

Study on Clinical Characteristics of COPD Patients Presented with Interstitial Lung Abnormalities

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is defined by recurrent respiratory symptoms and airflow restriction brought on by anomalies in the airways and/or alveoli that appear following prolonged exposure to noxious substances, such as tobacco smoke. The biggest risk factor for lung fibrosis and COPD is smoking.

Aims and Objectives: To analyze the various clinical characteristics of COPD patients which are attributed to Interstitial Lung Abnormalities (ILA).

Methods: This is a prospective cross-sectional, this study gathered data from patient's visits and data collection was done based on patient age, sex, BMI, FEV1, FVC, the mMRC dyspnea scale score, the CAT score, and the annualized incidence of COPD exacerbations per participant. Propensity score matching of 1 to 3 was done between the control groups and ILA and required statistical analysis was conducted.

Results: Patients without ILAs showed a range of airflow restriction severity from Global Initiative for Chronic Obstructive Lung Disease or GOLD 1 to 4. Contrary, the severity of the airflow limitation was distributed across GOLD 1 to 3 in patients with ILAs, with a small number of patients in each class. Patients with ILAs demonstrated numerically, but not substantially.

Conclusion: The study has concluded that ILA lesions in patients with COPD progressed slowly and that the growth of ILAs had no bearing on COPD flare-ups. The study further concludes that ILAs following COPD may involve interstitial fibrosis brought on by smoking, which is distinct from some types of fibrosing lung disease with bad prognoses.

Keywords: interstitial lung abnormalities, ILA, chronic obstructive pulmonary disease, airway obstruction.

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by progressive restriction of airflow and in severe long standing form, it causes irreversible damage to pulmonary parenchyma. COPD is caused on by prolonged exposure to dangerous

substances or particles. Like the coexistence of pulmonary fibrosis and emphysema is referred to as (CPFE). Patients with COPD frequently experience emphysematous lung changes as a result of the degradation of the alveolar wall brought

on by toxic inhalation (such as cigarette smoke) [1]. A preventable and curable illness known as a chronic obstructive pulmonary disease (COPD) is characterized by tissue loss and a growing restriction of airflow. Due to chronic inflammatory reactions brought on by extended exposure to irritating particles or gases, most often smoking cigarettes, it is linked to structural changes in the lungs [1,2]. Airway constriction and a reduction in lung recoil are the results of chronic inflammation. The illness frequently manifests as coughing, sputum production, and dyspnea. Asymptomatic conditions to respiratory failure are all possible symptoms [3]. Long-term exposure to hazardous chemicals or particles results in COPD. One of most major reasons for COPD globally is tobacco smoke. Other factors may include exposure to secondhand smoke, environmental, and occupational hazards, and a lack of alpha-1 antitrypsin enzyme . (AATD) [4,5].

Chronic obstructive pulmonary disease (COPD) is defined by recurrent respiratory symptoms and airflow restriction brought on by anomalies in the airways and/or alveoli that appear following prolonged exposure to noxious substances, such as tobacco smoke. The biggest risk factor for lung fibrosis and COPD is smoking [6,7]. Emphysema and pulmonary fibrosis co-exist, and this condition is known as combined emphysema and fibrosis (CPFE). Given that nearly all (98%) patients with CPFE are either current or past smokers, smoking is hypothesized to play a significant role in the disease. It is yet unknown if pulmonary fibrosis and emphysema co-existing in a person represent a distinctive clinical entity or even a coincidence of smoking-related diseases, as is the case with lung cancer and COPD [8,9]

The diverse condition known as chronic obstructive pulmonary disease (COPD) is defined by ongoing airflow restriction and chronic respiratory symptoms [10]. Due to

the deterioration of the alveolar wall brought on by toxic inhalation (such as cigarette smoke), patients with COPD typically see emphysematous alterations in the lung. As a result, the emphysematous lung's loss of its elastic recoil capacity which further reduces its maximal expiratory airflow. Small airway disease (SAD), which is characterized by inflammatory and peribronchial fibrosis in smaller conducting airways (less than 2 mm in diameter), is another significant pathologic alteration in COPD [11-15]. In addition, interstitial lung disease (ILD) is a group of illnesses marked by chronic inflammatory and fibrotic infiltration of the alveolar septa, which results in significant alterations to the capillary endothelium and alveolar epithelium. Despite having different characteristics, COPD and ILD may coexist in the same patient since they both share some of the same risk factors like old age, tobacco exposure, and males) [16-18].

