### Can high-frequency transthoracic sonography play a competitive role with high-resolution computed tomography in the assessment of dyspnea?

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### Background

Transthoracic ultrasound (TUS) can potentially give important complementary information in particular conditions like bedside rapid diagnostic evaluation of dyspneic patients who commonly present to emergency (ER) units.

### Objective

Assessing the significance and diagnostic utility of B-lines and pleural line abnormalities detected on TUS among patients presented to the ER unit for the assessment of dyspnea against high-resolution computed tomography findings.

Patients and methods

A prospective observational study including 240 consecutive patients was conducted. TUS was done for patients presenting to the ER for the assessment of dyspnea. B-lines and the pleural line were evaluated by a linear and convex transducers. Sonographic findings were reported against high-resolution computed tomography findings, which was considered the gold standard.

### Results

Slightly rough, fringed, irregular, interrupted, wavy, coexistence of more than one abnormal type of pleural line were detected in 30.8%, 35.4%, 19.2%, 17.9%, and 30% of cases, respectively. Warrick score classified patients with interstitial lung disease to mild (44.6%), moderate (36.3%), and severe (19.2%). Diffusing capacity for carbon monoxide (DLCO% predicted) and total lung capacity (TLC% predicted) predicted showed negative correlation with Warrick score (r=-0.66, r=-0.48respectively,  $P \leq 0.001$  for both) and positive correlation with distance between B lines (r=0.31 and 0.30 respectively, P<0.001 for both). Warrick score at a cutoff more than 7 showed 96.3% sensitivity and 64.3% specificity. Distance between B lines at cutoff more than 3 mm had 100% sensitivity and 40.4% specificity. Cutoff more than 3 for B lines number/scan showed 92.6% sensitivity and 31% specificity. Pleural thickness at cutoff more than 2 mm showed 100% sensitivity and 34% specificity. Abolished lung sliding showed 96.3% sensitivity and 50% specificity. Conclusion

TUS is an important tool for the diagnosis and assessment of pulmonary disorders. B-lines number and distance, pleural line abnormalities, lung sliding, and pleural thickness added diagnostic value for the ER assessment of dyspneic patients.

### **Keywords:**

B lines, dyspnea, pleural line, transthoracic ultrasound

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### Introduction

The gold standard imaging technique for the majority of pulmonary disorders is high-resolution computed tomography (HRCT) [1]. The hazard of ionizing radiation, high cost, and being nonportable are limitations to its bedside use [2].

Transthoracic ultrasonography (TUS) is nowadays progressively used for evaluating various pulmonary disorders. Owing to its relatively low cost, noninvasive nature, reproducibility of findings, and being portable for bedside use allowed its use for bedside rapid diagnostic evaluation of dyspneic patients who commonly present to emergency (ER) units [3].

B-lines is an important sign detected on TUS examination used for diagnostic appraisal [4], yet it cannot determine the definite underlying pathology [5].

Pathology of the lung parenchyma that reaches the surface of the lung leads to peculiar pleural line changes which can be detected via high-frequency TUS probe.

The current study aimed to assess the relevance and diagnostic utility of B-lines and pleural line

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abnormalities detected by TUS among admitted patients to the ER unit for the assessment of dyspnea against HRCT findings.

### Patients and methods

In all 240 patients admitted to the ER for dyspnea assessment during the period from May 2018 to January 2020 participated in this prospective observational study. TUS was performed followed by a thoracic noncontrast HRCT scan. The research ethics committee of Faculty of Medicine approved the study protocol. All participants gave informed written consent.

### Inclusion criteria

Inclusion criteria included those patients presented for dyspnea assessment at the ER unit.

### **Exclusion criteria**

- (1) Age less than 18 years.
- (2) Trauma.
- (3) Pneumothorax.
- (4) Massive pleural effusion with underlying atelectasis.
- (5) Subcutaneous emphysema.
- (6) Patients with more than 24 h interval between HRCT and TUS.
- (7) Patients with poor-quality of TUS image.

