RESEARCH ARTICLE

Functional impact of usual interstitial pneumonia pattern in interstitial lung diseases

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Abstract

Objective: To evaluate longitudinal changes in pulmonary function among patients with interstitial lung disease (ILD) presenting the pattern of Usual Interstitial Pneumonia treated with nintedanib. Secondary objectives involved comparing the evolution between idiopathic pulmonary fibrosis (IPF) and non-IPF progressive fibrosing ILDs and assessing the prognostic value of the Gender, Age, Physiology (GAP) score in relation to baseline functional parameters.

Methods: Between June 2021 and September 2025, a retrospective observational study at the Pneumology Clinic of Mureș County Clinical Hospital included 15 patients. Demographic data, high-resolution Computer Tomography findings, Forced Vital Capacity, Diffusing Capacity for Carbon Monoxide, and GAP scores were analyzed before and after treatment initiation. Data was assessed using Shapiro Wilk distribution test and paired t-tests.

Results: The study group consisted in 11 patients with IPF and 4 with non-IPF fibrosing ILDs, with a mean baseline GAP score of 3.83±1.69. Under antifibrotic therapy, FVC showed numerical stabilization (83.50 ± 22.09% to 94.00 ± 16.09%; p = 0.94), while DLCO suggested a non-significant, controlled decline (43.86 ± 13.23% to 40.90 ± 16.15%; p = 0.26). IPF patients had greater baseline functional impairment and a more pronounced DLCO decline evolution. GAP score negatively correlated with baseline DLCO.

Conclusions: Nintedanib was associated with clinically relevant functional stabilization in UIP-pattern ILDs. Baseline functional impairment and the GAP score were revealed to be valuable variables in terms of risk stratification. Larger prospective studies are needed to confirm long-term outcomes.

Keywords: Interstitial Lung Diseases, Functional Tests, antifibrotic treatment.

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Introduction

Interstitial lung diseases (ILD) are defined as a cluster of conditions that cause inflammation of the lung parenchyma, with or without fibrosis, primarily affecting gas exchange, and are characterized by symptoms such as progressive dyspnea, reduced exercise tolerance, and reduced quality of life [1]. While uncommon, they constitute a clinically important group of disorders, with incidence varying widely by geographic location, from 1 to 31.5 cases per 100,000 person years [2].

Usual Interstitial Pneumonia (UIP) is not a pathology by itself, but rather a radiological and histopathological pattern for ILD, mostly seen in Idiopathic Pulmonary Fibrosis (IPF), but also appearing in connective tissue diseases, chronic hypersensitivity pneumonitis, sarcoidosis, drug-induced lung injury (e.g., amiodarone), and nonspecific interstitial pneumonia (NSIP) variants [3, 4].

In terms of imaging, High-Resolution Computed Tomography (HRCT) stands out as the favored technique for conducting non-invasive diagnoses and characterizing the UIP pattern. The distinguishing features encompass honeycombing, bronchiectasis with traction, ground-glass or reticular opacities with a predilection for subpleural and basal areas [5, 6]. To enhance the connection with functional impairment, current most recent studies frequently incorporate quantitative CT measurements (like over-aerated lung tissue and the degree of fibrosis) [7].

From a functional standpoint, UIP is related with a progressively restrictive ventilatory dysfunction characterized by a decrease in static lung volumes, particularly Forced Vital Capacity (FVC) and Total Lung Capacity (TLC), as well as the Diffusing Capacity for Carbon Monoxide (DLCO)[8]. These values can be used to assess the severity of the fibrotic process and as a guide for antifibrotic therapy and regular monitoring [9].

The natural progression of interstitial lung diseases showing the UIP pattern is typically one of progressive and unalterable deterioration, characterized by persistent decline in lung function and a shortened life expectancy [10]. The introduction of antifibrotic agents, pirfenidone and nintedanib, marked an important change in treatment. While both pirfenidone and nintedanib have demonstrated efficacy in slowing forced vital capacity (FVC) decline in idiopathic pulmonary fibrosis (IPF) [11, 12], nintedanib has also been shown to be effective in progressive fibrosing interstitial lung diseases (PF-ILDs) beyond IPF, including those exhibiting a UIP pattern [13]. There-

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fore, nintedanib currently represents the antifibrotic therapy applicable across the spectrum of UIP-pattern fibrosing ILDs. Despite strong data from controlled trials, it is essential to assess how these therapies perform in real-world clinical practice to ensure long-term effectiveness across different patient groups.

