

Original article

Lung ultrasound B-lines in systemic sclerosis: cut-off values and methodological indications for interstitial lung disease screening

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Abstract

Objectives. Lung ultrasound (LUS), through assessment of B-lines and pleural line alterations, is able to evaluate interstitial lung disease (ILD), a frequent complication of SSc. Different scanning schemes and counting methods have been proposed but no clear cut-off values have been indicated for screening. We aimed to evaluate the accuracy of different LUS methodological approaches to detect ILD compared with high-resolution CT (HRCT) as the gold standard.

Methods. Sixty-nine SSc patients underwent LUS and chest HRCT on the same day. Both exams were scored by expert readers. The accuracy of different scanning schemes and counting methods was assessed and clinical and functional data were compared with imaging findings.

Results. B-lines were more numerous in patients with the diffuse skin subset and Scl70 autoantibody positivity. The number of B-lines correlated with the Scleroderma Lung Study (SLS) I HRCT score ($R = 0.754$, $P < 0.0001$). A total of >10 B-lines on the whole chest or >1 B-line on the postero-basal chest showed 97% sensitivity for detecting even very early ILD signs (corresponding to an SLS I score of 1). Sensitivity increased to 100% when pleural line alterations were included in the analysis.

Conclusions. LUS has a very high sensitivity in detecting SSc-related ILD. A cut-off value of >10 B-lines on the whole chest or >1 B-line on the postero-basal chest can be used for the screening of SSc-ILD. Assessing only the postero-basal chest seems to be mostly effective, combining high sensitivity with a less time-consuming approach.

Key words: systemic sclerosis, lung ultrasound, B-lines, interstitial lung disease, high-resolution computed tomography

Rheumatology key messages

- Lung ultrasound has a very high sensitivity for screening even very mild SSc-related ILD.
- Assessment of the postero-basal chest is the most effective scanning approach.

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Introduction

SSc is an inflammatory autoimmune disease evolving to fibrosis [1], with high morbidity and mortality [2]. Usually >50% of SSc patients develop interstitial lung disease (ILD) during the course of the disease [3]. Pulmonary function tests (PFTs) are routinely performed in the screening and follow-up of ILD, although sensitivity and specificity are quite low [4]. High-resolution CT (HRCT) is the gold standard for ILD evaluation [5], even if limited by exposure to ionizing radiation [6] and a lack of recommendations for its use in screening and follow-up [7].

In the last decade, lung ultrasound (LUS) has been used to detect ILD in SSc through assessment of B-lines [8]. B-lines are the sonographic sign of pulmonary interstitial involvement and are clearly visible in ILD [9]. The correlation between B-lines and HRCT signs of SSc-related ILD [10–14] and their prognostic role [15] have been definitely confirmed. LUS B-lines therefore seem a very promising tool for the screening of ILD [16], but no clear cut-off values have been proposed to identify the early phase of ILD in SSc [17].

The aim of our study was to define the cut-off values of LUS B-lines to detect even very mild ILD, using different B-line scanning and counting methods, with HRCT as the gold standard.

Methods

Consecutive patients >18 years of age, classified as SSc according to the 2013 ACR/EULAR classification criteria [18], and followed as outpatients by the Rheumatology Department of Careggi Hospital in Florence were enrolled. LUS examination was performed on the same day as HRCT. Data regarding clinical, instrumental and biochemical SSc-related features were recorded. The study was approved by the local ethical committee board (Comitato Etico Area Vasta Nord Ovest, no. 2849) and written informed consent was signed by each patient.

Chest HRCT

HRCT scans were performed using a spiral CT/Highspeed scanner (General Electric Medical Systems, Wauwatosa, WI, USA) carrying one row of detectors and a 1 s rotation time. All patients' evaluations were performed in a supine position and started with an antero-posterior and latero-lateral scout X-ray, followed by 35–55 scans acquired at the end of inspiration, in apnoea, from the apex to lung bases, without using contrast medium. The HRCT images were then independently reviewed by two thoracic radiologists, blinded to LUS findings, with specific expertise in pulmonary disease. The presence of ILD was then visually scored according to two previously described semiquantitative methods: the Wells score [19] and the Scleroderma Lung Study (SLS) I score [20]. The Wells score is a comparative grading system evaluating the extent of parenchymal disease relative to reticular

