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● *Original Contribution*

INTEGRATIVE CARDIOPULMONARY ULTRASOUND FOR INTERSTITIAL LUNG DISEASE ASSESSMENT: CORRELATION BETWEEN LUNG ULTRASOUND PERFORMANCE AND CARDIAC INVOLVEMENT

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Abstract—The aims of this study were to apply integrative cardiopulmonary ultrasound (thoracic ultrasound) to the evaluation of patients with interstitial lung disease (ILD) and to determine the relationship between lung ultrasound signs and echocardiographic parameters such as systolic pulmonary artery pressure (SPAP) and various right ventricular parameters. ILD patients and healthy controls underwent lung ultrasound (LUS) and echocardiographic tests. In addition to traditional echocardiographic parameters, right ventricular free wall longitudinal strain (RVLS_FW) was measured using 2-D speckle-tracking echocardiography. The degree of pulmonary fibrosis or the disease severity of each ILD patient was scored with a semiquantitative scoring method, taking into account multiple LUS signs. Statistical analyses were performed to compare various parameters between ILD patients with and those without pulmonary hypertension. Correlations between the different parameters were then evaluated, and the LUS scores were used to predict pulmonary hypertension using a receiver operating characteristic curve analysis. Among the 90 patients who qualified for entry into this study, 30% (n = 27) had pulmonary hypertension. The patients with pulmonary hypertension had larger right ventricular dimensions, lower RVLS_FW and higher LUS scores. An effective correlation was found between ILD LUS scores and echocardiographic parameters, especially SPAP ($r = 0.735$, $p < 0.001$). The groups were comparable with respect to most echocardiographic parameters, with mild, moderate and severe pulmonary fibrosis, whereas SPAP was significantly higher in the moderate and severe groups. RVLS_FW was obviously reduced in the group with severe pulmonary fibrosis. Although RVLS_FW in the mild pulmonary fibrosis group was in the normal range, it was slightly reduced compared with that of the controls. A cutoff of more than 16 LUS points had 85.2% sensitivity and 80.3% specificity in predicting elevated SPAP (>36 mm Hg). Thoracic ultrasound is useful in the assessment of ILD. As ILD progresses, the structure or function of the right ventricle gradually deteriorates. LUS not only detects lung conditions in ILD, but also indirectly reflects SPAP and right ventricular function. Integrated use of LUS and echocardiography will provide an invaluable point-of-care imaging modality to facilitate the diagnosis, management and treatment of patients with ILD. (E-mail: Lxz_echo@163.com) **© 2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Interstitial lung disease, Integrative cardiopulmonary ultrasound, Systolic pulmonary artery pressure, Right ventricular parameters.**

INTRODUCTION

Interstitial lung disease (ILD) is a heterogeneous group of lung disorders with similar clinical, radiographic, pathologic or physiologic manifestations, and is characterized by inflammation and fibrosis of the pulmonary parenchyma (Wallis and Spinks 2015). ILD patients frequently develop pulmonary hypertension (PH), which often leads to right ventricular dysfunction (Caminati et al. 2013). In particular, survival is directly related to the capacity of the right ventricle to adapt to the elevated pulmonary vascular load (Lettieri et al. 2006).

Although high-resolution computed tomography (HRCT) remains the gold standard for diagnosis of ILD, lung ultrasound (LUS) has emerged during the past 15 y as an important imaging tool in diagnosis of ILD and other lung conditions. Echocardiography (Echo) is used to evaluate cardiac involvement in ILD and remains the best non-invasive screening tool for PH.

In a cross-sectional study of patients with idiopathic pulmonary fibrosis, Nathan et al. (2008) found that echocardiographic assessment of systolic pulmonary artery

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pressure (SPAP) was not sufficiently accurate for the assessment of PH, as nearly a third of patients with normal SPAP measured by echocardiography had PH when diagnosed by right heart catheterization (RHC). Recently, Zheng et al. (2015) found that the number of B-lines positively correlated with SPAP, and the cutoff value (number of B-lines >4) predicted elevated SPAP (>30 mm Hg). However, their study took only the B-lines into account, which is just one of the parameters of the LUS test for ILD. So it is feasible to use LUS as a complement to evaluate SPAP.

