

# Pulmonary hypertension in idiopathic pulmonary fibrosis

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**Background** Pulmonary hypertension (PH) is a common finding in patients with idiopathic pulmonary fibrosis (IPF) and is associated with increased morbidity and mortality.

**Aim** This study was designed to detect the prevalence of PH in patients with IPF and to determine the correlation between pulmonary function test (PFT) parameters, radiological and echocardiographic findings, and PH among these patients. In addition, the effect of therapy for 1 month (long-term oxygen therapy ± drugs) on PH was evaluated.

**Patients and methods** PFTs, the composite physiologic index, multidetector chest computed tomography, and echocardiography were performed on 60 IPF patients (10 men and 50 women, mean age 51 years). Fifteen healthy age-matched and sex-matched volunteers were also studied as a control group.

**Results** PH was present in 46 (76.6%) patients of IPF. There was a high negative correlation between parameters of PFTs and composite physiologic index and the mean pulmonary arterial pressure (mPAP). In contrast, there was a significant positive correlation between

mPAP and main pulmonary artery diameter on computed tomography. There was also a positive correlation between echocardiographic findings and mPAP. There was no significant improvement of PH between those patients treated with drugs and oxygen and those on oxygen therapy alone.

**Conclusion** PH is common in patients with IPF. There is an inverse relationship between lung function measures and PH and a direct one with radiological and echocardiographic findings. The short-term use of oxygen therapy with or without drugs had no effect on PH in patients with IPF. *Egypt J Broncho* 2014 8:23–31  
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## Introduction

Idiopathic pulmonary fibrosis (IPF), the most common form of idiopathic interstitial pneumonias, is a chronic, progressive, irreversible, and usually lethal lung disease of unknown cause with an estimated survival of 2.5–5 years. IPF occurs in middle-aged and elderly adults, is limited to the lungs, and is associated with a histopathological or radiological pattern typical of usual interstitial pneum(UIP) [1–3].

The diagnosis of IPF often requires a multidisciplinary approach, involving pulmonologists, radiologists, and pathologists experienced in the field of interstitial lung diseases [4].

Pulmonary hypertension (PH) is a hemodynamic and pathophysiological condition defined as an increase in mean pulmonary arterial pressure (mPAP) to at least 25 mmHg at rest as assessed by right heart catheterization (RHC) [5,6]. PH often complicates the course of IPF and may even be found in patients with preserved lung function. PH in IPF patients is associated with decreased exercise capacity and a worse prognosis. Although pulmonary artery

pressures (PAPs) and other cardiac hemodynamic parameters can be accurately assessed by RHC, a simple, reliable, and noninvasive method to estimate PAPs and diagnosis of PH in patients with advanced lung disease is preferable. Doppler echocardiography has gained popularity in the last two decades for noninvasive estimation of systolic pulmonary artery pressure (SPAP) from the peak velocity of a tricuspid regurgitant jet. Doppler echocardiography is a useful tool for the detection of PH, which also provides additional information regarding associated cardiac abnormalities [7].

## Aim

The aims of this study were to:

- (1) Determine the prevalence of PH among patients with IPF.
- (2) Detect the correlation between pulmonary function tests (PFTs), echocardiographic parameters, radiological findings, and mPAP in these patients.
- (3) Compare the effect of oxygen therapy ± drugs in the form of corticosteroids, diuretics, and

immunosuppressive drugs on PH among patients with IPF.

### Patients and methods

This study was performed on 60 patients with IPF who were randomly selected from outpatient clinics of chest and internal medicine departments at the Minia University Hospital from April 2010 to June 2013.

This study was approved by the ethics committee of Faculty of Medicine, Minia University, and informed consent was obtained from patients and controls.