Materials and methods

Study design

This is a prospective cross-sectional study which was conducted on 70 patients who visited the hospital's outpatient department from October 2021 to October 2022. The data prospectively gathered from ongoing scheduled visits or newly registered patients in our hospital. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria were used to diagnose COPD in each patient. Repeated spirometry was utilized to demonstrate chronic airflow limitation, which is indicated by a post-bronchodilator ratio of 0.7 between forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1).

This study uses parameters like age, sex, BMI, FEV1, FVC, the mMRC dyspnea scale score, the CAT score, and the annualized incidence of COPD exacerbations per participant over the observational period were examined as

baseline parameters. The study, also uses age, gender, GOLD stage, and BMI as the dependent variables in logistic regression to create a propensity score in order to lessen selection bias. Propensity score matching of 1 to 3 was done between the control groups and ILA and required statistical analysis was conducted.

Inclusion and exclusion criteria

With an age group of 40 to 90 years old and a smoking history of at least ten pack-years, we enrolled individuals with stable COPD. If they granted their agreement, patients who had been diagnosed with COPD and whose status had been deemed stable were listed.

Current smokers, chronic bronchitis or emphysema without air supply restriction, hematological conditions, a background of lung resection, the consumption of oral corticosteroids, immunosuppressive medications, or antifibrotic medications, and the onset of a COPD exacerbation within the four weeks before data collection were the exclusion criteria. Additionally, individuals who were lost to follow-up, did not finish the 1-year follow-up, got radiation or chemotherapy within a year of registering or had apparent ILAs were not included in this analysis.

Statistical analysis

Data were presented as mean (standard deviation), and percentages were used to depict categorical data. Using the Mann-

Whitney U-test or Student's t-test, we evaluated for within-group differences in the continuous variables. Using Fisher's exact test, categorical variables were compared. We used R (The R Foundation for Statistical Computing, Vienna, Austria) and the graphical user interface EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) to perform all statistical analyses. The level of significance was considered to be $\alpha=0.05$.

Ethical approval

The patients were given a thorough explanation of the study by the authors before starting the study and gathering the data of the patients. The patients' permissions were obtained from each of the patient. The hospital's Ethical Committee has approved the whole study process.

Results

The characteristics of the study participants are shown in Table 1. The patient's average age was 73.2 years, with a standard deviation (SD) of 7.6 and 5 female patients. While the mean FEV1 percent predicted was 63.14% (SD = 21.2), the mean absolute FEV1 was 1.63 L (SD = 0.59). The patients' standard deviation (SD) was 7.6, their average age was 73.2 years, and 5 of them were female. When compared to patients without ILAs, patients with ILAs showed statistically, but not significantly, greater FEV1 and FEV1 percent predicted values, as well as lower mMRC dyspnea scale and CAT scores.

Table 1: Baseline characteristics of patients

Characteristics	Value
Age, years	73.2 (7.6)
BMI, (kg/m ² ; mean±sd)	24.1 (9.4)
Female; n(%)	5 (7.14%)
Smoking history (pack-years)	53.2 (29.6)
% FEV1 (mean±sd)	63.4 (21.2)
FEV1 (L)(mean±sd)	1.63 (0.59)
FVC (L)(mean±sd)	3.12 (0.79)
GOLD stage; n(%)	
1	17 (24.2%)
2	35 (50%)

3	15 (21.4%)
4	3 (4.28%)
CAT score (mean±sd)	6.2 (5.5)
mMRC dyspnea scale grade (mean±sd)	1.2 (0.8)
Death from any cause; n(%)	8 (11.42%)
Exacerbation history; n(%)	0.15 (0.40)

Patients without ILAs showed a range of airflow restriction severity from GOLD 1 to 4. Contrarily, the severity of the airflow limitation was distributed across GOLD 1 to 3 in patients with ILAs, with a small number of patients in each class.

