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Prediction of pulmonary function decline in fibrous interstitial lung abnormalities based on quantitative chest CT parameters

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Abstract

Background Interstitial lung abnormalities (ILA) are a proposed imaging concept. Fibrous ILA have a higher risk of progression and death. Clinically, computed tomography (CT) examination is a frequently used and convenient method compared with pulmonary function tests. This study aimed to correlate quantitative CT airway parameters with pulmonary function parameters in patients with fibrous ILA, with the goal of establishing a prediction model for abnormal pulmonary function parameters in patients with fibrous ILA.

Methods Ninety-five cases of fibrous ILA including CT images and 64 normal control cases were collected. All patients completed pulmonary function tests within one week. The airway parameters of the CT images of the two groups of cases were measured using a commercial software (Aview). Differences in airway parameters and lung function parameters between the two groups were analyzed by logistic multifactorial regression. The correlation between airway parameters and lung function parameters among 95 patients with fibrous ILA and a prediction model was determined for the decreased percentage forced vital capacity to predicted normal value (FVC%pred) in patients with fibrous ILA.

Results Logistic multifactorial regression correlated FVC%pred and bronchial wall thickness (WT) were correlated with fibrous ILA. The 95 patients with fibrous ILA were divided into normal FVC%pred ($n=69$) and decreased FVC%pred ($n=26$) groups at the 80% cut-off. Logistic multifactorial regression revealed that FVC%pred decline in patients with fibrous ILA was effectively predicted by age (odds ratio [OR]: 1.11, 95% confidence interval [CI]: 1.02–1.21, $p=0.014$), gender (OR: 4.16,95% CI: 1.27–13.71, $p=0.019$), luminal area of the sixth generation brochi (LA_6; OR: 0.87, 95%CI: 0.78–0.970,$p=0.015$), and airway wall area (WA; OR: 1.12, 95%CI: 1.02–1.24, $p=0.020$) were effective predictors of. The area under the curve of the prediction model based on the four parameters was 0.8428.

Conclusion WT is a quantitative CT biomarker and FVC%pred is a valid lung function parameter in fibrous ILA patients. Age, gender, LA_6, and WA are effective predictors of FVC%pred decline in fibrous ILA patients. The combined model has good predictive value.

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Keywords Interstitial lung abnormalities, Pulmonary function test, Quantitative computed tomography

Introduction

Interstitial lung abnormalities (ILA) are defined as non-dependent changes affecting more than 5% of any lung zone that are incidentally detected when patients undergo chest computed tomography (CT). ILA include non-dependent ground-glass or reticular abnormalities, non-emphysematous cysts, honeycombing, and traction bronchiectasis [1]. Depending on the type of lesion, ILA can be classified as fibrous (reticular abnormalities, honeycombing, tractional bronchiectasis) and non-fibrous (ground-glass, mosaic sign, consolidation) [2]. Subpleural reticular abnormalities, lower lobe predominant changes, traction bronchiectasis, and honeycomb-like changes are imaging features associated with disease progression in ILA [3].

The presence of ILA in smokers and former smokers are associated with mortality and lung function impairment [4]. Unlike the diagnosis of chronic obstructive pulmonary disease (COPD), according to the GOLD guidelines, the diagnosis of COPD is a ratio of <0.70 for forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) after inhalation of bronchodilation [5]. Study findings regarding changes in lung function in patients with ILA have not been entirely consistent; in a recent study, a lower FVC was an independent risk factor for patients with ILA compared to those without ILA [6]. In a cardiac-oriented study, patients with progressive ILA displayed an accelerated decline in spirometry (FVC) measurements compared to patients without ILA or non-progressive ILA; this decline was consistent with imaging progression [7]. Another study of patients with COPD featuring ILA reported a higher annual rate of decline in FVC and FEV_1 in patients with ILA progression compared to those without progression [8]. Due to the limitations of pulmonary function tests, quantitative CT parameters are used for airway characteristics in objective and noninvasive analyses, such as emphysema, large airway remodeling and expired air trapping. A study showed that an internal perimeter of 10 mm (Pi10) could be used as a biological marker of fibrous ILA and revealed that smoking affects airway remodeling [9]. Patients with COPD combined with ILA reportedly have higher wall thickness indices compared to those without ILA [10]. However, fewer studies have addressed the combination of lung function and quantitative CT parameters.

This paper describes a study undertaken to investigate the changes in lung function parameters and quantitative CT airway parameters in patients with fibrous ILA, as well as the airway changes in those with abnormal lung function parameters. The goal is to develop a prediction model for abnormal lung function parameters in patients with fibrous ILA.

