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INTERSTITIAL LUNG DISEASE

Oscillometry and computed tomography findings in patients with idiopathic pulmonary fibrosis

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ABSTRACT Although the utility of oscillometry for predicting disease severity in idiopathic pulmonary fibrosis (IPF) had been researched, little has been reported on the mechanism of why respiratory impedance reflects disease severity. In addition, traction bronchiectasis has been considered to reduce respiratory resistance and correlate negatively with airflow obstruction, but this hypothesis has not been validated. The present study aimed to investigate the correlations between oscillometric parameters and fibrosis-related lung abnormalities in IPF and to assess the utility of oscillometry as a surrogate marker for traction bronchiectasis and airflow obstruction.

Eighty Japanese patients with IPF underwent high-resolution computed tomography (HRCT), spirometry, and oscillometry and were retrospectively investigated. Fibrosis-related HRCT findings were scored regarding airspace consolidation, honeycombing, architectural distortion, traction bronchiectasis, and fibrosis. Correlations between the HRCT scores, spirometric parameters, and oscillometric parameters were analysed.

Respiratory reactance correlated positively with all fibrosis-related HRCT scores. Vital capacity and forced vital capacity (FVC) correlated negatively with oscillometric parameters and HRCT scores, reflecting the severity of restrictive ventilatory deficiency. Respiratory resistance was not related to any of the HRCT scores or forced expiratory volume in 1 s/FVC. However, forced expiratory volume in 1 s/FVC correlated positively with HRCT scores, which showed that airflow obstruction became milder as the disease progressed.

In conclusion, respiratory reactance reflects fibrosis and restrictive ventilatory deficiency in IPF. Moreover, respiratory resistance is independent of traction bronchiectasis and airflow obstruction in patients with IPF, which implies that respiratory resistance might reflect different properties of the airways.

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Introduction

Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause with a poor prognosis [1–3]. Since the clinical course of individual patients with IPF varies [4], many studies have been reported regarding developing clinical, physiological, and radiological markers to evaluate the clinical conditions and prognosis of patients with IPF [5–17]. As radiological and physiological markers, fibrosis-related high-resolution computed tomography (HRCT) findings and pulmonary function tests are used for predicting the prognosis of patients with IPF [10, 11, 13, 16, 17]. Notably, forced vital capacity (FVC), which reflects restrictive ventilatory deficiency, has been used as a surrogate marker for prognosis [13]. Restrictive ventilatory deficiency in IPF is primarily attributed to reduction of lung compliance [16]. Although the measurement requires placement of an oesophageal pressure probe to obtain transpulmonary pressure, lung compliance is useful for early IPF diagnosis because it is markedly reduced even in patients without abnormal HRCT findings [16, 18].

In addition to these markers, studies for evaluating patients with IPF using oscillometry, also called the forced oscillation technique, have been reported [14, 15]. Oscillometry, which involves measurements of within-breath changes in respiratory impedance, measures respiratory resistance (R_{rs}) and respiratory reactance (X_{rs}). R_{rs} represents the sum of the airway resistance and viscous resistance of lung and thoracic tissue [19], whereas X_{rs} reflects the dynamic elastance and inertia of the respiratory system [20]. Measuring respiratory impedance using oscillometry is less time-consuming and is technically easier to perform than spirometry because it is measured at rest with minimal respiratory effort [21, 22].

Regarding the utility of oscillometry as a physiological marker in IPF, respiratory reactance correlated with FVC and was useful as a surrogate marker for prognosis in IPF [14]. However, oscillometry and spirometry do not necessarily reflect the same physiological conditions of the respiratory tract system [23], and little has been reported on the mechanism of why respiratory reactance reflects the disease severity. In particular, no studies have validated the correlation of respiratory impedance with the degree of fibrosis and lung compliance in patients with IPF. As respiratory reactance correlates with lung compliance theoretically [24], we hypothesised that respiratory reactance reflects the degree of fibrosis and might be useful for early diagnosis in IPF.

Apart from the correlation between respiratory reactance and fibrosis, patients with IPF sometimes show traction bronchiectasis and increased forced expiratory volume in 1 s (FEV_1)/FVC [16]. Given that airway resistance is affected by the diameter of the airways [25], we hypothesised that traction bronchiectasis reduces respiratory resistance, allows more air to pass out of the lungs, and correlates negatively with airflow obstruction in patients with IPF.

The objectives of the present study regarding IPF were as follows: 1) to investigate the correlation of oscillometric parameters with fibrosis-related lung abnormalities; and 2) to assess the utility of oscillometry as a surrogate marker of traction bronchiectasis and airflow obstruction.

