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Original research article

Lung carbon monoxide diffusivity in patients with chronic obstructive pulmonary disease and interstitial lung disease: An observational study

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Abstract

Background and objective: The purpose of this study was to evaluate the severity of COPD and ILD by examining the pulmonary diffusion capacity of patients with these disorders. The purpose of this research is to establish if decreased D_{LCO} is related to an increase in morbidity. The goal of early diagnosis and effective treatment for chronic obstructive pulmonary disease and interstitial lung disease is to enhance patients' quality of life. The goal of this study is to evaluate the relationship between smoking and D_{LCO} in COPD and ILD.

Method: From January 2020 to November 2021, the Department of Pulmonary Medicine, Kakatiya Medical College, Warangal, Telangana, India, undertook a cross-sectional prospective observational study. 50 patients with chronic respiratory disorders such COPD and interstitial lung diseases met the inclusion criteria. Before the study, ethical committee approval was obtained. In their original language, subjects gave informed, written consent. Blood, CXR, HRCT, spirometry, D_{LCO}, and 6MWT were performed after a complete history, general, and systemic examination.

Result: COPD patients covered 365.45±79.26m and ILD patients 353.53±48.08m on the 6MWT. COPD patients had 95.64±1.87 pre-6MWT SpO2 and 93.18±2.83 post-6MWT. ILD patients had 96.18±1.88 pre-6MWT SpO2 and 93.12±2.78 post-6MWT. For COPD patients with 6MWT distances of 400-700 mtrs, mean DLCO levels were 71.75±21.59 and 51.10±14.41, respectively. For patients with 6MWT distances of 400-700 mtrs and <400 mtrs, mean DLCO levels were 49.317±10.90 and 62.40±9.76, respectively, in group ILD.

Conclusion: Connective tissue illnesses and COPD may benefit from early lung disease detection and treatment. Pack years lower smokers' D_{LCO}, indicating lung alveolar capillary membrane degradation. Stop smoking to preserve lung function. Since the research group has fewer anaemic individuals and normal Hb, anticipated and corrected D_{LCO} levels are similar.

Keywords: Carbon monoxide, COPD, interstitial lung disease

Introduction

One of the top three killers around the globe, 90% of those who succumb to chronic obstructive pulmonary disease (COPD) live in poor and middle-income nations (LMICs). Continued exposure to COPD risk factors and an aging population are expected to raise the global burden of COPD over the coming decades. Over 200 million individuals worldwide suffer from COPD, with 65 million dealing with the disease's moderate to severe forms [1, 2].

Diffuse lung disease (DLD) is a catch-all term for a wide variety of conditions that affect the pulmonary parenchyma and make it difficult for the lungs to exchange gas. It is a major health problem around the world, especially in children and the elderly. The broad meaning of this phrase reflects the complexity of the underlying pathophysiology, which typically involves severe alterations to the alveolar and airway architecture as well as alterations to the interstitial compartment. While "interstitial lung disease" (ILD) has been the standard nomenclature for these conditions, "Diffuse Parenchymal Lung Disease" is now the preferable term [3, 4].

The presence of airflow obstruction has been a primary diagnostic criterion, making spirometry a cornerstone of diagnosis. Recently, in order to accomplish a holistic evaluation, spirometry has been supplemented with assessments of symptoms, influence on health status, CT imaging for quantitative assessment of emphysema, and risk of exacerbations for those with COPD. Measurement of the lung's carbon monoxide diffusing capacity is a non-invasive and readily available diagnostic procedure that is not yet incorporated into standard COPD assessment models (D_{LCO}). Providing a quantitative measure of gas transfer in the lungs, the diffusing capacity for carbon monoxide is a popular and therapeutically

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important test. One of the earliest indicators of illness development is a decline in D_{LCO}. Patients with chronic lung disease are at a greater risk of dying from their condition if their D_{LCO} values are low (eg: COPD, ILD) [4, 5].

In their early stages, most of these diseases are both preventable and treatable. In addition to health education and public awareness, this situation calls for early diagnosis and the establishment of suitable management regimens. There is a pressing need for a test that can detect and discriminate between structural and functional lung impairment at an early stage. The purpose of this research was to determine whether or not decreased D_{LCO} was associated with greater disease severity and morbidity in individuals with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD). Because it is a non-invasive test, early identification and treatment of COPD and ILD can enhance patients' quality of life [6, 7, 8].

Material and Methods

The current study was a prospective cross-sectional observational study that was carried out in the Department of Pulmonary Medicine, Kakatiya Medical College, Warangal, Telangana, India, between January 2020 to November 2021. In total, fifty people who fulfilled the requirements for participation in the study were selected to have chronic respiratory disorders such as COPD and interstitial lung diseases. Before beginning the trial, approval was obtained from the ethical committee. A fully-informed signed consent was gained from the subjects after the study as well as the methods involved were explained to them in their local language. Subjects were examined with blood tests, a CXR, HRCT, spirometry, DLCO, and a 6MWT after a comprehensive history, general examination, and systemic examination were performed on them.

Inclusion criteria

1. Patients diagnosed with COPD and ILD
2. Age of patients more than 18 years
3. Patients who are hospitalized and outpatients suffering from COPD and ILD
4. Patients who were able to hold their breath for eight to ten seconds were moved to the DLCO waiting list.

Exclusion criteria

1. A younger age than 18 years old
2. Patients who are unable to complete the PFT.
3. Patients who are currently suffering from active pulmonary tuberculosis and have a history of a recent myocardial infarction (less than one month).

Results

A prospective study to evaluate the role of diffusion capacity of carbon monoxide (D_{LCO}) in assessing subjects with Chronic Obstructive Pulmonary Disease (COPD) and Interstitial Lung Disease (ILD) was carried.

