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Quantitative CT in mortality prediction in pulmonary fibrosis with or without emphysema

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Abstract. Aim: We aimed to evaluate the quantitative CT analysis of patients with CPFE in comparison with IPF and emphysema. **Methods:** Patients with CPFE(n:36), IPF(n:38) and emphysema(n:32) were retrospectively included in the study with the approval of the ethics committee. **Results:** There was a positive correlation between total lung volume and FVC%, TLCO% and 6 MWT, and negative correlation between mMRC and mortality. Negative correlation was found between right, left lung density and FVC%, TLCO% and 6 MWT, and positive correlation between mortality. Also, total lung volume, right and left lung densities were significant in predicting mortality and cut-off values are ≤3831,> -778 and> -775, respectively (p = 0.040, 0.020, 0.013). **Conclusion:** Quantitative CT are guiding in predicting mortality of the disease.

Key words: Combined pulmonary fibrosis and emphysema, idiopathic pulmonary fibrosis, emphysema, quantitative computerized tomography, pulmonary function test

Introduction

Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease with an unknown etiology, poor prognosis and clinical course differs between patients (1). Emphysema is a disease that causes air trapping and airflow restriction as a result of destruction and loss of elasticity in the alveolar wall and is seen as low attenuation areas (LAA) in computed tomography (CT) (2). Combined pulmonary fibrosis and emphysema syndrome (CPFE) appears radiologically as predominantly emphysema in the upper lobes, , fibrosis in the lower lobes. Lung volumes are partially preserved, carbon monoxide diffusion capacity (DLCO) decreases (3-5).

Today, CPFE is considered as a different syndrome than emphysema and fibrosis (4). Although its clinical, radiological and functional characteristics are similar to IPF in terms of prognosis, CPFE exhibits different features (6-7). Thoracic CT plays a major role in distinguishing CPFE from IPF and emphysema (7). Differences are seen in pulmonary function tests in emphysema and pulmonary fibrosis. Compliance and lung volumes increase, elastic recoil decreases in emphysema whereas compliance and lung volumes decrease and elastic recoil increases in fibrosis (8). While pulmonary fibrosis has a restrictive pattern, emphysema shows obstructive pattern and air trapping. In CPFE, where emphysema and fibrosis are together, air flow rates and lung volumes are preserved, while gas exchange decreases (9-11).

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Nowadays, the usage of quantitative CT techniques is gradually increasing. Quantitative CT is used not only in interstitial lung diseases but also in other diseases such as pulmonary embolism, chronic obstructive pulmonary disease (COPD), COVID-19(12-14). There are studies using these techniques related to the diagnosis, prognosis and mortality of interstitial lung diseases and IPF (15-19). However, there is not much study on quantitative CT in patients with CPFE, and even fewer studies comparing four groups which are CPFE, IPF, emphysema and control group.

CPFE, IPF and emphysema can be similar with their symptoms and clinical features. It can be difficult for clinicians to distinguish these three diseases and diagnose CPFE. In addition, survival of both IPF and CPFE is short, and predictors for mortality are important and may shed light on priority in transplant. There are a few studies on quantitative CT in CPFE patients. Generally, the quantitative CT studies is about IPF. Therefore, in our study; we aimed to compare the quantitative CT findings in patients diagnosed with CPFE, IPF and emphysema and evaluate the prediction for mortality.

Materials and Methods

Patients

Patients diagnosed with CPFE, IPF and emphysema, who were admitted to the interstitial lung diseases outpatient clinic between September 2013 and February 2019, were included retrospectively. A control group consisted of the patients without interstitial lung disease or chronic lung disease who have thorax CT for screening or examination. The diagnosis of IPF was made clinically, radiologically and/or pathologically according to ATS / ERS / JRS / ALAT diagnostic criteria (20). Patients with more than 10% of centrilobuler and/or paraseptal emphysema in the upper lobes and pulmonary fibrosis in the lower lobes were evaluated radiologically as CPFE described by Cottin et al. and Ryerson et al. (7,21). The pattern of fibrosis in CPFE patients was evaluated by radiologists. Pulmonary fibrosis, CPFE, emphysema and control groups were determined by evaluating the patients' CT by two independent radiologists. Obstructive disorder was present in the pulmonary function tests of 18 (56%) patients with emphysema. Patients diagnosed with sarcoidosis, connective tissue disease, hypersensitivity pneumonia, pneumoconiosis, lymphangioleomyomatosis, langerhans cell histiocytosis and eosinophilic pneumonia, and patients with environmental exposure to drug toxicity and asbestos or any fibrogenic agent were excluded from the study. Demographic and clinical data of all patients, pulmonary function parameters (PFT), 6-minute walk test (6 MWT), Short Form(SF)-36 quality of life assessment scale, modified Medical Research Council (mMRC) dyspnea score, systolic pulmonary artery pressure (sPAB) on echocardiography (ECHO) and CT findings were recorded.

