miscellaneous group (pulmonary lymphoma, amyloidosis, pulmonary hypertension, and pulmonary thromboembolism).[12] Our case showed the classic manifestation of simple silicosis: diffuse bilateral nodular pattern, predominantly in both upper lobes.

We believe that occupational exposure to silica must be taken into account in the evaluation of patients with autoimmune diseases and vice versa. Patients exposed to silica dust should be actively screened for signs and symptoms of autoimmune diseases, including SS.

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Miguel Martin Asenjo,[a,*] Javier Miguel Martín Guerra,[a] Claudia Iglesias Pérez,[b] José Maria Prieto de Paula[a]

[a] *Servicio de Medicina Interna, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[b] *Servicio de Neumología, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*

* Corresponding author.
E-mail address: miguel.martin.asenjo@gmail.com
(M. Martin Asenjo).

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Ultrasound Application With Acoustic Structure Quantification (ASQ) in Interstitial Lung Diseases☆

Aplicación ecográfica con cuantificación de la estructura acústica (ASQ) en las enfermedades pulmonares intersticiales

To the Editor:

Lung ultrasound (LUS) is currently an indispensable tool in pulmonology. It has great advantages, including reproducibility, low cost, and lack of ionizing radiation, but its main limitations are its incompatibility with air, and the fact that it is operator-dependent. LUS findings in healthy lung parenchyma generate various signs, such as the pleural shift sign, and artifacts called A and B lines.

Specifically, more than 3 B lines appearing in a scanned area can be interpreted as thickening of the interlobular septa. Roughness, thickening and destructuring of the pleural line, in addition, may be a sign of interstitial lung disease (ILD).[1–4]

To date, no ultrasound method has been able to quantify the severity of lung parenchyma involvement in patients with diffuse ILD, an application that might also be useful in follow-up. For this reason, high-resolution computed tomography (HRCT) continues to be essential for evaluating of the severity and progress of these patients.[5–8]

The most commonly used ultrasound technique for assessing fibrosis (more specifically, liver fibrosis) is ultrasound elastography, although conventional ultrasonography, based on morphological grayscale analysis, may contain more information than that provided by elastography. The acoustic structure quantification (ASQ) method is a non-invasive tool that is used to characterize tissues through the statistical analysis of ultrasound signals received. When tissue is normal, the echo pulse generated is smaller than the ultrasound wavelength, following the normal Rayleigh distribution (continuous distribution function). When tissue is fibrotic, the echo pulses become larger than the wavelength, and deviate from the Rayleigh distribution.[9–11]

ASQ is currently used for characterizing liver fibrosis. Unlike elastography, ASQ images are produced by ultrasound interference generated by innumerable reflective objects. According to this theory, tissue heterogeneity could be quantified by measuring the speckle pattern of tissue from an analysis of the probability density function. On the basis of these principles, and given that no studies have been previously published, we studied ASQ as a method for the evaluation of diffuse ILD.[12–15]

We thus performed the first prospective, observational, randomized case-control study to determine if the ASQ method could quantify severity in fibrosing diffuse ILD. Two groups of patients were recruited, after obtaining ethics committee approval and written informed consent. Group 1 comprised patients with ILD and involvement demonstrated on high-resolution computed tomography (HRCT). Group 2 were healthy patients without respiratory disease, no history of smoking, and normal results on lung auscultation, spirometry, and chest X-ray.

The study was conducted in the pulmonology clinic, where both patient groups underwent evaluation, first with ultrasound and then with the ASQ method. We used a convex transducer, and multiple images were captured in B-mode applied between the intercostal spaces. In patients with diffuse ILD, the point with most interstitial involvement previously visualized on HRCT was sought. In healthy patients, the best axial plane of the lung bases was used.

The acquired images were interpreted with ASQ analysis, drawing 3 randomly assigned regions of interest (ROI), which included the intercostal muscles, pleural line, and lung parenchyma. Mean

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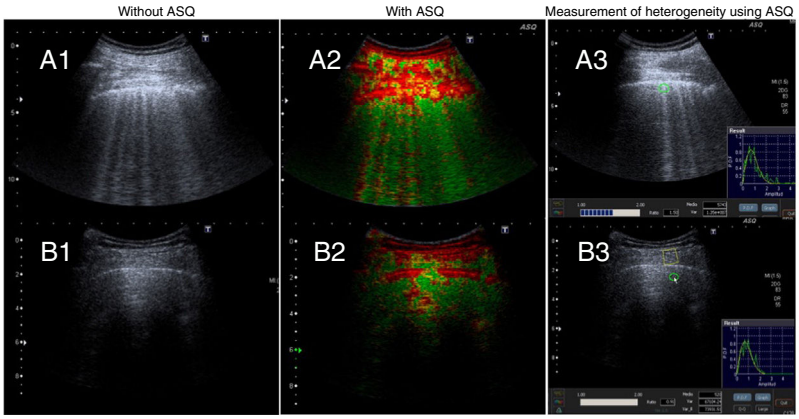

