# Research article Association between six-minute walk tests with lung diffusion capacity for carbon monoxide in chronic respiratory disease: A cross-sectional study

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#### ABSTRACT

**Introduction and Aim:** Interstitial lung disease (ILD) is a heterogeneous disorder that share common clinical, radiographic, and physiological features. Most patients with ILD usually experience an exertion – induced dyspnea as first symptom. A noticeable change in oxygen saturation was noticed in ILD patients while exercise. The study objective was to ascertain the functional parameter that correlates best with ILD by comparing age, sex, and smoking history with different ILD pattern.

**Materials and Methods:** A proforma (including Six Minute Walk Test and Pulmonary Function Test with lung diffusion capacity) for one-year period (September 2014 - November 2015) was taken for the 40 included participants. The study includes patients with Interstitial Lung diseases diagnosed by clinical, radiological and spirometric parameters. The study tests the sensitivity and the specificity of six-minute walk test versus lung carbon monoxide diffusing ability.

**Results:** A total of 40 participants were included (19 were males and 21 were females). 12 were smokers and 28 were non-smokers. 20 patients belonged to Usual Interstitial Pneumonia (UIP) pattern, 14 were Non-Specific Interstitial Pneumonia (NSIP) and 6 were others. The mean $\pm$ SD spirometric parameters were FEV1/FVC=101.71 $\pm$ 16.752, FVC=55.29 $\pm$ 17.322, FEV1=57.66  $\pm$  20.246.

**Conclusion:** There was no statistical significance between age, gender, smoking and ILD patterns. Spirometer and diffusion capacity indices co-relate best with NSIP pattern of ILD in our study. In a resource limited setting, clinical and radiological assessment of ILD with six-minute walking distance and spirometry should or need not be supplemented by DLCO for severity assessment.

Keywords: Diffusing capacity; lung disease; pneumonia; spirometer.

# INTRODUCTION

Interstitial lung disease (ILD) is a heterogeneous disorder that share common clinical, radiographic, and physiological features. Most patients with ILD usually experience an exertion – induced dyspnea as first symptom that can precede significant impairment in ventilatory mechanics and gas exchange (1). Also, patients with ILD often experience distressing dyspnea during exercise that may contribute to exercise limitation (1). Consequently, exercise testing can be highly useful for ILD patients' clinical assessment.

Incidence and prevalence rates of Diffuse Parenchymal Lung Disease (DPLD) have not been approximated because of varying diagnosis on a particular disease. The mortality rate of these patients continues to increase in many countries (2, 3). Several facets of this disease have been narrated in beaucoup of literatures (4 - 6). ILD is most prevailing and observed in males in towering frequency than females (7). A noticeable change in oxygen saturation was noticed in ILD patients using cycle ergometer or treadmill (8). However, these forms of exercise can be strange for some people and computation of the everyday exercising data may not be significant. Sixminute walk test (6MWT) was suggested to be an exercise activity that could appropriate be recommended to these patients (2). Hence, this study aimed to explore ILD in a large group of patients considering three outcome measures of 6MWT such as walk distance, oxygen saturation while walking, and after walk breathlessness experience relating to the baseline activity of lung. To ascertain the functional parameter that correlates best with ILD by comparing age, sex, and smoking history with different ILD pattern was the focus of the study.

#### MATERIALS AND METHODS

Participants with Interstitial Lung Disease attending Department of Chest medicine and Tuberculosis were considered and ethical approval was sanctioned. A proforma for one-year period (September 2014 -November 2015) was taken for the included participants in the age group between 40 - 70 years of both the genders. The inclusion criteria consisted of patients with High Resolution Computerized Tomography (HRCT) confirmed ILD cases, definitive Idiopathic Pulmonary Fibrosis (IPF) patients, predictable Forced Vital Capacity (FVC) > 50% and Lung Diffusion Capacity (DLCO)> 35%. The patients who could walk for six minutes with stable saturation and pre-operative cooperative patients with bronchial asthma, COPD and ILD were considered inclusion for 6MWT and pulmonary function test respectively. Those patients with walking disability due to neuro/ muscular conditions, severe pulmonary hypertension with resting heart rate > 120/minute, diastolic > 120mm hg, systolic > 180 mm hg and unstable angina / myocardial infraction in last 4 weeks were considered for exclusion for six-minute walk test. The exclusion criteria for pulmonary function test were hemoptysis, tuberculosis, hemiplegia, unstable angina, and recent surgeries.

# Main Survey

The study includes patients with Interstitial Lung diseases diagnosed by clinical, radiological and spirometric parameters. The participants were included in this study after receiving their consent.