Pulmonary function tests (PFT)

PFT was performed using the ZAN 300 device (ZAN Messgerate, Oberthulba, Germany) with the patient in a resting and sitting position. The test was repeated at least three times and those with less than 5% change between tests were evaluated. Forced vital capacity (FVC) with spirometry and body plethysmography, forced expiratory volume in the first second (FEV1), FEV1 / FVC, forced expiratory flow rate between 25% and 75% of vital capacity (FEF25-75), total lung capacity (TLC), residual volume (RV), RV / TLC, carbon monoxide transfer factor (TLCO)%, transfer coefficient (KCO)%, FVC% / TLCO% values were recorded. FEV1 and FVC were evaluated according to the European Respiratory Society (ERS) guidelines (22-24). Adjusted value of carbon monoxide transfer factor (TLCO) relative to hemoglobin was taken (25).

CT protocol

High-Resolution CT(HRCT) images (Hıthachı Whole Body X-ray System, Hıthachı, Ltd. 2-16-1, Highashi-Ueno, Taito-ku, Tokyo, 110-0015, Japan) obtained in supine position, full inspiration, with 16 detectors and 1.25 mm section thickness. The parenchyma window was evaluated between -700 and 1500 Hounsfield Units (HU). Thoracic HRCTs of all patients were examined by two independent radiologists. Volume analysis over the HRCT images was made with the program "Myrian version 2.4.2 (Intrasense, Montpellier, France)". Myrian software automatically divide

the lung parenchyma into segments, bronchial and vascular structures together with HU values, and automatically calculates lung volume by algorithms. Visual and numerical data and graphics, which were obtained automatically, were checked by the radiologist and if necessary, manual adjustments were made on the same program and recorded. Total lung volume (cm3), right and left lung volume (cm3), right and left lung average density (density) (HU), percentage of the low attenuation areas of the right and left lung and the whole lung (LAA%) were recorded separately. Pulmonary function tests performed in the similar period of HRCT scanning. This period is limited to a maximum of 30 days before or after HRCT.

Echocardiography (ECHO)

Philips iE33 echocardiography device (x4.1 transducer; Philips Medical Systems, Bothell, WA, USA) with matrix array ultrasonographic transducer was used for echocardiography(ECHO) (conventional 2DE). The echocardiographic views of each patient were obtained in compliance with the recommendations of the American and European Societies of Echocardiography (26). Systolic pulmonary artery pressures (sPAB) (mmHg) were recorded. Patients with sPAB≥35 mmHg were evaluated as pulmonary hypertension (PHT) (27-29).

Statistical Analysis

Analyses of data was performed with the Statistical Package for the Social Sciences (SPSS, Inc., Chicago IL), version 22, software for Windows and data were presented as mean ± standard derivation and numbers (n) and percent (%). Shapiro-Wilk and Kolmogorov-Smirnov normality tests were used to check whether continuous variables show normal distribution or not. Anova test and Kruskal- Wallis test were conducted to compare the continuous variables between the groups and the X^2 test and Fisher's Exact test were performed for the comparison of categorical variables. Pearson correlation test was used to determine whether there was any relationship between clinical parameters. P <0.05 was considered statistically significant. ROC analysis was performed to assess sensitivity and specificity. Kaplan-Meier survival analysis was used to assess overall survival. The results were presented with 95% confidence intervals.

Ethics

The study organized in accordance with good clinical practices and Helsinki Declaration were approved by the ethics committee of our hospital (No: 49109414- 806.02.02).

