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ORIGINAL ARTICLES

A feasibility study of a short lung ultrasound protocol as a screening method for fibrotic interstitial lung disease

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ABSTRACT

Aims: Interstitial lung disease (ILD) represents a common complication of connective tissue diseases (CTD). Early detection of ILD is critical since patients often remain asymptomatic during the initial stages. While numerous studies have proposed various ultrasound protocols for ILD evaluation, we find these protocols to be time-consuming in our clinical practice. The aim of this study is to introduce a concise lung ultrasound protocol for the screening of pulmonary fibrosis.

Methods: We conducted a prospective observational pilot study involving 28 patients followed in consultation for ILDs. By implementing this streamlined protocol, we established correlations between ultrasound findings at specific locations and their corresponding tomographic patterns. Following the assessment of the protocol's diagnostic accuracy, a multidisciplinary meeting was convened to scrutinize ultrasound images from several patients and evaluate the level of agreement among rheumatologists, pulmonologists, and radiologists.

Results: Our simplified protocol revealed significant correlations between ultrasonographic pleural irregularity, discontinuity and the number of B-lines, and the tomographic findings of reticulation and honeycombing in both the upper and lower lung regions. This protocol demonstrated high sensitivity and positive predictive value in identifying reticulation and honeycombing, as well as remarkable specificity and negative predictive value for the latter. The results obtained between the specialties showed strong agreement.

Conclusion: Preliminary results suggest a role of ultrasound to detect peripheral manifestations of fibrotic ILDs, such as reticulation and honeycombing. This assessment protocol can be adopted effectively by clinicians, such as rheumatologists, to evaluate lung involvement by CTDs. A larger study is necessary to achieve more robust and generalizable results as a screening tool.

Keywords: Interstitial lung diseases; Lung ultrasound; Connective Tissue Disease

INTRODUCTION

Interstitial lung diseases (ILD) comprise a diverse group of diffuse parenchymal pulmonary conditions that affect the interstitial space, alveolar epithelium, as well as perivascular and lymphatic tissues. These diseases often exhibit similar clinical, imaging, and pathological features[1]. They frequently manifest as secondary complications of connective tissue diseases (CTD), including systemic sclerosis (SSc), rheumatoid arthritis, myositis, Sjögren's syndrome, and lupus, and significantly contribute to morbidity and mortality in affected individuals[2,3,4].

While high-resolution computed tomography (HRCT) of the chest is a commonly utilized diagnostic tool for ILD, its high cost and associated radiation exposure limit its suitability for routine screening. In this context, several studies have suggested that lung ultrasound could serve as a viable method for diagnosing ILD[1,2,4,5,6]. It offers high sensitivity and diagnostic accuracy, is cost-effective, radiation-free, and well-received by patients[7]. Typical ultrasound findings associated with ILD include pleural line irregularity and discontinuity, pleural thickening (>3mm), subpleural nodules, and the

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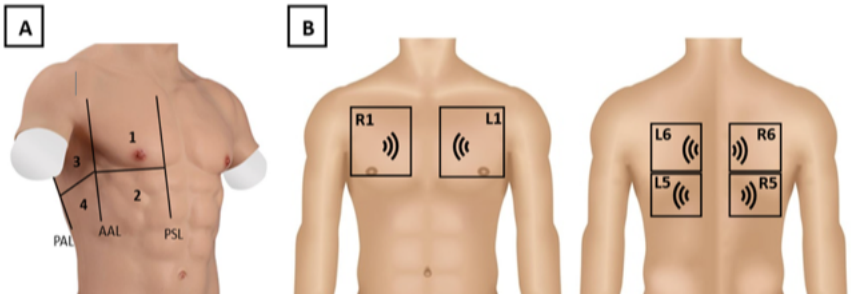

Figure 1. Lung Ultrasound Protocols. (A) The four chest areas per side considered for complete eight-zone lung ultrasound examination, used to evaluate the presence of interstitial syndrome. According to Volpicelli et al, the interstitial syndrome is present when there are ≥3 B-lines in two or more regions bilaterally of the anterior and lateral thorax. (B) Six chest zones assessed on short ultrasound examination.

