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Association of Single Breath Carbon Monoxide Diffusion Capacity with Exercise-Induced Oxygen Desaturation: Differences amongst Obstructive and Restrictive Respiratory Disorders

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Abstract

Background: While reduced DLCO is associated with impaired oxygenation, its relationship to exercise-induced oxygen desaturation (EID) across different lung disease phenotypes remains incompletely characterized. This study aimed to evaluate the association between DLCO and EID across obstructive, restrictive, and normal lung physiologies, and assess its utility and other pulmonary functions as identifying clinically significant EID. **Methods:** Of 600 patients screened, 196 adults underwent complete pulmonary function testing and exercise desaturation studies performed within six months. EID was defined as ≥4% decrease in oxygen saturation. Linear regression models assessed associations between desaturation and DLCO, adjusting for age, sex, ethnicity, height, smoking history, and disease classification. Receiver operating characteristic (ROC) curve analyses were performed to evaluate discriminatory ability of DLCO and other PFTs for predicting EID. **Results:** Higher DLCO values were significantly associated with smaller decreases in oxygen saturation during exercise. After adjustment, each 1-L increase in DLCO was associated with a 0.14% smaller desaturation ($p < 0.001$), and each 1% increase in percent predicted DLCO corresponded to a 0.035% smaller desaturation ($p < 0.001$). No significant interaction was observed between DLCO and lung disease classifi-

cation or smoking history. DLCO moderately associated with desaturation ($r = -0.35$, $p < 0.001$). ROC analyses showed modest discriminatory performance for DLCO, comparable to TLC and FVC; other pulmonary function variables performed less well. **Conclusions**: DLCO is inversely associated with EID across obstructive, restrictive, and normal lung function patterns. However, DLCO and other PFTs demonstrate only a modest association with clinically significant desaturation amongst disease categories.

Keywords

Desaturation Study, Diffusion Capacity, Exercise-Induced Hypoxemia, Gas Transfer, Obstructive Respiratory Disorders, Restrictive Respiratory Disorders, Ventilation-Perfusion Relationships

1. Introduction

The single breath diffusing capacity of carbon monoxide (DLCO) is commonly used as an indicator of gas transfer from alveoli to pulmonary capillaries. It is used to distinguish parenchymal involvement in obstructive lung diseases such as emphysema from chronic bronchitis, restrictive disorders such as interstitial lung disease (ILD) from neuromuscular disease and thoracic cage disorders, and to evaluate for pulmonary vascular disease. Few studies have attempted to compare the association of DLCO to desaturation during exercise amongst obstructive and restrictive disorders [1]-[11]. An association between DLCO and desaturation during exercise has the potential to be a useful screening tool for all patients undergoing routine pulmonary function testing (PFT) to see who would be at higher risk for desaturation on exercise and would require further testing.

While impaired gas transfer regardless of ventilatory mechanics plays a key role in causing hypoxemia, little is known about the differences in impact of impaired gas transfer on hypoxemia across different pulmonary pathologies. Gas transfer during exercise may vary amongst individuals with obstructive versus restrictive disorders because of different ventilation-perfusion relationships. For example, the relative increase in physiologic dead space due to gas trapping in COPD patients may exert a greater influence on exercise-induced desaturation than in patients with restrictive disorders [8] [9] [11]. The main objective of this study was to determine the association between degree of exercise-induced desaturation and DLCO and compare associations amongst cohorts with different pulmonary disease diagnoses. A secondary objective was to identify and compare other potential indices associated with exercise-induced oxygen desaturation in individuals with obstructive and restrictive disorders.

2. Methods

2.1. Patients

This single center retrospective cross-sectional study examined the association be-

tween exercise-induced oxygen desaturation and lung diffusion capacity of carbon monoxide (DLCO). The study population consisted of 600 patients at Los Angeles General Medical Center's chest clinic. One hundred ninety-six patients with complete pulmonary function tests (PFTs) and a desaturation study done within a period of 6 months were included in the study (**Figure 1**). The investigation was approved by the institutional review board of the University of Southern California Health Sciences Center (HS-24-00110).