Patients with IPF were diagnosed according to the following criteria:

- (1) Clinical diagnosis of IPF [8] in the form of progressive dyspnea, dry cough, and bilateral basal or widespread crackles. A restrictive ventilatory defect with a reduction in total lung capacity (TLC) and forced vital capacity (FVC) less than 80% predicted [2].
- (2) High resolution computed tomography (CT) criteria for UIP pattern in the form of subpleural, basal predominance, reticular abnormality, and honeycombing with or without traction bronchiectasis.

The absence of features listed as inconsistent with UIP pattern are: Upper or mid-lung predominance, peribronchovascular predominance, extensive ground glass abnormality, profuse micronodules, discrete cysts (multiple, bilateral, away from areas of honeycombing), diffuse mosaic attenuation/air-trapping (bilateral, in three or more lobes), and consolidation in bronchopulmonary segment(s)/lobe(s) [3].

Fig. 1



Idiopathic pulmonary fibrosis on multidetector chest computed tomography.

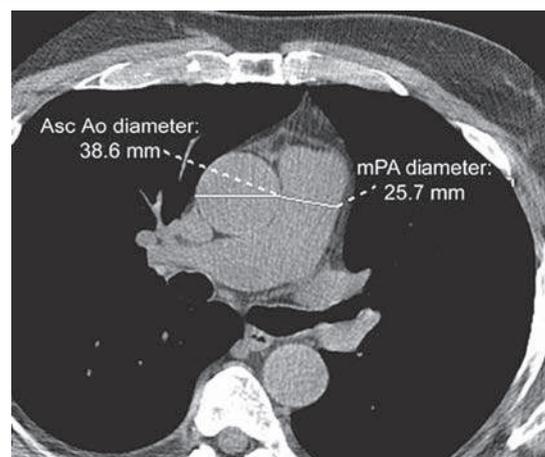
Patients with occupational exposure to a fibrogenic agent, those on medications that cause interstitial pulmonary fibrosis, and those with a history of connective tissue diseases were excluded.

All patients were subjected to the following:

- (1) Complete history taking and physical examination.
- (2) Routine laboratory investigations and collagen profile.
- (3) Plain chest radiography (PA) view.
- (4) PFTs: they were expressed as percentages of predicted values for the patient's age, sex, and height, and included the forced expiratory volume in 1 s ( $FEV_1$ ), FVC, and their ratio ( $FEV_1/FVC$ ); TLC and single-breath carbon monoxide diffusing capacity (DLCO) corrected for hemoglobin concentration were measured using ZAN 300 Device (Biomedica, Germany). Composite physiologic index (CPI) was calculated by the following equation [9]:  $91 - (0.65 \times DLCO\% \text{ predicted}) - (0.53 \times FVC\% \text{ predicted}) + (0.34 \times FEV_1\% \text{ predicted})$ .
- (5) Gender age physiology (GAP) index was also calculated [10].
- (6) Arterial blood gases analysis.
- (7) Multidetector chest computed tomography (MDCT) with contrast using GE bright speed 16 detector/slice (General Electric, Norway).

CT pattern and extent of IPF were determined either to be reticulonodular or honeycombing, basal subpleural or diffuse. The main pulmonary artery diameter (MPAD) was measured at its widest dimension; at this same level, the widest ascending aorta diameter (AD) was measured and the MPAD/AD ratio was calculated (Figs 1 and 2).

Fig. 2



Measurements of main pulmonary artery diameter (mPA) and ratio of the diameters of main pulmonary artery to ascending aorta.

