Med Ultrason 2014, Vol. 16, no. 1, 27-31
DOI: 10.11152/mu.2014.2066.161.am1so2

Comparison of a new, modified lung ultrasonography technique with high-resolution CT in the diagnosis of the alveolo-interstitial syndrome of systemic scleroderma

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Abstract

Aims: Pulmonary fibrosis is the main cause of mortality in patients with Systemic Scleroderma (SSc). This study was performed to investigate the utility of modified trans-thoracic ultrasound (TTUS) scoring system according to the comet tail sign (B-line artifacts) and to compare it with high-resolution computed tomography (HRCT) findings in patients with SSc and pulmonary involvement. **Patients and method:** Seventy subjects with SSc diagnosed according to the American College of Rheumatology criteria were enrolled. All subjects underwent HRCT followed by TTUS for comet tail sign detection in order to predict the degree of lung fibrosis. The modified TTUS assessment was performed at 10 intercostals spaces level. **Results:** A significantly positive correlation between TTUS and the severity of pulmonary involvement (Spearman's correlation coefficient= 0.695, $P < 0.001$), (LR=74.36, $P<0.001$) was found. When compared with HRCT as the gold standard method, the sensitivity, specificity, positive and negative predictive value of TTUS was 73.58%, 88.23%, 95.12% and 51.72% respectively. Kappa values for the intra-observer modified TTUS assessment was 0.838. **Conclusions:** Our study showed that the modified TTUS comet tails scoring system could be useful in the assessment of the pulmonary involvement in patients with SSc.

Keywords: systemic sclerosis, ultrasonography, high-resolution CT, Warrick score

Introduction

Systemic scleroderma (SSc) is a connective tissue disease (CTD) characterized by excessive fibrosis in different organs and systems, especially in skin, immunologic abnormalities, and vasculopathy [1]. Lung, gastrointestinal tract and kidneys are the most common internal organs affected by SSc [1]. Pulmonary involvement is present in 70-100% of patients [2], pulmonary fibrosis being one of the main causes of morbidity and the leading cause of mortality.

High-resolution CT (HRCT) is the gold standard method for diagnosis of SSc related interstitial lung disease [3]. The role of trans-thoracic ultrasound (TTUS) in the assessment of a various pulmonary conditions has been previously reported [4-6]. The ultrasonographic (US) feature of pulmonary fibrosis consists of detection and quantification of the US lung comet tail sign (B-line artifacts). This sign is generated by the reflection of the US beam from the thickened sub-pleural interlobar septum. Previous studies have reported extensive assessment of the lung by examining a great number of intercostal spaces, which is difficult and time consuming [4-6]. The aim of our study was to examine only selective intercostal spaces – 10 locations (modified TTUS) – and to compare the results of this new scoring system with the HRCT findings according to the Warrick score.

Received 15.11.2013 Accepted 12.01.2014
Med Ultrason
2014, Vol. 16, No 1, 27-31
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Patients and method

Seventy consecutive patients (62 females and 8 males) with SSc diagnosis referred to the Rheumatology outpatients Clinic of the tertiary referral hospital were enrolled. The diagnosis of SSc was made according to the American College of Rheumatology classification criteria for SSc by a qualified rheumatologist with 5 years experience. Patients with a history of pulmonary neoplasia, heart failure, asthma, and smoking were excluded from the study.

After clinical examination, all the patients were evaluated thoroughly by a cardiologist and a pulmonologist to exclude other causes of pulmonary and cardiac inducing US B-Line. All chest HRCT and TTUS examinations were performed in the radiology department. Chest HRCT examinations were interpreted and scored by one radiologist with experience in pulmonary HRCT and interstitial lung disease. Another radiologist with 8 years of experience performed all TTUS examinations. The radiologists were blinded to the clinical data's and HRCT or TTUS findings. Ethical approval was obtained from the University Ethics Committee and informed consent was obtained from all patients.

Ultrasonographic B-Line assessment:

TTUS examination was performed using a Medison Accuvix V20 (Medison, South Korea) equipped with 7 to 10 MHz broad band linear multi-frequency transducer. The US imaging parameters were set in each case in order to obtain the maximal contrast between the examined soft tissue structures. Patients were examined in supine position for assessment of anterior chest wall and in sitting position for the posterior chest wall. US images were obtained by moving the probe longitudinally along anatomical reference lines.

