Correlation between high-resolution computed tomography of the chest and pulmonary functions in idiopathic pulmonary fibrosis

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Background The idiopathic interstitial pneumonias are a heterogeneous group of non-neoplastic disorders resulting from damage to the lung parenchyma by varying patterns of inflammation and fibrosis. High-resolution computed tomography (HRCT) has become an integral part of the diagnosis and evaluation of the patient with idiopathic interstitial pneumonias.

Aim of the study The aim of this work was to correlate between HRCT findings and pulmonary functions in patients with idiopathic pulmonary fibrosis (IPF).

Patients and methods Thirty patients with features consistent with IPF as diagnosed by means of HRCT were included. The severity of IPF was scored using 'Kasr Al Ainy HRCT scoring of IPF' in which the lung was divided into six zones, three on each side, with a specific score given for each zone according to the extent of fibrosis. Transthorathic echocardiography was performed for all patients with the estimation of pulmonary artery systolic pressure (PASP).

Results The mean lower lung zone score according to the HRCT score for severity of IPF was 7.93±2.67, which is consistent with typical basal distribution of IPF. A negative correlation was noted between total HRCT score with forced vital capacity, partial pressure of oxygen, and 6 min walk test. There was a positive correlation between PASP detected using echocardiography and pulmonary artery size measured using HRCT (P=0.022).

Conclusion There is a positive correlation between PASP detected using echocardiography and pulmonary artery size measured using HRCT. There is a negative correlation between PASP using echo and partial pressure of oxygen in arterial blood gases and also between total lung zone HRCT score and pulmonary functions.

Egypt J Bronchol 2016 10:330–336

Egyptian Journal of Bronchology 2016 10:330–336

Keywords: high-resolution computed tomography, idiopathic pulmonary fibrosis, pulmonary function tests

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Received 4 January 2016 **Accepted** 29 January 2016

Introduction

The idiopathic interstitial pneumonias (IIPs) are a group of diffuse parenchymal lung diseases. The IIPs are a heterogeneous group of non-neoplastic disorders resulting from damage to the lung parenchyma by varying patterns of inflammation and fibrosis [1].

Idiopathic pulmonary fibrosis (IPF) is defined as a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause, occurring primarily in older adults, limited to the lungs, and associated with the histopathologic and/or radiologic pattern of usual interstitial pneumonia (UIP) [2].

IIPs generally share a common pattern of physiologic abnormality characterized by a restrictive ventilatory defect – that is, a reduction in lung volumes with preserved ratio of forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) and reduced diffusing capacity for carbon monoxide (DLCO) [3].

High-resolution computed tomography (HRCT) has become an integral part of evaluation of patients with IIP. The presence of reticular opacities, often associated with traction bronchiectasis, or honeycombing, is critical for making a definite diagnosis for UIP [4].

Pulmonary artery hypertension (PAH) is common in patients with IPF. When present, PAH is associated with increased mortality, and may explain the deterioration of some patients with preserved pulmonary function. PAH in IPF may develop as a consequence of, or disproportionate to, the underlying fibrotic lung disease [5].

Aim of the work

The aim of this work was to correlate between HRCT chest findings and pulmonary functions in patients with IPF.

Patients and methods

Thirty patients admitted to the Chest Department at Kasr Al Ainy Hospital with IPF as diagnosed by

 DOI: 10.4103/1687-8426.193633

HRCT were included in the study. The study was not subjected to IRB/Ethics committee approval.

Inclusion criteria

All patients proved as having IPF as diagnosed on HRCT according to official ATS/ERS statement [2] were included in the study.

High-resolution computed tomography features of usual interstitial pneumonia pattern

Subpleural, basal predominance.

(1) Reticular abnormality.
(2) Honeycombing with or without traction bronchiectasis.
(3) Absence of features listed as inconsistent with UIP pattern.

Inconsistent with usual interstitial pneumonia pattern

Upper or mid-lung predominance.

(1) Peribronchovascular predominance.
(2) Extensive ground-glass abnormality.
(3) Profuse micronodules (bilateral, predominantly upper lobes).
(4) Discrete cysts (multiple, bilateral, away from areas of honeycombing).
(5) Diffuse mosaic attenuation/air-trapping (bilateral, in three or more lobes).
(6) Consolidation in bronchopulmonary segment(s)/lobe(s).

Exclusion criteria

Presence of HRCT features inconsistent with UIP pattern.

