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RESEARCH **Open Access**

Significance of transthoracic ultra-sonography in early detection of patients with interstitial lung diseases in Aswan University Hospital

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Abstract

Background Recently, the diagnosis and follow-up of numerous pulmonary diseases such as pneumothorax, pneumonia, and pleural effusion were easily by use of conventional ultrasound, and the maximum usefulness of transthoracic ultrasonography (TUS) in pulmonary diseases especially diffuse parenchymal lung disease has not been detected yet. This study was conducted to determine the value of transthoracic ultrasonography in patients with interstitial lung disease (ILD). Moreover, the viable correlations of the ultrasound findings with the functional and radiological findings of ILDs had been assessed.

Results TUS diagnosis was positive in 73 cases, there was a substantial variation between the two groups classified according to ultrasonographic diagnosis regarding age and smoking history ($p = 0.003$ and 0.013 respectively). All the patients with usual interstitial pneumonia ($n = 42$) and Indeterminate UIP ($n = 49$) had positive ultra-sonographic findings [$p = 0.041$ and 0.001 accordingly]. Regarding pulmonary function tests, there was a considerable variance between both groups regarding FVC, PEF, FEF25-75, FEV1/VC ($p = 0.037$, 0.029, 0.015, and 0.000 accordingly). The most positive US diagnosis areas were upper lateral, lateral basal, and interscapular areas. There was a weak negative correlation between TUS diagnosis and FVC [$r = -0.25$, $p = 0.026$].

Conclusion We concluded the great significant value of TUS in the diagnosis and follow-up of patients with interstitial lung diseases. It had an extremely thoughtful role in the diagnosis of ILD by detection of multiple B-lines distribution emerging from pleura and extending in the entire lung surface. The use of TUS in early detection and follow-up of ILDs reduced the cost.

Keywords Transthoracic ultra-sonography, Interstitial lung disease, Usual interstitial pneumonia

Introduction

Diffuse parenchymal lung disease especially interstitial type (ILD), is a chronic, often progressive, fibrosing condition with a diverse pattern of lung involvement. It is classified on the basis of clinical manifestations and radiological findings. Some causes of interstitial lung disease have been documented, such as drugs (e.g., amiodarone, methotrexate), environmental factors, genetic factors, and connective tissue diseases (CTD). Undetectable causes are generally classified as idiopathic [1]. Recently, the transthoracic ultrasound (TUS) has become enormously sensitive to varieties of pulmonary content material and to stability among fluids and air. In healthy lungs transthoracic ultrasound (TUS) waves are totally reflected by air; however, in the diseased lung with

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reduced alveolar air content material and growing interstitial and alveolar fluids, unique artifacts will be imitated [2]. Ultrasonographic images of ILD have a specific character where numerous diffuse bilateral B-lines appear similar to separate laser-like longitudinal hyperechoic reverberation artifacts, with the same density and continuity, that start from the visceral pleural line, reaching to the bottom of the screen and moving at the same time and direction with lung sliding [3].

The purpose of this study was to assess the transthoracic ultrasonography capabilities in patients with ILDs. Moreover, the viable correlations of transthoracic ultrasound findings with practical and radiological findings of ILDs will be assessed.

Methods

Eighty patients with ILD were included in the current study which was a prospective cross-sectional one. This study was conducted according to ATS 2018 guidelines for HRCT chest findings for the diagnosis of UIP form in Aswan University Hospital in the chest department, during the period between January 2017 and December 2019 [4]. The current study was approved by the Institutional Ethics Committee, Faculty of Medicine, Aswan

