Combined pulmonary fibrosis and emphysema syndrome: clinical, functional, and radiological assessment

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Background The coexistence of pulmonary fibrosis and emphysema is increasingly recognized.

Objective To assess the clinical, physiological and radiological characteristics of patients with combined pulmonary fibrosis and emphysema (CPFE) and compare it with patients with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD) alone.

Patients and methods One hundred-twenty patients were enrolled and divided into three groups; 40 had COPD based on poorly reversible airflow obstruction in spirometry; 40 had ILD based on high-resolution computed tomography (HRCT); and 40 had CPFE based on the presence of emphysematous changes in the upper lung zones and pulmonary fibrosis in lower zones in HRCT. Modified Medical Research Council dyspnea scale, arterial blood gas analysis, spirometry, diffusion capacity for carbon monoxide (DLCO), polythesmography, HRCT chest, and echocardiography were done.

Results More than 57% of patients with CPFE were men and the majority of them were smokers. There was no significant difference in dyspnea grade between CPFE group and other groups ($P>0.05$). The rate of exacerbation per year was significantly higher in the CPFE group (4.2±1.02) compared with either COPD group (3.33±1.56) or ILD group (3.15 ±1.05). CPFE patients had both emphysematous and fibrotic changes on radiological examination. Lung volumes were preserved but DLCO% was significantly lower and the mean pulmonary artery systolic pressure was significantly higher in the CPFE group compared with COPD and ILD.

Conclusion CPFE is a distinct syndrome that has characteristic radiological findings and lung function profile with a significant reduction of DLCO and a significant increase in pulmonary artery systolic pressure.

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Keywords: diffusion capacity for carbon monoxide, high-resolution computed tomography, pulmonary hypertension

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Introduction

Combined pulmonary fibrosis and emphysema (CPFE) syndrome is a recently defined clinical entity. However, the histopathologic coexistence of pulmonary fibrosis and emphysema was first described in the literature in the 1970s [1]. Subsequently in the 1990s, the advent of computed tomography technology permitted enhanced clinical recognition of the coexistence of pulmonary fibrosis and emphysema in the same patients. Emphysema is usually encountered predominantly in the upper lobes followed by fibrosis of the lower lobe [2]. The prevalence of CPFE is not known although a wide variation in different studies is present. It has been estimated to represent between 8 and 51% of cases of diffuse interstitial lung disease [3].

On the other hand, in patients with emphysema the proportion of pulmonary fibrosis was estimated to be about 4.4–8% by HRCT [4,5]. Most patients are current or former smokers, predominantly men over 65 years of age, with severe dyspnea and exercise limitation [2].

High-resolution computed axial tomography (HRCT) of the chest is the mandatory tool to confirm the diagnosis in which centrilobular and/or paraseptal emphysemas in the upper lung zones coexist with pulmonary fibrosis in lower lobes in one individual. Pulmonary hypertension is highly prevalent in CPFE and is the main determinant of death. Tobacco smoking has been proposed as the leading factor in its etiology [6]. It is not known whether CPFE represents a unique disease entity or a coincidence of two pulmonary diseases related to cigarette smoking. Moreover, the extent of emphysema and fibrosis needed to distinguish the patient with CPFE from patients with predominant emphysema or predominant fibrosis is still unclear [7]. Usual interstitial pneumonia/idiopathic pulmonary fibrosis (IPF) appears to be the most common imaging or pathologic findings in CPFE; however, other fibrotic patterns have been reported in conjunction with emphysema [8]. The aim of this study was to assess the clinical, physiological and radiological characteristics of patients with CPFE syndrome and

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to compare it with patients with chronic obstructive pulmonary disease (COPD) and disease interstitial lung disease (ILD) alone.

Patients and methods

Patients

This study was done in the Chest Department, Assiut University Hospital during the period from August 2015 to August 2016. The study was approved by the Ethical Committee of Faculty of Medicine, Assiut University. An informed consent was obtained from all patients. The confidentiality of patient's information was maintained during all steps of the study.

