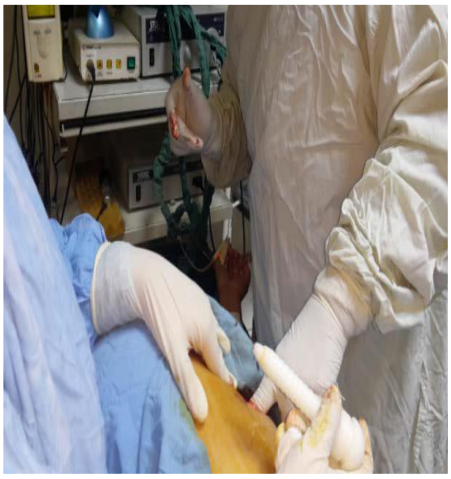

Figure [6]: Trocar insertion

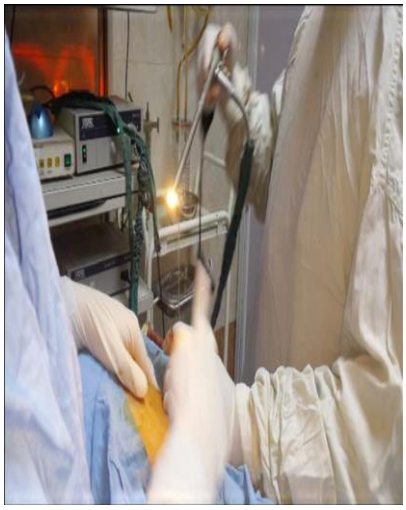

Figure [7]: Thoracoscope introduction

Figure [8]: Taking the biopsy

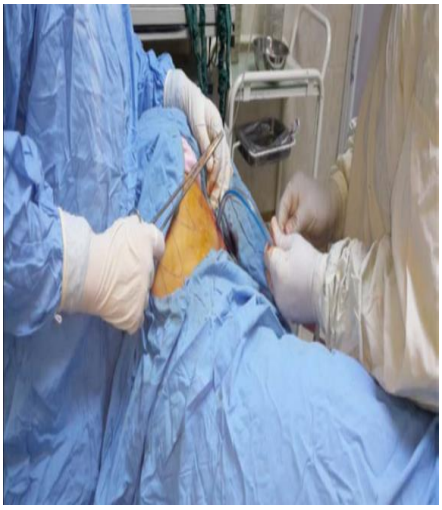

Figure [9]: Tube insertion and wound closure

Table [1]: Electrolytes, arterial blood gases, pulmonary function tests, electrocardiogram, and X-ray among studied populations

		Patients [n=50]
Electrolytes	Na [mEq/L]	133.02 ± 0.86
	K [mEq/L]	4.14 ± 0.15
	Ionized Ca [mg/dL]	3.65 ± 0.12
	Mg [mg/dL]	2.66 ± 0.78
ABGs	pH	7.41 ± 0.0557
	PaO_2	66.16 ± 6.62
	SaO_2	93.7 ± 2.91
	HCO_3	23.56 ± 5.076
Pulmonary function tests	FVC %	56.43 ± 14.76
	FEV_1 %	67.9 ± 7.17
	FEV1/FVC ratio	96.4 ± 10.53
ECG	Normal	36[72.0%]
	Sinus tachycardia	9[18.0%]
	P pulmonale	5[10.0%]
X-ray	Normal	26[52.0%]
	Nodular	8[16.0%]
	Reticular	2[4.0%]
	Hilar LN	4[8.0%]
	Small lung volume	10[20.0%]

