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Lung ultrasound in the follow-up of stable idiopathic pulmonary fibrosis

Oya BAYDAR TOPRAK*, Ezgi ÖZYILMAZ, İsmail HANTA, Sedat KULECİ Efraim GÜZEL

Department of Chest Diseases, Faculty of Medicine, Çukurova University, Adana, Türkiye

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Abstract

Idiopathic pulmonary fibrosis is the most common and severe form of idiopathic interstitial pneumonia and is responsible for 20% of interstitial lung disease (ILD) cases. In this study, it was planned to evaluate the relationship of these two methods in detecting lung changes in IPF using a 12-zone lung ultrasound protocol with the current standard evaluation method, high-resolution computed tomography. 22 patients diagnosed with idiopathic pulmonary fibrosis by multidisciplinary evaluation were included in the study, and HRCT and pulmonary function tests and LUS protocol of 12 lung regions were used. The mean age ± SD of the patients was 69.0 ± 7.59 years. 21 (95.5%) were male. While 17 (77.3%) of the patients included in the study were diagnosed with radiological evidence, the diagnosis of the rest was confirmed histopathologically. While 5 of the patients (22.7%) did not receive any special treatment, 13 of the remaining patients were taking pirfenidone, and 4 were taking nintedanib. When the HRCT total fibrotic score was evaluated with the total LUS score, a correlation coefficient of 0.702 (P:0.000) was obtained. In stable idiopathic pulmonary fibrosis, lung ultrasonography can be a readily accessible, non-irradiating, short-term, and rapidly informative monitoring technique that can be utilised at the bedside or during consultation instead of high-resolution thorax computerized tomography.

Keywords: idiopathic pulmonary fibrosis, lung ultrasonography, thoracic tomography, pulmonary function test, gap

1. Introduction

The most severe form of idiopathic interstitial pneumonia, idiopathic pulmonary fibrosis (IPF), has a dismal prognosis and primarily affects older persons, demonstrating a close correlation between the fibrosis process and ageing. In all ILD examinations, high-resolution computed tomography (HRCT) of the chest is presently regarded as the primary standard diagnosis, not only for the first assessment but also for disease monitoring and treatment effectiveness prediction (1). In cases of respiratory function impairment and during yearly follow-ups, HRCT is typically necessary. Tomography has some drawbacks, including repetitive radiation exposure, expense, accessibility, and occasionally challenging supine positioning. It is essential to be aware of the radio shielding issue since the cumulative dosage for each exam is 7 mSv, which is equivalent to 2 years of exposure to natural light (2). Alternative diagnostic techniques are required due to the radiation danger, even though HRCT is now the preferred approach for the assessment of IPF (3). This seems to be a promising application for lung ultrasonography (LUS). The key benefits of the LUS examination are that it doesn't involve radiation exposure and is affordable, repeatable, convenient, bearable, and non-invasive (4). There are still specific gaps in this area that are particular to illnesses like IPF, despite the fact that several studies have proven that lung ultrasound results are now connected with HRCT scores in various disease categories (5-7). The purpose of this study is to clearly demonstrate the association between radiological results and lung ultrasound findings in stable period IPF follow-up.

2. Materials and Methods

2.1. Hypothesis

Lung ultrasound (LUS) may be a suitable method for the follow-up of patients with idiopathic pulmonary fibrosis.

2.2. Primary endpoint

Evaluation of the efficacy and safety of LUS in stable IPF

2.3. Excepted benefits

- Reducing the total radiation dosage that IPF patients get through HRCT in light of the accurate information that will be gathered.
- Reducing Health expenditures if it is determined that the LUS examination is sufficient for the clinical care of IPF

2.4. Study design and population

Twenty-two individuals with a confirmed diagnosis of IPF from a multidisciplinary perspective were included in the study between 1.1.2020 and 1.5.2020 sequentially. The trial excluded patients who had symptoms of aggravation in the previous 4 weeks. After each patient signed the informed consent form, they were all enrolled in the research. The Cukurova University Non-Interventional Ethics Committee (96/2020) approved this

*Correspondence: oyabaydarr@yahoo.com.tr

cross-sectional study.

At the time of the visit, included patients completed a clinical evaluation that comprised a thoracic ultrasound, pulmonary functional tests, and mMRC score. The most recent thorax CT conducted within three months of enrollment and those completed while the patient was enrolled were assessed. During subsequent reassessments, the presence, location, and severity of ultrasound abnormalities were noted for each patient and compared to the development of clinical, functional, and CT scans.

2.5. Lung ultrasound (LUS)

A GE Logic e R7 pro, USA, equipped with a 2-5 MHz curve array (C5-2) and a 4-12 MHz linear array (L12-4), was used for all LUS studies. Imaging parameters were adjusted manually to ensure maximum contrast between the examined structures. The "12-lung regions" LUS protocol was used. The LUS protocol provided an equal assessment of the anterior, lateral, and posterior lung regions on both sides. LUS was performed in a sitting position with the arms raised above the head while breathing normally to evaluate the lateral chest wall.

