CHEST

Prognostic Value of Lung Ultrasound B-Lines in Systemic Sclerosis

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BACKGROUND: A high percentage of systemic sclerosis (SSc) patients experience interstitial lung disease (ILD) during the disease course. Recent data have shown that lung ultrasound (LUS) can assess ILD by the evaluation of B-lines, the sonographic sign of pulmonary interstitial involvement.

RESEARCH QUESTION: To establish the prognostic value of B-lines in a large number of patients with SSc.

STUDY DESIGN AND METHODS: A total of 396 consecutive patients with SSc, who were enrolled at three Rheumatology Departments, underwent a comprehensive LUS examination on the anterolateral and posterior chest for a total of 58 scanning sites. All available clinical, imaging, and functional data were recorded. Patients were followed after enrolment to establish the prognostic role of LUS.

RESULTS: The median number of B-lines was higher in patients with the diffuse cutaneous subset (44 vs 17 B-lines; $P < .0001$), topoisomerase I autoantibodies (39 vs 16 B-lines; $P < .0001$), and the presence of ILD at chest high-resolution CT (45 vs 9 B-lines; $P < .0001$). At multivariable analysis, the number of posterior B-lines ≥5 was associated with new development or worsening ILD (hazard ratio, 3.378; 95% CI, 1.137-9.994; $P = .028$), with additional value over topoisomerase I positivity. The prognostic value was further confirmed in the subgroup of patients with known ILD at baseline (hazard ratio, 1.010; 95% CI, 1.003-1.018; $P = .008$).

INTERPRETATION: Lung ultrasound B-lines are associated with worsening or development of pulmonary deterioration. In the near future, LUS might become part of the diagnostic and prognostic armamentarium in patients with SSc, which would allow a more sustainable and user-friendly approach to this very fragile population. CHEST 2020; 158(4):1515-1525

KEY WORDS: B-lines; interstitial lung disease; prognosis; systemic sclerosis; ultrasound

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ABBREVIATIONS: DLCO = capacity of the lung for carbon monoxide; HRCT = high-resolution CT; ILD = interstitial lung disease; PFT = pulmonary function test; SSc = systemic sclerosis

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Systemic sclerosis (SSc) is characterized by a complex pathophysiology that leads to fibrosis of the skin and of the main internal organs.[1] Interstitial lung disease (ILD) is one of the main causes of disease-related morbidity and death.[2] Over the last 40 years, although the mortality rate due to renal crisis has decreased significantly, the number of deaths due to pulmonary involvement, namely ILD and pulmonary arterial hypertension has increased.[3] Because more than one-half of patients with SSc experience ILD during the course of the disease,[3] strict monitoring of pulmonary signs and symptoms is mandatory.

Unfortunately, exertional dyspnea is nonspecific and often insidious, and a nonproductive cough may be absent at the early stages. Typical basilar velcro-like crackles at auscultation are specific, but not sensitive.[4] Imaging techniques and functional tests therefore are essential. Pulmonary function tests (PFTs), which include %FVC and total lung capacity, that are associated with diffusing capacity of the lung for carbon monoxide (%DLCO) are the mainstay of the diagnosis of pulmonary involvement. In patients with SSc, DLCO can be reduced either in ILD or in vascular abnormalities linked to pulmonary hypertension. Chest radiography is often the first imaging test of choice, although its sensitivity and specificity are both low in the assessment of ILD.[5] High-resolution CT (HRCT) is more accurate than chest radiography in the detection and characterization of pulmonary involvement and is now considered the noninvasive diagnostic gold standard for ILD evaluation.[6] The main limitations of HRCT are its cost and radiation exposure.[7] Promising data recently have been described on the use of lung ultrasound (LUS) B-lines to detect ILD.[8] B-lines are the sonographic sign of the pulmonary interstitial syndrome[9] and are visible in ILD, as reported by different studies.[9-15] The aim of our study was to assess the prognostic value of LUS B-lines to predict new development or worsening pulmonary involvement in a large population of patients with SSc who were enrolled in a multicenter study.

