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Original Research Article

Clinical Spectrum, Radiological Profile, and Outcomes of Interstitial Lung Disease: A Retrospective Study from a Tertiary Care Hospital

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Abstract:

Background: Interstitial lung disease (ILD) is a term used to describe a group of diffuse parenchymal lung diseases with a range of degrees of inflammation and fibrosis, that lead to progressive loss of lung function and cause hefty morbidity. Early diagnosis by clinical assessment, pulmonary function testing, and high-resolution computed tomography (HRCT) is critical for better outcomes for patients.

Aim: To assess the clinical spectrum, radiological profile, pulmonary function abnormalities, treatment pattern and clinical outcomes of patients presenting with ILD in the tertiary care hospital.

Methodology: This was a retrospective observational study of 105 adult patients with confirmed ILD seen at Department of Pulmonary Medicine, Rajan Babu Institute of Pulmonary Medicine and Tuberculosis, Delhi, India. Demographic parameters, clinical presentation, pulmonary function tests, HRCT, treatment received and outcomes were evaluated in clinical records. SPSS version 26.0 was used for data analysis, p-value <0.05 was regarded as statistically significant.

Results: The average age of the patients was 56.2 ± 13.8 years with male predominance of 58.1%. Dyspnea (92.4%) and dry cough (81.9%) were the commonest presenting symptoms. Ventilatory defects were seen in 81.9% of the patients and were restrictive. The most common HRCT findings were reticular opacities (70.5%), followed by ground-glass opacities (60.0%), traction bronchiectasis (44.8%), and honeycombing (32.4%). The most common ILD subtype was connective tissue disease-associated interstitial lung disease (CTD-ILD), accounting for 31.4% of cases. 74.3% of patients received corticosteroids. At follow-up 46.7% were clinically stable, 34.3% had disease progression and 7.6% were dead. A significantly high correlation was seen between the presence of honeycombing on HRCT and the disease progression ($p = 0.002$).

Conclusion: ILD predominantly affected middle-aged and elderly individuals and commonly presented with progressive respiratory symptoms, restrictive pulmonary dysfunction, and fibrotic changes on HRCT. CTD-associated ILD was the most common ILD subtype. Honeycombing was significantly associated with disease progression, highlighting the diagnostic and prognostic importance of HRCT. Timely multidisciplinary assessment and appropriate intervention are essential to improve clinical outcomes.

Keywords: Interstitial lung disease, Diffuse parenchymal lung disease, High-resolution computed tomography, Pulmonary function test, Connective tissue disease-associated interstitial lung disease, Clinical outcomes, Honeycombing.

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Introduction

Also known as diffuse parenchymal lung diseases (DPLDs), interstitial lung diseases (ILDs) are a diverse group of over 200 pulmonary diseases associated with differing extents of inflammation and fibrosis of the pulmonary interstitium, alveoli, and distal airways, as well as the pulmonary vasculature. Though very different at a clinical level, they present with similar features at a clinical-radiological, physiological and pathological level: progressive exertional dyspnea, persistent dry cough, ventilatory restriction, reduction of diffusing capacity of the lungs and typical features on high-resolution computed tomography (HRCT). Many ILDs eventually develop progressive fibrosis leading to end-stage lung disease, respiratory failure, poor quality of life and death, for which ILD is a significant contributor to chronic respiratory morbidity worldwide. Therefore, early diagnosis and prompt commencement of suitable therapy is very important in achieving good long-term outcomes [1-3]

The epidemiology of ILDs differs widely between geographical regions, due to various environmental exposures, occupational exposures, genetic susceptibility, smoking rates and prevalence, and access to health care, as well as diagnostic methods. The incidence in Europe and North America has been reported to be around 3 to 30 cases per 100,000 population with an increasing prevalence over the last few decades due to rising awareness, high use of HRCT, multi-disciplinary diagnostic approach and ageing population [4-6] The major subtypes are encountered in clinical practice include idiopathic pulmonary fibrosis (IPF), connective tissue disease-associated ILD (CTD-ILD), hypersensitivity pneumonitis (HP), sarcoidosis, and occupational lung diseases, but the frequency of these subtypes vary by population.