Out of 50 subjects, 33 were COPD patients and 17 were ILD patients. Among COPD patients, 27 were diagnosed as emphysema and 6 chronic bronchitis cases.

Table 1: Demographic profile of patients

Demographics		**Total Number (%)**
Sex	Female	13 (26%)
	Male	37 (74%)
Age Groups (in years)	20-40	5 (10%)
	40-60	24 (48%)
	60-80	20 (40%)
	>80	1 (2%)
	Mean±SD	56.78±12.97
	Min-Max	30-82
Residence	Rural	32 (64%)
	Urban	18 (36%)
Education	Illiterate	25 (50%)
	Primary	11 (22%)
	Secondary	8 (16%)
	Undergraduate	4 (8%)
	Postgraduate	2 (4%)

In this study we included 50 subjects out of which 74% (n=37) were males,26% (n=13)were females. Mean Age of the study population was 56.78±12.97 years, among which 48% (n=24) were in between 40

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to 60 years, followed by 40% (n=20) 60 to 80 years age group, 10%(n=5) were 20-40 years age group and 2%(n=1) is above 80 years.
64% (n=32) of the subjects were from rural background and 36%(n=18) were from urban background. Since the medical college is in a rural setting, many subjects were from rural background and few completed higher studies.
50% (n=25) in the study were illiterates, and 22% (n=11) took primary education,16%(n=8) took secondary education, whereas 4 subjects (8%) completed under graduation and 4%(n=2) subjects were postgraduates.

Table 2: Distribution of patients according to occupation

Occupation	%	N
Farmers	44%	22
Laborers	20%	10
Semiskilled workers	14%	7
Skilled workers	6%	3
Professionals	4%	2
House wives	12%	6
Total	100%	50

Out of 50 subjects 44% (n=22) were farmers, 20% (n=22) were laborers, 14% (n=7) were semiskilled workers, 6% (n=3) were skilled workers, 4% (n=4) were professionals and 12% (n=6) were housewives.

Table 3: Distribution of patients according to socioeconomic status

SES	Total
L	16 (32%)
LM	22 (44%)
M	10 (20%)
UM	1 (2%)
U	1 (2%)
Total	50 (100%)

In the study population, when socio-economic status was looked into, 22(44%) were lower middle class, 16(32%) were lower class, 10(20%) middle class, 1(2%) is upper middle class and 1(2%) belong to upper class.

Table 4: Distribution of patients according to smoking

Smoking	Total	COPD		ILD	
		Frequency	%	Frequency	%
Y (Yes)	29 (58%)	26	79%	3	18%
N (No)	14 (28%)	2	6%	12	71%
FS (Former Smokers)	7 (14%)	5	15%	2	12%
Total	50 (100%)	33	100%	17	100%
Mean Pack Years	34.53±8.67	36.39±7.7		23±4.47	

For COPD patients, it was observed that 79% of the patients had the habit of smoking while 6% of the patients didn't have the habit of smoking and 15% were former smokers. It was observed that mean pack years was 36.39±7.7.
For ILD patients, it was observed that 18% of the patients had the habit of smoking while 71% of the patients didn't have the habit of smoking and 12% were former smokers. It was observed that mean pack years was 23±4.47.

Table 5: Mean DLCO according to smoking in two groups

Smoking	COPD		ILD	
	n	Mean±SD (DLCO)	n	Mean±SD (DLCO)
No	2	75.00±22.633	12	55.83±10.75
Yes	31	57.55±19.54	5	46.40±13.43

It was observed that for the group COPD, mean DLCO level for non-smokers was 75.00±22.633 while for smokers mean DLCO level was 57.55±19.54. For the group ILD, mean DLCO level for non-smokers was 55.83±10.75 while for smokers mean DLCO level was 46.40±13.43. Therefore, in smokers, the diffusion capacity of lung for carbon monoxide decreased compared to non-smokers.

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Table 6: Mean DLCO according to pack years in two groups

Pack Years	COPD		ILD	
	n	Mean±SD	n	Mean±SD
20-30 yrs	8	72.88±25.17	5	46.40±13.43
30-40 yrs	15	56.07±15.77		-
40-50 yrs	8	45.00±7.27		-

It was observed that for the group COPD, mean DLCO level for 20-30 pack yrs group was 72.88±25.17, while for 30-40 pack yrs was 56.07±15.77 and for 40-50 pack yrs was 45.00±7.27. For the group ILD, mean DLCO level for the 20-30 pack yrs was 46.40±13.43. The above table shows that, among COPD patients, as pack years of smoking increases the diffusion capacity of lung decreases.

Table 7: Distribution of patients according to body mass index

BMI	Total Number (%)
Underweight	15 (30%)
Normal	24 (48%)
Overweight	7 (14%)
Obesity	4 (8%)
Total	50 (100%)
Mean±SD	21.43±4.80

As a part of the physical examination height and weight of each of the subjects were noted and BMI calculated. Majority of subjects had a BMI between 18.5-25. Out of 50 subjects 48%(n=24) had a BMI between 18.5-24,14%(n=7) had BMI between 25-29.9,30%(n=15) had BMI <18.5, 8%(n=4) had BMI >30.

Symptomatology

The predominant symptom among the study population was cough observed in 96% (n=48), 50%(n=25) had sputum production, 78%(n=39) had dyspnea of varying severity, 26%(n=13) had wheeze, 18%(n=9) had chest pain, and 6%(n=3) had fever, 12%(n=6) had joint pains, and 4%(n=2) had dermatological symptoms.