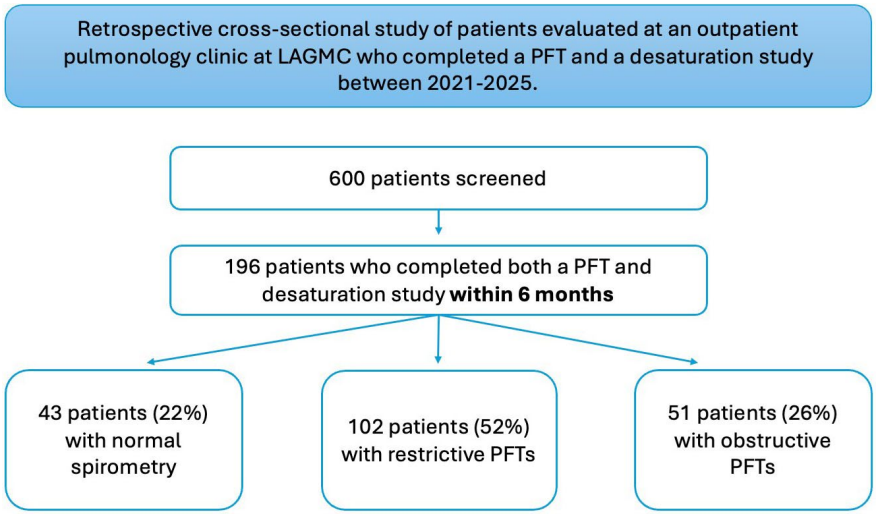


Figure 1. Flow chart of study groups.

2.2. Testing Methods

Data were collected in stable patients aged 18 - 80 years with obstructive and restrictive criteria based on American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines [12]. Patients with neuromuscular disorders, left ventricular heart failure, and those unable to perform lung function testing according to ATS/ERS guidelines were excluded. Patient characteristics included age, gender, height, weight, BMI, ethnicity, lung disease diagnosis, smoking history. Pulmonary function testing (PFT) was performed from January 1, 2021 to October 1, 2025. Testing was performed in seated patients, consisting of post-bronchodilator spirometry, lung volume subdivisions measured by body plethysmography, and DLCO (adjusted for hemoglobin) in ml/min/mmHg, and DLCO adjusted for alveolar volume, VA (DLCO/VA), according to American Thoracic Society guidelines [6] [12]. Patients receiving supplemental oxygen were placed on room air for five minutes before performing pulmonary function testing. Peripheral pulse oximetry (SpO_2) was measured with a Masimo ROOT with RAD-7 oximeter (Masimo, Irvine, CA) using a forehead sensor. The criteria for airways obstruction was a post-bronchodilator ratio of forced expiratory volume at one second (FEV1) to forced vital capacity (FVC) less than 0.7 [12]. The criteria for restrictive lung disease were an FEV1 less than 80% predicted and an FEV1/FVC greater than or equal to 0.7 [12]. Predicted values for spirometry indices, lung volumes, and

DLCO were from Schoenberg *et al.* [13], Crapo *et al.* [14] and Knudson *et al.* [15], respectively.

Desaturation studies were performed from January 1, 2021 to October 1, 2025. Patients were asked to walk along a hallway at their own pace for six minutes while SpO_2 and heart rate were monitored. If initial SpO_2 at rest on room air was less than or equal to 88%, they were tested while breathing oxygen at 2 L/min (approximate FiO_2 0.3) by nasal canula. SpO_2 was recorded in most cases with a forehead sensor. Whether the test was performed while the patient was breathing room air or required supplemental oxygen because of a resting SPO_2 of <88% on room air, the lowest SPO_2 recorded during walking was used for analysis. Desaturation was defined as a decrease in SpO_2 by 4% or more during exercise [7] [9].

2.3. Statistical Analysis

DLCO, DLCO corrected for alveolar volume (DL/VA), and other PFT variables (FVC, RV, TLC, FEV_1, FEV_1/FVC) were analyzed as continuous variables and modeled both as absolute values and as percent predicted values (accounting for age, sex, ethnicity, and height). The primary outcome was net oxygen desaturation with exercise.

Initial diagnostic evaluation of linear regression models visually revealed potentially influential outliers. Thus, robust linear regression models using MM-estimation were used to reduce the influence of extreme values. Robust models assessed the association between exercise-induced desaturation (dependent variable) and DLCO as well as DL/VA (independent variables), adjusting for the following covariates: adjusting for age, sex, ethnicity, height, smoking history, and lung disease classification (normal, restrictive, obstructive). As a sensitivity analysis, ordinary least squares (OLS) regression models were also fitted to assess stability of estimates.

