Transthoracic lung ultrasonography in idiopathic pulmonary fibrosis: correlation with high-resolution computed tomographic findings and evaluation of new imaging protocols

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Aims and objectives

Objectives

The objectives of the present study were to: (i) to compare a comprehensive transthoracic lung ultrasonographic (TLUS) protocol in two different patient positions (sitting/supine and lateral decubitus) with regard to feasibility, duration, patient convenience and assessment of B-lines, using high-resolution computed tomography (HRCT) as a reference standard and (ii) to compare a simplified TLUS protocol in two different patient positions (sitting and lateral decubitus) with the same-positioned comprehensive TLUS assessments, with regard to feasibility, duration, patient convenience and assessment of B-lines using HRCT as a reference standard, in patients with idiopathic pulmonary fibrosis (IPF).

Background

The role of TLUS in the assessment of lung interstitial syndrome (IS) has recently been established [1-6] with multiple B-lines representing its sonorographic hallmark [1]. Interstitial pulmonary fibrosis, described among others under the umbrella of IS, is increasingly being investigated with TLUS [5-12]. Research has focused mainly on pulmonary involvement in patients with systemic sclerosis and rheumatoid arthritis, showing that TLUS scores correlate with the extent and severity of pulmonary fibrosis on the "gold standard" chest HRCT [5-12]. However, there have been no studies investigating a potential correlation in patients with IPF.

Till today, various TLUS protocols have been proposed for the evaluation of IS. The international consensus conference guidelines, although suggest scanning in the sitting/supine position, do not define the optimal patients' position for TLUS assessment, in pulmonary fibrosis [1]. More importantly, there are no studies evaluating the impact of patients' positioning during TLUS in pulmonary fibrosis. A previous study on heart failure population suggests that patients' positioning may impact the number of B-lines during TLUS [13]. Adding to that, previous computed tomography (CT) studies show that lung attenuation varies in relation to the degree of lung inflation and the dependency of the region studied [14] and that changes in body position increase lung attenuation in the dependent lung areas [15, 16]. Lateral decubitus position ensures scanning mostly during deep inspiration because the non-dependent hemithorax facing up will be on inspiration and the dependent hemithorax abutting the examination table will be on expiration [17, 18]. Herein, we decided to study our patients in the lateral decubitus position because we assumed that the inspirational state of the examined hemithorax, being consistent with the respiratory phase that HRCT images are routinely acquired, together with the fact that the dependent lung segments are shifted paramediastinally, could provide TLUS scores that correlate better and more accurately with HRCT scores, than in the sitting/supine position.
In addition to concerns regarding patients' positioning, the optimal TLUS scanning protocol has to be defined. Most of the proposed protocols require extensive assessment of 50-72 lung intercostals spaces (LIS) [4, 5, 7, 10]. Comprehensive TLUS protocols, although potentially more suitable for detailed evaluation of the peculiar distribution of interstitial pulmonary fibrosis, may be time consuming, compromising their wider application and efficiency in everyday clinical practice. In the light of such limitations, the utility of TLUS has been further evaluated by employing simplified, 10-LIS or 14-LIS, methods in patients with systemic sclerosis and rheumatoid arthritis related pulmonary fibrosis, suggesting significant correlations between TLUS and HRCT scores [6, 7, 9, 10].
Methods and materials

1. Patients

The study was conducted according to the Declaration of Helsinki and local regulations. Ethical approval was obtained from the University Ethics Committee and written informed consent to undergo thorough TLUS examinations was obtained from all patients.

Between October 2013 and February 2016 25 consecutive patients with an IPF diagnosis were prospectively enrolled. The diagnosis of IPF was made following a team evaluation between pulmonologists, radiologists and pathologists, according to international criteria: (i) exclusion of other known causes of interstitial lung disease, including connective tissue disease, environmental exposure and medication; (ii) the presence of a usual interstitial pneumonia (UIP) pattern on chest HRCT and (iii) specific combinations of HRCT and pathology findings following surgical lung biopsy [19].

