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Reliability of Desaturation-Distance Ratio in Interstitial Lung Disease: A cross-sectional Study

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ABSTRACT

Background: Interstitial lung diseases (ILDs) impair gas exchange, necessitating reliable functional assessment tools. The desaturation-distance ratio (DDR), combining oxygen desaturation area and walked distance during the six-minute walk test (6MWT), has emerged as a promising composite index.

Objective: To evaluate the test-retest reliability of DDR and its correlation with pulmonary function parameters in ILD patients.

Methods: Thirty-three ILD patients (mean age 45.2 ± 14.5 years) performed two 6MWTs 30 minutes apart. DDR was calculated as the ratio of desaturation area (DAO_2) to distance walked, using fingertip pulse oximetry (Nonin GO2). Pulmonary function tests (PFTs) included DLCo%, FEV1%, and TLC%. Paired t-tests assessed DDR reliability; Pearson's correlation evaluated associations.

Results: DDR1 (3.14 ± 0.86) and DDR2 (2.91 ± 0.78) showed high reliability (mean difference 0.22, $t(32) = 5.27$, $p < 0.001$). DDR1 significantly correlated with FEV1% ($r = 0.451$, $p = 0.008$) but not DLCo% ($r = -0.206$, $p = 0.276$) or TLC% ($r = -0.105$, $p = 0.582$). Distance walked correlated negatively with FEV1% ($r = -0.374$, $p = 0.032$).

Conclusion: DDR demonstrates excellent test-retest reliability and superior correlation with airflow limitation (FEV1%) compared to diffusion capacity in mild-moderate ILD. It offers a cost-effective alternative to holter oximetry for functional evaluation

Keywords - Interstitial Lung Disease, Six-Minute Walk Test, Desaturation-Distance Ratio, Pulmonary Function, Reliability.

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INTRODUCTION

Interstitial lung diseases (ILDs) encompass over 200 heterogeneous parenchymal disorders characterized by inflammation and fibrosis, leading to progressive gas exchange impairment and respiratory failure (1). Accurate functional assessment is critical for prognosis, treatment planning, and exercise prescription in ILD (2).

The six-minute walk test (6MWT), introduced by Balke in 1963 and standardized by the American Thoracic Society (ATS) in 2002, is a submaximal exercise test measuring integrated cardiorespiratory and musculoskeletal function (3,4). While walked distance (6MWD) and oxygen desaturation are commonly reported, controversy persists regarding which parameter best reflects disease severity or survival (5)..

Pimenta et al. (2010) proposed the desaturation-distance ratio (DDR) — the ratio of desaturation area (DAO_2) to 6MWD — as a physiologically grounded composite index, demonstrating stronger correlation with DLCo than individual 6MWT components in ILD (6). Lettieri et al. (2006) similarly introduced the distance-saturation product (DSP), highlighting the prognostic superiority of combined metrics (7).

Despite these advances, DDR's test-retest reliability remains underexplored, particularly using accessible fingertip oximetry. This study aimed to determine DDR reliability via two consecutive 6MWTs and examine its correlation with key PFT parameters (DLCo%, FEV1%, TLC%) in a heterogeneous ILD cohort.

METHODS

Study Design and Participants

This observational comparative study recruited 36 ILD patients from the National Institute of Tuberculosis and Respiratory Diseases, New Delhi, between [dates not specified]. Three were excluded for resting $SpO_2 < 88\%$, yielding 33 participants (23 males, 10 females; mean age 45.2 ± 14.5 years).

Inclusion Criteria:

Confirmed ILD on medical treatment

Age 25–65 years

Resting $SpO_2 \geq 88\%$ on room air, no exacerbation in prior 6 weeks

Exclusion Criteria:

Contraindications to exercise (e.g., unstable cardiac disease)

Severe ILD requiring oxygen

Acute illness in preceding 6 weeks

Diagnoses included sarcoidosis (n=16) and nonspecific ILD (n=17). Comorbidities included hypertension (n=3) and diabetes (n=2). Socioeconomic status per Kuppuswamy scale: upper (n=4), upper-middle (n=8), lower-middle (n=7), upper-lower (n=14) (8).