- (8) Doppler echocardiography was performed using conventional clinical echocardiographic equipment (GE Vivid 3; General Electric) with 2.5 or 3.5 MHz transducers. Tricuspid regurgitant flow was identified by color flow Doppler techniques, and the maximum jet velocity was measured by continuous wave Doppler without the use of intravenous contrast. Right ventricular (RV) systolic pressure was estimated on the basis of the modified Bernoulli equation and was considered to be equal to the SPAP in the absence of RV outflow obstruction:  $SPAP$  (mmHg) = RV systolic pressure =  $(4 \times TRV^2 + RAP)$  where TRV is the tricuspid regurgitation velocity in m/s and RAP is the right atrium pressure [11,12]. RAP was estimated to be 5, 10, or 15 mmHg on the basis of the variation in the size of inferior vena cava with inspiration as follows [13]: complete total collapse, RAP = 5 mmHg; partial collapse, RAP = 10 mmHg; and no collapse, RAP = 15 mmHg.
- (a) mPAP was calculated as follows:  
 $mPAP = (0.61 \times SPAP + 2 \text{ mmHg})$  [14].
- (b) RV systolic function using right ventricular fractional area change (RV-FAC) was obtained from a four-chamber view, where the right ventricular end-diastolic area (RV-EDA) and right ventricular end-systolic area (RV-ESA) were measured, and the RV-FAC was calculated as follows:  $RV-FAC (\%) = (RV-EDA - RV-ESA) / RV-EDA \times 100$ . Normal value for RV-FAC is above 35% [15]. RV-FAC is a measure of RV systolic function that has been shown to correlate with RV ejection fraction by MRI [16,17].
- (c) Tei index was calculated using tissue Doppler imaging. Tei index = isovolumic contraction time + isovolumic relaxation time / ejection time. It is an index of RV performance; in adults, values for the RV less than 0.4 are considered normal [18].

PH is defined as mPAP of at least 25 mmHg at rest [5].

According to this definition the 60 patients of IPF were divided into two groups:

Group A: included 14 patients without PH.

Group B: included 46 patients with PH.

The study also included 15 healthy volunteers as a control group (group C) matched in age and sex with the studied patients.

According to the line of treatment they received as inpatients, group B was divided into two subgroups: group B1 included 24 patients who received continuous oxygen

therapy (15–20 h/day) only by venturi mask ranging from 28 to 31% and group B2 included 22 patients who received prednisolone 1 mg/kg/day, frusemide diuretics 60 mg/day, and azathioprine 50 mg/day increased by 25 mg every week; they also received continuous oxygen therapy by venturi mask ranging from 28 to 31%.

Follow-up echocardiography was performed after 1 month among both B1 and B2 subgroups.

### Statistical analysis

Statistical analysis was performed using the statistical package for social science (SPSS, version 16; SPSS Inc., Chicago, Illinois, USA) software on a personal computer. Statistical analysis was performed using the  $\chi^2$ -test and the independent sample *t*-test to assess differences between proportions. Differences were considered statistically significant when *P* value was less than 0.05. Bivariate correlation using Spearman's test was used.

### Results

Table 1 shows that the prevalence of PH in IPF patients was 76.7%. On studying the general characteristics of the studied groups, it was found that there was no difference in the mean age in group A versus group B. There was also no difference between both groups of IPF regarding duration of the disease. Considering GAP index stage, there was no significant difference in GAP stage among those with or without PH.

With respect to PFTs, there was a very highly significant decrease in FVC% predicted, FEV<sub>1</sub>% predicted, and TLC% predicted and a significant increase in CPI in group B compared with group A. In contrast, there was no significant difference between both groups of IPF regarding DLCO% predicted. There was a significant difference in the mean PaO<sub>2</sub> among group B versus group A (Table 2).

Table 3 shows echocardiographic findings among the studied groups. It was found that group B had a highly significant higher level of SPAP and mPAP than group A and the healthy control group (group C). Besides, there was a statistically significant difference between group A and group B regarding RV-FAC% and Tei index.

Figure 3 shows that there is a highly significant negative correlation between mPAP and FVC% predicted ( $r = -0.630, P = 0.0001$ ). Besides, there was also a highly significant negative correlation between mPAP, TLC% predicted, DLCO% predicted ( $r = -0.502, P = 0.0001$ ), and PaO<sub>2</sub> ( $r = -0.584, P = 0.001$ ). In contrast, there was highly significant positive correlation between mPAP and CPI ( $r = 0.550, P = 0.0001$ ).

