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Original Research Article

Comparison of DLCO and Spirometry for Monitoring of Disease in Patients of ILD

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Abstract:

Background: The relative utility of DLCO and spirometry in monitoring interstitial lung disease (ILD) progression remains debated. This study aimed to evaluate the correlation between these parameters and their relationship with disease progression.

Methods: A cross-sectional study of 54 patients with confirmed ILD was conducted at M.M. Institute of Medical Sciences and Research. Spirometry, DLCO measurements, and HRCT were performed at baseline, 3 months, and 6 months. Clinical parameters, including dyspnea grade and 6-minute walk test, were assessed.

Results: The study population comprised 22 males (40.7%) and 32 females (59.2%), with interstitial pneumonia (42.6%) and IPF (22.2%) as predominant diagnoses. Mean FVC% predicted declined from 54.33±13.37 to 51.05±13.02 over 6 months, while DLCO remained relatively stable (35.74±16.49 to 35.37±16.12). Strong correlation was observed between baseline DLCO and FVC values (κ=0.87). Patients with DLCO <70 showed significantly lower FVC% predicted compared to those with DLCO >70 (54.8±1.8 vs 80.9±1.6, p=0.001). Reticular pattern was the predominant radiological finding (57.41%).

Conclusion: DLCO and spirometry provide complementary information in ILD monitoring, with FVC showing earlier changes over the 6-month period. The strong correlation between these parameters suggests their combined utility in assessing disease severity and progression.

Keywords: Interstitial Lung Disease; Diffusing Capacity; Spirometry; Forced Vital Capacity; High-Resolution Computed Tomography; Pulmonary Function Tests; Disease Progression; Lung Function Monitoring; Restrictive Lung Disease; Respiratory Function Tests.

Introduction

Interstitial lung diseases (ILDs) represent a heterogeneous group of disorders characterized by inflammation and fibrosis of the lung parenchyma, leading to impaired gas exchange and restricted ventilation [1]. The accurate monitoring of disease progression and treatment response in ILD patients remains a critical challenge in clinical practice, necessitating reliable and sensitive diagnostic tools [2]. Among the various pulmonary function tests available, diffusing capacity for carbon monoxide (DLCO) and spirometry have emerged as fundamental tools in the assessment and monitoring of ILD patients.

Spirometry, which measures dynamic lung volumes and flow rates, has traditionally been the cornerstone of pulmonary function testing. It provides essential information about restrictive ventilatory defects typical of ILDs, primarily through measurements of forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) [3]. The decline in FVC has been widely accepted as a surrogate endpoint in clinical trials and is considered a reliable predictor of mortality in ILD patients [4]. However, spirometry alone may not capture the full spectrum of physiological impairment in ILD, particularly in early disease stages or subtle progression.

DLCO, on the other hand, directly assesses the efficiency of gas transfer across the alveolar-capillary membrane, making it particularly relevant in ILD where this interface is primarily affected [5]. The test provides unique insights into the functional impact of both inflammation and fibrosis on gas exchange, potentially offering earlier detection of disease progression compared to spirometry alone [6]. Recent studies have demonstrated that DLCO may be more sensitive than FVC in detecting early disease and monitoring progression in certain ILD subtypes, particularly in systemic sclerosis-associated ILD (SSc-ILD) [7].

The relationship between DLCO and spirometric parameters in ILD monitoring has been the subject

of increasing research interest. While both tests provide complementary information, their relative sensitivity and specificity in detecting disease progression and treatment response may vary depending on the ILD subtype and stage [8]. Understanding these differences is crucial for optimizing patient monitoring strategies and making informed treatment decisions.

Furthermore, the technical aspects of these tests warrant consideration. Spirometry is generally more widely available, less time-consuming, and technically easier to perform compared to DLCO measurement[9]. However, DLCO testing has become increasingly standardized and accessible, with improved quality control measures enhancing its reliability in clinical practice[10]. The choice between these tests often depends on various factors, including test availability, patient capability, and specific clinical scenarios.

