Poster

Incidence of Progressive Phenotype in Fibrosing Interstitial Lung Disease (PF-ILD) in a Tertiary Healthcare Center

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Incidence of Progressive Phenotype in Fibrosing Interstitial Lung Disease (PF-ILD) in a Tertiary Healthcare Center

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Introduction

- Progressive fibrotic interstitial lung disease (PF-ILD) is a heterogeneous group of chronic fibrotic lung diseases, characterized by progressive destruction of the lung parenchyma.
- The INBUILD trial (NCT02999178) demonstrated that Nintedanib was associated with a reduction in the rate of forced vital capacity (FVC) decline in PF-ILD over 12 months.
- It is important to understand characteristics of patients with fibrosing ILD who may be at higher risk of progression to ensure careful monitoring and access to treatment when appropriate.
- Evidence is lacking on what characteristics are associated with increased risk of developing the progressive phenotype among patients with fibrosing ILD

Methods

STUDY DESIGN

- Retrospective cohort study of fibrosing ILD patients using data from the Cleveland Clinic Health System electronic medical records (EMR).
- Patient population: adult patients with evidence of fibrosing ILD during the time-period 2009 - 2019.
- Index date was defined as the FVC date closest to first documented ILD diagnosis.

INCLUSION CRITERIA

- ≥2 ICD-9 or ICD-10 diagnosis on ≥2 separate dates for a relevant ILD between 2009 to 2019
- Two or more FVC values as per below –
  1. First documented FVC value between 12 months prior and 6 months following the initial documentation of ILD,
  2. At least one FVC measurement within the 3-28 months period following the initial FVC documentation
- Age ≥18 at first observed ILD diagnosis

EXCLUSION CRITERIA

- Lung transplant evaluation or successful transplant within 3 months of first encounter with ILD
- Enrollment in ILD specific randomized clinical trial

PRIMARY OUTCOME

- Progression: defined as an annualized greater than 10% relative decline in predicted FVC over the 28-month period from the index date.
- Lung transplant and all-cause death were considered competing risks if they occurred in the absence of progression

STATISTICAL ANALYSIS

- Continuous characteristics were described as mean (standard deviation), categorical patient characteristics were described with counts and percentages.
- Intergroup comparisons were analyzed using unpaired Student's t test or Mann-Whitney U test for continuous variables, as appropriate, and chi-square test/Fishers exact test for categorical variables.

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Table 1: Baseline Characteristics by Progression

* Missing values for 1001 patients

Characteristic	Overall, N = 5,934	FVC decline ≤ 10% N = 4,948	FVC decline > 10% N = 986
Age			
Age, Mean (SD)	62 (14)	61 (14)	66 (13)
Race			
Black N (%)	692 (12%)	602 (12%)	90 (9%)
White N (%)	4,945 (83%)	4,103 (83%)	842 (85%)
Gender			
Female, N (%)	3,101 (52%)	2,654 (54%)	447 (45%)
Smoking status			
Current, N (%)	476 (8.0%)	396 (8.0%)	80 (8.1%)
Former, N (%)	2,622 (44%)	2,128 (43%)	494 (50%)
Never, N (%)	2,479 (42%)	2,118 (43%)	361 (37%)
Unknown, N (%)	357 (6%)	306 (6.2%)	51 (5.2%)
Comorbidities			
COPD/Emphysema, N (%)	1,577 (27%)	1,277 (26%)	300 (30%)
GERD, N (%)	2,068 (35%)	1,710 (35%)	358 (36%)
OSA, N (%)	1,022 (17%)	828 (17%)	194 (20%)
Asthma, N (%)	1,253 (21%)	1,047 (21%)	206 (21%)
Coronary Artery Disease, N (%)	1,395 (24%)	1,090 (22%)	305 (31%)
Heart Failure, N (%)	959 (16%)	775 (16%)	184 (19%)
CKD, N (%)	590 (9.9%)	457 (9.2%)	133 (13%)
Pulmonary Hypertension, N (%)	401 (6.8%)	337 (6.8%)	64 (6.5%)
Charlson comorbidity index (IQR), N (%)	1, (0, 4)	1, (0, 4)	1, (0, 5)
Immunosuppression, N (%)	2,288 (39%)	1,928 (39%)	360 (37%)
Pulmonary Function on index testing (in Median (IQR))			
FEV1/FVC Ratio	83 (74, 97)	83 (74, 97)	84 (73, 97)
Baseline FVC (% predicted)	81 (66, 94)	81 (67, 95)	75 (62, 90)
DLCO (% predicted)*	41 (20, 67)	42 (20, 69)	37 (18, 56)

Table 2: Rate of progression by PF-ILD diagnosis subgroup at Index visit

Index ILD diagnosis	Cohort size (N, %)	Further Progression within 24 months [% (95% CI)]
Undifferentiated/other	3088 (52.0)	23.0 (14.1, 31.9)
Sarcoidosis	1417 (23.9)	9.0 (7.4, 10.6)
CTD-ILD	1054 (17.8)	14.6 (12.3, 16.8)
IPF	184 (3.1)	26.9 (20.0, 33.9)
Occupational ILD	100 (1.7)	21.4 (12.6, 32.1)
Hypersensitivity pneumonitis	79 (1.3)	22.4 (13.2, 31.7)
Idiopathic NSIP	12 (0.2)	16.7 (0, 38.7)

Results

- Mean age (SD) at time of first diagnosis was 62±14 years; patients with FVC decline > 10% had mean age of 66 years vs. 61 years for patients who did not experience this decline (Table 1)
- Baseline pulmonary function testing at time of cohort entry was significantly different in those who experienced a >10% relative decline in FVC (Table 1). Baseline Charlson Comorbidity Index did not show any difference.
- Within the first year of initial ILD diagnosis, prednisone was prescribed to 43% of patients; 39% received a prescription for an alternate immunosuppressive agent.
- 37% of patients with a >10% relative decline in FVC received a prescription for immunosuppression, compared with 39% of patients who did not experience decline.
- 52% of patients had undifferentiated ILD at the time of first diagnosis, 24% had sarcoidosis, 18% had CTD-ILD, and 3% had IPF (Table 2)
- 998 (16.8%) patients experienced >10% relative decline in FVC during 28 months post-index among all ILD patients, and progression was different by ILD sub-categories.
- IPF had the largest incidence of progression (26.9% (95% CI - 20.0, 33.9)), while sarcoidosis had the lowest incidence (9.0% (95% CI - 7.4, 10.6)) (Table 2).

Conclusions

- 16.8% of ILD patients experienced a ≥10% decline in FVC within 24 months of first FVC measurement around ILD diagnosis.
- Incidence of progression was observed to be higher in IPF patients, and lower in sarcoidosis patients.
- Identifying factors associated with an increased risk of PF-ILD prior to the onset of progression may help to guide early therapy initiation and improve our understanding of the prognosis in this patient population.

Limitations

- This study relies on a single metric of fibrotic ILD progression (FVC decline > 10%). The true incidence of progression (including worsening of HRCT and/or worsening symptoms) may be higher than reported within this sample.
- Study is limited to patients seeking care at tertiary hospital (Cleveland Clinic), hence may not be representative of general US population with fibrotic ILD.

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