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# A comparative study to evaluate factors affecting adverse outcomes in interstitial lung diseases with Idiopathic pulmonary fibrosis (IPF) and other non-IPF interstitial lung diseases at 6 months in a tertiary care centre

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## ABSTRACT

**Introduction and aim of the study:** The diagnosis and treatment of interstitial lung diseases (ILD), a class of diffuse parenchymal lung disorders that are associated with significant morbidity and death, provide challenges to the clinician. Multidisciplinary discussions (MDD) between a clinician, radiologist, and pathologist are used to diagnose ILD. There is a lack of information on the use of composite prediction models such as the ILD Gap Index and the Composite Physiologic Index. The main objective of the study was to evaluate factors affecting adverse outcomes in interstitial lung diseases with idiopathic pulmonary fibrosis (IPF) and other non-IPF interstitial lung diseases at 6 months in a tertiary care centre.

**Material and methods:** This was a retrospective cohort research carried out at a tertiary care centre at Howrah, a district of state West Bengal in India. The main inclusion criteria were to include all patients who had complete medical records after being diagnosed with ILD. Any patients who suffered from pulmonary TB or lung cancer were excluded. The study comprised 164 consecutive individuals with a multidisciplinary diagnosis of interstitial lung disease. At 6 months, clinical evaluation, spirometry and DLCO were performed on the patients. FVC reduction of less than 10% at 6 months and mortality were evaluated as outcome variables.

**Results:** Idiopathic pulmonary fibrosis (IPF) affected 27.2% of the 164 patients who were evaluated, while non-IPF affected 72.8% of the patients. At a 6-month follow-up, 15.2% of patients died, with 72% having IPF. At 6 months, the FVC of 51.2% had decreased by 10%. Age more than 60, male gender, BMI 18.5, smoking, the presence of pulmonary hypertension, mean saturation more than 90%, percentage predicted FVC more than 50%, percentage predicted DLCO more than 40 per cent, 6-minute walk distance more than 250 m at diagnosis, UIP pattern in HRCT, CPI score more than 50, and ILD-GAP index more than 4 are factors associated with mortality in interstitial lung diseases. Age more than 60 years old and IPF group were variables linked with death in multivariate analysis using logistic regression in bivariate analysis, the same factors were linked to a reduction in FVC of more than 10% at 6 months, whereas in multivariate analysis, smoking history and an initial projected DLCO of less than 40% were significant. In interstitial lung disorders, the ILD Gap index is a better predictor of death than a composite physiologic index. (AURO 0.912 vs., CPI 0.856).

**Conclusions:** Interstitial lung disease mortality indicators include age more than 60, idiopathic pulmonary fibrosis type, and FVC decline  $\geq 10\%$  at 6 months and less than 50% at baseline. Prediction methods like composite physiologic index (CPI) and ILD Gap index aid prognosis and clinical decision-making. The ILD Gap index predicted mortality better than the composite physiologic index. The main objective of the study was to evaluate factors affecting adverse outcomes in interstitial lung diseases with idiopathic pulmonary fibrosis (IPF) and other non-IPF interstitial lung diseases at 6 months in a tertiary care centre.

**Keywords:** lung disease, interstitial lung diseases, Idiopathic pulmonary fibrosis, non-IPF interstitial lung diseases

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## Introduction

The course of fibrosing interstitial lung disease (ILD) is rather variable. Some patients have a stable path or modest functional decline, while others advance rapidly [1]. Progressive fibrosing interstitial lung disease (PF-ILD) is a group of diseases marked by a high-resolution computed tomography (HRCT) documented increase in pulmonary fibrosis, a decline in lung function, deteriorating breathing symptoms and quality of life, and an elevated risk of early mortality despite treatment options. Its clinical course is similar to that of idiopathic pulmonary fibrosis (IPF) [1]. Given the diversity of patient- and disease-specific characteristics in ILDs, risk prediction is difficult. Given its simplicity of measurement, consistency, and capacity to predict prognosis at baseline and throughout time, with even slight changes giving prognostic information [2], forced vital capacity (FVC) may be the most suitable single prognostic indicator. The outcome measure that received the highest support from the consensus panellists for both connective tissue disease-associated interstitial lung disease (CTD-ILD) and IPF was FVC, which received unanimous support. Inconsistent results presently support the use of changes in FVC as a possible proxy for mortality or, conversely, progression-free survival [3]. A decline of more than 10% in the percentage of projected FVC is a reliable indicator of disease progression [4]. To assess the likelihood of an event, often a diagnosis or prognosis, clinical prediction models incorporate statistical information from the history, physical examination, and/or test results. Survival was also predicted by baseline diffusing capacity of the lungs for carbon monoxide (DLCO) and CPI scores [5]. ILD utilising the GAP model, a previously established clinical prediction model for ILD based on sex, age, and lung physiology [6]. The ILD-GAP model successfully predicts mortality across all disease stages and in the majority of chronic ILD subtypes [6]. The results of the different forms of ILD vary significantly, according to the research currently available. Studies examining risk factors for ILD mortality are few and far between in our environment. There is a dearth of information on the use of composite prediction models like the composite physiologic index and ILD Gap Index. Prospective disease registries may provide more accurate estimations of incidence and prevalence as well as insights into the aetiology, risk factors, course and results of a disease.