We performed a modified TTUS B-lines assessment, which consisted of a total of 10 intercostal space (ICS) examinations (table I). These sites were selected according to the higher prevalence of interstitial lung disease in SSc and accessibility by TTUS. US assessment of B-Line

Table I. The 10 intercostal sites used for ultrasound examination

Location	Anatomical line	US B- Line assessment (right and left)
Anterior	mid-clavicular	4th ICS
Lateral	anterior axillary	4th ICS
	mid-axillary	4th ICS
Posterior	sub-scapular	8th ICS
	posterior axillary	8th ICS

ICS – intercostals site

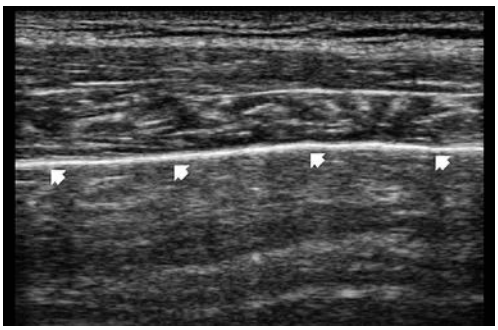

Fig 1. The normal smooth linear echogenic line of pleura.

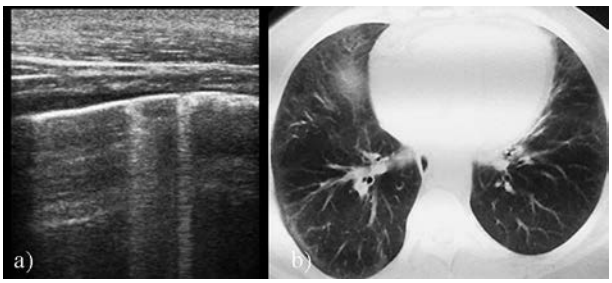

Fig 2. a) The comet tail sign (2 B-lines) in the mild form of alveolo-interstitial involvement in systemic sclerosis. b) HRCT showing the mild form of alveolo-interstitial involvement in systemic sclerosis (Warrick score=4).

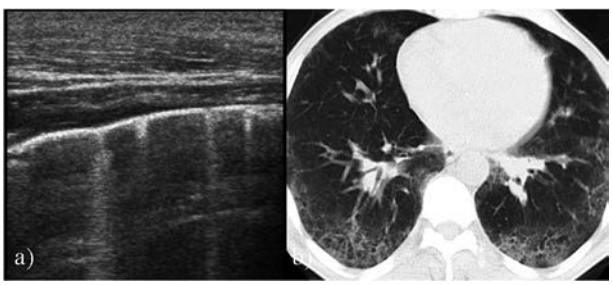

Fig 3. a) The comet tail sign (4 B-lines) in moderate form of alveolo-interstitial involvement in systemic sclerosis. b) HRCT showing moderate form of alveolo-interstitial involvement in systemic sclerosis (Warrick score=14).

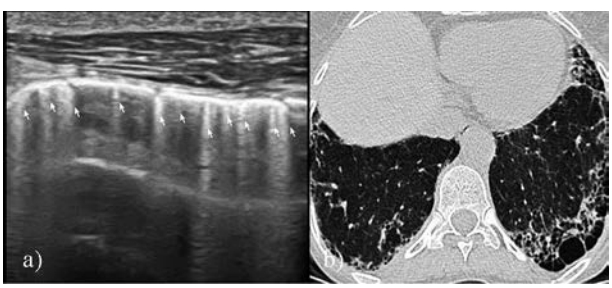

Fig 4. a) The comet tail sign (several B-lines) in the severe form of alveolo-interstitial involvement in systemic sclerosis. b) HRCT showed severe form of alveolo-interstitial involvement in systemic sclerosis (Warrick score = 30).