Table 8: Symptomatology in the study subjects

Symptoms	Percentage(n)
Cough	96%(n=48)
Sputum	50%(n=25)
Dyspnea	78%(n=39)
Wheeze	26%(n=13)
Chest pain	18%(n=9)
Fever	6%(n=3)
Joint Pains	12%(n=6)
Dermatological symptoms	4%(n=2)

In the study population, 78% (n=39) presented with dyspnea of varying severity. Of them 4 had grade 0 dyspnea, 15 had grade1 dyspnea, 14 had grade 2 dypnea, 6 had grade 3 dypnea, according to MMRC dyspnea grading. In our study no patient had grade 4 dypnea. The above graph depicts the distribution of patients according to various grades of dyspnea in COPD and ILD patients.

Table 9: Hemoglobin (Hb%) in the study subjects

	Hb%	
	Mean±SD	Min-Max
Total pts	12.15±1.70	9.6 – 16.0
COPD	12.297±1.74	9.6-16
ILD	11.865±1.63	9.6-14.5

The mean Hb of study population was 12.15±1.70. For COPD patients, it was observed that mean HB was 12.297±1.74 with a minimum of 9.6 and a maximum of 16. For ILD patients, it was observed that mean HB was 11.865±1.63 with a minimum of 9.6 and a maximum of 14.5.

Table 10: Mean DLCO predicted and mean DLCO corrected

	Mean DLCO Predicted	Mean DLCO corrected (for Hb)	P value

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Total pts (n=50)	56.72±17.60	52.653±16.5	>0.05
COPD pts (n=33)	58.60±19.79	54.29±18.29	>0.05
ILD pts (n=17)	53.06±12.01	49.48±12.18	>0.05

Hb corrected DLCO for study population was calculated by using formula: Hb corrected DLCO = predicted DLCO([Age-Sex-Factor+Hb g/dL]/[1.7 Hb]). For males 15 years old or older, the Age-Sex-Factor is 10.22. For females of any age and children less than 15 years old, the Age-Sex-Factor is 9.38. The above table shows, there is no significant difference between predicted DLCO values and corrected DLCO (for Hb) values. Since there are less anemic patients in the study and mean Hb of study population is 12.15, hemoglobin levels may not be an affecting factor for DLCO results.

HRCT Chest

Among 33 COPD patients, 27 were emphysema cases and 6 were bronchitis cases. In emphysema patients, upper lobe emphysematous changes was predominant finding.

Table 11: CT findings in COPD emphysema patients

CT Finding in Emphysema patients	Percentage(n)
Normal	18.5(5)
Upper lobe Emphysema	22.2(6)
Lower lobe Emphysema	7.4(2)
Pan lobular Emphysema	7.4(2)
Centrilobular Emphysema/Nodules	7.4(2)
Paraseptal Emphysema	11.1(3)
Hyperinflated areas	11.1(3)
Air trapping	14.8(4)
Subpleural blebs/cysts/bullae	18.5(5)

Out of 6 bronchitis cases, 4 showing normal CT finding, 2 with positive findings (bronchial wall thickening). In 17 ILD patients, 1 is showing normal CT findings, and 16 with positive findings.

Table 12: CT findings in ILD patients

CT Finding in ILD patients	Percentage(n)
Normal	5.8(1)
Ground glass opacities	35.2(6)
Reticulonodular/reticular	52.9(9)
Septal thickening	35.2(6)
Septal subpleural line	35.2(6)
Fibrosis	23.5(4)
Honey combing	17.6(3)
Traction bronchiectasis	23.5(4)
Irregular pleural margin	5.8(1)
Peribronchial fibrosis	11.7(2)
Bilateral hilar lymphadenopathy	5.8(1)

In patients with interstitial lung disease major CT abnormality was reticular or reticulonodular shadows (n=9). In the ILD group, there were 3 already diagnosed rheumatoid arthritis related ILD patients, 1 SLE patient, 1 sarcoidosis,1 HSP, 1 systemic sclerosis and 7 idiopathic ILD patients present.

Table 13: Mean DLCO and CT chest in study subjects

CT Chest	COPD		ILD	
	n	Mean±SD (DLCO)	N	Mean±SD (DLCO)
Normal	9	70.65±18.07	1	65.35±0.00
(+ve) Findings	24	51.83±14.07	16	51.62±10.79

It was observed that for the group COPD, mean D_{LCO} for normal CT subjects was 70.65±18.07, while for the (+ve) findings was 51.83±14.07. For the group ILD, meanD_{LCO} for normal CT patients was 65.35±0.00 while for the (+ve) finding was 51.62±10.79. Therefore mean D_{LCO} values were mildly decreased in patients with normal findings in CT chest.

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Spirometry

Spirometry was performed for all the subjects. Among ILD patients 16 showed restrictive pattern and 1 with normal spirometry values. The one with normal spirometry has NSIP pattern in HRCT chest with connective tissue disorder being etiological factor. In COPD patients 32 had obstructive pattern and 1 patient had shown normal spirometry study.

Table 14: Spirometryresults in study subjects

Spirometry	COPD			ILD		
	Mean±SD	Median (IQR)	Min-Max	Mean±SD	Median (IQR)	Min-Max
FEV1/FVC	53.52±6.71	54 (47.5-58)	39-65	88.18±6.45	88 (84-94.5)	76-98
FEV1 (%)	55.42±11.56	56 (47.5-60.5)	39-83	68.65±7.95	67 (62-76.5)	56-81
FVC	74.15±8.61	72 (66.5-80.5)	61-93	55.76±9.74	59 (49-63)	38-70
FEF 25 - 75%	55.33±12.94	59 (43-65.5)	26-76	56.24±16.38	59 (40-72.5)	33-75

The graph above shows the mean of the various spirometry parameters for the two groups of COPD and ILD.