Materials and Methods

Four hundred ten consecutive patients who were affected by SSc and were enrolled at three Rheumatology Departments in Italy (Florence, Milan, and Pisa) were evaluated prospectively during regular office visits. The inclusion criteria were (1) a previous diagnosis of SSc, according to the American College of Rheumatology/European League Against Rheumatism classification criteria,[16] independently from the stage of the disease and organ involvement; (2) age >18 years; (3) informed consent; and (4) available follow-up. All available clinical and instrumental data, including history, physical examination (such as history/presence of digital ulcers as defined by Suliman et al,[17] skin fibrotic involvement by modified Rodnan skin score, biochemical and immunologic data [in particular anticentromere and anti-Topoisomerase I antibody positivity], and PFTs with DLCO) were recorded. The local Ethical Committee Boards approved the study; informed consent was obtained from each patient (Comitato Etico Sperimentazione Clinica CEAVNO Area Vasta Nord-Ovest Toscana n° 2849 for Pisa/Florence, and Comitato Etico-Scientifico di Milano Area C n° 427-092015 for Milan).

Lung Imaging

LUS was performed the day of enrolment on the anterolateral and posterior chest, moving the sonographic probe along anatomic reference lines, as previously described.[10] Commercially available echographic equipment with 2.5 to 3.5 MHz cardiac sector transducers were used (Mylab50, Esaote, Genoa, Italy; IE33, Philips Medical Systems, Andover, MA; Vivid i, GE/Vingmed, Milwaukee, WI). Patients were in the supine position for the anterolateral scanning and in the sitting position for the posterior scanning. The anterolateral assessment included 28 scanning sites, and the posterior assessment included 30 scanning sites[10] for a total of 58 scanning sites (Fig 1). A B-line was defined as an echogenic, coherent, wedge-shaped signal with a narrow origin in the near field of the image.[9] At each scanning site, the number of B-lines was recorded, enumerated, and summed. Pleural line characteristics were also observed and recorded; the pleural line was considered abnormal in the presence of a distinct coarse appearance or subpleural alterations (Figs 2C, D); to maintain good specificity, subtle abnormalities of the pleural line were not considered as pleural line alterations. Convex (3.5-6.0 MHz) or linear transducers (7.0-10.0 MHz) were used in addition to the cardiac probe to better visualize the pleural characteristics (Fig 1). B-lines were quantified as previously described from 0 to 10 at each scanning site[9,10]; therefore, the number of total B-lines could range between 0 and 580 for total B-lines, 0 to 280 for anterolateral B-lines, and 0 to 300 for posterior B-lines. Two observers (G. A. and L. G.), who were both fellows in cardiology at the time of imaging with dedicated training and previous experience in LUS of at least 1 and 3 years, acquired and analyzed all LUS studies for the three centers. The observers were blind to the clinical status, chest HRCT, PFTs, and all medical information of the patients, apart from the information clearly inferable by the inspection (in particular the aspect of the skin of the face, trunk, and hands).

Follow Up

Patients were followed according to their clinical needs, with the use of good clinical practice principles. Follow-up data were obtained from at least one of four sources: review of the patient's hospital records, review of the patient's charts, a telephone interview with the patient conducted by physicians, or a staff physician visiting the patients in the out-patient clinic. The primary outcome was the

RIGHT mid-axillary	RIGHT anterior axillary	RIGHT mid-clavicular	RIGHT para-sternal	inter-costal space	LEFT para-sternal	LEFT mid-clavicular	LEFT anterior axillary	LEFT mid-axillary
				II				
				III				
				IV				
				V				

LEFT posterior axillary	LEFT linea scapularis	LEFT para-vertebral	inter-costal space	RIGHT para-vertebral	RIGHT linea scapularis	RIGHT posterior axillary
			II			
			III			
			IV			
			V			
			VI			
			VII			
			VIII			
			IX			

Figure 1 – *Ultrasound scanning sites for the anterolateral and the posterior chest*

combination of the development of ILD or the worsening of preexisting ILD. Given the lack of universally accepted definition of worsening ILD and the absence of recommendation in monitoring patients with SSc for ILD development, events were defined according to an integrated evaluation based on the clinical picture combined with all available assessments and were identified as predictors of progression in SSc-related ILD (≥10% decrease in FVC, ≥15% decrease in DLCO, extent of disease on HRCT scan, presence of honeycombing).[18-20] To adjudicate a case of new development of ILD, signs of SSc-ILD on HRCT that were not present in the previous HRCT as reported by the radiologist were always needed. Two physicians (blinded to baseline LUS count) evaluated each case separately; in the case of disagreement on the event, consensus was reached with a third expert (4 cases). Patients were censored at the time of the event, in case the event occurred, or on the day of the last available follow up.