Table II. The Warrick scoring system for alveolo-interstitial involvement

Parenchymal alteration	Severity score
Ground glass opacities	1
Irregular pleural margins	2
Septal/subpleural lines	3
Honeycombing	4
Subpleural cysts	5
Number of lung segments	
1–3	1
4–9	2
>9	3

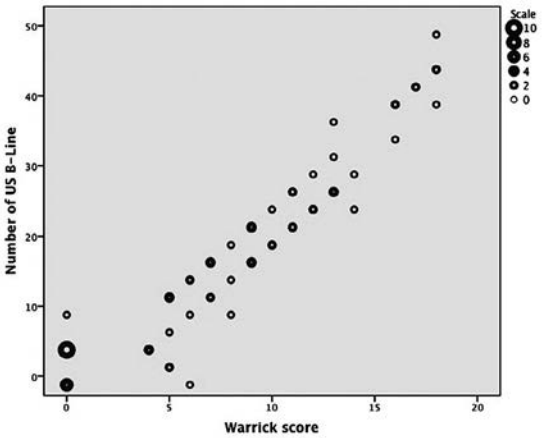

Fig 5. The correlation between HRCT and TTUS.

was performed applying the probe perpendicular to the skin in the intercostal spaces along the aforementioned anatomical reference lines Anterior ICS were evaluated with patients in supine position and posterior ICS with patients in sitting position. In TTUS, the artifact generated from the thickened interlobular septa at lung surfaces was considered TTUS B-line. TTUS- B Line is evident as a hyper echoic narrow-based reverberated artifact that is generally not visible in normal lung parenchyma. The ultrasonographic severity of pulmonary alveolo-interstitial involvement yielded a score according to the sum of all TTUS B-lines and was correlated with the HRCT findings. TTUS assessment was scored semi-quantitatively as 0 = normal, (≤ 5 B-lines), 1 = mild (from 6 to 15 B-lines), 2 = moderate (from 16 to 30 B-lines), and 3 = severe (> 30 B-lines) (fig 1-4).

High resolution computed tomography assessment:

Chest HRCT examinations were performed by using a MDCT (GE Light Speed RT 16 CT Scanner; GE, Milwaukee, Wl) scanner at full inspiration in the supine position (120 kV and 300 mAs). In subjects with increased opacification in the posterior portion of lung bases, we also performed prone sectioning in order to exclude gravity dependent perfusion.

The lung parenchyma was imaged from the apex to the base with a table increment of 10 mm, a slice thickness of 2 mm and a bone plus reconstruction with lung window. No intravenous contrast material was used. Pulmonary involvement identified and scored according to Warrick score (table II). A total Warrick score was obtained by summing the severity and the extension scores (0-30). For assessing the intra-observer reliability, reinterpretation of the TTUS stored imagines was performed 5 weeks after the first evaluation.

To accurately correlate the TTUS B-lines with HRCT findings, the scores obtained at HRCT assessment were evaluated and the results were expressed as a semi-quantitative scoring: 0 = normal (0 points); 1 = mild (< 8 points); 2 = moderate (from 8 to 15 points) and 3 = severe (> 15 points).

Statistical analysis was performed using SPSS software, version 16. Descriptive results were expressed as a mean and standard deviation (SD). Chi-square analysis was used to compare between US and HRCT data and the Spearman's rho correlation coefficient was used to calculate the respective correlation. P-values below 0.01 were considered statistically significant. To assess agreement between the TTUS and Warrick score and the intra-observer reliability weighted kappa statistics were calculated.

Results

Mean age ± SD was 50.29 ± 9.7 years (ranging from 30 to 70 years) and the mean ± SD disease duration was 88 ± 83.1 months (range 4 to 252 months). A total of 700 ICS were evaluated for B-lines assessment. The distribution of various grades of pulmonary involvement of SSc according to the HRCT Warrick score and semiquantitative TTUS scoring are shown in table III.

When the TTUS assessment was compared to the Warrick score a significant positive correlation for severity of pulmonary involvement appreciation (Spearman's correlation coefficient= 0.695, $P < 0.001$), (LR=74.36, $P<0.001$) was found. The scatter plots of HRCT scores versus US scores demonstrated the correlation between HRCT and TTUS (fig 5). The global kappa value of the agreement between two imaging methods was 0.553

Table III. Severity of lung interstitial disease assessed by TTUS and HRCT.

