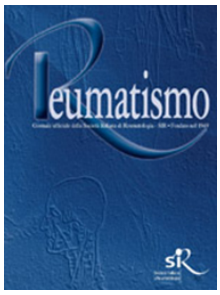

Reumatismo - The Italian Journal of Rheumatology

https://www.reumatismo.org/reuma

eISSN 2239-7132

Please cite this article as:

Tanten Zabaleta R, Marín J, Zacariaz Hereter JB, et al. **Clinical utility of lung ultrasound for the detection of interstitial lung disease in patients with rheumatoid arthritis**. *Reumatismo* doi: 10.4081/reumatismo.2024.1651

Submitted: 13-09-2023
Accepted: 23-05-2024

Clinical utility of lung ultrasound for the detection of interstitial lung disease in patients with rheumatoid arthritis

R. Tanten Zabaleta[1], J. Marín[1], J.B. Zacariaz Hereter[1], J. Maritano[2], M. Fullana[2], N. Alvarado[1], E.R. Soriano[1], J.E. Rosa[1]

[1]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, Argentina; [2]Pneumology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, Argentina

Corresponding author: Romina Tanten Zabaleta, Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, 4190 Teniente General Juan Domingo Perón; Zip: 1199, Ciudad Autónoma de Buenos Aires, Argentina.
Tel.: +54 (011) 49590200
E-mail: romina.tanten@hospitalitaliano.org.ar

Key words: interstitial lung disease, rheumatoid arthritis, lung ultrasound, high-resolution computed tomography.

Contributions: all the authors made a substantial intellectual contribution, read and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: all procedures were performed by the ethical standards of the Ethics Committee for Research Protocols (CEPI) of the Hospital Italiano de Buenos Aires (protocol number: 5925, approval date: 11/2/21), and the 1964 Declaration of Helsinki and its subsequent amendments, or comparable ethical standards.

Informed consent: all patients provided written informed consent.

Funding: this work was supported by a grant from the Pan-American League of Rheumatology Associations (PANLAR).

Availability of data and materials: data and materials are available from the corresponding author upon request.

Summary

Objective. To establish the diagnostic value of lung ultrasound (LUS) in patients with rheumatoid arthritis (RA) for the detection of interstitial lung disease (ILD).

Methods. A cross-sectional study was performed. Consecutive patients with RA (American College of Rheumatology/European League Against Rheumatism 2010 criteria) who had a chest high-resolution computed tomography (HRCT) performed within 12 months before inclusion, regardless of symptomatology, were included. Demographic, clinical, laboratory, and pharmacological data were recorded. Each patient underwent a LUS with assessment of B-lines (BL) and pleural irregularities (PI). HRCT was considered the gold standard for the confirmatory diagnosis of ILD. Receiver operating characteristic (ROC) curves were calculated to test the ability of LUS findings (BL and PI) in discriminating patients with ILD.

Results. A total of 104 RA patients were included, of which 21.8% had ILD. Patients with ILD had more BL (median 26 *versus* 1, $p<0.001$) and PI (median 16 *versus* 5, $p<0.001$) than patients without ILD. The diagnostic accuracy in ROC curves was: area under the curve (AUC) 0.88 and 95% confidence interval (CI) 0.78-0.93 for BL and AUC 0.82 and 95% CI 0.74-0.89 for PI. The best cut-off points for (ILD detection) discriminating the presence of significant interstitial lung abnormalities were 8 BL and 7 PI.

Conclusions. The presence of 8 BL and/or 7 PI in the LUS showed an adequate cut-off value for discriminating the presence of significant interstitial lung abnormalities, evocative of ILD.

Introduction

Interstitial lung disease (ILD) is one of the most common extra-articular manifestations of rheumatoid arthritis (RA). The risk of developing clinically important ILD in RA patients is about 7.7% (1). It is estimated that median survival for the total RA-ILD population ranges from 2 to 14 years (2). However, there are significant discrepancies in the estimation of the prevalence of ILD associated with RA, and this depends on the population studied and the methods applied for its diagnosis.

High-resolution computed tomography (HRCT) has been accepted as the standard imaging method for diagnosing and monitoring ILD in patients with rheumatic diseases, demonstrating a close correlation with open lung biopsy (3), and good sensitivity for the detection of ILD in patients with connective tissue diseases (3, 4). However, the use of HRCT as a screening method has disadvantages, such as its high cost and exposure to ionizing radiation.