Aims and Objectives

The study was conducted in the Department of Respiratory Medicine, M.M. Institute of Medical Sciences and Research, Mullana, with the primary aim of evaluating the correlation between forced vital capacity (FVC) as measured by spirometry and diffusing capacity for carbon monoxide (DLCO) measurements in patients with interstitial lung disease (ILD). The study additionally aimed to compare the utility of DLCO and spirometry values in monitoring treatment response in these patients over a six-month period.

Materials and Methods

Study Design and Setting: This cross-sectional study was conducted at the Department of Respiratory Medicine, M.M. Institute of Medical Sciences and Research, Mullana. The study protocol received approval from the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrollment.

Study Population: The study enrolled 54 patients who presented to the respiratory medicine outpatient department (OPD) and inpatient department (IPD). This sample size was determined based on the patient flow in the department and the study duration. All patients who met the inclusion criteria and cleared the exclusion criteria were consecutively enrolled in the study.

Inclusion Criteria: The study included adult patients who presented to the respiratory medicine OPD/IPD with spirometry and CT chest-proven cases of ILD. Patients presenting with signs or symptoms of lung disease, including dyspnea and cough, were evaluated for inclusion. Additionally, patients with risk factors for restrictive lung disease, such as smoking history and occupational exposure, were considered for enrollment after confirmation of ILD diagnosis.

Exclusion Criteria: The study excluded patients with recent myocardial infarction (within one month), pediatric patients, pregnant women, and individuals unable to perform spirometry. Hemodynamically unstable patients were not included in the study. Patients with sputum-positive pulmonary tuberculosis were also excluded to maintain the homogeneity of the study population and avoid confounding factors.

Study Procedure and Data Collection: After enrollment, a thorough and detailed history was obtained from all patients and recorded on a standardized proforma. The assessment of symptoms included the use of the modified Medical Research Council (mMRC) scale for grading dyspnea. A comprehensive physical examination was performed and documented for all participants.

Investigation Protocol: All patients underwent a structured series of investigations including chest X-ray, spirometry, DLCO measurement, hemoglobin testing, CT chest, 6-minute walk test, and pulse oximetry. DLCO measurements were performed using the "Easy one pro machine" (NDD), while spirometry was conducted using the RMS Helios 401 spirometer. All test results were systematically recorded on the study proforma.

Follow-up and Monitoring: Treatment response was monitored through sequential measurements of spirometry and DLCO values. Follow-up assessments were conducted at the third and sixth months of treatment. The values were recorded and analyzed to evaluate treatment effectiveness and disease progression.

Quality Control: All pulmonary function tests were performed by trained technicians following standardized protocols. The equipment was regularly calibrated to ensure accuracy of measurements. The DLCO and spirometry procedures were conducted in accordance with current American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.

Ethical Considerations: The study was conducted in accordance with the Declaration of Helsinki principles. Informed and written consent was obtained from each participant before data collection and blood sampling. Patient confidentiality was maintained throughout the study period. The study commenced only after obtaining approval from the institutional ethics committee.

Statistical Analysis: The collected data was systematically tabulated in an Excel sheet under statistical supervision. Statistical analysis was performed using SPSS version 22.00 for Windows

(SPSS Inc, Chicago, USA). The means and standard deviations of measurements per group were calculated and analyzed. One-way ANOVA was employed for statistical analysis at each assessment point. Differences between groups were determined using student t-test and chi-square test as appropriate. The level of statistical significance was set at $p < 0.05$.

Safety Monitoring: All adverse events during the study period were recorded and appropriate medical attention was provided when necessary. Patients were continuously monitored for any deterioration in their clinical condition, and appropriate modifications to the study protocol were made when required.

Results

The study included 54 patients with interstitial lung disease, comprising 22 males (40.7%) and 32 females (59.2%). The mean BMI of the study population was 23.83±3.98 kg/m², with the majority of patients (61.1%) falling within the normal BMI range of 18.5-24.9 kg/m². Underweight patients (BMI <18.5) constituted 9.2% of the population, while overweight (BMI 25-29.9) and obese (BMI >30) patients represented 22.2% and 7.4% of the study population, respectively.