Materials and methods

Study subjects

This retrospective study was approved by the Institutional Ethics Committee of Huadong Hospital Affiliated Fudan University (approval number: 2024K249). Informed consent was waived. We confirmed that the procedures were performed in full compliance with the relevant guidelines and regulations. Data were collected retrospectively from patients who had completed a chest CT examination and pulmonary function tests within a week of each other from August 2022 to September 2023. Patients with poor CT images and those with other serious diseases of the chest (e.g., asthma, COPD, and those who had undergone lung surgery) were excluded. Two radiologists (S.Y.L and L.D.C, with 10 and 3 years' experience, respectively, in thoracic radiology) separately evaluated CT images. Established diagnostic criteria [11] used were incidental identification of non-dependent abnormalities, including ground-glass with reticular abnormalities, lung distortion, traction bronchiectasis, honeycombing, and non-emphysematous cysts; involvement of at least 5% of a lung zone (upper, middle, and lower lung zones demarcated by the levels of the inferior aortic arch and right inferior pulmonary vein); and individuals not suspected of having interstitial lung disease. Finally, 95 patients with fibrous ILA were included in the study. Sixty-four healthy individuals were included as controls. The patients with fibrous ILA were divided into a group with normal percentage forced vital capacity to predicted normal value (FVC%pred; $n=69$) and a group with decreased FVC%pred ($n=26$) at a cut-off of 80%. The enrollment flowchart of patients is shown in Fig. 1.

Pulmonary function tests

All pulmonary function tests were performed within one week of the CT scan and followed the joint American Thoracic Society/European Respiratory Society pulmonary function test guidelines [12] on a Jaeger Master Screen Pro pulmonary function system (Jaeger Ltd., Hochberg, Germany). Prior to the lung function test, patients sat in a chair and the examining physician introduced and demonstrated the essentials of the lung function test in detail and guided practice. The following parameters were measured using a spirometer: FVC, FEV_1, FEV_1/FVC, maximal mid-expiratory flow, diffusing capacity of the lungs for carbon monoxide (DLCO), ratio of DLCO to change in concentration of inhaled gas after dispersal in the lungs (V_A) (DLCO/V_A), residual volume

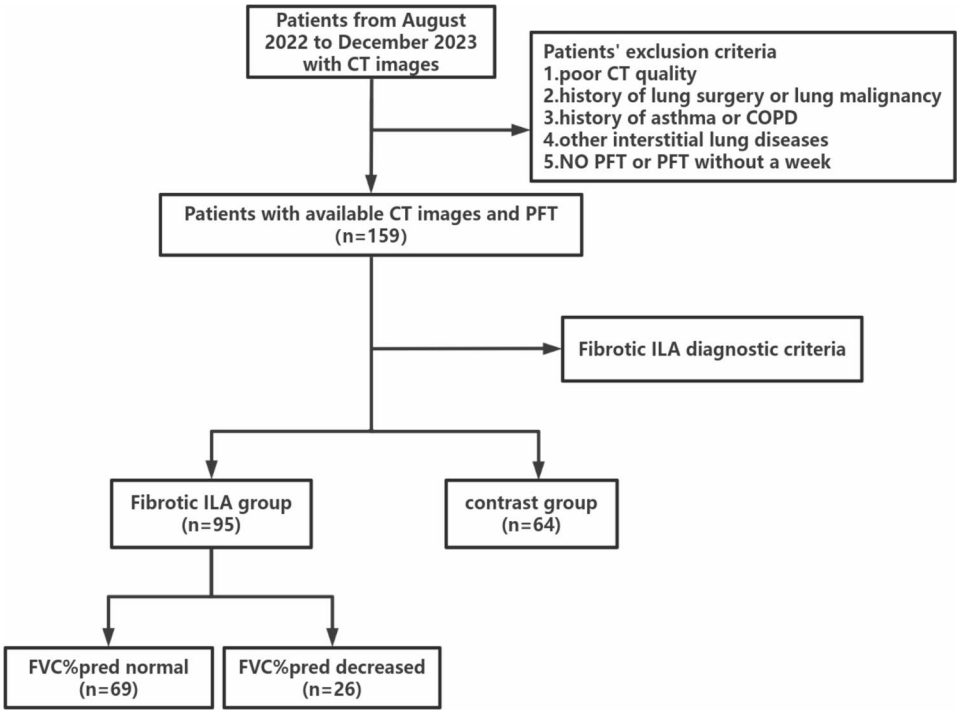

Fig. 1 Flowchart of the study population

of air (RV), total lung capacity (TCL), and RV/TCL. Each test was performed a maximum of three times, with the best value used for subsequent analyses.