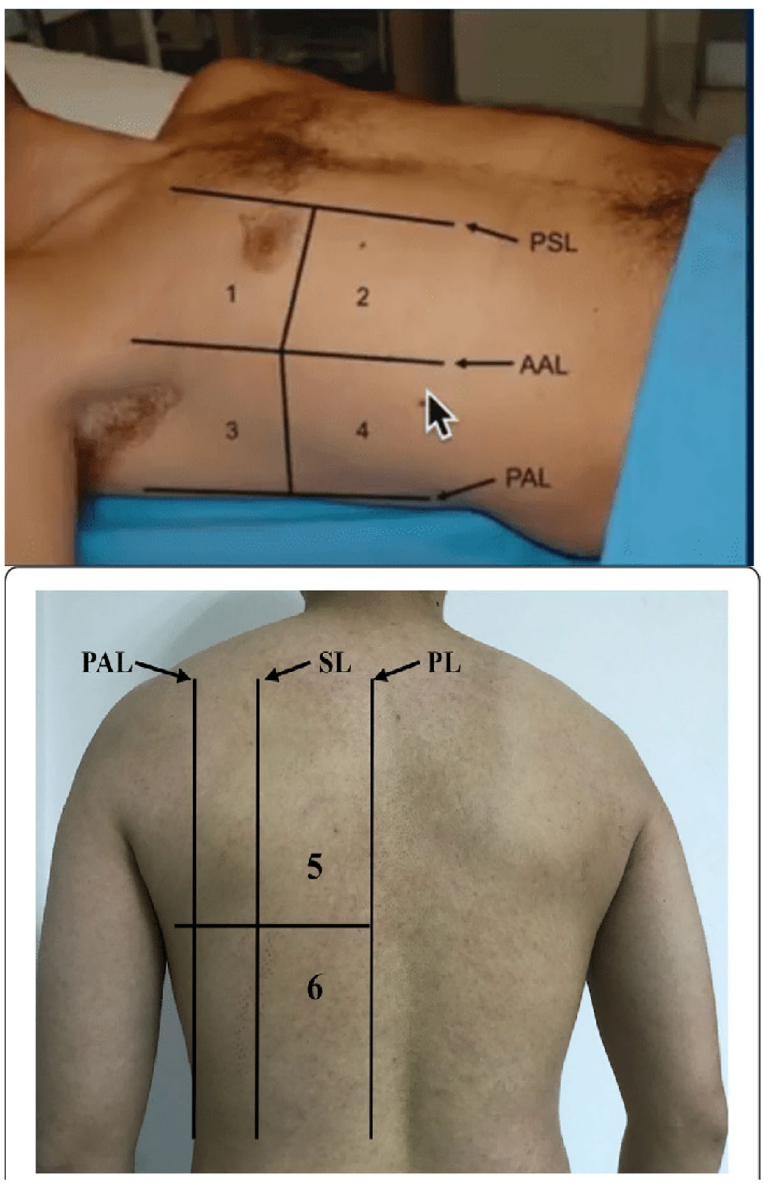

Fig. 1 Different areas of TUS application. Adapted from (Volpicelli et al. [2])

University. A written consent was obtained from each participant upon acceptance to take part in the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Exclusion criteria

- Patients with cardiac diseases (left-sided heart failure, pulmonary edema) [they may have findings of multiple B lines on transthoracic ultrasound examination which mimic ILD findings].
- Patients with chronic kidney diseases (as patients presented with nephrogenic pulmonary edema may have findings of multiple B lines on transthoracic ultrasound examination which mimic ILD findings).

All the included subjects were subjected to the following:

- ¤ Complete medical history including the assessment of the score of dyspnea by the Modified Medical Research Council dyspnea scale (MMRC). since it predicts the quality of life and survival (Functional Dyspnea).
- ¤ Complete clinical examination
- ¤ Plain chest X-ray postero-anterior view: the diffuse lung disease was described by the following main radiological patterns: Nodular, Reticular, and reticulonodular patterns [5].
- ¤ The laboratory investigations (kidney function tests and complete blood count).

