Prevalence and Characteristics of Progressive Fibrosing Interstitial Lung Diseases

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INTRODUCTION

- Interstitial lung diseases (ILDs) represent a spectrum of lung disorders involving the lung parenchyma that often result in fibrosis (scarring) of lung tissue.
- The prototypical fibrosing ILD is idiopathic pulmonary fibrosis (IPF)
- A subset of non-IPF patients with fibrosing ILD develop a progressive phenotype (PF-ILD).
- Antifibrotic therapy may help this subset of patients[1]; however, the local prevalence of PF-ILD unknown

OBJECTIVES

- To describe the local prevalence and clinical characteristics of patients with PF-ILD, and compare them to patients with fibrosing ILD without a progressive phenotype (non-progressors)

METHODS

- Participants of the Canadian Registry for Pulmonary Fibrosis (CARE-PF), McMaster University site, were studied.
- All participants with 1) evidence of fibrosis on CT scan, 2) diagnosis other than IPF, and had serial forced vital capacity (FVC) measurements recorded were included, from November 2015 to March 2020.
- Participants were classified as PF-ILD using the INBUILD study criteria[1]: relative forced vital capacity (FVC) decline ≥10%, or any 2 of: relative FVC decline 5-10%, worsening respiratory symptoms or worsening fibrosis on HRCT, over the preceding 24 months
- The remaining patients that did not meet criteria for PF-ILD, but had non-IPF fibrotic ILD, were classified as non-progressors
- The primary outcomes were the rate of lung function decline, as determined by the mean absolute fall in FVC over the prior year, measured in ml ± standard deviation, and the prevalence of PF-ILD
- Prevalence was reported per 100,000 persons, using Hamilton Niagara Haldimand Brant Local Health Integration Network (HNHB-LHIN) population data
- A sensitivity analysis was done stratifying prevalence estimates by the following age groups: under 40, 40-59, 60-79, and 80 and above

METHODS

- Descriptive measures for baseline characteristics were reported in means (±standard deviation), medians (interquartile range), and percentages.
- Differences in baseline characteristics between PF-ILD and non-progressors were compared using the $\chi 2$ test for categorical variables, by Student's t-test for normally distributed variables, and by the Kruskal-Wallis test for non-normally distributed continuous variables

RESULTS

	PF-ILD	Non-progressors	P-value
n	101 (43%)	133 (57%)	
Age (years)	65±12	64±12	0.41
Male sex	40 (40%)	59 (44%)	0.47
Ethnicity			0.15
Caucasian	86 (89%)	116 (92%)	
Asian	8 (8.2%)	6 (4.8%)	
Other	3 (3%)	2 (1.5%)	
Smoking History			0.006
Non-smoker	36 (36%)	64 (48%)	
Ex-smoker	64 (63%)	60 (45%)	
Current smokers	1 (1%)	9 (90%)	
Family history of ILD	8 (8%)	10 (8%)	0.97
ILD Diagnosis			0.59
CTD-ILD	41 (40%)	47 (35%)	
Chronic HP	14 (14%)	15 (11%)	
Sarcoidosis	8 (8%)	17 (13%)	
Inorganic dust exposure-ILD	5 (5%)	6 (5%)	
Other	33 (33%)	48 (36%)	
BMI	30±7	31±7	0.55
Baseline PFT's			
FVC (L)	2.50±0.86	2.72±0.96	0.08
FVC % predicted	71±18	74±18	0.27
FEV1 (L)	1.98±0.66	2.12±0.73	0.11
FEV1 % predicted	73±19	75±19	0.50
DLCO (ml/min/mmHg)	12.09±4.03	14.78±6.39	0.006
DLCO % predicted	51±15	60±19	0.003
GAP score			0.36
Stage I	69 (68%)	101 (76%)	
Stage II	31 (31%)	30 (23%)	
Stage III	1 (1%)	2 (2%)	

Table 1: Baseline characteristics. Data presented as mean ± SD; or count (column percentage). CTD-ILD (connective tissue disease associated ILD), HP (hypersensitivity pneumonitis), BMI (body mass index), FEV_1 (forced expiratory volume in 1st second, L), FVC (forced vital capacity, L), DLCO (transfer capacity for carbon monoxide ml/mmHg/min), GAP (Gender-Age-Physiology) score, a validated mortality risk score for ILD that uses gender, age, %predicted FVC and %predicted DLCO

RESULTS

- 234 participants with non-IPF fibrosing ILD were included.
- Of these, 101 (43%) met criteria for PF-ILD and 133 (57%) were non-progressors.
- PF-ILD and non-progressors did not differ by age, sex, ethnicity, underlying ILD diagnosis or GAP score. Compared to non-progressors, PF-ILD were more likely to have a smoking history, and a trend towards lower baseline FVC and DLCO (Table 1).
- The mean annual FVC decline in patients with PF-ILD was 173±250ml; in comparison, no decline in lung function was evident in non-progressors (mean annual FVC change +39±262ml)

Age category	Local population size	Number of patients with PF-ILD	Age-specific prevalence per 100,000 persons
Under 40	**683,630**	**4**	**0.59**
40-59	**413,120**	**25**	**6.05**
60-79	**286,703**	**59**	**20.58**
80 and above	**75,000**	**13**	**17.33**
Total	**1,458,453**	**101**	**6.93**

Table 2: Total and age-specific prevalence of PF-ILD (per 100,000 persons)

- Based on a local catchment area of 1,458,453 people, the prevalence of PF-ILD was 6.93 per 100,000 people of all ages.
- The prevalence of PF-ILD was highest in the 60-79 age group, followed by the 80 and above age group and the 40-59 age group.
- PF-ILD was uncommon in those under 40

CONCLUSIONS

- PF-ILD is prevalent in the local community, with case rates highest in those in the 60-79 age group.
- Smoking and lower baseline lung function were important risk factors for PF-ILD
- PF-ILD were most commonly patients with CTD-ILD, specifically RA-ILD, followed by patients with chronic hypersensitivity pneumonitis
- The rate of disease progression in patients with PF-ILD, as measured by annual FVC decline, was 173±250ml, which matches disease progression rates seen in IPF[2]
- The rate of lung function decline was similar to the placebo arm of the INBUILD study, a recent randomized control trial showing that nintedanib, an antifibrotic drug, slows the rate of progression of FVC decline in PF-ILD
- This data highlights the importance of identifying patients who meet criteria for PF-ILD, so that they may benefit from evidence-based therapy with antifibrotics

REFERENCES

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