CT examination

All CT scans were performed using Somatom Definition Flash, Somatom and Sensation-16 (Siemens Medical Solutions, Malvern, PA, USA), and GE Discovery CT750 HD, 64-slice LightSpeed VCT (GE Medical Systems, Chicago, IL, USA) scanners. The scan parameters were: 120 kVp; 100–200 mAs; pitch, 0.75–1.5; and collimation, 1–1.5 mm. All image data used a standard (STND)/medium sharp reconstruction algorithm. Patients underwent chest CT scan at full inspiration in the supine position.

Quantitative CT assessment of airway parameters

All CT images were evaluated using commercial software (Aview, Coreline Soft, Seoul, Korea). Airways were automatically segmented using a three-dimensional quantitative algorithm. All quantitative parameters were automatically collected from inspiratory CT. Airway parameters included: Pi10; branchcount, mean luminal area (LA), mean airway wall thickness (WT), mean wall area (WA), and airwall area percent (WAF); emphysema parameters (whole-lung volume, whole-lung mean, whole-lung count, whole-lung skewness, whole-lung kurtosis, whole-lung E-kurtosis, whole-lung LAA (low attenuation area), and whole-lung LAA%). Pi10 was the square root of the WA of a hypothetical airway with 10 mm internal perimeter, which was a useful measure of airway WT obtained by calculating a regression line plotted from the square root of the WA of internal perimeters of multiple airways at different locations [13]. WT, airway WA percent (WA%), and LA were calculated from the average of whole-lung fifth-, sixth-, seventh-, and eighth-generation, and whole-lung bronchial values. All quantitative parameters were automatically measured by the software and manually corrected in case of deviation. The tracheobronchial tree generated by three-dimensional reconstruction is shown in Fig. 2.

Statistical analyses

SPSS (Version 24.0, IBM SPSS Statistics Software, Chicago, IL, USA) was utilized for statistical analyses and plotting. Parametric data are expressed as mean ± standard deviation. Nonparametric data are expressed as numbers and percentages. Independent sample t-test was used to compare normally distributed continuous variables. The Mann–Whitney U test was used for non-normally distributed data. Clinical and imaging factors with $p < 0.05$ between the two groups were used as input variables for binary logistic regression with a stepwise selection method to identify predictors. A nomogram model was constructed using the R language (Version 4.4.0, R Core Team, Vienna, Austria), and calibration curves were plotted to evaluate the goodness of fit of the nomogram graphs. Receiver Operating Characteristic (ROC) curves

