Transthoracic ultrasonographic features of diffuse parenchymal lung diseases

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Objectives The value of transthoracic ultrasonography (TTUS) in diffuse parenchymal lung disease (DPLD) has not been established yet. This prospective study was conducted to assess pleural and parenchymal alterations in patients with DPLD by TTUS and to compare the results with chest high-resolution computed tomography (HRCT). The results of TTUS were compared with some arterial blood gas (ABG) parameters and 6-min walk test (6MWT).

Patients and methods This study was conducted on 50 patients. All patients underwent HRCT, resting ABGs, and 6MWT, in addition to TTUS to evaluate (a) the presence and number of B-line and distance between them, (b) pleural effusion, (c) pleural thickening, (d) an irregular, fragmented pleural line, and (e) subpleural alterations.

Results The studied group showed female predominance, wide range of age, and most of them were nonsmokers. All patients had diffuse bilateral B-lines. B-line numbers were inversely correlated with severity of pulmonary fibrosis detected by HRCT modified Warrick score; however, distance between B-lines was directly correlated with severity of pulmonary fibrosis. Some ABGs (resting PaO_2, resting SpO_2%, $AaDO_2$) and 6MWT parameters were correlated with B-line number and distance between them. As detected by TTUS, the majority of patients (82%) had irregular thickened pleural line, whereas 44% of them had absent lung sliding.

Conclusion TTUS can play a complementary role in the diagnosis and monitoring of DPLD patients. Multiple B-lines distributed over the entire lung surface in combination with a thickened, irregular, and fragmented pleural line are strongly suggestive of the presence of DPLD. TTUS gives an idea about diffuse or limited, early, or advanced DPLD.

Egypt J Bronchol 2017 11:179–187

Egyptian Journal of Bronchology 2017 11:179–187

Keywords: B-lines, interstitial lung disease, lung ultrasound

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Received 11 January 2017 **Accepted** 6 March 2017

Introduction

In recent years, transthoracic lung ultrasound (TTUS) has risen as a new, promising technique for assessment of numerous pulmonary abnormalities [1]. It has been highlighted that lung sonography is highly sensitive to variations of the pulmonary content and balance between air and fluids. Of late, lung US has been considered a valid method for the assessment of interstitial pulmonary fibrosis compared with high-resolution computed tomography (HRCT) [2]. Interstitial lung disease (ILD) can be imaged by the presence of B-lines (also called US lung comets). B-lines are a sonographic sign of interstitial syndrome, originating from thickened interlobular septa [3].

Aim

The aim of this study was to assess pleural and parenchymal alterations in patients with diffuse parenchymal lung disease (DPLD) by TTUS and to compare the results with the severity of changes in chest HRCT. In addition, the results of TTUS examination were compared with some arterial blood gas (ABG) parameters and 6-min walk test (6MWT), which reflect the degree of pulmonary impairment secondary to fibrosis.

Patients and methods

This descriptive cross-sectional study was conducted at our institute. The ethical committee of university hospital institute approved the study. An informed written consent was obtained from all participants before their enrolment into the study. Fifty patients with DPLD were included in this study. They were selected from the chest department and the chest outpatient clinic. All patients were diagnosed according to diagnostic algorithm of ILD [4]. The diagnosis of these cases was based on clinical presentation, serological markers, pulmonary function tests, HRCT pattern and distribution, bronchoscopy with bronchoalveolar lavage, and biopsy [Transthoracic Ultrasonography (TTUS) or by mediastinoscopy].

Exclusion criteria

Patients with pulmonary edema of various causes, pneumonia, atelectasis, chronic obstructive pulmonary disease, pulmonary embolism, and pleural disease were excluded from the study, as B-lines may be detected in all mentioned cases [3,5,6]

 DOI: 10.4103/ejb.ejb_3_17

Study design

All patients were subjected to the following:

(1) Detailed medical history and clinical examination, including demographics, family, smoking, drug, environmental, and occupational exposures history, with emphasis on the onset, course, and duration of the presenting symptoms, and the symptoms and signs of extrapulmonary systems affection [4].
(2) Laboratory tests: these tests included complete blood count, erythrocyte sedimentation rate, urine analysis, fasting and postprandial blood sugar, liver function tests, creatinine, blood urea nitrogen and serological markers such as antinuclear antibody, lupus erythematosus cells, rheumatoid factor, cytoplasmic antineutrophil cytoplasmic antibodies, perinuclear antineutrophil cytoplasmic antibodies, and antiscleroderma 70 antibodies (when indicated according to clinical diagnosis of the case) [4].
(3) Resting ABGs analysis: ABGs were analyzed by 'rapid lap analyzer 248' apparatus; the following values were recorded and then calculated: O_2 saturation% (SaO_2%), PaO_2 mmHg, $PaCO_2$ mmHg, HCO_3 mEq/l and pH, and AaO_2 gradient.
(4) Six-min walk distance (6MWD): it is supervised measurement of the distance that patients can quickly walk on a flat, hard surface in a period of 6 min. 6MWD was carried out before and after interventions to determine the patient functional capacity [7]. Reference values are 576 m for healthy male patients and 494 m for healthy female patients [8]. Before and after the test, oxygen saturation% (SpO_2%) was measured by a pulse oximeter, and desaturation was defined as a fall in oxygen saturation to 88% or less during the 6MWT [9].
(5) HRCT
HRCT examination was performed by standard protocol using Aquilion 160 helical scanner (Toshiba, Otawara, Japan). Scans were obtained at full inspiration from the apex to the lung base with the patients in the supine position. The acquisition parameters were as follows: sequential mode, 1–1.5 mm collimation and 10 mm interval, 180–260 mA average tube current (depending on body built), and 120–140 kV tube voltage. In the current study, pulmonary involvement was identified and scored according to a semiquantitative modified Warrick score [10].
Modified Warrick scoring was obtained by summing the point values of parenchymal abnormality pattern (severity score) ranging from 0 (normal) to 15 (all lesions present) and (the extension score) by localizing the number of pulmonary segments involved of both the lungs and adding +1 for each segment involved. An additional score of +3 was assigned when the lesions were bilateral. The extension score ranged from 0 (normal) to 15 (more than nine pulmonary segments involved). The total Warrick score ranged from 0 (no involvement) to 30 (the worst involvement). The results were expressed as normal (0 point); 1, mild (>8 points); 2, moderate (8–15 points); and 3, severe (<15–30 points) (Table 1) [10].
(6) Trans-thoracic ultrasonography (TTUS)
TTUS was performed using (Sonoscape A8, Mobile Ultrasonic Diagnostic System, model: A8, SN18006751, SonoScape Co., Ltd. China SONOMED) and (Sonoscape SSI- 6000, Digital Color Doppler Ultrasound System, Model: SSI- 6000 SonoSape Co., Ltd. China SONOMED) equipped with a 3.5-MHz convex probe and 8-MHz linear probe. The patient was examined in a supine or near supine position with the anterior chest wall exposed rising his/her arms above his/her head to widen the intercostal spaces and facilitate scanning.

We used convex probe and then linear probe in the same manner for effective assessment of the pleura; scanning was performed using the intercostal spaces as acoustic windows.

In the evaluation of interstitial fibrosis, thoracic sonography was performed for each patient using the protocol described by Volpicelli *et al.* [3] and Anderson *et al.* [2]. The sonographic technique ideally consists of scanning eight zones. Four chest areas per side, areas 1 and 2 on right side, as well as areas 5 and 6 on left side denote the upper anterior and

Table 1 Semiquantitative modified Warrick score

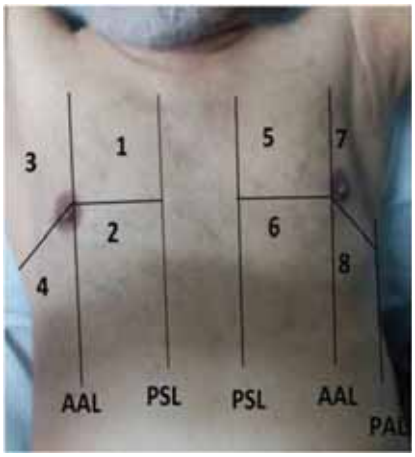
	Grading
Severity scores (parenchymal alteration pattern)	
Ground glass opacities	1
Irregular pleural margins	2
Septal/subpleural lines	3
Honeycombing	4
Subpleural cysts	5
Maximal severity score	15
Extension scores (number of bronchopulmonary segments involved)	
1–3 segments	+1
4–9 segments	+1
>9 segment involved	+1
Bilateral involvement	+3
Note that extent of disease measured for each of the abnormalities	
Maximal extent score	15

lower anterior chest areas, respectively. Areas 3 and 4 on the right side, as well as areas 7 and 8 on left side, denote the upper lateral and basal lateral chest areas, respectively (Fig. 1).