Results

Clinical characteristics: CPFE, IPF, emphysema and control

The average age of four groups, CPFE (n = 36), IPF (n = 38), emphysema (n = 32) and control group (n = 36), respectively, was 66.9 ± 7.5, 67.8 ± 7.0, 63.0 ± 6.2 and 67.5 ± 3.7 (p = 0.008). Percentage of male patients (97.2%, p = 0.008), rate of smoking (smoker, ex-smoker) (97.2%, p <0.001), presence of comorbidity (72.2%, p = 0.009), mean mMRC score (2.4 ± 1.3,p<0.001), mean annual attack number(1.1±1.7, p=0.001), mean annual hospitalization number (0.7±1.2,p=0.046) in the CPFE group were more than the other two groups. While mean SF-36 total score ((64.5 ± 25.5), p <0.001) was lower in CPFE group(Table 1).

In echocardiographic evaluation; the mean systolic pulmonary artery pressure (sPAB) was higher in the CPFE group (p = 0.006). The number of patients with pulmonary hypertension (PHT) was similar in the CPFE and IPF group and was significantly higher than the emphysema group (p = 0.008) (Table 1).

The number of patients receiving long term oxygen therapy (LTOT) was highest in the CPFE (n = 15, 41.7%), followed by IPF (n = 7, 18.4%) and emphysema (n = 3, 9.4%), respectively (p = 0005). While 30.5% of patients with CPFE and 94.7% of patients with IPF received antifibrotic treatment, 78.1% of patients with emphysema were receiving bronchodilator treatment.

Pulmonary function tests parameters: CPFE, IPF and emphysema

FVC; 77.2 ± 18.2% in CPFE, 63.6 ± 15.7% in IPF and 81.0 ± 14.9% in emphysema, and the

Table 1. Demographic and clinical features of patients

	CPFE n=36	IPF n=38	Emphysema n=32	Control n=36	P value
Age, year (mean)	66.9±7.5	67.8±7.0	63.0±6.2	67.5±3.7	0.008
Gender (n,%) **Male** **Female**	 35, 97.2% 1, 2.8%	 26, 68.4% 12, 31.6%	 28, 87.5% 4 12.5%	 30 83.3% 6 16.7%	 0.008
Smoking(non-smoker/ smoker/ex-smoker)(%)	2.8/13.9/83.3	44.7/15.8/39.5	3.1/40.6/56.3		<0.001
Pack year (n=87)	51.6±40.6	24.4±14.9	51.9±28.4		0.004
Comorbidity (%) **Yes/No (%)**	 72.2% /27.8%	 65.8% /34.2%	 37.5% /62.5%		 0.009
DM **HT** **CAD** **COPD** **Hyperlipidemia** **Lung cancer**	4, 11.1% 12, 33.3% 12, 33.3% 15, 41.7% 1, 2.8% 0, 0.0%	16, 42.1% 11, 28.9% 14, 36.8% 2, 5.3% 1, 2.6% 2, 5.3%	2 6.3% 5 15.6% 4, 12.5% 22, 68.8% 0, 0.0% 0, 0.0%		<0.001 0.231 0.056 <0.001 0.652 0.161
Dyspnea **Cough** **Sputum**	32, 88.9% 28, 77.8% 13, 36.1%	35, 92.1% 31, 81.6% 10, 26.3%	20, 62.5% 12, 37.5% 4, 12.5%		0.002 <0.001 0.082
Clubbing	13, 36.1%	8, 21.1%	0, 0.0%		0.001
BMI (kg/m²)	26.1±3.1	27.4±3.8	24.9±4.0		0.020
SF-36 total score (mean)	64.5±25.5	81.5±13.1	68.3±27.2		0.004
mMRC score(mean)	2.4±1.3	2.0±0.9	0.7±0.8		<0.001
6MWT(mean)(n=86)	320.2±77.2	340.8±97.4	371.3±95.3		0.140
Attack number (median) (min-max)	0.0 (0.0-7.0)	0.0 (0.0-3.0)	0.0 (0.0-2.0)		0.002
Hospitalization number (median) (min-max)	0.0 (0.0-6.0)	0.0 (0.0-2.0)	0.0 (0.0-3.0)		0.045
SPAP(mmHg) mean (n=100)	36.5±20.9	33.2±14.1	24.5±7.2		0.006
PHT (n=100) **Yes / No (%)**	40.0/ 60.0	39.4/ 60.6	9.45/ 90.6		0.008
Mean Pulmonary arterial diameter(mm)	27.3±3.7	28.2±3.7	24.5±3.8		<0.001