disease, differentiating five separate levels: parenchymal opacification alone, parenchymal opacification more extensive than a reticular pattern, parenchymal opacification equal in extent to a reticular pattern, reticular pattern more extensive than parenchymal opacification and a reticular pattern alone; lobes are scored independently of each other and each lobe can get a maximum score of 5. The SLS I score is a semiquantitative scoring method where the extent of the pulmonary abnormality in each of six zones is graded using a scale from 0 to 4 (0, absent; 1, 1–25%; 2, 26–50%; 3, 51–75%; 4, >75%) to evaluate the four categories of parenchymal abnormalities: pure ground-glass opacities (GGOs); lung fibrosis including thickened reticular markings, bronchiectasis and bronchiolectasis; honeycombing and emphysema. The two readers scrolled all slices from the apex to the base of each HRCT scan. The scoring was performed in three zones (upper, extending from the apex to the aortic arch; middle, from the aortic arch to the inferior pulmonary vein; and lower, from the inferior pulmonary vein to the diaphragm) of each lung.

LUS

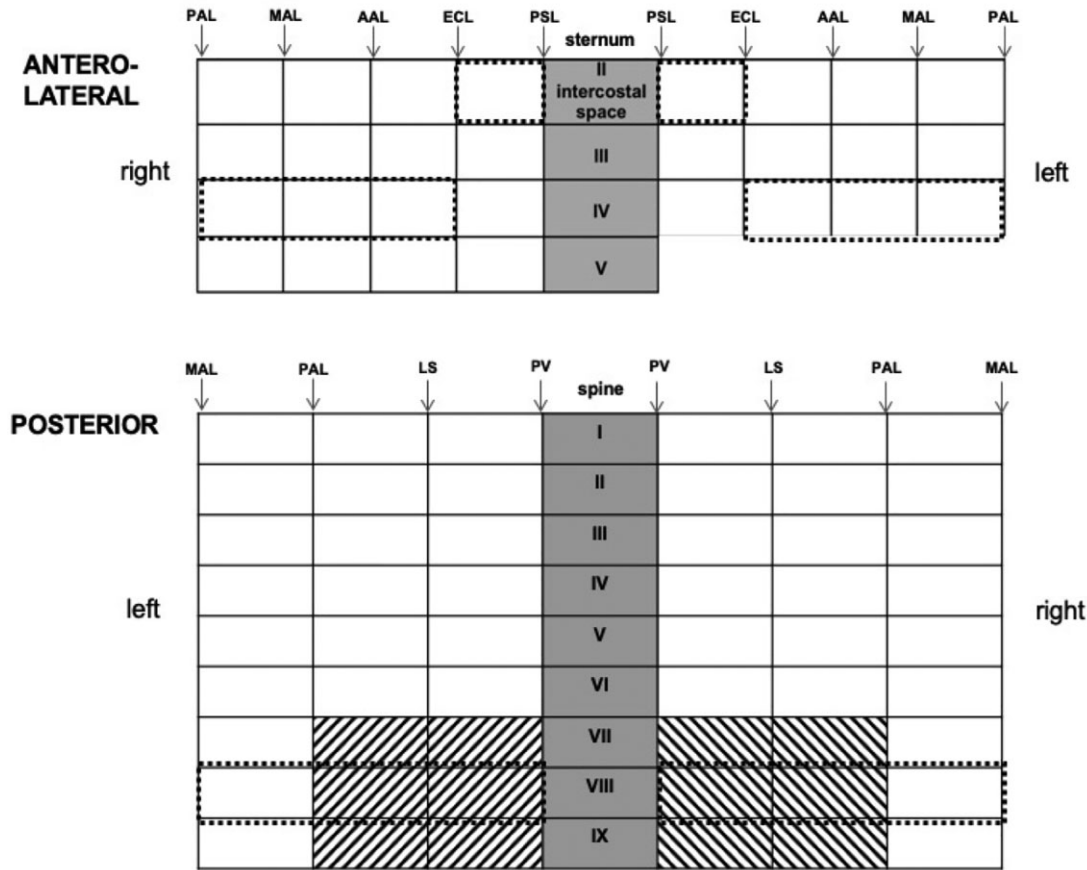
LUS was performed as previously described [9] on the antero-lateral (28-site scanning technique) and on the posterior thorax (30 additional scanning sites), for a total of 58 scanning sites, using 2.5–3.5 MHz cardiac sector transducers (2.5 cm long) on commercially available echographic equipment (Vivid i, GE/Vingmed, Milwaukee, WI, USA). Patients were supine during the antero-lateral scanning and sitting on the bed during the posterior scanning.