Fig. 2 Chest ultrasound image showing multiple B-lines and high-resolution HRCT image of the same patient

High-resolution chest computed tomography

By using the standard protocol for HRCT examination through using Aquilion 64, Toshiba 160-slice CT scanner, aquilion TM prime as the unique usual criterion for the diagnosis of ILD. The scans were done while holding breathing after complete inspiration starting from the apex of the lung to its base while the patients lying in the supine position. The acquisition parameters were 180–260 mA common tube current (relying on a body built), Sequential mode, 1-mm collimation, 10-mm interval, and 120–140 kV tube. HRCT examination without contrast media agent. Idiopathic pulmonary fibrosis (IPF) diagnostic algorithm by HRCT depends on the existence of the usual interstitial pneumonia (UIP) pattern allied with honeycombing appearance and reticular abnormalities in subpleural at the base of lungs and the absence of honeycombing appearance was considered as a probable UIP pattern [4].

Standard spirometry

Standard spirometry was done for all patients by use of (WinsproPRo PFT) machine. The following parameters were measured [Forced Expiratory Volume in first second (FEV1), Forced Vital Capacity (FVC), FEV1/FVC%, Peak Expiratory Flow (PEF), FEF 25–75 (Forced expiratory flow at 25% to 75% of forced vital capacity) and FEV1/ VC].

Arterial blood gases analysis

Transthoracic ultrasonography (TUS)

TUS was performed for all patients using (Philips ClearVue 350 ultrasound, USA) ultrasound machine equipped with a convex phased array probe (bandwidth 2–5 MHz). For the evaluation of interstitial syndrome, we scanned 12 regions. each side of the chest was divided into Six areas for lung ultrasound examination [areas 1 and 2 denote (the upper and lower) anterior chest areas respectively, correspondingly]. [areas 3 and 4 denote (the upper and basal) lateral chest areas respectively], and [areas 5 and 6 denote (interscapular and intrascapular area) as shown in Fig. 1) [2]. Transthoracic ultrasound was done through a pulmonologist properly educated in chest sonography (not known any clinical or hemodynamic data of patients). For the sonographic diagnosis of diffuse interstitial syndrome, we based on the appearance of B Lines, which had been previously referred to as artifacts in the shape of comet-tail, fashioned from the thickening interlobular septa at the interface of the lung wall. These have been documented as well-defined sharp demarcated, longitudinal, hyperechoic, dynamic traces that emerge from the pleural line and spread like a laser ray as much as the brink of the screen [6, 7].

Significant area is described via way means of the existence of 3 or extra B-line in a longitudinal sector among two ribs and a significant exam was defined by the presence of two or more affected areas on both sides of the chest [2], as shown in Fig. 2. The distance

Table 1 Demographic and clinical data of all the patients included in the study

Demographic data	
➢ Total number of patients	80 (42 females and 38 males)
➢ Age (years) (mean ± SD)	49.62 ± 11.82
➢ Weight " kg" (mean ± SD)	74.58 ± 10.18
➢ Height" Cm" (mean ± SD)	160 ± 7.75
➢ Smoking history (*n* %)	34 (42.5%)
➢ Exposure to occupational hazards (*n* %)	27 (33.75%)
ABG (mean ± SD)	
➢ PH	7.409 ± 0.039
➢ PCo2 (mmHg)	35.75 ± 12.36
➢ Po2 (mmHg)	50.23 ± 14.12
➢ HCO3 (mmol/l)	24.79 ± 5.046
➢ O2 saturation (%)	81.58 ± 8.63
CXR abnormalities pattern (*N* %)	
➢ Reticular pattern	30 (37.5%)
➢ Nodular pattern	6 (7.5%)
➢ Reticulo-nodular pattern	44 (55%)
Pulmonary function tests (mean ± SD)	
➢ FVC (%)	56.3 ± 18.008
➢ FEV1 (%)	58.2 ± 18.38
➢ FEV1/FVC (%)	85.05 ± 7.73
➢ PEF (L/S)	42.76 ± 15.55
➢ FEF 25–75 (L/S)	49.98 ± 16.23
➢ FEV1/VC (%)	52.79 ± *14.02*
HRCT findings N (%)	
UIP pattern	42(52.50%)
Indeterminate UIP pattern	49(61.25%)
Probable UIP pattern	61(76.25%)
Alternative diagnosis	38 (47.50%)

Data were presented as mean ± SD, or number and percentage (%)

Table 2 ECHO findings of the study population

	Mean (SD)
LVEF % by M mode (%)	62.21% (± 4.78)
PASP MmHg (mmHg)	51.37 MmHg (± 19.25)
RT atrium area (cm2)	24.56 cm^2 (± 2.18 cm^2)
TR peak gradient (mmHg)	36.4 mmHg (± 16.9)
RT ventricular dimension mid (cm)	4 cm (± 0.56 cm)

which separates B-lines from each other was calculated and expressed in milliliters.