presence of B-lines[1,8]. B-lines are defined as distinct, laser-like, hyperechoic vertical reverberations originating from the pleural line, extending to the bottom of the ultrasound screen without fading, and moving in synchrony with lung sliding. It's worth noting that a few B-lines, particularly at the lung bases, can be present in healthy individuals and may not be indicative of disease. The term "interstitial syndrome" is used when three or more B-lines appear between two ribs in at least two regions bilaterally on the anterior and lateral thorax (Figure 1A)[9]. Various factors, aside from ILD, can cause interstitial syndrome, including cardiogenic or non-cardiogenic pulmonary edema, with the latter being associated with pneumonia, embolism, or malignancy[9,10,11].

Over the years, multiple studies have proposed different lung ultrasound protocols for investigating ILD[7]. However, many of these protocols are time-consuming and may not be practical for everyday clinical use. In this feasibility study, we aimed to evaluate a concise ultrasound protocol designed to identify ultrasonographic changes indicative of ILD, and to correlate these ultrasound findings with the corresponding tomographic features, including mosaic, ground glass, honeycombing, traction bronchiectasis, and reticulation, in cases of both fibrotic and nonfibrotic ILDs. Additionally, we evaluated the practicality of training other healthcare professionals in this ultrasound protocol. The intention was to enable these professionals to use this method as a screening tool in their clinical practice, providing a valuable resource for attending clinicians.

MATERIAL AND METHODS

Study Design

A single-centre prospective observational pilot study with non-probability sampling was conducted over a two-months period in a referral center for ILD care at the University Hospital São João in Porto, Portugal. The study included patients aged 18 and older who were being followed in consultation for diffuse parenchymal lung disease. Inclusion in the study required the mandatory signing of informed consent. We excluded cases that lacked a HRCT scan available within 6 months of the ultrasound assessment. Additionally, patients with a history of decompensated heart failure and those showing evidence of respiratory infection or pleural effusion during the assessment were also excluded. Demographic and clinical data, such as age, gender, smoking habits, lung function tests, and HRCT characteristics, were systematically collected. The HRCT patterns analyzed included honeycombing, traction bronchiectasis, reticulation, ground glass, and mosaic attenuation.

Lung ultrasound short protocol

Lung ultrasound scans were conducted on all cases by two trained pulmonologists in simultaneous using a Mindray DP-10 ultrasound device equipped with a 7.5 MHz linear probe, and all conclusions were based on interobserver agreement. As recruiting observers, they were not blinded to clinical and diagnostic data, but the ultrasound examination was performed without any knowledge of the HRCT findings.

The probe was consistently positioned longitudinally during the examinations. In instances where the thickness of the thoracic wall impacted image quality, particularly in obese patients, a 3.5 MHz curvilinear probe was employed to assess deeper structures.

A concise ultrasound examination was performed in the following zones (Figure 1B):

- R1/L1: The probe was positioned in the second intercostal space anteriorly, on the right (R1) and left (L1) sides, as medially as possible to avoid any underlapping tissues, such as breast and muscle.