Potential effect modification was assessed by including interaction terms between DLCO or DL/VA and (1) lung disease classification, and (2) smoking history in separate adjusted robust models. Interaction terms were evaluated individually to test whether the association between DLCO or DL/VA and desaturation differed across these groups. Non-significant interactions were removed from final models, and covariates were retained as adjustment variables.

Spearman rank correlation coefficients were calculated to provide a nonparametric assessment of monotonic association between DLCO and desaturation, given the presence of mild outliers and potential non-normality. Similar regression models and correlations were evaluated for DL/VA and desaturation.

Missing values were excluded from analysis, and regression model assumptions were evaluated using diagnostic plots of residuals. Benjamini-Hochberg was used to correct for multiple hypothesis testing over regression models. Receiver operating characteristic (ROC) analyses were conducted for each PFT to estimate sensitivity, specificity, and area under the curve (AUC) for predicting ≥4% desaturation. Sensitivity and specificity were calculated at the optimal Youden threshold

for each PFT. All analyses were conducted in R Version 4.5.2 (R Foundation for Statistical Computing, Vienna, Austria) and a p-value ≤ 0.05 was considered statistically significant.

3. Results

3.1. Study Population

Baseline and clinical characteristics are described using median and interquartile range (IQR) for continuous variables and count with frequency for categorical variables (Table 1). Across all subgroups of lung disease, the median age was 59.5 years (IQR 50 - 67 years) with a larger proportion of females (56%). A majority were Hispanic (84%) and most of the population did not have a history of smoking (60%). Twenty-two percent of the cohort was classified as having normal lung function, compared to 52% classified as having restrictive and 26% as having obstructive disorders. Seven patients (16%) with normal lung spirometry experienced desaturation of SpO_2 of 4% or more; 51 patients (50%) with restrictive lung spirometry and 18 patients (35%) with obstructive lung spirometry experienced desaturation.

Table 1. Study population characteristics by lung disease classification.

Variable	N	Normal N = 43[1]	Restrictive N = 102[1]	Obstructive N = 51[1]	Overall N = 196[1]
Age (years)	196	62 (49, 69)	56 (49, 64)	64 (55, 70)	59.5 (50, 67)
Gender	196				
Female		30 (70%)	56 (55%)	24 (47%)	110 (56%)
Male		13 (30%)	46 (45%)	27 (53%)	86 (44%)
Ethnicity	196				
Hispanic		38 (88%)	93 (91%)	34 (67%)	165 (84%)
Non-Hispanic		5 (12%)	9 (8.8%)	17 (33%)	31 (16%)
Smoking History	196				
No		30 (70%)	69 (68%)	19 (37%)	118 (60%)
Yes		12 (28%)	31 (30%)	31 (61%)	74 (38%)
Unknown		1 (2.3%)	2 (2%)	1 (2%)	4 (2%)
DLCO (ml/min/mmHg)	196	15.1 (10.9, 20.7)	11.2 (7.8, 14.9)	11.8 (10.1, 15.2)	12.2 (9.1, 15.8)
DLCO (%)	196	68 (58, 85)	51 (38, 68)	60 (45, 77)	59 (44, 72)
DL/VA (ml/min/mmHg/L)	196	4.2 (3.3, 4.9)	3.7 (2.6, 4.4)	4.2 (3.3, 4.8)	4.1 (3.1, 4.7)
DL/VA (%)	196	101 (82, 119)	90 (68, 117)	95 (80, 116)	95 (78.5, 116.5)
FVC (L)	196	2.7 (2.1, 3.4)	2.0 (1.7, 2.4)	2.2 (1.7, 2.6)	2.1 (1.8, 2.7)
FVC (%)	196	90 (83, 100)	61 (50, 71)	65 (54, 82)	69.5 (56, 83)
RV (L)	195	1.7 (1.2, 1.8)	1.3 (1.0, 1.6)	2.6 (2.0, 3.6)	1.5 (1.2, 2.1)

Continued

Missing		0	1	0	1
RV (%)	195	98 (81, 110)	76 (65, 94)	157 (121, 189)	94 (71, 122)
Missing		0	1	0	1
TLC (L)	195	4.3 (3.9, 5.3)	3.4 (2.7, 4.0)	4.9 (4.2, 6.5)	4.0 (3.1, 4.8)
Missing		0	1	0	1
TLC (%)	195	95 (89, 105)	69 (60, 77)	106 (88, 120)	79 (67, 101)
Missing		0	1	0	1
FEV1 (L)	196	2.3 (1.7, 2.7)	1.6 (1.3, 2.0)	1.2 (1.0, 1.5)	1.6 (1.3, 2.0)
FEV1 (%)	196	99 (86, 107)	67 (53, 76)	43 (37, 63)	69 (49, 84)
FEV1/FVC	196	80 (76.3, 83)	83 (79, 87)	53 (47, 66)	79.5 (70, 85)

[1]Median (Q1, Q3); n (%).