Lung ultrasound (LUS) is a non-invasive, low-cost, safe, non-ionizing, and easily performed diagnostic tool. Currently, several studies demonstrate its sensitivity and diagnostic use in the detection of ILD in patients with RA and other connective tissue diseases (1, 5, 6).

LUS plays an important role in the detection of pulmonary diseases based on the identification and quantification of B-lines (BL), which are comet-like artifacts generated by the reflection of the ultrasound beam from the thickened subpleural interlobar septa, identifiable between the intercostal spaces (7). There are different scoring systems to assess lung involvement, but several of them can be time-consuming for the physician and the patient in routine daily clinical practice and are also impractical in follow-up (1). A simplified scoring system has shown a good correlation with the more extensive system and has been validated with HRCT as the gold standard method (8). In addition to the detection of BL by LUS, pleural involvement is also adequately described, which manifests itself with pleural irregularities (PI) clearly identifiable in the ultrasound study and defined as the loss of regularity of the pleura, which may be associated with an increase in thickness (either focal, diffuse, linear, or nodular) (9, 10).

However, few studies have correlated both LUS characteristics with HRCT in patients with RA (5, 11). The present study aimed to investigate the diagnostic value of LUS in ILD for RA patients, using chest HRCT as the gold standard.

Materials and Methods

Patients

We performed a cross-sectional study at the Hospital Italiano de Buenos Aires in Argentina. Consecutive outpatients fulfilling RA 2010 American College of Rheumatology/European League Against Rheumatism classification criteria (12) who had at least one chest HRCT in the 12 months prior to the inclusion visit, regardless of symptomatology, were included between January 2021 and August 2022.

We excluded patients with other chronic inflammatory joint diseases (psoriatic arthritis, crystalline arthritis, spondylarthritis, systemic lupus erythematosus, Sjögren's syndrome, mixed connective tissue disease, and overlap syndromes), as well as those who exhibited signs of respiratory infections within the month preceding the HRCT and LUS dates, evidence of moderate to severe pleural effusion, signs of heart failure, and moderate/severe heart valve disease and/or severe obstructive pulmonary disease.

The electronic medical records of each patient included were manually reviewed and demographic, clinical, laboratory, and treatment data were recorded.

Interstitial lung disease and chest high-resolution computed interpretation

For the diagnosis of ILD, HRCT was considered the gold standard. All HCRTs were assessed by an ILD-expert pulmonologist, who was blinded to the clinical symptoms and LUS findings. When interstitial involvement was found, its extension and pattern were determined. The extent of involvement was visually defined at the discretion of the ILD expert pulmonologist. The extension was defined as the percentage of lung parenchyma with interstitial involvement. Considering previous

reports, ILD was defined as present when an extension ≥10% of lung involvement was found irrespective of the pattern (13). Different radiological features were assessed (ground-glass or reticular abnormalities, traction bronchiectasis, honeycombing, and non-emphysematous cysts) to classify the ILD according to the following HRCT patterns: usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), organizing pneumonia (OP), interstitial lymphoid pneumonia (ILP), and indeterminate. Other tomographic findings, such as location, were also assessed (subpleural, peri broncho vascular, and random). For the comparison with other diagnostic methods, patients were divided into two groups according to HRCT results: i) normal (HRCT without interstitial involvement); ii) ILD (HRCT with interstitial involvement with an extension ≥10%).

Lung ultrasound examination

LUS examination was performed by two ultrasonography-trained rheumatologists, blinded to HRCT results and clinical data, using an Esaote Mylab class C machine equipped with a multi-frequency (MHz) linear transducer (8-18 MHz) and a curved transducer (4-8 MHz). LUS was performed through transverse scans of intercostal spaces, using a simplified published anatomical score, including 14 intercostal spaces (ICS) grouped in 2 chest wall regions (8).

Description of the anatomical sites:

- anterior region (bilateral):
  - 2^{nd} ICS, para-sternal line
  - 4^{th} ICS, mid-clavear line
  - 4^{th} ICS, anterior axillary line
  - 4^{th} ICS, mid-axillary line
- posterior region (bilateral):
  - 8^{th} ICS, paravertebral line
  - 8^{th} ICS, sub-scapular line
  - 8^{th} ICS, posterior axillary line

PI and BL were assessed at each space. PI was defined as the loss of regularity, that may be associated with an increase in thickness (either focal, diffuse, linear, or nodular) (10). BL was defined as vertical artifacts reminiscent of comet tails arising from the pleural line and projecting downwards (7). BL and PI evaluation included quantifying the total number of BL and of PI.