Table [2]: Different data according to Warrick score among the studied patients

Parameters		Mild[n=23]	Moderate[n=22]	Severe[n=5]	p
Warrick score		11.12 ± 3.41	20.18 ± 3.26	29.2 ± 0.936	***<0.001****
6-min walk test		454.5 ± 107.1	431.8 ± 82.37	218.1 ± 34.21	***<0.001****
B-lines distance		4.82 ± 1.33	5.29 ± 1.34	5.46 ± 1.31	***0.003****
PaO_2		69.21 ± 6.55	67.09 ± 6.83	64.43 ± 7.39	***0.003****
FVC		62.13 ± 7.04	59.36 ± 5.73	56.45 ± 8.61	***0.001****
Symptoms	Dyspnea	8 [34.8%]	7 [31.8%]	1 [20%]	0.752
	Dry cough	8 [34.8%]	8 [36.4%]	1 [20%]	
	Easy fatigability	6 [26.1%]	5 [22.7%]	3 [60%]	
	Fever	1 [4.3%]	2 [9.1%]	0 [0.0%]	

Table [3]: Complications and hospital stay among studied populations

		Patients [n=50]	
		N	%
Complications	Bulla in partnehymea	6	12.0%
	Plural Disear	2	4.0%
	Pneumothorax	1	2.0%
	Mortality	1	2.0%
Hospital stay duration	Mean ± SD	4.94 ± 0.77	
	Median [Range]	5 [4 - 6]	
Follow up duration	Mean ± SD	5.28 ± 0.83	
	Median [Range]	6 [4 - 6]	

Table [4]: Relation between computed tomography and histopathology reports

	CT findings				
	GGO [n=22]	CP [n=5]	Cons. [n=10]	RIP [n=19]	HC. [n=7]
Alveolar proteinosis	1 [4.5]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
Alveolar hemosidrosis	0 [0.0]	1[20.0]	0 [0.0]	0 [0.0]	0 [0.0]
Hypersensitivity pneumonitis	10[45.5]	1[20.0]	0 [0.0]	3[15.8]	0 [0.0]
Sarcoidosis	0[0.0]	0[0.0]	0 [0.0]	4[21.1]	0 [0.0]
Nonspecific interstitial pneumonia	2[9.1]	1[20.0]	4[40.0]	3[15.8]	2[28.6]
Idiopathic pulmonary fibrosis	3[13.6]	0[0.0]	0 [0.0]	3[15.8]	3[42.9]
Respiratory bronchiolitis ILD	6[27.3]	1[20.0]	0 [0.0]	6[31.6]	2[28.6]
Desquamative ILD	0[0.0]	1[20.0]	6[60.0]	0 [0.0]	0 [0.0]

GGO: Ground glass opacity; CP: Crazy paving; Cons.: consolidation; RIP: Reticular interstitial pattern; HC: honeycombing

Here, we presented a male patient, 50 years old, who had diabetes, hypertension, and ischemic heart disease [IHD]. He presented with dyspnea and easy fatigability. Clinically, he had cyanosis, clubbing, bilateral basal consonating [Velcro] crepitation. Chest X-ray [figure 10] revealed bilateral central infiltration [increased bronchovascular markings]. The ultrasound revealed multiple B lines and thick pleural line; while CT Chest revealed reticulonodular opacification and ground-glass appearance.