The pleural line was evaluated and was considered abnormal when clearly irregular, indented, with subpleural alterations or a coarse appearance. Convex (3.5–6.0 MHz) or linear transducers (7.0–10.0 MHz) were used, when needed, to better identify pleural alterations.

B-lines were defined as discrete laser-like vertical hyperechoic reverberation artefacts that arise from the pleural line, extend to the bottom of the screen without fading and move synchronously with the lung sliding [9]. In each scanning site, B-lines were quantified from 0 to 10, as previously described [21]. The total number of B-lines was evaluated through different counting methods: summing up the number of B-lines found in all scanning sites ('total B-lines') [9, 22]; dividing the total B-lines for the number of assessable scanning sites ('B-line score'); and summing up B-lines only when there were at least three B-lines in a single scanning site, thus ignoring for the count those sites with one or two B-lines [point-of-care (POC) score] [9].

We then considered four different scanning schemes (Fig. 1): antero-lateral and posterior chest [10, 23], posterior chest only [10], simplified evaluation [24] and postero-basal chest only. One physician, blinded to other pulmonary imaging tests and functional study results, with dedicated training and >10 years of experience in LUS, performed and analysed all LUS images.

Fig. 1 LUS scanning schemes



The whole chest scheme includes the antero-lateral chest and the posterior chest; the posterior chest scheme includes only the posterior chest; the simplified scheme includes those scanning sites framed with the dotted line; the postero-basal chest scheme includes those scanning sites with the hatched pattern. PAL: posterior axillary line; MAL: medium axillary line; AAL: anterior axillary line; ECL: emiclavicular line; PSL: parasternal line; LS: linea scapularis; PV: paravertebral line.

Echocardiography

To exclude a cardiogenic origin of B-lines, all patients underwent a comprehensive two-dimensional trans-thoracic echocardiogram using conventional methods with commercially available US machines equipped with 2.5–3.5 MHz phased-array transducers, second harmonic technology and coupled with tissue Doppler imaging (TDI), as previously described. Pulmonary artery systolic pressure was derived from the maximal velocity of tricuspid Doppler tracing according to the Bernoulli equation and adding the value of right atrial pressure, estimated on the basis of the collapsibility index of the inferior vena cava. All measurements were performed according to the recommendations of the European Association of Cardiovascular Imaging/American Society of Echocardiography.

Statistical analysis

Continuous variables are presented as mean (s.d.) or as median [interquartile range (IQR)], as appropriate.

Two-sample comparisons were performed using a *t*-test if variables were normally distributed, the Mann–Whitney *U* test for non-normally distributed data and the chi-squared test for categorical data. Parametric Pearson or non-parametric Spearman correlation coefficient analyses were used to test the correlation between parameters, as appropriate. Survival rates were estimated with Kaplan–Meier curves and compared by the logrank test. A Cox proportional hazards model employing univariable and stepwise multivariable procedures tested association between selected variables and outcome. A *P*-value <0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (version 20; IBM, Armonk, NY, USA).

Results

Of 71 SSc patients, 69 were eligible for data analysis. Two patients were excluded because of cryptogenic

TABLE 1 Clinical characteristics of the study population (*n* = 69)

Age, years, median (IQR)	52 (41–63)
Female, <i>n</i> (%)	60 (87.0)
Duration of disease, years, median (IQR)	3 (1–5)
Diffuse skin subset, <i>n</i> (%)	11 (15.9)
Modified Rodnan skin score, median (IQR)	0 (0–5)
Anti-topoisomerase I positivity, <i>n</i> (%)	21 (30.4)
ACA positivity, <i>n</i> (%)	28 (40.6)
VEDOSS patients, <i>n</i> (%)	26 (37.7)
Smoke exposure, <i>n</i> (%)	30 (43.5)
FVC, %, median (IQR)	106 (88–129)
TLC, %, median (IQR)	102 (89–111)
DLCO, %, median (IQR)	81 (64–92)
History/presence of digital ulcers, <i>n</i> (%)	24 (34.8)
Pleural alterations on LUS, <i>n</i> (%)	37 (53.6)
Scleroderma pattern on nailfold videocapillaroscopy, <i>n</i> (%)	53 (76.8)
ILD on chest HRCT, <i>n</i> (%)	37 (53.6)
SLS I HRCT score, median (IQR)	0 (0–4)
Wells HRCT score, median (IQR)	0 (0–2)

organizing pneumonia (one patient) and lung nodules with suspicion of malignancy (one patient). Clinical and demographic characteristics are shown in Table 1.