Methods

Patients

All 343 Japanese patients with interstitial pneumonia who attended clinics at the National Hospital Organization Osaka Toneyama Medical Center between 2013 and 2019 were screened in this study. Patients were excluded if they had secondary interstitial pneumonia, as well as patients who did not undergo spirometry, oscillometry, or HRCT. The usual interstitial pneumonia (UIP) diagnosis was based on the presence of UIP pattern on HRCT not subjected to surgical lung biopsy or specific combinations of HRCT findings and surgical lung biopsy patterns [26]. Patients with combined pulmonary fibrosis and emphysema (CPFE) or with FEV_1/FVC <70% (*i.e.* suspected of having COPD) were also excluded. The diagnosis of CPFE was based on the criteria developed by Cottin *et al.* [27]. Patients were excluded if they had malignancy, severe heart diseases, or severe cerebral diseases. Only patients with at least 3 months of convalescence were included. Figure 1 shows the inclusion flowchart. In total, 80 patients qualified for this study and were evaluated using the examinations and analysis described in the following sections.

Study design

Respiratory impedance was measured in all patients using oscillometry. Spirometry and oscillometry were performed on the same day. Oscillometry was performed at first, and thereafter, spirometry was measured. Short-acting β_2-agonists were not used for at least 12 h before tests in all patients. Chest HRCT scans were performed within 3 months from the measurement of oscillometry and spirometry, and patients were stable until the completion of these measurements. Treatment for IPF was not changed at least 1 month before the initial data measurement to the completion of all data measurements. The HRCT findings were quantified by calculating HRCT scores described in the latter section. Correlations between the HRCT scores, respiratory impedance, and spirometric parameters were analysed regarding the total patients

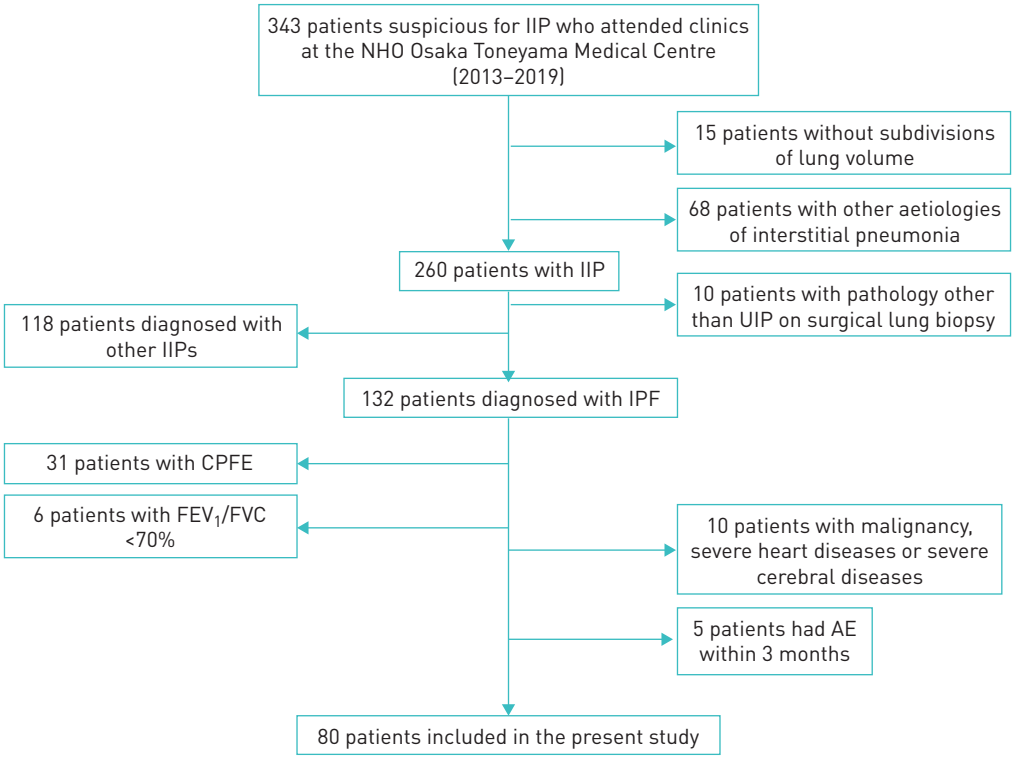

FIGURE 1 Patient inclusion flowchart. AE: acute exacerbation; CPFE: combined pulmonary fibrosis and emphysema; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; IIP: idiopathic interstitial pneumonia; IPF: idiopathic pulmonary fibrosis; NHO: National Hospital Organization; UIP: usual interstitial pneumonia.

included in this study. The Institutional Review Board of the National Hospital Organization Osaka Toneyama Medical Center approved the study protocols and chose an opt-out system for obtaining patients' informed consent (approval number: TNH-R-2020005).