Fig. 1. Pulmonary ultrasound without ASQ and with ASQ. Group 1. A1: without ASQ, showing roughness, thickening, and destructuring of the pleural line and multiple B lines. A2 and A3: with ASQ, multiparametric representation and measurement of lung heterogeneity, respectively. Group 2. B1: without ASQ, showing normal, fine pleural line, B lines (less than 3) and A lines. B2 and B3: with ASQ, multiparametric representation and measurement of lung heterogeneity, respectively.

and standard deviation were calculated for each measurement (data derived directly from the ultrasound equipment). In addition, a multiparametric map based on echo amplitude distribution was generated, in which high C_m2 values (a statistical parameter derived from the varying echo amplitude distribution) are represented in a darker gray and low values in a lighter gray. In liver fibrosis, dispersion increases proportionally with the distortion of the parenchymal architecture and produces a red color, so we applied this same premise in this study, but associating it with pulmonary fibrosis.

The values of heterogeneity of data obtained in the ROI were collected as mean and standard deviation, and comparisons among groups were performed using the Mann–Whitney test. Probability values were considered significant at $P < 0.05$.

The study included a total of 20 patients (10 per group). In group 1, mean age was 74.7 ± 8.8 years, and 60% were men. Pulmonary interstitial patterns with fibrotic component on HRCT were distributed as follows: usual interstitial pneumonia in 5 patients, non-specific interstitial pneumonia in 3, and chronic hypersensitivity pneumonitis in 2. LUS without ASQ (Fig. 1A) showed roughness, thickening and destructuring of the pleural line and multiple B lines (more than 3) per field explored. LUS with ASQ (Fig. 1A2 and A3) was represented with a multiparametric map, measuring heterogeneity in the pulmonary parenchyma (1.42 ± 0.086), pleural line (1.58 ± 0.172), and extrapleural line (1.16 ± 0.138). In group 2, mean age was 44.1 ± 5.8 years, and 30% were men. LUS without ASQ 1B1) showed a normal, fine pleural line, B lines (less than 3) and A lines. LUS with ASQ (Fig. 1A2 and A3) showed the multiparametric map, and measured the heterogeneity ratio in the pulmonary parenchyma (1.05 ± 0.118), pleural line (1.43 ± 0.178), and extrapleural line (1.32 ± 0.150).

Statistically significant differences were observed in the association between the quantification of tissue heterogeneity in pulmonary parenchyma ($P < 0.01$) and extrapleural tissue ($P < 0.05$) between both groups.

Our study is limited by its small sample size. However, given the findings of this first preliminary study, we conclude that LUS with ASQ could quantify the degree of interstitial involvement and guide the management of these patients. However, a study with a larger sample size and reproduction of the measurements obtained by ultrasound will be necessary.

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Conflict of Interests

The authors declare that they have no conflict of interests directly or indirectly related with the contents of this manuscript.

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Aurelio L. Wangüemert Pérez,[a,*] Cristina González Delgado,[b] Julián Fernández Ramos[b]

[a] Servicio de Neumología, Hospital San Juan de Dios, Santa Cruz de Tenerife, Spain
[b] Servicio de Radiología, Hospital San Juan de Dios, Santa Cruz de Tenerife, Spain

Corresponding author.
E-mail address: aureliowp@hotmail.com (A.L. Wangüemert Pérez).

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Need for Portable Oxygen Titration Using 6-Minute Walk Tests☆

Necesidad de titular el oxígeno portátil mediante pruebas de marcha de 6 minutos

To the Editor:

Oxygen therapy improves survival, quality of life, and exercise capacity in patients with chronic obstructive pulmonary disease (COPD) and severe respiratory failure at rest.[1–3] Portable oxygen (O_2) devices facilitate compliance with oxygen therapy and help avoid restrictions in physical activity. The SEPAR guidelines for oxygen therapy recommend that O_2 flow be adjusted during stress testing to achieve a mean arterial oxyhemoglobin saturation (SpO_2) of ≥90%.[4] The 6-minute walk test (6MWT) is the method most widely used.[5] Often, however, O_2 is inappropriately adjusted for exercise, since it is a laborious process and can sometimes be contraindicated.[6,7] Some countries recommend using the same O_2 flow rate as that indicated at rest or recommend increasing O_2 by an additional 1 l.[8]

The aim of this study was to determine if the prescribed oxygen flow after titrating portable oxygen therapy for the 6MWT is similar to the flow that would be indicated if an additional liter were added to the prescribed O_2.