Table 2: Before 1-to-3 propensity score matching, characteristics of the study participants with and without ILAs were compared.

Parameters	ILAs (+) (n=10)	ILAs (-) (n=60)	p-value
Age, years	73.9 (6.5)	72.6 (7.8)	0.178
BMI, (kg/m ² ; mean±sd)	24.5 (3.3)	23.5 (9.8)	0.723
Female; n(%)	1 (10)	6 (10)	1
Smoking history (pack-years)	61.4 (33.2)	53.8 (29.1)	0.166
% FEV1 (mean±sd)	67.9 (19.3)	62.3 (21.3)	0.176
FEV1 (L)(mean±sd)	1.76 (0.51)	1.63 (0.62)	0.297
FVC (L)(mean±sd)	3.12 (0.65)	3.18 (0.75)	0.895
GOLD stage; n(%)			
1	3 (30)	14 (23.3)	
2	5 (50)	30 (50)	
3	2 (20)	13 (21.67)	
4	0 (0)	3 (5)	
CAT score (mean±sd)	5.0 (4.3)	6.3 (5.4)	0.228
mMRC dyspnea scale grade (mean±sd)	1.1 (1.1)	1.1 (1.0)	0.166
Death from any cause; n(%)	1 (10)	7 (11.6)	0.758
Exacerbation history; n(%)	0.05 (0.11)	0.15 (0.38)	0.111

Table 3 displays the averages for the patients in both groups' FEV1, FEV % predicted, CAT scores, and mMRC dyspnea scale scores. Patients with ILAs demonstrated numerically, but not substantially, higher FEV1 and FEV1 percent predicted values as well as reduced mMRC dyspnea scale and CAT scores when compared to patients without ILAs.

Table 3: After 1-to-3 propensity score matching, characteristics of the study participants with and without ILAs were compared.

Parameters	ILAs (+) (n=10)	ILAs (-) (n=60)	p-value
Age, years	73.9 (6.5)	72.6 (7.8)	0.779
BMI, (kg/m ² ; mean±sd)	24.5 (3.3)	23.5 (9.8)	0.756
Female; n(%)	1 (10)	5 (8.3)	1
Smoking history (pack-years)	61.3 (33.4)	50.8 (29.3)	0.095
% FEV1 (mean±sd)	68.3 (19.3)	64.2 (21.8)	0.355
FEV1 (L)(mean±sd)	1.75 (0.51)	1.59 (0.58)	0.185
FVC (L)(mean±sd)	3.15 (0.65)	3.03 (0.67)	0.443
CAT score	4.8 (4.3)	6.5 (5.5)	0.182
mMRC dyspnea scale grade (mean±sd)	0.8 (0.8)	1.1 (1.0)	0.08
Death from any cause; n(%)	1 (10)	7 (11.6)	0.726
Exacerbation history; n(%)	0.05 (0.09)	0.24 (0.45)	0.042

Discussion

To evaluate interstitial lung disease patients' health-related quality of life, a well-validated, user-friendly instrument is required (ILD). A recently developed, brief, and easy-to-use questionnaire for COPD patients, the COPD Assessment Test (CAT), demonstrates good and valid measuring features. The efficacy of the CAT in individuals with ILD was examined in this study. The study concludes that the CAT is a brief, easy-to-complete questionnaire with reliable measuring qualities for evaluating individuals with ILD's health state [19,21].

Interstitial lung abnormalities brought on by smoking are distinct from particular types of fibrosing lung disease that may have poor prognoses. Although they are regarded as separate conditions, pulmonary fibrosis and chronic obstructive pulmonary disease with concomitant interstitial lung abnormalities may be on the same continuum. We set out to assess the clinical traits of patients with concomitant interstitial lung abnormalities and chronic obstructive pulmonary disease. The results show that interstitial lung abnormality lesions in people with pre-existing chronic obstructive pulmonary disease grow slowly. Additionally, the development of interstitial lung abnormalities had no discernible impact on the worsening of chronic obstructive pulmonary disease. The study hypothesizes that smoking-related interstitial fibrosis, as opposed to particular types of fibrosing lung disease linked with poor prognoses, may be responsible for post-chronic obstructive pulmonary disease interstitial lung abnormalities [20,22].