**Table 1 Demographic data of the studied groups**

Variables	Group A	Group B	Group C	$P_1$	$P_2$	$P_3$
Number (%)	14 (23.3)	46 (76.7)	15			
Age (years)	50.2 ± 7.8	52.3 ± 7.6	50.4 ± 7.6	0.8	0.4	0.3
Sex						
Male	5 (36)	5 (11)	7 (46)	0.35	0.13	0.02*
Female	9 (64)	41 (89)	8 (54)	0.59	0.13	0.02*
Smoking						
Nonsmokers	13 (93)	44 (95)	15 (100)	0.29	0.4	0.67
Smokers	1 (7)	2 (5)	—	—	—	0.67
Duration of illness (years)	2.85 ± 2.53	4.54 ± 3.82	—	—	—	0.1
MMRC grade						
Grade II	5 (35)	5 (11)	—	—	—	0.02*
Grade III	7 (50)	18 (39)	—	—	—	0.47
Grade IV	2 (15)	23 (50)	—	—	—	0.01*
GAP stage						
Stage I	12 (86)	29 (63)	—	—	—	0.11
Stage II	2 (14)	17 (37)	—	—	—	0.11

Data are expressed as number (%) or mean ± SD;  $P_1$ , group A vs. group C;  $P_2$ , group B vs. group C;  $P_3$ , group A vs. group B; \*Significant.

**Table 2 Pulmonary function test parameters and arterial blood gases among the studied groups**

Variables	Group A	Group B	Group C	$P_1$	$P_2$	$P_3$
FVC% pred						
Range	47–84	21–84	83–100			
Mean ± SD	63.1 ± 1.16	46.5 ± 1.4	90 ± 6.9	0.0001*	0.0001*	0.001*
FEV <sub>1</sub> % pred						
Range	41–86	20–86	79–90			
Mean ± SD	62.5 ± 1.4	46.4 ± 1.5	81.6 ± 3.5	0.0001*	0.0001*	0.001*
TLC% pred						
Range	40–85	23–90	87–110			
Mean ± SD	67.3 ± 1.43	55.5 ± 1.3	95 ± 7.4	0.0001*	0.0001*	0.008*
DLCO% pred						
Range	21–79	21–79	80–112			
Mean ± SD	52.28 ± 1.9	43 ± 1.58	90.1 ± 1	0.0001*	0.0001*	0.07
CPI						
Range	25–60	15–83	0.35–20			
Mean ± SD	44.6 ± 1.11	53.9 ± 1.3	11.6 ± 8.0	0.0001*	0.0001*	0.02*
PaO <sub>2</sub> (mmHg)						
Range	40–86	39–87	82–95			
Mean ± SD	79.4 ± 1.15	70 ± 1.4	90.6 ± 4.01	0.002*	0.0001*	0.02*
PaCO <sub>2</sub> (mmHg)						
Range	38–55	38–77	37–45			
Mean ± SD	42.6 ± 4.1	46 ± 9.5	39.8 ± 2.09	0.02*	0.01*	0.19

$P_1$ , group A vs. C;  $P_2$ , group B vs. group C;  $P_3$ , group A vs. group B; CPI, composite physiologic index; DLCO, carbon monoxide diffusing capacity; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity; TLC, total lung capacity; \*Significant.

**Table 3 Echocardiographic parameters among the studied groups**

Variables	Group A	Group B	Group C	$P_1$	$P_2$	$P_3$
SPAP (mean ± SD) (mmHg)	32.3 ± 4.14	52.6 ± 1.1	32.5 ± 4.05	0.9	0.0001*	0.0001*
mPAP (mean ± SD) (mmHg)	21.4 ± 2.6	34.02 ± 7.22	21.5 ± 2.55	0.9	0.0001*	0.0001*
RV-FAC (mean ± SD) (%)	53.3 ± 1.2	44.5 ± 1.1	53.8 ± 1.1	0.92	0.01*	0.01*
Tei index (mean ± SD)	0.34 ± 0.02	0.45 ± 0.15	0.34 ± 0.02	0.32	0.004*	0.009*

$P_1$ , group A vs. group C;  $P_2$ , group B vs. group C;  $P_3$ , group A vs. group B; mPAP, mean pulmonary arterial pressure; RV-FAC, right ventricular fractional area change; SPAP, systolic pulmonary artery pressure; \*Significant.