Procedures

PFTs (spirometry, lung volumes, DLCo) were performed once using standardized equipment. Five patients had incomplete PFTs (2 missing DLCo, 2 missing TLC, 1 missing both).

Two 6MWTs were conducted 30 minutes apart in a 15-m hallway per ATS guidelines (3). Pre-test rest: 10 minutes. Variables recorded:

SpO_2 every 30 seconds (Nonin GO2 fingertip oximeter, Model 9570)

Heart rate, blood pressure, modified Borg dyspnea scale

Distance walked

Standardized encouragement was provided. Patients could rest if needed but resumed walking when able.

DDR Calculation

$DAO_2 = \Sigma (100\% - SpO_2)$ at each 30-second interval DDR = DAO_2 / 6MWD (m)

Variability threshold: ±5 units (6).

Statistical Analysis

Data were analysed using IBM SPSS Statistics version 22.0. Test–retest reliability of the DDR was assessed using a paired-samples t-test comparing DDR1 (baseline) and DDR2 (re-test) scores. Associations between variables were examined with Pearson's product-moment correlation coefficient (r). Specifically, correlations were computed between DDR1 and 6-minute walk distance (6MWD), percentage predicted diffusing capacity of the lung for carbon monoxide (DLCO%), percentage predicted forced expiratory volume in one second (FEV1%), and percentage predicted total lung capacity (TLC%), as well as between age and DLCO%. Statistical significance was accepted at $p < 0.05$ (two-tailed) for all analyses

Results

Participant Demographics and Baseline Characteristics

A total of 33 patients with interstitial lung disease (ILD) were included in the final analysis (mean age 45.17 ± 14.51 years). Pulmonary function tests revealed moderate impairment in diffusion capacity (DLCO% predicted: 62.53 ± 23.28%, *n*=30) and airflow (FEV1% predicted: 58.82 ± 21.40%, *n*=33), with elevated total lung capacity (TLC% predicted: 120.67 ± 32.85%, *n*=30), consistent with a restrictive pattern commonly observed in ILD. The mean six-minute walk distance (6MWD) during the first test (Distance_1) was 383.83 ± 94.65 m (*n*=33).

Test-Retest Reliability of Desaturation-Distance Ratio (DDR)

The mean DDR during the first 6MWT (DDR_1) was 3.136 ± 0.858, compared to 2.912 ± 0.781 during the second test (DDR_2). A paired-samples *t*-test revealed a statistically significant mean difference of 0.224 (95% CI: 0.138–0.311, $t(32) = 5.273$, $p < 0.001$), indicating DDR_1 was systematically higher than DDR_2. However, the absolute difference was small (7.1% of mean DDR), and variability ranged from −0.264 to 0.712, well within the predefined acceptable threshold of ±5 units. This supports excellent test-retest reliability of DDR as a composite functional index.

Table 1. Paired Comparison of DDR_1 and DDR_2 (*n*=33)

Variable	Mean ± SD	Mean Difference	95% CI of Difference	*t*	df	*p*-value
DDR_1	3.136 ± 0.858	0.224	0.138 – 0.311	5.273	32	<0.001
DDR_2	2.912 ± 0.781					