For COPD patients it was observed that mean FEV1/FVC was 53.52±6.71, mean FEV1 (%) was 55.42±11.56, while mean FVC was 74.15±8.61.

For ILD patients, it was observed that mean FEV1/FVC was 88.18±6.45, mean FEV1 (%) was 68.65±7.95, while mean FVC was 55.76±9.74.

Obstruction grading of COPD patients (based on FEV_1)

Grading of obstruction was based on FEV1 (as per GOLD criteria)[87]

Mild: FEV1%predicted ≥80

Moderate: FEV1%predicted 50-79

Severe: FEV1%predicted ≤59.

Table15: Obstruction severity grading in COPD patients

Obst Grading	COPD	
	Frequency	%
Normal	1	3%
Mild	2	6%
Moderate	19	58%
Severe	11	33%
Total	33	100%

The table above shows the distribution of COPD patients on the basis of obstruction grading. It was observed that 6% of the patients had mild obstruction, while 58% of the patients had moderate and 33% had severe obstruction. 1(3%) patient has normal spirometry.

Restriction grading of ILD patients (based on FVC)[68]

Grading of restrictionwas based on FVC

Normal: FVC% predicted ≥80

Mild: FVC%predicted 60-79

Moderate: FVC%predicted 51-59

Severe: FVC%predicted ≤50.

Table 16: Restriction grading in ILD patients

Rest. Grading	ILD	
	Frequency	%
Normal	1	6%
Mild	6	35%
Moderate	6	35%
Severe	4	24%
Total	17	100%

The table and graph above shows the distribution of ILD patients on the basis of restriction grading. It was observed that 35% each had mild and moderate restriction. While 24% had severe restriction and 1(6%) patient has normal spirometry study.

DLCO

For COPD patients, it was observed that mean DLCO% predicted was 58.61±19.8 with a minimum of 36 and a maximum of 121. Mean DLCO correction (for Hb) was 54.287±18.3 with a minimum of 33.76 and

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a maximum of 106.3 while mean VA was 78.48±11.18. Mean KCO was 66.91±13.27. Mean TLC was 131.03±13.54.

For ILD patients, it was observed that mean DLCO% predicted was 53.06±12.01 with a minimum of 36 and a maximum of 76. Mean DLCO correction (for Hb) was 49.4812±12.18 with a minimum of 30.27 and a maximum of 70 while mean VA was 61.65±9.99. Mean KCO was 68.94±13.25. Mean TLC was 73.24±11.91.

Table 17: DLCO results in study population

DLCO	COPD			ILD		
	Mean±SD	Median (IQR)	Min-Max	Mean±SD	Median (IQR)	Min-Max
DLCO% predicted	58.61±19.8	56 (43-65.5)	36-121	53.06±12.01	54 (43-63.5)	36-76
DLCO correction (for Hb)	54.287±18.3	51.99 (37.71-63.32)	33.76-106.3	49.4812±12.18	47.86 (39.045-60.87)	30.27-70
VA	78.48±11.18	78 (71.5-86)	58-102	61.65±9.99	65 (51.5-69.5)	48-78
KCO	66.91±13.27	68 (52.5-78)	43-84	68.94±13.25	71 (57.5-81.5)	49-90
TLC	131.03±13.54	131 (121-142)	104-157	73.24±11.91	76 (60-83.5)	56-91

Grading of DLCO: Based on% predicted DLCO (corrected) values.
Normal: 75-140%
Mild: >60 but less than lower limit of normal (LLN)
Moderate: 40- 60%
Severe: <40%.

Table 18: DLCO severity grading

Grading of DLCO	COPD		ILD	
	Frequency	%	Frequency	%
Normal	6	18%	0	0%
Mild	3	9%	4	24%
Moderate	14	42%	8	47%
Severe	10	30%	5	29%
Total	33	100%	17	100%

The table above shows the distribution of patients under the study on the basis of DLCO grading. Among COPD patients with chronic bronchitis (n=6), showed normal DLCO values with obstructive pattern on spirometry.

For COPD patients, it was observed that 9% of the patients had mild DLCO while 42% of the patients had moderate DLCO, 18% had normal DLCO and 30% had severe DLCO.

For, ILD patients, it was observed that 24% of the patients had mild DLCO while 47% of the patients had moderate DLCO and 29% had severe DLCO.

In a COPD patient with normal values on spirometry, showed decrease in DLCO with HRCT chest showing hyperinflated areas.

Table19: Mean DLCO according to division of cases by spirometry (fev1) in COPD

Division of cases by spirometry (FEV1)	COPD		p value
	n	Mean DLCO±SD	
Normal	1	56±0.00	<0.001
Mild	2	85.71±29.12	
Moderate	19	58.50±15.28	
Severe	11	41.13±12.02	

The table above shows the mean DLCO level for COPD patients across the three division of cases by spirometry (FEV1). It was observed that mean DLCO for mild division was 85.71±29.12 while for moderate division was 58.50±15.28 and for severe mean DLCO was 41.13±12.02. One COPD patient with normal spirometry has DLCO value of 56.

Further it was observed that there was a significant difference in mean DLCO level when compared between the three Division of cases by spirometry (FEV1) (p value <0.001).