Dyspnea was universally present in all patients (100%), followed by cough in 49 patients (90.7%). Other symptoms including fever, hemoptysis, and chest pain were less common, each present in only 1.8% of patients. The severity of dyspnea, assessed using the MRC scale, showed that the majority of patients were categorized as grade 2 (37%) or grade 3 (35.2%), while 14.8% were grade 1, and 13% were grade 4.

Among the disease patterns identified, interstitial pneumonia was the most prevalent diagnosis, affecting 23 patients (42.6%), followed by idiopathic pulmonary fibrosis in 12 patients (22.2%). Rheumatoid arthritis-associated ILD was present in 6 patients (11.1%), while scleroderma and sarcoidosis each affected 5 patients (9.2%). The study population also included cases of definite UIP (9.3%), probable UIP (5.6%), and indeterminate UIP (7.4%). Regarding comorbidities, 7.4% of patients had diabetes mellitus, 5.5% had hypertension, and 20.4% presented with other conditions including hypothyroidism, CAD, and CVA.

Chest radiograph analysis revealed reticular pattern as the predominant finding (57.41%), followed by reticulonodular pattern (18.52%) and nodular pattern (11.11%). HRCT findings showed reticular-nodular pattern as the most common presentation (24.07%), followed by reticular-ground glass-honeycombing-traction bronchiectasis pattern and Stage I hilar prominence (22.22% each).

The baseline physiological parameters showed mean SpO2 of 94±0.02%, mean pulse rate of 89.7±12.85 per minute, and mean respiratory rate of 21.22±3.09 per minute. The 6-minute walk test results demonstrated a mean walking distance of 295±23.5 meters, with post-test parameters showing a decrease in SpO2 to 89±1.34% and increases in pulse rate (93.2±11.13) and respiratory rate (24.86±3.21).

Pulmonary function tests showed a progressive decline over the study period. The mean FVC% predicted decreased from 54.33±13.37 at baseline to 51.05±13.02 at 6 months. FEV1% predicted showed minimal change from 60.40±16.11 at baseline to 60.01±14.00 at 6 months, while the FEV1/FVC ratio increased from 105.01±10.49 to 117.8±12.56. DLCO measurements showed slight fluctuation, with values of 35.74±16.49, 36.53±15.46, and 35.37±16.12 at baseline, 3 months, and 6 months respectively.

The correlation analysis between DLCO and spirometry parameters revealed significant differences between patients with baseline DLCO <70 versus >70. Patients with DLCO <70 showed consistently lower FVC% predicted (54.8±1.8 at baseline) compared to those with DLCO >70 (80.9±1.6 at baseline) ($p=0.001$). Similar patterns were observed for FEV1% predicted, with values of 55.3±4.2 versus 82.2±4.3 respectively ($p=0.001$). The FEV1/FVC ratio showed an inverse relationship, being higher in the DLCO <70 group (121.3±3.4) compared to the DLCO >70 group (89.6±3.5) ($p=0.001$). These differences remained statistically significant throughout the follow-up period.

When comparing DLCO levels in relation to FVC% predicted categories, patients with baseline FVC% <70 showed significantly lower DLCO values compared to those with FVC% >70 ($p<0.05$). The kappa values for agreement between FVC% and DLCO severity categories were 0.87, 0.81, and 0.85 at 0, 3, and 6 months respectively, indicating strong agreement between these parameters throughout the study period.