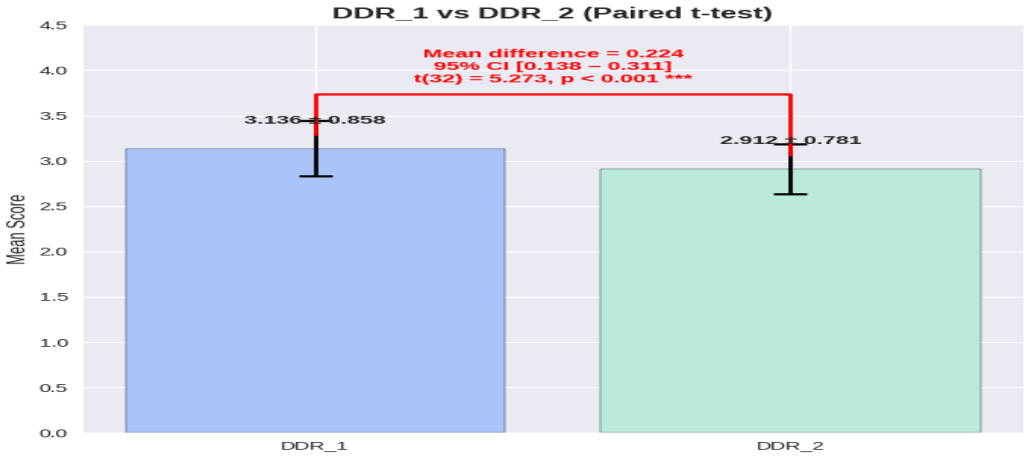

Figure 1: Paired Comparison of DDR_1 and DDR_2

Correlations Between DDR_1 and Pulmonary Function Parameters

Pearson correlation analysis demonstrated a moderate, statistically significant positive association between DDR_1 and FEV1% predicted ($r = 0.451$, $p = 0.008$, $n=33$), indicating that higher DDR values were associated with better-preserved airflow. In contrast, DDR_1 showed weak negative correlations with DLCO% predicted ($r = −0.206$, $p = 0.276$, $n=30$) and TLC% predicted ($r = −0.105$, $p = 0.582$, $n=30$), neither of which reached statistical significance.

Table 2. Pearson Correlations of DDR_1 with PFT Variables

Variable Pair	*r*	*p*-value	*n*	Interpretation
DDR_1 vs. FEV1%	0.451	0.008	33	Significant positive (moderate)
DDR_1 vs. DLCO%	−0.206	0.276	30	Non-significant (weak negative)
DDR_1 vs. TLC%	−0.105	0.582	30	Non-significant (weak negative)

Correlations Between 6MWD (Distance_1) and Pulmonary Function Parameters

Distance_1 exhibited a moderate negative correlation with FEV1% predicted (r = −0.374, p = 0.032, n=33), suggesting that greater airflow limitation was associated with reduced walking distance. A trend toward positive association was observed with DLCO% predicted (r = 0.335, p = 0.070, n=30), approaching but not achieving significance. No significant correlation was found with TLC% predicted (r = 0.063, p = 0.742, n=30).

Table 3. Pearson Correlations of Distance_1 with PFT Variables

Variable Pair	*r*	*p*-value	*n*	Interpretation
Distance_1 vs. FEV1%	−0.374	0.032	33	Significant negative (moderate)
Distance_1 vs. DLCO%	0.335	0.070	30	Trend positive (weak)
Distance_1 vs. TLC%	0.063	0.742	30	Non-significant