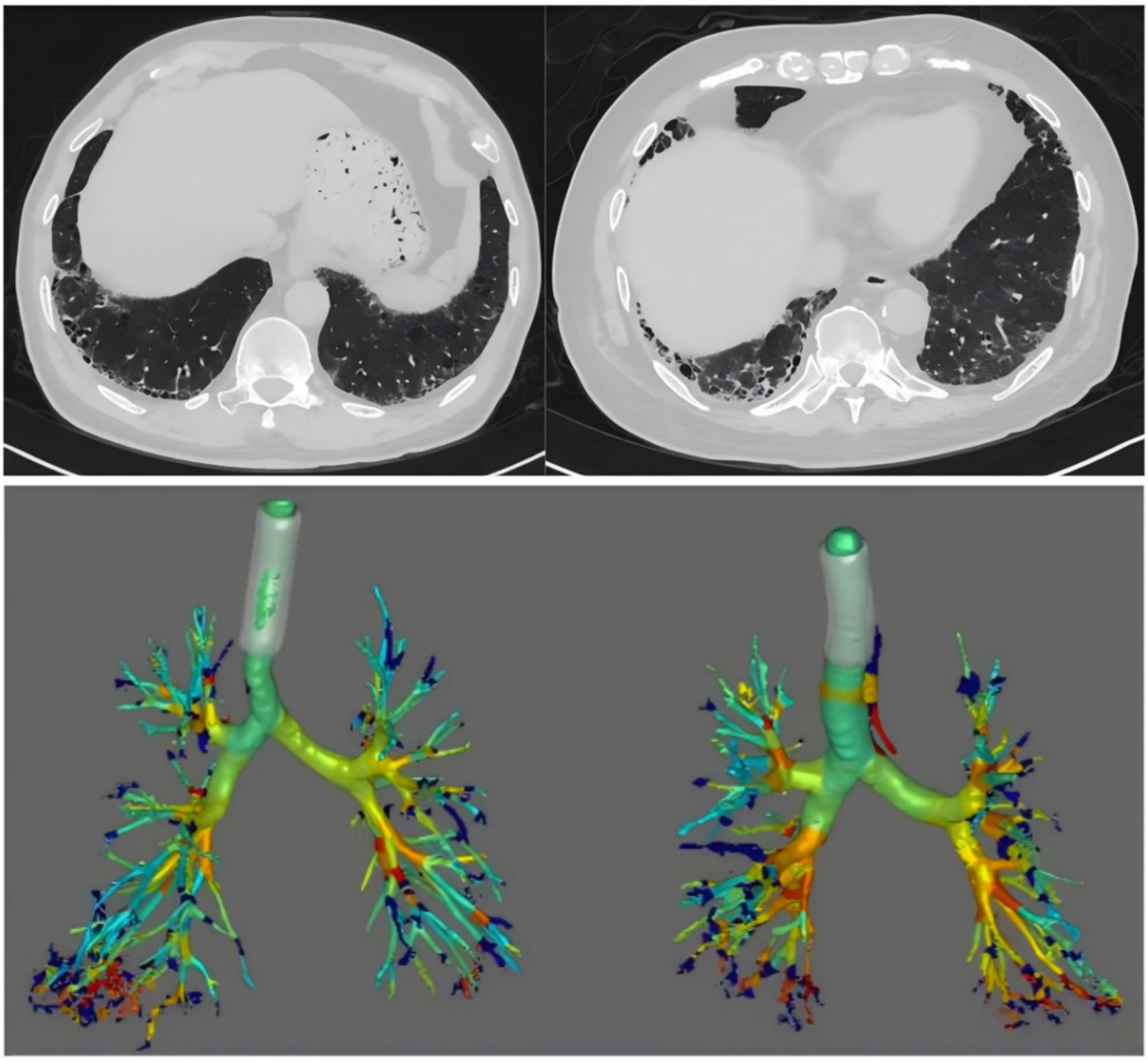

Fig. 2 CT images and tracheobronchial tree generated by three-dimensional reconstruction in two fibrous ILA patients. A: Case with a normal FVC%pred of 85%. The luminal area of the sixth bronchi was 15.9 mm^2 and the wall area was 19.3mm^2. B: Case with a declined FVC%pred of 65%. The luminal area of the sixth bronchi was 14.0 mm^2 and the wall area is 27.8 mm^2

were plotted using MedCalc (Version 16.8.4, MedCalc Software, Ostend, Belgium) and the model and each predictor efficacy were evaluated using the DeLong test was used to compare the differences in Area under curve (AUC) of each ROC curve.

Results

Multivariate regression analysis in fibrous ILA group and control group

Multivariable logistic regression analyses revealed significant difference between the fibrous ILA normal control groups for age (odds ratio [OR]: 1.21, 95% confidence interval [CI]: 1.12–1.30, $p < 0.001$), FVC% (OR: 0.94, 95%CI: 0.90–0.99, $p < 0.001$), DLCO% (OR: 0.96, 95%CI: 0.93–0.99, $p < 0.001$), WT (OR: 16.15, 95%CI: 1.65-158.02, $p = 0.002$), whole-lung LAA (OR: 1.47, 95%CI: 0.93–2.33, $p = 0.005$).

Univariable regression analysis in the decreased FVC%pred group and normal group

The 95 patients with fibrous ILA were divided into a group with normal FVC%pred (n = 69) and a group with decreased FVC%pred (n = 26) at a cut-off of 80%. The aforementioned parameters were differentiated; gender; age; Pi10 and Pi10 of the sixth-, seventh-, and eighth-generation bronchi; branchcount of the seventh- and