Measurement of respiratory impedance using oscillometry

Respiratory impedance was measured at rest with broadband oscillometry using a commercially available device (Mostgraph-01; Chest M.I. Co., Ltd., Tokyo, Japan). Oscillometry was performed according to the recommendations of the European Respiratory Society [28]. Whole-breath respiratory impedance was measured, and the average data of each oscillometric parameter were used. As indicators of the frequency dependence of R_{rs}, R_{rs} at 5 and 20 Hz (R_5 and R_{20}, respectively) and the difference between these (R_5–R_{20}) were used. In addition, X_{rs} at 5 Hz (X_5), resonant frequency (F_{res}), and low-frequency reactance area (ALX) were measured as indicators of respiratory reactance. F_{res} indicates the point at which X_{rs} crosses zero and elasticity and inertia balance each other, and ALX is defined as the integral of X_5 to F_{res} [23]. Predicted respiratory impedance values were calculated according to the formula developed by Oostveen *et al.* [29].

Spirometry

All patients underwent spirometry using the CHESTAC 8800 spirometer (Chest M.I., Inc.) according to the recommendations of the American Thoracic Society and the European Respiratory Society [30]. Predicted FVC and FEV_1 were calculated according to the formula for Japanese patients developed by the Japanese Respiratory Society [31].

HRCT scores

Chest HRCT scans were conducted with 1 mm section thickness. HRCT images were reviewed independently by two pulmonologists trained in HRCT scoring, and average HRCT scores were adopted. The presence, extent, and distribution of HRCT findings were evaluated based on the presence of airspace consolidation, honeycombing, architectural distortion, traction bronchiectasis, and fibrosis, because these lung abnormalities reportedly correlate with the prognosis of patients with IPF [11].

The HRCT scores were evaluated based on the definition of HRCT findings and the scores developed by SUMIKAWA *et al.* [11] (supplementary tables 1 and 2). The observers evaluated the extent of all radiological abnormalities that were present in both lungs to determine the percentage of lung parenchyma occupied by the disease. The lungs were divided into six zones (upper, middle, and lower on both sides), and each zone was evaluated separately. The upper lung zone was defined as the area of the lung above the level of the tracheal carina, the lower lung zone was defined as the area of the lung below the level of the inferior pulmonary vein, and the middle lung zone was defined as the area of the lung between the upper and lower zones [11]. When abnormal HRCT findings were present, the extent of lung involvement was evaluated visually and independently for each of the six lung zones. The airspace consolidation and honeycombing scores were based on the percentage of the lung parenchyma with these abnormalities and were estimated to the nearest 5% of parenchymal involvement. The overall percentage of lung involvement was calculated by averaging the six lung zones. The extent of architectural distortion, traction bronchiectasis, and interstitial fibrosis was quantified by adding the HRCT scores of the six lung zones (supplementary table 2).

Statistical analysis

Spearman's rank correlation coefficient (r_s) was used for bivariate correlation analysis between HRCT scores and parameters of oscillometry and spirometry. Univariate and multivariate analyses were used for interaction analyses. For all analyses, p-values <0.05 were considered statistically significant. Furthermore, all statistical analyses were performed using EZR version 1.38 (based on R version 3.5.2 and R commander version 2.5-1; Jichi Medical University Saitama Medical Center, Saitama, Japan) [32].

Results

Baseline characteristics

Among the 80 patients included in the present study, 6 patients were diagnosed by a combination of surgical biopsy and HRCT findings, and 74 patients without pathology were diagnosed with UIP on HRCT. Table 1 summarises the patients' baseline characteristics. Many of the patients had been treated with pirfenidone (800–1800 mg daily), nintedanib (200–300 mg daily), inhaled N-acetylcysteine (350 mg diluted with saline to a total volume of 10 mL, twice a day), and/or oral corticosteroids (2–10 mg daily). No treatment for IPF affected oscillometric parameters (supplementary table 3). Moreover, multivariate analysis showed that age and body mass index did not affect any oscillometric parameters (all p-values >0.05). Table 2 lists the results of the HRCT scores, oscillometric parameters, and spirometric parameters. The average FEV_1/FVC was higher than the predicted FEV_1/FVC of healthy subjects (men, 76.7%; and women, 76.8%) [31].

Correlations of respiratory impedance with spirometry

Oscillometric parameters variously correlated with spirometric parameters in patients with IPF (table 3). All oscillometric parameters correlated with vital capacity (VC), FVC, and FEV_1. Of note, respiratory

TABLE 1 Patient baseline characteristics

Parameter	Value	Range
Patients n	80	
Age years	74.2±7.8	50–88
Sex male/female n	51/29	
Height cm	159.2±9.5	130.0–178.2
Weight kg	55.8±13.9	27.6–97.5
BMI kg·m^{-2}	21.8±3.9	13.2–31.6
Smoking pack-years	27±26	0–135
mMRC dyspnoea scale 0/1/2/3/4 n	28/21/12/11/8	
LDH U·L^{-1}	220±37	156–356
KL-6 U·mL^{-1}	1002±647	222–4348
Medications n (%)		
Pirfenidone	21 (26.3)	
Inhaled N-acetylcysteine	16 (20.0)	
Nintedanib	9 (11.3)	
Oral corticosteroids	6 (7.5)	

Data are presented as mean±SD and range, unless otherwise stated. BMI: body mass index; LDH: lactate dehydrogenase; mMRC: modified Medical Research Council.