Radiographic interstitial lung abnormalities and emphysema are linked to cigarette smoking. It is unknown how much emphysema and decreased total lung capacity are related to interstitial lung abnormalities. The presence of COPD shows how interstitial lung abnormalities affects both emphysema and total lung capacity. Greater exposure to cigarette

smoke and smoking habits were both positively associated with interstitial lung abnormalities. Interstitial lung abnormalities in smokers were related to decreased total lung capacity and less emphysema. These abnormalities were seen on roughly 1 in 12 high-resolution computed tomographic (HRCT) scans [23].

An increasingly recognized discrete condition with different clinical, physiological, and radiological features is combined pulmonary fibrosis and emphysema (CPFE). The goal of the study was to pinpoint the physiological and radiographic indicators that can foretell death in CPFE. Patients with typical interstitial pneumonia (UIP) plus emphysema (CPFE group) and those with IPF alone were evaluated in terms of clinical features, pulmonary function, high-resolution computed tomography (HRCT), and therapy (IPF group). At diagnosis and during follow-up, the HRCT and Composite Physiologic Index (CPI) scores were evaluated. According to our study findings, patients with CPFE had distinctive clinical, physiological, and radiographic characteristics and were primarily male smokers. Compared to IPF, they had a worse prognosis. In these individuals, PAH and a 5-point increase in CPI score annually were predictive of mortality [24,25].

Conclusion

The study has concluded that ILA lesions in patients with COPD progressed slowly and that the growth of ILAs had no bearing on COPD flare-ups. The study further concludes that ILAs following COPD may involve interstitial fibrosis brought on by smoking, which is distinct from some types of fibrosing lung disease with bad prognoses. Airflow obstruction that persists over time and persistent respiratory symptoms are characteristics of the complex disorder known as a chronic obstructive pulmonary disease (COPD). Patients with COPD frequently experience emphysematous lung changes because of

the weakening of the alveolar wall brought on by toxic inhalation.

References

- Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. *Am J Respir Crit Care Med.* 2017; 195: 557–582.
- Cottin V, Nunes H, Brillet PY, Delaval P, Devouassoux G, Tillie-Leblond I, et al. Combined pulmonary fibrosis and emphysema: a distinct underrecognised entity. *Eur Respir J.* 2005; 26: 586–593.
- Cottin V, Cordier JF. Combined pulmonary fibrosis and emphysema in connective tissue disease. *Curr Opin Pulm Med.* 2012; 18: 418–427.
- Jankowich MD, Rounds SIS. Combined pulmonary fibrosis and emphysema syndrome: a review. *Chest.* 2012; 141: 222–231.
- Kobayashi S, Hanagama M, Yamanda S, Ishida M, Yanai M. Inflammatory biomarkers in asthma-COPD overlap syndrome. *Int J Chron Obstruct Pulmon Dis.* 2016; 11: 2117–2123.
- The Japanese Respiratory Society. Guidelines for the diagnosis and treatment of COPD (chronic obstructive pulmonary disease) 4th ed. Medical Review Company, Ltd, Tokyo, 2013.
- Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of COPD [updated 2017]. <http://www.goldcopd.org/>. Accessed 17 November 2016.
- Global Initiative for Chronic Obstructive Lung Disease . Global Initiative for Chronic Obstructive Lung Disease; 2021. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease, 2021 report [Internet] [cited 2020 Dec 23]. Available from: <https://goldcopd.org/wp-content/uploa>ds/2020/11/GOLD-REPORT-2021-v1.1-25Nov20_WMV.pdf.
- Broaddus VC, Mason RJ, Ernst JD, King TE, Jr, Lazarus SC, Murray JF, et al. Philadelphia: Elsevier; Murray and Nadel's textbook of respiratory medicine. 6th ed. 2016.
- Hage R, Gautschi F, Steinack C, Schuurmans MM. Combined pulmonary fibrosis and emphysema (CPFE) clinical features and management. *Int J Chron Obstruct Pulmon Dis.* 2021;16:167–77
- Huie TJ, Solomon JJ. Emphysema and pulmonary fibrosis: coincidence or conspiracy? *Respirology.* 2013;18:116 3–4.
- Selman M, Martinez FJ, Pardo A. Why does an aging smoker's lung develop idiopathic pulmonary fibrosis and not chronic obstructive pulmonary disease? *Am J Respir Crit Care Med.* 2019; 199:279–85.
- Alsumrain M, De Giacomo F, Nasim F, Koo CW, Bartholmai BJ, Levin DL, et al. Combined pulmonary fibrosis and emphysema as a clinicoradiologic entity: characterization of presenting lung fibrosis and implications for survival. *Respir Med.* 2019;146:106–12.
- Cottin V, Nunes H, Brillet PY, Delaval P, Devouassoux G, Tillie-Leblond I, et al. Combined pulmonary fibrosis and emphysema: a distinct underrecognised entity. *Eur Respir J.* 2005;26:586–93.
- Cottin V, Nunes H, Mouthon L, Gamondes D, Lazor R, Hachulla E, et al. Combined pulmonary fibrosis and emphysema syndrome in connective tissue disease. *Arthritis Rheum.* 2011 ;63:295–304.
- Koo BS, Park KY, Lee HJ, Kim HJ, Ahn HS, Yim SY, et al. Effect of combined pulmonary fibrosis and emphysema on patients with connective tissue diseases and systemic sclerosis: a systematic review and meta-analysis. *Arthritis Res Ther.* 2021; 23:100.

17. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med.* 2017 Sep;5(9):691-706.
18. Stockley RA. Neutrophils and protease/antiprotease imbalance. *Am J Respir Crit Care Med.* 1999 Nov;160(5 Pt 2):S49-52.
19. Mattos WL, Signori LG, Borges FK, Bergamin JA, Machado V. Accuracy of clinical examination findings in the diagnosis of COPD. *J Bras Pneumol.* 2009 May;35(5):404-8
20. Parker CM, Voduc N, Aaron SD, Webb KA, O'Donnell DE. Physiological changes during symptom recovery from moderate exacerbations of COPD. *Eur Respir J.* 2005 Sep; 26 (3):420-8.
21. Nagata K., Tomii K., Otsuka K., Tachikawa R., Otsuka K., Takeshita J., Tanaka K., Matsumoto T., & Monden K. Evaluation of the chronic obstructive pulmonary disease assessment test for measurement of health-related quality of life in patients with interstitial lung disease. *Respirology*, 2012;17(3): 506–512.
22. Washko G. R., Hunninghake G. M., Fernandez I. E., Nishino M., Okajima Y., Yamashiro T., Ross J. C., Estépar R. S. J., Lynch D. A., Brehm J. M., Andriole K. P., Diaz A. A., Khorasani R., D'Aco K., Sciurba F. C., Silverman, E. K., Hatabu H., & Rosas I. O. Lung Volumes and Emphysema in Smokers with Interstitial Lung Abnormalities. *New England Journal of Medicine*, 2011; 364(10): 897–906.
23. Ono M., Kobayashi S., Hanagama M., Ishida M., Sato H., Makiguchi T., & Yanai M. Clinical characteristics of Japanese patients with chronic obstructive pulmonary disease (COPD) with comorbid interstitial lung abnormalities: A cross-sectional study. *PLOS ONE*, 2020;15(11): e0239764.
24. Zhang L., Zhang C., Dong F., Song Q., Chi F., Liu L., Wang Y., & Che C. Combined pulmonary fibrosis and emphysema: a retrospective analysis of clinical characteristics, treatment and prognosis. *BMC Pulmonary Medicine*, 2016;16(1).
25. Roy D. S., Alqifari D. S. F., & Walia C. Cyclopedic analysis of medication-related osteonecrosis of the jaws in patients with diabetes mellitus. *Journal of Medical Research and Health Sciences.* 2022;5(8): 2153–2164.