Inclusion criteria comprised: (i) an established diagnosis of IPF and (ii) a recent (within 2 weeks prior to referral) chest HRCT. Exclusion criteria included: (i) causes of lung interstitial fluid (heart failure, diastolic dysfunction, pneumonia, asthma, pulmonary edema); (ii) pleural effusion; (iii) history of pulmonary neoplasia; (iv) inability to complete all TLUS examinations. Identification and exclusion of patients with lung interstitial fluid or pleural effusions was made on the basis of clinical data, echocardiographic results and HRCT findings which were available in all cases.

2. Chest HRCT

2.1. Technique

All chest HRCT examinations were performed with a 16-row scanner using a standard protocol. Acquisition parameters were as follows: 120-140 kV and 300 mAs; slice thickness: 1 mm; slice spacing: 10 mm. A bone reconstruction with lung window was used. Images were obtained at full inhalation from lung apices to bases with the patients in supine position. Patients with increased opacification in the postero-caudal segments underwent additional sections in the prone or lateral decubitus position, in order to define gravity-dependent changes. No intravenous contrast material was administered.

2.2. HRCT analysis

HRCT studies were analyzed by a senior radiologist (18 years of experience) who was blinded to clinical data and TLUS results. Pulmonary involvement was evaluated according to the Warrick semi-quantitative scoring system [20] and the Warrick score (WS) was calculated for all patients.
3. Lung US

3.1. Technique

TLUS studies were performed by a 5\textsuperscript{th}-year radiology resident, supervised by a senior chest radiologist (20 years of experience), with a GE Logiq 7 machine, equipped with a 3-9 MHz micro-convex transducer.

All patients were examined during two sessions, with comprehensive and simplified TLUS protocols. The distribution and anatomic landmarks of the TLUS protocol are shown on Table 1.

During session 1 patients were evaluated twice with a 56-LIS protocol in two different positions: the supine/sitting (supine/sitting comprehensive protocol) and the lateral decubitus (decubitus comprehensive protocol). During the supine/sitting comprehensive protocol, patients were placed in the supine and sitting positions for the examination of the anterior and posterior chest respectively, while during the decubitus comprehensive protocol, they were examined in the left lateral decubitus position for the evaluation of right hemithorax and in the right lateral decubitus position for the evaluation of the left hemithorax. Assessment of the left anterior 5\textsuperscript{th} LIS was not included in any protocol, as heart impairs optimal evaluation.

During session 2, patients were examined twice with a 16-LIS protocol in two different positions, the sitting (sitting simplified protocol) and the lateral decubitus (decubitus simplified protocol) accordingly: During the sitting simplified protocol, patients were examined in the sitting position while during the decubitus simplified protocol they were placed in the left lateral decubitus position for the evaluation of the right hemithorax and reversely. The 16-LIS were chosen based on the known and predicted prevalence of IPF-related changes [19].

The study was randomized regarding the order in which protocols were performed.

3.2. TLUS analysis

TLUS studies were analyzed by the same investigators who performed them, who were blinded to clinical data and HRCT findings.

During all TLUS protocols, the number of B-lines was recorded in each LIS. B-line is defined as a vertical, hyperechoic reverberation artefact which originates from the pleural line, extends deeply to the edge of the screen and moves synchronously with the pleural line during the breathing cycle [1]. The sum of B-lines in all LIS during supine/sitting comprehensive protocol, decubitus comprehensive protocol, sitting simplified protocol and decubitus simplified protocol resulted in supine/sitting comprehensive ultrasound (US) score (supine/sitting cUS score), decubitus comprehensive US score (decubitus
cUS score), sitting simplified US score (sitting sUS score) and decubitus simplified US score (decubitus sUS score), respectively.

4. Statistical analysis

For the statistical analysis we used MedCalc, version 10.0. Standard descriptive results were expressed as mean and standard deviation (SD). Univariate comparisons were made with two-sample t-tests. Correlation between parameters was made with Pearson correlation. A P-value less than .005 was considered statistically significant. For the assessment of intraobserver and interobserver variability between the two investigators, weighted kappa values were calculated.
Table 1: Anatomical sites assessed during comprehensive 56-lung intercostal spaces (LIS) and simplified 16-LIS ultrasonographic protocols, separate for the left and right hemithoraces.