LUS was feasible in 100% of the cases and the time needed for the scanning and interpretation of the whole chest was always <10 min. Pleural alterations were detected in 37 (53.6%) patients, who also showed a significantly higher number of total B-lines compared with patients without pleural line alterations (Table 2). The number of scanning sites with pleural alteration [median 1 (0–2), range 0–40] significantly correlated with the total number of B-lines ($R = 0.49$, $P < 0.001$).

Clinical correlations of LUS B-lines

The total number of B-lines was lower in patients fulfilling the criteria for very early diagnosis of SSc (VEDOSS) and higher in those with dcSSc and anti-topoisomerase I autoantibody positivity (see Table 2). No association was found between the number of B-lines and age ($P = 0.41$), smoke exposure ($P = 0.148$), New York Heart Association functional class ≥ 3 ($P = 0.180$), digital ulcers ($P = 0.263$) and duration of disease ($P = 0.087$). No significant correlation was found with ejection fraction ($P = 0.462$), E/e' ($P = 0.105$), estimated pulmonary artery systolic pressure on echocardiography ($P = 0.517$), tricuspid annular plane systolic excursion ($P = 0.727$) and N-terminal prohormone of brain natriuretic peptide serum levels ($P = 0.268$), thus confirming the non-cardiogenic origin of the detected B-lines. Conversely, significant correlation was found with the modified Rodnan skin score ($R = 0.375$, $P = 0.002$), diffusion capacity for carbon monoxide (DLCO; $R = -0.471$, $P < 0.0001$), forced vital capacity (FVC; $R = -0.442$, $P < 0.001$), forced expiratory volume in 1 s (FEV₁; $R = -0.376$, $P < 0.01$), total lung capacity (TLC; $R = -0.355$, $P < 0.01$), vital capacity (VC; $R = -0.442$,

$P < 0.001$), but not with FEV₁/VC ($R = 0.109$, $P = 0.41$). Patients with a DLCO of <80% had a higher number of total B-lines compared with patients with a DLCO $\geq 80\%$ [median 40 (IQR 17–87) vs 13 (4–24); $P < 0.0001$], as well as patients with an FVC <80% compared with patients with an FVC $\geq 80\%$ [median 85 (IQR 22–101) vs 15 (6–32); $P = 0.008$].

No difference in the number of total B-lines was found in patients on calcium antagonists ($P = 0.74$), sildenafil ($P = 0.86$), bosentan ($P = 0.13$), prostanoids ($P = 0.31$) or hydroxychloroquine ($P = 0.85$), whereas patients on corticosteroids had a higher number of total B-lines compared with patients not on corticosteroids [median 88 (IQR 23–108) vs 16 (5–44); $P < 0.01$].

Correlation of LUS B-lines and HRCT

Signs of ILD on HRCT were detected in 33/69 patients (47.8%), with a median SLS I HRCT score of 3 (IQR 1–7.5) and a median Wells score of 2 (IQR 2–4). In the overall population, the median SLS I HRCT score was 0 (IQR 0–4) and the median Wells score was 0 (IQR 0–2). The HRCT alterations were distributed as follows: GGO alone ($n = 4$), thickened reticular markings alone ($n = 11$), GGO + honeycombing ($n = 1$), GGO + thickened reticular markings ($n = 13$), honeycombing + thickened reticular markings ($n = 3$) and GGO + thickened reticular markings + honeycombing ($n = 1$). The total number of B-lines significantly correlated with both the SLS I score ($R = 0.754$, $P < 0.001$) and the Wells score ($R = 0.691$, $P < 0.001$). The HRCT and LUS of one SSc patient are shown in Fig. 2.