TTUS interpretation:

(1) B-lines
   (a) The presence of B-lines, which were previously called comet-tail artifacts, generated from the thickened interlobular septa at the lung wall interface was assessed. These were defined as well-defined, vertical, hyperechoic, dynamic lines originating from the pleural line, and spreading like a laser ray up to the edge of the screen. These artifacts are best visible under real-time examination, because some of them appear less pronounced on frozen sonograms. A positive region is defined by the presence of three or more B-lines in a longitudinal plane between two ribs and a positive exam is defined by the presence of two or more positive regions bilaterally [3]. The numbers of B-lines per scan were counted and then the total number of B-lines in all previously mentioned areas was calculated [3].The distance between each two adjacent B-lines was measured and then the average was calculated and was expressed in millimeters.
(2) Pleura
   (a) Detection of lung sliding under real-time examination.
   (b) Estimating whether the pleural line is fragmented and irregular or smooth.
   (c) Detection of presence or absence of pleural nodule or pleural effusion.
   (d) Estimation of pleural thickness: we measured the thickness of pleural lines in all zones and then calculated the mean value. Pleura was considered thickened if its thickness was more than 3 mm [11].

Figure 1



Chest areas and lines for complete TTUS examination in DPLD patients. AAL, anterior axillary line; PAL, posterior axillary line; PSL, parasternal line.

Statistical analysis

Data were analyzed by the statistical package for the social science software, version 20, Armonk, NY: IBM Corp. Descriptive results were expressed as mean±SD, and non-numerical data were expressed as number and percentage. Graphics were performed using Microsoft excel 2010. χ^2 analysis was used to compare between TTUS and HRCT data. Study of the relationship between variables was performed using 'Pearson correlation'. Linear correlation coefficient (r) was used for the detection of the correlation between two quantitative variables in one group. Both the direction and strength of relation were expressed by calculating the correlation coefficient (r). The strength is expressed by a number ranging between 0 (absent correlation) and 1 (perfect correlation). In practice, it is usually fractions where the more close to 1 the stronger the correlation. The following can serve as a guide to interpret the magnitude of correlation coefficient.

Results

Fifty patients with DPLD were included in this study (34 women and 16 men with extended age ranging from 26 to 83 years, mean age of 51.92±13.28 years); 19 patients were recently diagnosed with DPLD (38%, n=19), and 31 patients were previously diagnosed with DPLD and were attending the outpatient clinic for follow-up (62%, n=31). Clinical characteristics and demographic data of the study group are summarized in Table 2. This table shows that large portions of DPLD participant patients (80%) were nonsmokers, and presented with more than one symptom. All of them (100%) presented with dyspnea and cough, followed by chest wheeze in 58% of patients. Additional extrapulmonary manifestations were recorded in 22% of patients. The majority of our patients were diagnosed with hypersensitivity pneumonitis (HP) (54%, n=27), and sarcoidosis was recorded in 8% (n=4).

To assess severity of pulmonary fibrosis, the patients were divided into three groups (mild, moderate, and severe) according to HRCT semiquantitative modified Warrick score (Table 3) [10]. Most of our patients were classified as moderate (48%, n=24), followed by severe (34%, n=17), and lastly mild (18%, n=9).

Table 2 Demographic data of the studied groups

Variables	*N* (%)
Age (year)	
Mean±SD	51.92±13.28
Range	26–83
Sex	
Male	16 (32)
Female	34 (68)
Smoking	
Smoker	9 (18)
Exsmoker	1 (2)
Nonsmoker	40 (80)
The main presenting symptoms	
Dyspnea	50 (100)
Cough (dry, productive)	50 (100)
Chest pain	2 (4)
Chest wheeze	29 (58)
Cyanosis	8 (16)
Clubbing	15 (30)
Extrapulmonary symptoms	11 (22)
Diagnosis	
HP	27 (54)
Sarcoidosis	4 (8)
IPF	12 (24)
Rheumatoid	3 (6)
SLE	3 (6)
Scleroderma	1 (2)
Methods of diagnosis	
History+HRCT+exclusion criteria	39 (78)
History+HRCT+LN biopsy	4 (8)
History+HRCT+serological markers	7 (14)

HP, hypersensitivity pneumonitis; HRCT, high-resolution computed tomography; IPF, idiopathic pulmonary fibrosis; SLE, systemic lupus erythmatosis.

Table 3 Classification of diffuse parenchymal lung disease severity according to total Warrick score

Item	Mild (S=>8)	Moderate (S=8–15)	Severe (S=<15–30)
Total Warrick score (mean±SD)	3. 9 ±0.33	9.6±1.7	20.3±4.2
N (%)	9 (18)	24 (48)	17 (34)

S, total Warrick score.

Table 4 shows total B-line number, mean B-distance, and pleural thickness for all studied patients as mean± SD. In addition, this table shows that most of the cases had thickened and irregular pleural line (62 and 82%, respectively), whereas 44% had reduced or absent lung sliding.