(1) Any known cause of interstitial lung disease.
(2) Presence of acute exacerbation of IPF.
(3) Mechanically ventilated patients.

All our patients were subjected to the following:

(1) Thorough history taking with particular attention to dyspnea and its grading according to the New York Heart Association (NYHA) functional classification system.
(2) Full routine laboratory investigations.
(3) Full spirometric testing (flow volume loop) using Sensor Medics V_{max} 229 (Becton, Dickinson and Co., New Jersey, USA).
(4) Arterial blood gases (ABGs) on ambient air.
(5) Six-min-walk test (6MWT).
(6) Transthoracic echocardiography: estimation of pulmonary artery systolic pressure (PASP).
(7) HRCT chest: the severity of IPF was scored using 'Kasr Al Ainy HRCT scoring of IPF' (which is a modification of the Remy-Jardin classification described in 1994) [6], in which the lung is divided into six zones, three on each side. The upper zones were demarcated above the level of the main carina, the middle zones between the level of the main carina and the inferior pulmonary veins, and the lower zones under the level of the inferior pulmonary veins.

Each zone was scored as follows:

0: no interstitial disease.

1: ground-glass attenuation.

2: fine intralobular interstitial thickening.

3: coarse intralobular interstitial thickening.

4: coarse intralobular interstitial thickening with traction bronchiectasis or traction brochiolectasis.

5: honeycombing.

For measuring the main pulmonary artery caliber in the mediastinal images, the following scoring system was installed:

0: pulmonary artery caliber less than 29 mm (i.e. within normal).

1: pulmonary artery caliber between 29 and 35 mm.

2: pulmonary artery caliber greater than 35 mm.

Main pulmonary artery caliber was measured at its widest dimension [7].

Statistical methods

Data were statistically described in terms of mean±SD, median and range, or frequencies (number of cases) and percentages, when appropriate. Correlation between various variables was made using Pearson moment correlation equation for linear relation in normally distributed variables and Spearman rank correlation equation for non-normal variables. *P* values less than 0.05 were considered statistically significant. All statistical calculations were carried out using

computer program SPSS release 15 for Microsoft Windows, 2006 (SPSS Inc., Chicago, Illinois, USA).

Results

This study included 30 patients admitted to the Chest Department, Kasr Al Aini University Hospital, with a mean age of 49.37±14.61 years; the youngest patient was 20 years old and the oldest patient was 75 years old (Tables 1–9 and Fig. 1).

Discussion

There is an unmet need for an accurate noninvasive measure of disease severity in IPF. As well as refining prognostic evaluation, a reliable measure of severity would improve the precision with which disease is monitored and would allow accurate stratification in clinical studies [8].

HRCT is an integral aspect of the evaluation of patients with suspected IPF. Moreover, the overall extent of lung fibrosis on HRCT (i.e. combined extent of reticulation and honeycomb change) is a strong independent predictor of mortality in patients with IPF [9]. This study was conducted to correlate between HRCT of the chest findings and pulmonary functions in IPF.

This study was conducted in the Chest Department, Kasr Al Ainy Hospital, Cairo University; it included 30 patients admitted with IPF diagnosed using HRCT.

Demographic data of patients involved in this study

Eighteen patients were female (60%) and 12 patients were male (40%) (Table 1). This indicates a higher incidence of IPF in the female population compared with the male population in the studied group. This is contradictory to the official ATS/ERS/JRS/ALAT statement on evidence-based guidelines for the diagnosis and management of Idiopathic Pulmonary Fibrosis 2011 [10]. However, female prevalence in this study is consistent with that reported in other Egyptian studies, including the study by Rifaat *et al.* [11].

In this study, the mean age of the patients was 49.37 years. The official ATS/ERS/JRS/ALAT guidelines 2011 stated that IPF typically occurs in the sixth and seventh decades [10].

Table 1 Sex distribution in the study

	Frequency	%
Female	18	60.0
Male	12	40.0
Total	30	100.0

In the present study, we used the NYHA functional classification system for grading of dyspnea. This system relates symptoms to everyday activities and the patient's quality of life (QoL).

We noticed that 10% of the patients presented with dyspnea class II, 50% of the patients presented with dyspnea class III, and 40% of the patients presented with dyspnea class IV (Table 2).