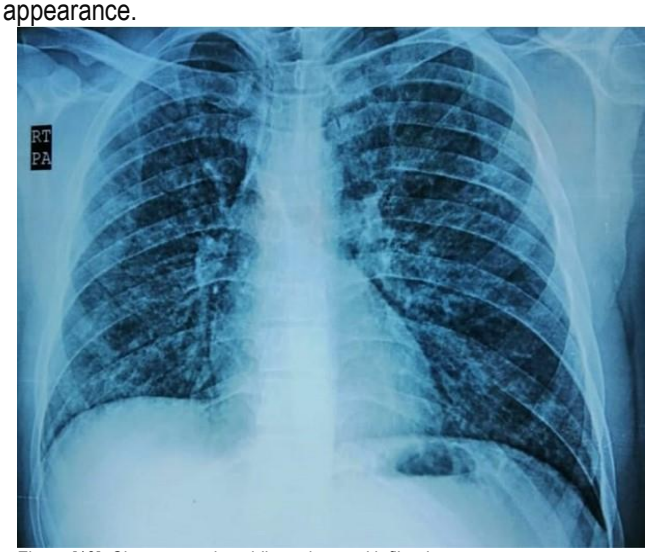

Figure [10]: Chest x-ray show bilateral central infiltration

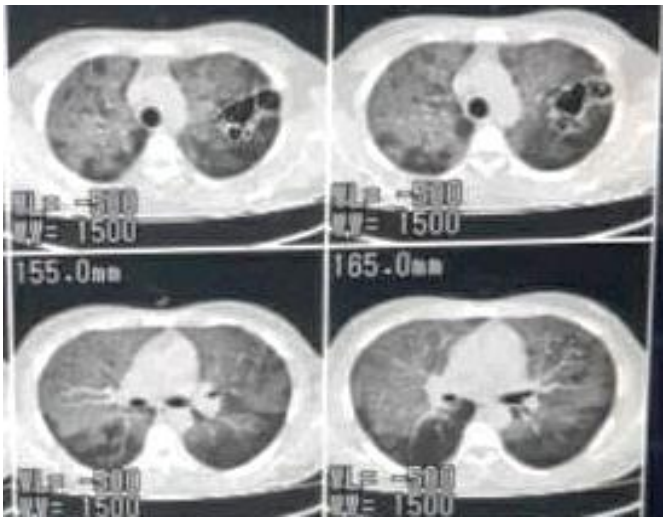

Figure [11]: HRCT showed multiple areas of central alveolar consolidation with air trapping and cystic change

DISCUSSION

A specific diagnosis remains unavailable to one-third of all patients with ILD even after using computerized tomography, bronchoscopy, bronchoalveolar lavage examination, and transbronchial Lung Biopsies [TBLBs]. So, for this sizeable group of patients, the only option remaining is the SLB. However, surgery had its risks. In recent years Video-assisted Thoracoscopic Surgery [VATS] has replaced the older, more invasive method of performing a mini-thoracotomy in these patients [10]. The current work aimed to evaluate thoracoscopic lung biopsy's safety and efficacy in patients with interstitial lung diseases. A prospective study was conducted in the endoscopy unit in the chest department, Al-Azhar University hospital [Damietta]. It included 50 patients with suspected ILD. Results are in line with Lieberman *et al*. [11], who included Forty-seven patients with suspicious ILD for SLB. The mean age was 57.4±12.8, and 55.3% were females, 44% were smokers, and there were 33 diabetic patients and 17 COPDs. Furthermore, Kreider *et al*. [12] revealed an average age of 58 years [range, 38 to 84 years], and 56% were women. Fifty percent were current or former smokers. Also, the current work results are in line with Fibla *et al*. [13]. They reported that mean FVC was 75% [56.43 ±14.76% in the current work]; FEV1: 76.1% [67.9±7.17% in the current study] FEV1/FVC was 86%, TLC was 74%.

Regarding CT findings, the current study showed that the most prevalent finding was ground-glass opacity [GGO; 44%], and the least prevalent finding was crazy paving [10%]. These findings are supported by Goldin *et al*. [14]. They reported that HRCT revealed 92.9% pulmonary fibrosis [PF], 49.4% pure ground-glass opacity [pGGO], and

37.2% honeycomb cysts [HCs]. Furthermore, Luo *et al*. [15] revealed that distinguishing HRCT features were ground-glass opacities, reticular lines, patchy consolidation, bullae, pleural thickening, honeycombing, subpleural lines, emphysematous changes, pleural effusion and enlargement of mediastinal lymph nodes patchy nodules among 87.5%, 65.6%, 43.8%, 25%, 21.9%, 21.9%, 18.8%, 12.5%, 6%, 6% and 6% in a successive order.

Because the use of X-ray for ILD detection is not sensible [as it is normal in the majority of patients, especially in early disease stages [52% were normal in the current study]], HRCT is the "gold" standard imaging modality for the diagnosis and monitoring of ILD. HRCT images and characteristic histopathological data can be highly suggestive for characteristic diagnoses in such patients. Current data supports the use of LUS, to detect ILD by the detection of and evaluation of B-lines, a sonographic marker of the diffuse pulmonary interstitial syndrome [16].