As the burden of ILD in India is yet to be comprehensively understood, due to lack of epidemiological data, under-recognition, and absence of national disease registries. Patients tend to be referred late, and primary healthcare providers do not have a clear understanding of the disease's symptoms. In addition, there is often overlap between chronic respiratory symptoms and diffuse radiological infiltrates, which are seen in pulmonary tuberculosis (TB), which is still very common in the country. This means that many patients with ILD will start empirical anti-tubercular therapy prior to diagnosis, which ultimately delays treatment, leads to further disease progression, exposes patients to unnecessary drug therapy, and increases health care costs [7,8]. This diagnostic dilemma calls for enhanced awareness and systematic screening of ILD in endemic TB areas.

In the age of HRCT, the diagnostic strategy for ILD has changed dramatically, as the technique has allowed the characterization of parenchymal abnormalities and detection of specific HRCT patterns like usual interstitial pneumonia (UIP), probable UIP, nonspecific interstitial pneumonia (NSIP), organizing pneumonia (OP), and hypersensitivity pneumonitis (HP). The multidisciplinary diagnosis of HRCT, which is based on clinical history, serological investigations, pulmonary function testing (PFTs), bronchoscopy, and, if necessary, histopathological examination, is the basis of international recommendations [9,10]. Radiological assessment is not just used to help classify the disease but can also give helpful prognosis and inform therapy decisions.

The clinical features of ILD are generally non-specific and are most commonly characterized by increasing dyspnea and chronic cough. Other clinical features including digital clubbing, inspiratory 'Velcro' crackles, constitutional features, extrapulmonary autoimmune features and exercise-induced oxygen desaturations may hint to specific disease types. PFT usually shows a restrictive ventilatory defect with decreased forced vital capacity (FVC) and impaired diffusing capacity for CO (DLCO); sometimes mixed or obstructive patterns are seen depending on the cause of the problem. The clinical course is very variable, and some patients have stable diseases, whereas other patients may develop a very rapid progression of diseases that may require long-term oxygen therapy, antifibrotic treatment and/or lung transplantation in selected patients [11].

The importance of outcome assessment in ILD has been growing with consideration of several clinical and radiological parameters to the prognosis of the disease. Advanced age, male sex, extensive fibrosis in the HRCT, UIP pattern, severe deterioration of pulmonary function, pulmonary hypertension and late diagnosis have been shown regularly to be associated with poor survival. In contrast, very early recognition and timely commencement of corticosteroid therapy, immunosuppressive drugs, antifibrotic therapy, pulmonary rehabilitation, and supportive care have been shown to help manage síntomas and slow the progression of the disease in the appropriate patient populations [12,13]. A knowledge of the clinical presentation, radiological features, and outcomes of treatment is, therefore, crucial to the management of patients in a way that is most beneficial to them and cost-effective to the healthcare system.

Thus, the present retrospective study was done in Pulmonary Medicine department of Rajan Babu Institute of Pulmonary Medicine and Tuberculosis (RBIPMT), Delhi, India, to assess the clinical spectrum, radiological profile and outcomes of patients with ILD. This study aims to improve the understanding of the pattern of ILD in North India and to offer some evidence which can help in early diagnosis, help in clinical decision making and contribute to the growing body of literature on ILD in India by analyzing the demographic characteristics, clinical features, HRCT patterns, pulmonary function findings and treatment outcome.

Methodology

Study Design: This is a retrospective observational study to assess the clinical spectrum, radiological spectrum and outcomes of ILD. A retrospective design was selected to allow full analysis of the existing hospital records to determine the demographic characteristics, clinical presentation, radiological findings, diagnostic investigations, treatment details and clinical outcome, without influencing the management of patients. The study followed the principles of the Declaration of Helsinki and institutional ethical guidelines for biomedical research.

Study Area: The study was done in the Department of Pulmonary Medicine, Rajan Babu Institute of Pulmonary Medicine and Tuberculosis (RBIPMT), Delhi, India.

Study Duration: Medical records of eligible patients managed during 1 year of the study.

Sample Size: 105 patients with a diagnosis of Interstitial Lung Disease (ILD) were included in the study who met the inclusion criteria.