Baseline dyspnea has been shown to correlate with QoL and survival in several studies [12]. A variety of different metrics for dyspnea have been used, including the medical research council scale, the baseline dyspnea index, QoL measurement tools with respiratory questionnaires, the Borg scale, University of California, San Diego shortness of breath questionnaire, and the clinical–radiological–physiological dyspnea score developed by Watters *et al.* [13]. It remains unclear as to which dyspnea metric has most predictive of outcome in patients with IPF. Change in dyspnea over time has also been shown to predict survival as concluded by Collard *et al.* [14].

Functional affection of the studied patients

Mean 6MWT was 235.43±101.40 m. The 6MWT is a widely used measure of exercise tolerance that has been validated in a variety of cardiac and pulmonary diseases. Du Bois *et al.* [15] stated that the 6MWT is a reliable, valid, and responsive measure of exercise tolerance in patients with IPF. Swigris *et al.* [16] noted that shorter walk distance and delayed heart rate recovery after walk test have been associated with an increased risk for subsequent mortality. Some authors such as Hallstrand *et al.* [17] have suggested that desaturation below 88% during 6MWT is a marker for increased risk for mortality (Table 3).

Optimal reference equations from healthy population-based samples using standardized 6MWT methods are not yet available. A mean 6MWD of 630 m for 51 healthy adults was reported by Troosters *et al.* [18].

Table 2 Classes of dyspnea in the patients according to the New York Heart Association classification

	Frequency	%
I	0	0
II	3	10.0
III	15	50.0
IV	12	40.0
Total	30	100.0

Mean PO_2 in ABG was 58.13±12.716 mmHg and mean sulfur dioxide in ABG was 87.57±7.519. Characteristic ABG abnormalities in IPF include resting hypoxemia and increased alveolar–arterial oxygen pressure difference [19]. These abnormalities are more evident during exercise, where hypoxemia is quite prevalent. According to ATS/ERS international consensus statement 2000, the resting ABGs may be normal or reveal hypoxemia (secondary to ventilation/perfusion ratio mismatch and diffusion abnormalities) and respiratory alkalosis [20].

In our trial to correlate between PO_2 in ABG and 6MWT, we noticed that there was a strong positive correlation between PO_2 in ABG and 6MWT, with a *P* value of 0.001 denoting high statistical significance.

Other studies such as that by Du Bois *et al.* [15] tried to correlate between changes in 6MWD and changes in measures of physiologic function and dyspnea, but they found that the correlations were in the expected direction, although generally weak. Caminati *et al.* [21] reported moderate correlations between 6MWD and both percentage-predicted FVC and percentage-predicted DLCO.

In this study, the mean FVC% was 53.43±15.72, mean FEV_1/FVC was 89.20±6.01, denoting restrictive pattern, and mean forced expiratory flow at 25–75% was 67.17±17.56, denoting small airway affection.

A restrictive defect is the most frequent ventilatory abnormality in patients with pulmonary fibrosis, which is a common consequence of many interstitial lung diseases. It is a typical finding in patients with IPF. The presence of airflow obstruction may reflect coexistent chronic obstructive pulmonary disease or asthma. Lung volumes may be relatively preserved in smokers with IPF due to coexisting emphysema, with the FEV_1/FVC ratio remaining normal [22].

Baseline pulmonary function test values have shown mixed associations with survival in IPF. This may be, in part, due to comorbid conditions such as emphysema, pulmonary vascular disease, and obesity, or technical differences in testing. Baseline FVC is of unclear predictive value [23]. DLCO (single breath, and hemoglobin corrected) is more reliably predictive of survival at baseline, and a threshold of ~40% predicted has been associated with an increased risk for mortality [24].

In this study, we modified a scoring system for severity of IPF 'Kasr Al Ainy HRCT scoring of IPF' in which the lungs were divided into six zones and each zone was scored from 0 to 5, where 0 denotes no interstitial affection and 5 denotes the presence of honeycombing.

After adding the right and left lung zones, the following findings were noticed: the mean upper lung zone score was 6.27±3.16, mean middle lung zone score was 6.43±3.40, and the mean lower lung zone score was 7.93±2.67 (Table 4 and Fig. 1). This is consistent with the typical distribution of IPF, which is predominantly basal according to the official ATS/ERS/JRS/ALAT guidelines, 2011 [10].