All study participants underwent the following:

- (1) History taking, clinical examination, dyspnea grading (modified Medical Research Council).
- (2) Arterial blood gases analysis (Rapid lab 850; CHIRON/Diagnostics, Halstead, UK).
- (3) HRCT (GE Lightspeed VCT, Siemens Healthcare, Germany, WI; 64 slices) Lung parenchymal involvement was identified and scored according to the semiquantitative modified Warrick score [6].
- (4) TUS (Aloka Echo Camera SSD-3500; Aloka Prosound, Yokohama, Japan).

All participants were examined by TUS using a 3.5 and 7.5 MHz probes [3].

Assessment was done for:

(1) B-lines:

Represent hyperechoic non fading vertical lines starting at the pleural line and running toward the screen end. The positive zone was identified by the detection of more than or equal to three Blines. The positive examination was identified by the detection of more than or equal to 2 positive zones on each side. The B-lines number was estimated per zone [7].

(2) The lung sliding

The to and fro lung movement with respiration seen at the pleural line.

- (3) The pleural line
  - (a) Thicknening: diffuse or focal echogenic lesions originating from parietal or visceral pleura, its width measured more than 3 mm with or without irregularity of the pleural line.
  - (b) Abnormal pleural line:
    - Slightly rough pleural line: the pleural line contour was blurred with difficulty to discern the pleural thickness.
    - (2) Irregular and interrupted pleural line: obvious and interrupted disorderly changes of the pleural surface.
    - (3) Fringed pleural line: uniform, thickened, and continuous distribution of the granular surface throughout the pleural line.
    - (4) Wavy pleural line: wavy lines possibly harboring B-lines in the concavities.

### **Pulmonary function tests**

Spirometry (Cosmed SrL, Quark PFTs ergo, P/N Co9035-12-99, made in Italy).

Measurements were done and interpreted according to the American Thoracic Society criteria [8].

Single-breath diffusing capacity for carbon monoxide (DLCO) 'D 97723; Zan 300, Oberthulba, Germany, CO/CH4 analyzer."

Hemoglobin and carbon monoxide (CO) level corrections were made for DLCO values [9].

Whole body plethysmography (D 97723; Zan 300, Oberthulba, Germany).

Measurements were done by a constant-volume variable pressure body plethysmography.

### Six-minute walk test

It measures the distance the patient walks quickly on a hard flat surface for a duration of 6 min [10]. Desaturation was defined as a decline in SpO<sub>2</sub> to less than or equal to 88% measured by a pulse oximeter during the 6 min walk test [11].

### Statistical analysis

SPSS (Statistical Package for the Social Sciences, version 20, IBM, Armonk, New York, USA) was

Transthoracic ultrasound findings of enrolled patients

Fringed pleural line was the most frequent abnormal

pleural line (35.4%). Coexistence of more than a type of

abnormal pleural line was present in 72 (30%) patients

used for analysis of data. Mean±SD or median (range) and frequency (percentage) were used for data expression.  $\chi^2$  test, Student's *t* test, and analysis of variance test were used to compare differences between study groups as appropriate. Diagnostic accuracy of TUS and Warrick score was assessed by receiveroperating characteristics curve. Correlation between Warrick score and other continuous variables was estimated by Spearman correlation. A *P* value of 0.05 or less was considered statistically significant.

### Results

### Clinical data of enrolled patients

This study included 240 patients (Fig. 1). The mean age of enrolled cases was 55.38±10.58, 55.4% of the cases were females and 44.6% were males (Table 1).

# The mean Warrick score was 10.42±6.44. Out of the enrolled patients 107 (44.6%), 87 (36.3%), and 46 (19.2%) patients had mild, moderate, or severe

Warrick score among patients of the study

Warrick score respectively (Table 3).

# Transthoracic ultrasound and pulmonary function parameters based on Warrick score

Significant differences were found in forced vital capacity (FVC) % predicted, DLCO % predicted, total lung capacity (TLC) % predicted, and 6 min

#### Figure 1



(Table 2).

Flowchart of the study.