Statistical Analysis

Continuous variables are expressed as mean ± SD or median and interquartile ranges, as appropriate. Two-sample comparisons were performed using *t*-tests if variables were normally distributed, the Mann-Whitney *U* test for nonnormally distributed data, and the chi-squared test for categoric data. Correlations between parameters were assessed with parametric Pearson or nonparametric Spearman correlation coefficient analysis, as appropriate. The association of selected variables with the outcome was assessed by Cox's proportional hazard model with the use of univariable and multivariable procedures (allowing variables with $P < .10$ at univariable to enter the model). The event rates were estimated with Kaplan-Meier curves and compared by the log-rank test. The interobserver variability in LUS assessment was examined by intraclass correlation coefficient on 40 LUS videos that were evaluated by two expert readers. An ex-post power calculation has been performed: for a hazard ratio of 2.5, the calculated power is

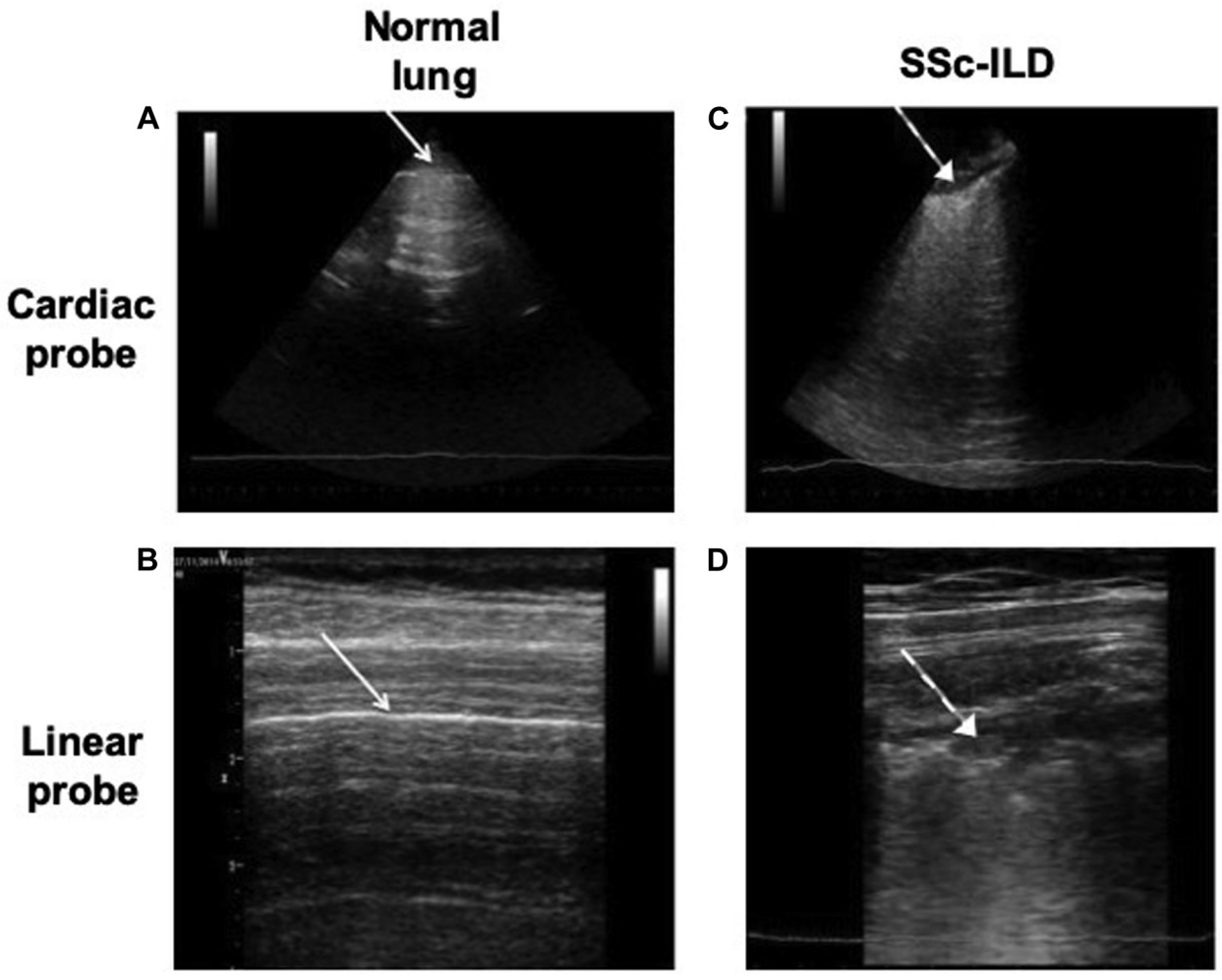

Figure 2 – *Normal lung ultrasound pattern (A, cardiac probe and B, linear probe) compared with interstitial lung disease pattern (C, cardiac probe and D, linear probe). The white arrows in A and B indicate the normal pleural line; the dotted-line arrows in C and D indicate pleural line alterations.*

0.90; for a hazard ratio of 3, the calculated power is 0.98. A probability value of $<.05$ was considered statistically significant. All statistical analyses were performed with the Statistical Package for the Social Sciences (version 20; SPSS Inc, Chicago, IL).

