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Research Article

MORTALITY IN IPF BY COMPOSITE PHYSIOLOGICAL INDEX AND GAP MODEL

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A B S T R A C T

Idiopathic Pulmonary Fibrosis (IPF) is one of the most aggressive form of Idiopathic Interstitial Pneumonias and its clinical course is highly variable. Many tools have been used in past like pulmonary functional test (PFT), but none of them can actually predict the extent of disease. So there is unmet need of development of a tool which can predict the course of disease. Composite Physiological Index (CPI) on comparison with already established GAP model of IPF helps us to predict the course of the disease so that appropriate medical and surgical intervention like lung transplantation could be planned.

In this study mortality rate in IPF Patients were studied retrospectively for period of two years. In our study, it was found that mortality rate in IPF increases with increase of mean composite physiological Index, hence it indicates the poor prognosis of disease.

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is the most common and most aggressive of the idiopathic interstitial pneumonias. Its clinical features are dypnea on exertion, cough, clubbing of fingers and bibasal crackles on auscultation the chest with consistent radiological and histopathological features of UIP.[1]Natural history of IPF is not well understood due tolimited epidemiological studies done in past. Life expectancy in patients having IPF is about 2.5 to 3.5 years[1, 2] however, there is variability in survival due to inconstant clinical course. Usually symptoms appears 1-2 years preceding a diagnosis.[3]Now a days subclinical IPF is more frequently detected due to increase in frequency of performance of thoracic imaging, leading to a median survival between 2 and 4 years from time of diagnosis[4-6]. There are no proper consensus stating measures to assess prognosis and response of treatment in patients having IPF[7-9].

Several models with multifaceted scoring systems have been developed by combination of single factors which have been proved beneficial in predicting prognosis in patients having IPF. However these models are cumbersome to use and never got widely accepted as a prognostic tool [6]. In previous models exercise testing, histoptahological and radiological testing was given preference over pulmonary function test (PFT) so new entity composite physiologic index (CPI) was developed which only contained pulmonary function test (PFT) and gas transfer values and was easy to use as compared to previous models[10].

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Another multidimensional index combining gender (G), age (A) and two lung physiology variables (P), i.e. forced vital capacity (FVC) and diffusion capacity to carbon monoxide (DLCO) was developed in the GAP model having three stages proposing 2- year mortality rate of 11, 30 and 62%[11].

The aim of our study was to determine whether mortality is accurately predicted by composite physiological index in patients with IPF using the GAP model, a clinical prediction model based on sex, age, and lung physiology, that has been validated in patients with idiopathic pulmonary fibrosis.[11]

MATERIALS AND METHODS

A two year retrospective study was done from March 2017 to March 2015 in 33 already diagnosed and registered cases of idiopathic pulmonary fibrosis at department of respiratory medicine, JLN medical college Ajmer, Rajasthan. IPF was diagnosed on the basis of the 2011 criteria of the American Thoracic Society/European Respiratory Society (ATS/ERS).Diagnostic criteria comprised (*1*) bilateral basal or widespread crackles, (*2*) a restrictive ventilatory defect or isolated depression of DL_{CO}, (*3*) CT appearances compatible with IPF (discussed later here), and (*4*) no environmental exposure to a fibrogenic agent (4). Patients with connective tissue diseases were excluded.[1]

CT criteria for inclusion in the study consisted of (*1*) predominantly basal and subpleural distribution of disease, (*2*) a variable mixture of reticular abnormalities and ground-glass attenuation (when ground-glass attenuation was prominent [in a minority of cases], evidence of underlying fine fibrosis, consisting of traction bronchiolectasis, was required), (*3*) the absence of consolidation, nodular abnormalities, or other

parenchymal abnormalities (except for centrilobular emphysema).[1]

Patients were divided into three different groups by using GAP score, which was calculated using the method suggested by Ley *et al* (Image 1). All four clinical variables were examined: gender (woman: 0 points, man: 1 point), age (0-2 points), FVC (%) (0-2 points), and DL_{CO} (%) (0-3 points).[2]The CPI was derived for each individual in all groups by the formula as follows: CPI = 91.0 − (0.65 × percent predicted diffusing capacity for carbon monoxide [DL_{CO}]) − (0.53 × percent predicted FVC) + (0.34 × percent predicted FEV_1).[10]

Mean CPI was calculated in each group, and mean CPI of the patients who expired in two years was calculated and compared in each group.

RESULTS

Baseline mean composite physiological index in 11 patients of group1 was 48.10, in 11 patients of group II was 54.61 and in 11 patients of group III was 64.19(Table 1).