Severity	TTUS (n / %)	HRCT (n / %)
Normal	29 / 41.4%	17 / 24.3 %
Mild	12 / 17.1%	21 / 30%
Moderate	21 / 30%	23 / 32.9 %
Severe	8 / 11.4 %	9 / 12.9%

n – number of patients

($p<0.001$). When compared with HRCT as the gold standard method, the sensitivity, specificity, positive and negative predictive value of TTUS was 73.58%, 88.23%, 95.12% and 51.72% respectively.

The global kappa values for the intra-observer reliability of TTUS B-lines assessment was 0.838.

Discussions

Nowadays, chest HRCT is considered the "gold-standard" method to detect disease activity in early pulmonary and subclinical lung involvement [3,4].

TTUS was previously described for assessing some pulmonary condition such as pulmonary interstitial edema, atelectasis and pleural effusions [7-13]. It has also been used as a guide for interventional lung procedures such as biopsy of pleural lesions [7-13]. The role of TTUS to investigate pulmonary fibrosis in systemic sclerosis has also been described [4].

The results of recent research on TTUS in pulmonary alveolo-interstitial disease have shown promising correlation with HRCT as the "gold standard" method [3]. US can be a valuable diagnostic modality for the assessment of the chest, being a bedside procedure, widely available, and inexpensive. Also from a technical point of view, the lung surfaces can be easily investigated by TTUS and the comet tail sign "artifacts" could be detected quickly using a small surface, high frequency probe [14].

Our main obstacle with the previous US scoring systems is the necessity to assess the US B-lines in more than 50 ICS, which is both time consuming and difficult to perform on a regular basis [3- 6]. In our study we assessed by US10 ICS for detecting the B-line. These spaces were chosen based on the prevalence of lung segment involvement during HRCT assessment in patients with scleroderma. To the best of our knowledge, our work is the first study providing evidence for the utility of using a smaller number of ICS evaluations for TTUS B-lines assessment in pulmonary involvement in SSc patients.

Diagnosis and quantification of the lung involvement in patients with SSc has both prognostic and therapeutic significance [4,15,16]. According to our study, TTUS can be helpful in identifying and quantifying pulmonary fibrosis. Taking into account the cost-effectiveness, accessibility, and the performing time (5.4 min) for TTUS, the clinical impact of this method is more promising. There was a prominent difference in time spent on comprehensive (mean 23.3 ± SD 4.5 minutes) and simplified US assessment (mean 8.6 ± SD 1.4) [3] when compared to our method (mean 5.4± 1.8 minutes).

HRCT remains the gold-standard method to assess the alveolo-interstitial involvement, allowing the investigation of the entire lung parenchyma compared to TTUS that can assess only the lung surface. TTUS can be useful as an adjunctive method to follow-up the SSc patients especially during treatment, reducing the radiation exposure especially in young women who have a higher risk of developing radiation related cancers [4].

Gargani et al [4] showed that US B-Lines are more frequent in the diffuse form of SSc rather than the limited form and have a good correlation with HRCT on assessment of lung fibrosis. They reported that US B-Lines has a potential diagnostic value to detect pulmonary fibrosis. Gutierrez et al [3] reported that a simplified US B-lines assessment of interstitial lung fibrosis could be an adjunctive method in patients with connective tissue disease. They showed that there was a significant correlation between the simplified US assessment and HRCT findings ($P=0.0006$) and between classic ultrasound and simplified US assessment ($P=0.0001$).

TTUS is usually performed by low to medium (3.5-5 MHz) frequency transducers [13,17] whereas high frequency linear transducers are considered to be the best tools in the investigation of the pleural line. A diffuse bilateral lung comet tail artifact is indicative for the presence of an alveolo-interstitial syndrome and it can be seen in different clinical conditions as pulmonary fibrosis, acute respiratory distress syndrome, interstitial pneumonia and pulmonary edema [18]. Cardiogenic causes of US B-Lines such as pulmonary edema that can cause thickened interlobar septa are the main differential diagnosis of US B-Lines [19].