Prior to the study, an evaluation of the degree of agreement among the participating sonographers was carried out. BL (quantifying their total number) and PI (quantifying their total number) were evaluated through an exercise of reading images in videos.

Inter-observer reliability for the definition of BL was excellent [intraclass correlation coefficient (ICC)=0.97] and moderate for PI (ICC=0.78). The intra-observer correlation coefficient for BL was (ICC=0.76), and the intra-observer agreement percentage for PI was (ICC=0.79).

Statistical analysis

Descriptive and analytical statistics were performed. Continuous variables were reported as means and standard deviations or median and interquartile ranges (IQR) for non-normally distributed data and compared with the Student *t*-test or Mann-Whitney, respectively. Bonferroni adjustment was used for multiple comparisons. Categorical variables were reported as proportions [with their corresponding 95% confidence Interval (CI)] and compared using the χ^2 or Fisher test for a binary outcome. Cut-off points were calculated for BL and PI using receiver operating characteristic (ROC) curves. Sensitivity, specificity, predictive values, and likelihood ratios were calculated for each cut-off point.

The sample size calculation was performed following the proposal of Carley *et al.* (14). For sensitivity the lung HRCT was considered as the gold standard. For an expected sensitivity of 70%, with a hemi-amplitude of 15% and a prevalence of pulmonary involvement of 33%, 109 patients with RA are required.

Data were analyzed with the STATA v.12 programs (Stata Corp, College Station, TX, USA).

Ethical considerations

All procedures were performed by the ethical standards of the Ethics Committee for Research Protocols (CEPI) of the Hospital Italiano de Buenos Aires (protocol number: 5925, approval date: 11/2/21), the 1964 Declaration of Helsinki and its subsequent amendments, or comparable ethical standards. All patients provided written informed consent.

Results

A total of 104 patients with RA were included; 82.7% (95% CI 74.0-89.4) were women with a median age at RA diagnosis of 57.5 years (IQR 47.3-67.2) and a median disease duration of 8.7 years (IQR 3.3-15.8). Baseline characteristics are shown in Table 1, according to the presence or not of ILD.

96.2% of patients (95% CI 90.5-98.9) were seropositive for rheumatoid factor and/or anti-citrullinated protein antibodies. The median disease activity score-28 for rheumatoid arthritis with erythrocyte sedimentation rate (ESR) was 3.19 (IQR 2.6-4.6), at the moment of LUS. Fifty-six (53.8%) patients were on conventional synthetic disease-modifying antirheumatic drugs (DMARDs) only, 64.3% were in monotherapy with methotrexate, and 46.2% were under biological/targeted synthetic DMARDs treatment at inclusion. Table 1 shows the different treatment combinations. Twenty-one patients (21.8%) had ILD according to the chest HRCT definition (HRCT extension ≥10% of lung involvement). They were older at the time of RA diagnosis (64 *versus* 54 years old, p=0.002) and had higher ESR and C-reactive protein (48 *versus* 29 mm/h, p=0.02, and 5.9 *versus* 3 g/L; p=0.002, respectively) than patients without ILD.

Patients with ILD were classified on the following HRCT patterns: i) indeterminate, 9 (42.9%); ii) NSIP, 6 (28.6%); iii) UIP, 4 (19%); iv) others, 2 (9.5%) (OP, ILP) (Table 2).

Regarding LUS examination, patients with ILD had significantly more BL (median 26 *versus* 1, p<0.001) and PI (median 16 *versus* 5, p<0.001) than patients without ILD (Figures 1 and 2). Seventy-one % of the patients underwent LUS within 3 months after performing the HRCT, median time between HRCT and LUS was 1.42 months (IQR 0.5-7.36) in patients without ILD, and 2.67 months (IQR 0.92-9.25) in patients with ILD, without a statistically significant difference (p=0.34). The diagnostic accuracy of ROC curves was: area under the curve (AUC) 0.88 (95% CI 0.78-0.93) for BL and AUC 0.82 (95% CI 0.74-0.89) for PI. The best cut-off point for ILD detection was 8 BL and 7 PI (Figure 3). The diagnostic performance of LUS for the detection of ILD is shown in Table 3.

Discussion

The present study showed high sensitivity and specificity of LUS for the detection of ILD in patients with RA.

First of all, and in line with previous studies, our study confirms that the findings of LUS for BL and PI allow discrimination of significant interstitial lung abnormalities. We found that patients with ILD had significantly more BL and PI than patients without ILD. Our cut-off value was 8 BL and 7 PI, with a sensitivity greater than 80% and a specificity close to 80% in agreement with other studies, in which a cut-off value of 9 and 10 BL was found, respectively (1, 15). A possible explanation for this subtle difference could be that our patients had less interstitial involvement on HRCT, which could explain the lower number of BL found in our study.