In this analytic cross-sectional study 120 patients were enrolled and divided to three groups. The COPD group included 40 patients; 32 men and eight women. The ILD group included 40 patients; 16 men and 24 women and the CPFE group included 40 patients; 23 men and 17 women. The age range was from 38 to 70 years. COPD was diagnosed according to Global Initiative for Chronic Obstructive Lung Disease criteria by the presence of postbronchodilator fixed ratio of FEV1/FVC less than 0.70 [9]. ILD was diagnosed using HRCT by the presence of reticular abnormality, ground glass abnormality, nodular or micronodular opacities, honeycombing with or without traction bronchiectasis [10]. CPFE was diagnosed by the presence of emphysematous changes on HRCT, in the form of well-demarcated areas of decreased attenuation in comparison with the surrounding normal lung and marginated by a very thin (1 mm) or no wall, and/or multiple bullae (1 cm) with upper zone predominance combined with diffuse parenchymal lung disease with significant pulmonary fibrosis in the form of reticular opacities, and/or honeycombing, architectural distortion, traction bronchiectasis, bronchiolectasis and focal ground-glass opacities with peripheral and basal predominance [2]. Patients with connective tissue disease, drug-induced interstitial lung disease, pneumoconiosis, hypersensitivity pneumonitis or sarcoidosis were not included in the CPFE group.

Methods

Patients were subjected to:

(1) Detailed medical history with an attention to demographic data, symptoms including dyspnea and its grade according to MRC scale [11] and the presence of comorbidities.
(2) Physical examinations: with special attention to the presence of cyanosis finger clubbing, signs of airflow obstruction, signs of cor-pulmonale, crackles and signs of hyperinflation.
(3) Plain chest radiography: posteroanterior and lateral views to search for emphysematous changes in COPD, fibrotic changes in ILD and both in CPFE.
(4) Arterial blood gases: Arterial blood samples were taken from all patients to check gases tension and acid base status using blood gases analyzers (Rapid lab 850; Chiron Diagnostics, Halstead, UK).
(5) High-resolution computed axial tomography (HRCT): HRCT examination (using Aquilion 64; Toshiba Medical Systems, Otawara, Japan) was performed by standard protocol scans were obtained at full inspiration from the apex to the lung base with the patients in the supine position.
(6) Echocardiogaraphy: (Philips xMATRIX Echo System; Philips, Eindhoven, The Netherlands) to measure pulmonary artery systolic pressure.
(7) Pulmonary function tests: Pulmonary function tests were done when the patient condition becomes stable. Standard spirometry and polythesmography were performed in all patients by means of a fully equipped computerized system (using Cosmed SrL, Quark PFTs ergo, P/N Co9035-12-99; Cosmed SrL, Rome, Italy, and D 97723, Zan 300; Zan, Oberthulba, Germany, respectively). Single-breath diffusing capacity for carbon monoxide (DLCO) was also measured using a single breath (using D 97723, Zan 300; Zan).

Statistical analysis

The data were tested for normality using the Anderson–Darling test and for homogeneity variances before further statistical analysis. Categorical variables were described by number and percent, where continuous variables were described by mean±SD. χ^2-Test and Fisher's exact test were used to compare between categorical variables where comparison between continuous variables by analysis of variance was followed least significant difference. A two-tailed P value less than 0.05 was considered statistically significant. All analyses were performed with the SPSS for windows version 16 (SPSS Inc., Chicago, IL, USA).

Results

As regards demographic data, the mean age of patients with CPFE (55.48±13.77 years) was significantly lower than that of COPD patients (62.05±8.1 years) and significantly higher than that of ILD patients (48.33± 10.04 years) ($P<0.01$ for each). Men were the