Results

Three hundred ninety-six patients with SSc (365 women; median age, 55 years [interquartile range (IQR), 44-66 years]) satisfied the inclusion criteria and were enrolled in the study. The median duration of disease was 4 years (IQR, 1-9 years). The diffuse skin subset was present in 22.5% of patients with a prevalence of digital ulcers of 32.6%, and of ILD on HRCT of 42.2% (Table 1).

LUS assessment was feasible in all patients, and none was excluded for technical reasons. Increased skin thickness nor high BMI (maximum BMI, 38 mg/m^2) limited LUS feasibility. The intraclass correlation coefficient between the two expert readers on B-lines number assessment was 0.948, which is consistent with previous data. The median number of B-lines was 8 (IQR, 3-23) on the anterolateral chest and 11 (IQR, 3-31) on the posterior chest, respectively, thus determining a median B-lines total number of 19 (IQR, 8-55).

Significant pleural line alterations were detected in 40% of the patients, and their presence was associated with a significantly higher number of B-lines (51 [IQR, 22-99] vs 11 [IQR, 4-24); $P < .0001$). The median number of B-lines was significantly higher in patients with HRCT positive for ILD (45 [IQR, 17-99] vs 9 [IQR, 4-19]; $P < .0001$) and showed a significant inverse correlation with %FVC (R, -0.34; $P < .0001$), total lung capacity (R, -0.35; $P < .0001$) and %DLCO (R, -0.50; $P < .0001$); a weak correlation was found between the

TABLE 1] B-lines Number According to Clinical Characteristics

Clinical Characteristic	No. (%)	Total No. of B-lines, Median (IQR)	*P* value
Sex			.015
Female	365 (92.2)	19 (7-51)	
Male	31 (7.8)	36 (11-155)	
American College of Rheumatology/European League Against Rheumatism systemic sclerosis score			< .0001
>9 points	314 (79.3)	25 (10-73)	
9 points	82 (20.7)	10 (4-20)	
Skin involvement			< .0001
Limited	307 (77.5)	17 (7-40)	
Diffuse	89 (22.5)	44 (17-91)	
Antibodies			< .0001
Anti-Topoisomerase I	123 (31.1)	39 (15-89)	
Anti-Centromere	166 (41.9)	14 (5-32)	
Nailfold Videocapillaroscopy			< .0001
Late systemic sclerosis pattern	357 (90.2)	49 (22-90)	
Early/active/undifferentiated systemic sclerosis pattern	39 (9.8)	18 (8-49)	
New York Heart Association functional class			< .0001
I or II	367 (92.7)	18 (7-49)	
III or IV	29 (7.3)	89 (24-174)	
Modified Rodnan skin score			<.0001
<3	218 (55.1)	12 (4-24)	
≥3	178 (44.9)	39 (15-98)	
Digital ulcer			< .0001
History or presence	129 (32.6)	31 (12-87)	
No history	267 (67.4)	17 (6-43)	
Diffusion capacity of lung oxide			< .0001
≥80%	245 (61.9)	10 (3-19)	
<80%	151 (38.1)	29 (11-76)	
High-resolution CT			< .0001
Negative for interstitial lung disease	229 (57.8)	9 (4-19)	
Positive for interstitial lung disease	167 (42.2)	45 (17-99)	
Diagnosis			.84
Pulmonary arterial hypertension	13 (3.3)	19 (10-33)	
No pulmonary arterial hypertension	383 (96.7)	19 (8-59)	

IQR = interquartile range.

number of B-lines and disease duration (R, −0.18; $P <$ .001). Similar results were obtained by analyzing the number of anterolateral and posterior B-lines separately.