TABLE 2 Results of spirometry, oscillometry, and high-resolution computed tomography scores

Parameter	Value	Range
Subjects n	80	
Spirometry		
FEV_1 L	2.05±0.62	0.76–3.33
FEV_1 % pred	88.9±16.8	54.1–142.3
FEV_1/FVC %	85.0±7.3	71.3–100.0
VC L	2.45±0.83	0.79–4.15
FVC L	2.46±0.83	0.76–4.14
FVC % pred	83.3±18.0	41.5–127.1
IC L	1.60±0.60	0.47–3.12
IRV L	0.74±0.42	0.08–2.40
ERV L	0.85±0.37	0.19–2.00
V_T L	0.86±0.36	0.28–1.82
Oscillometry		
R_5 $cmH_2O{\cdot}L^{-1}{\cdot}s^{-1}$	3.14±1.04	1.21–5.96
R_5 % pred	153.7±56.5	39.0–388.1
R_{20} $cmH_2O{\cdot}L^{-1}{\cdot}s^{-1}$	2.39±0.77	1.10–4.32
R_{20} % pred	92.6±29.4	32.9–196.8
R_5–R_{20} $cmH_2O{\cdot}L^{-1}{\cdot}s^{-1}$	0.75±0.37	0.05–1.99
X_5 $cmH_2O{\cdot}L^{-1}{\cdot}s^{-1}$	−1.24±0.76	−3.04–0.00
X_5 % predicted	94.5±56.2	0.0–246.4
F_{res} Hz	12.11±3.34	4.30–20.89
F_{res} % pred	102.4±30.3	36.0–184.2
ALX $cmH_2O{\cdot}L^{-1}{\cdot}s^{-1}{\times}Hz$	6.99±5.69	0.04–24.66
ALX % pred	232.8±197.3	1.1–857.9
HRCT scores		
Airspace consolidation	1.9±2.7	0.0–11.7
Honeycombing	10.8±11.9	0.0–55.8
Architectural distortion	1.4±1.7	0–6
Traction bronchiectasis	6.7±4.4	0–18
Interstitial fibrosis	18.8±4.8	7–24

Data are presented as mean±SD and range, unless otherwise stated. ALX: low-frequency reactance area; ERV: expiratory reserve volume; FEV_1: forced expiratory volume in 1 s; F_{res}: resonant frequency; FVC: forced vital capacity; HRCT: high-resolution computed tomography; IC: inspiratory capacity; IRV: inspiratory reserve volume; % pred: % predicted; R_5 and R_{20}: respiratory system resistance at 5 and 20 Hz, respectively; V_T: tidal volume; VC: vital capacity; X_5: respiratory system reactance at 5 Hz.

reactance strongly correlated with VC and FVC, but FEV_1 correlated with both respiratory resistance and reactance almost equally (tables 3 and 4). FEV_1/FVC was increased as F_{res} and ALX became higher and X_5 became more negative (table 3), but no correlations were observed between FEV_1/FVC and respiratory resistance (figure 2 and supplementary table 4). The results showed that airflow obstruction became milder as respiratory reactance was increased, and that respiratory resistance did not correlate with airflow obstruction.

Regarding subdivisions of VC, respiratory reactance correlated both with inspiratory reserve volume (IRV) and expiratory reserve volume (ERV). However, respiratory resistance correlated only with ERV (table 3 and figure 3). Both respiratory reactance and resistance correlated with tidal volume, but no oscillometric parameters were related to tidal volume with clinical significance (table 4). Based on the results described above, respiratory reactance correlated with VC stronger than respiratory resistance, and respiratory resistance correlated with spirometric parameters that were related to forced expiration.

Correlations of HRCT scores with respiratory impedance and spirometry

Respiratory reactance significantly correlated with all HRCT scores, but respiratory resistance did not correlate with any of the scores (table 5). Even traction bronchiectasis score did not correlate with respiratory resistance. The HRCT scores became more severe as F_{res} and ALX became higher and X_5 became more negative. The results showed that only respiratory reactance correlated positively with fibrosis-related HRCT findings in the lungs of IPF patients.