- R5/L5: The probe was placed in the lower part of

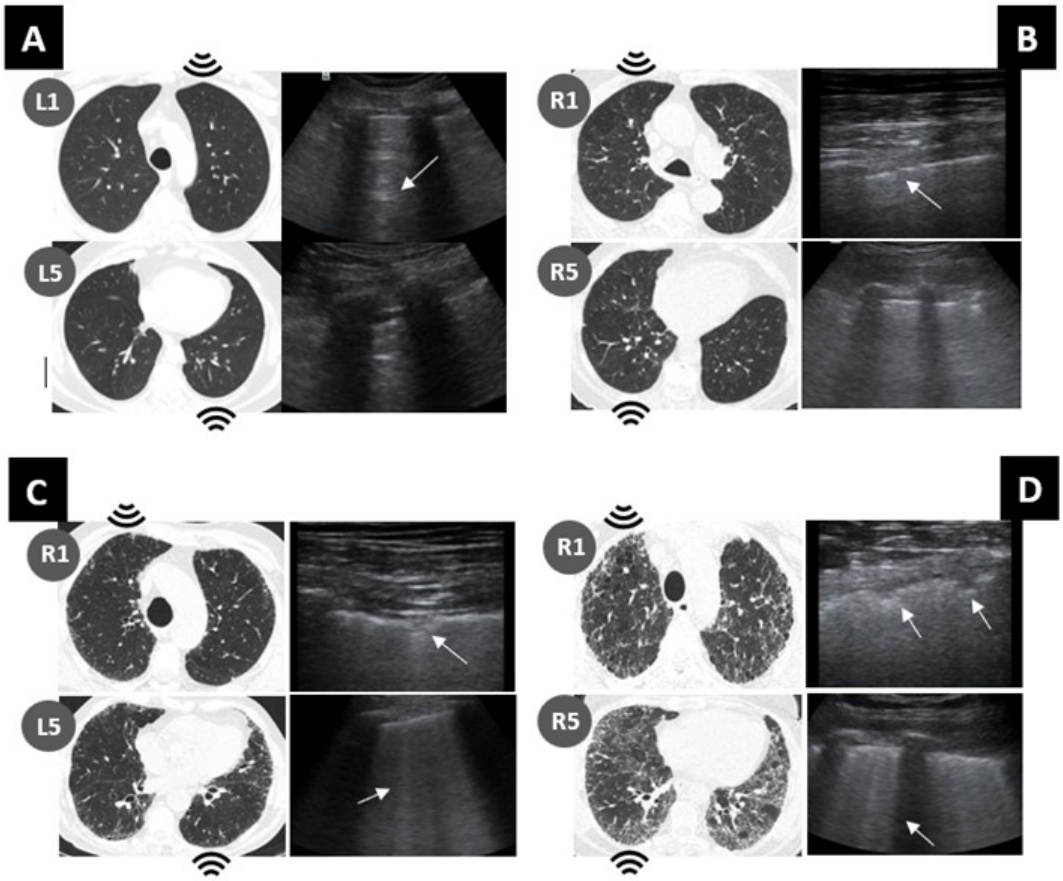

Figure 2. Correlation between sonographic and tomographic images. A) 52-year-old male patient with asthma, no pleural line changes, presence of multiple A lines, in relation with hyperinflation; B) 87-year-old male patient with non-fibrotic HP. R1: Ground glass and mosaic attenuation pattern on HRCT, correlating with pleural line discontinuity on ultrasound (US); R5: no HRCT or pleural line changes on US. C) 86-year-old male patient with IPF. R1: reticulation pattern on HRCT, correlating with pleural line irregularity on US; L5: reticulation pattern on HRCT, producing B-lines on US. D) 61-year-old female patient with fibrotic desquamative interstitial pneumonia. R1: honeycombing pattern on HRCT, irregularity and discontinuity; R5: honeycombing pattern on HRCT, creating abundant B-lines, commonly present in the interstitial syndrome.

the chest, posteriorly, below the scapula, on the right (R5) and left (L5) sides. It's worth noting that placing the probe more medially would increase the distance to the pleura, resulting in a thicker appearance on the image and potentially decreasing the accuracy of the findings.

- R6/L6: Zone 6 was utilized in cases where the patient's body composition posed challenges to ultrasound accuracy in Zone 5, as often seen in obese patients. In these instances, the probe was positioned on the medial border of the scapula, even more medially than in Zone 5, on the right (R6) and left (L6) sides. In order to obtain a larger sonographic area for examination, patients were asked to place the hand of the side being scanned on the contralateral shoulder.

During the ultrasound examination, the following changes were meticulously recorded: continuity/discontinuity of the pleural line, regularity/irregularity of the pleural line, thickness of the pleural line (measured in millimeters, and subsequently categorized into four strata: 0-1 mm, 1-2 mm, 2-3 mm, and greater than 3 mm) and number of B-lines (which includes absence (0 or 1 line), less than 5 lines, and 5 lines or more) located between two adjacent ribs. Pleural thickening was stratified based on the observation that the average thickness across all patients was <2 mm (with only three patients exhibiting pleural thickness >3 mm), and the significant variability of underlying diseases. A threshold of 5 B-lines was chosen to improve diagnostic specificity, particularly given the shorter ultrasound protocol, which excluded certain ultrasonographic zones.