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Table 20: Mean DLCO according to division of cases by spirometry (FVC) in ILD

Division of cases by spirometry (FVC)	ILD		p value
	n	Mean DLCO±SD	
Normal	1	65.22±0.00	<0.001
Mild	6	56.02±11.53	
Moderate	6	49.56±8.81	
Severe	4	35.61±3.99	

The table above show the mean DLCO level for ILD patients across the three Division of cases by spirometry (FVC). It was observed that mean DLCO for mild division was 56.02±11.53 while for moderate division was 49.56±8.81 and for severe division mean DLCO was 35.61±3.99. One ILD patient with normal spirometry has DLCO value of 65.22.
It was observed that there was a significant difference in mean DLCO level when compared between the three Division of cases by spirometry (FVC) (p value <0.001).
The two patients in the study with normal spirometry values showed mild decrease in DLCO.

6MWT

Table 21: 6 minute walk test results in study subjects

6 minute walk test	COPD		ILD	
	Mean±SD	Min-Max	Mean±SD	Min-Max
Distance (metres)	365.45±79.26	220-500	353.53±48.08	270-420
pre 6MWT spo2	95.64±1.87	91-99	96.18±1.88	93-98
post 6MWT spo2	93.18±2.83	88-98	93.12±2.78	88-97

The mean 6MWT distance covered in COPD patients was 365.45±79.26m and for ILD patients 353.53±48.08m.
For COPD patients, pre 6MWT SpO2 was 95.64±1.87 and post 6MWT SpO2 was93.18±2.83.For ILD patients, pre 6MWT SpO2 was 96.18±1.88 and post 6MWT SpO2 was 93.12±2.78.
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Table 22: Mean DLCO and 6 MWT distance (metres)

6 MWT (metres)	COPD		ILD		P value
	n	Mean±SD	n	Mean±SD	
<400 m	21	51.10±14.41	12	49.317±10.90	>0.05
Normal (400-700m)	12	71.75±21.59	5	62.40±9.76	>0.05

It was observed that for the group COPD, mean DLCO level for patients with 6MWT distance of <400 mtr was 51.10±14.41 while for patients with normal 6MWT distance of 400-700 mtrsmean DLCO level was 71.75±21.59.
For the group ILD, mean DLCO level for patients with 6MWT distance of <400 mtr was 49.317±10.90 while for patients with 6MWT distance of 400-700 mtrsmean DLCO level was 62.40±9.76.
In present study, it was observed that, there is no statistically much difference between patients 6 MWT distance and D_{LCO} values with p value > 0.05

Discussion
Tracer gas diffusion capacity is measured by its ability to pass the alveolar-capillary membrane in inspired air and bind to hemoglobin in the red blood cells within the capillary. Two separate processes, membrane conductance (Dm) and the chemical interaction between carbon monoxide and hemoglobin, make up the entirety of the process of CO absorption. Diffusion across the alveolar-capillary interface is reflected in the membrane conductance. After CO2 has been transferred over the membrane, the uptake rate is affected by the response rate and the blood volume in the pulmonary capillaries. When performed properly, there are no known risks or complications [9, 10].
There are six stages in the transport of environmental carbon monoxide into the bloodstream via the pulmonary capillaries.

There are a few ways that carbon monoxide can be introduced into the lungs
1. Through a steady stream of gas;
2. Carbon monoxide diffusion and mixing in the alveolar ducts, air sacs, and alveoli;
3. Carbon monoxide transfer across the gas-liquid interface of the alveolar membrane;
4. Carbon monoxide diffusion and mixing in the lung parenchyma and alveolar capillary plasma;
5. Diffusion across the red-cell membrane and within the interior of the red blood cell; 6) chemical reaction with constituents of blood Hb [10, 11].

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Reduced lung volume, tobacco use, Hb alterations, and high altitude are all contributors to this phenomenon. Age, sex, height (and maybe ethnicity), body position, PIO2, and exercise also affect DLCO. Total lung capacity is the sweet spot for diffusing capacity because of this relationship. For this reason, measuring alveolar volume concurrently has been the norm. As a result, DLCO can be seen as a global indicator of the health of the air-blood interface. If the structure or function of this interface is disrupted in any way, the diffusing capacity will change, and this change can be measured to aid in the early diagnosis of respiratory disease. When interstitial fibrosis is very widespread or when the pulmonary vasculature is weakened by vascular blockage or nonperfusion, the values for diffusing capacity will be lower. As a result of these restrictions at the interface, diffusing capacity is altered. Once the parenchyma and interstitium interface are involved, the diffusing capacity will change well before the spirometry or lung volume measurements become aberrant. Diffuse parenchymal/interstitial lung disorders and idiopathic pulmonary fibrosis are two examples of conditions that illustrate this point. Therefore, decreased diffusing capacity shows desaturation even in the presence of normal spirometry or lung sizes [11, 12].

Multiple clinical situations call for determining the lung's ability to diffuse carbon monoxide. In smokers with airway obstruction, the DLCO is a great indicator of the extent of anatomic emphysema.

Restrictive lung disease, characterized by decreased total lung capacity and vital capacity, can be diagnosed with the aid of DLCO. This might be useful in distinguishing between an intrapulmonary and an extrapulmonary cause of limitation.

Mild (early or preclinical) interstitial lung disease can also be detected through DLCO testing in high-risk patients with conditions like Sarcoidosis, hypersensitivity pneumonitis, chest irradiation and cancer chemotherapy, rheumatic diseases like systemic sclerosis, and pulmonary toxicity-inducing drugs like amiodarone [12, 13].

In addition to determining whether or not a patient needs oxygen therapy, measuring DLCO may be necessary before lung resection surgery (lung volume reduction surgery), in disability evaluation (a low DLCO below 40% predicted may qualify a patient for total disability), and in assessing whether or not a patient has a disability.

When exercising, oxygen desaturation is most reliably predicted by a DLCO that is low (50% of expected). In individuals presenting with dyspnea on exertion, a DLCO test can be advised as a screening test; however, a normal DLCO does not rule out desaturation on exercise [13, 14].