The integrative cardiopulmonary ultrasound approach, also called thoracic ultrasound (TUS), is an emerging technique that combines LUS and Echo to evaluate lung and cardiac conditions simultaneously, especially in the critical care setting (Lichtenstein and Karakitsos 2012). Moreover, TUS is easily available at the bedside and is a real-time procedure that is free of radiation hazards compared with conventional imaging modalities. However, few studies have applied TUS to the diagnosis and management of ILD.

Thus, in the present study, we employed the TUS approach to comprehensively assess the pulmonary and cardiac condition of ILD patients. We further determined various clinical and ultrasound parameters associated with pulmonary hypertension in ILD patients and investigated the relationship between ILD LUS and echocardiographic parameters.

METHODS

Study population

The diagnosis of ILD was based on clinical manifestations, serologic tests, pulmonary function tests (PFTs) and HRCT findings. Computed tomography-guided percutaneous lung biopsy was also performed for some cases (n = 34). Exclusion criteria were (i) infection of the respiratory tract as well as serious left ventricular failure; (ii) another underlying lung disease such as chronic obstructive pulmonary disease; (iii) history of pulmonary surgery; and (iv) poor imaging quality. The study was approved by the Faculty of Medicine Ethics Committee of Capital Medical University, and informed consent was freely obtained from all participants. In addition, 30 age- and sex-matched healthy controls were also recruited as a comparison cohort.

Lung ultrasound

Lung ultrasound was performed using a Philips iE33 ultrasound machine (Philips Healthcare, Andover, MA, USA) with the patient in the sitting or supine position. Each intercostal space available in the tests was assessed. To facilitate the recording of lesion locations, they were divided into upper, middle and lower fields. A multiphase-array probe (1.0–5.0 MHz) and a linear probe (3.0–11.0 MHz) were used to scan B-lines and pleural lines, respectively.

A semiquantitative LUS evaluation method (Buda et al. 2016) was used to analyze the sonographic findings for ILD (Table 1). B-Lines were defined as well-defined, vertical, hyper-echoic dynamic lines originating from the pleural lines and spreading like a laser ray up to the edge of the screen (Lichtenstein et al. 1997) (Fig. 1a), and were counted in real time when they were most clearly visible.

Echocardiography

Standard echocardiography was performed with a multiphase-array probe in accordance with the recommendations of the American Society of Echocardiography (Lang et al. 2015). Chamber dimensions and left ventricular ejection fraction (LVEF) were measured using the two-dimensionally guided M-mode method and the biplane Simpson method, respectively. Right ventricular fractional area change (RV FAC) was measured in an apical four-chamber view. Right ventricular dimensions were defined as basal, mid-cavity in an apical four-chamber view. RV outflow tract dimensions (at the proximal or subvalvular level at the distal or pulmonic valve and tricuspid annular plane systolic excursion [TAPSE]) were also measured. Similarly, we measured the diameters of the main, left and right pulmonary arteries. In addition, some tissue Doppler echocardiography parameters were measured, including tricuspid annulus peak velocity (S', e', a') and myocardial performance index (MPI). SPAP was estimated on the basis of peak tricuspid regurgitation (TRV), taking into account the right atrial pressure (RAP) as described by the simplified Bernoulli equation. The severity of tricuspid regurgitation was reflected by the regurgitation area.

Table 1. Semiquantitative method used to score lung ultrasound (Buda et al. 2016)

Lung ultrasound abnormality*	Grade	Extent score†		
		Pulmonary field 1	Pulmonary field 2	Pulmonary field 2
White lung	1	2	3	4
Irregular pleural line	2	3	4	5
B-Lines (<3)	3	4	5	6
B-Lines (≥4)	4	5	6	7
Blurred pleural lines	5	6	7	8
Am lines	6	7	8	9

* Irregular pleural line and blurred pleural lines revealed in Figure 1(b,c). Am-lines are Subpleural, horizontal and numerous reverberation artifacts (arranged in parallel, one under the other) arising from pleural lines and running to the edge of the screen—wide at the base and narrow at the top.

† Mild pulmonary fibrosis, 3–14 points; moderate pulmonary fibrosis, 15–20 points; severe pulmonary fibrosis, 21–35 points.