Study Population: The study population included adult patients with ILD, visiting the outpatient department or admitted to the Department of Pulmonary Medicine, Rajan Babu Institute of Pulmonary Medicine and Tuberculosis, Delhi, during the study period. Patients were diagnosed with ILD by clinical assessment, HRCT scan, pulmonary function testing, laboratory tests and, when available, histopathological studies. The American Thoracic Society/European Respiratory Society (ATS/ERS) criteria for ILD and idiopathic interstitial pneumonias were used to classify patients. We used well-defined international diagnostic criteria for the diagnosis of cases of connective tissue disease-associated ILD (CTD-ILD), hypersensitivity pneumonitis (HP), sarcoidosis, occupational ILD, and other ILD subtypes.

Data Collection: Medical records were analyzed and data were extracted from the medical record with a standardized data extraction form, in a retrospective manner. Recorded variables were clinical presentation, demographic factors (age, gender, residence, smoking habits, occupational and environmental exposure, family history), physical examination findings, laboratory investigations, pulmonary function tests (PFTs), radiological findings, bronchoscopic findings, histopathological findings, treatment details and clinical outcomes.

Lab tests performed included basic hematology, basic chemistry, serum angiotensin-converting enzyme (ACE) and, if available, antinuclear antibody (ANA), rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), anti-double stranded DNA (anti-dsDNA), anti-Scl-70 antibody, c-ANCA, and p-ANCA. Pulmonary function assessment consisted of FVC, FEV_1, FEV_1/FVC ratio, DLCO (if available) and the Six-Minute Walk Test (6MWT). Radiological assessment included chest radiography and high-resolution computed tomography (HRCT) of thorax to examine the characteristic patterns of ILD. When available, bronchoscopy and histology were examined. The diagnosis was done using the multidisciplinary approach, clinical, radiological, laboratory and histopathological findings, following ATS/ERS recommendations. Follow-up records were used to collect clinical outcomes such as disease progression, hospitalization, oxygen requirement and mortality.

Inclusion Criteria

All patients who met the following criteria were included:

- Age ≥18 years.
- Confirmed diagnosis of Interstitial Lung Disease based on ATS/ERS diagnostic recommendations.
- HRCT Chest findings are available.
- Complete medical records containing clinical and radiological information.
- Patients who were treated at RBIPMT during the study period.

Exclusion Criteria

The next groups of patients have been excluded:

- Children under 18 years of age.
- Lack of full or proper medical history.
- Active pulmonary TB patients.
- Those who have primary lung cancer.
- Patients with isolated pleural diseases but no ILD.
- Patients who were not diagnosed with ILD.

Study Procedure: Following institutional approval patients who were diagnosed with Interstitial Lung Disease (ILD) in the hospital during the study period were screened from hospital medical records. Cases were identified from the inpatient and outpatient records of the Department of Pulmonary Medicine, eligible cases meeting the inclusion criteria were selected. Standardized case record form was used to extract the data.

Demographic data, smoking history, occupational/environmental exposure, signs and symptoms at onset, length of illness, physical exam, lab investigations, pulmonary function test results and radiological findings were recorded. HRCT images and radiology reports were reviewed to find the characteristic patterns of ILD. Where available, bronchoscopic findings, bronchoalveolar lavage reports, transbronchial lung biopsy findings or histopathology reports were reviewed.

The diagnosis of ILD was made based on clinical assessment, HRCT imaging, laboratory tests, pulmonary function tests, bronchoscopy findings, histopathology (when available) and on multidisciplinary discussion following the guidelines of the ATS/ERS. Follow-up records provided clinical outcomes such as disease progression, disease stability, treatment response, hospitalization, oxygen usage, and mortality. All of the data retrieved was checked for completeness prior to statistical analysis.

Statistical Analysis: The data collected were analyzed by means of Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA) and entered into a computer spreadsheet.

All continuous data were summarized as mean ± SD or as the median with interquartile range (IQR) if they were not normally distributed. Categorical variables were presented as Frequency and Percentage.

The Chi-square test or Fisher's exact test was used for comparisons between categorical variables, as appropriate. The Independent Student's t-test was used to compare the Continuous variables with normal data distribution and the Mann–Whitney U test was used with non-normally distributed data. One-way Analysis of Variance (ANOVA) or Kruskal–Wallis test was used to make comparisons between more than two groups.

The clinical and HRCT features, as well as pulmonary function parameters, were analyzed using binary logistic regression for relationship with patient outcomes, if applicable. All analyses were performed with a two-tailed p value <0.05 being considered statistically significant".