Two of 43 patients (5%) with normal lung spirometry exhibited an SpO_2 of less than or equal to 88%, requiring supplemental oxygen at baseline. The average SpO_2 of all patients with normal lung spirometry on room air was 98.7% (SD 2.9%). In comparison, 11 out of 51 patients (22%) with obstructive lung spirometry had an SpO_2 less than or equal to 88% requiring supplemental oxygen at baseline, with an average SpO_2 on room air of 97.7% (SD = 3.2). Twenty of 102 patients (20%) with restrictive lung spirometry exhibited an SpO_2 less than or equal to 88% requiring supplemental oxygen at baseline, with an average SpO_2 on room air of 97.5 percent (SD 3.5). There was no statistical difference in baseline SpO_2 on room air between the three groups ($p = 0.1$).

3.2. DLCO vs. Desaturation; Disease Classification and Effects of Smoking

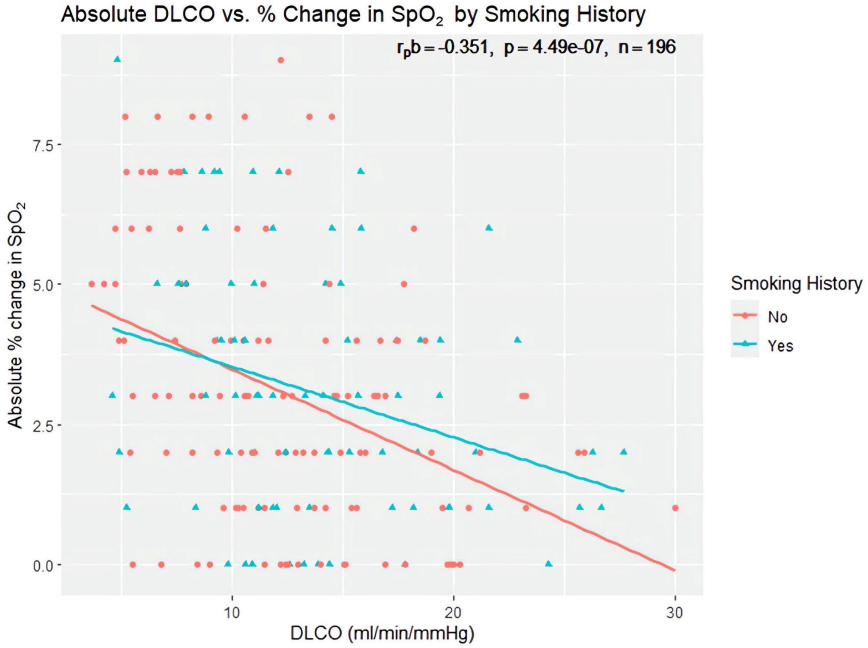
Table 2 summarizes the associations between exercise-induced oxygen desaturation and DLCO. Higher DLCO values were significantly associated with smaller decreases in oxygen saturation during exercise. After adjusting for age, sex, ethnicity, height, smoking history, and lung disease classification, each unit increase in DLCO (in ml/min/mmHg) was associated with a 0.14% smaller desaturation (adjusted $\beta = -0.14$, 95% CI: −0.21 to −0.07, $p < 0.001$). With percent predicted DLCO, each 1% increase corresponded to a 0.04% decreased desaturation (adjusted $\beta = -0.04$, 95% CI: −0.05 to −0.017, $p < 0.001$). Spearman correlation revealed a statistically significant negative correlation between DLCO and desaturation (Figure 2; rho = −0.35, $p < 0.001$).

Tests for interaction between DLCO and lung disease classification were not statistically significant, indicating that the association between DLCO and desaturation did not significantly differ across lung disease subgroups. This association also did not significantly differ across smoking history subgroups. Both variables were retained as covariates in the final adjusted models (Figure 2).

Table 2. Estimated associations between DLCO and desaturation.