On the other hand, in our study, we evaluated PI as loss of regularity, which may be associated with an increase in thickness (either focal, diffuse, linear, or nodular) (10). It was defined as present or absent in the evaluated intercostal spaces. Our results demonstrate a high correlation between these findings (BL and PI), allowing for reliable discrimination of patients with significant interstitial lung abnormalities. Similarly, in the study conducted by Pinal-Fernandez *et al*. (one of the first studies to evaluate PI as ultrasound findings), PI was defined as the loss of the normal hyperechoic linear pleural contour and classified semi-quantitatively as mild, moderate, and severe, showing high specificity as a sign in LUS of ILD (9). Subsequently, other studies have corroborated these results (5, 11).

In other published papers, the percentage of patients with reported ILD was higher, between 33 and 34% (1, 15). This difference can be explained by the selection of patients, since in these groups, they

included only those with suspicion and/or previous diagnosis of ILD. Our study involved consecutive RA patients with an HRCT within the previous year, regardless of the symptoms and previous diagnosis of ILD.

Regarding the HCRT patterns, we found the most frequent to be indeterminate (42.9%), followed by NSIP (28.6%) and UIP (19%). This is in disagreement with what is described in the literature, where the most prevalent pattern in RA is UIP (3, 16). This difference may also be attributed to our selection since we took consecutive patients, many of whom had no history of ILD or symptoms. Our patients may have had earlier ILD (preclinical), where it is not possible to define a subtype of ILD.

Some limitations should be mentioned. One is that the study was carried out in a single center, thus limiting possible external validation and generalization to the rest of the population with ILD. Another limitation is that we selected patients because they had an HRCT in the previous 12 months, but we did not record if they were symptomatic, as we have mentioned. Also, the HRCT and LUS were not performed simultaneously with each other, but the 3-month interval is close. In the majority of cases, both studies were performed within a few months, a period in which no major changes are expected and reflecting usual clinical practice. On the other hand, the strengths of this study are the combined work of both rheumatologists and lung disease specialists and the number of patients involved; moreover, it is one of the few evaluating the sensitivity and specificity of both BL and PI.

According to these results, we can say that LUS has a high negative predictive value. Therefore, we consider that LUS could avoid performing HRCT in patients who have had a normal LUS or a BL and PI count below the cut-off point.

Conclusions

The presence of 8 BL and/or 7 PI in the LUS showed adequate diagnostic performance for ILD, with a good negative prognostic value. Our study shows that LUS is a potential screening method to detect ILD in patients with RA since it is an accessible, non-invasive, and easy-to-perform method. A normal LUS or with values below the cut-off may avoid the need, cost, and toxicity of unnecessary HRCT.