The Gender, Age, Physiology (GAP) score is a validated multidimensional index and staging system widely utilized in the management of ILDs for risk stratification, severity assessment and mortality prediction. This tool integrates simple clinical and demographic variables with objective physiological markers to provide a standardized evaluation of disease status. The score is calculated based on four primary parameters divided into two domains: demographical variables, which include patient gender and age; and physiological parameters obtained through respiratory function tests, specifically Forced Vital Capacity (FVC% of predicted) and Diffusing Capacity for Carbon Monoxide (DLCO% of predicted). The cumulative point score stratifies patients into three distinct disease stages, each directly correlating with estimated 1-, 2-, and 3-year mortality rates: stage I (0-3 points) characterized by mild disease severity, stage II (4-5 points) indicating a moderate disease severity and stage III (6-8 points) associated with severe, advanced pulmonary fibrosis [14].

The objective of this research is to assess the long-term alterations in respiratory function in patients with pulmonary interstitial disease and a UIP pattern who are receiving nintedanib therapy, with the goal of understanding how the treatment affects functional decline and the progression of the disease. Additional goals focused on comparing the functional progression of idiopathic UIP patients with those having non-IPF, progressive fibrosing ILDs displaying a UIP pattern, and investigating the connection between baseline functional parameters and prognostic scores, such as the GAP score, to assess their utility for disease severity stratification and clinical decision making.

Methods

We conducted a retrospective observational study including 15 patients admitted to the Pneumology Clinic of Mureș County Clinical Hospital between June 2021 and September 2025 focusing on the clinical evolution of patients with interstitial lung disease (ILD) treated with nintedanib. The study obtained the agreement of the Ethics Committee with number 15434/09.10.2025.

Inclusion criteria were patients diagnosed with ILD, aged≥18 years, treated with Nintedanib, with available pre- and post-treatment functional and imaging data. All consecutive eligible patients diagnosed during the study period were screened for inclusion. No patients were excluded because of treatment refusal. One patient discontinued nintedanib due to gastrointestinal adverse effects after the follow-up functional assessment and was therefore retained in the final analysis.

Patients for whom advanced functional explorations (body pletismography and DLCO) prior and post-treatment were not available and those for whom imaging exposures did not include HRCT were excluded from the study.

The medical care of the patients involved continuous inpatient, day hospital, and specialized ambulatory services at Mureș County Clinical Hospital. All participants provided written informed consent for research purposes.

For the patients included in the study, the following parameters were analyzed: demographic data (age, gender), type of interstitial lung disease (IPF or non-IPF), respiratory function tests (DLCO, plethysmography), imaging findings (High-Resolution Computer Tomography, using a Siemens SOMATOM go.All. CT scanner), and mortality prediction score (GAP score). All patients received a standardized follow-up assessment six months after initiating nintedanib, which included pulmonary function tests (body plethysmography and DLCO), clinical evaluations, and follow-up HRCT, when clinically indicated. Reassessment of imaging was conducted only when clinically necessary, particularly in patients showing clinical deterioration and/or functional decline.

Statistical analysis was performed using GraphPad Prism version 8.0.2. Continuous variables were expressed as mean ± standard deviation or median, depending on the distribution. Data normality was tested using the Shapiro-Wilk test. For the pre- and post-treatment comparison, we employed the Paired Samples t-test (for normally distributed data) or the Wilcoxon Signed-Rank test (for non-parametric data). A p-value of <0.05 was considered statistically significant.

Ethical statement

The study obtained the agreement of the Ethics Committee of Clinical County Hospital Mureș with number 15434/09.10.2025.

Results

This study included 15 patients diagnosed with interstitial lung disease presenting the UIP pattern (Figure I). The mean age was 73.2±8.14 years, with a predominance of male patients (n=11; 73.3%). Most cases were represented by idiopathic pulmonary fibrosis (IPF), recording a share of 73.3% (n=11), while the remaining 26.7% (n=4) were diagnosed with non-IPF forms of diffuse interstitial lung disease. The severity of disease at study entry, assessed using the GAP prognostic score, revealed a mean of 3.83±1.69 points, indicating a group with moderate risk of progression.