The receiver operating characteristics (ROC) curve analysis confirmed the analytical relationship between the number of B-lines and the presence of ILD on HRCT [area under the curve (AUC) 0.91 (95% CI 0.84, 0.98), $P < 0.0001$]. The presence of a total number of B-lines >10 was found to maximize the overall diagnostic accuracy, with a sensitivity of 97.0%, but with a specificity of 64%.

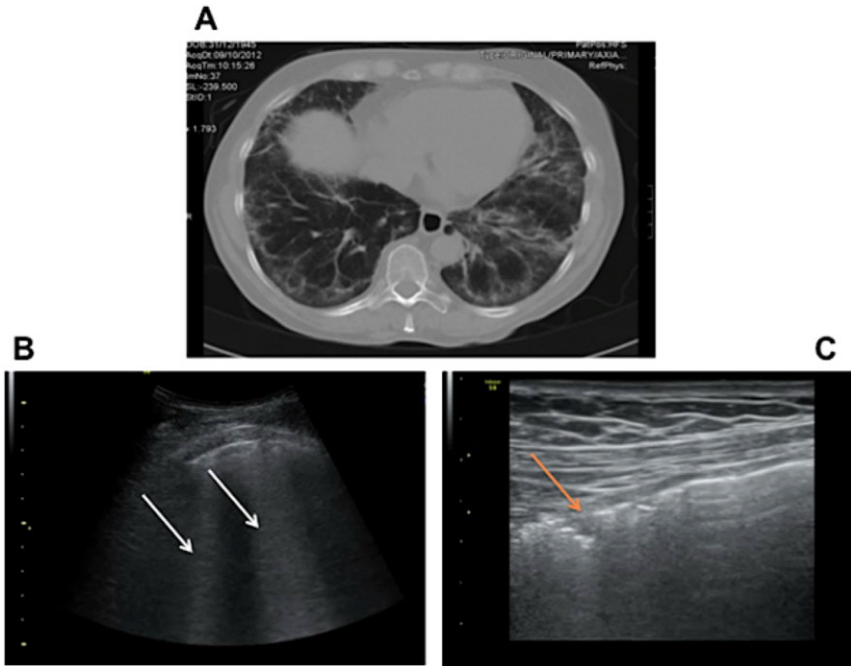
Individual patient analysis comparing LUS and HRCT findings showed an 80% concordance between the two examinations. In 13 patients, LUS results were considered false negative, because some B-lines were present whereas HRCT was negative. In these 13 cases, the median number of B-lines was lower when compared with true positive cases [19 (IQR 13–31) vs 51 (24–92); $P < 0.001$]. The total number of B-lines was <20 in 8/13 of these cases; 4/13 had a reduced DLCO value <80% (none of them had pulmonary hypertension) and 6 had previous/current smoking exposure. In five of these patients, some apical micronodules were present on HRCT; these patients also had some B-lines at the more apical scanning sites. More detailed information on discordant false-positive cases are presented in Table 3. One false-negative case was detected: a patient with a very small (<1%) ground-glass area located in the paracardiac position (SLS I score 1, Wells score 0), with LUS pleural alterations in a single scanning site but without

TABLE 2 B-lines distribution according to different parametric variables

Variables		Number of B-lines, median (IQR)	P-value
Female	Yes	15 (5–44)	0.007
	No	55 (28–98)	
Arterial hypertension	Yes	33 (15–88)	0.075
	No	17 (5–45)	
Diabetes mellitus	Yes	14 (10–17)	0.646
	No	18 (7–46)	
Current smoker	Yes	19 (10–53)	0.643
	No	17 (6–45)	
Current or former smoker	Yes	19 (10–60)	0.148
	No	14 (5–44)	
VEDOSS criteria	Yes	8 (3–16)	<0.001
	No	29 (14–77)	
Diffuse skin involvement	Yes	88 (33–108)	<0.001
	No	15 (5–36)	
Anti-topoisomerase I antibody positivity	Yes	29 (14–77)	0.002
	No	10 (2–25)	
NVC SSc pattern	Yes	19 (9–48)	0.007
	No	7 (3–15)	
Pleural alterations on LUS	Yes	33 (14–76)	<0.001
	No	10 (3–18)	

NVC: nailfold videocapillaroscopy. Bold values are those $P < 0.05$, thus statistically significant.