TABLE 3 Results of Spearman's rank correlation coefficient for parameters of oscillometry and spirometry (n=80)

Parameter	R_5		R_{20}		R_5–R_{20}		X_5		F_{res}		ALX	
VC	−0.465	**	−0.437	**	−0.304	**	0.517	**	−0.562	**	−0.523	**
FVC	−0.450	**	−0.423	**	−0.291	**	0.506	**	−0.541	**	−0.509	**
FEV_1	−0.485	**	−0.468	**	−0.306	**	0.497	**	−0.530	**	−0.497	**
FEV_1/FVC	0.092	NS	0.041	NS	0.063	NS	−0.250	*	0.286	*	0.261	*
IC	−0.154	NS	−0.331	**	−0.127	NS	0.444	**	−0.504	**	−0.454	**
IRV	−0.144	NS	−0.128	NS	−0.076	NS	0.422	**	−0.530	**	−0.445	**
ERV	−0.551	**	−0.479	**	−0.474	**	0.406	**	−0.414	**	−0.403	**
V_T	−0.355	**	−0.377	**	−0.176	NS	0.272	*	−0.232	*	−0.265	*

ALX: low-frequency reactance area; ERV: expiratory reserve volume; FEV_1: forced expiratory volume in 1 s; F_{res}: resonant frequency; FVC: forced vital capacity; IC: inspiratory capacity; IRV: inspiratory reserve volume; R_5 and R_{20}: respiratory system resistance at 5 and 20 Hz, respectively; V_T: tidal volume; VC: vital capacity; X_5: respiratory system reactance at 5 Hz. NS: not statistically significant; *: p<0.05; **: p<0.01, as measured by Spearman's rank correlation coefficient.

Consistent with the correlation of oscillometric parameters with the HRCT scores, VC, FVC, and FEV_1 correlated negatively with the HRCT scores. Meanwhile, FEV_1/FVC correlated positively with all HRCT scores (table 5). This showed that restrictive ventilatory deficiency became more severe and airflow obstruction became milder as fibrosis-related lung abnormalities progressed in patients with IPF. Regarding subdivisions of VC, IRV correlated with all HRCT scores, but ERV was not related to any of the scores. These data showed that fibrosis-related lung abnormalities correlated not with forced expiration but rather forced inspiration in patients with IPF.

Discussion

The present study highlights two major findings regarding the utility of oscillometry in IPF: 1) respiratory reactance correlates positively with fibrosis-related lung abnormalities in patients with IPF; and 2) respiratory resistance can be independent of traction bronchiectasis and airflow obstruction in patients with IPF. To the best of our knowledge, this is the largest study to date that assessed the correlation of HRCT findings with oscillometry in patients with IPF.

Respiratory reactance correlates positively with lung fibrosis-related HRCT findings in patients with IPF. In patients with IPF, FVC is a reliable measurement that reflects the clinical conditions [13]. Respiratory reactance correlated positively with FVC and was useful for evaluating disease progression [14]. However, no studies have thoroughly reported the mechanism of how respiratory reactance correlates with FVC. Therefore, the present study investigated the mechanism by analysing the correlations between HRCT scores, spirometry, and oscillometry.

In patients with IPF, reduction of lung compliance tightly correlates with lung fibrosis and occurs in patients with an early stage of IPF [16, 18]. This leads to restrictive ventilatory deficiency and is reflected in the decrease in FVC [16]. Even IPF patients without restrictive ventilatory deficiency have reduction of lung compliance [33]. Lung compliance was considered to correlate with respiratory reactance theoretically [24], but earlier studies failed to show the correlation of lung compliance with respiratory impedance in a small number of patients with IPF [34, 35]. The present study first showed that respiratory reactance correlated with fibrosis-related lung abnormalities in patients with IPF (table 5). Given that respiratory reactance also correlated with FVC that reflects lung compliance and predicts the disease severity in patients IPF [13], respiratory reactance might correlate with lung compliance in patients with IPF. Lung compliance is useful for early diagnosis of IPF because it is markedly reduced even in IPF patients without abnormal HRCT findings [16, 18]. Therefore, assessing the utility of respiratory reactance as a substitute for lung compliance might be useful for early and effortlessly diagnosing IPF patients without abnormal HRCT findings because the measurement of lung compliance requires an invasive technique for patients compared with that of oscillometry [16, 21, 22]. Thus, further studies are necessary to validate this hypothesis and the utility of respiratory reactance.

FEV_1/FVC and respiratory resistance can be independent in patients with IPF. As the progressive increase in elastic recoil occurs with worsening pulmonary fibrosis, FEV_1/FVC increases as lung compliance is reduced in IPF [36]. Apart from lung fibrosis and restriction, IPF is understood to primarily involve the alveolar regions, but some previous studies have suggested the involvement of the airways [16, 37–39].