Follow-up data available on the 396 patients, with a median time of observation of 28 months (IQR, 11-44 months), identified 50 patients with new development or worsening of ILD. New development of ILD occurred in 16 patients with a median time of 30.8 months (IQR, 16.6-44.3 months), whereas worsening of ILD occurred in 34 patients with a median time 20.8 months (IQR, 6.6-36.2 months). At univariable analysis, the total number of B-lines (anterolateral + posterior chest B-lines) and the posterior B-lines alone (as continuous variable) were associated significantly with events (hazard ratio, 1.011; 95% CI, 1.006-1.016; $P <$ .0001). The area under the

TABLE 2] Univariable and Multivariable Analysis for Association With Outcomes in the Study Population (n = 396)

Variable	Univariable, hazard ratio (95% CI)	*P* Value	Multivariable HR (95% CI)	*P* Value
Age	0.991 (0.972-1.010)	.358	…	…
Diffuse skin subset	1.119 (0.581-2.156)	.737	…	…
Anti-Topoisomerase I antibody positivity	2.886 (1.642-5.072)	.0001	2.987 (1.474-5.596)	.002
Modified Rodnan skin score	1.020 (0.989-1.052)	.216	…	…
Forced vital capacity, % predicted	0.996 (0.983-1.009)	.565	…	…
Diffusion capacity of lung oxide, % predicted	0.986 (0.970-1.002)	.081	1.010 (0.989-1.031)	.368
Total lung capacity, % predicted	0.976 (0.961-0.991)	.002	0.985 (0.967-1.003)	.101
Total posterior B-lines ≥ 5	5.557 (1.998-15.452)	< .001	3.378 (1.137-9.994)	.028

curve for posterior B-lines to predict events was 0.67 (0.59-0.75; $P < .0001$). A cut-off value of ≥5 posterior B-lines was then determined through receiver operating characteristic curve analysis to optimize sensitivity and negative predictive value, and its association with events was confirmed (Table 2). Individual patient analysis plotting the presence of ≥5 posterior B-lines at LUS with events showed a high number of false-positive cases (84%), but a very low number of false-negative cases (4%), a sensitivity of 92.0%, specificity of 16%, a negative predictive value of 92%, and a positive predictive value of 16% (Table 3). On multivariable analysis posterior B-Lines ≥5 and anti-topoisomerase I positivity were the two parameters associated to events (Table 2). When only the subgroup of patients with anti-topoisomerase I positivity was analyzed, posterior B-Lines were still associated to events (HR, 1.008; 95% CI, 1.000-1.015; $P = .01$). A total number of posterior B-Lines ≥5 was thus able to discriminate patients at higher risk of worsening pulmonary involvement, as confirmed by Kaplan-Meier curves (Fig 3). When only the subgroup of patients with known ILD at the time of LUS (167 patients) was analyzed, the association of posterior B-Lines with events was confirmed (Table 4).

Discussion

To the best of our knowledge this is the first study to address the prognostic value of ultrasound B-lines for the prediction of new development or worsening ILD in a multicentric study with a large population of patients with SSc. Our data show that B-lines may predict a new development or worsening ILD, with additive value over anti-topoisomerase I positivity.

HRCT is the noninvasive gold-standard technique for ILD diagnosis and assessment.[21,22] It enables the diagnosis of ILD and provides relevant information that may help in the choice of therapeutic strategies. Frequently, HRCT is also used as a follow-up tool, but the radiation exposure still remains an issue,[7,23,24] because patients with SSc are often young women of reproductive age who are moreover at increased risk of cancer.

Previous studies have shown that LUS may identify ILD in SSc[10,11,14,25,26] and other rheumatic diseases[27] and in other diffuse parenchymal lung diseases, which includes idiopathic pulmonary fibrosis and sarcoidosis.[11,28,29] In SSc, a significant positive linear correlation has been found between the number of B-lines and the HRCT 30-point Warrick score.[10] In particular, B-lines have shown excellent sensitivity and negative predictive value, compared with HRCT,[14] which suggests a potential role of LUS in the screening of ILD-SSc in patients who are asymptomatic or with nonspecific symptoms.

Pleural line alterations are another relevant characteristic of LUS examinations, but their role in ILD is still unclear.[9,30-32] In severe ILD, pleural line alterations are almost always clearly visible; this feature

TABLE 3] Individual Patient Analysis According to the Presence of ≥5 Posterior B-Lines at Lung Ultrasound Scan and Events

Variable	Posterior B-lines <5	Posterior B-lines ≥5	Total
No interstitial lung disease worsening/development	98	248	346
Interstitial lung disease worsening/development	4	46	50
Total	102	294	396