References

1. Cogliati C, Antivalle M, Torzillo D, Birocchi S, Norsa A, Bianco R, et al. Standard and pocket-size lung ultrasound devices can detect interstitial lung disease in rheumatoid arthritis patients. Rheumatology 2014; 53: 1497-503.
2. Farquhar HJ, Beckert N, Beckert L, Edwards AL, Matteson EL, Frampton C, et al. Survival of adults with rheumatoid arthritis associated interstitial lung disease - a systematic review and meta-analysis. Semin Arthritis Rheum 2023; 60: 152187.
3. Cavagna L, Monti S, Grosso V, Boffini N, Scorletti E, Crepaldi G, et al. The multifaceted aspects of interstitial lung disease in rheumatoid arthritis. Biomed Res Int 2013.
4. Kadura S, Raghu G. Rheumatoid arthritis-interstitial lung disease: manifestations and current concepts in pathogenesis and management. Eur Respir Rev 2021; 30: 210011.
5. Moazedi-Fuerst FC, Kielhauser SM, Scheidl S, Tripolt NJ, Lutfi A, Yazdani-Biuki B, et al. Ultrasound screening for interstitial lung disease in rheumatoid arthritis. Clin Exp Rheumatol 2014; 32: 199-203.
6. Gutierrez M, Ruta S, Clavijo-Cornejo D, Fuentes-Moreno G, Reyes-Long S, Bertolazzi C. The emerging role of ultrasound in detecting interstitial lung disease in patients with rheumatoid arthritis. Joint Bone Spine 2022; 89: 105407.
7. Gutierrez M, Tardella M, Rodriguez L, Mendoza J, Clavijo-Cornejo D, García A, et al. Ultrasound as a potential tool for the assessment of interstitial lung disease in rheumatic patients. Where are we now? Radiol Med 2019; 124: 989-99.
8. Gutierrez M, Salaffi F, Carotti M, Tardella M, Pineda C, Bertolazzi C, et al. Utility of a simplified ultrasound assessment to assess interstitial pulmonary fibrosis in connective tissue disorders - preliminary results. Arthritis Res Ther 2011; 13: R134.
9. Pinal-Fernandez I, Pallisa-Nuñez E, Selva-O'Callaghan A, Castella-Fierro E, Simeon-Aznar CP, Fonollosa-Pla V, et al. Pleural irregularity, a new ultrasound sign for the study of interstitial lung disease in systemic sclerosis and antisynthetase syndrome. Clin Exp Rheumatol 2015; 33: S136-41.
10. Delle Sedie A, Terslev L, Bruyn GAW, Cazenave T, Chrysidis S, Diaz M, et al. Standardization of interstitial lung disease assessment by ultrasound: results from a Delphi process and web-reliability exercise by the OMERACT ultrasound working group. Semin Arthritis Rheum 2024; 65: 152406.
11. Mena-Vázquez N, Jimenez-Núñez FG, Godoy-Navarrete FJ, Manrique-Arija S, Aguilar-Hurtado MC, Romero-Barco CM, et al. Utility of pulmonary ultrasound to identify interstitial lung disease in patients with rheumatoid arthritis. Clin Rheumatl 2021; 40: 2377-85.
12. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010; 69: 1580-8.
13. Hatabu H, Hunninghake GM, Richeldi L, Brown KK, Wells AU, Remy-Jardin M, et al. Interstitial lung abnormalities detected incidentally on CT: a position paper from the Fleischner Society. Lancet Respir Med 2020; 8: 726-37.
14. Carley S, Dosman S, Jones SR, Harrison M. Simple nomograms to calculate sample size in diagnostic studies. Emerg Med J 2005; 22: 180-1.
15. Di Carlo M, Tardella M, Filippucci E, Carotti M, Salaffi F, Carlo M Di, et al. Lung ultrasound in patients with rheumatoid arthritis: definition of significant interstitial lung disease. Clin Exp Rheumatol 2022; 40: 495-500.
16. Joy GM, Arbiv OA, Wong CK, Lok SD, Adderley NA, Dobosz KM, et al. Prevalence, imaging patterns and risk factors of interstitial lung disease in connective tissue disease: a systematic review and meta-analysis. Eur Respir Rev 2023; 32: 220210.