The lung ultrasound characteristics were subjected to a detailed analysis and were then compared with the HRCT images of the corresponding zones (Figure 2).

Assessment of health professionals Agreement for Ultrasound Findings

To assess the agreement between health professionals in diagnosing interstitial syndrome and other ultrasono-

TABLE I. Patients' characteristics and distribution according to diagnosis

Characteristics	
Age, mean ±SD, years	68 ± 12
Male, n (%)	19 (67.9)
Former/current smokers, n (%)	17 (60.7)
FVC, mean ±SD	85.4 ± 16.1
FEV1, mean ±SD	90.6 ± 17
FEV1/FVC, mean ±SD	81.4 ± 9.3
TLC, mean ±SD	80.6 ± 14.2
DLCO, mean ±SD	56.1 ± 18.2
DLCO/VA, mean ±SD	80.1 ± 22.1
Diagnosis	
Idiopathic pulmonary fibrosis	5
Fibrotic Hypersensitivity Pneumonitis	5
Non-fibrotic HP	4
Fibrotic CTD-ILD	3
Familial pulmonary fibrosis	2
CPFE	1
Unclassifiable fibrotic ILD	2
Fibrotic NSIP	1
Fibrotic DIP	1
Sarcoidosis - Scadding stage II	1
ANCA-negative vasculitis	1
Granulomatous Disease probably infectious	1
Systemic Sclerosis without ILD	1

CPFE: Combined Pulmonary Fibrosis and Emphysema; CTD-ILD: Connective Tissue-related Interstitial Lung Disease; DIP: Desquamative interstitial pneumonia; DLCO: Diffusing capacity of the lung for carbon monoxide; FVC: Forced Vital Capacity; ILD: Interstitial Lung Disease; NSIP: Nonspecific Interstitial Pneumonia; SD: standard deviation; TLC: Total Lung Capacity; VA: alveolar volume.

graphic manifestations of ILDs, we extended invitations to two rheumatologists with prior training in musculoskeletal ultrasound and two thoracic radiologists. A one-hour consensus meeting was organized, overseen by the two pulmonologists who had conducted the initial ultrasound assessments. The purpose of this meeting was to present the study protocol and establish standardized definitions for pleural line regularity, pleural line continuity, and the number of B-lines.

The session commenced with a review of fundamental concepts related to chest ultrasound, subsequently delving into its specific applications in the context of ILD. Following this comprehensive introduction, the six reviewers individually assessed the ultrasound images with respect to pleural line regularity, pleural line continuity, and number of B-lines. A total of 36 pre-selected images were evaluated for pleural regularity and continuity, and 15 images were scrutinized for the number of B-lines.

Statistical Analysis

Data presentation included counts and proportions for categorical variables, while mean or median values with standard deviations were applied for continuous variables.

The statistical analysis employed the Chi-square test and Fisher's exact test for independent samples, with results considered statistically significant if the *p*-value was <0.05.

Intra-specialty agreement, involving two evaluators, and inter-specialty agreement, spanning three different specialties, were evaluated regarding the responses provided by the six reviewers for each ultrasound image. This assessment was carried out using the Cohen's Kappa test and the Fleiss Kappa test, respectively. Weighted-kappa coefficients were categorized to reflect the extent of agreement: poor ($0<\kappa w\leq 0.20$), fair ($0.20<\kappa w\leq 0.40$), moderate ($0.40<\kappa w\leq 0.60$), good ($0.60<\kappa w\leq 0.80$), and excellent ($0.80<\kappa w\leq 1.00$). Weighting the kappa coefficient allowed us to quantify the degree of disagreement, placing greater emphasis on significant score differences. This approach has been previously applied in the field of ILD[12]. Statistical analysis was conducted using IBM SPSS version 26 software.

RESULTS

Lung ultrasound short protocol examination

We conducted an assessment of 28 patients, among whom 19 (67.9%) were male and 9 (32.1%) were female, with ages ranging from 34 to 87 years (as detailed in Table I). Among the patients, twenty were diagnosed with pulmonary fibrosis, while seven presented with non-fibrotic ILD and one presented without ILD.