After two years 1 patient expired in group I, 3 patients expired in II, and 6 patients expired in group III. Two year mortality rate in group I was 9.09%, in group II was 27.27% and in group III was 54.54%. Composite physiological index and mortality rate significantly increases with each stage of IPF patients (derived from GAP INDEX).

DISCUSSION

Our study shows that mortality rate is higher in patients with high gap staging (III>II>I). Composite physiological index (CPI) which reflects the extent of disease can also be used as predictor of mortality in IPF patients. In our study a mean CPI value of 58.22 and above predicts increased two years mortality in patients with IPF.

In idiopathic pulmonary fibrosis, the quantification of disease severity using pulmonary function tests is often confounded by emphysema. Previous histopathological and CT studies have shown that DL_{CO} levels most closely reflects the extent of fibrosis, so DL_{CO} was included in the CPI which quantifies the functional defect attributable to pulmonary fibrosis.[12,13,14]FVC and FEV_1 levels were integrated in the CPI and more weight age was given to FVC than FEV_1 as higher ("restrictive") FEV_1 level results in an increased CPI score, because in that case, reductions in DL_{CO} and FVC are largely or wholly due to fibrosis rather than emphysema[13] . As several studies have shown that decline in FVC levels are more significantly related to prognosis in patients with proven UIP so spirometric volumes were applied along with DL_{CO} levels in CPI.[15, 16]

The CPI offers two distinct advantages. First, it does not necessitates the use of radiological or histopathological variables. A second advantage of the CPI index is the use of DL_{CO} levels which relates to the extent of fibrosis, rather than exercise data is used. Previously used indexes such as CRP score cannot be used in all patients having IPF as there exercise tests are limited by cardiac disease or resting hypoxia.[6]

The CPI is a new "severity variable" that reconciles functional severity and the global morphologic extent of disease. Our observations show that the CPI correlates with predicted mortality rate calculated by GAP model and is linked to mortality (in histologically proven UIP and in IPF diagnosed using clinical and CT criteria) more closely than individual pulmonary function indices. The CPI accounts for coexisting emphysema in patients having IPF (a major confounding influence on pulmonary function indices). In patients without emphysema on CT, the CPI reflected the extent of fibrosis no better than DL_{CO} levels.[14, 17, 18]

CONCLISION

Our study shows that mortality rate is higher in patients with high gap staging (III>II>I). Composite physiological index (CPI) which reflects the extent of disease can also be used as predictor of mortality in IPF patients.

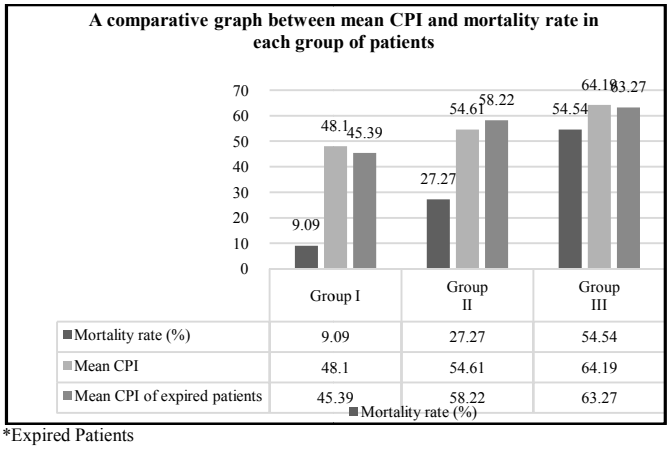
Image 1

	Predictor	Points
G	Gender	
	Female	0
	Male	1
A	Age, y	
	≤60	0
	61–65	1
	>65	2
P	Physiology	
	FVC, % *predicted*	
	>75	0
	50–75	1
	<50	2
	D_{LCO}, % *predicted*	
	>55	0
	36–55	1
	≤35	2
	Cannot perform	3
	Total Possible Points	8

Stage	I	II	III
Points	0–3	4–5	6–8
Mortality			
1-y	5.6	16.2	39.2
2-y	10.9	29.9	62.1
3-y	16.3	42.1	76.8

Table 1

	Composite Physiological Index(CPI)		
S. No.	**Group I**	**Group II**	**Group III**
1.	49.87	53.98	61.29*
2.	49.45	62.7*	61.8
3.	50.95	48.81	68.11*
4.	45.39*	53.86	68.72
5.	45.98	59.42	59.98*
6.	50.01	49.53	63.75*
7.	46.78	54.65*	61.76
8.	44.86	53.92	62.84*
9.	49.34	56.54	63.66*
10.	46.35	57.31*	64.71
11	50.15	55.64	69.91
Total	529.13	600.74	706.13
Mean CPI	48.1	54.61	64.19
Mean CPI of expired patients	45.39	58.22	63.27



*Expired Patients

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