As regards pulmonary hypertension (PH) and its relation with IPF, 16 patients (53.3%) in this study had PAH as evidenced by increased PASP detected by

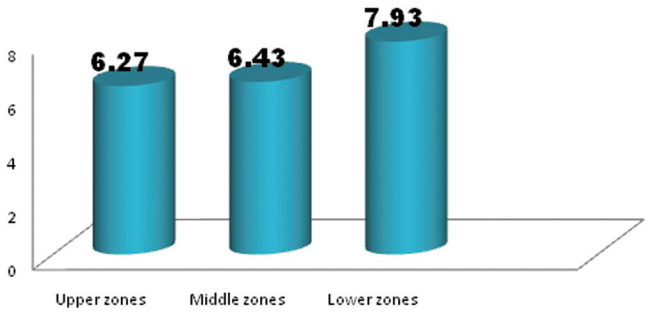
Table 3 Functional affection of the study group

	Minimum	Maximum	Median	Mean	SD
6MWT	100	600	200	235.43	101.40
PCO_2	34	56	40	40.47	4.47
PO_2	35	84	56	58.13	12.71
SO_2	60	96	89	87.57	7.51
FVC%	22	87	55.5	53.43	15.72
FEV_1/FVC	76	100	90	89.20	6.01
FEF 25–75%	30	94	67	67.17	17.56

Table 4 High-resolution computed tomography scoring system among lung zones

	Minimum	Maximum	Median	Mean	SD
Score of upper zones	0	10	7.5	6.27	3.16
Score of middle zones	0	10	8	6.43	3.40
Score of lower zones	2	10	8.5	7.93	2.67
Total score	4	30	24	20.63	8.07

Figure 1



HRCT scoring system among lung zones. According to HRCT score for the severity of IPF, range of upper lung zone score was from 0 to 10, with a mean of 6.27±3.16, range of middle lung zone score was from 0 to 10, with a mean of 6.43±3.40, and range of lower lung zone score was from 2 to 10, with a mean of 7.93±2.67. This is consistent with typical distribution of IPF, which is predominantly basal. HRCT, high-resolution computed tomography; IPF, idiopathic pulmonary fibrosis.

Table 5 Pulmonary hypertension in the patients as detected using echocardiography

	Frequency	%
Yes	16	53.3
No	14	46.7
Total	30	100.0
Mean±SD	54.56±12.35	

Table 6 Pulmonary artery score depending on pulmonary artery size in high-resolution computed tomography

	Frequency	%
0	11	36.7
1	16	53.3
2	3	10.0
Total	30	100.0

Table 7 Correlation between PASP in echo and pulmonary artery size in HRCT

	Pulmonary artery size
PASP in echo	
Pearson correlation	0.568
P value	0.022
N	16

Table 8 Correlation between pulmonary artery size and total HRCT score

	Total HRCT score
Pulmonary artery size	
Pearson correlation	0.174
P value	0.358
N	30

means of echocardiography (Table 5). The mean PASP was 54.56±12.35.

The recent guidelines for the diagnosis and treatment of PAH classify PAH in IPF in the third group of 'PH due to lung diseases and/or hypoxia' [25].

Despite its critical role, the epidemiology of PAH in IPF has not been extensively studied, and the reported incidence is wide, ranging from 32 to 84% [26], which is consistent with the current study results.

The development of PAH in IPF patients is associated with worse survival [27]. In this study, we measured the main pulmonary artery caliber in the mediastinal images using a scoring system starting from 0 to 1, in which 0 represents the normal pulmonary artery caliber (i.e. <29 mm), 1 represents pulmonary artery caliber between 29 and 35 mm, and 2 represents pulmonary artery caliber greater than 35 mm (Table 6).

According to Ng *et al.* [28], on computed tomography (CT), enlargement of the main pulmonary artery (>29 mm), right ventricular dilatation, and an increased diameter of the pulmonary artery as compared with the aorta are indicative of the development of PAH.

As regards the efficiency of measuring pulmonary artery size in HRCT in relation to PASP in echocardiography, there was a strong positive correlation (r=0.568) between PASP detected using echocardiography and pulmonary artery size measured using HRCT, with a *P* value of 0.022 denoting high statistical significance (Table 7). This is consistent with the study by Devaraj *et al.* [29], in which the ratio of the diameter of the main pulmonary artery to the diameter of the ascending aorta had a strong correlation with mean pulmonary artery pressure (mPAP). Our findings are also in agreement with the study by Grosse and Grosse [30], which stated that a pulmonary artery with a diameter more than 29 mm has a positive predictive value of 97%, a sensitivity of 87%, and a specificity of 89% for diagnosing PAH. Similarly, Peña *et al.* [31] concluded that PH can be predicted reliably when the CT demonstrated a diameter of the main pulmonary artery greater than 29 mm and a segmental artery-to-bronchus diameter ratio of 1 : 1 or more in three or four lobes.

