Platythorax increases residual volume/total lung capacity in idiopathic pleuroparenchymal fibroelastosis

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To the Editor:

Idiopathic pleuroparenchymal fibroelastosis (iPPFE) is a chronic progressive interstitial lung disease (ILD) characterised by upper lobe-dominant elastofibrosis [1]. Patients with iPPFE exhibit physical features such as emaciation, platythorax and deepened suprasternal notch [1]. In most patients with restrictive lung disease, the vital capacity (VC), residual volume (RV) and total lung capacity (TLC) decrease proportionately without affecting the RV/TLC ratio [2, 3]. Pulmonary physiology in patients with iPPFE is notable due to the markedly decreased VC and increased RV/TLC ratio [1, 4–6]. This deviation from the typical pattern observed in most patients with restrictive lung diseases raises questions regarding the mechanism underlying increased RV/TLC ratio in patients with iPPFE. Researchers have postulated that platythorax and hyperinflation in the lower lobes are potential contributors to an increase in the RV/TLC ratio in patients with iPPFE [4, 6–11]. This study aimed to elucidate the mechanism underlying the increase in the RV/TLC ratio in patients with iPPFE.

We conducted an observational retrospective study including patients diagnosed with iPPFE between 2011 and 2022 at the Fukuoka University Chikushi Hospital (Japan). The inclusion criteria were patients aged ⩾20 years who were diagnosed according to the proposed criteria for iPPFE [5], and who underwent simultaneous chest computed tomography (CT) and pulmonary function tests at diagnosis. Patients with concurrent pneumonia, pneumothorax, pneumomediastinum or lung cancer detected on CT examination at diagnosis were excluded. We estimated the flat chest index as the radiological extent of platythorax [8, 12]. The flat chest index was defined as the ratio of the anteroposterior diameter of the right thoracic cage to the transverse diameter of the thoracic cage on chest CT images at the level of the sixth thoracic vertebra, as previously described [8, 12]. ILD complicated in the lower lobes of patients with iPPFE was defined as any fibrotic lesion other than PPFE in the lower lobes. Three-dimensional (3D) images were constructed and volumetric analysis was performed to quantify lung volume in each lobe using SYNAPSE VINCENT (version 5.3; Fujifilm Medical Systems, Tokyo, Japan). The quantified lung volumes were standardised by dividing them by the predicted value of forced vital capacity (FVC), as previously described [13]. If a patient underwent CT or pulmonary function tests 12±6 months after diagnosis, the annual changes in standardised lung volume, flat chest index and pulmonary function parameters were calculated using the following formula:

$$\text{Annual change in parameter} = \frac{(\text{value at } 12 \pm 6 \text{ months after diagnosis}) - (\text{value at diagnosis})}{\text{interval, years}}$$

Continuous data are presented as mean±SD. The paired t-test or Wilcoxon test was used to evaluate differences in paired data. Pearson's correlation coefficients were used to examine the associations between the parameters. Statistical significance was set at $p<0.05$. All statistical analyses were performed using the R software (version 4.1.0; R Foundation for Statistical Computing, Vienna, Austria).

This study consisted of 57 patients with iPPFE (38 men and 19 women) with a mean age of 72.7 years. The body mass index was 17.9±3.11 $kg \cdot m^{-2}$, FVC 69.3±23.0% pred, forced expiratory volume in 1 s (FEV_1)/FVC 90.4±9.39%, RV 93.3±26.9% pred, TLC 80.9±19.1% pred, RV/TLC 118±29.6% pred and diffusion capacity for carbon monoxide 94.3±33.9% pred.

Shareable abstract (@ERSpublications)
Platythorax significantly contributes to the increase in residual volume/total lung capacity ratio in patients with idiopathic pleuroparenchymal fibroelastosis https://bit.ly/3uZ0rmP

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Correlation analysis between the flat chest index and pulmonary function parameters at diagnosis showed that the flat chest index positively correlated with FVC % pred (r=0.557, p<0.001) and TLC % pred (r=0.548, p<0.001), and inversely correlated with RV/TLC % pred (r= −0.404, p=0.007) (figure 1a). Furthermore, in the analyses of annual changes, the flat chest index positively correlated with FVC % pred (r=0.469, p=0.008) and TLC % pred (r=0.494, p=0.032), and inversely correlated with RV/TLC % pred (r= −0.526, p=0.021) (figure 1a). The RV/TLC % pred increases in patients with obstructive lung disease or air trapping, as well as in those with platythorax or hyperinflation [2, 3]. To investigate their influence, we examined the correlation between RV/TLC %pred and FEV_1/FVC and between RV/TLC %pred and VC-FVC. However, no correlations were observed between RV/TLC % pred and FEV_1/FVC (r=0.247, p=0.111), or between RV/TLC % pred and VC−FVC (r= −0.012, p=0.935) at diagnosis.