Table 5 and Fig. 3 show that the degree of interstitial affection on chest HRCT detected by modified Warrick score is significantly inversely correlated with total B-line number and positively correlated with B-line distance between each two adjacent B-lines among all patients involved– mild, moderate, and severe groups.

Table 4 Thoracic ultrasound parameters in total studied patients

Parameters	Values
Total B-lines number (mean±SD)	72.1±9.05
Mean B-distance (mm) (mean±SD)	4.12±0.76
Pleural thickness in mm in total studied patients (mean±SD)	3.205±0.34
Pleural thickness for the group with normal pleural thickness (mean±SD) [*N* (%)]	2.95±0.05 [19 (38)]
Pleural thickness for the group with thickened pleural line (mean±SD) [*N* (%)]	(3.36±0.35) [31 (62)]
Irregular pleural line [*N* (%)]	41 (82)
Regular pleural line [*N* (%)]	9 (18)
Pleural effusion [*N* (%)]	0
Pleural nodules [*N* (%)]	3 (6)
Reduced or absent lung sliding [*N* (%)]	22 (44)
Normal lung sliding [*N* (%)]	28 (56)

Table 6 and Fig. 4 show that there was no statistical significant difference in total number of B-lines and B-line distance detected by TTUS between mild, moderate, and severe total Warrick score (P=0.79 and 0.73, respectively), whereas there was a significant difference in pleural thickness of all patients involved in each group and pleural thickness of patients with thickened pleura in each group (P=0.012 and .026, respectively).

Table 7 shows that there was no statistical significant difference in resting PaO_2, resting SaO_2%, $AaDO_2$, 6MWD, and post-6MWT SpO_2% among all patients in mild, moderate, and severe groups.

Table 8 shows that B-line number is inversely correlated with B-line distance in mm and AaO_2 gradient, whereas it is positively correlated with resting PaO_2, resting SpO_2%, post-6MWT SpO_2%, and 6MWD among all patients involved – mild, moderate, and severe groups.

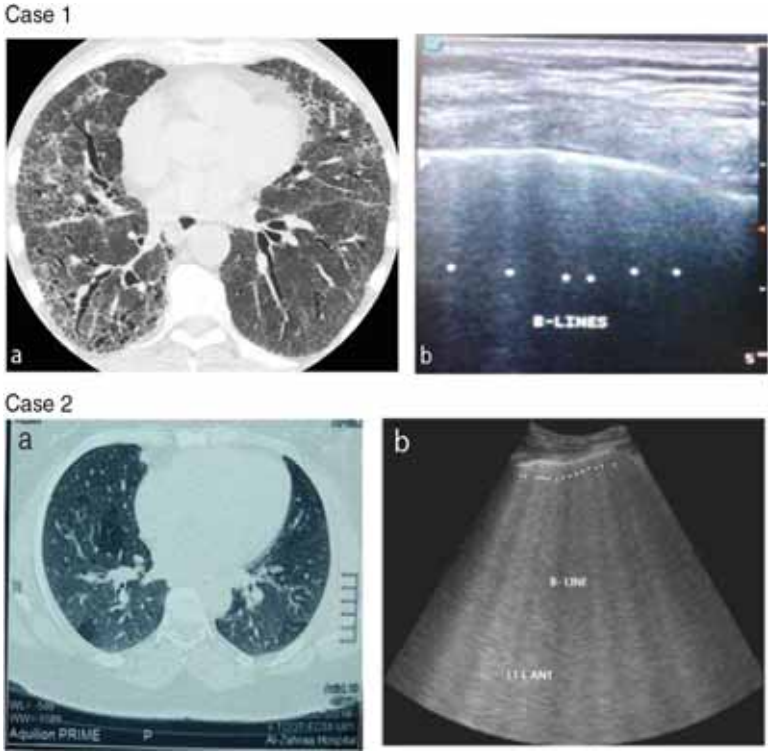
Table 9 shows that B-line distance is positively correlated with AaO_2 gradient, whereas it is negatively correlated with resting PaO_2, resting SpO_2%, post-6MWT SpO_2%, and 6MWD among all patients involved – mild, moderate, and severe groups (Fig. 2).

Discussion

Lung ultrasound is a reliable tool to evaluate DPLD. The presence of multiple B-lines is the primary sonographic sign in DPLD. Pleural line abnormalities are often present in patients with DPLD. The distribution of B-lines correlates with computed tomography signs of fibrosis [2].