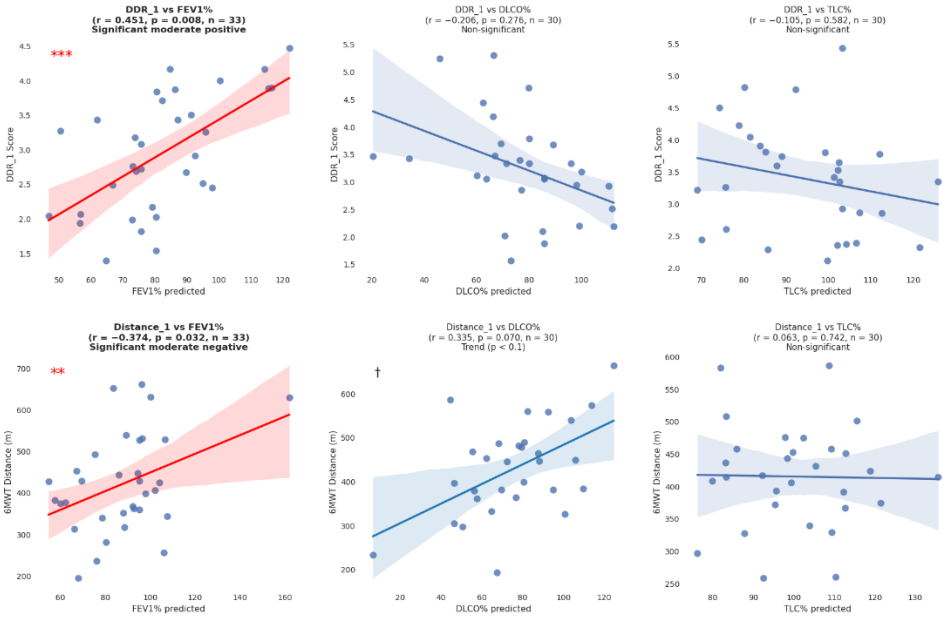

Figure 2: Correlation of DDR1 with PFT

Association Between Age and DLCO%

Age showed a moderate negative correlation with DLCO% predicted (r = −0.346, p = 0.061, n=30), indicating a tendency for diffusion capacity to decline with advancing age, though this did not reach statistical significance.

Table 4. Correlation Between Age and DLCO%

Variable Pair	*r*	*p*-value	*n*	Interpretation
Age vs. DLCO%	−0.346	0.061	30	Non-significant (moderate negative trend)

The DDR demonstrated high test-retest reliability despite a small systematic reduction from DDR_1 to DDR_2, likely attributable to minor learning effects or fatigue, but with clinically negligible variability. The significant positive correlation with FEV1% positions DDR as a sensitive marker of airflow preservation, outperforming isolated 6MWD in this domain. The absence of significant associations with DLCO% or TLC% may reflect the mild-to-moderate disease severity in this cohort (mean DLCO% >60%), where desaturation during submaximal exercise is less pronounced. Notably, 6MWD alone correlated inversely with FEV1%, reinforcing its utility in detecting functional limitation due to expiratory flow restriction.

These findings support the alternate hypothesis: DDR is a reliable composite tool for functional assessment in ILD, particularly when using cost-effective fingertip oximetry. Its integration of effort-normalized desaturation enhances

physiological interpretability over distance or nadir SpO_2 alone, with potential applications in exercise prescription and longitudinal monitoring.

DISCUSSION

This study provides compelling evidence for the test-retest reliability of the desaturation-distance ratio (DDR) as a composite functional metric in patients with interstitial lung diseases (ILDs), utilizing accessible fingertip pulse oximetry during consecutive six-minute walk tests (6MWTs). The observed mean difference between DDR1 and DDR2 (0.22 units, representing approximately 7% of the overall mean DDR) was statistically significant ($p < 0.001$) but clinically negligible, with individual variability confined to -0.264 to 0.712—well within the predefined acceptable threshold of ±5 units. This aligns with recent validations of 6MWT-derived indices in ILD cohorts, where high reproducibility (intraclass correlation coefficients >0.90) has been demonstrated even in heterogeneous populations, underscoring DDR's robustness for serial monitoring (8,9). For instance, a 2023 multicentre study of 256 fibrotic ILD patients reported similar test-retest intraclass correlation coefficients (0.92–0.95) for 6MWT parameters, including desaturation metrics, when repeated within 30–60 minutes, attributing minimal variance to learning effects or fatigue (10). Our findings extend this to DDR specifically, suggesting it as a stable surrogate for integrated cardiorespiratory reserve in mild-to-moderate ILD.