The annual changes in standardised lung volume were quantified in 42 patients. Among the 42 patients or patients with iPPFE with ILD in the lower lobes (n=25), standardised total lung volume, upper-lobe volume and lower-lobe volume decreased significantly between diagnosis and 12±6 months after diagnosis (figure 1b). In patients with iPPFE without ILD in the lower lobes (n=17), the standardised total lung volume and lower-lobe volume were equivalent between diagnosis and 12±6 months after diagnosis, but upper-lobe volume decreased significantly. An increase in the standardised lower-lobe volume between diagnosis and 12±6 months after diagnosis was observed in 10 (23.8%) of the 42 patients. We compared the clinical characteristics between patients with increased lower-lobe volume and those with decreased lower-lobe volume. However, there were no significant differences in the clinical characteristics between the groups.

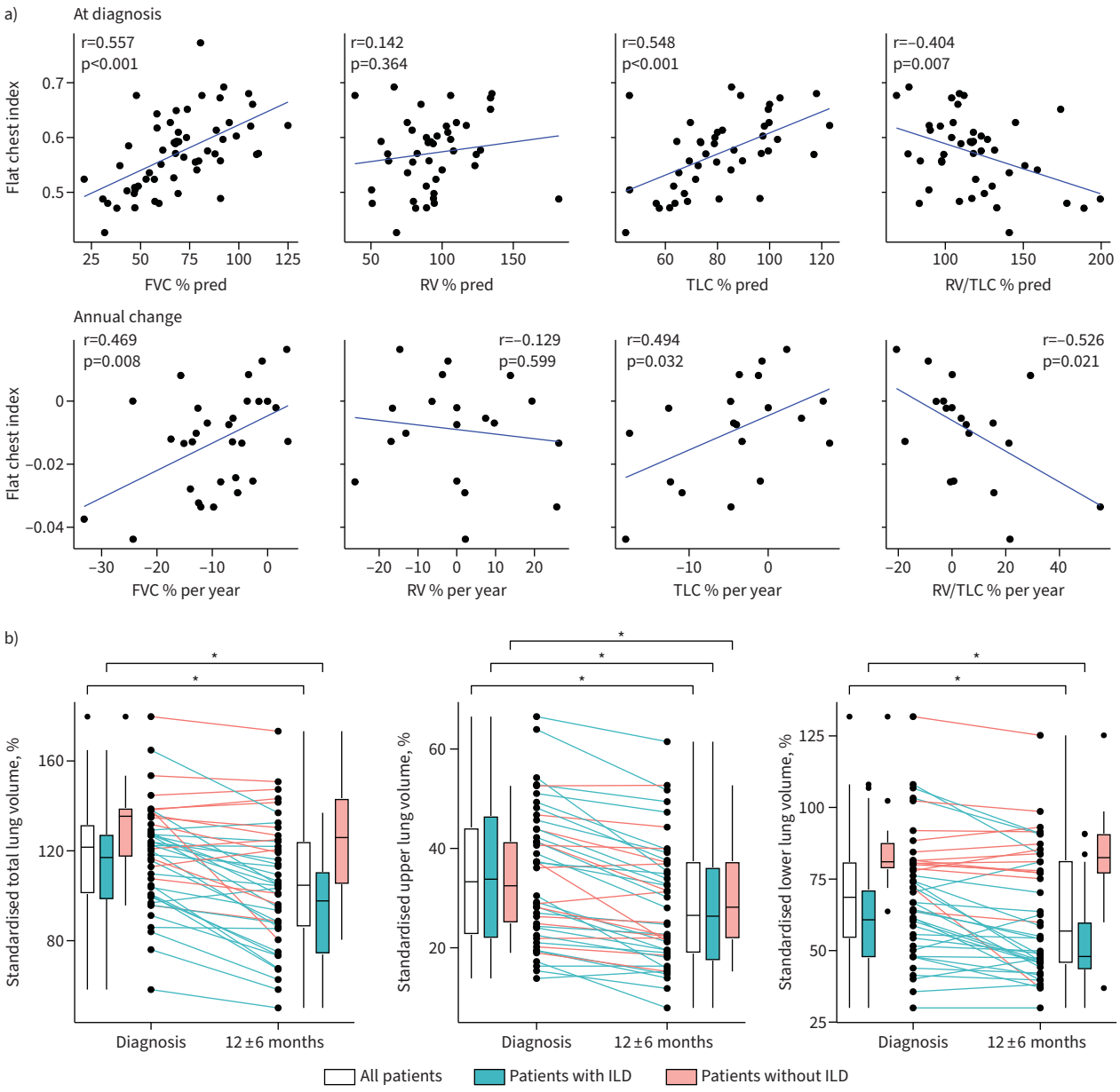
Correlation analysis between standardised lung volume and pulmonary function parameters at diagnosis showed moderate or strong correlations between the standardised total lung volume and FVC % pred (r=0.665), RV % pred (r=0.643) and TLC % pred (r=0.877); between upper-lobe volume and FVC % pred (r=0.416) and TLC % pred (r=0.545); and between lower-lobe volume and RV % pred (r=0.552) and TLC % pred (r=0.578) (figure 1c). In the analyses of annual changes, moderate or strong correlations were found between the standardized total lung volume and FVC % pred (r=0.677) and TLC % pred (r=0.613), upper-lobe volume and FVC % pred (r=0.590), and lower-lobe volume and FVC % pred (r=0.410) and TLC % pred (r=0.674) (figure 1c). However, no correlation was observed between RV/TLC % pred and standardised lung volume at diagnosis and in an annual change analysis.