predominant sex in the COPD and the CPFE group (80 and 57%, respectively). Most patients with CPFE (87.5%) were exposed to tobacco smoke. There was no statistically significant difference regarding the residence or the presence of other comorbidities including hypertension or diabetes mellitus between the three groups ($P>0.05$ for each) as shown in Table1. Table 2 represented the clinical data of the studied patients. There was no statistical significant difference in Modified Medical Research Council (mMRC) dyspnea scale among the three groups ($P>0.05$). All patients with COPD had productive cough while most patients with CPFE and ILD had dry cough. Chest wheeze was significantly higher in COPD than either CPFE or ILD group. Finger clubbing was significantly higher in either CPFE group or ILD group compared with the COPD group ($P<0.001$, <0.01 respectively). Most patients with COPD and CPFE had hyperinflation. The presence of velcro crackles was significantly higher in either ILD group or CPFE group compared with COPD ($P<0.001$ for each). The rate of exacerbation per year was significantly higher in patients with CPFE than in COPD or ILD patients. In contrast to COPD who had hyperinflation and emphysematous changes and ILD who had reticulonodular and fibrotic changes, patients in the CPFE group had both hyperinflation and emphysematous changes combined with reticular, nodular, ground glass opacity, honeycombing and fibrotic changes on radiological examination (Tables 3 and 4, and Fig. 1).

Table 5 showed that the mean PaO_2 and SaO_2 and DLCO% were significantly lower in the CPFE group compared with the COPD group or ILD group and the mean pulmonary artery systolic pressure was significantly higher in the CPFE group in comparison to either COPD group or ILD group ($P<0.001$ for each). The mean FVC% was significantly lower in the ILD group in comparison to either COPD or CPFE groups ($P<0.001$, <0.05, respectively) and significantly lower in the CPFE group than the COPD group ($P<0.001$). The mean total lung capacity (TLC)%, mean residual volume (RV)%, mean RV/TLC%, and mean percentage function residual capacity were significantly higher in the COPD group when compared with either CPFE group or ILD group, and were significantly higher in the CPFE group in comparison with the ILD group ($P<0.01$ for each).

Discussion

In the past few years there is an increasing recognition of clinical, radiological, and pathological coexistence of variable degrees of emphysema and pulmonary fibrosis in the same patient, resulting in a clinical syndrome known as CPFE. That syndrome is characterized by shortness of breath and great abnormalities of gas exchange, frequently complicated by pulmonary hypertension and had significant mortality [7]. We conducted this study to describe the characteristic of this syndrome in comparison to emphysema and pulmonary fibrosis alone.

In the current study, the mean age of patients with CPFE was 55.48±13.77 years which was significantly

Table 1 Demographic data of patients with combined pulmonary fibrosis and emphysema syndrome compared with chronic obstructive pulmonary disease and interstitial lung disease patients

Variables	COPD	CPFE	ILD	*P* value	P_1	P_2	P_3
Age	62.05±8.1	55.48±13.77	48.33±10.04	<0.001**	0.008**	<0.001**	0.004**
Sex							
Male	32 (80.0)	23 (57.5)	16 (40.0)	0.001**	0.029*	0.001**	0.117
Female	8 (20.0)	17 (42.5)	24 (60.0)				
Smoking history							
Current smoker	15 (37.5)	14 (35.0)	10 (25.0)	0.104	0.637	0.032*	0.237
Ex-smoker	7 (17.5)	8 (20.0)	5 (12.5)				
Passive smoker	16 (40.0)	13 (32.5)	13 (32.5)				
Nonsmoker	2 (5.0)	5 (12.5)	12 (30.0)				
Residence							
Urban	11 (27.5)	8 (20.0)	11 (27.5)	0.312	0.431	1.000	0.431
Rural	29 (72.5)	32 (80.0)	29 (72.5)				
Comorbidities							
HTN	8 (20.0)	9 (22.5)	6 (15.0)	0.825	0.869	0.788	0.843
DM	10 (25.0)	8 (20.0)	8 (20.0)				

Data expressed as *n* (%) or mean±SD; COPD, chronic obstructive pulmonary disease; CPFE, combined pulmonary fibrosis and emphysema syndrome; DM, diabetes mellitus; HTN, hypertension; ILD, interstitial lung disease; *P* value: comparison between all studied groups; P_1: comparison between COPD and CPFE groups; P_2: comparison between COPD and ILD groups; P_3: comparison between CPFE and ILD groups; $^*P<0.05$, statistically significant difference; $^{**}P<0.01$, statistically significant difference.

