



Response to “Subclinical interstitial lung disease in patients with systemic sclerosis. A pilot study on the role of ultrasound”*

Respuesta a «Intersticiopatía pulmonar subclínica en pacientes con esclerosis sistémica. Estudio piloto sobre el papel del ultrasonido»

Dear Editor,

We have conscientiously read the study by Reyes-Long et al.¹, recently published in REUMATOLOGÍA CLÍNICA, which analyses the role of the pulmonary ultrasound (EchoPulm) for the screening of interstitial lung diseases (ILD) in patients with systemic sclerosis (SS). The study design is meticulous, with blinding of the different evaluators and a narrow time window between the (simultaneous) clinical-ultrasound assessments and the high-resolution computed tomography (HRCT) (7 days later).

The selection of patients with no clinical respiratory manifestations and a mean duration of 4 years provides a clinical context closer to the early diagnosis of ILD than most previous studies that included more advanced forms of SS². The finding of subclinical ILD in 41.2% of patients is in line with the previous results of Barskova et al.³, whose population included 58% of very early SS, which showed evidence of ILD by HRCT in 41%, the concordance between EchoPulm and HRCT being 83%. However, we have detected a discordance regarding the percentage of subclinical ILD in this study by Reyes-Long et al.¹ that we consider relevant to correct. In the text it is described as present in 28 of the 68 patients included (41.2%), but Table 1 shows 40 patients with a pathological ultrasound scan (58.83%).

Contributions on the comparative validity of EchoPulm with respect to pulmonary auscultation, chest X-ray, respiratory function tests and HRCT support its usefulness as a screening tool for ILD. In support of this role, a negative predictive value of EchoPulm of up to 100% has been described in previous studies², so it would be very useful to have the additional negative predictive value of EchoPulm in this SS population without respiratory symptoms.

The significant association between EchoPulm and anticentromere antibodies is unexpected in light of the clinical profiles associated with these antibodies in multicentre studies⁴. We wondered whether it might be related to the strikingly high rate of double positivity of antitopoisomerase ($n=63$) and anticentromere ($n=38$) antibodies estimated in this population (48.5%–55.9%) based on the data in Table 1. This double positivity has been described as an exceptional phenotype present in .3%–.6% of SS patients and whose clinical features are not clearly different from those of patients with only antitopoisomerase antibodies^{5,6}.

With respect to the ultrasound parameters used, we are missing details on relevant settings such as harmonics, gain or time gain compensation, the number of foci or their position, due to their potential impact on the visualisation of the B lines^{7,8}. We are also surprised by the frequency range selected for the study of the B lines; although these are the recommended frequencies for the study of the pleural line, it has been described that increasing the frequency from 6 to 11 MHz can attenuate the B⁷ lines, which could be a limiting factor in the study.

The limitations mentioned by the authors and the suggestions previously mentioned do not detract from the value of this great work, which advances knowledge on the usefulness of EchoPulm

monography for the early diagnosis of ILD in SS. We share the authors' interest in this safe and accessible technique and its consideration as a promising and complementary screening tool for ILD in light of the evidence in the literature⁹. The validation of EcoPulm has not yet been completed, but preliminary results from multicentre longitudinal studies are very promising and bring us closer to its implementation in clinical practice¹⁰.

Financing

This study did not receive any type of financing.

References

1. Reyes-Long S, Gutierrez M, Clavijo-Cornejo D, Alfaro-Rodríguez A, González-Sámano K, Cortes-Altamirano JL, et al. Intersticiopatía pulmonar subclínica en pacientes con esclerosis sistémica. Estudio piloto sobre el papel del ultrasonido. Reumatol Clin. 2021;17:144–9, <http://dx.doi.org/10.1016/j.reuma.2019.05.004>.
2. Vicente-Rabaneda EF, Bong D, Castañeda S, Möller I. Use of ultrasound to diagnose and monitor interstitial lung disease in rheumatic diseases. Clin Rheumatol. 2021, in press.
3. Barskova T, Gargani L, Guiducci S, Randone SB, Bruni C, Carnesecchi G, et al. Lung ultrasound for the screening of interstitial lung disease in very early systemic sclerosis. Ann Rheum Dis. 2013;72:390–5, <http://dx.doi.org/10.1136/annrheumdis-2011-201072>.
4. Walker UA, Tyndall A, Czirják L, Denton C, Farge-Bancel D, Kowal-Bielecka O, et al. Clinical risk assessment of organ manifestations in systemic sclerosis: a report from the EULAR Scleroderma Trials And Research group database. Ann Rheum Dis. 2007;66:754–63, <http://dx.doi.org/10.1136/ard.2006.062901>.
5. Heijnen IAFM, Foocharoen C, Bannert B, Carreira PE, Caporali R, Smith V, et al. Clinical significance of coexisting antitopoisomerase I and anticentromere antibodies in patients with systemic sclerosis: a EUSTAR group-based study. Clin Exp Rheumatol. 2013;31:96–102.
6. Alkema W, Koenen H, Kersten BE, Kaffa C, Dinnissen JWB, Damoiseaux JGMC, et al. Autoantibody profiles in systemic sclerosis: a comparison of diagnostic tests. Autoimmunity. 2021;54:148–55, <http://dx.doi.org/10.1080/08916934.2021>.
7. Kameda T, Kamiyama N, Kobayashi H, Kanayama Y, Taniguchi N. Ultrasonic B-line-like artifacts generated with simple experimental models provide clues to solve key issues in B-lines. Ultrasound Med Biol. 2019;45:1617–26, <http://dx.doi.org/10.1016/j.ultrasmedbio.2019.03.003>.
8. Schmickl CN, Menon AA, Dhokarh R, Seth B, Schembri F. Optimizing B-lines on lung ultrasound: an in-vitro to in-vivo pilot study with clinical implications. J Clin Monit Comput. 2020;34:277–84, <http://dx.doi.org/10.1007/s10877-019-00321-z>.
9. Vicente-Rabaneda EF, Acebes C, Castañeda S. Utilidad de la ecografía extraarticular aplicada a las enfermedades inflamatorias sistémicas en la práctica clínica. Reumatol Clin. 2021;17:229–36, <http://dx.doi.org/10.1016/j.reuma.2020.04.005>.
10. Gargani L, Bruni C, Romei C, Frumento P, Moreo A, Agoston G, et al. Prognostic value of lung ultrasound B-lines in systemic sclerosis. Chest. 2020;158:1515–25, <http://dx.doi.org/10.1016/j.chest.2020.03.075>.

Esther F. Vicente-Rabaneda^{a,*}, David Bong^b, Ingrid Möller^c, Santos Castañeda^{a,d}

^a Servicio de Reumatología, Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Spain

^b Facultad de Medicina, Universidad de Barcelona-Bellvitge Campus, Instituto Poal de Reumatología, Barcelona, Spain

^c EULAR Working Group Anatomy for the Image, Instituto Poal de Reumatología, Universidad de Barcelona, Universidad Internacional de Cataluña, Barcelona, Spain

^d Cátedra ROCHE-UAM, EPID-Futuro, Universidad Autónoma de Madrid, Madrid, Spain

* Corresponding author.

E-mail address: efvicenter@gmail.com (E.F. Vicente-Rabaneda).

* Please cite this article as: Vicente-Rabaneda EF, Bong D, Möller I, Castañeda S. Respuesta a «Intersticiopatía pulmonar subclínica en pacientes con esclerosis sistémica. Estudio piloto sobre el papel del ultrasonido». Reumatol Clin. 2022;18:624.