Clinically, changes in diffusing capacity can occur when either the surface area of gas exchange or the pulmonary vascular bed is impacted. Illnesses such as emphysema, diffuse parenchymal lung disorders, and pulmonary vascular diseases typically exhibit aberrant values of diffusing capacity at an early stage in the disease's progression.

Diseases affecting the airways, such as chronic bronchitis, asthma, and non-cystic fibrosis bronchiectasis, do not significantly change the lung's diffusing capacity. However, conditions like acute diffuse alveolar hemorrhage will boost the body's ability to disperse oxygen. The examination of this disorder's diffusing capacity was left out of the current investigation.

Age, sex, and height are highlighted as factors that affect a person's ability to spread out an impact. It is a measure of the pulmonary membrane's effective surface area and is highly correlated with FRC (FRC). FRC varies with both height and sex. Women of same age and height record poorer diffusing capacities due to lower functional residual capacities [15, 16].

The Current Study: This research was conducted on 50 patients. Thirty-three of the 50 participants had COPD, and 17 had ILD. There were 27 emphysema patients and 6 chronic bronchitis patients among the COPD group.

Participants' ages have to be 18 or older to be included in the analysis. About 48% of the participants in the study were in the middle-aged range (40-60 years old). Our sample cohort had a mean age of 56.78+12.97 years old, and 74% (N=37) were men and 26% (N=13) were women.

The following criteria were not changed to correlate with the projected values of the Indian population because the study population is chosen from people with chronic respiratory disease in order to determine the level of anomalies in diffusing abilities. We performed DLCO and DLCO/VA measurements in accordance with accepted practices. The ability to diffuse is rarely researched, and there are only a few of studies that have done so in Indian participants [16, 17].

Sex

The majority of the participants in this study were male (74%), while only 26% were female. Many of the research listed below primarily involved male participants, while others had female participants. Aparna Balasubramanian *et al.* and Weinreich UM *et al.* found that men were overrepresented among those with COPD in their respective study populations. This discovery lends credence to the results of the current investigation.

Researchers Nermine M.Riad *et al.* found that men were more likely to have ILD than women. This result corroborate the findings of the current study. The majority of Rajkumar *et al* ILD.'s study

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participants were female. This result contradicts what we've found in our current investigation. The majority of people in our study had a body mass index (BMI) between 20 and 30, and the average BMI was 21.43+4.80. Fifteen (30%) of the participants were considered to be underweight, whereas only four (8%) were considered to be obese.
Aparna Balasubramanian *et al*., Weinreich UM *et al*., Diaz AA *et al*., Sahin H *et al*., and others all found that men were overrepresented in their study populations. This discovery lends credence to the results of the current investigation [18, 19].

Clinical Presentation: Cough was the most common symptom, occurring in 48/48 (96%) of the patients in this study. Another major symptom was dyspnea, which was present in 39 of 50 patients (78 percent).
Similar symptoms, such as cough and shortness of breath, have been reported in previous studies on COPD and ILD by Rajkumar *et al*. and Anton xaubet*et al*. Among the 50 participants, 33 had COPD and 17 had ILD. Four patients had idiopathic pulmonary fibrosis (23.5% of ILD cases) and six had non-specific interstitial pneumonia (35.2%). Six of the COPD patients had bronchitis (18.2%) and the remaining 27 had emphysema (81.8%).
The average hemoglobin level is between 9.6 and 16 grams per cent. It is widely known that only anemic levels of hemoglobin are correlated negatively with DLCO when DLCO is adjusted according to the hemoglobin level. Standardization recommendations from the American Thoracic Society (ATS) and the European Respiratory Society (ERS) recommend using the equation proposed by Cotes and coworkers to correct DLCO for Hb concentration, so we did so in our study.
Patients with COPD had a mean DLCO% predicted of 58.61+19.8 in the current study. For Hb, the average DLCO correction was 54.287+18.3. Results showed that the average projected DLCO for patients with ILD was 53.06+12.01. The average value of the DLCO adjustment (for Hb) was 49.4812+12.18. When comparing projected DLCO values to corrected DLCO (for Hb) readings, there is no statistically significant difference. Because of the very small number of anemic participants and the relatively normal mean Hb of the study sample, it is possible that hemoglobin levels will not be a significant confounder in DLCO analyses.
Weinreich UM *et al*. found a mean Hb of 8.4 in their research. This result contradicts the results of the current study. Hb averaged 13.9 in Thomas *et al* study.'s This discovery lends credence to the results of the current investigation [20, 21].
Regarding smoking, 29 of the 50 participants (58%) in this study had either COPD or ILD, while 14 (28%) were never smokers and 7 (14%) were ex-smokers. The results of the diffusing abilities of these patients were impacted by the factor of smoking, and the results represent the underlying condition that caused the interference. It has been found that smokers have a lower value of diffusing capacity for the single-breath DLCO.
In comparison to other research on COPD and ILD, the current mean smoking pack years of 34.53+8.6 years is closer to the results of the aforementioned studies by Silvestro Ennio D'Anna *et al*., Kirby M. *et al*., and Thomas *et al*. The present study is supported by the findings of Bhakti P *et al*., who found that in middle-aged asymptomatic male smokers, transfer factor levels decreased and showed an inverse association with severity and duration of smoking.

In contrast to the typical DLCO values
Cigarette smokers in our cohort of patients with COPD had a lower mean DLCO (57.55+19.54) than did those who were never smokers (75+22.63). In smokers, DLCO drops with increasing pack-years smoked, suggesting that alveolar capillary membrane damage in the lungs will worsen. For the group COPD, the mean DLCO level was 72.88+25.17 for the pack 20-30 years old, 56.07+15.77 for the pack 30-40 years old, and 45.00+7.27 for the pack 40-50 years old. The average DLCO level for the pack 20-30 year olds in the ILD group was 46.40+13.43 [21, 22].