Fig. 2 The HRCT and LUS images of one SSc patient



(A) HRCT shows a typical non-specific interstitial pneumonia pattern with ground-glass areas. LUS **(B)**, convex probe; **(C)**, linear probe) shows B-lines (arrow in B) and pleural line alterations (arrow in C).

detectable B-lines; the trivial ground-glass area remained stable on HRCT follow-up.

On the posterior chest, the highest number of B-lines (mean number ≥ 0.8 B-lines per scanning site) was

consistently found in the two lower (more basal) inter-costal spaces along the posterior axillary line, linea scapularis and paravertebral line on both the right and the left.

TABLE 3 Comparison between HRCT and LUS false-positive cases

Patient	HRCT description	Anterior B-lines	Posterior B-lines	Total B-lines
1	Apical pleural irregularities	5	6	11
2	Calcific apical micronodules	7	6	13
3	Calcific apical micronodules	0	13	13
4	Normal HRCT	3	11	14
5	Normal HRCT	8	7	15
6	Small areas of parenchymal dysventilation at the lung left base, some small thickened apical and paracardiac interlobular septa	8	9	17
7	Parenchymal nodule of the right inferior lobe	8	11	19
8	Apical fibrotic striae (previous radiotherapy for breast cancer)	14	5	19
9	Small areas of parenchymal dysventilation	3	20	23
10	Calcific apical micronodules	6	24	30
11	Thickened interlobular septa and micronodules not SSc-related	6	27	33
12	Mosaic attenuation pattern	26	17	43
13	Normal HRCT	28	17	45

When the presence of pleural alteration as a sign of positive LUS examination was considered, the combination of B-lines >10 and/or pleural alteration (in at least one scanning site) yielded a sensitivity of 100%, a specificity of 47%, a positive predictive value of 71.2% and a negative predictive value of 100%. When the same analysis was repeated for only the posterior chest area, an ROC cut-off of four B-lines showed the same sensitivity as the full chest examination (sensitivity 97.0%, specificity 64%), as well as when pleural alterations were included (sensitivity 100%, specificity 39%). Similarly, using the simplified score proposed by Gutierrez *et al.* [12] with a cut-off of six B-lines as identified by ROC curve analysis, a sensitivity of 85% with a specificity of 78% in predicting the presence of ILD on HRCT was still detected (Table 4).

When only the basal part of the posterior chest was considered (Fig. 1), the sensitivity was the same as the whole chest (antero-lateral) and the whole posterior chest (sensitivity 97%), but assessed only 12 scanning sites (Table 4). Even with this scanning scheme, including pleural line alterations increased the sensitivity to 100%. The scanning sites related to the postero-basal chest are approximately the seventh through ninth intercostal spaces, between the inferior angle of the scapula and the diaphragm (Fig. 1). When assessing only this basal part of the posterior chest, the cut-off to maximize diagnostic accuracy was more than three B-lines, with a sensitivity of 79% and a specificity of 81%.

The performances of the three different counting methods, matched with the four scanning schemes, are summarized in Table 4. These results show a high sensitivity for all the combinations (always >85%), with a wide range of specificity values (31–78%).

Discussion

Our data confirm that LUS B-lines correlate with HRCT, independent from the LUS scanning technique and counting method. Moreover, LUS B-lines have a very high sensitivity in detecting parenchymal modifications, even in the very early phase of ILD. The assessment limited to the postero-basal area of the chest seems the most effective approach, combining a very high sensitivity with a quicker and simpler scanning scheme.

In SSc, HRCT is the pivotal tool for the identification and monitoring of parenchymal modifications in everyday practice [24]. However, the clinical usefulness of HRCT is jeopardized by radiation exposure, which is particularly relevant in SSc patients, often young women of childbearing age, who are exposed to a greater oncologic risk [25].

It has been clearly shown that LUS can identify ILD in SSc patients [10, 26, 27]. When compared with previous articles, the present study has the following strengths: a rather large SSc population; LUS examination performed on the same day as HRCT and by the same expert sonographer; all HRCTs independently and blindly evaluated by two thoracic radiologists expert in ILD, with a standardized score specifically developed for SSc-ILD [20] and with the same machine; the data analysis performed with three different counting methods over four different scanning techniques; a regional assessment of pleural line alterations of the overall chest; and a detailed individual analysis of discordant cases.