Result

Table 1 presents the baseline demographic characteristics of the 105 patients diagnosed with interstitial lung disease (ILD). The mean age of the study population was 56.2 ± 13.8 years, with the highest proportion of patients belonging to the 46–60 years age group (37.1%), followed by those aged >60 years (32.4%). Male patients constituted 58.1% of the cohort, while females accounted for 41.9%. Most patients were from urban areas (65.7%), whereas 34.3% were from rural areas. Regarding smoking status, 59.0% were never smokers, 25.7% were former smokers, and 15.2% were current smokers. Occupational and environmental exposures were reported in 27.6% and 22.9% of patients, respectively, while a positive family history of ILD was observed in 6.7% of cases.

Table 1: Baseline Demographic Characteristics of Patients with ILD (N = 105)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
18–30	8	7.6
31–45	24	22.9
46–60	39	37.1
>60	34	32.4
Mean age (years)	**56.2 ± 13.8**	
Gender		
Male	61	58.1
Female	44	41.9
Residence		
Urban	69	65.7
Rural	36	34.3
Smoking Status		
Never smoker	62	59
Former smoker	27	25.7
Current smoker	16	15.2
Occupational Exposure	29	27.6
Environmental Exposure	24	22.9
Positive Family History	7	6.7

Table 2 summarizes the clinical presentation and comorbidities of the study population. Dyspnea (92.4%) was the most common presenting symptom, followed by dry cough (81.9%). Other symptoms included weight loss (21.9%), sputum production (18.1%), chest pain (14.3%), fever (11.4%), and hemoptysis (5.7%). The duration of symptoms ranged from less than six months in 31.4% of patients to more than one year in 29.5%, while 39.0% had symptoms lasting between six and twelve months. Among comorbid conditions, hypertension (36.2%) was the most frequent, followed by connective tissue disease (31.4%), diabetes mellitus (29.5%), gastroesophageal reflux disease (20.0%), and coronary artery disease (13.3%).

Table 2: Clinical Presentation and Comorbidities of Patients with ILD (N = 105)

Variable	Frequency (n)	Percentage (%)
Presenting Symptoms		
Dyspnea	97	92.4
Dry cough	86	81.9
Sputum production	19	18.1
Chest pain	15	14.3
Fever	12	11.4
Weight loss	23	21.9

Hemoptysis	6	5.7
Duration of Symptoms		
<6 months	33	31.4
6–12 months	41	39
>12 months	31	29.5
Comorbidities		
Hypertension	38	36.2
Connective tissue disease	33	31.4
Diabetes mellitus	31	29.5
Gastroesophageal reflux disease	21	20
Coronary artery disease	14	13.3

Table 3 depicts the pulmonary function test (PFT) findings among patients with ILD. The mean predicted forced vital capacity (FVC) was 63.8 ± 16.2%, while the mean forced expiratory volume in one second (FEV_1) was 69.4 ± 15.8%. The mean FEV_1/FVC ratio was 0.86 ± 0.08, consistent with a predominantly restrictive ventilatory defect. The mean diffusing capacity for carbon monoxide (DLCO) among the patients in whom it was available was 49.6 ± 14.3%, indicating impaired gas exchange. The mean six-minute walk distance (6MWD) was 342.5 ± 91.7 meters. Overall, 81.9% of patients demonstrated a restrictive pattern on spirometry, while 11.4% had a mixed ventilatory defect and 6.7% showed normal pulmonary function.

Table 3: Pulmonary Function Test Findings of Patients with ILD (N = 105)		
Variable	**Mean ± SD / Frequency**	
FVC	63.8 ± 16.2	
FEV_1	69.4 ± 15.8	
FEV_1/FVC ratio	0.86 ± 0.08	
DLCO	49.6 ± 14.3	
Six-minute walk (m)	342.5 ± 91.7	
PFT Pattern	**Mean ± SD / Frequency**	**Percentage (%)**
Restrictive	86	81.9
Mixed	12	11.4
Normal	7	6.7

Table 4 shows the radiological findings on high-resolution computed tomography (HRCT) and the final ILD diagnoses. The most frequent HRCT abnormality was reticular opacity (70.5%), followed by ground-glass opacity (60.0%), traction bronchiectasis (44.8%), septal thickening (39.0%), honeycombing (32.4%), and mosaic attenuation (17.1%). Based on multidisciplinary evaluation, connective tissue disease-associated interstitial lung disease (CTD-ILD) was the most common ILD subtype, accounting for 31.4% of cases, followed by idiopathic pulmonary fibrosis (23.8%), hypersensitivity pneumonitis (17.1%), sarcoidosis (11.4%), non-specific interstitial pneumonia (9.5%), and occupational ILD (6.7%).