Table 1 Clinic features and imaging parameters of patients

Variables	Total ($n=95$)	0 ($n=69$)	1 ($n=26$)	p
Hight	1.66 ± 0.08	1.67 ± 0.08	1.65 ± 0.08	0.289
Weight	66.01 ± 9.76	66.91 ± 9.74	63.62 ± 9.57	0.144
BMI	23.89 ± 2.78	24.09 ± 2.88	23.37 ± 2.44	0.262
Age	72.92 ± 8.62	71.28 ± 9.09	77.27 ± 5.28	< 0.001
Gender	M (44.21)	M (34.78)	M (69.23)	0.003
PI10-LEVEL5	5.14 ± 1.30	5.06 ± 1.36	5.38 ± 1.09	0.288
PI10-LEVEL6	4.13 ± 1.11	3.98 ± 1.09	4.54 ± 1.07	0.027
PI10-LEVEL7	3.70 ± 0.80	3.57 ± 0.70	4.04 ± 0.97	0.011
PI10-LEVEL8	3.47 ± 0.81	3.35 ± 0.65	3.80 ± 1.10	0.048
PI10	3.67 ± 0.73	3.53 ± 0.62	4.05 ± 0.86	0.002
BRANCH-COUNT-LEVEL5	12.97 ± 3.85	13.01 ± 3.84	12.85 ± 3.97	0.851
BRANCH-COUNT-LEVEL6	26.13 ± 6.75	26.65 ± 6.70	24.73 ± 6.80	0.218
BRANCH-COUNT-LEVEL7	43.36 ± 11.63	45.25 ± 11.14	38.35 ± 11.62	0.009
BRANCH-COUNT-LEVEL8	53.80 ± 17.76	56.68 ± 16.48	46.15 ± 19.08	0.009
BRANCH-COUNT	326.21 ± 148.19	341.96 ± 139.59	284.42 ± 164.55	0.092
LA-LEVEL5	25.34 ± 10.82	26.64 ± 11.55	21.90 ± 7.77	0.057
LA-LEVEL6	16.46 ± 6.59	17.35 ± 6.75	14.12 ± 5.60	0.033
LA-LEVEL7	11.06 ± 4.34	11.61 ± 4.57	9.62 ± 3.35	0.047
LA-LEVEL8	8.67 ± 3.59	9.04 ± 3.57	7.69 ± 3.52	0.047
LA	9.86 ± 2.37	10.02 ± 2.33	9.46 ± 2.47	0.309
WT-LEVEL5	2.23 ± 0.41	2.20 ± 0.44	2.28 ± 0.32	0.400
WT-LEVEL6	1.67 ± 0.43	1.66 ± 0.40	1.71 ± 0.50	0.575
WT-LEVEL7	1.20 ± 0.28	1.18 ± 0.27	1.25 ± 0.32	0.251
WT-LEVEL8	0.95 ± 0.24	0.93 ± 0.21	1.01 ± 0.31	0.147
WT	1.10 ± 0.26	1.05 ± 0.23	1.23 ± 0.31	0.010
WA%-LEVEL5	67.44 ± 7.60	66.41 ± 7.80	70.15 ± 6.41	0.032
WA%-LEVEL6	62.98 ± 8.44	61.93 ± 8.29	65.78 ± 8.35	0.047
WA%-LEVEL7	58.11 ± 8.69	56.76 ± 7.70	61.69 ± 10.21	0.013
WA%-LEVEL8	55.24 ± 8.76	53.85 ± 7.63	58.92 ± 10.51	0.011
WA%	57.71 ± 8.82	56.09 ± 7.84	62.02 ± 9.93	0.003
WA-LEVEL5	57.24 ± 16.08	57.31 ± 16.86	57.06 ± 14.11	0.946
WA-LEVEL6	38.24 ± 16.22	38.69 ± 14.64	37.04 ± 20.11	0.662
WA-LEVEL7	22.31 ± 7.94	22.37 ± 7.89	22.16 ± 8.22	0.912
WA-LEVEL8	15.53 ± 6.33	15.51 ± 6.05	15.59 ± 7.14	0.954
WA	19.52 ± 5.55	18.36 ± 4.71	22.61 ± 6.47	0.004

Abbreviations: BMI body-mass index, Pi10 the square root of the wall area of a hypothetical airway with 10 mm internal perimeter, LA luminal area, WA airway wall area, WT wall thickness, WA% airway wall area percent

Table 2 Logistic regression analysis for prediction of fibrous ILA patients with declined FVC%pred

variables	OR (95%CI)	p
gender	4.16(1.27–13.71)	0.019
age	1.11 (1.02 ~ 1.21)	0.014
LA_6	0.87 (0.78 ~ 0.97)	0.015
WA	1.12 (1.02 ~ 1.24)	0.020

Abbreviations: CI confidence interval, OR odds ratio, LA_6 luminal area of the sixth generation brochi, WA airway wall area

eighth-generation bronchi; WT; WAF and WAF of the fifth-, sixth-, seventh-, and eighth-generation bronchi; WA (Table 1).

The 95 patients with fibrous ILA were additionally divided into a group with normal DLCO%pred ($n=20$) and a group with decreased DLCO%pred ($n=75$), with a cut-off of 80% for differentiation. The aforementioned airway parameters were not statistically significant ($p>0.05$).

Nomogram and calibration curves

After including the above variables with $p<0.05$ as input variables in the multivariate regression, age (71.28 ± 9.09 vs. 77.27 ± 5.28, $p=0.014$), gender (male (34.78%) vs. male (69.23%), $p=0.019$), LA_6 (17.35 ± 6.75 vs. 14.12 ± 5.60, $p=0.015$), and WA (18.36 ± 4.71 vs. 22.61 ± 6.47, $p=0.020$) were statistically significant in the decreased FVC%pred group. Four parameters were selected to construct the nomogram (Table 2). The nomogram of the model and the calibration curve used to visualize the performance of the nomogram are shown in Fig. 3, with the AUC values shown in Fig. 4. To demonstrate the clinical advantages of the nomogram, we compared the ROC curves of the single variables against the model. Respective age, gender, LA_6, and WA subject work characteristics (ROC) curves were 0.7074 (95%CI: 0.6009–0.8138), 0.6722 (95%CI: 0.5655–0.7789), 0.6583 (95%CI: 0.5295–0.7871), and 0.6927 (95%CI: 0.5613–0.8244). The data demonstrate that the model outperforms either single parameter.