Our findings have some clinical implications for the use of LUS in SSc patients. We found that B-lines have a good correlation with the HRCT score specific for SSc-ILD, despite the methodology used for both the

TABLE 4 Comparison between different LUS counting methods and scanning schemes: correlation with SLS I score and accuracy in predicting the presence of ILD on HRCT

Counting methods	Scanning schemes			
	Whole chest (58 sites) [10, 23]	Posterior (30 sites) [10]	Simplified (14 sites) [12]	Postero-basal (12 sites) [10]
Total B-lines [9, 22]	$R = 0.75, P < 0.0001$ AUC = 0.91, $P < 0.0001$ Cut-off >10 Sensitivity 97% Specificity 64%	$R = 0.70, P < 0.0001$ AUC = 0.875, $P < 0.0001$ Cut-off >3 Sensitivity 97% Specificity 50%	$R = 0.67, P < 0.0001$ AUC = 0.871, $P < 0.0001$ Cut-off >6 Sensitivity 85% Specificity 78%	$R = 0.70, P < 0.0001$ AUC = 0.875, $P < 0.0001$ Cut-off >1 Sensitivity 97% Specificity 56%
B-lines score	$R = 0.74, P < 0.0001$ AUC = 0.90, $P < 0.0001$ Cut-off ≥ 0.45 Sensitivity 97% Specificity 73%	$R = 0.68, P < 0.0001$ AUC = 0.86, $P < 0.0001$ Cut-off ≥ 0.10 Sensitivity 97% Specificity 50%	$R = 0.66, P < 0.0001$ AUC = 0.86, $P < 0.0001$ Cut-off ≥ 0.10 Sensitivity 97% Specificity 31%	$R = 0.66, P < 0.0001$ AUC = 0.86, $P < 0.0001$ Cut-off ≥ 0.04 Sensitivity 94% Specificity 61%
POC score [9]	$R = 0.72, P < 0.0001$ AUC = 0.90, $P < 0.0001$ Cut-off >1 Sensitivity 97% Specificity 36%	$R = 0.63, P < 0.0001$ AUC = 0.84, $P < 0.0001$ Cut-off >1 Sensitivity 88% Specificity 53%	$R = 0.64, P < 0.0001$ AUC = 0.86, $P < 0.0001$ Cut-off >1 Sensitivity 94% Specificity 52%	$R = 0.18, P = 0.885$ AUC = 0.49, $P = 0.85$

Counting methods: Total B-lines = sum of the number of B-lines found in all scanning sites [9, 22]. B-line score = total B-lines divided by the number of assessable scanning sites. POC score = sum of the number of B-lines found in those scanning sites with three or more B-lines [9]. Scanning schemes: Whole chest (antero-lateral and posterior chest), total of 58 sites [10, 23]. Posterior chest only, total of 30 sites [10]. Simplified evaluation, total of 14 sites [12]. Postero-basal only, total of 12 sites [9].

scanning and counting, with the most effective approach—combining high sensitivity with a simpler scanning scheme—obtained by assessing the postero-basal chest.

ROC analysis allowed the identification of cut-offs that might be employed for screening purposes. In particular, a total of >10 B-lines on the overall chest or >1 B-line on the postero-basal chest were found to be the best cut-offs to maximize sensitivity. When pleural line alterations were added to these cut-off values, the sensitivity reached 100%. In our cohort, B-lines assessment missed only one patient who had a trivial involvement in the paracardiac region. This may be explained by the fact that this ground-glass area was medially located and surrounded by aerated parenchyma and therefore could not be reached by the LUS beam. For this reason, LUS must be integrated into the clinical context, as with any other examination, and in the case of significant clinical suspicion of ILD dictated by impaired pulmonary function tests, even with a normal LUS pattern, HRCT should always be performed.

Our cut-off is similar to the one proposed by Tardella *et al.* [28], although the number of 10 B-lines, apparently identical to our cut-off, was obtained on the 14-site scanning simplified score [29] and predicted an HRCT Warrick score of at least 7, which identifies an already significant ILD involvement; however, the main message about the high sensitivity of LUS is in line with our

results. This cut-off of more than one B-line in the postero-basal chest can be further used for the screening of even mild involvement, with this thoracic region easily identified by the anatomical references of the inferior angle of the scapula and the diaphragm (Fig. 1).