It was found that there was a significant positive correlation between mPAP, age, duration of illness, Modified Medical Research Council (MMRC) scale, GAP index stage, PA

diameter, and its ratio with the ascending aorta (PA/A). In contrast, there was no correlation between mPAP and both pattern and extent of IPF in MDCT (Table 4).

Figure 4 reveals that there is a significant positive correlation between mPAP and RV Tei index.

Regarding correlation of RV systolic function as represented by RV-FAC% and PFT parameters, there was a significantly positive correlation between RV-FAC% and DLCO% predicted. In contrast, there was a significantly negative correlation between RV-FAC% and CPI. There was a significantly negative correlation between Tei index and all PFTs parameters and a significantly positive correlation between Tei index and CPI. In contrast, there was no significant correlation between RV-FAC% and Tei index and PaO<sub>2</sub> (Table 5).

**Discussion**

PH is a common accompaniment of IPF and has a significant impact on outcomes [8,19]. Some studies have investigated transthoracic echocardiography (TTE) as a noninvasive means of detecting PH and have demonstrated that elevated estimated SPAP is associated with reduced survival using thresholds of 40–50 mmHg [8,20].

In our study, SPAP is estimated by echocardiography as it is a simple, noninvasive, and nonexpensive method. The prevalence of PH in IPF patients in the present study was 76.7% on the basis of mPAP.

Most studies on PH in IPF were in patients referred for lung transplantation, in which the reported prevalence of PH is 32–46% [9,21–23]. These studies determine PH by RHC as a routine investigation before lung transplantation. Nadrous *et al.* [8]

**Table 4 Correlation coefficient between mean pulmonary artery pressure and clinical and radiological data of the studied groups**

Variables	r	P value
Age	0.242	0.03*
Duration of illness	0.314	0.01*
MMRC scale	0.5000	0.0001*
GAP index stage	0.351	0.006*
Pattern of IPF on CT	0.103	0.433
Extent of IPF on CT	-0.165	0.207
Pulmonary artery diameter	0.588	0.0001*
Ratio PA/A	0.330	0.01*

CT, computed tomography; IPF, idiopathic pulmonary fibrosis; PA/A, pulmonary artery to ascending aorta ratio; \*Significant.

**Table 5 Correlation coefficient between right ventricular echocardiographic parameters, pulmonary function tests, and PaO<sub>2</sub>**

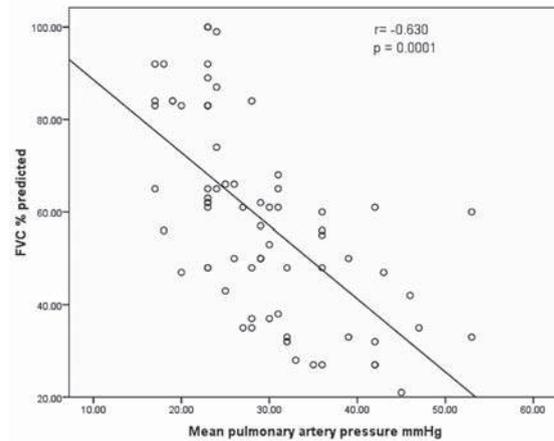
Variables	FVC% pred		TLC% pred		DLCO% pred		CPI		PaO <sub>2</sub> (mmHg)	
	r	P	r	P	r	P	r	P	r	P
RV-FAC%	0.15	0.20	0.11	0.34	0.24	0.03*	-0.25	0.02*	0.11	0.34
Tei index	-0.27	0.01*	-0.28	0.01*	-0.25	0.02*	0.27	0.01*	-0.17	0.14