Our ultrasound examinations of the lower lobes revealed the strongest correlations with fibrotic changes observed in HRCT, particularly concerning pleural irregularity, pleural discontinuity, and number of B-lines. These ultrasound findings were significantly associated with the presence of honeycombing and pulmonary reticulation (Figure 3, and Suppl. Table I to III of Supplemental Digital Content).

In the upper lobes, notable associations were found between the number of B-lines observed ultrasonographically and the presence of honeycombing, traction bronchiectasis, and reticulation in HRCT. Additionally, pleural discontinuity was more pronounced in the upper lobes of patients with traction bronchiectasis or reticulation. Ultrasonographic pleural irregularity in the upper lungs ex-

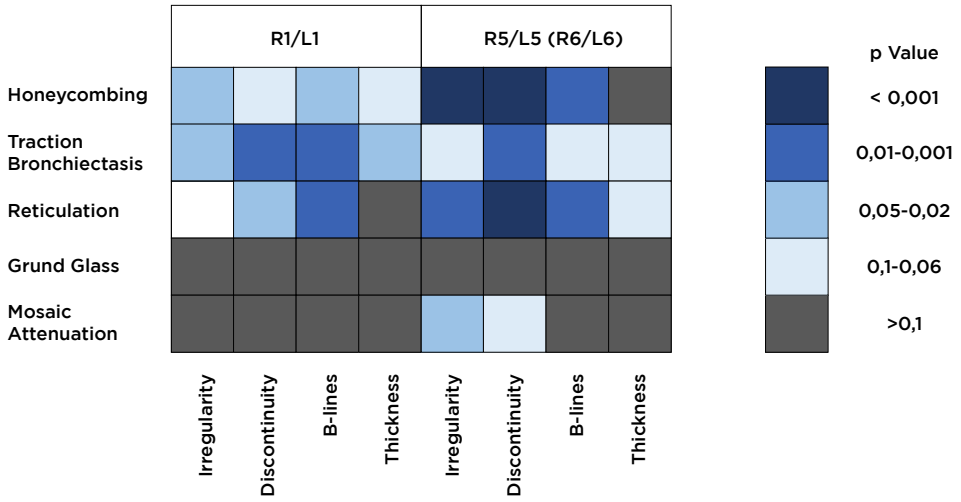

Figure 3. Relationship heatmap between tomographic and ultrasound characteristics. The strength of association is reflected by the significance (p-value).

TABLE II. Accuracy Relation between HRCT reticulation and honeycombing and ILD features on short lung ultrasound

Presence of ILD features*1	Reticulation on HRCT				Honeycombing on HRCT			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
Upper Lobes	94%	45%	73%	83%	100%	63%	56%	100%
Lower Lobes	81%	100%	100%	64%	50%	100%	100%	67%
Full Protocol*2	95%	33%	84%	66%	87%	77%	81%	83%

HRCT: high resolution computed tomography; ILD: Interstitial Lung Disease; PPV: Positive predictive value; NPV: Negative predictive value.
*1 ILD features for Reticulation: pleural line irregularity and/or discontinuity and presence of ≥2 B lines
ILD features for Honeycombing: pleural line irregularity plus discontinuity and 5 or more B lines
*2 Full protocol ILD features: Reticulation – Presence of the defined criteria for reticulation in any sonographic area; Honeycombing - Presence of the defined criteria for honeycombing in any sonographic area.

hibited association with traction bronchiectasis and honeycombing. The measurement of pleural line thickness using ultrasound was found to be significantly associated with the presence of traction bronchiectasis in the upper lobes (Table IV, Supplemental Digital Content).

The mean pleural line thickness in the upper regions was 1.1±0.4 mm (ranging from 0.6 to 2.1 mm), while in the lower regions, it averaged 1.9±0.7 mm (ranging from 0.1 to 4.3 mm). No statistically significant associations were observed between the studied ultrasonographic features and the presence of ground glass opacities on HRCT or the evidence of mosaic attenuation, except for pleural irregularity in the lower lobes in the latter case.