Distance covered in a six-minute walk test (6MWT)
In cross-sectional investigations, a low DLCO has been associated to a lower 6MWD, suggesting that this functional measure of the lung reflects the quality of alveolar-capillary gas transfer. Patients with chronic obstructive pulmonary disease ran a median of 365.45 meters (79.26 meters) on the 6-minute walk test. In the present investigation, all of the patients were given a 6-minute walk test, a diffusion capacity measurement, and a spirometry. All participants completed the 6-minute walk test, and while 34% of those tested had normal results, 42% of those with COPD and 24% of those with ILD exhibited a decrease in 6MWT distance. Those with COPD completed a 6-MWD of 365.45+79.26 meters, while patients with ILD completed a shorter distance of 353.53+48.08 meters.
The mean 6MWT distance (365.45 mts) in the present investigation is similar to that found in studies on COPD and ILD by VHF Mak *et al*, Sahin H *et al*, [11], Amir Farkhooy *et al*, and Kirby M *et al*. The present study is supported by the findings of a previous study on ILD conducted by Someya *et al*., who found a mean 6MWT distance of 353.53 mts. The present study is not supported by previous research on ILD by Hoda Ali AbouYoussuf *et al*, because their study did not find a similar mean 6MWT Distance

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(353.53mts) [22, 23].

Spirometry and DLCO for COPD studies

The mean FEV1 (%) of the COPD study population was 55.42+11.56, and the mean DLCO correction(for Hb) was 54.287+18.3.

Patients with COPD were divided into three groups based on their forced expiratory volume in one second (FEV1) spirometry results, with those in the mild group having a mean DLCO of 85.71+29.12, those in the moderate group having a mean of 58.50 15.28, and those in the severe group having a mean of 41.13+12.02. A DLCO of 56 was found in a COPD patient whose spirometry was normal.

Thirty-three (66%) of the 50 participants in this study had COPD. Out of these, spirometry revealed that 2% (6%) had mild blockage, 19% (58%) had moderate obstruction, and 33% (11 patients) had severe obstructive defect. Mean DLCO was found to be 85.71+29.12 for the mild division, 58.50+15.28 for the moderate, and 41.13+12.02 for the severe.

The DLCO for one COPD patient whose spirometry is normal is 56 0.00. There was also a statistically significant difference in mean DLCO levels (p value 0.001) across the three spirometry (FEV1) divisions of cases.

Patients with normal spirometry had a mean DLCO% corrected of 60.61, those with obstructive defects had a mean of 54.287+18.3, and those with a restrictive pattern had a mean of 49.4812+12.18. The DLCO was observed to be significantly decreased in five people with a restricted spirometry pattern. The efficacy of DLCO to predict exercise desaturation was recently investigated utilizing a large database with mixed pulmonary illness. Patients with a restrictive pattern were more likely to have a low DLCO (56%) than those with an obstructive pattern (33%). They found that a threshold of -62% projected worked best across the board. Using the Miller *et al*. reference equation, the sensitivity and specificity for O2 desaturation were both about 75% when DLCO was below the anticipated value of 62% [23].

Based on the findings of these studies, it is recommended that patients with COPD who have a low DLCO also undergo a 6-minute walk distance test in addition to measuring their exercise O2. Patients with COPD who have a normal DLCO measurement can rule out exercise-induced O2 desaturation, and subgroups who respond to certain treatment protocols cannot be defined only by pulmonary function test patterns. Twenty participants reported dyspnea following the 6MWT, and 14 had significantly decreased DLCO. Those with a low DLCO and COPD need activity measurements to prove desaturation, while those with a normal DLCO can rule out exercise-induced O2 desaturation.

In the present investigation, all of the patients were given a 6-minute walk test, a diffusion capacity measurement, and a spirometry. All participants completed the 6-minute walk test, and while 34% of them had normal results, 42% of those with COPD and 24% of those with ILD exhibited a decrease in 6MWT distance. Patients with COPD completed a 6-MWD of 365.45+79.26 meters, while patients with ILD completed a shorter distance of 353.53+48.08. The mean FEV1 (%) of the present study is very similar to those of previous COPD studies by Aparna Balasubramanian *et al*., Weinreich UM *et al*., Thomas *et al*., Afroditi K Boutou *et al*., Diaz AA *et al*., VHF Mak *et al*., and Silvestro Ennio D'Anna *et al* [24,25].

The present work is supported by previous research on COPD, including those of Aparna Balasubramanian *et al*., Weinreich UM *et al*., Thomas *et al*., Afroditi K Boutou *et al*., Diaz AA *et al*., VHF Mak *et al*., and Silvestro Ennio D'Anna *et al*. Emphysema can also be diagnosed using DLCO testing. Having a limited diffusion capacity is a hallmark of emphysema in patients with airflow obstruction. As a result, a low DLCO is one PFT metric that best correlates with the severity of emphysema on histology.

Division of cases by spirometry and diffusing capacity for carbon monoxide (DLCO) in ILD studies: the overall mean DLCO for ILD patients (FVC). When comparing DLCO across severity levels, researchers found that mild division had a mean value of 56.02+11.53, moderate division had a mean value of 49.56 8.81, and severe division had a mean value of 35.61+3.99. When spirometry is normal, the DLCO for one patient with ILD is 65.22.