## Material and methods

This was a retrospective cohort research carried out at a tertiary care centre at Howrah, a district of state

West Bengal in India. The main inclusion criterion was to include all patients who had complete medical records after being diagnosed with ILD. Any patients who suffered from pulmonary TB or lung cancer and also did not have all relevant details in records were excluded. The main objective of the study was to contrast the adverse outcome as measured by a decline in FVC/DLCO at 6 months in patients with idiopathic pulmonary fibrosis (IPF) and other non-IPF interstitial lung disease who were registered and presented to a tertiary care centre in Howrah, a district of the Indian state of West Bengal, for 2 years. The secondary objective of the study was to identify the elements influencing the negative effects of interstitial lung disorders and to assess the predictive efficacy of the ILD GAP score and the composite physiologic index (CPI) in interstitial lung disorders.

The paper does not report on primary research. All data analysed were collected as part of routine diagnosis and treatment. The program was not set up as a study or research project but as a treatment program; hence ethics approval was not required. The paper examines the information gathered from the patient visits' medical records using a pre-made, standardised form. None of the participants got any financial reward. The Helsinki Declaration's guiding principles are followed by this research.

The study comprised 164 consecutive individuals with a multidisciplinary diagnosis of interstitial lung disease. A thorough history, spirometry, HRT, DLCO, peripheral oxygen saturation (SpO<sub>2</sub>) 6-minute walk test, ECG and 2-dimensional eco results were documented in a well-completed proforma. Wherever appropriate, the ANA profile, serum angiotensin-converting enzyme, serum calcium, and 24-hour urine calcium were noted from the electronic OPD registry. According to the current recommendations of the American Thoracic Society/European Respiratory Society, IPF was diagnosed after ruling out the known causes and HRCT data suggesting a UIP pattern. At 6 months, clinical evaluation, spirometry and DLCO were performed on the patients at the clinic and data was captured from the electronic patient registry of clinic OPD. FVC reduction of less than 10% at 6 months and mortality were evaluated as outcome variables.

Data were imported into Microsoft Excel and EPI info version 7 was used for analysis. Quantitative variables were characterised by mean and standard deviation for descriptive statistics. A percentage distribution was used to characterise qualitative factors. For inferential statistics comparing groups, the chi-square test was used to compare qualitative variables, while the student t-test was used to compare quantitative data. P-values less than 0.05 were regarded as significant. The Kaplan–Meier survival plot was used to evaluate the survival pattern.

**Table 1.** Interstitial lung disease mortality risk factors (Bivariate analysis)

Parameters	Survived		Not survived		RR	95% CI	P-value
	N	%	N	%			
Age > 60 (years)	32	23.2	17	68	1.4	1.15–1.75	0.002
Ever smoker (N)	32	23.02	14	56	1.3	1.06–1.5	< 0.001
Sex male (N)	40	28.78	16	64	1.29	1.08–1.53	< 0.001
BMI < 18.5 (kg/m <sup>2</sup> )	8	5.76	11	44	2.14	1.26–3.84	< 0.001
Pulmonary hypertension (N)	32	23.02	17	68	1.42	1.15–1.75	< 0.001
GERD	96	69.06	18	72	1.02	0.8–1.17	0.4
DLCO < 40%	19	16.3	20	86.96	2.1	1.4–2.9	< 0.001
FVC < 50%	68	48.92	22	88	1.26	1.1–1.4	0.003
HRCT UIP pattern	36	25.9	19	76	1.4	1.18–1.75	< 0.001
6 MWD < 250 m	46	34.07	20	83.3	1.3	1.16–1.6	< 0.001
ILD Gap index > 4	17	16.3	20	86.96	2.1	1.4–2.9	< 0.001
CPI score > 50	40	34.9	24	100	1.6	1.3–1.9	< 0.001

BMI — body mass index; CI — confidence interval; CPI — composite physiologic index; DLCO — diffusing capacity of the lungs for carbon monoxide; FVC — forced vital capacity; GERD — gastro-esophageal reflux disease; HRCT UIP — high-resolution computed tomography for usual interstitial pneumonia; ILD — interstitial lung diseases; N — number of patients; RR — risk ratio

## Results

Idiopathic pulmonary fibrosis (IPF) affected 27.2% of the 164 patients who were evaluated, while non-IPF affected 72.8% of the patients.