Our data may also clarify the issue of ‘apparent’ false-positive cases of LUS, where >10 B-lines were detected over the entire chest, whereas HRCT was negative. In these patients, although HRCT did not show specific signs of SSc-ILD, the exams were not completely normal: in seven cases, HRCT showed some fibrotic lines in the apical regions that were considered ‘false positive’ for SSc-ILD, but found small de-aeration areas of the pulmonary parenchyma generating some B-lines. In three patients with >10 B-lines, HRCT was completely negative; these B-lines could be partly related to dynamic small atelectatic striae in dependent areas due to the supine position. This does not impact on the clinical role of LUS, since it is known that it is not possible to distinguish those B-lines originating from initial SSc-ILD from other fibrotic lines or small de-aeration areas. However, this helps us understand those cases of ‘apparently’ false-positive LUS compared with HRCT and the consequent low specificity of LUS.

Pleural line alterations may be a relevant LUS feature that can disclose ILD in rheumatic diseases [9, 22, 30–32], but their role in screening still remains limited. In our cohort, only one patient with <10 total B-lines and

minimal ILD was identified thanks to pleural line alterations and not to B-lines. In severe ILD, pleural line alterations are clearly visible, whereas patients with early ILD may not show any pleural line modification on LUS. Moreover, since the evaluation of the pleural line is qualitative and many conditions can determine small pleural line alterations (including tiny old scarring following pulmonary infections), only a significant coarse appearance of the pleural line should be considered as abnormal (Fig. 2). Pleural line alterations can be better visualized by convex or linear probes compared with phased-array probes, although clear, unequivocal alterations can be seen, or at least suspected, even with a phased-array probe.

It must be pointed out that despite its utility in several lung conditions, LUS cannot replace HRCT, which remains of paramount importance in ILD, providing detailed imaging of any area of the chest. Furthermore, LUS cannot distinguish between the different radiological ILD patterns (ground glass, reticulation, honeycombing) shown by HRCT. In clinical practice, LUS can have a role as a screening tool for early ILD detection and can be combined with PFTs to identify those patients who need a chest HRCT. The low cost, feasibility, short duration (<10 min for a complete chest scan), short learning and interpretation curves [22, 33] and the possibility of being performed by hand-held devices [33, 34] suggest that LUS might be employed more frequently in rheumatic patients where ILD may be an issue. Even medical personnel without previous experience in US can be effectively trained in a relatively short time on B-line detection and counting [35]. In patients with normal PFTs, a completely normal LUS could actually exclude the presence of ILD, with chest X-ray completing the information on the overall overview of the chest; in patients with impaired DLCO and ≤ 10 B-lines, the probability of SSc-ILD on HRCT is low (Supplementary Figs S1 and S2, available at *Rheumatology* online). Of course, the flow-chart proposal (Supplementary Fig. S2, available at *Rheumatology* online) is intended as a schematic approach, always to be integrated and adjusted according to the overall clinical picture.

It is important to reiterate that B-lines are non-specific, because they may be detected in other pulmonary conditions of parenchymal air reduction/increased parenchymal density, i.e. cardiogenic pulmonary oedema. For this reason, cardiac function was carefully checked in all our patients. In the clinical arena, rheumatologists should be aware of the non-specificity of B-lines, and if a patient has a significant cardiac involvement, the potential cardiac aetiology of B-lines should be considered. However, fibrotic pneumogenic B-lines usually originate from an irregular, abnormal pleural line—apart from the very early stages—whereas in patients with cardiogenic B-lines the pleural line is thin and regular. Moreover, cardiogenic B-lines at rest would be present in advanced phases of cardiac involvement in decompensated patients, a condition that is not so common in patients who need to be screened for ILD.

In conclusion, LUS shows a very high sensitivity for early ILD detection. The evaluation of LUS could be practically limited to the postero-basal chest areas as a highly sensitive, simple and rapid scanning scheme. We propose <10 B-lines on the entire chest or <1 B-line in the postero-basal chest as cut-offs to detect early ILD in SSc. Overall, LUS is user- and patient-friendly and, when combined with PFTs, may serve as a reliable screening tool for detecting early ILD in SSc patients.

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Data availability statement

Data are available on request.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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