Clinical use of lung ultrasound short protocol examination in ILD

The identification of reticulation in HRCT represents one of the earliest indicators of fibrotic ILD. This observation prompted us to investigate the viability of employing a concise lung ultrasound protocol during a standard consultation to detect early ultrasonographic signs of pulmonary fibrosis. In contrast, honeycomb changes observed in HRCT signify advanced disease and have been linked to prognostic significance[13]. We calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of lung ultrasound when these specific sonographic features of ILD were present for the detection of reticulation and honeycombing (Table II). The highest accuracy for identifying reticulation was achieved when either pleural irregularity or discontinuity, combined with the presence of 2 or more B-lines, were observed on ultrasound. For honeycombing, the most robust correlation with ultrasonographic findings was found when both pleural line irregularity and discontinuity, along with 5 or more B-lines, were present.

The short lung ultrasound protocol demonstrated its

highest sensitivity and NPV in the upper lobes, while it exhibited the highest specificity and PPV in the lower lobes for the detection of both pulmonary reticulation and honeycomb changes. When considering all ultrasonographic areas (R1, L1, R5, and L5), the full protocol yielded an overall sensitivity of 95% and a specificity of 33% for reticulation. Additionally, it achieved a sensitivity of 87% and a specificity of 77% for honeycombing (Table II). The majority of patients were correctly classified (PPV) as having reticulation (84%) or honeycombing (81%) when utilizing this protocol. Notably, the short ultrasound protocol, with its highly specific ultrasonographic criteria for detecting honeycomb alterations (resulting in a high true negative rate and low false positive rate), significantly reduced false negative outcomes, thereby achieving a correspondingly high NPV of 83%. The NPV for detecting reticulation was comparatively more modest, standing at 66%.

Multidisciplinary meeting and agreement between the participants' results

Remarkably, excellent intraspecialty agreement was observed for all three specialties concerning the number of B-lines, with κw values of 0.91 for pulmonology, 0.81 for rheumatology, and 0.81 for radiology. Good agreement was noted among rheumatologists for pleural regularity (κw=0.79) and continuity (κw=0.62), and similarly, pulmonologists demonstrated good agreement for both pleural regularity and continuity (κw=0.70 for both). Radiologists displayed fair agreement for pleural line regularity and continuity (κw=0.60 for both) (Table III).

Following the initial evaluation, cases where discordant results were found within specialties were reviewed to reach a consensus, facilitating the calculation of interspecialty agreement. The results showed excellent interspecialty agreement for the number of B-lines (κw=0.94) and pleural line regularity (κw=0.93), while pleural line continuity exhibited a moderate agreement (κw=0.51).

DISCUSSION

We present a concise lung ultrasound protocol capable of identifying features that correlate with pulmonary fibrosis, specifically in line with HRCT evidence of honeycombing, traction bronchiectasis and reticulation. The application of this streamlined lung ultrasound examination during routine follow-up consultations for patients with CTD holds the potential to unveil early signs of ILD. This is particularly evident when ultrasonographically detecting pleural abnormalities (irregularity and/or discontinuity) along with at least 2 B-lines, a combination that demonstrates high sensitivity and delivers a robust positive predictive value for subpleural reticulation, which often represents the earliest finding of fibrosis on HRCT.

Beyond diagnostic utility, ultrasound may also hold prognostic significance in the context of CTD-ILD. Specifically, more advanced fibrotic changes associated with honeycombing were consistently observed when a combination of ultrasound features—pleural line irregularity, discontinuity, and the presence of 5 or more B-lines—was present.

While ultrasonographic findings in the lower lobes were more specific, more correctly excluding patients without the condition (commonly affecting this region of the lungs), the sensitivity was maximized anteriorly in the upper half of the lungs when reticulation or honeycombing was present in the upper lobes. This reflects the higher image quality obtained in this part of the thorax due to fewer interposing tissues.