CPI, composite physiologic index; DLCO, carbon monoxide diffusing capacity; FVC, forced vital capacity; RV-FAC, right ventricular fractional area change; TLC, total lung capacity; \*Significant.

performed TTE on 88 patients with IPF who were evaluated for lung transplantation. Eighty-four percent had PH (defined as an estimated SPAP > 35 mmHg at rest). Studies by Agarwal *et al.* [24] and Laz and Ahmad [25] found that the prevalence of PH in IPF patients was 36 and 33.3%, respectively, as detected by TTE.

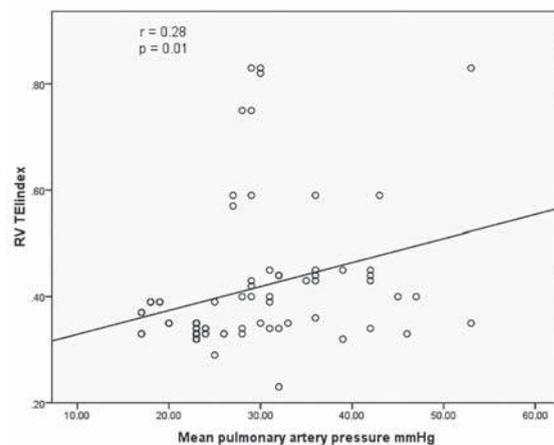
PH develops over time in patients with IPF, as

**Fig. 3**



Correlation coefficient between mean pulmonary artery pressure and the forced vital capacity (FVC) % predicted in all studied groups.

**Fig. 4**



Correlation coefficient between mean pulmonary artery pressure and the right ventricular (RV) Tei index among the studied groups.

demonstrated by the rise in prevalence of PH in IPF patients awaiting transplantation from 33% at initial assessment up to 85% immediately before transplantation [8].

This wide range in the prevalence of PH reported likely reflects the timing of the measurement during the course of the patient's disease, with patients who are later in their disease course manifesting more evidence of pulmonary arterial hypertension (PAH). It is possible that the high prevalence of PH in our study could be due to the fact that the studied patients as a whole were in relatively late stages of IPF when they underwent the study, as 67% of them had diffuse honeycombing pattern in MDCT and the mean duration of illness was 4.5 years.

The onset of PH correlates with the magnitude of reduction in lung volumes and DLCO. In the present study, it was found the mPAP had an inverse correlation with all parameters of pulmonary functions (FVC, TLC, and DLCO) and PaO<sub>2</sub> and had direct correlation with CPI. In addition, it was found that 22 patients of the 27 (81.48%) patients with FVC less than 50% predicted and 24 (88.8%) patients with DLCO less than 40% predicted had PH (Table 6).

It was also found that seven of the 13 patients (53.8%) with FVC%/DLCO% greater than 1.5 had PH (Table 6). Nadrous *et al.* [8] and Hamada *et al.* [26] found a negative correlation between mPAP and DLCO% predicted and PaO<sub>2</sub>. In contrast, Nathan *et al.* [9] failed to demonstrate a significant relationship between various PFTs and mPAP. Somewhat better correlation was noted with DLCO% less than 30 having a two-fold higher prevalence of PH (56.4%) compared with DLCO% more than 30 (28.6%). They also found that a FVC%/DLCO% greater than 1.5 was associated with a nearly two-fold increased risk for PH.

Our study revealed that there was a positive significant correlation between mPAP, age, duration of IPF, MMRC scale, and GAP index. Laz and Ahmad [25]

observed significant positive correlation between dyspnea scale and SPAP in patients with IPF-PH ( $r = 0.67, P = 0.017$ ).

It has been reported that easily accessible CT parameters, such as the MPAD, correlate well with hemodynamic measurements on RHC and can therefore be used to assess the probability of PH [27–29].

Previous studies had shown that the MPAD and its ratio PA/A correlate well with mPAP [29–31], whereas others report no correlation [32–34].