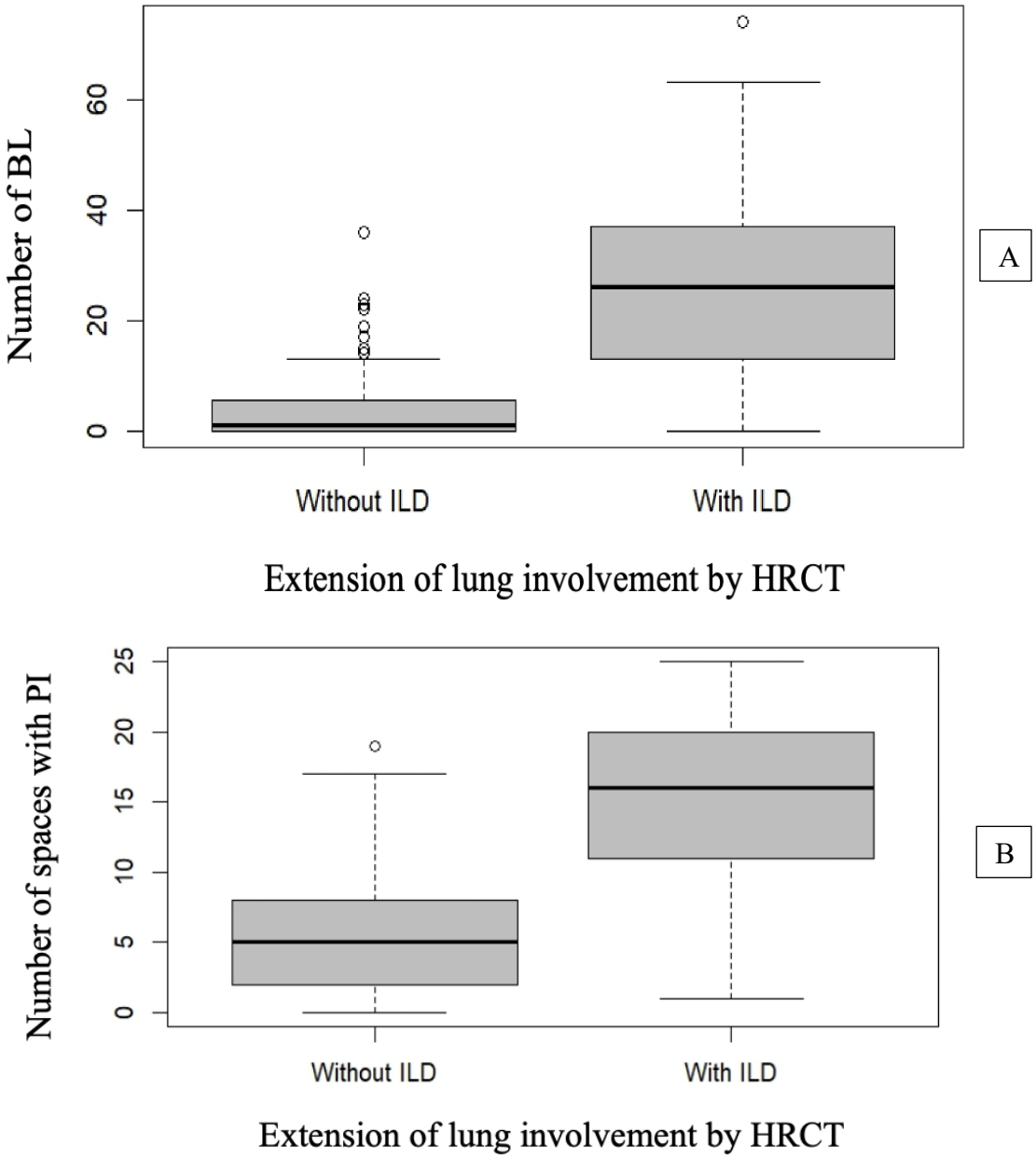

Figure 1. A) Number of B-lines (BL) according to the extension of pulmonary interstitial involvement measured by high-resolution computed tomography (HRCT); B) number of spaces with pleural irregularities (PI) according to the extension of pulmonary interstitial involvement measured by HRCT. ILD, interstitial lung disease.

a) B line b) Irregular pleural line

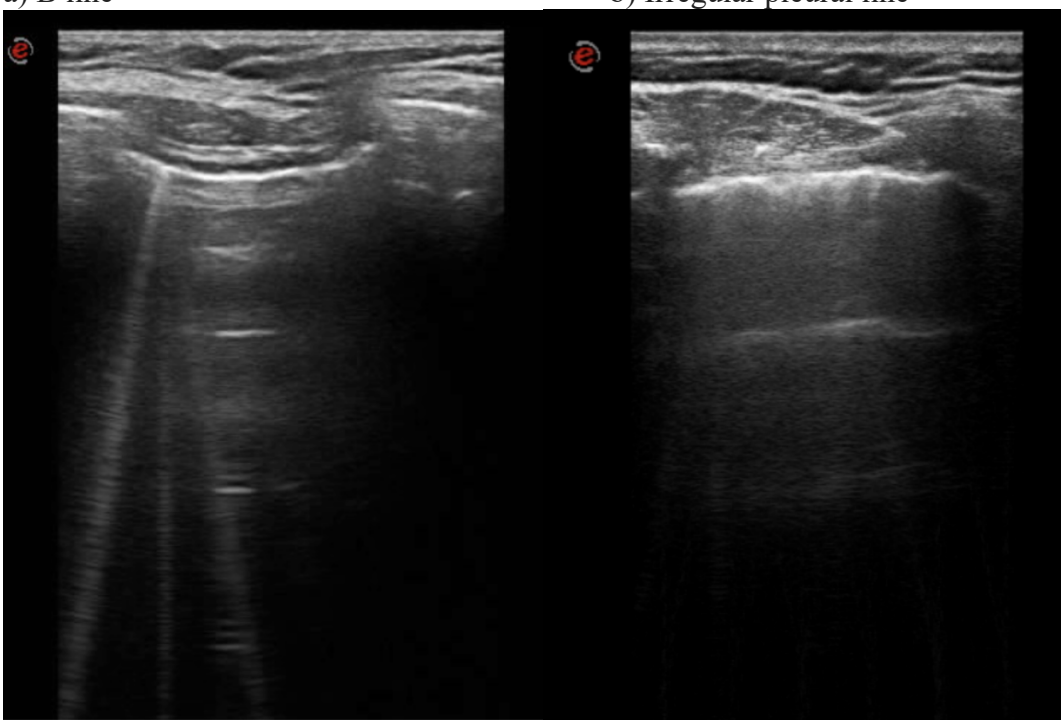

Figure 2. Lung ultrasound showing B-lines and pleural irregularities.