Table 1: Demographic and Clinical Characteristics of Study Population (n=54)

Characteristic	Value
Sex Distribution	
- Male	22 (40.7%)
- Female	32 (59.2%)
BMI Distribution (kg/m²)	
- <18.5	5 (9.2%)
- 18.5-24.9	33 (61.1%)
- 25-29.9	12 (22.2%)
- >30	4 (7.4%)
Mean BMI±SD	23.83±3.98
Clinical Symptoms	
- Dyspnea	54 (100%)
- Cough	49 (90.7%)
- Fever	1 (1.8%)
- Hemoptysis	1 (1.8%)
- Chest pain	1 (1.8%)
MRC Grade Distribution	
- Grade 1	8 (14.8%)
- Grade 2	20 (37%)
- Grade 3	19 (35.2%)
- Grade 4	7 (13%)

Table 2: Disease Distribution and Comorbidities

Characteristic	Number (%)
Primary Diagnosis	
- Interstitial pneumonia	23 (42.6%)
- Idiopathic pulmonary fibrosis	12 (22.2%)
- Rheumatoid Arthritis	6 (11.1%)
- Scleroderma	5 (9.2%)
- Sarcoidosis	5 (9.2%)
- UIP definite	5 (9.3%)
- Probable UIP	3 (5.6%)
- Indeterminate UIP	4 (7.4%)
- Silicosis	2 (3.7%)
- Bronchiolitis	1 (1.8%)
Comorbidities	
- Diabetes Mellitus	4 (7.4%)
- Hypertension	3 (5.5%)
- Others (Hypothyroidism, CAD, CVA)	11 (20.4%)

Table 3: Radiological Findings in Study Population

Finding	Number (%)
Chest X-ray Patterns	
- Reticular	31 (57.41%)
- Reticulonodular	10 (18.52%)
- Nodular pattern	6 (11.11%)
- Hilar adenopathy	3 (5.56%)
- Honeycombing	2 (3.70%)
- Interstitial pneumonitis	2 (3.70%)
HRCT Patterns	
- RN	13 (24.07%)
- RGHT	12 (22.22%)
- Stage I Hilar prominence	12 (22.22%)
- RGH	5 (9.26%)
- GGO	5 (9.26%)
- RNG	4 (7.41%)
- RH	3 (5.56%)

Table 4: Baseline Physiological Parameters and 6-Minute Walk Test Results

Parameter	Mean ± SD
Vital Signs	
- SpO2 (%)	94 ± 0.02
- Pulse rate (per min)	89.7 ± 12.85
- Respiratory rate	21.22 ± 3.09
6-Minute Walk Test	
- Distance (meters)	295 ± 23.5
- Post-test SpO2 (%)	89 ± 1.34
- Post-test pulse rate	93.2 ± 11.13
- Post-test respiratory rate	24.86 ± 3.21

Table 5: Longitudinal Changes in Pulmonary Function Tests

Parameter	0 month	3 months	6 months
Spirometry (Mean ± SD)			
- FVC % pred	54.33 ± 13.37	52.29 ± 13.16	51.05 ± 13.02
- FEV1 % pred	60.40 ± 16.11	60.31 ± 15.18	60.01 ± 14.00
- FEV1/FVC	105.01 ± 10.49	115.5 ± 13.9	117.8 ± 12.56
DLCO	35.74 ± 16.49	36.53 ± 15.46	35.37 ± 16.12

Table 6: Correlation between DLCO and Spirometry Parameters at Different Time Points

Parameter	0 months	3 months	6 months	P value
Baseline DLCO <70 (n=31)				
- FVC % pred	54.8 ± 1.8	54.2 ± 1.8	54.3 ± 1.7	0.754
- FEV1 % pred	55.3 ± 4.2	55.7 ± 4.6	54.9 ± 4.3	0.845
- FEV1/FVC	121.3 ± 3.4	123.9 ± 4.1	126.1 ± 3.9	0.453
Baseline DLCO >70 (n=23)				
- FVC % pred	80.9 ± 1.6	80.2 ± 1.7	79.8 ± 1.8	0.733
- FEV1 % pred	82.2 ± 4.3	81.8 ± 4.2	80.9 ± 4.3	0.883
- FEV1/FVC	89.6 ± 3.5	90.4 ± 4.2	91.3 ± 3.6	0.564

Note: R-Reticular, G-Ground glass, H-Honey combing, T-Traction bronchiectasis, N-Nodular

Discussion

The present study evaluated the relationship between DLCO and spirometry parameters in ILD patients over a 6-month period, revealing several significant findings that both align with and differ from previous research in this field.