# Spirometry with diffusing capacity of the lungs for carbon monoxide (DLCO)

The difference in the carbon monoxide pressure quantification during inhalation and exhalation implies diffusing capacity of the lungs carbon monoxide. Pulmonary function tests were conducted in a lab located close to the chest unit as per American Thoracic Society (ATS) recommendation. COSMED micro quark system is diagnostic equipment and was used for spirometric assessment for forced expiratory volume in 1 second (FEVI). Forced Vital Capacity (FVC) and Peak Expiratory Flow Rater (PEER) are examined employing spirometry tested using computerized spirometer. Three forced expired activity satisfying ATS recommendation were extracted for every single participant considering the inflated rate. The participants experienced single breath hold method for lungs diffusing capacity for carbon monoxide twice and the mean of the values were captured.

# Six-minute walk test (6MWT)

The extent that a person can cover in an interval of six minutes is estimated through 6MWT. The procedure was carried out in an aerated chest-ward covering an area of 30 meters. The intensity that a patient could breathe was documented comparing 10-point Borg scale (No exertion - 0 and maximum exertion - 10). The levels of heartrate, blood pressure and oxygen saturation were checked and captured before and after this procedure. To avoid unanticipated consequences, the participants were informed to wait for minimum of

15 minutes after the procedure. The values in meters were calculated for 6MWT and the result of 6MWT and saturation (SPO2) was analyzed for distance saturation product (DSP).

# Statistical analysis

SPSS software version 17 was carried out for this analysis. To compare the parameters connecting the groups were assessed through independent sample student t test. The comparison between two attributes and association between two parameters were analyzed through chi-square test and Pearson correlation coefficient analysis respectively. Anova test comparing means in more than two different groups was done and statistical significance was set at a p value of < 0.05.

# RESULTS

Parametric tests were executed since the results were distributed normally and represented numerically. Forty ILD participants were involved with the age range of  $55.83 \pm 11.57$ . Of these patients, 19 were men and 21 were female (Table 1). 12 were smokers and 28 were non-smokers. 20 patients belonged to Usual Interstitial Pneumonia (UIP) pattern, 14 were Non –Specific Interstitial Pneumonia (NSIP) and 6 were others. There was no statistical significance between genders and ILD patterns (p value = 0.59) (Fig. 1). Also, association between ILD pattern and smoking was found to have no statistical significance (p value = 0.12) (Fig. 2). The association between age and ILD patterns revealed statistical significance with p value 0.04 (Fig. 3).

Variables		<b>Participants</b> n (%)
Gender	Male	19 (47.5)
	Female	21 (52.5)
Smokers	Yes	12 (30)
	No	28 (70)
Diagnosis	UIP	20 (50)
(ILD	NSIP	14 (35)
Patterns)	Others	6 (15)
Ground	Yes	17 (42.5)
Glass Opacity	No	23 (57.5)
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 Table 1: Patients' pre-procedural parameters (n =40)

UIP= Usual Interstitial Pneumonia NSIP=Non –Specific Interstitial Pneumonia

There were no association found between ILD and baseline saturation, ILD and desaturation, ILD pattern and the distance walk (Table 2). In addition, there was a greater reduction in DLCO in NSIP group compared to the other groups. RV/TLC was reduced equally in UIP and NSIP group. NSIP group was found to be with a greatest drop in FVC, RV and TLC when compared with the other groups (Table 2). p-value < 0.05 was tested by using the one-way Anova. The mean  $\pm$  SD on comparison between spirometric

parameters with ILD pattern were as follows: FEV1/FVC=101.7±16.7,FVC=55.2±17.3, FEV1=57.6 ± 20.2, TLC =  $52.8 \pm 15.8$ , RV =  $59.3 \pm 31.1$ , KCO =  $80.2 \pm 29.3$ , DLCO= $32.8 \pm 18.2$  and RV/TLC Ratio =  $119.5 \pm 46.8$  (Table 2). There was statistically significant positive correlation between baseline saturation and desaturation, baseline distance walk and desaturation, DLCO and FEV1, DLCO and FVC, DLCO and RV, DLCO and TLC, RV/TLC ratio and RV, FEV1 and FVC, FEV1 and FEV1/FVC, FEV1 and TLC, FVC and TLC, RV and TLC using Pearson's correlation (Fig. 4). Among spirometric values: DLCO, FEV1, FVC, Residual Volume (RV) and Total Lung Capacity (TLC) were found to be much reduced in NSIP pattern when compared to other ILD'S pattern.