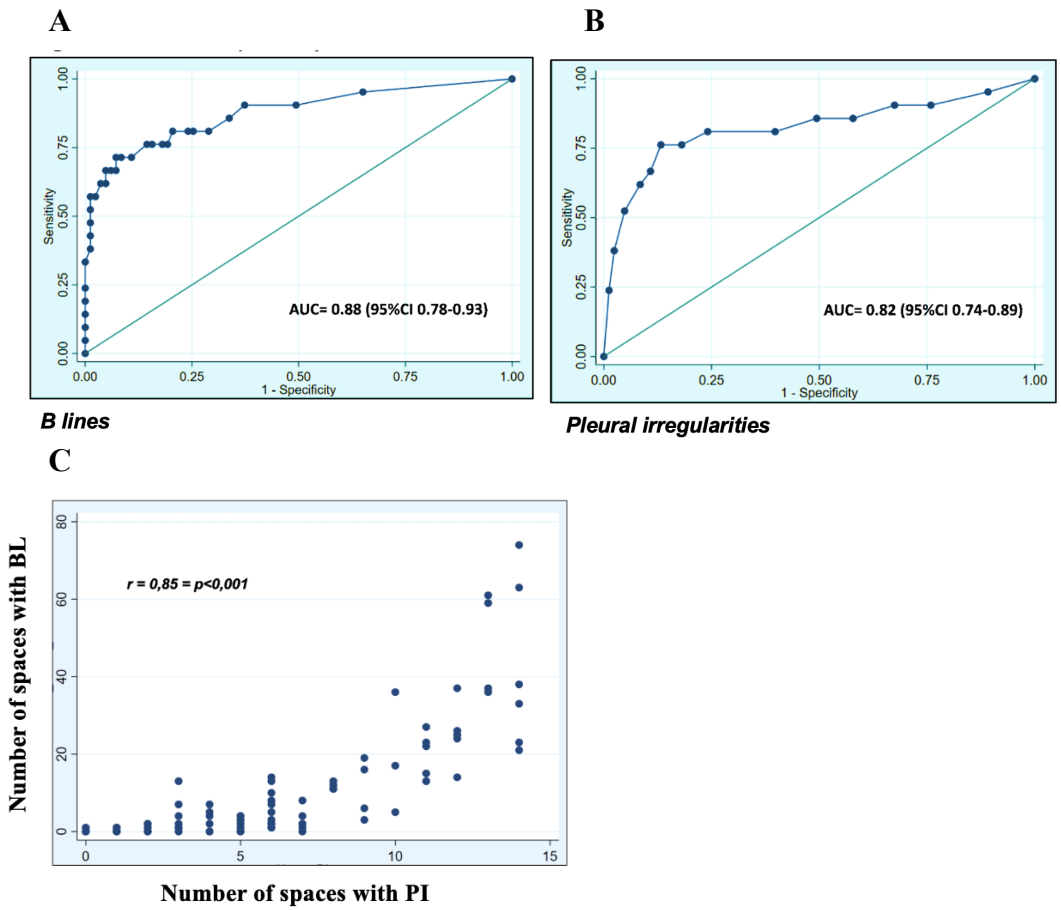

Figure 3. A) Diagnostic accuracy of B-lines (BL) in lung ultrasound (LUS) for interstitial lung disease (ILD) detection: receiver operating characteristic (ROC) curve and estimation of the area under the curve (AUC); B) diagnostic accuracy of pleural irregularities in LUS for ILD detection: ROC curve and estimation of AUC; C) correlation between the total number of BL and the number of spaces with PI.

Table 1. Clinical and demographic characteristics.