We prospectively included all patients with chronic respiratory failure seen in the oxygen therapy clinic between October 2015 and September 2018 who were prescribed a continuous flow portable O_2 device. They were in a stable phase, met criteria for home O_2 therapy, had the autonomy to carry out activities outside the home, and were capable of performing a 6MWT.[6] Patients who were prescribed a device with a valve were not included in the study.

O_2 was initially adjusted to the at rest rate following SEPAR recommendations.[4] At least 1 6MWT was then performed, using a WristOx$_2$ pulse oximeter, Model 3150, with continuous flow O_2 using the device that we considered most appropriate, depending on the estimated flow requirement and the patient's mobility and preferences. The 6MWTs were performed following SEPAR recommendations.[6] If mean SpO_2≥90% was not achieved in the first test, the test was repeated after a minimum rest period of 30 min, increasing flow by 1 l/min until the objective was achieved. We compared the flow rate after adjustment for the 6MWT with the flow that would be prescribed if 1 l was added to the O_2 at-rest flow rate.

The SPSS package version 20.0 was used for the statistical analysis. A descriptive analysis of patient characteristics was performed, and the Student's *t*-test was used for comparison of means. A *p* value<0.05 was considered statistically significant.

A total of 165 patients, 113 (68.5%) of whom were men, mean age 70.9 (SD 9.31) years, were included. Mean O_2 flow prescribed for the portable device was 3.64 (SD 0.95) l/m. Seventy-seven patients (46.7%) used continuous flow concentrators and 88 (53.3%) had liquid O_2 backpacks. After titration for the 6MWT, the prescribed O_2 was only the same if 1 l had been added to the resting O_2 rate in 49 patients (29.7%) (p<0.0001). We increased the O_2 flow rate in 88 patients (53.3%) and reduced it in 28 (17%). Table 1 shows the diseases causing chronic respiratory failure and the relationship between both methods for prescribing portable O_2 flow. The prescriptions coincided in 36% of the COPD patients, but in only 17.5% of the interstitial diseases, and in 11% of the patients with pulmonary hypertension, in whom desaturation with exertion is greater. Twenty-one patients refused the liquid O_2 backpack, despite requiring more than 3 l/min. In 10 patients, desaturation experienced during the 6MWT could not be corrected.

The results show the superiority of titration by 6MWT over the alternative of adding 1 l of O_2 to the resting flow rate for correcting desaturation during activities of daily living. This is because with the latter, 53.3% of patients (72.5% and 66.7%, in the case of diffuse interstitial pulmonary disease and pulmonary hypertension, respectively) continue to desaturate during exertion. Patients with chronic respiratory failure who are stable often present prolonged periods of hypoxemia that are associated with reduced exercise tolerance and an increased rate of complications, such as pulmonary hypertension, right heart failure, and polycythemia.[9] Arterial blood gas at rest is not useful for adjusting portable O_2 flow.[10] Stress tests, in contrast, allow us to assess the effectiveness of therapeutic interventions.[5,11] The most widely used is the 6MWT,[7] in its different modalities,[6,12] though cycle ergometers have also been used to titrate O_2.[13]

Other factors to bear in mind are the mobility profile of each patient, their preferences, and the mobility permitted by each of the O_2 sources.[14] Thus, 21 patients (12.7%) refused to change their device to a liquid O_2 backpack, despite needing to increase their flow by more than 3 l/min O_2, because that would limit their autonomy.

At the present time, no portable devices are available that meet the needs of the more severe patients, as the liquid O_2 backpack can only provide a flow of up to 5 l/min. In fact, despite having liquid O_2 backpacks providing 5 l/min, 10 patients in our study experienced desaturation during the 6MWT that could not be corrected, with a mean sustained SpO_2 of <90%.

In the future, an alternative to the current titration procedures may be to individualize the provision of home oxygen supply to each patient by integrating sensors in portable O_2 devices that would measure SpO_2 in real time and automatically adjust the flow of O_2, according to patient needs.[15]

In summary, it currently seems necessary to titrate the portable O_2 flow with a stress test if we want to adequately correct desaturation during exercise. Even so, this method has its limitations and is not the only factor to be taken into account when prescribing portable O_2.

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