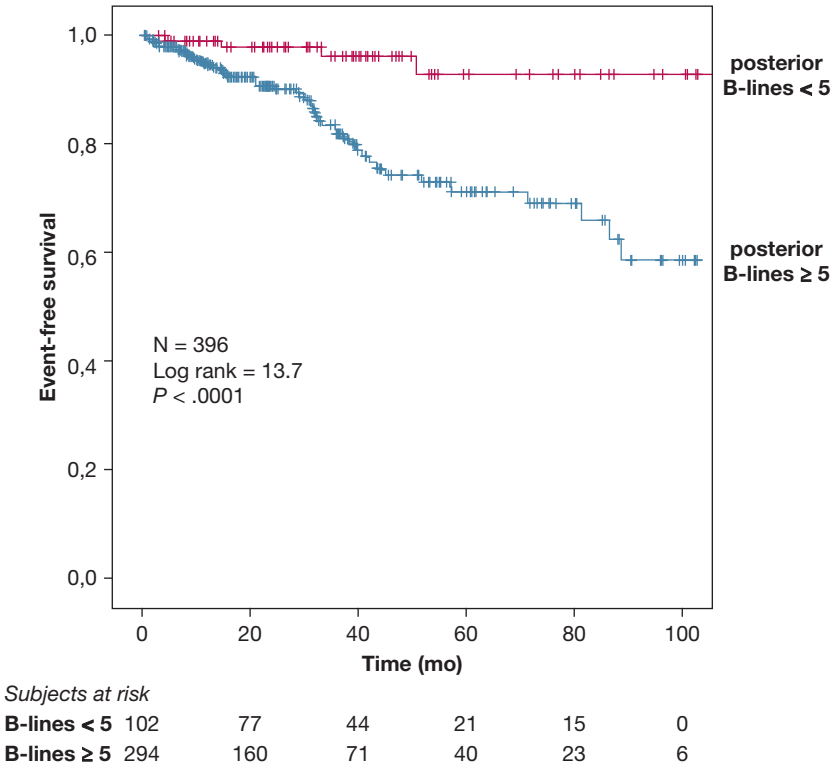

Figure 3 – *Kaplan-Meier curves and estimates of event-free survival in patients with <5 or ≥5 posterior B-lines.*

helps in differentiating "cardiogenic" B-lines (because of extravascular lung water consequent to increased left ventricular filling pressures) from "fibrotic" B-lines (because of deposition of collagen tissue in the interstitial space). Of course, this differential diagnosis is based mainly on the patient's history and cannot rely only on the ultrasound appearance of the pleural line. However, from an imaging point of view, extravascular lung water in patients with decompensated heart failure yields multiple diffuse bilateral B-lines, with a gravity-related distribution (ie, more B-lines in the dependent areas). In these cases, the pleural line appears as a hyperechoic, well-defined, thin, horizontal line. Instead, collagen-thickened interlobular septa generate multiple diffuse B-lines, usually, but not necessarily, bilateral in early phases, more numerous on the posterior chest at lung bases, and often associated with alteration of the pleural line. In these cases, the pleural line appears coarse, indented, and irregular (Fig 2C and D). These pleural line alterations are more often visible in more advanced phases of the disease, although sometimes they may be present even with a very few B-lines. In our experience, pleural line alterations have been detected in the absence of a significant number of B-lines only in a

TABLE 4] Univariable and Multivariable Analysis for Association With Outcomes in Patients With Known Interstitial Lung Disease at the Time of the Lung Ultrasound Scan (n = 167)

Variable	Univariable, HR (95% CI)	*P* Value	Multivariable, HR (95% CI)	*P* Value
Age	0.985 (0.961-1.011)	.257	…	…
Diffuse skin subset	0.853 (0.360-2.019)	.717	…	…
Anti-Topoisomerase I antibody positivity	2.218 (1.099-4.478)	.026	3.177 (1.257-8.028)	.015
Modified Rodnan skin score	1.021 (0.985-1.058)	.262	…	…
FVC, % predicted	0.989 (0.974-1.004)	.141	…	…
Diffusion capacity of lung oxide, % predicted	0.988 (0.969-1.007)	.204	…	…
Total lung capacity, % predicted	0.981 (0.964-0.999)	.034	0.994 (0.975-1.014)	.552
Total posterior B-lines	2.763 (1.313-5.812)	< .007	1.010 (1.003-1.018)	.008

very limited number of patients; therefore, from a clinical point of view, pleural line alterations can be considered in most patients as a proxy for numerous B-lines. It should also be noted that gross alterations of the pleural line make the identification and counting of B-lines more difficult, thus leading to a possible underestimation of the number of B-lines.[31,33]