When comparing the mean DLCO levels of the three spirometry (FVC) case divisions, a statistically significant difference was found (p<0.001). In restrictive spirometic patterns, the mean DLCO% prediction was 49.4812+12.18ml/min/mm Hg. It was discovered that the DLCO was drastically decreased in five patients with a restrictive pattern on spirometry. The 6 minute walk distance (6MWD) was also lower among these patients, with a mean value of 304 meters. The present study is supported by previous research on ILD by Nermine M.Riad *et al*. and Khaled Hussein *et al*., in which the mean FVC (percent) and mean DLCO (percent) age were quite similar to the present mean values [25].

Of the 50 participants, 17 (34%). had ILD. Spirometry testing revealed that 6 (or 35%) had mild restriction, 6 (or 35%) had moderate restriction, and 4 (or 24%) had severe restrictive defect. Average DLCO was found to be 56.02 11.53 for mild division, 49.56 8.81 for moderate division, and 35.61+3.99 for severe division. When spirometry is normal, the DLCO for one patient with ILD is 65.22. It was also shown that the three spirometry-based case divisions had significantly different mean DLCO levels (p value <0.001).

In restrictive spirometic patterns, the mean projected DLCO% was 49.4812+12.18 ml/min/mm. Hg. It

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was discovered that the DLCO was drastically decreased in five patients with a restrictive pattern on spirometry. The 6 minute walk distance (6MWD) was also lower among these patients, with a mean value of 304 meters.

Idiopathic pulmonary illness (in 29.4% of patients) and nonspecific interstitial pneumonia (in 35.2% of patients) were the most common causes of interstitial lung disease in the current investigation (NSIP). Five (30.4%) of the participants in the current study had interstitial lung disease caused by connective tissue disorders (CT-ILD). It is possible that the course of rheumatoid arthritis could be slowed down if lung illness in individuals was diagnosed and treated sooner rather than later.

Forty individuals with early rheumatoid arthritis and no respiratory symptoms participated in a prospective observational research by Robles-Perez A *et al*. Pulmonary function was altered in 18 individuals (45 percent). There was no significant drop in FVC values and all cases had DLCOs of 80% of prediction. In this sample of people, the DLCO averaged 68%. Patients with HRCT abnormalities, with diffuse cylindrical bronchiectasis being the most common finding (58%), all had low DLCO levels. These findings indicate that lung disease may be present from the outset of the rheumatic process, especially in those with higher serum ACPA levels, and without displaying respiratory symptoms. The non-invasive DLco process is trusted as an accurate means of diagnosing this lung illness.

Systemic lupus erythematosus is another example of an autoimmune disease that causes anomalies in diffusion capacity and leads to a restrictive lung condition (SLE). Interstitial lung disease is one of the major respiratory consequences of systemic lupus erythematosus and a leading cause of mortality in patients with SLE. Diffusion capacity for carbon monoxide in one breath (DLCO) fell first, before any other indices.

For their research on SLE, Masaaki Nakano and colleagues followed 110 consecutive Japanese patients. In 52 patients, or 47%, they found a decrease in DLCO, and in 9 patients, or 8%, they found a restrictive impairment of pulmonary function. 13 percent of the population had pulmonary fibrosis. Patients without lung fibrosis or a restrictive pattern usually displayed decreased DLCO.

Alveolar membrane diffusing capacity and pulmonary capillary blood volume, the two components of DLCO, were evaluated in a study including 24 patients with pulmonary sarcoidosis by Christine Lamberto and colleagues. Both membrane diffusing capacity and DLco are strongly predictive of gas exchange problems after exercise in individuals with sarcoidosis, and this study shows that a decrease in membrane diffusing capacity accounts for most of the reduction in DLCO at rest. This study shows that the membrane diffusing component of DLCO is primarily responsible for the reduction in DLCO in sarcoidosis, and is the strongest predictor of aberrant gas exchange during exercise, regardless of whether or not pulmonary fibrosis is present. Capillary blood volume in the lungs is likely only slightly affected due to vascular recruitment while at rest.

Conclusion

Despite controlling for spirometry and CT indications of emphysema, an impairment in DLCO was related with higher COPD symptoms and lower exercise performance. In light of these results, it is reasonable to think about include DLCO in future multidimensional instruments diagnosing COPD.

Patients with normal CT chest findings and mild symptoms had somewhat lower mean DLCO values than the population with abnormal CT chest findings and severe symptoms in both COPD and ILD, demonstrating that DLCO can be used to estimate disease severity.

Low DLCO is associated with higher symptomatology and diminished exercise ability, suggesting its usefulness in morbidity assessment. For the purposes of determining total impairment and the necessity of determining if oxygen therapy is required, a DLCO below 40% of the projected value may be used.

Patients with COPD can be better evaluated with both DLCO and FEV1 data included in the analysis. Pulmonary rehabilitation is more likely to succeed if this metric is improved.

Quality of life is significantly correlated with DLCO and FVC measurements, making them valuable tools in the management of patients with interstitial lung disease.

In the initial evaluation of patients with connective tissue diseases such as SLE, rheumatoid arthritis, systemic sclerosis, sarcoidosis, and hypersensitivity pneumonitis, DLCO can be recommended for the detection of mild (early or preclinical) interstitial lung disease because it is a non-invasive procedure.

Finding and treating lung disease early in adults with connective tissue diseases and COPD may slow the course of these conditions.

To prevent further deterioration in lung functions, it may be recommended that smokers quit. Among smokers, DLCO is decreased as pack years of smoking increased, implying that there will be more lung alveolar capillary membrane damage.

There is no statistically significant difference between the projected DLCO values and the corrected DLCO (for Hb) values since there are fewer anaemic patients in the study and the mean Hb of the study population is within normal ranges.

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