CPFE: Combined pulmonary fibrozis and emphysema, IPF: İdiopathic pulmonary fibrosis, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary arterial disease, COPD: Chronic obstructive pulmonary disease, BMI: Body Mass index, SF 36: Quality of life score, mMRC: Modified Medical Research Council dyspnea scale, 6MWT:6 minute walk test, SPAP: Systolic pulmonary arterial pressure, PHT: Pulmonary hypertension.

difference was significant (<0.001). TLC, RV and RV/TLC values were highest in the emphysema group and higher in the CPFE group than IPF (p <0.001). While TLCO (33.8 ± 13.4%, p <0.001) and KCO (45.4 ± 18.2%, p = 0.002) are lower in CPFE than IPF and emphysema group, FVC% / TLCO% (2.5 ± 1.1, p <0.001) ratio was significantly higher in the CPFE than the other two groups (Table 2).

Volumetric measures of Quantitative CT: CPFE, IPF, emphysema and control

When we compare four group for quantitative HRCT; Total lung volume, including right and left lung volumes, was highest in the emphysema group and was gradually decreasing in the control group, CPFE and IPF group, respectively (p <0.001). Compared to the control group, both right and left lung

Table 2. Pulmonary function test parameters of the patients

	CPFE n=36	IPF n=38	Emphysema n=32	P value
TLC % (n=93)	78.0±13.0	63.3±14.9	114.6±60.5	<0.001
RV % (n=93)	99.7±32.3	73.0±24.8	174.5±152.3	<0.001
RV/TLC (n=93)	96.9±45.9	48.8±18.2	127.1±40.5	<0.001
FEV1 %	78.1±19.1	71.6±15.7	70.9±16.1	0.150
FVC %	77.2±18.2	63.6±15.7	81.0±14.9	<0.001
FEV1/FVC	80.6±12.0	90.1±7.0	69.1±11.8	<0.001
FEF 25-75	67.9±30.4	96.3±30.9	45.1±24.2	<0.001
TLCO(mmol/min/kPa) % (n=93)	33.8±13.4	43.3±13.5	52.1±14.8	<0.001
FVC%/TLCO%(n=93)	2.5±1.1	1.6±0.5	1.7±0.7	<0.001
KCO %(n=93)	45.4±18.2	75.3±32.7	76.0±59.6	0.002

CPFE: Combined pulmonary fibrozis and emphysema, IPF: Idiopathic pulmonary fibrosis, TLC: Total lung capacity, RV: Reziduel volume, FEV1: forced ekspiratuar volume in 1 second, FVC: forced vital capacity, FEF 25-75: forced ekspirauar flow rate between%25-%75of vital capacity, TLCO: Carbonmonokside transfer factor, KCO: Transfer factor (TLco/alveolar volume)

density (HU) decreased in the emphysema group, whereas it was found to increase significantly in CPFE and IPF (p <0.001). The % of total lung LAA was lowest in the control group, and increased in the IPF, CPFE and emphysema groups, respectively (p <0.001) (Table 3).

While there was a positive correlation between total lung volume in quantitative HRCT, and FVC% (r = 0.326 p = 0.001), TLCO% (r = 0.226 p = 0.028) , 6 MWT (r = 0.290 p = 0.007); negative correlation between mMRC (r = - 0.312 p = 0.001) and mortality (r = -0.236 p = 0.015) in all patients (Figure 1a). There was negative correlation between right- left lung density and FVC% (r = -0.370, p <0.001 and r = -0.399, p <0.001), TLCO% (r = -0.232, p = 0.024 and r = -0.239, p = 0.020) and 6 MWT (r = -0.268, p = 0.013 and r = -0.288, p = 0.007) and positive correlation with mortality (r = 0.230 p = 0.018 and r = 0.290 p = 0.003) (Figure 1b-1c).