Currently, the role of SLB is still debated. However, its main advantage over different radiological investigations [X-ray, ultrasound, or CT chest] is the pathology's definite diagnosis, which leads to a change in the treatment regimen. For example, the diagnosis of sarcoidosis shortens therapy [from a whole life treatment to a few months]. Besides, it differentiates the prognosis of different conditions [e.g., desquamative ILD had a good prognosis, which advocates continuous treatment].

Despite the advent of video-assisted thoracoscopic surgery [VATS] for lung biopsy and the progress of post-surgery intensive care, many physicians are overcautious on the balance between the efficacy of VATS on diagnosis and the risks of SLB [17]. Luo *et al*. [15] included a total of 811 patients diagnosed as ILD during 5 years, and only 32 [3.9%] patients accepted VATS. In these selected ILD patients, the diagnosis was changed from the previous diagnosis in 84.4% after SLB. The site and number of biopsies may affect the diagnostic efficacy of VATS. Morell *et al*. [18] found that diagnoses from the lingula and middle lobes coincided with those from other lobes. In their study with 41 biopsies, the biopsy site was determined by the abnormalities on CT scan with one biopsy site in most cases and no biopsy obtained from the lingula or middle lobe. These data were compared to the study published by Fibla *et al*. [13]. They reported that a single biopsy site might be sufficient to obtain a definite diagnosis for most patients [71.9%]. Morris and Zamvar [19] revealed that a definite pathological diagnosis was made in 74.2% of cases following VATS biopsy. A change in treatment was initiated in 47.2% of patients, including in 80% of patients diagnosed with hypersensitivity pneumonitis and 60% of patients diagnosed with sarcoidosis. A positive response to treatment was experienced in 58% of patients who changed treatment. Only 54% of patients who received a consensus diagnosis of UIP after VATS lung biopsy had been given a differential diagnosis of "probable UIP" at CT scan. 15% of patients who received a differential diagnosis of "probable UIP" at CT scan had their diagnosis changed to Hyper-sensitivity Pneumonitis after lung biopsy.

As regard complications of the patients show that 6[12%] had Bulla in partnehymea, two [4%] had plural disear, one [2%] had Pneumothorax, and one [2%] died. Hospital stay duration was ranged between 4–6 days with a mean value of 4.94±0.77 days. Follow-up duration was ranged between 4–6 months with a mean value of 5.28±0.83 months. Lieberman *et al*. [11] included 47 patients. Lung tissue was obtained via a thoracoscopic approach in all, but two had mini-thoracotomy. The mean operative time was 51.1 minutes [18-123], median hospital stay was two days [1-18]. Most [87.2%] of the patients were discharged within 72 hours. Thirty-day mortality for elective surgery was 4.5% [2/44]. Post-operative complications occurred in about one-third of the patients. Complications in elective procedures included pneumothorax [10.4%], re-intubation [5.4%] and prolonged intubation [2.7%]. Full concordance of radiographic diagnosis with the final diagnosis was significantly higher when reviewed by a cardiothoracic radiologist [60.5% vs. 21.3%]. The preoperative clinical diagnosis was fully concordant with the final diagnosis in only 28.2% of cases. Furthermore, Jeon *et al*.[20] revealed that no major surgical complications or deaths were reported in either group, and non-intubated VATS biopsies were safely performed in subjects with relatively low carbon monoxide diffusing capacity [P=0.08] or poor American Society of Anesthesiologists physical status scores [ASA] [P=0.02].

In conclusion, thoracoscopic lung biopsy is an effective and relatively safe procedure to reach the final diagnosis in undiagnosed patients with suspected interstitial lung disease. However, as an invasive procedure, it must be resorted to undiagnosed patients irrespective of the use of computed tomography or promising lung ultrasound. Besides, thoracoscopic lung biopsy provides significant therapeutic benefit and could be considered the gold standard in diagnosing ILD. However, as the small number of included patients represented a limiting step of the current work, we could not generalize our results, and future studies are still required.

Financial and Non-financial Relationships and Activities of Interest

None

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