Fig. 1: Association between gender and ILD patterns. Pearson's Chi-square test p-value < 0.05



Fig. 2: Association between smoking and ILD patterns. Pearson's Chi-square test p-value < 0.05



Fig. 3: Association between age group and ILD patterns. Pearson's Chi-square test p-value < 0.05

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Variables	Overall (n=40)	UIP (n=20)	NSIP (n=14)	Others (n=6)	P- value
Baseline saturation	95.7±2.1	95.7±1.6	95.7±2.3	95.8±3.1	0.53
Desaturation	88.1±4.7	87.9±4.3	89±4.6	87.1±7.2	0.91
Distance walk	198.2±54.6	198.4±51.8	206.5±61.2	178.3±51.5	0.50
DLCO	32.8±18.2	34.9±21.3	27.5±12.7	38±17.5	0.68
RV / TLC Ratio	119.5±46.8	117.1±37.1	115±47	138.1±75.2	0.44
FVCex	55.3±17.3	59.2±17.5	48.9±13.7	57±22.3	0.54
RV	59.3±31.1	59.4±28.5	54.3±23.6	70±52.5	0.80
TLC	52.8±15.8	55.3±16.0	48±14.5	56±18.4	0.75

**Table 2:** Comparison between spirometric parameter with ILD pattern of the study participants (n=40)

p-value < 0.05 was tested using one-way Anova



Fig. 4: Correlation between studied variables using Pearson's correlation p-value <0.05 considered as statistically significant

# DISCUSSION

In comparison between smokers and ILD we found that smoking plays a role in Non-Specific Interstitial Pneumonia (NSIP) and it does not seem to play a role in incidence of UIP and others. Literatures concentrating IPF patients suggested a greater chance was seen in smokers and case-control evidence pointing smoking as the etiology for the disease (8,9). In contrast few research has reported that smoking does not influence the life span of ILD patients (8,9). There were significant relations seen in respiratory bronchiolitis associated ILD, desquamative interstitial pneumonitis, Langerhans cell histiocytosis, cryptogenic fibrosing alveolitis and eosinophilic pneumonia (8). А homogenous histopathologic characteristic observed in was respiratory bronchiolitis (RP) and DIP where collection of pigmented macrophages was noticed in the alveoli (9).

Also, the former (RP) was a symptomless disease that was present even after quitting smoking.

In correlation between age and diagnosis, ILD's are generally uncommon in patients' age group < 40. In our study, the maximum incidence of ILD'S seems to be in 40 - 60 years. However, this could be biased due to a small sample size. Sarcoidosis and disease relating to connective tissues were noticed in middle aged patients ranging between 20 and 40 years. In contrary, IPF was more detected in elderly patients of age above 60 years (10). The degree of desaturation during 6MWT and the baseline saturation did not differ in the three patterns of ILD group and so did the walking distance. An evident finding that was prominent and distinct in our results was that the recurrence and drop in the saturation level while 6MWT has no striking variability in comparison between NSIP, UIP and others.

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The IPF patient's life expectancy was predicted to be a minimum of one year since the start of the treatment in 58 IPF studied participants as reported by Hanson et al., (10). In addition, the author has stated that if a consistent or ameliorated FVC was seen in IPF patients then the expectant life span was greater and vice versa in IPF patient showing a 10 percent decline in the FVC spirometry tests (10). Adding to the above statement, further diminishing DLCO levels of equal to or more than 20 percent post treatment of 12 months experienced unfortunate life expectancy (10). The prognosis of the disease depends on the baseline pulmonary function tests(PFTS) and they serve as an important diagnostic fact. The features of 6MWK being uncomplicated, economical and consistency makes the tests more engaging and acceptable for the patients and for long-term studying of patients' condition. The lethal nature of IPF creates an unfavorable prognosis with varying mortality rates. Belloli and Lama concluded that the viability of patients with UIP and NSIP could be related with the desaturation levels that were observed while 6MWT (11). However, the physiologic status and imaging features should be considered (11). Hunninghake et al., suggested that patients can reasonably be spared lung biopsy if an assessment of the clinical-radiologic data by experienced pulmonologists and radiologists confidently supports a diagnosis of IPF (12). HRCT features alone have a specificity of 90% but a sensitivity of only 78.5%.

#### CONCLUSION

SMWT is a simple and reliable objective tool in the functional assessment of ILD irrespective of the pattern. Smoking and UIP Pattern of ILD did not correlate whereas spirometer and diffusion capacity indices co –relate best with NSIP Pattern of ILD in our study. In addition, in a resource limited setting, clinical and radiological assessment of ILD with sixminute walking distance and spirometry should or need not be supplemented by DLCO for severity assessment.

# CONFLICT OF INTEREST

The authors declare no conflict of interest.

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