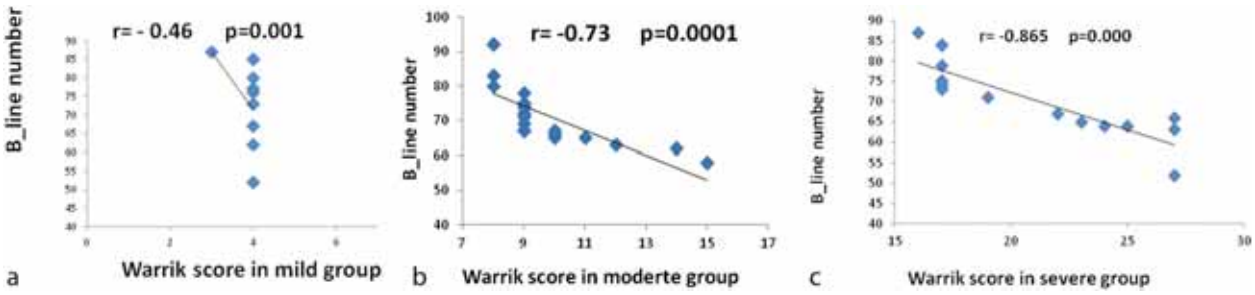
In the current study, about 80% of DPLD participant patients were nonsmokers, and presented with more

Figure 2



Selected examined cases HRCT versus TTUS CASE (1): Male patient 76 y old, smoker, clubbing +ve, (IPF). (a) HRCT at the level of the lower lobes shows a subpleural "reticular pattern" characterized by thickened interlobular septae, thickened intralobular interstitium, traction bronchiectasis, subpleural plebe and minimal honeycombing. (b) TTUS for the same patient showed diffuse B-lines with a wide distance between them (about 7 mm), pleural line is fragmented and irregular, pleural thickness: were 4.1 mm. CASE (2): Female patient, 43 y old non-smoker diagnosed as hyper-sensitivity pneumonitis. (a) HRCT at the level of the lower lobes shows ground glass opacity with mosaic pattern. (b) TTUS for same patient showed diffuse B-lines with narrow distance between them (less than 3 mm), pleural line is smooth, no pleural thickness (2.8 mm).

Figure 3



Correlation of modified Warrick score and B-line numbers in three studied groups. (a) Mild group. (b) Moderate group. (c) Severe group.

Table 5 Correlation of Warrick score between B-line numbers and distance in three studied groups

Total Warrick scores	Severity of DPLD by HRCT Warrick score					
	Mild		Moderate		Severe	
	r	*P*	*r*	*P*	*r*	*P*
Total B-line numbers	–0.46	<0.001*	–0.73	<0.001*	–0.865	<0.001*
B-distance (mm)	0.47	<0.001*	0.88	<0.001*	0.873	<0.001*

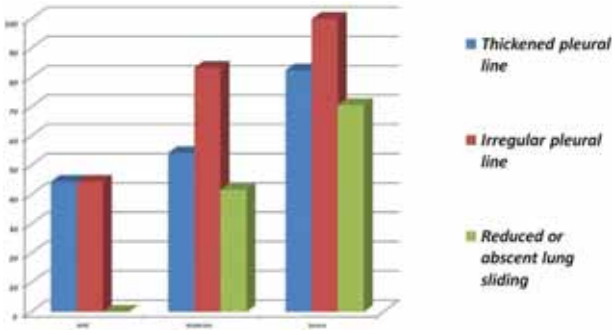
DPLD, diffuse parenchymal lung disease; HRCT, high-resolution computed tomography. *Significant.

than one symptom. All patients presented with dyspnea and coughing; however, chest wheezes were recorded in 58% of them. Extrapulmonary manifestations were observed in 22% of patients. This can be clarified by female predominance in our study (68%, *n*=34) versus male (32%, *n*=16); in addition, the majority of our

patients were diagnosed with HP (54%, *n*=27), and sarcoidosis was recorded in 8% (*n*=4).

These results were in agreement with Behr [12], who concluded that dyspnea at rest or on exertion is a common presenting symptom in 90% of cases of ILD. Dry or productive cough of nonpurulent sputum is also a common feature in up to 80% of ILD patients. In addition, Leslie [13], reported that HP and sarcoidosis are less likely to occur in smokers.

Figure 4



Pleural assessment by TTUS in three studied groups.