Clinical implications

LUS is a highly versatile technique.[34] It is inexpensive and can be performed at the patient's bedside with a hand-held device.[15,35] Feasibility is very high, close to 100%; only severe obesity, which is rare in SSc, can pose some issues during the scanning, whereas up-to-date skin thickening has never been reported as a main limitation for LUS. Moreover, the learning curve is short,[35,36] and the examination is nonionizing; the time needed that is reported in the literature is variable between <10 minutes and an average of 23 minutes.[8,12] In our experience, a whole LUS examination, assessment of the number of B-lines on both the anterolateral and posterior chest, requires an average time of 10 minutes for nonnovice sonographers, with a shorter time duration in patients without or with a few B-lines (in whom the time needed to quantify B-lines is reduced) and a longer duration in patients with more numerous B-lines. For all these reasons, LUS could allow a tighter follow up compared with what is feasible with chest radiography and HRCT. LUS can also be easily coupled with standard echocardiography to assess cardiac morphology and function and to estimate pulmonary hemodynamics. Clearly, LUS cannot replace HRCT, which provides a detailed definition of the pulmonary parenchyma; our study was not aimed to compare LUS with HRCT, which is an irreplaceable imaging tool for the management of ILD. Moreover, LUS is able to detect peripheral abnormalities but may miss suspicious nodules or other parenchymal modifications that are located in proximity of the hilum. Therefore, LUS may be considered a more appealing screening tool for ILD in the early phases of SSc and may help with the establishment of the appropriate timing of HRCT.

We used a quite comprehensive scheme that included scanning sites on the anterolateral and posterior chest, as previously described. It would be desirable to have a simplified scheme with similar accuracy; more limited LUS scanning schemes have been proposed for the diagnosis of SSc-ILD,[8,12,13] but no data are available on their prognostic role. However, our data show that the assessment limited to the posterior chest alone, which is less time-consuming than studying the anterolateral and posterior chest, is also associated with events.

Our data show that B-lines not only have a role in the screening of SSc-ILD but also are associated with outcome in these patients. Presence of ≥5 posterior B-lines predicts ILD worsening in the following years. This suggests that LUS is an independent predictor of events, with additional value to anti-topoisomerase I positivity, a well-known prognostic marker in SSc.[37] The prognostic value of posterior B-lines is also confirmed in those patients who already have received a diagnosis of ILD at the time of B-lines evaluation. We selected a cutoff value of <5 posterior B-lines on the receiver operating characteristic curve to prioritize sensitivity and negative predictive value because, in our perspective, this would translate to a higher clinical impact in patients with SSc, compared with prioritizing specificity. In our study population, this cutoff would have classified 102 patients (26%) as carrying a very low risk to experience worsening pulmonary involvement in the following months, with a very low rate of false negative (4%). On the other hand, in patients with ≥5 posterior B-lines, it is not possible to draw specific conclusions, because these patients could either show further deterioration (16% of cases) or not (84%). Obviously, these results depend on the prevalence of events of our population; therefore, the cutoff cannot be generalized to different populations with different prevalence of events.

Limitations

Some study limitations should be highlighted. HRCT was performed in high-volume centers with expertise in chest imaging, but there was no core-laboratory centralized reading or semiquantitative scoring evaluations for all HRCT; a core-laboratory reading was done in a subgroup of 69 patients with similar results at multivariable analysis compared with the overall population. LUS examinations were performed by expert physicians; perhaps the same good accuracy would not be achieved by less expert readers, although the B-lines learning curve is quite short.[35,36] B-lines are a