Table 4: HRCT Thorax Findings and Final ILD Diagnosis (N = 105)		
Variable	**Frequency (n)**	**Percentage (%)**
HRCT Findings		
Reticular opacity	74	70.5
Ground-glass opacity	63	60
Traction bronchiectasis	47	44.8
Septal thickening	41	39
Honeycombing	34	32.4
Mosaic attenuation	18	17.1
Final Diagnosis		
CTD-associated ILD	33	31.4
Idiopathic Pulmonary Fibrosis	25	23.8
Hypersensitivity Pneumonitis	18	17.1
Sarcoidosis	12	11.4
NSIP	10	9.5
Occupational ILD	7	6.7

Table 5 presents the treatment profile and clinical outcomes of the study population. Corticosteroids were the most frequently prescribed treatment (74.3%), followed by pulmonary rehabilitation (39.0%), immunosuppressive therapy (32.4%), long-term oxygen therapy (27.6%), and antifibrotic therapy (25.7%). Regarding clinical outcomes during follow-up, 46.7% of patients remained clinically stable, while 34.3% experienced disease progression. Clinical improvement was observed in 11.4% of patients, whereas 7.6% died during the study period. Additionally, 29.5% of patients require hospitalization during follow-up.

Table 5: Treatment Profile and Clinical Outcomes (N = 105)

Variable	Frequency (n)	Percentage (%)
Treatment Received		
Corticosteroids	78	74.3
Immunosuppressive therapy	34	32.4
Antifibrotic therapy	27	25.7
Long-term oxygen therapy	29	27.6
Pulmonary rehabilitation	41	39
Clinical Outcome		
Stable disease	49	46.7
Disease progression	36	34.3
Improved	12	11.4
Death	8	7.6
Hospitalization during follow-up	31	29.5

Table 6 demonstrates the association between the presence of honeycombing on HRCT and disease progression. Among patients with honeycombing, 55.9% experienced disease progression compared with 23.9% of patients without honeycombing. Conversely, 44.1% of patients with honeycombing and 76.1% of those without honeycombing did not exhibit disease progression. The association between honeycombing and disease progression was found to be statistically significant (Chi-square = 9.64, p = 0.002), indicating that the presence of honeycombing on HRCT was significantly associated with an increased likelihood of disease progression in patients with ILD.

Table 6: Association Between Honeycombing on HRCT and Disease Progression

HRCT Honeycombing	Disease Progression n (%)	No Disease Progression n (%)	Total	p-value
Present	19 (55.9)	15 (44.1)	34	**0.002**
Absent	17 (23.9)	54 (76.1)	71	
Total	**36**	**69**	**105**	

Discussion

This retrospective study aims to analyze the clinical spectrum, radiological findings, pulmonary function abnormalities, treatment pattern and outcome of 105 patients with interstitial lung disease (ILD) from a tertiary care hospital. The study population was mostly aged above 40 years (56.2 ± 13.8 years), with the largest proportion of patients being above 40 years (37.1%) followed by 46–60 years (32.4%). These results show that ILD is mainly found in the middle-aged and elderly and suggest a progressive and chronic course of fibrotic lung disease. In a few studies from India, the mean age at diagnosis has been found to be 50-60 years, indicating that age is a significant risk factor for developing ILD. The current study revealed a male preponderance (58.1%), similar to that reported by Singh et al. [7] and Udwadia et al. [14] and other western registries, which showed that ILD was more common in men, especially in fibrotic diseases like idiopathic pulmonary fibrosis (IPF). Kumar et al. [15] and various Indian registry-based studies, however, reported a slight female predominance with a large proportion of women having connective tissue disease-associated ILD (CTD-ILD) and nonspecific interstitial pneumonia (NSIP). Our study showed that most subjects were from urban areas (65.7%) which may be due to greater access to tertiary healthcare facilities and increased diagnostic availability in metropolitan areas. In addition, most patients were never smokers (59.0%) and the predominance of never smokers also emphasized the importance of evaluating secondary causes of ILD, particularly an underlying connective tissue disease.