TABLE 4 Results of univariate analysis for parameters of oscillometry and spirometry (n=80)

Parameter	R_5			R_{20}			R_5–R_{20}			X_5			F_{res}			ALX		
	std β	Adjusted R^2		std β	Adjusted R^2		std β	Adjusted R^2		std β	Adjusted R^2		std β	Adjusted R^2		std β	Adjusted R^2	
VC	−0.437	0.181	**	−0.445	0.188	**	−0.309	0.084	**	0.467	0.208	**	−0.520	0.262	**	−0.439	0.183	**
FVC	−0.418	0.164	**	−0.425	0.170	**	−0.295	0.075	*	0.459	0.201	**	−0.501	0.241	**	−0.426	0.171	**
FEV_1	−0.449	0.192	**	−0.459	0.201	**	−0.313	0.087	**	0.461	0.202	**	−0.493	0.233	**	−0.427	0.172	**
FEV_1/FVC	0.072	−0.008	NS	0.076	−0.007	NS	0.041	−0.011	NS	−0.190	0.024	NS	0.271	0.062	*	0.031	0.019	NS
IC	−0.290	0.072	**	−0.219	0.037	*	−0.168	0.006	NS	0.418	0.164	**	−0.480	0.221	**	−0.380	0.134	**
IRV	−0.135	0.005	NS	−0.149	−0.010	NS	−0.069	−0.008	NS	0.344	0.087	**	−0.450	0.192	**	−0.323	0.093	**
ERV	−0.505	0.245	**	−0.486	0.226	**	−0.415	0.162	**	0.366	0.123	**	−0.384	0.136	**	−0.365	0.122	**
V_T	−0.324	0.093	**	−0.344	0.107	*	−0.199	0.028	NS	0.291	0.073	*	−0.272	0.062	*	−0.254	0.053	*

ALX: low-frequency reactance area; ERV: expiratory reserve volume; FEV_1: forced expiratory volume in 1 s; F_{res}: resonant frequency; FVC: forced vital capacity; IC: inspiratory capacity; IRV: inspiratory reserve volume; NS: not significant; R_5 and R_{20}: respiratory system resistance at 5 and 20 Hz, respectively; std β: standardised regression coefficient; V_T: tidal volume; VC: vital capacity; X_5: respiratory system reactance at 5 Hz. *: p<0.05; **: p<0.01, as measured by univariate analysis.

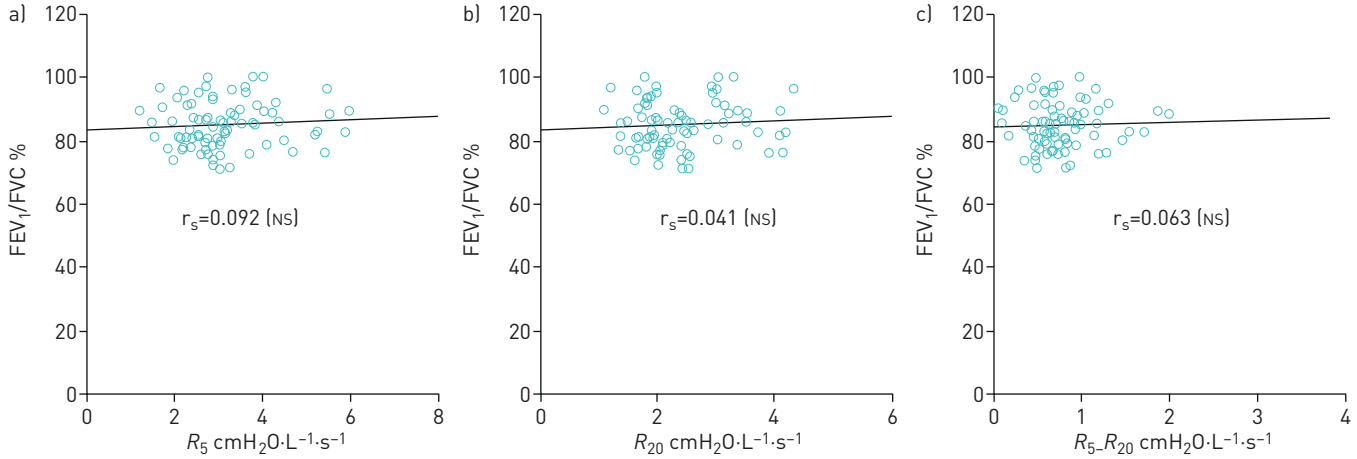

FIGURE 2 Spearman's rank correlation coefficient (r_s) for respiratory resistance and FEV_1/FVC (n=80). a) R_5, b) R_{20} and c) R_5–R_{20}. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; R_5 and R_{20}: respiratory system resistance at 5 and 20 Hz, respectively; NS: not statistically significant.