Discussion

In this paper, we describe our investigated concerning the changes in quantitative airway parameters on CT in patients with fibrous ILA and the development of a model for predicting lung function abnormalities on CT images in patients with fibrous ILA.

In patients with fibrous ILA, the mean WT was thicker. Thus, airway abnormalities may play a role in or be associated with the early pathogenesis of pulmonary fibrosis. This is consistent with a recent study that concluded that patients with ILA develop airway wall thickening, even when ILA lesions are confined to the lower lobes of both lungs. The authors also observed that thicker airway WT in the upper lobes of both lungs and the right middle lobe

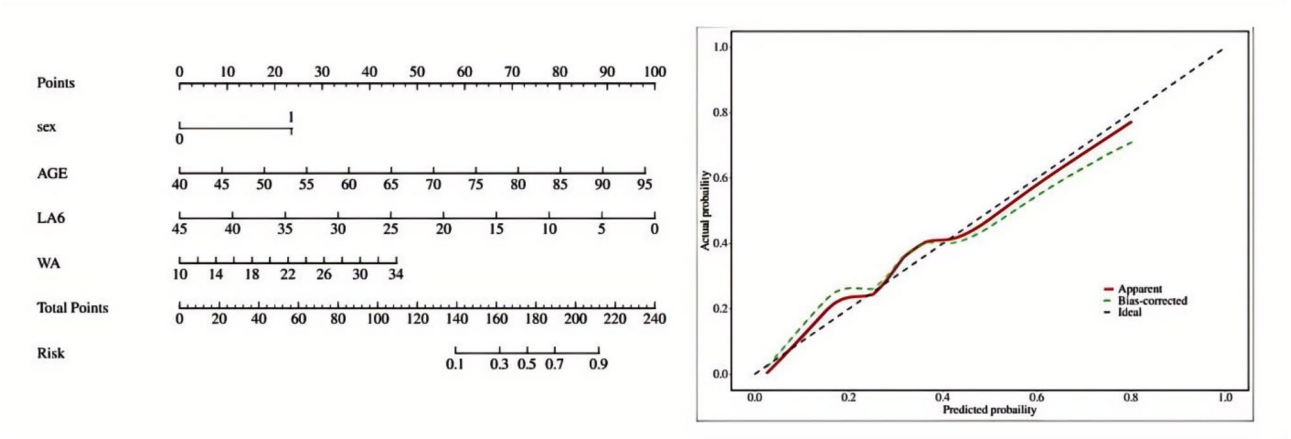

Fig. 3 Construction of the nomogram. a Nomogram predicting FVC%pred decline in fibrous ILA. b Calibration curves for the nomogram. Notes: 1 for males, 0 for females; $LA_{6,}$ the luminal area of the sixth- generation bronchi; WA, airway wall area

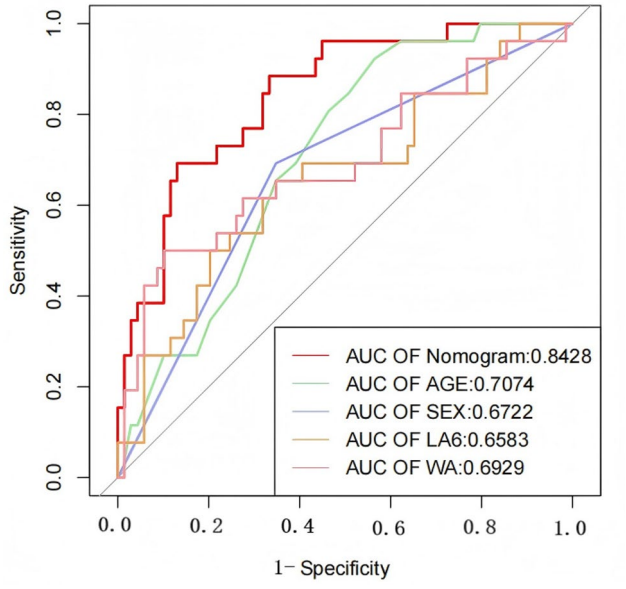

Fig. 4 ROC curves of the nomogram and the single variables. Notes: Combined is the model incorporating sex, age, luminal area of the sixth- generation bronchi (LA_6) and airway wall area (WA)