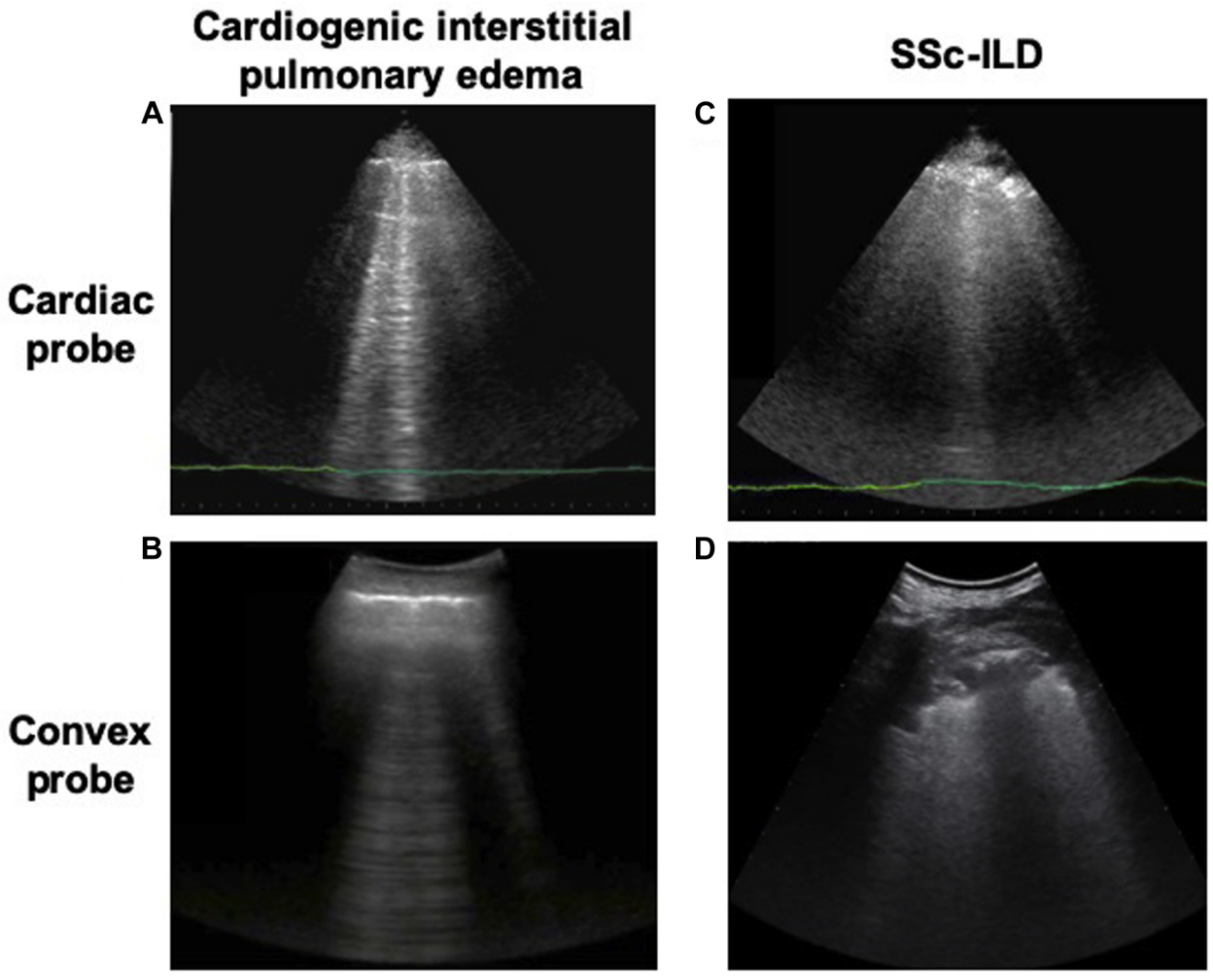

Figure 4 – *A-B, Multiple B-lines in a patient with cardiogenic interstitial pulmonary edema: A, cardiac probe; B, convex probe. Multiple B-lines in a patient with systemic sclerosis-interstitial lung disease: C, cardiac probe; D, convex probe. SSc-ILD = systemic sclerosis-interstitial lung disease.*

nonspecific sonographic sign of partial pulmonary deaeration, so they are also visible in cardiogenic pulmonary edema. However, the differential diagnosis is usually clear from the patient's history and/or from dynamic serial evaluation, because only cardiogenic B-lines significantly decrease after diuretic therapy; moreover, the appearance of the pleural line in cardiogenic pulmonary edema is quite different from the pleural line in ILD (Fig 4). In our population, all patients had at least an echocardiogram performed very close to the LUS evaluation, and no patient had a significant left ventricular involvement to justify presence of "cardiogenic" instead of "pneumogenic" B-lines. The LUS examination was done at different timing among the population, because patients were studied consecutively as soon as LUS was available, which corresponded to different moments in the course of the disease in different patients.

No standardized criteria are available to define ILD worsening; therefore, we preferred an integrated clinical-instrumental evaluation to assign the event, compared with a purely numeric parameter, that was linked only to a decrease in FVC and DLCO.

LUS B-lines depict modifications of the lung parenchyma in SSc-ILD and are an independent predictor of further pulmonary deterioration, whose value is additional to the prognostic stratification of anti-topoisomerase I antibody positivity. In the near future LUS might become part of the diagnostic and prognostic armamentarium in patients with SSc, which would allow a more sustainable and user-friendly approach to this very fragile population.

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