Survival analysis

The mean follow-up was 30.4 (± 15.2) months. During follow-up, 25% of all patients died. 9 (25.0%) of them were in CPFE, 9 (23.7%) were in IPF and 1 (3.1%) was in emphysema. When the patients compared for the existence of the mortality, the total lung volume was lower in the mortal group (p = 0.028), and the right and left lung density was higher (p = 0.027, p = 0.008, respectively). In the ROC analysis; sensitivity of the total lung volume for mortality is 78.95% (95% Cl 54.4-93.9), specificity is 52.63% (95% Cl 39.0-66.0), cut-off ≤3831 (AUC = 0.645; p = 0.04) (Figure 2a) and sensitivity

Table 3. Volumetric measures of Quantitative CT of Patients

	CPFA n=36	IPF n=38	Emphysema n=32	Control n=36	P value
Right lung volume (cm3)	2386.8±590.6	1769.4±562.5	3197.2±713.5	2790.9±642.1	<0.001
Left lung volume (cm3)	2021.5±601.8	1420.5±537.1	2774.5±731.2	2442.5±814.2	<0.001
Total lung volume(cm3)	4408.3±1161.6	3142.5±1071.3	5970.7±1382.5	4630.8±1605.7	<0.001
Right lung density (HU)	-804.4±49.9	-737.7±55.3	-846.7±33.6	-825.1±29.1	<0.001
Left lung density (HU)	-793.9±62.9	-719.9±60.7	-841.0±35.4	-821.1±35.2	<0.001
Right lung LAA (%)	18.3±11.4	9.1±8.2	19.1±12.4	4.2±4.4	<0.001
Left lung LAA (%)	17.7±11.8	8.0±7.4	17.2±12.4	4.3±4.6	<0.001
Total lung LAA (%)	18.3±11.6	8.1±7.8	19.0±11.9	4.3±4.5	<0.001

CPFE: Combined pulmonary fibrozis and emphysema, IPF: Idiopathic pulmonary fibrosis, LAA: Low attenuation area

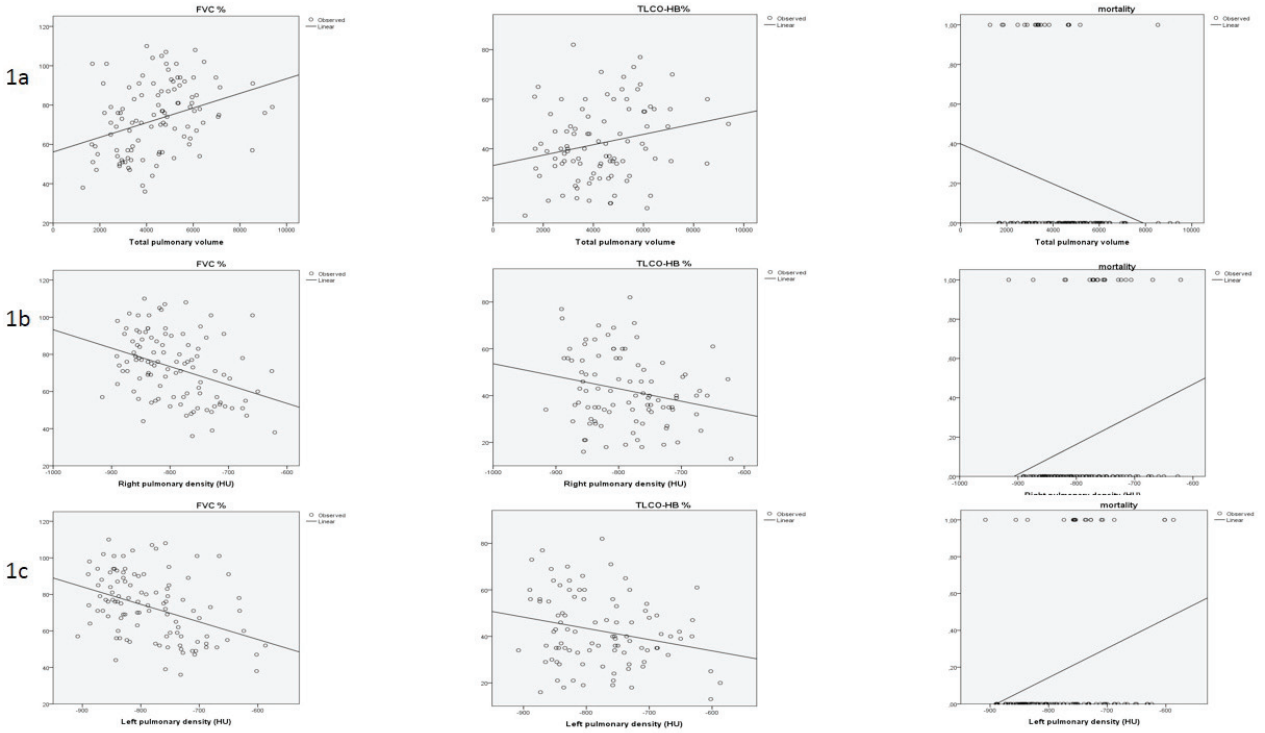

Figure 1. a) Correlation between total lung Volume and FVC%, TLCO%, mortality, b) Correlation between right lung density and FVC%, TLCO% , mortality, c) Correlation between left lung density and FVC%, TLCO%, mortality