Airway epithelial cells proliferate and differentiate with increased numbers of bronchioles in patients with IPF [37–39], and airway dilation occurs as part of the disease process [16]. Therefore, FEV_1/FVC of patients with IPF is higher than that of healthy subjects, which shows that airflow obstruction becomes milder in IPF [40]. Hence, respiratory resistance, which is obtained theoretically by dividing respiratory

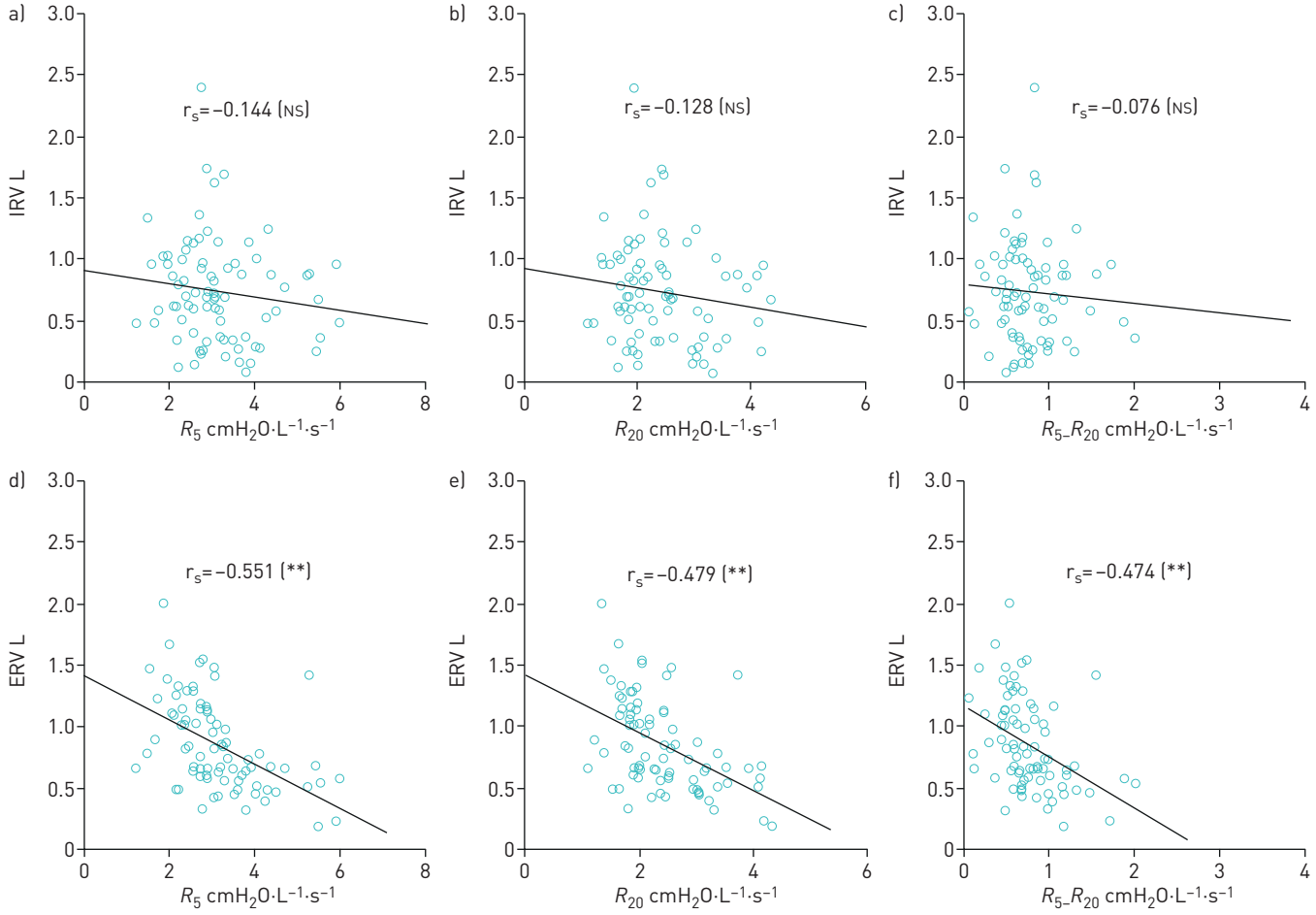

FIGURE 3 Spearman's rank correlation coefficient (r_s) for respiratory resistance with a–c) IRV and d–f) ERV (n=80). ERV: expiratory reserve volume; IRV: inspiratory reserve volume; R_5 and R_{20}: respiratory system resistance at 5 and 20 Hz, respectively; NS: not significant. **: p<0.01, as measured by r_s.