Statistical analysis

Statistical Package for Social Sciences (SPSS-model 25) software program turned into used for the evaluation of the results.

Results

Table 1 illustrates the demographic, clinical, and radiological data of all the subjects who participated in our study.

Table 2 displays the echo findings of the study cohort.

Comparison between the demographic data of the subjects included in the study classified according to the result of transthoracic U/S was shown in Table 3, where there was a substantial variance between both groups regarding age and smoking history ($p=0.003$ and 0.013 respectively).

Table 4 displays the comparison between HRCT pattern and PFT results of the study population according to the result of transthoracic u/s, Regarding HRCT pattern, all the patients with UIP ($n=42$) and Indeterminate UIP ($n=49$) had positive ultra-sonographic findings [$p=0.041$ and 0.001 accordingly], while regarding pulmonary function tests, there was a considerable variance between both groups regarding FVC, PEF, FEF25-75, FEV1/VC ($P=0.037$, 0.029, 0.015, and 0.000 accordingly).

Figure 2 shows a chest ultrasound image showing multiple B lines and a high-resolution CT image of the same patient. The most positive US diagnosis areas were upper lateral, lateral basal, and interscapular areas as illustrated in Fig. 3. The strength of association between TUS diagnosis and FVC was done using a 2-sided Spearman's rho correlation where there was a weak negative correlation between TUS diagnosis and FVC [(r = -0.25, $P=0.026$) as displayed in Table 5.

Table 3 Comparison between demographic data of the patients included in the study according to the transthoracic ultrasonography results

		U/S diagnosis				
		Positive (*n* = 73)		Negative (*n* = 7)		
		N	%	*N*	%	*P* value
Gender	Male (38)	37	(97.4)	1	(2.6%)	0.112
	Female (42)	36	(85.7%)	6	(14.3%)	
Exposure to Occupational hazards	No (53)	47	(88.7%)	6	(11.3%)	0.413
	Yes (27)	26	(96.3%)	1	(3.7%)	
Smoking history	No (46)	39	(84.8%)	7	(15.2%)	0.013*
	Yes (34)	34	(100%)	0	(0%)	
Age (years) (mean ± SD)		37.1 ± 9.04		50.82 ± 11.49		0.003*

Data are presented as mean ± SD, or number and percentage (%). *P* value below 0.05 is significant. (T) Student *t* test of significance

* mean significant

Table 4 Comparison between HRCT pattern and PFT results of the study population according to the result of transthoracic u/s

HRCT	Positive Findings by US (*n* = 73)	Negative findings by US (*n* = 7)	*P* value
HRCT pattern	*N* (%)	*N* (%)	Fisher's Exact test
➢ UIP (*n* = 42)	42 (100%)	0 (0%)	0.041
➢ Indeterminate UIP (*n* = 49)	49 (100%)	0 (0%)	0.001*
➢ Probable UIP (*n* = 61)	58 (95.1%)	3 (4.9%)	0.051
➢ Alternative diagnosis (*n* = 38)	34(89.5%)	4 (10.5%)	0.703
Pulmonary function tests	mean ± SD	mean ± SD	Student's t test
➢ FVC (L)	53.59 ± 14.0	84.57 ± 30.79	0.037*
➢ FEV1(L)	56.14 ± 15.82	79.71 ± 30.13	0.085
➢ FEV1/FVC (%)	85.05 ± 8.14	85.0 ± 1.63	0.962
➢ PEF	41.6 ± 14.8	55.0 ± 20.1	0.029*
➢ FEF (25–75)	48.6 ± 15.5	64.1 ± 14.8	0.015*
➢ FEV1/VC (%)	50.9 ± 12.9	72.3 ± 11.2	0.000*