The normality of data distribution was confirmed using the Shapiro-Wilk test ($p>0.05$), allowing for the application of parametric test (Paired Samples t-test).

Different clinical profiles were found by etiological subanalysis at study entrance. Patients included in the IPF subgroup were older and presented greater levels of functional impairment compared to the non-IPF subgroup. (Table I)

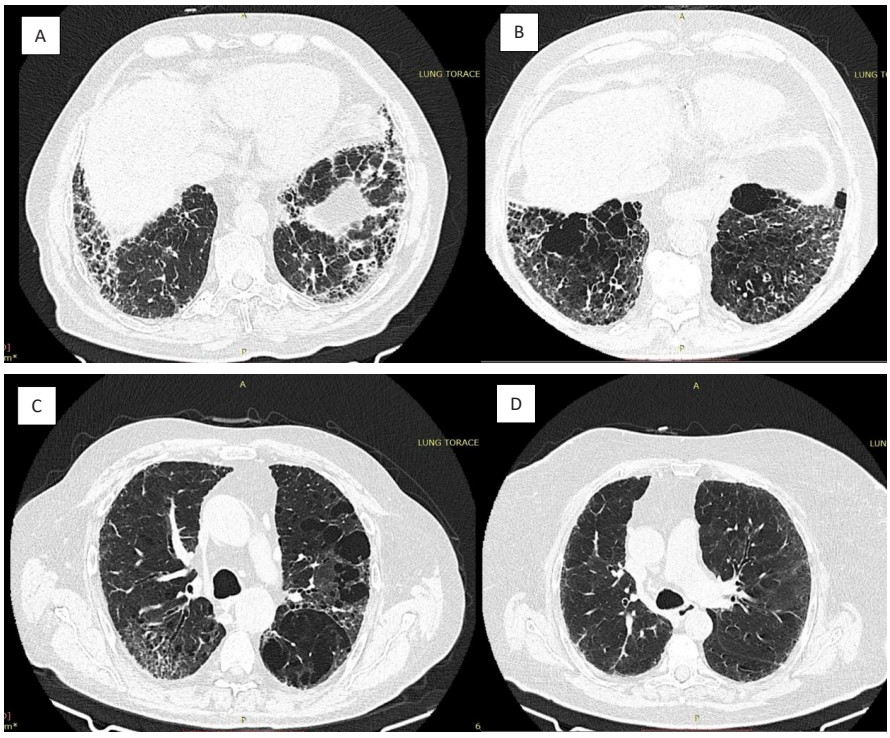


Fig. 1. High-resolution computer tomography demonstrates a typical UIP pattern:
A: Extensive subpleural honeycombing areas in the basal area; B: Dense reticular opacities, emphysema and honeycombing;
C: Progression of fibrosis in the upper perihilar level with severe architectural modifications and traction bronchiectasis;
D: Milder subpleural reticulation in the carinal level

Table I. Baseline Clinical and Functional Comparison by Etiology

Parameter	IPF Subgroup (n=11)	non-IPF Subgroup (n=4)
Age (years)	74.72 ± 5.19	69.00 ± 13.68
GAP Score	4.00 ± 1.60	3.50 ± 2.08
Baseline FVC (%)	81.60 ± 21.21	88.25 ± 26.87
Baseline DLCO (%)	42.60 ± 14.92	47.00 ± 8.48

The mean FVC at baseline was 83.50 ± 22.09% of predicted value. At re-evaluation, this parameter was observed to evolve at a mean of 94.00 ± 16.09%. Statistically, the paired t-test generated p value = 0.94. Although statistically insignificant, this functional outcome is clinically meaningful, indicating progress stagnation of fibrosis under nintedanib treatment.

When analyzing the entire study cohort, the DLCO parameter, considered a more sensitive indicator of alveolar-capillary membrane integrity, decreased from an average of 43.86 ± 13.23% to 40.90 ± 16.15%. Whilst a numerical decrease was recorded, the p = 0.26 value indicates that this decline is not statistically significant and may be interpreted as a controlled functional deterioration.