Patients with iPPFE have a markedly decreased VC, mild decrease in TLC, and normal or mildly increased RV, resulting in an increased RV/TLC % pred [6]. This distinctive pattern is labelled as “complex restriction pattern” and is associated with conditions that impair lung emptying, such as chest wall restriction, occult obstruction or neuromuscular disease [2, 3]. The causes of chest wall restriction include chest wall deformities (congenital or acquired), burn scars on the chest wall, obesity and respiratory muscle weakness [3, 14]. Although the previous study showed that the flat chest index correlated with RV/TLC % pred at diagnosis in patients with iPPFE [15], this study showed that the flat chest index consistently and inversely correlated with RV/TLC % pred in patients with iPPFE, not only at diagnosis but also in the annual change analysis. Therefore, it is reasonable to postulate that chest wall restriction contributes to the increase in RV/TLC % pred in patients with iPPFE.

Decreased compliance of the upper lobes in patients with iPPFE could trigger compensatory hyperinflation in the lower lobes [7]. Fukada *et al.* [13] measured lung volume in patients with iPPFE using 3D-CT and showed that the standardised lower-lung volume were larger in patients with iPPFE without ILD in the lower lobes compared to healthy controls. The present study showed that 23.8% of patients with iPPFE exhibited an increase in standardised lower-lung volume during 1-year follow-up. Therefore, in some patients with iPPFE, the lower lobes may be inflated over time. Meanwhile, as our study revealed no correlation between the standardised lower-lobe volume and RV/TLC % pred, hyperinflation is unlikely to contribute to the increase in RV/TLC % pred in patients with iPPFE.

The present study had several limitations. First, this was a single-centre retrospective study with a relatively small number of patients because of the rarity of the disease, potentially introducing patient selection bias. Second, the 1-year interval may be too short to examine time-dependent changes in lung volume in patients with iPPFE. Nonetheless, given the progressive nature of PPFE, with a poor prognosis, further extension of the interval may have increased the number of deaths and made the analysis more difficult.

In conclusion, the flat chest index consistently and inversely correlated with RV/TLC % pred at diagnosis and in an annual change analysis among patients with iPPFE. Meanwhile, no correlation was found between the standardized lower-lobe volume and RV/TLC % pred in patients with iPPFE. Hence, the



c)

	FVC % pred	RV % pred	TLC % pred	RV/TLC % pred
At diagnosis				
Standardised total lung volume	0.665*	0.643*	0.877*	−0.046
Standardised upper lobe volume	0.416*	0.337*	0.545*	0.04
Standardised lower lobe volume	0.377*	0.552*	0.578*	−0.016
Annual change				
Standardised total lung volume	0.677*	0.185	0.613*	−0.168
Standardised upper lobe volume	0.59*	0.015	0.381	−0.278
Standardised lower lobe volume	0.41*	0.272	0.674*	−0.098

FIGURE 1 a) Correlation between the flat chest index and each pulmonary function parameter in patients with idiopathic pleuroparenchymal fibroelastosis (iPPFE). The upper panels show the scatterplot at diagnosis and the lower panels show the annual change analyses. b) Standardised total lung volumes, upper-lung volumes and lower-lung volumes at diagnosis and 12±6 months after diagnosis in patients with iPPFE. In patients with iPPFE, the standardised total lung volume, upper-lobe volume and lower-lobe volume decreased significantly between diagnosis and 12±6 months after diagnosis (118±23.3% *versus* 104±27.6%, p<0.001; 34.4±13.7% *versus* 28.9±12.6%, p<0.001; 69.7±21.4% *versus* 63.1±21.9%, p<0.001). In patients with iPPFE with interstitial lung disease (ILD) in the lower lobes, the standardised total lung volume, upper-lobe volume, and lower-lobe volume also decreased significantly (111±21.6% *versus* 94.8±22.8%, p<0.001; 35.0±15.1% *versus* 28.3±13.5%, p<0.001; 61.9±19.7% *versus* 53.6±6.2%, p<0.001). In patients with iPPFE without ILD in the lower lobes, the standardised total lung volume and lower-lobe volume were equivalent (132±20.9% *versus* 124±26.1%, p=0.111; 85.3±16.0% *versus* 82.1±19.6%, p=0.251), but upper-lobe volume decreased significantly (33.4±10.6% *versus* 30.0±10.9%, p=0.022). *: p<0.05. c) Correlation coefficients (r) between pulmonary function parameters and standardised lung volume in patients with iPPFE. FVC: forced vital capacity; RV: residual volume; TLC: total lung capacity. *: p<0.05.

platythorax plays a central role in increasing RV/TLC in patients with iPPFE. Understanding these mechanisms sheds light on the complex physiology of patients with iPPFE and has implications for its diagnosis and management.

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