Data are presented as mean ± SD, or number and percentage (%). *P* value below 0.05 is significant

* mean significant

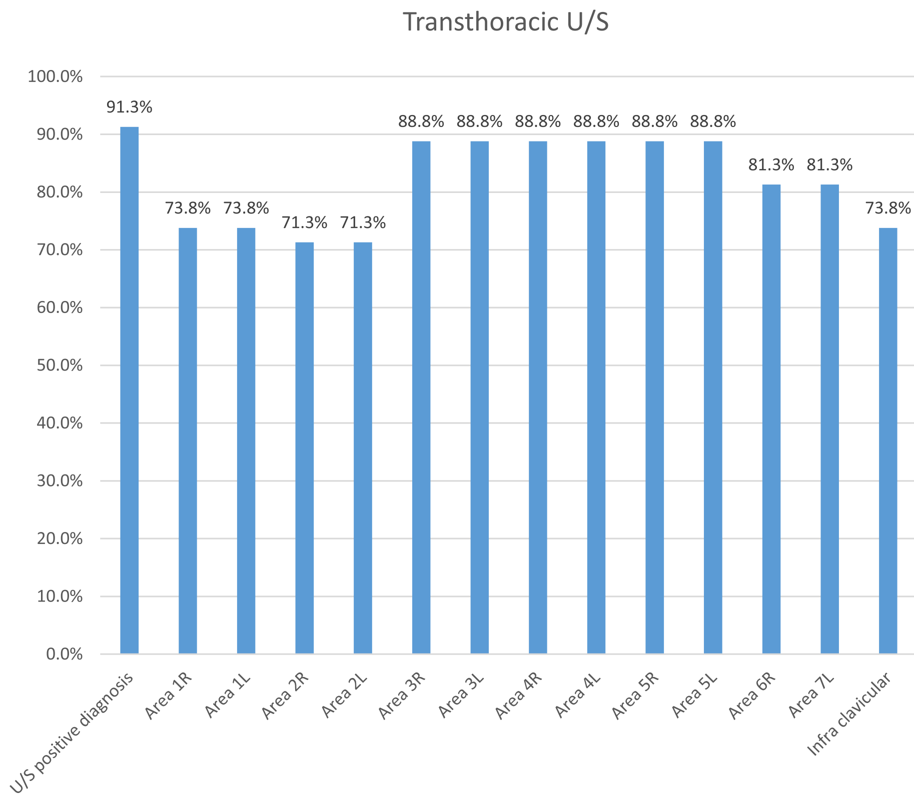

Fig. 3 Percent of positivity of TUS diagnosis among the diverse areas on both sides of the chest

Table 5 The correlation between U/S Diagnosis and FVC

		FVC
U/S diagnosis	*r*	−0.25
	P value	0.026*

*mean significant

Discussion

High-resolution computed tomography (HRCT) for a long time was deliberated as the standard investigation in the early diagnosis of ILD as it is a sensitive investigation to evaluate the degree and the pattern of pulmonary affection. Reticular pattern appearance, ground-glass opacities, micro-nodular and nodular pattern, and honeycombing shape are the most common HRCT signs of pulmonary involvement [4]. Recently, it has been highlighted that lung sonography is valuable in the early detection of interstitial lung diseases, characterized by the existence of multiple B-lines on both sides that seem to separate laser-like longitudinal hyperechoic reverberation artifacts that begin from the pleural line and extend to the end of image [3].