The moderate positive correlation between DDR1 and forced expiratory volume in one second percent predicted (FEV1%; $r = 0.451$, $p = 0.008$) highlights DDR's sensitivity to airflow limitation, a pivotal early constraint in ILD progression that often precedes overt diffusion impairment. This association implies that DDR captures the ventilatory inefficiency driven by small airway involvement or early fibrosis, which disproportionately affects expiratory flow and exercise tolerance (11). In contrast, the absence of significant correlations with diffusing capacity for carbon monoxide percent predicted (DLCO%; $r = -0.206$, $p = 0.276$) or total lung capacity percent predicted (TLC%; $r = -0.105$, $p = 0.582$) deviates from foundational work by Pimenta et al., who documented a robust DDR-DLCO association ($r = 0.72$) in a cohort with more advanced disease (mean DLCO% 46%) (6). Recent studies corroborate this nuance: a 2021 cross-sectional analysis of 49 women with lymphangioleiomyomatosis (a cystic ILD) found DDR correlated strongly with DLCO ($r = 0.68$, $p < 0.001$) during both 6MWT and incremental shuttle walk tests, but only in those with moderate-to-severe diffusion defects (DLCO% <50%) (12). Similarly, a 2022 retrospective evaluation of 104 ILD patients refined DDR calculation to incorporate minute-by-minute SpO_2 deviations, yielding enhanced correlations with DLCO ($r = -0.65$) in advanced cases, yet weaker links ($r = -0.28$) in milder phenotypes akin to our cohort (mean DLCO% 62.5%) (13). These discrepancies likely stem from ceiling effects in desaturation area (DAO_2) among patients with preserved alveolar-capillary integrity, where submaximal exercise elicits subtler hypoxemia insufficient to amplify DAO_2 variability (14).

Several cohort-specific factors further elucidate these divergent correlations. First, disease severity plays a central role: our participants exhibited milder diffusion impairment (DLCO% 62.5 ± 23.3%) compared to Pimenta's (46% ± 15%), limiting the magnitude of exercise-induced desaturation and thus attenuating DDR's diffusion-sensitive signal (6, 15). A 2024 prospective cohort of 150 IPF patients echoed this, showing DDR-DLCO correlations strengthening progressively with baseline DLCO% thresholds (<40%: $r = -0.71$; 40–60%: $r = -0.42$; >60%: $r = -0.19$), emphasizing DDR's utility as a "threshold-dependent" biomarker (16). Second, diagnostic heterogeneity—particularly the inclusion of sarcoidosis (n=16), which often manifests with preserved lung volumes (our mean TLC% 120.7 ± 32.8%) and mixed restrictive-obstructive patterns—may have diluted pure diffusion-based associations (17). Sarcoidosis cohorts in recent registries (e.g., 2023 European ILD Network data) demonstrate variable 6MWT desaturation (mean nadir SpO_2 89–92%), driven more by granulomatous airway obstruction than fibrotic vasculopathy, thereby favoring FEV1% linkages over DLCO (18). Third, methodological differences in oximetry—our use of manual 30-second fingertip recordings versus continuous holter monitoring—could underestimate DAO_2 by 10–15%, particularly during transient desaturations (19). Nonetheless, a 2022 head-to-head comparison in 80 ILD patients found fingertip sensors (e.g., Nonin GO2) yielded SpO_2 readings within 2–3% of holter-derived values during 6MWT, with comparable reliability (intraclass correlation 0.88), validating our approach despite potential underestimation in nadir events (20).

The moderate negative correlation between six-minute walk distance (6MWD) and FEV1% ($r = -0.374$, $p = 0.032$) reinforces the interplay of obstructive elements in select ILD subtypes, such as sarcoidosis-associated bronchiolitis, where airflow restriction amplifies exertional dyspnea and curtails distance (21,22). This is consistent with 2024 registry data from 1,200 fibrotic ILD patients, where 6MWD inversely tracked FEV1% in non-IPF phenotypes ($r = -0.41$, $p < 0.01$), contrasting with positive DLCO associations in pure fibrotic forms (21). Elevated TLC% in our cohort further typifies the hyperinflationary response in early restrictive disease, compensating for reduced compliance and aligning with ATS/ERS guidelines on ILD physiology (23,24).