In the current study, newly diagnosed cases of DPLD were 38% (*n*=19) and previously diagnosed DPLD attending outpatient clinic for follow up were 62% (*n*=31). All patients were diagnosed according to diagnostic algorithm of ILD [4]. Final diagnosis was either by clinical diagnosis, serological markers, pulmonary function tests, and HRCT pattern and distribution or by clinical diagnosis, HRCT, bronchoalveolar lavage, and biopsy [lymph-node biopsy through bronchoscopy (TBLB), or mediastinoscopy]. These results coincide with Launay *et al.* [14], who reported that for the diagnosis of ILD as it is a sensitive method to assess the extent and the pattern of pulmonary fibrosis. However, Kanne [15], concluded that a complete lack of pulmonary

Table 6 Comparison of transthoracic ultrasonography parameters between mild, moderate, and severe Warrick score

TTUS findings	Severity of DPLD by HRCT Warrick score			
	Mild (*n*=9; 18%)	Moderate (*n*=24; 48%)	Severe (*n*=17; 34%)	*P*-value
Total B-lines number (mean±SD)	73.2±11.2	70.9±7.5	71.6±9.0	0.79
Mean B-Distance (mean±SD)	3.9±0.45	4.2±0.66	4.1±1.0	0.73
Pleural thickness (mm) (mean±SD)	3.09±0.2	3.11±0.2	3.4±0.47	0.012*
Thickened pleural line [*n* (%)]	4/9 (44.4)	13/24 (54.2)	14/17 (82.4)	0.09
Irregular pleural line [*n* (%)]	4/9 (44.4)	20/24 (83.3)	17/17 (100)	0.002*
Reduced or absent lung sliding [*n* (%)]	0/9 (0)	10/24 (41.6)	12/17 (70.6)	0.002*

DPLD, diffuse parenchymal lung disease; HRCT, high-resolution computed tomography; TTUS, transthoracic ultrasonography. *Significant.

Table 7 Comparison of some arterial blood gas and 6-min walk test parameters between mild, moderate, and severe Warrick score

Parameters	Severity of DPLD by HRCT Warrick score			
	Mild (*n*=9; 18%)	Moderate (*n*=24; 48%)	Severe (*n*=17; 34%	*P*-value
Resting PaO_2	75.1±12.1	69.1±10.1	65.5±13.3	0.14
Resting SaO_2%	95.2±2.8	93.9±3.6	91.3±5.6	0.06
$AaDO_2$	30.1±10.7	33.9±11.6	37.5±11.6	0.28
6MWD	264.1±48.9	246.3±102.2	227.7±64.9	0.46
Post-6MWD SpO_2%	93.5±2.7	92.4±4.9	88.8±7.2	0.06

DPLD, diffuse parenchymal lung disease; HRCT, high-resolution computed tomography; 6MWD, 6-min walk distance.

Table 8 Correlation between B-line numbers and some measured parameters in mild, moderate, and severe groups

Total B-line numbers	Severity of DPLD by HRCT Warrick score					
	Mild (*n*=9; 18%)		Moderate (*n*=24; 48%)		Severe (*n*=17; 34%)	
	r	*P*	*r*	*P*	*r*	*P*
Mean B-distance (mm)	−0.95	0.000	−0.92	<0.001*	−0.97	<0.001*
Resting PaO_2	0.96	0.000	0.91	<0.001*	0.88	<0.001*
Resting SpO_2%	0.702	0.035	0.680	<0.001*	0.755	<0.001*
$AaDO_2$	−0.91	0.000	−0.84	0.011	−0.96	<0.001*
Post-6MWD SpO_2%	0.825	0.036	0.773	0.04	0.714	<0.001*
6MWD	0.197	0.000	−0.97	<0.001*	0.92	<0.001*

DPLD, diffuse parenchymal lung disease; HRCT, high-resolution computed tomography; 6MWD, 6-min walk distance. *Significant.

Table 9 Correlation between B-line distance and different studied parameters in mild, moderate, and severe groups

Mean B-distances (mm)	Severity of DPLD by HRCT Warrick score					
	Mild (*n*=9; 18%)		Moderate (*n*=24; 48%)		Severe (*n*=17; 34%)	
	r	*P*	*r*	*P*	*r*	*P*
Resting PaO_2	−0.822	0.007	−0.78	0.003	−0.94	<0.001*
Resting SpO_2%	−0.738	0.023	−0.775	0.001	−0.786	<0.001*
$AaDO_2$	0.824	0.006	0.88	0.001	0.97	<0.001*
Post-6MWD SpO_2%	−0.64	0.015	−0.639	0.012	−0.743	<0.001*
6MWD	−0.92	<0.001*	0.89	0.011	−0.89	<0.001*

DPLD, diffuse parenchymal lung disease; HRCT, high-resolution computed tomography; 6MWD, 6-min walk distance. *Significant.

parenchymal changes on HRCT imaging virtually excludes a diagnosis of ILD. Moreover, Meyer [16], detailed that HRCT of the thorax could give data that strongly support a specific diagnosis and may be diagnostic [e.g. typical changes of usual interstitial pneumonia (UIP)] such that further testing with bronchoscopy or surgical lung biopsy is not required.