#### Table 1 Clinical data of enrolled patients

	<i>N</i> =240
Age (years)	55.38±10.58
Sex	
Male	107 (44.6)
Female	133 (55.4)
Dyspnea score (mMRC)	3.25±1.03
Aerial blood gases	
рН	7.39±0.08
PaCo <sub>2</sub>	39.50±7.18
PaO <sub>2</sub>	61.06±10.23
HCO <sub>3</sub>	25.16±3.21
SaO <sub>2</sub>	88.21±5.33

Data expressed as n (%) and mean±SD. HCO<sub>3</sub>, bicarbonate; mMRC, modified Medical Research Council; PaCO2, partial pressure of carbon dioxide in blood; PaO2, partial pressure of oxygen in blood; SaO2, oxygen saturation as measured by blood analysis.

### Table 2 Transthoracic ultrasound findings among enrolled patients

N\_040

74 (00 0)
74 (30.8)
85 (35.4)
38 (44.7)
47 (55.3)
46 (19.2)
43 (17.9)
8 (3.3)
72 (30)
1.04±1.23
6.37±2.02
92 (38.3)
48 (61.7)
2.27±0.51

Data expressed as mean±SD, n (%). Data expressed as frequency (%).

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Table 3 Warric	k score	among	enrolled	patients
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	Mild	Moderate	Severe	Total
n (%)	107 (44.6)	87 (36.3)	46 (19.2)	240 (100)
Mean±SD	5.76±0.67	11.47±0.98	23.04±1.05	10.42±6.44
Range	5–8	10–12	22–25	5–25

Data expressed as n (%), mean±SD.

### Table 4 Transthoracic ultrasound and pulmonary functions parameters based on Warrick score

Parameters	Mild score (N=107)	Moderate score (N=87)	Severe score (N=46)	P value
FVC (% predicted)	67.35±18.40	53.27±15.09	40.52±11.16	0.029*
FEV1/FVC	83.34±8.03	81.60±8.14	80.69±8.87	0.34
DLCO (% predicted)	64.02±9.17	50.92±8.57	33.48±4.80	<0.001*
TLC (% predicted)	70.24±18.02	62.07±13.82	42.17±7.27	<0.001*
6 min walk test (m)	322.8±20.3	244.5±26.8	219.1±30.6	0.010*
Type of pleural lines				
Slightly rough line	50 (46.7)	24 (27.6)	0	<0.001*
Fringed pleural line	33 (30.8)	40 (46)	12 (26.1)	0.030*
Irregular interrupted	8 (7.5)	4 (4.6)	34 (73.9)	<0.001*
Wavy line	4 (3.7)	39 (44.8)	0	<0.001*
Normal line	8 (7.5)	0	0	0.040*
Coexistance of >1 abnormal type of lines	0	26 (29.9)	46 (100)	<0.001*
Number of B lines/scan	7.8±1.31	5.39±1.47	4.01±1.62	0.012*
B-line distance (mm)	4.29±0.83	7.61±0.62	11.06±1.08	<0.001*
Lung sliding				
Present	101 (94.4)	37 (42.5)	0	<0.001*
Abolished	6 (5.6)	40 (45.9)	46 (100)	
Pleural thickness (mm)	4.04±0.43	7.28±0.45	12.78±0.41	<0.001*

Data expressed as mean $\pm$ SD, *n* (%). DLCO, diffusion coefficient for carbon monoxide; FEV1, forced expiratory volume in first second; FVC, forced vital capacity; TLC, total lung capacity. \*Significant *P* value if less than 0.05.

### Table 5 Correlation of Warrick score with transthoracic ultrasound and pulmonary function parameters

Warrick score	r value	P value
PaO <sub>2</sub>	-0.01	0.89
6-MWT	-0.04	0.83
FVC% predicted	-0.13	0.10
FEV1/FVC	-0.03	0.62
DLCO (% predicted)	-0.66	< 0.001
TLC (% predicted)	-0.48	< 0.001
Pleural line thickness (mm)	0.53	< 0.001
Number of B lines/scan	-0.38	< 0.001
B-lines distance (mm)	0.77	< 0.001

*r* value (strength of correlation). 6-MWT, 6 min walk test; DLCO, diffusion coefficient for carbon monoxide; FEV1, forced expiratory volume in first second; FVC, forced vital capacity; PaO2, partial pressure of oxygen in blood; TLC, total lung capacity. *P* value (significance of correlation, significant if <0.05).

walk test (P=0.029, P<0.001, P< 0.001, P=0.010, respectively) among the patients with mild, moderate, and severe degree of Warrick score (Table 4).