Independent Variable	Unadjusted Coefficient β (95% CI)	p-value	Adjusted Coefficient β (95% CI)*	Adjusted p-value
DLCO (ml/min/mmHg)	−0.154 (−0.207, −0.102)	<0.001	−0.140 (−0.212, −0.067)	<0.001
DLCO (% predicted)	−0.043 (−0.058, −0.027)	<0.001	−0.035 (−0.053, −0.017)	<0.001

*Beta estimates from robust linear regression models after adjusting for age, sex, ethnicity, height, smoking history, and lung disease classification.



Absolute DLCO vs. % Change in SpO_2 by smoking history showing a statistically significant moderate relationship between DLCO and desaturation ($r_pb = -0.35$, $p < 0.001$). No statistically significant difference was found between smoking and non-smoking groups.

Figure 2. Robust correlation between DLCO and desaturation by smoking history.

3.3. DL/VA vs. Desaturation

Table 3. Estimated associations between DL/VA and desaturation.

Independent Variable	Unadjusted Coefficient β (95% CI)	p-value	Adjusted Coefficient β (95% CI)*	Adjusted p-value
DL/VA (ml/min/mmHg/L)	−0.275 (−0.552, 0.001)	0.05	−0.135 (−0.406, 0.136)	0.33
DL/VA (%)	−0.007 (−0.017, 0.004)	0.20	−0.003 (−0.013, 0.006)	0.48

*Beta estimates from robust linear regression models after adjusting for age, sex, ethnicity, height, smoking history, and lung disease classification.

DL/VA demonstrated an inverse association of borderline significance with de-

saturation; however, this association was not statistically significant after adjustment for covariates (adjusted $\beta = -0.135$; 95% CI, −0.406 to 0.136; p = 0.33, Table 3). Similarly, percent predicted DL/VA was also not significantly associated with desaturation (adjusted $\beta = -0.003$; 95% CI, −0.013 to 0.006; p = 0.48). Spearman correlation demonstrated a non-significant inverse association between DL/VA and exercise-induced desaturation (rho = −0.11, p = 0.15; n = 192).

3.4. Sensitivity Analysis

Sensitivity analyses using ordinary least squares (OLS) regression demonstrated that results were largely consistent with the primary robust regression models (Table A1 and Table A2, **Appendix**). For absolute DLCO, the adjusted coefficient differed by approximately 1% between robust and OLS models ($\beta = -0.140$ vs −0.138), indicating minimal influence of extreme observations. DLCO percent predicted showed a modest difference of approximately 11%, although statistical significance and direction of association were unchanged. For absolute DL/VA, the adjusted coefficient differed by approximately 15% between models ($\beta = -0.135$ vs −0.155), suggesting mild sensitivity to influential observations; however, inference remained non-significant in both specifications. Differences for DL/VA percent predicted were small in absolute magnitude despite a larger relative percentage change. Overall, conclusions were consistent across modeling approaches, and robust regression results are presented as the primary estimates given their reduced sensitivity to influential observations.

3.5. Analysis of Predictive Ability

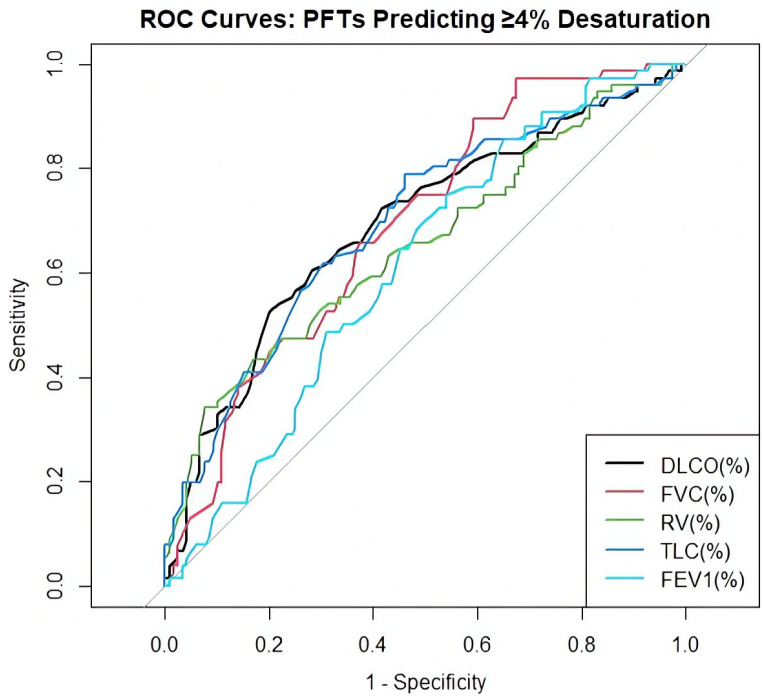
Receiver operating characteristic (ROC) analysis amongst lung volumes demonstrated weak to moderate discrimination for predicting ≥4% desaturation (Table 4 and Figure 3). TLC and DLCO demonstrated the highest overall discrimination (AUC = 0.70 and 0.69, respectively), followed closely by FVC (AUC = 0.69). In contrast, RV and FEV1 showed weaker moderate discrimination (AUC = 0.65 and 0.61), whereas DL/VA appeared to show limited discriminatory ability (AUC = 0.57). Sensitivity and specificity varied substantially by test: FVC, TLC, FEV1, and DL/VA demonstrated higher sensitivity (0.89, 0.79, 0.75, 0.58, respectively), whereas DLCO and RV achieved higher specificity (0.80 and 0.92). These patterns suggest that while no individual PFT provided strong discrimination, TLC, DLCO, and FVC showed comparable and moderately better performance than DL/VA, RV, or FEV1 in identifying individuals who desaturated during exercise.