Semiquantitative HRCT scoring methods have been developed to give more exact evaluation of quantity and type of DPLD abnormalities. In the current study, pulmonary involvement identified and scored according to semiquantitative HRCT modified Warrick score into three groups – mild (18%, *n*=9), moderate (48%, *n*=24), and severe group (34%, *n*=17). Total Warrick score (mean±SD) for each group was 3. 9±0.33, 9.6±1.7, and 20.3±4.2, respectively.

Semiquantitative HRCT modified Warrick scoring system has been used by Hasan and Makhlouf [17], and other several studies [18–20].

In patients with DPLD, the subpleural interlobular septa are thickened by deposition of collagen and fibrous tissues. By investigating the lung surface by TTUS, the great impedance gradient between the thickened septa and air in the lung causes reflection of ultrasound beams, creating diffuse B-lines all over the lung surface.

In our study, by TTUS examination, all patients had diffuse and more than three B-lines on both sides of the lung. These B-lines were best visible under real-time examination, as some of them seem less declared on frozen sonograms. Similarly, we observed that the B-lines appear clearly visible and widely separated from each other (7 mm) corresponding to well-established pulmonary fibrosis with reticular pattern or honeycombing in HRCT, whereas there were numerous B-lines with a narrow distance between them (3 mm), making the lung more hyperechoic, giving the description of white lung that was observed corresponding to ground glass areas in HRCT.

These outcomes were in agreement with Hasan and Makhlouf [17], as they concluded that B-lines appear obvious and widely separated from each other in patients with well-established fibrosis in HRCT; in addition, the B-lines seem numerous with a narrow distance between them in those with early ILD. They proposed that numerous B-line artifacts with a narrow distance between them might be because of the fact that the area between two adjacent interlobular septa became filled with inflammatory cells and edema. Bouhemad *et al.* [21], also stated that multiple B-lines 7 mm apart are caused by thickened interlobular septa, characterizing interstitial edema, whereas B-lines 3 mm or less apart are caused by ground glass areas characterizing alveolar edema. Same conclusions were also reached by Lichtenstein *et al.* [22].

In our study, the total B-lines number and mean B-distance for all studied patients (mean±SD) were 72.1 ±9.05 and 4.12±0.76, respectively. Despite this, there was no significant difference in total number of B-lines and B-line distance identified by TTUS, between mild, moderate, and severe modified Warrick score (*P*=0.79 and 0.73 respectively); we found that the degree of interstitial affection on chest HRCT detected by modified Warrick score is significantly inversely correlated with total B-line number and positively correlated with B-line distance between each two adjacent B-lines among all patients involved – mild, moderate, and severe groups.

These results were in concurrence with Hasan and Makhlouf [17], as they reported that the distance between each two adjacent B-lines positively correlated with Warrick score (r=0.693) (P<0.001). Moreover, Cogliati *et al.* [18], concluded that the B-line score was significantly correlated with HRCT score (r=0.806). Nearly same results were obtained by Mohammadi *et al.* [19], as they reported that

Warrick score was significantly correlated with severity of pulmonary involvement (r=0.695, P<0.001).

Different results were reported by Gargani *et al.* [20], who found that mean US B-lines for total studied patients with systemic sclerosis (SSc) was 37±50. This score is more frequent in the diffuse form of SSc rather than in the limited form (73±66 vs. 21±35; P<0.05) and has a good correlation with HRCT on assessment of lung fibrosis (r=0.72, P<0.001). Likewise, mean Warrick score was higher in the diffuse form than in the limited form (6.9±4.1 vs. 1.6±2.5; P<0.001). Therefore, they concluded that US B-lines have a potential diagnostic value to detect pulmonary fibrosis. The contrast between this outcome and our outcome is most presumably because they studied mean B-lines number and Warrick score in diffuse versus limited form of interstitial lung infiltration in SSc only, just while our study was on different types of DPLD.

In the present study, we used linear probe for more details about the pleural line. We recognized that pleural thickness in all studied patients as mean±SD was 3.205±0.34 mm. The majority of cases had thickened pleural line (62%, n=31), whereas 38% (n=19), had normal pleural thickness with mean thickness±SD as 3.36±0.35 and 2.95±0.05 mm, respectively. In addition, there was irregular and fragmented pleural line in most cases (82%, n=41), whereas 18% (n=9), of patients had regular pleural line. On the other hand, we identified that 44% (n=22), of our studied patients showed reduced or absent lung sliding, whereas 56% (n=28), had ordinary lung sliding.

Comparable results were accounted for by Reissig and Kroegel [23], as they found that 84.9% (n=45) of their DPLD cases had thickened pleural surface, whereas 98.1% (n=52) of cases had irregular pleural surface.