The transducer was placed perpendicular to the chest wall to provide a short-axis view of the intercostal space. During the LUS protocol, the number of B lines was re-registered in each preset IC. B-lines were defined as vertical hyperechoic reverberation artifacts originating from the pleural line and extending to the edges of the screen. In order to determine the degree of IPF severity, the total number of B lines per patient was scored by adding B lines from each of the 12 lung regions.

2.6. Thorax HRCT

Thoracic HRCT scans were evaluated in all patients in the last three months prior to participation in the radiological evaluation. Radiological images were assessed and graded by a single specialist physician in Çukurova University Faculty of Medicine, Department of Radiology. In the computed tomography that has been taken contrast in the early arterial phase, the section thickness is 1 mm.

Images were acquired while the patient was supine position with full inspiration covering the entire chest area. Additional sections were made in the prone decubitus position to exclude changes due to gravity. An intravenous contrast agent was not administered. In the early arterial phase, the section thickness is 1 mm. Major HRCT images have been described in international standard terminology defined by the Fleischner Society dictionary and in the peer-reviewed literature on viral pneumonia using terms such as ground-glass opacities (GGO), crazy-paving pattern, and consolidation (8). Image analysis was evaluated by expert radiologists in our institution using the institutional digital database system (HBYS Mergentech PACS, version v3.22.03.1-20220314).

Fibrotic changes were scored using a semi-quantitative technique. An HRCT fibrotic index was obtained by counting the presence and extension of reticulation and honeycomb for each lobe (9):

0—no reticulation,

1—reticulation without honeycombing,

2—septal reticulation with honeycomb in <25% of a lobe

3— septal reticulation with honeycomb in 2-49% of a lobe

4— septal reticulation with honeycomb in 50-75% of one lobe

5— septal reticulation with honeycomb in >75% of one lobe

Radiological involvements are divided into three;

Mild: scores ≤6

Medium: scores 7-13

Severe: scores ≥14

Gender-Age-Physiology (GAP) model – The most widely validated clinical prediction model is the GAP model, which incorporates age, sex, FVC, and DLCO into a simple score-score index and staging system that predicts one-, two-, and three-year mortality (10). The severity of the disease was determined according to this model.

2.7. Pulmonary function tests (PFTs)

PFTs were performed with a calibrated Sensor Medics V-Max 20 Spirometer (Jaeger MS-PFT Analyzer Unit, Wiasys Healthcare GmbH, Höchberg, Germany) in accordance with the ATS guideline. Basal forced expiratory volume for 1 second (FEV1) and forced vital capacity (FVC) were measured three times, and the best values were recorded. Total lung capacity was measured with the helium dilution technique (Jaeger MS-PFT Analyzer Unit), and Transfer Factor for Carbon Monoxide (TLCO) was measured with the single breath method. It was measured with a single breath technique in which 10% helium and 0.3% carbon monoxide were rapidly inhaled, held for 10 seconds, and then exhaled by measuring the remaining carbon monoxide (11). Test results are presented as a percentage of predicted values. The results of pulmonary function tests were interpreted according to the ATS/ERS recommendations (12).

3. Results

3.1. The characteristics of the participants

The mean age ± SD of the patients was 69.0 ± 7.59 years (range 58 to 81 years). 21 (95.5%) were male. Five patients were non-smokers, and 17 (77.2%) were active smokers or had a smoking history. While 17 (77.3%) of the patients included in the study were diagnosed with radiological evidence, the diagnosis of the rest was confirmed histopathologically. It was observed that hypoxemia developed at rest in 8 (36.4%) of the patients.

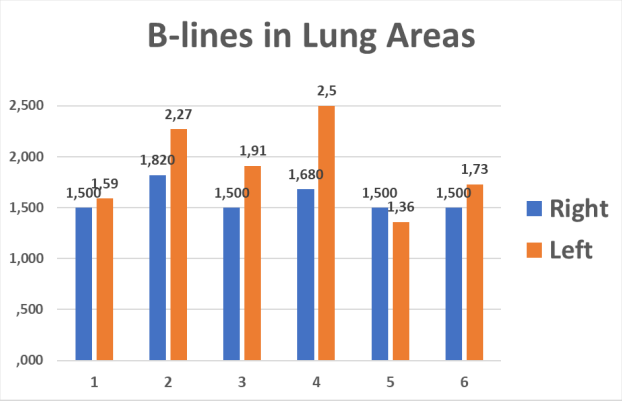

Fig. 1: Distribution of B-Lines in Lung Ultrasound Fields

The GAP stage was 1 in 10 (45.5%) of the participants, 2 in 10 (45.5%) and 3 in 2 (9.1%). While 5 of the patients (22.7%) did not receive any special treatment, 13 of the remaining patients were taking pirfenidone, and 4 were taking nintedanib. Table 1 summarizes the clinical characteristics of individuals.