Table 2 Clinical data of patients with combined pulmonary fibrosis and emphysema syndrome compared with chronic obstructive pulmonary disease and interstitial lung disease patients

Variables	COPD	CPFE	ILD	*P* value	P_1	P_2	P_3
Dyspnea grade by mMRC							
Group I	0 (0.0)	1 (2.5)	0 (0.0)	0.750	0.538	0.644	0.766
Group II	6 (15.0)	9 (22.5)	8 (20.0)				
Group III	28 (70.0)	23 (57.5)	24 (60.0)				
Group IV	6 (15.0)	7 (17.5)	8 (20.0)				
Cough							
Dry	0 (0.0)	26 (65.0)	31 (77.5)	<0.001**	<0.001**	<0.001**	0.217
Productive	40 (100.0)	14 (35.0)	9 (22.5)				
Hemoptysis							
No	40 (100.0)	39 (97.5)	39 (97.5)	0.601	0.314	0.314	1.000
Yes	0 (0.0)	1 (2.5)	1 (2.5)				
			Chest wheeze				
No	4 (10.0)	19 (47.5)	39 (97.5)	0.001**	<0.001**	<0.001**	<0.001**
Yes	36 (90.0)	21 (52.5)	1 (2.5)				
Chest pain							
No	29 (72.5)	26 (65.0)	29 (72.5)	0.700	0.469	1.000	0.469
Yes	11 (27.5)	14 (35.0)	11 (27.5)				
Rate of exacerbations/year	3.33±1.56	4.2±1.02	3.15±1.05	<0.001**	0.002**	0.527	<0.001**
Central cyanosis							
No	2 (5.0)	1 (2.5)	0 (0.0)	0.359	0.556	0.152	0.314
Yes	38 (95.0)	39 (97.5)	40 (100.0)				
Finger clubbing							
No	39 (97.5)	22 (55.0)	28 (70.0)	<0.001**	<0.001**	0.001**	0.166
Yes	1 (2.5)	18 (45.0)	12 (30.0)				
Crepitations							
Dry (velcro crackles)	0 (0.0)	31 (77.5)	40 (100.0)	<0.001**	<0.001**	<0.001**	0.001**
Wet	40 (100.0)	9 (22.5)	0 (0.0)				
Rhonchi							
Sibilant	24 (60.0)	24 (60.0)	0 (0.0)	<0.001**	<0.001**	<0.001**	<0.001**
Sonorous	16 (40.0)	1 (2.5)	0 (0.0)				
No	0 (0.0)	15 (37.5)	40 (100.0)				
Signs of hyperinflation							
Yes	40 (100.0)	38 (95.0)	0 (0.0)	<0.001**	0.396	<0.001**	<0.001**
No	0 (0.0)	2 (5.0)	40 (100.0)				

Data expressed as *n* (%); COPD, chronic obstructive pulmonary disease; CPFE, combined pulmonary fibrosis and emphysema syndrome; DM, diabetes mellitus; HTN, hypertension; ILD, interstitial lung disease; mMRC, Modified Medical Research Council; *P* value: comparison between all studied groups; P_1: comparison between COPD and CPFE groups; P_2: comparison between COPD and ILD groups; P_3: comparison between CPFE and ILD group; *$P<0.05$, statistically significant difference; **$P<0.01$, statistically significant difference.

lower than that of COPD patients (62.05±8.1 years) and higher than that of ILD patients (48.33±10.04 years). This was in agreement with previous studies which found that the mean age of COPD was higher in comparison to CPFE [12]. However, in the study of Akagi *et al.* [13] and Sugino *et al.* [14] the mean age of ILD patients was higher than CPFE patients (66.5±9.2 and 73.7±6.3, respectively).The cause beyond the difference from the results of this study may be due to the nature of patients as they studied only patients with IPF, which is predominant in elderly while this study also included patients with other ILD which had relatively younger age than IPF patients.