Table 4. Sensitivity, specificity, and AUC for PFTs.

Pulmonary function variable	Sensitivity	Specificity	Threshold	AUC (95% CI)
DLCO (%)	0.53	0.80	48.5	0.69 (0.61, 0.77)
DL/VA (%)	0.58	0.56	94.5	0.57 (0.49, 0.65)

Continued

FVC (%)	0.89	0.41	78.5	0.69 (0.62, 0.76)
RV (%)	0.34	0.92	66.5	0.65 (0.57, 0.73)
TLC (%)	0.79	0.54	88.5	0.70 (0.62, 0.77)
FEV1 (%)	0.75	0.46	75	0.61 (0.53, 0.69)



ROC curve analysis—TLC and DLCO demonstrated the highest overall discrimination (AUC = 0.70 and 0.69, respectively), followed closely by FVC (AUC = 0.69). In contrast, RV and FEV1 showed weaker performance (AUC = 0.65 and 0.61).

Figure 3. ROC curves for PFTs.

4. Discussion

The key findings of this study were: (a) Higher DLCO values were significantly associated with smaller decreases in oxygen saturation during exercise, (b) there was a moderate relationship between DLCO and desaturation, and (c) amongst functional indices, TLC, DLCO, and FVC moderately better identified individuals who desaturated during exercise.

4.1. Association between Desaturation with DLCO, and Other Functional Variables

DLCO exhibited a modest association with exercise-induced desaturation. With a cutoff of 48.5% predicted, DLCO was 53% sensitive and 80% specific for predicting desaturation of greater than 4% and an AUC of only 0.69. These findings are concordant with Hadeli *et al.* [11] who found that a DLCO of 62% predicted was only 75% sensitive and specific for predicting desaturation in a cohort of 8000

patients. Amongst PFTs, lung volumes and flows are not considered predictive of exercise-induced oxygen desaturation [9] [11] [16].

Generally, any variable with a ROC AUC of greater than 0.8 is considered to have good predictive potential. Other studies have shown a stronger predictive potential of DLCO [1] [16]-[19]. In a study of 80 patients with systemic sclerosis-related lung disease, Someya *et al.* [18] found that a DLCO of 56% or less predicted was highly predictive of desaturation, with an ROC curve analysis demonstrating 0.92 AUC, a sensitivity of 83%, and a specificity of 86%. In 48 patients with chronic obstructive pulmonary disease (COPD) Owens [9] found that a DLCO greater than 55% predicted was 82% sensitive and 100% specific for excluding desaturation during exercise. Kelley *et al.* [17] evaluated a cohort of 106 patients with interstitial lung disease and found that DLCO <50% predicted was 89% sensitive and 93% specific for detecting a desaturation.

There are several potential explanations for our discordant results. For instance, our study of nearly 200 patients is larger than most that have examined this relationship. [8]-[10] [17]. Previous studies examined patients with specific disease processes in isolation, such as COPD [10] or connective tissue disease-associated interstitial lung disease (CTD-ILD) [8] [16] [18] and cystic fibrosis [19]. Our initial analysis examined all patients as one group regardless of the disease process to determine the predictive potential of pulmonary function testing for a more generalized population. Additionally, the definition of desaturation varies in previous studies between 3% and 4% [11] [17] [20]. The American Thoracic Society defines desaturation as a decrease in SpO_2 of 4% or more [20]. Having used a SPO_2 cutoff of 4% decrease in this study, it may be difficult to compare some historical results with ours. While some studies [11] [17] report specific DLCO cutoffs with strong sensitivities and specificities, they do not provide receiving operating characteristic curve analysis, a more robust indicator of predictive potential as it indicates performance across all cutoffs.