# Correlation of Warrick score with transthoracic ultrasound and pulmonary function parameters

Warrick score showed significant positive correlation with pleural thickness and B-line distance; meanwhile,

### Table 6 Correlation of distance between B lines with pulmonary functions parameters and $PaO_2$

Distance between B lines (mm)	TLC% predicted	FVC% predicted	DLCO% predicted	PaO <sub>2</sub>
r	-0.65	-0.25	-0.70	-0.11
Р	<0.001	< 0.001	< 0.001	0.33

*r* value (strength of correlation). *P* value (significance of correlation, significant if <0.05). DLCO, diffusion coefficient for carbon monoxide; FVC, forced vital capacity; PaO2, partial pressure of oxygen in blood; TLC, total lung capacity.

it had negative correlation with the number of B lines/ scan, DLCO% predicted, and TLC% predicted (Table 5).

## Correlation of distance between B lines with pulmonary function parameters and PaO<sub>2</sub>

Negative correlation was found between each of TLC%, DLCO%, and FVC% predicted and the distance between B lines (P < 0.001) (Table 6).

# Correlation of B lines number with pulmonary function parameters and $\mbox{PaO}_2$

Number of B lines/scan showed positive correlation with TLC% predicted and DLCO% predicted (*r*=0.30 and 0.31, respectively, *P*<0.001) (Table 7).

# Diagnostic accuracy of Warrick score for the diagnosis of interstitial lung disease

Warrick score at a cutoff point more than 7 showed 96.3% sensitivity and 64.3% specificity for the diagnosis of interstitial lung disease with 67.5% overall diagnostic accuracy (Table 8, Fig. 2).

### Table 7 Correlation of B lines number/scan with pulmonary function parameters and $PaO_2$

B lines number/scan	TLC%	FVC%	DLCO%	PaO2
r	0.30	0.21	0.31	0.10
Р	< 0.001	0.20	< 0.001	0.22

*r* value (strength of correlation). DLCO, diffusion coefficient for carbon monoxide; FVC, forced vital capacity;  $PaO_2$ , partial pressure of oxygen in blood; TLC, total lung capacity. *P* value (significance of correlation, significant if <0.05).

### Table 8 Diagnostic accuracy of Warrick score in the diagnosis of interstitial lung disease

Indices	Value
Sensitivity	96.3%
Specificity	64.3%
Positive predictive value	53%
Negative predictive value	95%
Positive likelihood ratio	2.70
Negative likelihood	0.05
Accuracy	67.5%
Cutoff point	>7
Area under curve	0.88

### Figure 2

# Table 9 Diagnostic accuracy of transthoracic ultrasound findings in the diagnosis of acute dyspnea Indices Distance B lines Pleural Abolish

Indices	Distance between B lines (mm)	B lines number/ scan	Pleural thickness (mm)	Abolished sliding
Sensitivity	100%	92.6%	100%	96.3%
Specificity	40.4%	31%	34%	50%
Positive predictive value	17.5%	14.5%	16%	20%
Negative predictive value	100%	97%	100%	99.1%
Positive likelihood ratio	1.70	1.34	1.51	1.94
Negative likelihood ratio	0	0.24	0	0.07
Accuracy	47%	37.5%	41.2%	55%
Cutoff point	>3	>3	>2	-
Area under the curve	0.62	0.58	0.65	0.72

# Diagnostic accuracy of transthoracic ultrasound findings in diagnosing the etiology of acute dyspnea

Abolished lung sliding had the best diagnostic accuracy among TUS findings in diagnosing the etiology of acute dyspnea where it had 54% overall accuracy, 94% sensitivity, and 50% specificity (Table 9, Fig. 3).