of the lungs of COPD patients with ILA than in patients without ILA [10]. In a histopathologic evaluation of lungs from patients with ILA, significant peribronchial inflammation (25% of samples) and peribronchial fibrosis (42% of samples) were present in early disease specimens [14], further evidence of wall remodeling occurred in the bronchi of the small and medium airways. The results of surgical resection of lung tissue, lung autopsy specimens, and transbronchial biopsy specimens indicate that bronchial wall thickening in the central and peripheral airways is due to subepithelial fibrosis, increased airway smooth muscle, increased vascularization of the airway wall, and mucus hypersecretion [15]. Studies have shown an increasing prevalence of ILA by age group; in one study, there were 4% of patients under 60 years of age compared to 47% of patients over 70 years of age [16]. Similarly, in our study, increasing age is a risk factor for the presence of ILA and the decreased FVC%pred (OR: 1.11, 95%CI: 1.02–1.21, $p=0.014$). In our study, we also showed that aging is a risk factor for ILA. In our study, gender was also a risk factor for the decreased FVC%pred gender (OR: 4.16, 95%CI: 1.27–13.71, $p=0.019$). In previous ILA studies, gender and smoking status were not identified as independent risk factors [8]. In the present study, male ILA patients were more likely to show a decreased FVC%pred. We speculate that gender might be related to smoking status and thus affect airway remodeling. Therefore, older men with fibrous ILA patients should be more closely monitored.

ILA has been demonstrated to cause changes in lung function in several studies, but the findings are not entirely consistent. Pulmonary function tests are important for assessing disease severity and predicting the risk of disease progression or death in patients with interstitial lung disease, in particular for measuring changes in FVC and DLCO, parameters that reflect the degree of restrictive ventilatory impairment of the lungs. At baseline, the degree of FVC and DLCO impairment is associated with short- and medium-term prognosis [17]. The trend of lung function changes in ILA is similar to the changes in lung function in ILD patients. In our study, significant decreases were evident in FVC%pred and DLCO%pred in fibrous ILA patients, which is more consistent with previous studies. Decreased lung function, especially FVC, were significantly associated with an increased risk of death from IPF [18]. Fibrous interstitial lung abnormalities are thought to represent early or mild pulmonary fibrosis [19]. Therefore, early recognition of the decreased FVC is important for the monitoring of fibrous ILA disease. Compared to patients with normal FVC%pred, increased airway wall thickness

(including the directly measured parameter of WT and the indirectly measured parameters of Pi10 and WA%) were increased in 26 patients with fibrous ILA with decreased FVC%pred. Multivariate logistic regression analysis revealed the significant association of WA (OR: 1.12, 95%CI: 1.02–1.24, $p = 0.020$) with decreased FVC%pred in fibrous ILA. Recent data have also shown that increased wall thickening of the central airways may be involved in the pathogenesis of ILA and IPF, and wall thickening may affect the prognosis of patients with IPF [20]. In addition, patients with fibrous ILA were associated with the lumen area of the sixth- generation bronchi (LA_6; OR: 0.87, 95%CI: 0.78–0.970, $p = 0.015$), suggesting that mucus accumulation may decrease the airway lumen area [21]. Therefore, WA and LA_6 can be used as effective quantitative CT biomarkers of the decreased FVC%pred, which can indicate the early stage of lung function changes in clinical practice and better control disease progression.

We selected age, gender, LA_6, and WA to construct a nomogram. The calibration curve used to visualize the performance of the nomogram was shown in Fig. 3. The nomogram evaluated the accuracy of the model and any potential model overfitting through a bootstrap verification of 1000 resamplings. The comparison between the actual and predicted risks displayed good consistency. To demonstrate the clinical advantages of the nomogram, we compared the ROC curves of the single variables against the model (Fig. 4). Age, gender, LA_6, and WA subject work characteristics (ROC) curves were 0.7074 (95%CI: 0. 0.6009–0.8138), 0.6722 (95%CI: 0.5655–0.7789), 0.6583 (95%CI: 0.5295–0.7871), and 0.6927 (95%CI: 0.5613–0.8244). The data demonstrate that the model outperforms either single parameter.