Our results suggest that FVC, RV, and FEV1 are less closely associated with desaturation than DLCO, in keeping with studies that found other PFTs to be less or equally predictive as DLCO [9]-[11] [18] [19]. These lung volumes vary with structural changes such alveolar-capillary membrane thickness, alveolar volume, small airway dysfunction and dead space, with differing effects on exercise-induced hypoxemia.

4.2. Desaturation amongst Subgroups

We found no significant differences in degree of exercise-induced desaturation across different lung disease subgroups (restrictive versus obstructive). While obstructive and restrictive diseases can cause hypoxemia from different mechanisms (such as increased dead space in obstructive diseases [V/Q >1], and other impaired ventilation/perfusion matching [V/Q <1] in restrictive parenchymal lung disease), that the relationship between DLCO and desaturation exhibited no significant differences across different pathologies highlights DLCO as an independ-

ent marker of gas transfer across the alveolar-capillary membrane regardless of the mechanism of ventilation-perfusion mismatch.

In addition to DLCO, TLC and FVC exhibited a higher sensitivity for predicting desaturation. Increase in alveolar surface area associated with larger lung volumes enhance gas transfer across the alveolar-capillary membrane [1] [2] [5]-[7]. That said, while PFTs distinguish lung disease subgroups under resting conditions, breathing pattern changes during exertion [21]. Individuals with normal lung function compensate for increased metabolic demand by increasing minute ventilation and recruiting and/or dilating pulmonary capillaries; those with respiratory pathology cannot do so given mechanical restraints based on respective physiologies [22].

4.3. Association of DL/VA with Desaturation

While we observed a significant inverse relationship between DLCO and degree of exercise-induced desaturation we found no significant relationship between DL/VA and degree of desaturation. DL/VA (sometimes also referred to as KCO [23]) adjusts gas transfer according to the difference between TLC and dead space (=alveolar volume) and includes the effects of changes in pulmonary capillary blood volume, factors that induce variability in response to exercise and depend on the relative degrees of disease-induced parenchymal and vascular changes [1]-[4] [8] [23]. Variability in DL/VA amongst subgroups may also have accounted for the decrease in the discriminatory ability of DL/VA for desaturation. We did not adjust for VA in the determination of DLCO and KCO. By adjusting for VA, Johnson [23] showed that KCO and DLCO are inversely related in healthy subjects. Unadjusted DLCO and KCO % predicted values often differ; values adjusted for VA are nearly identical. Discrepancies arise from using prediction formulas based on normal subjects holding their breath near TLC. In patients with interstitial lung disease, the arterial oxygen tension during exercise correlates well with DLCO and KCO when adjusted for alveolar volume <80% [23] [24]. In our study, not adjusting for VA may have contributed for the association of DLCO with exercise-induced desaturation but not in the case for DL/VA.

Kaminsky *et al.* [1] compared the diagnostic utility of DLCO and DLCO/VA for predicting exercise-induced desaturation by comparing their respective ROC curves in a retrospective review of patients who had concurrent measurement of diffusing capacity and exercise oximetry. They showed that DLCO exhibited a slightly better ability to predict oxygen desaturation than DLCO/VA, with a cut-off of normal being 55% predicted. However, when the DLCO and DLCO/VA were adjusted for VA, neither measure outperformed the other in terms of predicting oxygen desaturation, with both measures exhibiting equally poor positive predictive value in the 50% - 70% range [1].

4.4. Effects of Smoking on Desaturation

We found no statistically significant difference between smoking and non-smok-

ing groups (Figure 2). Carboxyhemoglobin can influence the uptake of CO by producing an "anemia effect" influence the uptake of CO by producing an "anemia effect" and by decreasing the driving pressure for CO transport from alveolus into the capillary blood [5] [6]. While smoking is known to cause V/Q mismatching it failed to show a significant impact on changing the relationship between DLCO and degree of desaturation, suggesting DLCO can be used as a generalized marker of lung physiology irrespective of exposure history or underlying disease classification [25]. DLCO adjusted for CO is not significantly decreased in smokers without additional underlying pathology that would impair gas exchange (*i.e.*, emphysema, pulmonary fibrosis) [26] [27]. DLCO reflects only a component of V/Q mismatch, as seen in previous literature correlating V/Q scanning and positron emission tomography/computed tomography with PFTs [28].