### Discussion

Dyspnea is a prevalent symptom in ER units and therefore its differential diagnosis is crucial for



Receiver-operating characteristics for accuracy of Warrick score in the diagnosis of ILD.

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#### Figure 3



Receiver-operating characteristics for the accuracy of TUS findings in the diagnosis of etiology of acute dyspnea. TUS, transthoracic ultrasound.

correct management. This study was done to estimate the implementation and the value of abnormalities of the pleural line in comparison with computed tomographic findings in the assessment of dyspneic patients.

The current study identified four characteristic pleural line abnormalities on TUS. Slightly rough pleural line with confluent B-lines was detected in cases with ground-glass opacities in HRCT, while cases with parenchymal infiltration in HRCT had irregular and interrupted pleural line with confluent B-lines. Fringed pleural line with scattered **B**-lines coincided with irregularly thickened interlobular septa. Fringed pleural line with confluent B lines was found in superimposed ground-glass and irregular reticular opacities. Wavy pleural line was identified in the presence of subpleural emphysema. These findings were concordant with Li et al. [3]. In this study, modified Warrick HRCT score was used to estimate the degree of pulmonary involvement. Higher Warrick scores were associated with the lowest mean of FVC %predicted, which clarifies that advanced pulmonary fibrosis in HRCT is mostly associated with more derangement of pulmonary functions; this was supported by El Fatah et al. [12].

Also cases with severe Warrick score showed a significantly increased pleural line thickness and irregularity in comparison to cases with a mild score. This agreed with the results of El Fatah *et al.* [12] and Farag *et al.* [13].

The B-lines were more numerous with narrower distances between them in patients with mild Warrick score; however, in patients with reticular and honeycomb abnormalities, the distances between B-lines were significantly wider and their number was relatively smaller. Similar results were obtained by Hasan and Makhlouf [4] and El Fatah *et al.* [12].

Lung sliding was abolished in 100% of cases with severe Warrick score, 45.9% of moderate cases, and 5.6% of mild cases. These results were concordant with Farag *et al.* [13].

Sayed *et al.* [14] concluded that abolished lung sliding could be explained by visceral pleural fibrosis leading to the limitation of lung expansion and ventilation, ending into lung sliding impairment. The current results found that the B-line number showed an inverse correlation with the distance between B-lines in millimeters and significant positive correlation was found between Warrick score and B line distance and pleural line thickness. Similar results were obtained by Hasan and Makhlouf [4], El Fatah *et al.* [12], Mohammadi *et al.* [15], and Farag *et al.* [13]

Diot *et al.* [16] showed that a HRCT score of 7 achieved the best compromise between sensitivity (60%), specificity (83%), and positive predictive value (82%).

Tardella *et al.* [17] agreed with the results of this study and found that the receiver-operating characteristic curve analysis showed 96.3% sensitivity, 92.3% specificity, and positive likelihood ratio 12.52 when applying a cutoff value of 7 for Warrick score for the existence of systemic sclerosis-ILD.

Delle Sedie *et al.* [18] studied interstitial pulmonary fibrosis in systemic sclerosis patients. They illustrated 85% sensitivity and 70% specificity for LUS findings regarding the number of B lines in comparison to the chest HRCT findings.

Aghdashi *et al.* [19] considered more than 5 TUS B lines as positive pulmonary involvement.

### Limitations of the study

The current study had some limitations. First, the anterior and lateral chest areas only were examined by TUS to prevent displacing patients, which may yield to false-negative cases. Second, visualizing the pleural line is usually challenging in some cases and is determined by the experience of TUS operators. Third, the domain of this study was limited to the pleural line abnormalities and corresponding B-lines, meanwhile combining more abnormal TUS signs is more potential to increase the diagnostic yield.

### Conclusion

TUS is an important tool for the evaluation and diagnosis of pulmonary disorders. B-lines number and distance, pleural line abnormalities, lung sliding, and pleural thickness added diagnostic value for the evaluation of dyspneic patients in ER units.

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### **Conflicts of interest**

There are no conflicts of interest.

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