In the present study, it was found that patients with IPF-PH had a significantly higher PA diameter than those without PH and healthy controls (mean value was  $27.9 \pm 4.8$  vs.  $24.16 \pm 2.16$  and  $23.7 \pm 1.9$  mm, respectively,  $P = 0.02$ ). We also found that the ratio PA/A was significantly higher among both controls and IPF patients without PH ( $0.97 \pm 0.16$  vs.  $0.85 \pm 0.1$  and  $0.88 \pm 0.12$ , respectively,  $P = 0.01$ ).

We found that there was a significant positive correlation between both PA diameter and ratio PA/A on MDCT and mPAP in IPF patients ( $r = 0.58, P = 0.001$  and  $r = 0.3, P = 0.01$ , respectively). Nayar *et al.* [35] found that the main PA greater than 29 mm on CT scan compared with RHC mPAP had a correlation coefficient of 0.56 ( $P < 0.0001$ ), and CT prediction of MPAD/AA diameter greater than 1 had a coefficient of 0.42 ( $P = 0.004$ ) in patients with advanced lung disease. Another study by Lang *et al.* [31] found that the MPAD on CT correlated with mPAP ( $r = 0.496, P < 0.001$ ) and pulmonary vascular resistance ( $r = 0.445, P < 0.001$ ), and could predict borderline PH.

In contrast, Zisman *et al.* [36] found that there was no significant correlation between mPAP and any of the chest CT-determined measures such as extent of pulmonary fibrosis, MPAD, and the ratio of the PA to AD.

RV systolic dysfunction has been identified as a key element in determining prognosis of patients with chronic PH [37,38]. Therefore, identification of early RV dysfunction is of utmost clinical importance because as many as two-thirds of the deaths in patients with chronic PH may be attributed to RV failure [39]. It was documented that IPF patients exhibited impairment of both systolic and diastolic RV function. In the current study, we assessed one of the RV systolic functions through detection of RV-FAC% and it was found that IPF patients with PH had a statistically significant difference than those without PH and healthy controls ( $44.5 \pm 1.1$  vs.  $53.3 \pm 1.2$  and  $53.8 \pm 1.1$ , respectively,

**Table 6 Prevalence of pulmonary hypertension in idiopathic pulmonary fibrosis patients according to the cutoff values of pulmonary function tests**

Item	All IPF patients	IPF patients with FVC < 50% pred	IPF patients with DLCO < 40% pred	IPF patients with FVC%/DLCO% > 1.5
N (%)	60 (100)	27 (45)	27 (45)	13 (21)
mPAP $\geq$ 25 (mmHg)	46 (76.7)	22 (81.48)	24 (88.8)	7 (53.8)

Data are represented by n (%); DLCO, carbon monoxide diffusing capacity; FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; mPAP, mean pulmonary arterial pressure.

$P = 0.01$ ). Papadopoulos *et al.* [40] also found that IPF patients with PH had a worse RV-FAC% than controls ( $42 \pm 5$  vs.  $57 \pm 6$ ,  $P < 0.001$ ).

The myocardial performance index, also known as Tei index, incorporates elements of both systolic and diastolic phases in the assessment of global ventricular function [18]. The Tei index can be estimated for both the left ventricle and the RV. The RV Tei index is a candidate to increase the noninvasive diagnosis of PH because it reflects the RV function, is easy to assess, and can be estimated in the same session as the echocardiographic pulmonary artery systolic pressure (PASP). The normal value of the RV Tei index is less than 0.4 [18]. An elevated RV Tei index should be the result of either diastolic dysfunction or PH [41,42].

Our study showed that the mean RV Tei index in patients with IPF-PH increased substantially than normal controls and those with IPF and without PH. The RV Tei index was elevated in 56.5% of the patients with PH, suggesting that they had RV dysfunction. There was also a significant correlation between RV Tei index and mPAP.