5. Strengths and Limitations

Our study has strengths. It comprises a larger sample size compared with previous studies [8]-[10] [17], analysis of both lung disease subgroups and our data set as a whole, and advanced statistical methods including ROC curve analysis which is absent from some previous studies [11] [17] [18]. The pulse oximeter used in this study, the Masimo Root, has a root mean square error (derived from calculations of bias and precision) of 1.95, comparable to other models [29]. Utilizing the Massey-Martin scale to assess the impact of skin color on the accuracy of one pulse oximetry device, a recent study of this device and another oximeter [30] found differences in arterial oxygen saturation (SaO_2) and SpO_2 to be within the expected range of error of the devices and not clinically significant.

This study also had limitations. It was a single center retrospective study. Another is that we used pre-Global Lung Function Initiative (GLI)/ATS reference values for classifying PFT patterns, such as an FEV1/FVC ratio of less than 0.7 to indicate obstructive pathology. These traditional methods have limitations, including the inability to account for normal changes in lung function with aging that are better captured in the GLI equations that utilize Z scores [31]. Additionally, since original methodologies for PFT interpretation were based on data collected from predominantly Caucasian individuals, our predominantly Hispanic population can be misclassified using these methods.

6. Conclusion and Future Directions

Our study shows a strong inverse relationship between DLCO and the magnitude of exercise-induced oxygen desaturation. This relationship did not significantly vary amongst different lung disease subgroups or by smoking history. However, our findings also reveal a modest predictive potential of certain lung volumes, and DLCO, for patients who desaturate more than 4% with exercise. These results support the continued use of complete PFTs and desaturation studies in the evaluation of patients with lung disease as both provide unique clinical data. As our study failed to demonstrate any meaningful difference between lung disease sub-

groups, we suggest that other predictors of desaturation should be investigated, such as advanced CT methods including parametric response mapping [32], which can distinguish different COPD phenotypes (emphysematous vs. small airway disease) based off CT imaging comparing inspiratory and expiratory scans, not relying on spirometry. Parametric response mapping in lung transplant patients has been used to assess airway changes, however not specifically those with ILD [33]. Yang *et al.* [34] showed that in some instances, CT defined pathologies (namely emphysema), has been linked to exercise induced desaturation, a tool that has the potential to be used to predict desaturation. Further investigation needs to be conducted to examine this relationship with other pulmonary pathologies.

Author Contributions

Dr. Karim Merchant collated and gathered data; submitted the protocol and design of the study to the institutional review board. Dr. Ryan Williams collated and arranged data. Dr. Austin Lee collated and arranged data; wrote the initial draft of the manuscript. Dr. Tracy Chen performed the statistical analysis. Mr. Darren May extracted the raw data of patients who underwent both desaturation and pulmonary function studies to be collated and analyzed by others. Dr. Ahmet Baydur conceived of the project and directed other members in their roles.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

Table A1. Sensitivity analyses using ordinary least squares (OLS) regression for DLCO.

Independent Variable	Unadjusted Coefficient β (95% CI)	p-value	Adjusted Coefficient β (95% CI)*	Adjusted p-value
DLCO (ml/min/mmHg)	−0.156 (−0.214, −0.098)	<0.001	−0.138 (−0.211, −0.066)	<0.001
DLCO (%)	−0.038 (−0.053, −0.023)	<0.001	−0.031 (−0.048, −0.015)	<0.001

*Beta estimates from linear regression models after adjusting for age, sex, ethnicity, height, smoking history, and lung disease classification.

Table A2. Sensitivity analyses using ordinary least squares (OLS) regression for DL/VA.

Independent Variable	Unadjusted Coefficient β (95% CI)	p-value	Adjusted Coefficient β (95% CI)*	Adjusted p-value
DL/VA (ml/min/mmHg/L)	−0.293 (−0.582, 0.004)	0.05	−0.155 (−0.469, 0.158)	0.33
DL/VA (%)	−0.007 (−0.019, 0.003)	0.17	−0.004 (−0.016, 0.007)	0.47

*Beta estimates from linear regression models after adjusting for age, sex, ethnicity, height, smoking history, and lung disease classification.