This study was accomplished in Aswan University Hospital in the chest department, of 80 patients diagnosed with ILD according to ATS/ERS International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias 2018 [4]. The whole study group was diagnosed as ILD by HRCT with its diverse types. We found that the result of chest ultra-sonography was positive in 73 cases (91.25%), while it was negative in 7 cases (8.75%) and B lines were the most common type of chest US artifact among patients with ILD. In harmony with our study, the latest study of the sonographic lung surface in 12 sarcoidosis patients associated with pulmonary involvement revealed that all patients had an unsmooth, corrugated pleural surface associated with many comet tail artifacts [8]. Gargani et al. disclosed that about half of the patients diagnosed with systemic sclerosis in their study had B lines as a hallmark of interstitial pulmonary fibrosis [9]. Sayed et al. displayed that ILD patients had a considerable percentage of B lines compared with controls (73.8 vs.0%) ($P=0.001$) [10]. Similarly, a previous study shows that all patients of ILD diagnosed by HRCT were positive in transthoracic chest ultrasonography in the form of multiple bilateral

B-lines on the lungs. Also, the presence of more than six B-lines per scan [7]. Tardella et al. summarized that the cutoff point highly suggestive of the presence of ILD affection in systemic sclerosis patients was detection of ten B-line on lung Sonography (representative for "lung interstitial syndrome") [11]. Gigante et al. found a considerable significant correlation between the number of B-lines detected on lung Sonography and Warrick score HRCT assessment [12]. Also, Man et al. determined that the usage of LUS in ILD sufferers has numerous advantages in the form of a useful, less costly, easily accessible, and no radiation investigation [13]. Furthermore, Man et al. also found a considerable correlation between both HRCT and ultrasound scores and this approves with our result [14].

Regarding ABG, there was a considerable correlation between both Pao2 and O2 saturation and positive lung ultra-sonographic findings. This is approved by a previous study, which found that the space between B-lines was inversely correlated with Pao2 [7]. Concerning PFT, we found a considerable variation between the 2 groups classified according to the result of ultrasonographic diagnosis at FVC, at PEF, FEF25-75, and FEV1/VC. This was in harmony with the findings of Sayed et al. who established that there was a substantial inverse relationship between B-line distance detected ultra-sonographically and FVC% predicted ($r = -0.46$, $P = 0.03$) [9]. Similarly, a previous study summarized that there was a substantial negative correlation between the B-lines score and FVC while no substantial correlation was present between FEV1 and the total number of B-lines. moreover, Hasan and Makhlouf also found that the space between B-lines was inversely correlated with FVC and total lung capacity (TLC) [7].

However, this study had limitations including the small number of patients in our study. also, we did not compare chest radiographic findings with sonographic findings among patients with ILD.

Conclusion

Transthoracic ultrasound is a less costly, non-invasive, and easily used modality that prerequisites less contrast and radiation. It is a complementary technique for analysis of ILDs especially in conditions where chest CT is not always selected or is contraindicated. It is a reliable technique for early diagnosis of ILD particularly among individuals with a significant risk for developing ILDs. Bilateral B lines as a transthoracic ultrasound sign are highly suggestive of the presence of ILD. It can be used as a predictor marker of deterioration of the lung function parameters and the presence of fibrosis on the CT chest.

Abbreviations

CTD	Connective tissue disease
CT	Computed tomogram
FEF 25-75	Forced expiratory flow at 25% to 75% of the total flow of forced vital capacity
FEV1	Forced expiratory volume in first second
FVC	Forced vital capacity
HRCT	High-resolution computed tomography
ILD	Interstitial lung disease
IPF	Idiopathic pulmonary fibrosis
LUS	Lung ultrasound
MMRC	Modified Medical Research Council dyspnea scale
PaO2	Partial pressure of O2 in arterial blood
PEF	Peak expiratory flow
TLC	Total lung capacity
TUS	Transthoracic ultrasonography
UIP	Usual interstitial pneumonia

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None.

Authors' contributions
SB analyzed and interpreted the patient data regarding the transthoracic ultra-sonographic images and examination of interstitial lung disease patients and was a major contributor to writing the manuscript. SS contributed to the diagnosis of interstitial lung disease patients. SA contributed to the technical support. MG contributed to the collection of the data and clinical examination of interstitial lung disease patients. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by Aswan University, faculty of Medicine Ethics Committee–IRB: aswu/196/12/17.

Consent for publication
The manuscript has been read and approved by all the authors.

Competing interests
The authors declare that they have no competing interests.

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