TABLE 5 Results of Spearman's rank correlation coefficient for high-resolution computed tomography scores, oscillometry, and spirometry (n=80)

Parameter	Airspace consolidation		Honeycombing		Architectural distortion		Traction bronchiectasis		Interstitial fibrosis	
Oscillometry										
R_5	0.005	NS	−0.080	NS	−0.041	NS	−0.072	NS	−0.119	NS
R_{20}	−0.057	NS	−0.114	NS	−0.059	NS	−0.092	NS	−0.153	NS
R_5–R_{20}	0.065	NS	−0.078	NS	−0.008	NS	−0.048	NS	−0.096	NS
X_5	−0.375	**	−0.264	**	−0.345	**	−0.297	**	−0.206	NS
F_{res}	0.435	**	0.296	**	0.396	**	0.348	**	0.236	*
ALX	0.396	**	0.285	**	0.366	**	0.324	**	0.222	*
Spirometry										
VC	−0.386	**	−0.271	**	−0.393	**	−0.373	**	−0.181	NS
FVC	−0.406	**	−0.259	**	−0.386	**	−0.371	**	−0.159	NS
FEV_1	−0.350	**	−0.181	NS	−0.329	**	−0.301	**	−0.100	NS
FEV_1/FVC	0.438	**	0.413	**	0.459	**	0.436	**	0.293	**
IC	−0.421	**	−0.301	**	−0.415	**	−0.431	**	−0.199	*
IRV	−0.492	**	−0.367	**	−0.465	**	−0.496	**	−0.297	**
ERV	−0.181	NS	−0.074	NS	−0.172	NS	−0.124	NS	−0.031	NS
V_T	−0.121	NS	−0.068	NS	−0.142	NS	−0.196	NS	0.013	NS

ALX: low-frequency reactance area; ERV: expiratory reserve volume; FEV_1: forced expiratory volume in 1 s; F_{res}: resonant frequency; FVC: forced vital capacity; IC: inspiratory capacity; IRV: inspiratory reserve volume; NS: not significant; R_5 and R_{20}: respiratory system resistance at 5 and 20 Hz, respectively; V_T: tidal volume; VC: vital capacity; X_5: respiratory system reactance at 5 Hz. *: p<0.05; **: p<0.01, as measured by Spearman's rank correlation coefficient.

pressure by respiratory airflow, has been considered to decline in IPF [16]. From these observations, both respiratory reactance and resistance were hypothesised to correlate with FEV_1/FVC. In fact, the results of this study showed the correlation of FEV_1/FVC with respiratory reactance (table 3). However, the present study showed no correlations between respiratory resistance and FEV_1/FVC (table 3 and figure 2) and between traction bronchiectasis and respiratory resistance (table 5). These results implied that respiratory resistance and FEV_1/FVC reflected different properties of the airways in IPF. The change of FEV_1/FVC might have been attributed to fibrosis-related structural abnormalities of the lungs (table 5). However, given that respiratory resistance correlated with ERV but not with fibrosis-related structural abnormalities in the lung (table 5 and figure 3), other mechanisms related to forced expiration might have increased respiratory resistance.

Two possible hypotheses for the mechanism can be explained. First, reduced airway distensibility might increase respiratory resistance during forced expiration. Proximal airways of healthy subjects can expand and decrease airway pressure during forced expiration, but patients with IPF fail to reduce airway pressure because the proximal airways show reduced distensibility [41]. Hence, respiratory resistance might be higher only during forced expiration as the airway distensibility declines. Second, lung surfactant abnormalities might affect respiratory resistance. IPF induces lung surfactant abnormalities and subsequently decreases surface activity of the airways [42]. Reduced surface activity of the airways leads to increased airway resistance and lung compliance [16, 43]. Thus, increased respiratory resistance as a result of reduced surface activity might affect impaired force expiration of IPF. Further investigations are necessary to verify these hypotheses.

The present study had some limitations. First, it was a single-centre retrospective study, and some selection bias might have affected the findings. Second, the present study included only patients with IPF; thus, whether the results can be applicable to patients with CPFE remains unknown. Third, this study did not include healthy subjects, and whether the results are specifically applicable to patients with IPF remains unknown. Finally, this study did not mention the correlation of within-breath changes of oscillometric parameters with spirometric parameters and HRCT findings to generalise the results because oscillometric devices do not necessarily measure inspiratory and expiratory oscillometric parameters separately. Respiratory impedance reportedly changes between inspiratory and expiratory phases in IPF and chronic obstructive pulmonary disease [14, 21]. In particular, inspiratory oscillometric parameters correlated with spirometric parameters in IPF [14]. Therefore, further studies to investigate the utility of inspiratory and expiratory oscillometric parameters are needed in patients with IPF and CPFE.

In conclusion, the present study assessed the correlation of respiratory impedance with fibrosis and traction bronchiectasis in IPF. Respiratory reactance correlates with fibrosis-related HRCT findings. The utility of respiratory reactance should be investigated for early diagnosis of IPF without abnormal HRCT findings because respiratory reactance might be a substitute for lung compliance. Respiratory resistance can be independent of traction bronchiectasis and airflow obstruction in patients with IPF because respiratory resistance might show different properties of the airways. This study provides a theoretical foundation of the utility of oscillometry in IPF.

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