Table 1. Sociodemographic And Clinical Caharcateristics of The Participants

	n	%
Gender		
Female	1	4.5
Male	21	95.5
Age (mean±*SD*)	69.0+7.59	
Radiological Pattern		
UIP	15	68.2
Probable IPF	4	18.2
Indeterminate IPF	3	13.6
mMRC Score		
1	4	18.2
2	9	40.9
3	6	27.3
4	3	13.6
GAP Score		
2	2	9.1
3	8	36.4
4	4	18.2
5	6	27.3
6	1	4.5
7	1	4.5
FEV1L	1.98±0.47	
FEV1%	79.3±21.1	
FVCL	2.48±0.69	
FVC%	77.2±22.9	
FEV1/FVC	81.3±10.4	
DLCO%	40.5±22.1	
DLCO/VA%	63.6±29.6	

3.2. HRCT and LUS Scores

In the present study group, none of the participants had mild IPF according to the HRCT severity score, while 8 (36.4%) had moderate and 14 (63.6%) had severe IPF. The distribution of B-lines in both lungs is shown in Fig.1. When the HRCT total fibrotic score was evaluated with the total LUS score, a correlation coefficient of 0.702 (P:0.000) was obtained (Fig. 2.).

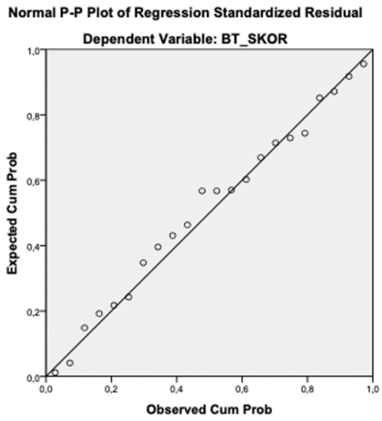

Fig. 2. Linear correlation of HRCT severity score and LUS fibrotic score

4. Discussion

The presence of many B lines with diverse distribution in both lungs is the key characteristic in the LUS assessment of fibrotic interstitial involvement. In stable IPF, the current investigation showed a substantial correlation between thoracic HRCT and LUS.

Today, with the rapid increase in the use of antifibrotic drugs, the use of HRCT has expanded not only for initial evaluation but also for monitoring the course of the disease and possible response to treatment. The main HRCT changes in a UIP pattern include reticulation and honeycombing, but evidence of ground glass changes is less common and has limited predictive value for the diagnosis of IPF (13). When dealing with radiation exposure, especially the biological effect of the cumulative dosage, attention should be used since people with IPF have a higher chance of developing lung cancer (14). Although HRCT is the reference standard diagnostic technique, the increasing role of LUS as a nonradiative tool in lung assessment has emerged to avoid radiation risk. In LUS, first in patients with interstitial lung disease associated with scleroderma; the presence of multiple B lines has been shown to be an indicator of pulmonary diffuse interstitial disorder and a significant linear correlation between the total number of B lines and the tomographic score, laying the groundwork for future research.[5] Studies of LUS are increasingly focusing on various interstitial lung illnesses other than IPF. IPF patients have been a part of several pieces of research, yet there is still a shortage of information on how to assess IPF patients (6,15). This study contributes to the literature showing a positive correlation between LUS fibrotic scores and HRCT severity scores. With this data and further studies to support it, the early detection of ultrasound signs of worsening interstitial changes will provide an additional argument for earlier evaluation with an HRCT scan or even initiation of treatment.

The first restriction of the presented study is the short sample size. Because IPF is an uncommon disease with a median survival duration of 2 to 5 years following diagnosis, enrolling on this population may be challenging. More extensive

investigations are required to corroborate the experimental and encouraging results. However, despite the fact that it was single-centre research and hence had a smaller patient population, it allowed a single skilled practitioner to complete all of the ultrasonographic examinations. The consistency of the data and a better understanding of the role of ultrasonography in the follow-up may be gained if follow-up research employing a comparative assessment can be carried out.

In conclusion; LUS can be an additional and reliable tool for IPF, which is a rapidly progressing disease that requires a multidisciplinary approach, that can be used at the bedside or during a consultation, is easily accessible, does not emit radiation, can be reached in a short time and is instantly informative.

Conflict of interest

The authors declare that they have no potential conflict of interest, including any financial, personal or other relationships with the other people or organisations that could inappropriately influence or be perceived to influence the presented work. The authors have no relevant financial or non-financial interests to disclose.

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Informed consent was obtained from all individual participants included in the study. Informed consent was obtained from legal guardians. All participants signed the document stating they participated in the study.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Approval was granted by the Ethics Committee of Cukurova University (96/2020).

Authors' contributions

Concept: O.B.T, E.Ö., İ.H., S.K., E.G. Design: O.B.T, E.Ö., İ.H., S.K., E.G. Data Collection or Processing: O.B.T, E.Ö., İ.H., S.K., E.G., Analysis or Interpretation: O.B.T, E.Ö., İ.H., S.K., E.G., Literature Search: O.B.T, Writing: O.B.T, E.Ö., İ.H., S.K., E.G.

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