At a 6 month follow-up, 15.2% (95% CI: 10.11%, 21.68%) of patients died, with 72% having IPF. At 6 months, the FVC of 51.2% (95% CI: 41.3%, 59%) had decreased by 10%. IPF and other ILDs had different death proportions, and this difference was statistically significant. (RR:1.62, 95% CI: 1.25, 2.09) with a p-value less than 0.001.

Compared to non-IPF (39.6%), FVC reduction was greater in IPF (83.7%). It was statistically significant that the percentage of FVC drop of 10% differed between the 2 groups (RR 1.59, 95% CI: 1.3, 1.94, p-value 0.001).

Age more than 60, male gender, BMI 18.5, smoking, the presence of pulmonary hypertension, mean saturation more than 90%, percentage predicted FVC more than 50%, percentage predicted DLCO more than 40%, 6-minute walk distance more than 250 m at diagnosis, UIP pattern in HRCT, CPI score more than 50, and ILD-GAP index more than 4 are factors associated with mortality in interstitial lung diseases (Tab. 1). Age more than 60 years old and IPF group were variables linked with death on multivariate analysis using logistic regression in bivariate analysis, same factors were linked to a reduction in FVC of more than 10% at 6 months, whereas in multivariate analysis, smoking history and an initial projected DLCO of less than 40% were significant. In interstitial lung disorders, the ILD Gap index is a better

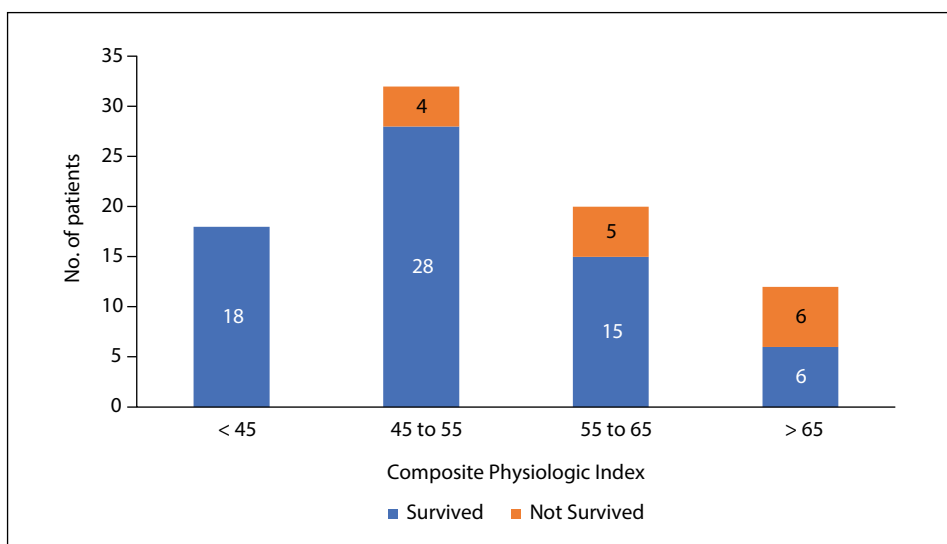
predictor of death than the composite physiologic index. (AURO 0.912 vs. CPI 0.856) (Tab. 1).

CPI had a mean value of 50.1811.6. Patients with IPF had a higher mean CPI (56.58.9) than those with other ILDs (47.4111.7),  $p < 0.004$  (Fig. 1).