In the present study, dyspnea was the most common clinical presentation (92.4%) followed by dry cough (81.9%) while constitutional symptoms like weight loss (21.9%), fever (11.4%) and hemoptysis (5.7%) were relatively uncommon. The results were similar to those of earlier Indian and international studies in

which the most common symptoms of ILD were progressive exertional dyspnea and chronic dry cough [17]. About 39.0% had been ill for 6–12 months before presentation, suggesting a considerable lag between onset of symptoms and diagnosis, a problem that often occurs because the early symptoms are vague. Limited awareness and overlapping with other chronic respiratory illnesses like pulmonary tuberculosis have been reported by Udwadia et al. as key factors in the late diagnosis of tuberculosis in India. In the present study, hypertension (36.2%) was the most common comorbidity, followed by connective tissue disease (31.4%), diabetes mellitus (29.5%), gastroesophageal reflux disease (20.0%), and coronary artery disease (13.3%). The relatively high frequency of connective tissue disease was consistent with CTD-associated ILD being the most common ILD subtype in the present cohort. Previous reports have also shown a high prevalence of cardiovascular and metabolic disorders in patients with ILD, and gastroesophageal reflux disease (GERD) has been shown to be a significant factor in worsening the disease, especially in patients with IPF.

Reticular opacities (70.5%) and ground-glass opacities (60.0%) were the most common HRCT abnormalities, followed by traction bronchiectasis (44.8%), septal thickening (39.0%), and honeycombing (32.4%). These findings represent a combination of inflammatory and fibrotic changes commonly observed across the spectrum of interstitial lung diseases. CTD-associated ILD was the most frequent ILD subtype in the present study, accounting for 31.4% of cases, followed by IPF (23.8%), hypersensitivity pneumonitis (17.1%), sarcoidosis (11.4%), NSIP (9.5%), and occupational ILD (6.7%). The predominance of never smokers, together with the frequent occurrence of reticular and ground-glass opacities, highlighted the importance of evaluating patients for an underlying connective tissue disease. Differences in the distribution of ILD subtypes across studies may be related to variations in referral patterns, geographic distribution, autoimmune screening practices, environmental exposures, and diagnostic criteria.

The statistically significant correlation between honeycombing on HRCT and the disease progress was an important finding of the present study ($\chi^2 = 9.64$, $p = 0.002$). More than half of patients with honeycombing (55.9%) experienced disease progression compared with only 23.9% of patients without honeycombing. This finding confirms previous findings which have shown that the honeycombing pattern is an irreversible late-stage fibrosis and is an independent predictor of worse prognosis.

This finding is consistent with previous observations indicating that honeycombing represents advanced and irreversible fibrosis and is associated with a worse prognosis and greater functional deterioration across fibrosing interstitial lung diseases. Therefore, honeycombing should be interpreted as a prognostic marker of advanced fibrosis rather than as evidence of IPF alone.

Therefore, HRCT findings, particularly presence of honeycombing, should be viewed as important prognostic indicators at initial evaluation, and follow-up. Overall, the current results are consistent with previous studies that showed ILD is more common in older individuals, often associated with progressive dyspnea and restrictive pulmonary physiology, often with fibrotic abnormalities on HRCT, and continues to be a source of high morbidity despite recent advances in diagnosis and treatment.

Conclusion

This retrospective study showed that interstitial lung disease predominantly affected middle-aged and elderly individuals and commonly presented with progressive respiratory symptoms, restrictive pulmonary function impairment, and fibrotic changes on HRCT. CTD-associated ILD was the most frequent ILD subtype, accounting for 31.4% of cases, while IPF accounted for 23.8%. The predominance of never smokers and the frequent occurrence of reticular and ground-glass opacities highlighted the importance of evaluating patients for an underlying connective tissue disease. Honeycombing showed a significant association with disease progression and may serve as an important marker for risk stratification. Early diagnosis, multidisciplinary assessment, subtype-specific treatment, and regular follow-up are essential to improve clinical outcomes.

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