In our study, we found a positive correlation (r=0.174) between pulmonary artery size measured in HRCT and total lung zone HRCT score but with no statistical significance (Table 8).

This is consistent with the findings of several studies, including Todd *et al.* [32], in which they noticed that PFTs and ABGs are necessary to identify the contribution of parenchymal lung disease to PH. Interestingly, a poor association between PH and pulmonary function has been found in several studies. Lettieri *et al.* [26] did not find a significant difference in lung function indices, except for DLCO, between IPF patients with and without PH. The combination of a DLCO of less than 40% predicted and the need for supplemental oxygen determined in individuals with a resting SpO_2 less than 88% identified the presence of PH with a sensitivity and specificity of 65 and 94.1%, respectively. Similarly, in the study by Nadrous *et al.* [33], none of the lung function tests correlated with estimated right ventricle systolic pressure, with the exception of DLCO, to which right ventricle systolic pressure was inversely related. Zisman *et al.* [34] developed a method to screen for PH based on a formula to predict mPAP from standard lung function tests. In this equation,

Table 9 Correlation between total HRCT score together with FVC%, PO_2 in ABG, and 6MWT

Total lung zone HRCT score	FVC%	PO_2	6MWT
Correlation coefficient	–0.151	–0.227	–0.192
P value	0.427	0.228	0.311
N	30	30	30

resting room air pulse oximetry (SpO_2) together with percentage FVC and DLCO% of predicted were found to be important indices for the calculation of mPAP.

High-resolution computed tomography scoring of idiopathic pulmonary fibrosis modified in this study

There was a negative correlation (r=–0.151) between total lung zone HRCT score and FVC%. There was a negative correlation (r=–0.227) between total lung zone HRCT score and PO_2, and there was a negative correlation (r=–0.192) between total lung zone HRCT score and 6MWT; however, none of these correlations was statistically significant (Table 9).

The relationship between HRCT findings and pulmonary function tests in IPF has been investigated by several authors. Wells *et al.* [35] analyzed the changes in serial CT scans and showed that improvement in pulmonary function tests was associated with regression of ground-glass pattern. Other studies such as that by Staples *et al.* [36] have shown that HRCT findings significantly correlate with several functional parameters, such as static lung volumes, FEV_1, or DLCO. However, some of these studies evaluated only the significance of ground-glass opacification or reticular pattern, but not the global extent of the disease in HRCT. Xaubet *et al.* [37] described a moderate correlation between overall abnormality on HRCT scan in 39 untreated IPF patients with both DLCO and FVC.

Watters *et al.* [13] created a composite score of clinical (dyspnea), radiographic (chest radiograph), and physiologic parameters, the CRP score. The physiologic component of the CRP includes spirometric measures, lung volume (thoracic gas volume), and DLCO corrected for alveolar volume. The overall CRP score demonstrated better correlation with a semiquantitative histologic total pathology score. Wells *et al.* [38] also confirmed a correlation between DLCO, exercise desaturation, and the physiologic component of the CRP score and the overall extent of fibrosis on HRCT scan in patients with IPF but without emphysema.

A modified CRP scoring system has been created by King *et al.* [12] that incorporates additional clinical and radiologic findings while giving less weight to physiologic parameters. This modified CRP score correlated with the extent of fibrosis, cellularity, granulation/connective tissue, and total pathologic derangement.

Wells *et al.* [8] extended these observations by creating a composite score that included spirometric (FEV_1 and FVC) and DLCO measurements. This composite physiologic index correlated better compared with individual parameters with the extent of disease on HRCT scan abnormality, which the authors thought likely reflected adjustment for concomitant emphysema.

Few studies have considered both HRCT findings and pulmonary function data in the same logistic analysis as a predictor of survival. Lynch *et al.* [9] studied 315 patients with IPF and found that a higher extent of fibrosis score and a lower DLCO increased the risk for death. Similarly, Mogulkoc *et al.* [39] studied 115 patients with IPF and found that the best prediction of survival was derived from a combination of DLCO percentage of predicted and HRCT fibrotic score. Shin *et al.* [40] studied 108 patients with UIP and fibrotic nonspecific interstitial pneumonia and came to the same conclusion.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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