One of the limitations of our studies is related to the absence of the control group (healthy people and patients with other etiology of the alveolo-interstitial syndrome). Also, we did not assess the inter-observer reliability.

Conclusions

The severity of the alveolo-interstitial involvement in patients with SSc can be appreciated by TTUS. The pres-

ence and number of US B-lines at TTUS examination have a significant positive correlation with alveolo-interstitial involvement at HRCT. The modified TTUS evaluation of 10 ICS could be a useful and rapid imaging modality in the evaluation of pulmonary involvement in SSc patients.

Conflict of interest: none

References

1. Assayag D, Kaduri S, Hudson M, Hirsch A, Baron M. High resolution computed tomography scoring system for evaluating Interstitial Lung Disease in Systemic Sclerosis Patients. Rheumatology: Current Research 2012; S1-003. doi:10.4172/2161-1149.S1-003.
2. Diot E, Boissinot E, Asquier E, et al. Relationship between abnormalities on high-resolution CT and pulmonary function in systemic sclerosis. Chest 1998; 114: 1623-1629.
3. Gutierrez M, Salaffi F, Carotti M, 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.
4. Gargani L, Doveri M, D'Errico L, et al. Ultrasound lung comets in systemic sclerosis: a chest sonography hallmark of pulmonary interstitial fibrosis. Rheumatology 2009; 48: 1382-1387.
5. Doveri M, Frassi F, Consensi A, et al. Ultrasound lung comets: new echographic sign of lung interstitial fibrosis in systemic sclerosis. Reumatismo 2008; 60: 180-184.
6. Jambrik Z, Monti S, Coppola V, et al. Usefulness of ultrasound lung comets as a nonradiologic sign of extravascular lung water. Am J Cardiol 2004; 93: 1265-1270.
7. Soldati G, Copetti R, Sher S. Sonographic interstitial syndrome: the sound of lung water. J Ultrasound Med 2009; 28: 163-174.
8. Lichtenstein DA, Mezière GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. Chest 2008; 134: 117-125.
9. Soldati G. Sonographic findings in pulmonary diseases. Radiol Med 2006; 111: 507-515.
10. Frassi F, Gargani L, Gligorova S, Ciampi Q, Mottola G, Picano E. Clinical and echocardiographic determinants of ultrasound lung comets. Eur J Echocardiogr 2007; 8: 474-479.
11. Picano E, Gargani L, Gheorghiade M. Why, when and how to assess pulmonary congestion in heart failure: pathophysiological, clinical, and methodological implications. Heart Fail Rev 2010; 15: 63-72.
12. Sperandeo M, Varriale A, Sperandeo G, et al. Transthoracic ultrasound in the evaluation of ulmonary fibrosis: our experience. Ultrasound Med Biol 2009; 35: 723-729.
13. Copetti R, Soldati G, Copetti P. Chest sonography: a useful tool to differentiate acute cardiogenic pulmonary edema from acute respiratory distress syndrome. Cardiovasc Ultrasound 2008; 6: 16.
14. Delle Sedie A, Doveri M, Frassi F, et al. Ultrasound lung comets in systemic sclerosis: a useful tool to detect lung interstitial fibrosis. Clin Exp Rheumatol 2010; 28: S54.
15. Wells AU, Rubens MB, du Bois RM, Hansell DM. Functional impairment in fibrosing alveolitis: relationship to reversible disease on thin section computed tomography. Eur Respir J 1997; 10: 280-285.
16. Latsi PI, Wells AU. Evaluation and management of alveolitis and interstitial lung disease in scleroderma. Curr Opin Rheumatol 2003; 15: 748-755.
17. Bouhemad B, Zhang M, Lu Q, Rouby JJ. Clinical review: Bedside lung ultrasound in critical care practice. Crit Care 2007; 11: 205.
18. Volpicelli G, Mussa A, Garofalo G, et al. Bedside lung ultrasound in the assessment of alveolar-interstitial syndrome. Am J Emerg Med 2006; 24: 689-696.
19. Picano E, Frassi F, Agricola E, Gligorova S, Gargani L, Mottola G. Ultrasound lung comets: a clinically useful sign of extravascular lung water. J Am Soc Echocardiogr 2006; 19: 356-363.