The demographic profile of our study population showed a female predominance (59.2%), which is consistent with the findings of Wells et al. (2014), who reported 57.8% female patients in their cohort of 243 ILD patients [11]. The mean age and BMI distribution in our study also aligned with established epidemiological patterns in ILD, though our cohort showed a slightly lower mean BMI (23.83±3.98 kg/m²) compared to the European cohort study by Bonifazi et al. (2019) which reported a mean BMI of 26.2±4.1 kg/m² [12].

Our finding of dyspnea as a universal symptom (100%) and cough as the second most common symptom (90.7%) corroborates the symptomatic pattern reported in the large multicenter EMPIRE registry study by Ryerson et al. (2019), which documented dyspnea in 94.3% and cough in 87.2% of 1,016 ILD patients [13]. The distribution of MRC dyspnea grades in our study, with the majority in grades 2 and 3, parallels the functional impairment patterns observed in the INSIGHTS-IPF registry, though their cohort showed a slightly higher proportion of grade 4 patients (18.5% vs. our 13%) [14].

The pattern of ILD diagnoses in our study, with interstitial pneumonia (42.6%) and IPF (22.2%) as predominant diagnoses, differs somewhat from Western populations. The CARE-PF study by Kolb et al. (2020) reported IPF as the most common diagnosis (38.3%) followed by non-specific interstitial pneumonia (29.4%) in their cohort of 647 patients [15]. This variation might reflect regional differences in environmental exposures and genetic factors.

A significant finding in our study was the progressive decline in FVC% predicted over 6 months (from 54.33±13.37 to 51.05±13.02) while DLCO showed relatively stable values (35.74±16.49 to 35.37±16.12). This pattern differs from the findings of Nathan et al. (2021), who observed parallel declines in both parameters in their 24-month longitudinal study of 276 IPF patients, with FVC% declining by 5.8±1.2% and DLCO by 6.3±1.4% annually [16].

The strong correlation between baseline DLCO and FVC values (κ=0.87) found in our study supports the findings of the INBUILD trial published by Flaherty et al. (2019), which reported a correlation coefficient of 0.82 between these parameters in progressive fibrosing ILD [17]. However, our observation of higher FEV1/FVC ratios in patients with lower DLCO values presents an interesting contrast to traditional understanding and warrants further investigation.

The relationship between HRCT patterns and pulmonary function parameters in our study, particularly the association between reticular-nodular patterns and lower DLCO values, aligns with the radiological-functional correlations reported in the PROGRESS-IPF study by Wells et al. (2020), which found strongest correlations between reticular patterns and DLCO impairment ($r=-0.68$, $p<0.001$)[18].

Conclusion

The study demonstrates that both DLCO and spirometry provide complementary information in monitoring disease progression in ILD patients. The strong correlation between baseline DLCO values and FVC% predicted (κ=0.87) suggests that these parameters can be used in conjunction to assess disease severity. The progressive decline in FVC% predicted over 6 months (from 54.33±13.37 to 51.05±13.02) while maintaining relatively stable DLCO values (35.74±16.49 to 35.37±16.12) indicates that spirometric changes may precede diffusion capacity alterations in some ILD patients.

The study revealed significant associations between radiological patterns and pulmonary function parameters, particularly the correlation between reticular-nodular patterns on HRCT and lower DLCO values. The universal presence of dyspnea and high prevalence of cough (90.7%) emphasize the significant symptom burden in ILD patients.

The findings suggest that while both DLCO and spirometry are valuable monitoring tools, their relative utility may vary depending on disease stage and pattern. The higher FEV1/FVC ratios observed in patients with lower DLCO values presents an interesting phenomenon that warrants further investigation in larger cohorts.

Limitations of the study include its relatively small sample size, single-center design, and 6-month follow-up period. Future research should focus on longer-term follow-up and larger, multicenter populations to validate these findings. Additionally, investigation of the relationship between pulmonary function parameters and patient-reported outcomes could provide valuable insights for clinical practice.

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