Notable differences were observed between the two subgroups from the moment of presentation. IPF patients started therapy with a more severe functional impairment compared to non-IPF patients. This suggests either a greater biological aggressiveness of IPF or a delayed diagnosis. In the non-IPF group, DLCO stability was remarkable. In the IPF group, a more pronounced trend towards a decrease in DLCO was observed, although it remained statistically insignificant. (Table II)

Table II. Longitudinal Functional Evolution: IPF versus Non-IPF Subgroups

Etiology	Parameter	Baseline -> Follow-up (%)	p-value
IPF	FVC	81.60 -> 90.28	0.93
	DLCO	42.60 -> 38.42	0.23
Non-IPF	FVC	88.25 -> 102.66	0.75
	DLCO	47.00 -> 46.66	0.49

Also, the relationship between the GAP prognostic score and baseline functional values was investigated. A negative correlation was observed between the GAP score and baseline DLCO value. Patients with a higher GAP score had significantly lower DLCO values, confirming its usefulness as a triage and severity assessment tool in the study group.

Nintedanib therapy was generally well tolerated. Out of a total of 15 patients, only one of them required discontinuation of treatment because of the adverse gastrointestinal effects.

The management of interstitial lung diseases exhibiting a UIP pattern has been evolved by the introduction of antifibrotic therapies. Landmark randomized clinical trials established nintedanib as an effective antifibrotic therapy for IPF, while the INBUILD trial subsequently demonstrated that nintedanib reduced the annual rate of FVC decline in progressive fibrosing ILDs beyond IPF [13,15]. Aligned with these findings, our real-world group showed functional stabilization under nintedanib therapy despite moderate baseline disease severity.

Diffusing capacity for carbon monoxide (DLCO) revealed a non-significant decline. The relative stability ob-

served in DLCO may suggest preservation of gas-exchange function under nintedanib therapy, consistent with the antifibrotic effect demonstrated in previous clinical trials.

Even though forced vital capacity (FVC) values showed a numerical increase during follow-up, this change did not reach statistical significance. In the context of such a progressive and irreversible disease, these results may be interpreted as clinically relevant. These findings are consistent with results from the INPULSIS and SENSCIS trials [15, 17], which demonstrated the significance of nintedanib in reducing the annual rate of FVC decline in fibrosing ILDs. Subgroup analysis revealed that patients with idiopathic pulmonary fibrosis (IPF) were older and presented with more impaired baseline lung function compared with those in the non-IPF group. In contrast, patients with non-IPF interstitial lung diseases exhibiting a UIP pattern demonstrated a notable stability in DLCO over the follow-up period. The functional stability observed in the non-IPF subgroup was consistent with the hypothesis that nintedanib treatment may have beneficial effects across fibrosing ILDs [18].

The observed negative correlation between the GAP prognostic score and baseline DLCO further supports the validity of this index as a marker of disease severity in this cluster of diseases. These results reinforce the utility of the GAP score as a practical triage tool for identifying patients with more advanced functional impairment who may benefit from early initiation of nintedanib therapy [19].

This study had several limitations, including a small number of patients (n=15) and a relatively short follow up period (6 months), which may limit the detection of long-term functional decline. Nevertheless, real-world evidence remains valuable in confirming that the benefits observed in randomized clinical trials are reproducible in clinical practice and across a broad spectrum of UIP-pattern ILDs [20].

Conclusion

A more complete understanding of the disease course in ILD with UIP pattern under nintedanib treatment was provided by combining functional and prognostic evaluation. Longitudinal assessment suggested that treatment was associated with functional stabilization, especially in terms of FVC, while DLCO score revealed only a limited, non-significant decline.

Baseline physiological impairment and prognostic score converged to identify patients at increased risk of progression, supporting the role of multidimensional assessment in routine clinical stratification. The differences observed between fibrosing interstitial lung diseases with and without IPF indicated potentially distinct functional trajectories, although these trends required cautious interpretation. Systematic functional monitoring, use of a prognostic index, and early antifibrotic intervention should be integrated into care pathways for fibrosing lung disease with UIP pattern. Given the limited cohort size, these findings were considered to support the hypotheses and highlighted the need for larger prospective studies to further clarify long-term functional outcomes.

Authors' contributions

GVD (Conceptualization; Formal analysis; Investigation; Writing – original draft; Visualization)
DEP (Data curation; Resources)
ECB (Conceptualization; Resources; Methodology; Project administration; Validation; Writing – original draft; Writing – review & editing; Supervision; Visualization)

Conflict of interest

No conflict of interest.

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