As regards sex distribution, this study was in concordance with previous studies regarding male sex predominance in CPFE syndrome. The male preponderance of cases of CPFE could be explained by greater exposure to smoking and other CPFE risk factors as dust and minerals in men than women [7]. As in the case of emphysema, IPF is also more common in men than in women, especially in older age groups [15]. Most patients with CPFE syndrome (87.5%) have been exposed to cigarette smoking. This is compatible with recent studies of CPFE which have shown a strong association with cigarette smoking [7]. The relationship between CPFE and smoking may be explained by the associations between smoking and both COPD/emphysema and IPF, where a unique group of patients exposed to cigarette smoke is vulnerable to develop extensive CPFE disease. In the present study, there was no statistically significant difference in the grade of dyspnea based on mMRC dyspnea scale among the study groups.

Table 3 Chest radiography findings among patients with combined pulmonary fibrosis and emphysema syndrome compared to chronic obstructive pulmonary disease and interstitial lung disease patients

Chest radiography	COPD	CPFE	ILD	*P* value	P_1	P_2	P_3
Emphysematous changes							
Hyperinflation	40 (100)	38 (95.0)	0 (0.0)	0.002**	0.002**	–	–
Low flat diaphragm	28 (70.0)	11 (27.5)	0 (0.0)				
Bulla	4 (10.0)	4 (10.0)	0 (0.0)				
Hyper lucent lung	9 (22.5)	1 (2.5)	0 (0.0)				
Narrow mediastinum	2 (5.0)	2 (5.0)	0 (0.0)				
Wide costophrenic angle	29 (72.5)	5 (12.5)	0 (0.0)				
Fibrotic changes							
Reticulonodular opacity	0 (0.0)	31 (77.5)	30 (75.0)	<0.001**	<0.001**	<0.001**	0.224
Honey combing opacity	0 (0.0)	1 (2.5)	0 (0.0)				
Normal	40 (100.0)	3 (7.5)	0 (0.0)				
Reticular opacity	0 (0.0)	4 (10.0)	8 (20.0)				
Nodular opacity	0 (0.0)	1 (2.5)	2 (5.0)				

Data expressed as *n* (%); COPD, chronic obstructive pulmonary disease; CPFE, combined pulmonary fibrosis and emphysema syndrome; DM, diabetes mellitus; HTN, hypertension; ILD, interstitial lung disease; *P* value: comparison between all studied groups; P_1: comparison between COPD and CPFE groups; P_2: comparison between COPD and ILD groups; P_3: comparison between CPFE and ILD group; $^{**}P<0.01$, statistically significant difference.

Table 4 High-resolution computed tomography findings of patients with combined pulmonary fibrosis and emphysema syndrome compared to chronic obstructive pulmonary disease and interstitial lung disease patients

HRCT	COPD	CPFE	ILD	*P* value	P_1	P_2	P_3
Emphysematous changes							
Centrilobular emphysema	6 (15.0)	24 (60.0)	0 (0.0)	0.028*	0.028*	–	–
Paraseptal emphysema	1 (2.5)	6 (15.0)	0 (0.0)				
Panlobular emphysema	1 (2.5)	9 (22.5)	0 (0.0)				
Bulla	3 (7.5)	5 (12.5)	0 (0.0)				
Hyperinflation	40 (100)	38 (95.0)	0 (0.0)				
Fibrotic changes							
Ground glass opacity	0 (0.0)	24 (60.0)	32 (80.0)	<0.001**	0.005**	<0.001**	0.111
Honey combing opacity	0 (0.0)	19 (47.5)	23 (57.5)				
Reticular opacity	0 (0.0)	28 (70.0)	21 (52.5)				
Traction bronchiactasis	0 (0.0)	3 (7.5)	1 (2.5)				
Architectural or bronchial distortion	1 (2.5)	4 (10.0)	0 (0.0)				

Data expressed as *n* (%); COPD, chronic obstructive pulmonary disease; CPFE, combined pulmonary fibrosis and emphysema syndrome; HRCT, high-resolution computed tomography; DM, diabetes mellitus; HTN, hypertension; ILD, interstitial lung disease; *P* value: comparison between all studied groups; P_1: comparison between COPD and CPFE groups; P_2: comparison between COPD and ILD groups; P_3: comparison between CPFE and ILD groups; $^{*}P<0.05$, statistically significant difference; $^{**}P<0.01$, statistically significant difference.