In the current study, despite the fact that there was no significant difference (P=0.09) in percentage of patients (mild, moderate, and severe groups) with thickened pleura distinguished by TTUS, there was a significant difference (P=0.012) in the pleural thickness in millimeter (mean±SD) between all groups involved. However, there was a significant difference in percentage of patients with irregular pleura and absent or reduced lung sliding between mild, moderate, and severe groups (P=0.002 and 0.002, respectively). Moreover, all severe cases showed irregular pleural line over the whole lung (100%), thickened pleura, and nearly absent lung sliding in the vast majority of them (83.3 and 70.6%, respectively). On the other hand, the moderate group showed less value for irregularity, thickening, and sliding of the pleura (83.3, 54.2, and 41.6%), and these abnormalities were identified essentially at the base of the lung. Conversely, all mild cases demonstrated normal lung sliding while they had irregular thickened pleural line just at the lung base in 44.4% of them. These outcomes showed that the pleural abnormalities were better distinguishable in the lower part of the lung, and the degree of fibrosis turned out to be more pronounced as the disease progress.

These results were in agreement with those of Sperandeo *et al.* [24]. They investigated the role of TTUS features of mild, moderate, and severe pulmonary fibrosis (based on clinical, PFT and radiological finding). They reported that severe pulmonary fibrosis cases showed irregular and thickened pleural line over the whole lung (100%, 33/33) with reduced lung sliding in 20/33 (61%). Moderate group showed 32/32 (100%) with irregular thickening at both lung bases with reduced lung sliding in 13/32 (41%). Mild cases showed normal lung sliding, whereas irregular pleural thickening was observed just at the lung base in 19/19 (100%). This slight contrast between Sperandeo *et al.*[24] study and our own might be because they had bigger studied cases (n=84 vs. 50) and majority of them were IPF. Furthermore, Soldati *et al.* [25], concluded that in DPLD the degree of the pleural involvement can vary within the same patient, and usually a thickened and fragmented pleural line with multiple B-line is better detectable in the lower part of the lung, which reflects the extent of the fibrosisIn the current study, there was no statistically significant difference in resting PaO_2, resting SaO_2%, $AaDO_2$, 6MWD, and post-6MWT SpO_2% among all studied groups. We have observed that all the parameters measured as mean±SD decrease as the disease has become more advanced, with the exception of increasing gradient (AaO_2) directly with the severity of the illness, which indicates more impairment in gas exchange.

In the current study, B-line number is inversely correlated with B-line distance in millimeter, and AaO_2 gradient, whereas it is positively correlated with resting PaO_2, resting SpO_2%, post-6MWT SpO_2%, and 6MWD among all patients involved – mild, moderate, and severe groups. On the other hand, B-line distance is positively correlated with AaO_2 gradient, whereas it is negatively correlated with resting PaO_2, resting SpO_2%, post-6MWT SpO_2%, and 6MWD among all patients involved – mild, moderate, and severe groups. These results indicated that PaO_2, AaO_2 gradient, and 6MWD correlated with severity of DPLD, as numerous B-lines with narrow distances between them represent early

alveolar wall affection and little impairment in lung function, whereas less B-line number with wide distances between them indicate thickened septa and great functional impairment.

These results were in agreement with Hasan and Makhlouf [17], as they reported that the distance between B-lines inversely correlated with PaO_2 (r=–1.811) (P<1.110).

Conclusion

Thoracic US is favored by lower cost, no radiation exposure and bedside examination. In addition, it can play a complementary role in the diagnosis and monitoring of DPLD patients, especially when HRCT unavailable or cannot be done. Diffuse bilateral B-lines distributed over the lung surface in combination with a thickened, irregular, and fragmented pleural line are strongly suggestive of the presence of DPLD. HRCT can give an idea about the probable histopathological types; however, TTUS gives an idea about diffuse or limited, early, or advanced DPLD.

Recommendations

Future or new blinded study to assess the sensitivity, specificity, and diagnostic accuracy of TTUS in patients with DPLD versus PCX-Ray and HRCT. Further studies are recommended to attain DPLD severity score assessment via TTUS and to compare them with other severity scores such as severity of symptoms, ABG, 6MWT, HRCT, spirometry, and DL_{CO}.

Limitations

The study has a few limitations. First, TTUS had been act upon patients already diagnosed as DPLD, and this may be regarded as a bias for the interpretation. However, in this study, we do not assess the diagnostic accuracy of TTUS in DPLD patients, but we study the role of TTUS in evaluation of DPLD patients and whether it can play a complementary role in the diagnosis and follow-up of DPLD patients. Second, interstitial fibrosis is usually not homogeneously disseminated. This limitation is not considered, as the majority of the studied patients had diffuse disease and on TTUS examination nearly all of the affected areas were assessed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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