It is important to note that lung ultrasound demonstrates remarkable accuracy when identifying ILD with tomographic patterns involving the pleural or subpleural regions[5, 6]. In contrast, its accuracy diminishes when detecting changes in HRCT patterns that extend less peripherally into the lung[6,15,16]. This observation may explain the lack of association between the sonographic characteristics of ILD and the patterns of ground glass and mosaic attenuation. Similarly, pleural thickness on ultrasound did not correlate with such tomographic patterns, which contradicts results from other studies[5,17]. This discrepancy might be attributed to the relatively small number of cases with CTD-ILD included in the study, which frequently affect the pleura in the form of pleuritis, pleural effusion or pleural thickening.

TABLE III. Kappa value for intra and interspecialty agreement regarding patients' ultrasound characteristics.

	Pulmonologists	Radiologists	Rheumatologists	MDTM
Regularity	0.7	0.6	0.79	0.93
Continuity	0.7	0.6	0.62	0.51
B lines	0.91	0.81	0.81	0.94

MDTM: Multidisciplinary team meeting

Both the stethoscope and lung ultrasound provide physical evidence of ILD. However, ultrasound may offer more informative insights at an earlier stage of the disease. While HRCT shows subpleural reticulation, reflecting the thickening of interlobular and intralobular septa in the early course of ILD, on auscultation this often manifests as crackles on chest. In congestive heart failure, subpleural interstitial septa thicken due to edema and produce similar crackling sounds on auscultation, along with the appearance of hyperechoic B-lines in a sonogram[14]. Nevertheless, pleural abnormalities are typically absent in this context, as the pleural line remains regular and smooth[9]. Moreover, auscultation hardly differentiates reticulation from other causes than fibrosis with great accuracy, as coarse crackles also occur in conditions like chronic bronchitis, bronchiectasis, pneumonia, and severe pulmonary edema.

Over the years, various lung ultrasound protocols have been proposed, each focusing on different characteristics, all with the common goal of establishing an easy-to-perform, reproducible, and accurate method for identifying and monitoring ILD in daily clinical practice[18]. A meta-analysis conducted by Song *et al.* revealed a high accuracy of lung ultrasound in diagnosing CTD-ILD, with a sensitivity of 91.5% and a specificity of 81.3%, relying solely on the number of B-lines. It's worth noting that different ultrasound zones and B-line cutoffs were utilized across various studies[19]. Another meta-analysis by Xie *et al.*, based on 11 articles, aimed to determine the most effective approach to assess CTD-ILD using lung ultrasound, focusing exclusively on B-lines. This analysis achieved a remarkable sensitivity of 98% and specificity of 86% by examining 14 intercostal spaces in the anterior, lateral, and posterior regions[7]. In addition to the number of B-lines, which tend to have low specificity for ILD, Lacedonia *et al.* emphasized the significance of other features, such as pleural line thickness, irregularity, interruption, and the presence of subpleural nodule[6]. Some protocols concentrated solely on pleural changes, such as the one developed by Fairchild *et al.* for patients with systemic sclerosis (SSc)[20]. However, these approaches are often time-consuming and frequently exclude the posterior basal regions of the lungs.

The short ultrasound protocol we propose involves the examination of only 2 to 3 zones bilaterally, with a strong emphasis on the pulmonary areas that are frequently affected by inflammation and/or fibrosis in CTD-ILD. These areas correspond to the "four corners" sign observed in high-resolution CT scans, which disproportionately impact the bilateral posterosuperior lower lobes and anterolateral mid-upper lobes. This specific pattern on CT scans has been described as characteristic of SSc-ILD[21].

Our results revealed a substantial level of agreement among assessments conducted by healthcare professionals from different medical specialties, suggesting that the widespread implementation of this protocol for outpatient management of these patients is not only feasible but highly practical. Notably, we demonstrate that rheumatologists can achieve consistent results comparable to those of more experienced pulmonologists and radiologists. While the interspecialty reliability measured by kappa was only moderate for pleural line continuity, the impact on the final decision was mitigated by the excellent agreement attained for pleural regularity and the number of B-lines. Furthermore, in the presence of honeycombing, regularity and continuity of the pleural line are often concurrently altered. These findings lay the foundation for rheumatologists, following appropriate training, to utilize this simplified lung ultrasound protocol during consultation when fibrotic CTD-ILD suspicion arises