This result was in agreement with Tomioka *et al.* [16], who conducted a retrospective observational study on 17 CPFE patients and 49 COPD patients and found that mMRC dyspnea grade were comparable between the two groups. However, other authors reported that CPFE patients had more dyspnea at rest and following effort than COPD patients as those patients had extensive pathology than patients with either disease alone [12].

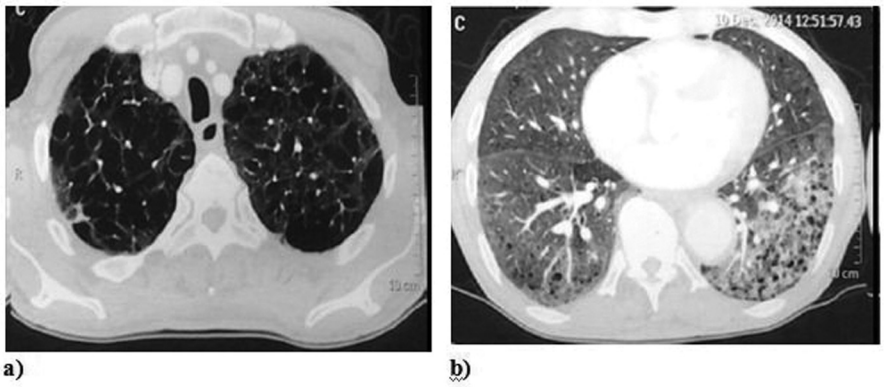
In this study patients with CPFE had a significantly higher rate of exacerbation per year than patients with COPD and ILD. This may be attributed to the great functional impairment of those patients. Although a consensus definition of CPFE syndrome does not currently exist, the diagnosis can be established using HRCT imaging. Characteristic radiologic findings in the CPFE syndrome include upper-lobe emphysema and lower-lobe interstitial fibrotic changes. The emphysema in CPFE includes bullous, paraseptal, and centrilobular changes and is typically distributed in the upper lobes [2,17,18]. In the current study centrilobular, paraceptal and panlobular emphysema were significantly higher in CPFE than in COPD patients. This was in agreement with that of Kitaguchi *et al.* [18] who have found that paraseptal emphysema was more common in the CPFE population than in the control group of patients with COPD (33.3 vs. 8.5%, respectively). Honeycombing, reticular abnormalities and ground glass attenuation are frequent in our study and comparable to that of ILD. Cottin *et al.* [2] support this finding.

Table 5 Arterial blood gas, pulmonary artery systolic pressure, and PFT among patients with combined pulmonary fibrosis and emphysema syndrome compared to chronic obstructive pulmonary disease and interstitial lung disease patients

	COPD (*n*=40)	CPFE (*n*=40)	ILD (*n*=40)	*P* value	P_1	P_2	P_3
pH	7.41±0.05	7.40±0.04	7.44±0.04	0.002**	0.443	0.007**	0.001**
$PaCO_2$	53.33±12.23	49.18±8.93	40.65±7.78	<0.001**	0.061	<0.001**	<0.001**
PaO_2	51.23±9.23	46.55±7.84	48.23±8.99	0.056	0.018*	0.126	0.391
HCO_3–	33.45±7.61	30.43±5.06	27.93±4.9	<0.001**	0.026*	<0.001**	0.064
SaO_2	82.5±10.04	77.53±9.45	82.5±8.8	0.028*	0.020*	1.000	0.020*
PASP*	43.58±18.29	68.35±13.88	47.53±20.71	<0.001**	<0.001**	0.324	<0.001**
FVC% predicted	83.93±12.15	65.7±18.28	58.63±9.67	<0.001**	<0.001**	<0.001**	0.024*
FEV1/FVC%	57.55±6.83	65.68±11.04	83.78±4.78	<0.001**	<0.001**	<0.001**	<0.001**
FEV1% predicted	52.53±12.92	52±15.02	56.44±10.9	0.255	0.858	0.182	0.131
LCO% predicted	68.83±5.13	41.68±13.45	54.76±10.8	<0.001**	<0.001**	<0.001**	<0.001**
TLC% predicted	171.03±26.74	94.1±42.74	54.3±17.98	<0.001**	<0.001**	<0.001**	<0.001**
RV/TLC%	55.31±10.74	46.03±17.84	25.92±8.96	<0.001**	0.004**	<0.001**	<0.001**
FRC% predicted	181.97±29.6	95.65±44.16	58.78±18.69	<0.001**	<0.001**	<0.001**	<0.001**
RV% predicted	196.11±50.23	118.16±53.95	64.03±20.83	<0.001**	<0.001**	<0.001**	<0.001**