Results

Patients

Mean age±SD of 25 patients included in the present study (19 males and 6 females) was 69.8±7.56 years (age range: 55 to 83 years). The mean WS±SD of the enroled patients was 18±4.72 (range 8-27).

TLUS

A total of 1.400 LIS was assessed, for each comprehensive TLUS protocol with four exceptions: the examination of the left 4\textsuperscript{th} LIS along the parasternal line in one patient, the examination of the left 3\textsuperscript{rd} and 4\textsuperscript{th} LIS along the parasternal line in another patient and the depiction of the left 11\textsuperscript{th} LIS along the paravertebral line in a third patient. The depiction of 3\textsuperscript{rd} and 4\textsuperscript{th} LIS was not feasible due to excessive pericardial fat, as seen on the corresponding HRCT images, while the examination of the 11\textsuperscript{th} LIS was impaired, probably due to variation in the attachment of the hemidiaphragm.

A total of 400 LIS was evaluated for each simplified US protocol with one exception: the depiction of the left 11\textsuperscript{th} LIS along the paravertebral line.

Correlations

A significant correlation was found between all US scores and WS (P<.0001) (Fig. 1). The decubitus cUS score and decubitus sUS score correlated better with WS compared to supine/sitting cUS score and sitting sUS score, respectively ($r^2=.95$ versus .94 and .88 versus .83, respectively) (Fig. 2).

A positive correlation was found between supine/sitting cUS score and sitting sUS score ($r^2=.9$; P<.0001) as well as between decubitus cUS score and decubitus sUS score ($r^2=.91$; P<.0001).

There was no significant difference between supine/sitting and decubitus cUS scores (P=.297) as well as between sitting and decubitus sUS scores (P=.065); however, US scores in the lateral decubitus position were lower than those in the supine/sitting position, in all patients (Fig. 3)

Mean duration of decubitus comprehensive protocol and supine/sitting comprehensive protocol was 19.2 and 22.8 minutes, respectively (P<.0001) and mean duration of
decubitus simplified protocol and sitting simplified protocol was 4.76 and 6.2 minutes, respectively (P<.005).

Twenty-four out of 25 patients (96%) reported preference for decubitus vs supine/sitting comprehensive protocol, while 14 patients (56%) preferred decubitus vs sitting simplified protocol.

For supine/sitting and decubitus comprehensive protocols, the kappa values for interobserver/intraobserver variability were .809/.817 and .825/.812, respectively. For sitting and decubitus simplified protocols, the kappa values for interobserver/intraobserver variability were .794/.828 and .834/.846, respectively.
**Fig. 1:** Chest HRCT and corresponding lung ultrasonography images in different patients with mild (a), moderate (b) and severe (c) pulmonary fibrosis. Lung ultrasonography image in (a) corresponds to the right 4th lung intercostal space, in (b) to the right 6th intercostal space and in (c) to the 9th intercostal space, along the paravertebral line.

Fig. 2: Correlation between the Warrick score (WS) and supine/sitting comprehensive ultrasonographic score (a), decubitus comprehensive ultrasonographic score (b), sitting simplified ultrasonographic score (c) and decubitus simplified ultrasonographic score (d).

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Fig. 3: A 55-year-old man with idiopathic pulmonary fibrosis. Lung ultrasonographic images corresponding to the left 8th lung intercostal space along the sub-scapular line. During supine/sitting comprehensive protocol (a) six B-lines were counted while during decubitus comprehensive protocol (b), seven minutes later, two B-lines were documented.

Conclusion

IPF could be evaluated with TLUS. TLUS scores correlated with WS, regardless patient positioning; however decubitus scores showed better correlation. Decubitus protocols were faster and preferred by patients. Simplified TLUS scores correlated with the corresponding, same-positioned comprehensive scores and WS.

The presented protocols may have the potential to be regarded as additional tools for the evaluation of IPF, especially in the context of follow up and treatment response. HRCT remains undoubtly the "gold standard" for the evaluation of patients with pulmonary fibrosis. However, in the light of the evolving role of TLUS in the assessment of pulmonary fibrosis, the establishment of accurate, reproducible as well as simplified TLUS methods that maximize their efficacy appears to be more than appealing, at least from a practical viewpoint.
References