of the right lung density is 84.21% (95% Cl 60.4-96.6), specificity 54.39% (95% Cl 40.7-67.6), cut-off> -778 (AUC = 0.665; p = 0.02) (Figure 2b), sensitivity of the left lung density 89.47% (95% Cl 66.9-98.7), specificity% 49.12 (95% Cl 35.6-62.7) and cut-off> -775 (AUC = 0.676; p = 0.013) (Table 4) (Figure 2c).

Kaplan meier plots according to cut-off values showing the best specificity and sensitivity are shown in Figure 3. The mean survival time was 53.9 ± 5.5 months in patients with total lung volume ≤3831 (cm3), while 64.2 ± 5.8 months (p Log Rank p = 0.019) (Figure 3a) in those with> 3831, 52.8 ±5.5 months in those with right lung density> -778 (HU),

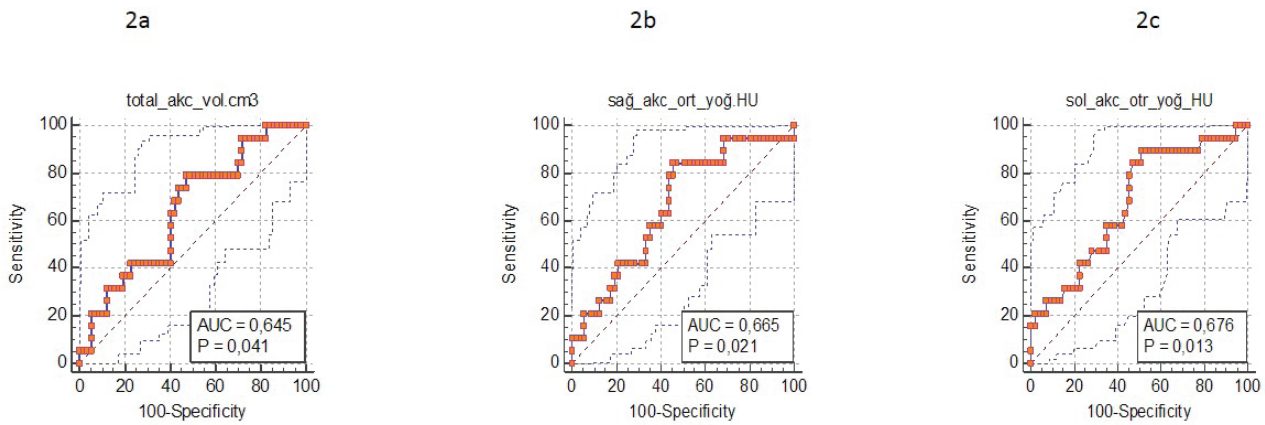

Figure 2. a) ROC graphic of total Lung Volume, b) ROC graphic of right lung density, c) ROC graphic of left lung density

Table 4. ROC analysis of Quantitative CT parameters

	AUC (95% Cl)	P value	Cut off value	Sensitivity (95% Cl)	Specificity (95% Cl)	PPV (95% Cl)	NPV (95% Cl)	Positive Likelihood Ratio (95% Cl)	Negative Likelihood Ratio (95% Cl)
Total lung vol	0.645 (0.527-0.752)	0,040	≤3831	78.95% (54.4-93.9)	52.63 (39.0-66.0)	35.7% (28.0-44.3)	88.2% (75.2-94.9)	1.67 (1.2-2.4)	0.40 (0.2-1.0)
Mean right lung density	0.665 (0.547-0.769)	0.020	>- 778	84.21% (60.4-96.6)	54.39% (40.7-67.6)	38.1% (30.4-46.5)	91.2% (78.1-96.8)	1.85 (1.3-2.6)	0.29 (0.1-0.8)
Mean left lung density	0.676 (0.559-0.779)	0.013	>-775	89.47% (66.9-98.7)	49.12 (35.6-62.7)	37.0% (30.3-44.1)	93.3% (78.6-98.2)	1.76 (1.3-2.4)	0.21 (0.06-0.8)
Emphysema ratio of total lung%	0.560 (0.441-0.673)	0.445	≤9.55	57.89% (33.5-79.7)	57.89% (44.1-70.9)	31.4% (21.9-42.8)	80.5% (70.0-88.0)	1.38 (0.8-2.2)	0.73 (0.4-1.3)