Vonk *et al.* [43] found a significant correlation between the RV Tei index and the catheterization parameters such as SPAP, diastolic PAP, and mPAP among patients with PH due to systemic sclerosis.

The current therapeutic options are quite limited for IPF, and even more so for IPF-associated PH. The major problem in treating both fibrosis and pulmonary vascular disease is the amount of organized scar tissue inside the fibrotic lung. These areas represent regions of final, nonreversible damage, not only to the interstitium, but also very likely to the pulmonary vasculature [44].

Finally, we compared the effect of oxygen therapy alone versus oxygen with drugs in the form of corticosteroids, diuretics, and immunosuppressive drugs on PH among patients with IPF and PH.

There was no significant difference between both groups of patients who received oxygen therapy alone or when oxygen was augmented by drugs regarding mPAP before and after treatment ( $P > 0.05$ ) (Table 7).

**Table 7 Comparison of mean pulmonary arterial pressure before and after treatment among both B1 and B2 subgroups**

Variable	B1 (N = 24)	B2 (N = 22)
mPAP before treatment	33.7 $\pm$ 6.2	34.09 $\pm$ 8.01
mPAP after treatment	30.33 $\pm$ 7.2	31.4 $\pm$ 8.6
P value	0.14	0.3

Data are represented as mean  $\pm$  SD; mPAP, mean pulmonary arterial pressure.

Previous study was performed on 18 patients with idiopathic lung fibrosis [45]. Ten patients received standard treatment (prednisone 10–15 mg/day) and supplementary oxygen therapy that was supplied at their homes (mean 16.4 h/day) for a period of 4 years. Eight patients who received the same treatment without home oxygen served as controls. At study entry, lung function test, blood gases, hematocrit, hemodynamic parameters of the pulmonary circulation, and thermodilution cardiac output were measured in all patients. The measurements were repeated after 4 years of follow-up. At follow-up examination, no differences in pulmonary function parameters were shown between the groups. mPAP and pulmonary vascular resistance were significantly lower in patients receiving home oxygen therapy as compared with those treated pharmacologically only. The lack of improvement in mPAP in the present study could be attributed to the short duration of oxygen therapy (1 month) and drugs in comparison with the long duration (4 years) in Polonski *et al.*'s [45] study.

Douglas *et al.* [46] found that there was no significant difference in survival between those patients of IPF treated with colchicine or prednisone and those on no therapy, and no difference between those on oxygen therapy and those without oxygen.

Cochrane review on the use of corticosteroids in IPF [47] showed that no existing evidence supported the efficacy of corticosteroids for treatment of IPF patients. In 2010, the Cochrane meta-analysis on the use of corticosteroids for IPF was updated and showed that there was still no evidence to support the efficacy of corticosteroids in the management of IPF, but there was also no evidence to rule out the use of corticosteroids in IPF.

The present study had some limitations. First of these limitations was the difficulty in measuring mPAP by cardiac catheterization, as it is more invasive and expensive technique. Second, the comorbid conditions that may contribute to PH were not included in this study. Finally, other shortcoming of this study was that the duration of treatment was limited to 1 month. This was because admission of these patients was not feasible for longer periods.

In conclusion, PH is common in IPF. Our study revealed a significant negative correlation between PFTs (FVC%, TLC%, DLCO%), PaO<sub>2</sub>, and PH. There was also a significant positive correlation of mPAP with both CPI and RV Tei index. Age, duration of IPF, MMRC scale, and GAP index stage also had a significant positive correlation with PH. In contrast, both the extent and pattern of IPF on CT had no correlation with PH.

Measurement of MPAD and its ratio to the ascending aorta as seen in CT chest can be easily performed by the clinician to discover the early presence of PH. Evaluation of the presence of PH in patients with IPF is useful in determining prognosis and effect of therapy.

Further studies are required to validate our findings and to evaluate therapy directed to prevent or treat this complicating comorbidity.

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### Conflicts of interest

There are no conflicts of interest.

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