We also established a model of quantitative CT parameters incorporating LA_6, and WA to predict the decreased FVC%pred in patients with fibrous ILA. The model displayed good predictive ability (AUC = 0.8428), indicating that quantitative CT parameters can reflect the degree of lung function impairment to a certain extent. Lung function testing is important for assessing disease severity and predicting risk of disease progression or death in patients with interstitial lung disease. Unfortunately, performing lung function testing can be challenging and requires active patient cooperation [22]. In the process of testing, often because of a lack of cooperation by patients, the test results will be seriously affected. For patients with severe disease, it may not even be possible to complete a lung function test, so the effectiveness of the test is greatly reduced. Therefore, qualified lung function tests are not appropriate for elderly patients who cannot cooperate and patients with acute exacerbations or advanced stages. The accuracy of a pulmonary function test depends on the degree of patient cooperation, and CT scans require much less patient cooperation than lung function tests. Therefore, quantitative CT analysis may show greater value when patients are in poor physical condition or poorly matched. Moreover, with the implementation of lung cancer screening programs, CT tests have become more popular, but routine tests may not include lung function tests. Therefore, this model can be added to the lung cancer screening program in the future to facilitate timely monitoring of the course of the disease, especially when the patient has no obvious symptoms, the change of FVC may be an effective marker of disease deterioration and progression. The preferred Food and Drug Administration clinical trial end-point for therapeutic trials in ILD studies is change in FVC over time, which is acknowledged as an accepted surrogate for mortality [23]. Therefore, based on the results of the predictive model, a personalized screening and follow-up plan can be developed for patients, and patients with FVC decline can receive more frequently.

In addition, we found little difference in airway parameters in patients with decreased DLCO%pred. In a study on COPD, there was a mild correlation between DLCO and airway parameters, and only in patients with severe COPD was the correlation more significant [24]. Because ILA is an early manifestation, its early airway changes do not cause abnormalities in diffusion function, and it is only at a certain stage of ILA progression that the decreased DLCO%pred is affected. In addition, increased airway WT may reflect bronchial inflammation, in which increased angiogenesis and increased pulmonary blood flow may increase gas diffusion [25]. Therefore, the DLCO%pred mainly reflects the gas exchange capacity of the alveolar-capillary interface. Early changes in airway structure may affect the pulmonary ventilation function, but will not directly significantly change the DLCO%pred value. However, approximately 80% of patients in our study experienced a decrease in DLCO, possibly due to ILA primarily affecting the lung interstitium (including alveolar walls and capillaries), resulting in thickening of the gas diffusion membrane and decreased efficiency of alveolar gas exchange. In a study on early idiopathic pulmonary fibrosis that confirmed our suspicion, endobronchial optical coherence tomography revealed a significant loss of bronchioles (between 30% and 50%) in early IPF, even in areas least affected by the disease [26]. These findings support small airway disease as a feature of early IPF. Fibrosis of the lung interstitium disrupts the capillary network, further reducing the ability to exchange gas. Small blood vessel loss may also be a feature of ILA-related vascular disease [27].

There are some limitations of our study. Firstly, we have limited data about concurrent lung function and CT examination. The small sample size may have reduced the confidence of the study and increased the margin of error.

Future studies should be prospective and multicenter in design, with larger sample sizes. Secondly, due to the limited clinical information we obtained, patients' smoking history and other clinical information will be further included in the future using standardized survey tools or questionnaires to supplement missing data. Although smoking may affect airway remodeling to some extent, in previous ILA studies, smoking status was not identified as independent risk factors [1].Thirdly, even at high resolution, CT does not allow direct visualization of the small airways (< 2 mm in diameter), which consist mainly of the last eight parts of the airways, including the respiratory fine bronchi, alveolar ducts, and alveolar sacs [28]. Even though some studies have found that airways < 2 mm in diameter are in the seventh (or higher) generation bronchi [29], due to the limited resolution of CT, the WT of airway with diameter < 2 mm may be underestimated. In the future, we will continue to collect dual-phase images of patients and apply the more accurate algorithm [30–33] to further study small airway changes.

In summary, WT is a biological marker of quantitative CT in patients with fibrous ILA and FVC%pred is a validated lung function parameter in patients with fibrous ILA. In patients with decreased FVC%pred, increased wall area and decreased LA_6, age, gender, 、 LA_6, and WA were effective predictors of FVC%pred decline in patients with fibrous ILA. The combined model has good predictive value to guide early lung function monitoring and early intervention for fibrous ILA.

Abbreviations

ILA	Interstitial lung abnormality
COPD	Chronic obstructive pulmonary disease
FEV_1	Forced expiratory volume in 1 s
FVC	Forced vital capacity
PFT	Pulmonary function test
QCT	Quantitative computed tomography
WT	Wall thickness
LA	Luminal area
WA	Wall area
WA%	Wall area percent

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Author contributions
Dechun Li and Yingli Sun contributed to study design, manuscript writing and data analysis. Zonjing Ma contributed to data acquisition and analysis.Bin Chen and Liang jin contributed to study design and data interpretation. Ming Li contributed to study design and manuscript revision. All authors have read and approved the manuscript.

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Data availability
The data presented in this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate
This study was approved by Huadong Hospital Affiliated Fudan University institutional review boards. This was a retrospective study approved by Huadong Hospital Affiliated Fudan University institutional ethics committee and informed consent was waived. We confirmed that the procedures were performed in full compliance with the relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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