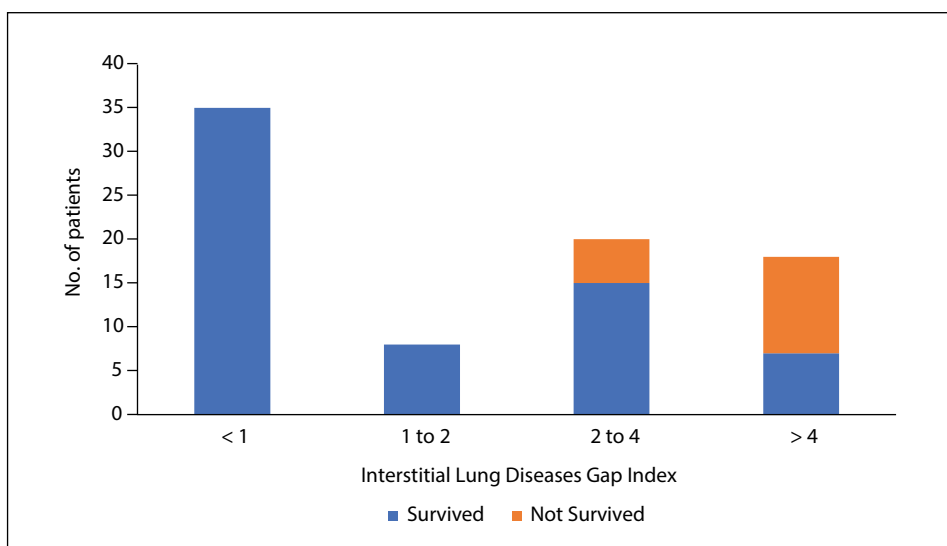
## Discussion

Because the condition is heterogeneous, it is difficult to determine risk in chronic interstitial lung disease [6]. We currently know very little about the factors that predict death in IPF patients, and studies in this field have not produced any prediction models that can be relied upon to accurately estimate each patient's risk of mortality [2]. Given its simplicity of measurement, consistency, and capacity to predict prognosis at baseline and throughout time, with even slight changes giving prognostic information [2], FVC is often the most suitable single prognostic indicator. Clinical prediction models are statistical models that include clinical observations from the past, present, and/or outcomes of tests to calculate the likelihood of an event [2]. The purpose of this research is to identify characteristics that predict survival, the clinical and physiological outcome of ILD at a 6-month follow-up, and to assess prediction models such as CPI and ILD-GAP Index in ILD.

A hospital-based cohort study including 164 individuals with ILD was done by the study team. Similar to what Sharma et al. [16] observed, out of the



**Figure 1.** Scores for the composite physiologic index that predicts death



**Figure 2.** Interstitial Lung Diseases Gap Index mortality prediction score

164 individuals evaluated, 26.2% had idiopathic pulmonary fibrosis (IPF), and 73.78% did not. According to Somenath Kundu et al., IPF was the most prevalent ILD (38.04%), followed by CTD-ILD (31.5%) [17].

At the 6-month follow-up in the present investigation, 15.2% of the study population had passed away, with IPF having a greater death rate than non-IPF. Mortality was significantly different between IPF and non-IPF ILDs (41.8% vs. 5.8%). Amandine Vial et al.'s study also emphasised IPF's poor prognosis in comparison to other ILDs [6].

Age > 60, male gender, BMI 18.5, smoking, the presence of pulmonary hypertension, mean saturation > 90%, per cent predicted FVC > 50%, per cent

predicted DLCO > 40%, 6-minute walk distance > 250 m at diagnosis, UIP pattern in HRCT, CPI score > 50, and ILD- GAP index > 4 are factors in the study that are linked to mortality in interstitial lung diseases. Age more than 60 years old and IPF group were variables related to mortality in a multivariate analysis. In research by Assayag D et al., older age, male gender, reduced carbon monoxide diffusion capacity, degree of fibrosis, and the presence of the typical interstitial pneumonia pattern were significant predictors of death on multivariate analysis [9].

51.2% of the participants in the trial saw a decline in FVC of 10% or more at 6 months. Bivariate analysis revealed factors comparable to those linked to mortality

that were also related to declines in FVC of more than 10% at 6 months; however, multivariate analysis revealed that history of smoking and initial % anticipated DLCO 40% were significant.

Our research revealed that IPF patients (83.7%) had a greater FVC drop of >10% than non-IPF patients (39.6%). According to Dinesh Khanna et al., the fall in FVC % over a year was 12.8% [18–20].

Similar to the finding by Solomon JJ that a lower baseline % predicted forced vital capacity and a 10% decline in FVC % predicted from baseline to any time during follow-up were independently associated with an increased risk of death [10], FVC 50% at baseline is associated with mortality in the present study. King TE Jr > 10% decrease in the percentage of expected FVC is a reliable indicator of the course of the illness [3].

The results of this study's evaluation of composite prediction models, such as the composite physiologic index and the ILD Gap index, again show that IPF patients have a worse prognosis than those with other ILDs. The ILD-GAP model successfully predicted mortality in the majority of chronic ILD subtypes and at all disease phases, according to earlier research [6]. The efficacy of GAP and CPI as multidimensional measures in IPF prognostication was further supported by a study by Charles Sharp et al. [7]. In the present investigation, the ILD Gap score outperformed the Composite Physiologic score as a predictor of death in interstitial lung disorders, which is consistent with Hanna M. et al.'s findings [5].

## Conclusion

Age more than 60 years, idiopathic pulmonary fibrosis as the ILD type, and drop in FVC 10% at 6 months as well as FVC 50% at baseline were variables linked to ILD mortality. When it comes to prognostication and clinical decision-making, trustworthy prediction models like the composite physiologic index (CPI) and ILD Gap index are readily available. The ILD Gap index outperformed the composite physiologic index as a predictor of death.

## Article information

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