AUC: area under curve, PPV: positive predictive value, NPV: negative predictive value, Cl: confidence interval

it was 59.6 ± 3.8 months (Log Rank p = 0.016) (Figure 3b) in those with ≤-778. 52.7 ± 5.1 months in those with left lung density> -775 (HU) and 55.9 ± 2.7 months (Log Rank p = 0.024) (Figure 3c) in those with ≤-775 (HU).

Discussion

Unlike other studies; lung volume, density and emphysema rate (low attenuation area, LAA%) calculated by quantitative HRCT, pulmonary function tests and clinical characteristics of the patients in groups as CPFE, IPF, emphysema and control were evaluated comparatively in our study. Diffusion capacity was the lowest in CPFE and increased in IPF and emphysema, respectively. Lung volumes (FVC, RV, TLC) were higher in CPFE than IPF and lower than emphysema.

In the quantitative HRCT, right and left lung volume and total lung volume were highest in the emphysema group and decreased gradually in the control group, CPFE and IPF group, respectively. Both the right and left lung density levels were lower in the emphysema group than in the control group and higher in CPFE and IPF, respectively. The percentage of total lung LAA was lowest in the control group, and increased gradually in the IPF, CPFE and emphysema group, respectively. In addition, while there was a positive correlation between total lung volume in quantitative HRCT and FVC%, TLCO% and 6 MWT, there was a significant negative correlation between mortality. Both right and left lung density were negatively correlated with FVC%, TLCO%, 6 MWT and mMRC, and significantly positively correlated with mortality. In addition, total lung volume, right and left lung density predicted mortality significantly, and cut-off values were ≤3831,> -778 and> -775, respectively.

In accordance with other studies, male gender and smoking were found to be significantly higher in CPFE, and also compared to IPF, additionally lung volumes were preserved in CPFE, while diffusion decreased more (30).

In a meta-analysis involving 13 studies, IPF and CPFE patients were compared; no statistically significant difference was found between one, three and five-year survival rates, and it was reported that CPFE had a poor prognosis similar to IPF (30). In the literature, there are studies indicating that CPFE has a worse prognosis than IPF (31-33), but there are also stating that there is no significant difference between them (30). In our study, CPFE was worse in terms of parameters such as mMRC, 6MWT, SF-36 quality of life, and the number of hospitalizations. However, our mortality rate in IPF and CPFE group was similar. The different results in these studies may be attributed to the variability of emphysema and fibrosis rates and patients' heterogeneity (34-36).