Data expressed as mean±SD; ANOVA, analysis of variance; COPD, chronic obstructive pulmonary disease; CPFE, combined pulmonary fibrosis and emphysema syndrome; DLCO, diffusion lung capacity for carbon monoxide; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; FRC, function residual capacity; HCO_3–, bicarbonate; DM, diabetes mellitus; HTN, hypertension; ILD, interstitial lung disease; LSD, least significant difference; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; PASP, pulmonary artery systolic pressure; RV, residual volume; SaO_2, O_2 saturation; TLC, total lung capacity; *P* value: comparison between all studied groups by ANOVA followed by LSD multiple comparison; P_1: comparison between COPD and CPFE groups; P_2: comparison between COPD and ILD groups; P_3: comparison between CPFE and ILD group; *$P<0.05$, statistically significant difference; **$P<0.01$, statistically significant difference.

Figure 1



Upper lobe centrilobular and paraseptal emphysema (a) and lower lobe fibrosis (b).

In the present study, there is significant hypoxemia and significant decrease in DLCO in the CPFE group when compared with either COPD group or ILD group. The severe impairment of gas exchange in CPFE is likely due to reduced vascular surface area and pulmonary capillary blood volume plus alveolar membrane thickening resulting from the two coexistent diseases [7]. Pulmonary hypertension is a well-known complication of CPFE syndrome. It appears to be more frequent and more severe in the CPFE population than in patients with emphysema or ILD alone [19]. In one study most CPFE patients have moderate to severe PAH whereas that in COPD or ILD alone it is usually mild to moderate [20]. The current study coincides with this and demonstrated that the mean pulmonary artery systolic pressure in CPFE patients was significantly higher than in COPD or ILD patients. This may be attributed to the presence of additional or synergistic effect of pulmonary vasoconstriction caused by hypoxemia and reduced capillary beds caused by the combination of emphysema and pulmonary fibrosis in CPFE [21].

In this study, we have found that in patients with CPFE despite extensive radiological changes, lung volumes are nearly preserved where TLC, RV, and function residual capacity were around normal values, while they are increased in COPD patients and decreased in ILD patients. The relatively normal lung volumes in CPFE usually are attributed to the counterbalancing effects of the restrictive defect of pulmonary fibrosis and the propensity to

hyperinflation seen in emphysema [7]. Gas exchange is markedly impaired in CPFE. This is manifested by a marked reduction in DLCO, PaO_2, and SaO_2. This may be due to the overlapping negative effects of both emphysema and pulmonary fibrosis on the gas exchange [7,22].

Conclusion

This study proved that CPFE is a distinct clinical syndrome with a characteristic presentation. HRCT is the main tool to confirm the diagnosis. Patients with CPFE syndrome had a characteristic functional profile, with preserved lung volumes and strongly impaired DLCO. Cigarette smoking and male sex were two major clinical characteristics linked to this syndrome. All patients with CPFE should be screened for possible complicating pulmonary hypertension as it was found in the majority of patients screened in this study.

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Conflicts of interest

There are no conflicts of interest.

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