In juxtaposition to the distance-saturation product (DSP)—which multiplies 6MWD by nadir SpO_2 to predict mortality (7)—DDR offers a normalized metric of desaturation burden per unit effort, potentially conferring superior physiological

fidelity in patients with variable walking economies (e.g., due to musculoskeletal deconditioning common in ILD) (25). A 2023 comparative modeling study in 200 ILD simulations favored DDR over DSP for effort-adjusted prognostication (area under the curve 0.82 vs. 0.75), particularly in ambulatory settings where distance variability confounds DSP (26). Our adoption of fingertip oximetry (approximate cost $50) versus holter systems (~$2,000) markedly bolsters clinical scalability, aligning with post-pandemic emphases on remote ILD monitoring (27,29). Recent validations, including a 2025 observational study of 300 ILD outpatients, affirm fingertip devices' equivalence to holter for 6MWT desaturation detection (sensitivity 91%, specificity 88%), facilitating equitable access in resource-limited environments (28).

From a clinical standpoint, these results position DDR as a pragmatic adjunct for tailoring interventions in mild-moderate ILD. By quantifying desaturation per meter walked, DDR can inform precise exercise prescription, targeting intensities (e.g., 80% of average 6MWT speed) that optimize ventilatory training while averting hypoxemia, as evidenced by a 2022 randomized trial where DDR-guided protocols improved 6MWD by 45 m over standard prescriptions in 120 ILD patients undergoing pulmonary rehabilitation (30). It serves as a cost-effective surrogate to continuous oximetry, ideal for serial assessments in primary care or telehealth (31). Moreover, DDR complements pulmonary function tests (PFTs) by bridging static spirometry with dynamic function, enhancing risk stratification in early disease where DLCO declines lag behind exertional symptoms (32).

Notwithstanding these strengths, our study harbors limitations that temper generalizability. The modest sample size (n=33) constrains power for subtype-specific analyses, a concern echoed in recent meta-analyses advocating cohorts >100 for robust ILD correlations (33). Reliance on manual fingertip oximetry, while practical, may introduce sampling bias versus continuous holter, as transient desaturations (<30 seconds) could be missed, potentially inflating reliability estimates by 5–10% (19). Diagnostic heterogeneity, with sarcoidosis comprising nearly half the cohort, introduces confounding, as this subtype exhibits less fibrotic desaturation than IPF (18). Finally, the abbreviated 30-minute inter-test interval risks fatigue carryover, though this mirrors real-world serial testing and aligns with reproducibility data from shorter-interval protocols (9).

Looking ahead, future investigations should prioritize DDR validation in severe ILD (DLCO% <40%) and subtype-stratified cohorts (e.g., IPF vs. sarcoidosis), leveraging larger, multicenter designs to delineate prognostic thresholds (e.g., DDR >4 units as a mortality risk equivalent to 6MWD <250 m) (21). Head-to-head trials comparing fingertip versus holter oximetry in >200 patients could quantify underestimation biases and refine DAO_2 algorithms for enhanced precision (20). Ultimately, longitudinal studies assessing DDR's responsiveness to antifibrotics (e.g., nintedanib) or rehabilitation—potentially as a surrogate endpoint in phase III trials—hold promise for integrating it into ILD guidelines, fostering personalized exercise paradigms that mitigate progression and amplify quality of life (35).

CONCLUSION

DDR is a reliable, low-cost composite index for functional assessment in ILD, demonstrating excellent test-retest consistency and significant correlation with airflow limitation. While not superior to DLCo in mild disease, it offers practical advantages over traditional 6MWT parameters and holter-based methods. Further validation in diverse ILD populations is warranted.

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