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.
Patients and method

Seventy consecutive patients (62 females and 8 males) with SSc diagnosis referred to the Rheumatology outpatient Clinics 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 induc- ing 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.

Ultrasoundographic 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 or- der 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 sit- ting position for the posterior chest wall. US images were obtained by moving the probe longitudinally along anatomic 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 accord- ing to the higher prevalence of interstitial lung disease in SSc and accessibility by TTUS. US assessment of B-Line

was applied performing the probe perpendicular to the skin in the intercostal spaces along the aforementioned anatomical reference lines. Prior ICS were evaluated with patients in supine position and posterior ICS with patients in sitting position. In TTUS, the artifact generat- ed 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 ul- trasonographic severity of pulmonary alveolo-interstitial involvement yielded a score according to the sum of all TTUS B-lines and was correlated with the HRCT find- ings. 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, Mil- waukee, WI) 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 grav- itative dependent perfusion.

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

Table II. The Warrick scoring system for alveolo-interstitial in- volvement

<table>
<thead>
<tr>
<th>Parenchymal alteration</th>
<th>Severity score</th>
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<tbody>
<tr>
<td>Ground glass opacities</td>
<td>1</td>
</tr>
<tr>
<td>Irregular pleural margins</td>
<td>2</td>
</tr>
<tr>
<td>Septal/subpleural lines</td>
<td>3</td>
</tr>
<tr>
<td>Honeycombing</td>
<td>4</td>
</tr>
<tr>
<td>Subpleural cysts</td>
<td>5</td>
</tr>
</tbody>
</table>

Number of lung segments

1-3  
4-9  
>9

The correlation between HRCT and TTUS. 

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 soft- ware, version 16. Descriptive results were expressed as a mean and standard deviation (SD). Chi-square analy- sis 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 distribu- tion of various grades of pulmonary involvement of SSc according to the HRCT Warrick score and semiquanita- tive TTUS scoring are shown in table III.

When the TTUS assessment was compared to the Warrick score a significant positive correlation for sever- ity 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 I. The 10 intercostal spaces used for ultrasound examination

<table>
<thead>
<tr>
<th>Location</th>
<th>Anatomical line</th>
<th>US B-Line assessment (right and left)</th>
</tr>
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<tbody>
<tr>
<td>Anterior</td>
<td>mid-clavicular</td>
<td>4º ICS</td>
</tr>
<tr>
<td>Lateral</td>
<td>anterior axillary</td>
<td>4º ICS</td>
</tr>
<tr>
<td></td>
<td>mid-axillary</td>
<td>4º ICS</td>
</tr>
<tr>
<td>Posterior</td>
<td>sub-ascapular</td>
<td>8º ICS</td>
</tr>
<tr>
<td></td>
<td>posterior axillary</td>
<td>8º ICS</td>
</tr>
<tr>
<td>ICS – intercostals site</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 showing severe form of alveolo-interstitial involve- ment in systemic sclerosis (Warrick score = 30).

Fig 5. The correlation between HRCT and TTUS.
Table III. Severity of lung interstitial disease assessed by TTUS and HRCT.

<table>
<thead>
<tr>
<th>Severity</th>
<th>TTUS (n / %)</th>
<th>HRCT (n / %)</th>
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<tbody>
<tr>
<td>Normal</td>
<td>29 / 41.4%</td>
<td>17 / 24.3%</td>
</tr>
<tr>
<td>Mild</td>
<td>12 / 17.1%</td>
<td>21 / 30%</td>
</tr>
<tr>
<td>Moderate</td>
<td>21 / 30%</td>
<td>23 / 32.9%</td>
</tr>
<tr>
<td>Severe</td>
<td>8 / 11.4%</td>
<td>9 / 12.9%</td>
</tr>
</tbody>
</table>

n = number of patients

TTUS B-lines assessment in pulmonary 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 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 presence 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