	Without interstitial lung disease (n=83)	With interstitial lung disease (n=21)	p
Female sex, % (95% CI)	85.5 (75.7-92.0)	71.4 (47.7-87.8)	0.19
Age at diagnosis of RA (years), mean (SD)	55 (13.4)	64 (14.5)	0.004
Follow-up time (years), mean (SD)	12.5 (5.7)	14 (6.2)	0.27
Smoking status, % (95%CI)			0.35
Never	48.2 (37.2-59.4)	33.3 (15.5-56.9)	
Former smoker	41.0 (30.5-52.3)	47.6 (26.4-69.7)	
Current smoker	10.8 (5.4-20.1)	19.0 (6.3-42.6)	
History of tuberculosis, % (95% CI)	3.6 (0.9-10.9)	0	1
PPD positive (>5 mm) ever, % (95% CI)	8.6 (3.2-19.7)	5.9 (0.3-30.8)	1
Rheumatoid factor positive, % (95% CI)	83.1 (73.0-90.1)	95.2 (74.1-99.7)	0.29
ACPA positive, % (95% CI)	89.2 (78.0-94.6)	95.2 (74.1-99-7)	0.35
Highest ACPA title recorded, median (IQR)	200 (200-500)	340 (200-1690)	0.41
Erosive disease, % (95% CI)	39.8 (29.4-51.1)	33.3 (15.5-56.9)	0.59
DAS28, mean (SD)	3.45 (1.32)	3.59 (1.2)	0.66
CDAI, median (IQR)	5 (2-12)	4 (2-13)	0.84
Erythrocyte sedimentation rate, median (IQR)	29 (21-48)	48 (28-67)	0.02
Bio-naive patients, % (95% CI)	51.8 (40.6-62.8)	61.9 (38.7-81.1)	0.47
CRP (mg/L), median (IQR)	3 (1.3-7.3)	5.9 (3.1-18.5)	0.02
Use of csDMARDs (bio-naïve patients), % (95% CI)			0.87
Methotrexate monotherapy	32.5 (22.9-43.8)	42.8 (22.6-65.6)	
Other csDMARD monotherapy	2.4 (0.4-9.2)	4.8 (0.2-25.9)	
Methotrexate combined with other csDMARD	15.7 (8.9-25.7)	9.5 (1.7-31.8)	
Other csDMARDs combinations	1.2 (0.06-7.5)	4.8 (0.2-25.9)	
Use of b/tsDMARDs at inclusion, % (95% CI)	48.2 (37.2-59.4)	38.1 (18.9-61.3)	0.56
Monotherapy	19.3 (11.7-29.7)	9.5 (1.7-31.8)	
Combined with csDMARDs	28.9 (19.7-40.1)	28.6 (12.2-52.3)	
Number of biologics received, median (IQR)	1 (1-2)	1 (1-2)	0.86
Type of b/tsDMARDs at inclusion, % (95%CI)			0.36
TNF inhibitors	42.5 (27.0-59.1)	25.0% (3.9-65.1)	
Abatacept	5.0 (0.6-16.9)	0	
Rituximab	2.5 (0.0-13.2)	0	
Tocilizumab	5.0 (0.6-16.9)	25.0% (3.2-65.9)	
Jak inhibitors	45.0 (29.2-61.5)	50.0% (15.7-84.3)	

CI, confidence interval; RA, rheumatoid arthritis; SD, standard deviation; PPD, purified protein derivate ACPA, anti-citrullinated protein antibodies; IQR, interquartile range; DAS28, Disease Activity Score in 28 joints; CDAI, clinical disease activity index; CRP, C-reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; b/tsDMARDs, biological/targeted synthetic disease-modifying antirheumatic drugs.

Table 2. Characteristics of patients with tomographic interstitial abnormalities (any extension).

Tomographic characteristics	Interstitial involvement ≥10% (n=21)
Pattern, n (%, 95% CI):	
UIP	19.0 (5.4-41.9)
NSIP	28.6 (11.3-52.2)
OP	4.7 (0.1-23.8)
ILP	4,7 (0.1-23.8)
Indeterminate	42.9 (21.8-65.9)
Predominant location of the alterations, n (%, 95% CI):	
Subpleural	95.2 (76.2-99.9)
Peribronchovascular	0
Random	4.8 (0.1-23.8)
Extent of subpleural involvement, median (IQR)	30 (20-60)

CI, confidence interval; UIP, usual interstitial pneumonia; NSIP, non-specific interstitial pneumonia; OP, organizing pneumonia; ILP, interstitial lymphoid pneumonia.

Table 3. Diagnostic performance of lung ultrasound for the detection of interstitial lung disease.

Test	Sensitivity (%)	Specificity (%)	+ LR	- LR	Positive prognostic value	Negative prognostic value	AUC
BL (≥8)	80.95	79.52	3.95	0.24	50	94.30	0.88 (0.78-0.93)
PI (≥7 spaces)	80.95	75.90	3.36	0.25	45.95	94.03	0.82 (0.74-0.89)

BL, B-lines; PI, pleural irregularities; +LR, positive likelihood ratio; -LR, negative likelihood ratio; AUC, area under the curve.