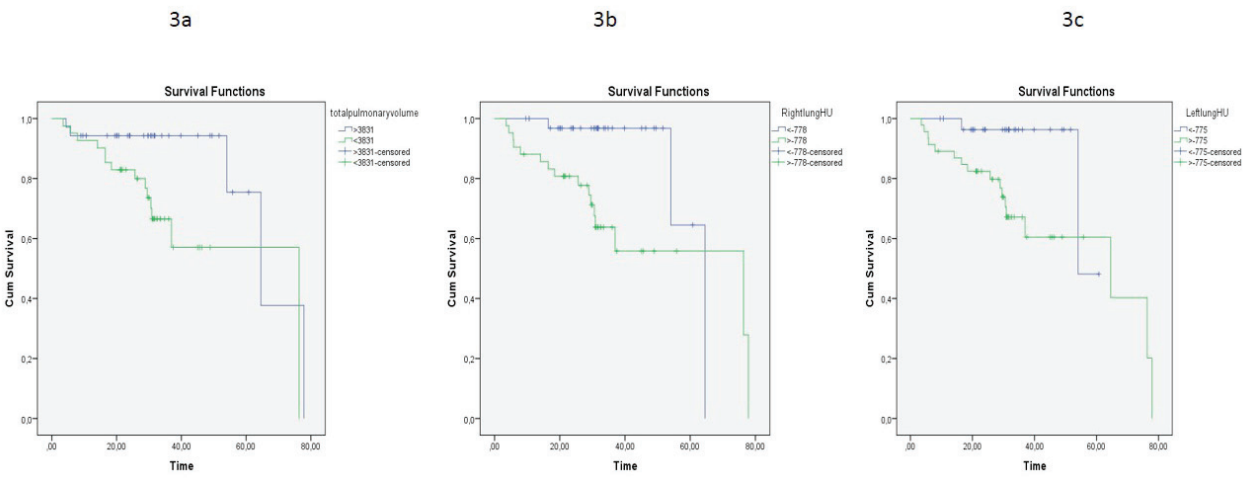

Figure 3. a) Total Lung Volume - Kaplan–Meier plot of survival probability. b) Right lung density- Kaplan–Meier plot of survival probability. c) Left lung density- Kaplan–Meier plot of survival probability.

Cottin et al. reported that patients with CPFE are often complicated with pulmonary hypertension (37). In our study, the mean sPAB was higher in the CPFE group. The proportion of patients with pulmonary hypertension (PHT) was similar in the CPFE and IPF group and higher than in the emphysema group.

In the study of Çiftçi et al; mean arterial PO2 was lower and mean sPAB was higher in CPFE group compared to IPF (8). In our study, we found the number of patients receiving LTOT due to hypoxemia and the mean sPAB value significantly higher in the CPFE group than in the emphysema and IPF group.

Nakagawa et al. reported that honeycomb rate predicted mortality by measuring the areas of honeycomb in IPF patients by quantitative HRCT (16). In the study by Jacob et al. evaluating the volume, density and heterogeneity of the vessels with quantitative HRCT in IPF patients; they reported that disease severity related with the vascular measurements (17). Bak et al investigated the quantitative HRCT in the evaluation of emphysema and fibrosis in patients with IPF and stated that it predicts prognosis and clinical outcomes (18). In the study of Torrisi et al. they evaluated survival in IPF patients using quantitative HRCT. They found that quantitative CT findings correctly predicted survival in IPF patients and correlated with the pulmonary function parameters (38).

Suzuki et al. They evaluated the percent of low attenuation area (LAA%, emphysema), the percent of high attenuation area (HAA%, fibrosis) and the percent of abnormal area obtained by the combination of low and high attenuation areas (AA%, emphysema + fibrosis) in quantitative CT of 46 patients with CPFE. A greater negative correlation was observed with DLCO% in AA% compared to LAA% or HAA % alone. In addition, AA% was found to be most strongly associated with hospitalization(34).

In the retrospective study in which Nemoto et al. included 228 patients with CPFE; They investigated the prognostic value of the degree of fibrosis detected with the automated CT technique. According to the rate of fibrosis, they divided the patients into 3 groups as <5%, 5% -10% and ≥ 10%. Those with ≥ 10% fibrosis had the worst overall survival and the most acute exacerbation (39).

254 patients with biopsy-proven fibrotic IIP were retrospectively included in the study by Choi et al. 66 patients were in CPFE, 188 patients were in the only fibrotic-IIP group. They investigated the relationship between emphysema index (EI) / fibrosis scores (FS) and mortality/survi in quantitative HRCT. Median survival was 6 years in CPFE and 10 years in only fibrotic IIP(p = 0.013). In the multivariate analysis, FVC and FS were found to be associated with high mortality in the CPFE group (p= 0.04, 0.03, respectively) (40).

In Akyıl et al.'s study; IPF without emphysema and CPFE had a median survival of 34 and 9 months, respectively. They showed radiologically that the presence of emphysema and honeycomb, male gender, hypoalbuminemia, hypoxemia, low FVC and low DLCO predicted mortality(41).

In our study, we found that the quantitative HRCT parameters were significantly different in

the control, emphysema, IPF and CPFE groups. We also found that these parameters (total lung volume and right-left lung density reflecting the degree of fibrosis) correlated significantly with FVC, TLCO, 6MWT, mMRC, and mortality, and predicted mortality significantly.

Limitations of the study

The limitations of our study are that it is primarily a retrospective observational study. Because the four groups compared, the number of cases is limited. Right heart catheterization is the gold standard in the diagnosis of pulmonary HT, but because it is an invasive procedure and our study is retrospective, ECHO findings were used, not right heart catheterization.

Conclusion

Quantitative HRCT measurements are guiding in predicting disease severity and mortality in IPF and CPFE patients. This is especially of important in directing to the lung transplant for patients who cannot perform PFT and 6MWT.

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