This study has several limitations that warrant consideration. First and foremost, the sample size is relatively small, which could potentially impact the results, although it's worth noting that most of the findings align with conclusions drawn from other studies. Despite showing high sensitivity and PPV in detecting early and advanced fibrosis, the NPV value was only moderate regarding reticulation and honeycombing, compromising the diagnostic value of ultrasound protocol at screening early disease. Given that only high-risk patients from ILD consultation were included, the study lacked negative cases for a valid estimation of NPV. Another potential limitation is the lack of ultrasound operator's blinding for the clinical data, which presumably could affect the assessment. A larger population set, including more patients with established CTD and control subjects, with ultrasound examination performed by an observer blinded for the underlying diagnosis, should be conducted to fully explore the potential of the study protocol.

In conclusion, the results demonstrated a promising role for ultrasound at detecting reticulation and honeycombing, with highest sensitivity in the upper lobes, and the highest specificity for the lower lobes. Although HRCT will remain the standard for the diagnosis and monitoring of ILDs, lung ultrasound has the potential to serve as a complementary method for a fast, cheap, radiation-free assessment at bedside.

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SUPPLEMENTARY MATERIAL

SUPPL. TABLE I. Presence of sonographic pleural line irregularity according to HRCT patterns

	R1/L1			R5/L5 (R6/L6)		
	Irregularity of the pleural line					
	Absence (n=7)	Presence (n=21)	p Value	Absence (n=15)	Presence (n=13)	p Value
Honeycombing	0	10	0,03	2	12	<0,001
Traction Bronchiectasis	2	16	0,04	8	11	0,1
Reticulation	2	15	0,06	8	13	0,007
Ground Glass	1	9	0,4	8	4	0,3
Mosaic Attenuation	0	6	0,3	6	0	0,02

SUPPL. TABLE II. Presence of sonographic pleural line discontinuity according to HRCT patterns

	R1/L1			R5/L5 (R6/L6)		
	Discontinuity of the pleural line					
	Absence (n=6)	Presence (n=22)	*p* Value	Absence (n=12)	Presence (n=16)	*p* Value
Honeycombing	0	10	0,06	1	13	<0,001
Traction Bronchiectasis	1	17	0,01	4	15	0,001
Reticulation	1	16	0,02	5	16	<0,001
Ground Glass	2	8	1	5	7	1
Mosaic Attenuation	1	5	1	5	1	0,06

SUPPL. TABLE III. Presence of sonographic B lines according to HRCT patterns

	R1/L1					R5/L5 (R6/L6)				
	Number of B Lines									
	≥5 Bilateral (n=17)	≥5 Unilateral (n=1)	<5 Bilateral (n=6)	Absence (n=4)	*p* Value	≥5 Bilateral (n=5)	≥5 Unilateral (n=3)	<5 Bilateral (n=16)	Absence (n=4)	*p* Value
Honeycombing	10	0	0	0	0,02	5	3	6	0	0,005
Traction Bronchiectasis	15	0	3	0	0,003	5	3	10	1	0,06
Reticulation	14	1	2	0	0,007	5	3	13	0	0,002
Ground Glass	7	0	2	1	0,8	2	0	9	1	0,3
Mosaic Attenuation	3	1	1	1	0,3	0	0	5	1	0,4

Suppl. Table IV. Pleural line thickness according to HRCT patterns.

	R1/L1				R5/L5 (R6/L6)			
	Thickness of the pleural line							
	0-1mm (n=11)	1-2mm (n=15)	2-3mm (n=2)	*p* Value	1-2mm (n=18)	2-3mm (n=8)	>3mm (n=2)	*p* Value
Honeycombing	2	6	2	0,08	7	6	1	0,2
Traction Bronchiectasis	4	12	2	0,04	10	8	1	0,07
Reticulation	5	10	2	0,3	11	8	2	0,08
Ground Glass	4	4	2	0,1	10	1	1	0,1
Mosaic Attenuation	3	3	0	0,7	5	1	0	0,5
	Mean: 1.14 ± 0.4mm (minimum:0,6;maximum:2,1)				Mean: 1.9 ± 0.7mm (minimum:0,11;maximum:4,3)			