HIV is Associated with Worse Pulmonary Diffusing Capacity Independent of Emphysema

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Introduction

- HIV is associated with accelerated decline in lung function (notably the FEV_1) and increased risk for Chronic Obstructive Pulmonary Disease (COPD)
- The Diffusing Capacity of the Lung for Carbon Monoxide (DLCO) is a marker of pulmonary gas transfer, closely associated with health outcomes (quality of life, respiratory symptoms, and mortality)
- Previous studies demonstrated a link between HIV and DLCO impairment – presumed to be related to increased emphysema and COPD
- The relationship between HIV and DLCO impairment has not been analyzed after accounting for emphysema severity, in individuals both with and without COPD

Objectives

Utilizing epidemiologically matched HIV-infected and uninfected participants from the Study of HIV in Etiology Lung Disease (SHIELD) we aimed to:

1) Describe the association between HIV and DLCO independent of emphysema severity
2) Identify the joint influence of HIV and Chronic Obstructive Pulmonary Disease on DLCO impairment

Methods

Data Collection

- Participant data from the SHIELD COPD Sub-study in Baltimore, Maryland
  - Designed to characterize COPD among participants with and without HIV
- Data analyzed from 353 participants with:
  - Lung Function Testing (Spirometry and DLCO Measurements)
  - Chest CT Imaging (to estimate emphysema)
- Primary Outcome: % Predicted DLCO (corrected for age, sex, and hemoglobin)
- CT Emphysema severity was evaluated quantitively via standard methods calculating the percent of lung volume with attenuation of -950 or less
- COPD was defined as Post-Bronchodilator FEV_1/FVC ratio <0.70
  - The parent study oversampled HIV-uninfected participants with COPD to better identify characteristics unique to PLWH and COPD
- Clinical and Laboratory evaluation at the time of Lung Function and CT Included:
  - Demographics (Age, Sex, Education)
  - Lab Measurement: Hemoglobin and Serum Markers of HIV Status (RNA Levels, CD4 T-Cell Count, and HIV antibodies)
  - Risk Assessment (Injection Drug Use (IDU), Smoking)

Analysis Plan

- Linear regression models analyzing the association between HIV and DLCO % predicted
- Logistic regression estimated odds of moderate-severe DLCO impairment (<60% predicted)
- Models adjusted for Demographics, Smoking (Current and Pack Years), IDU, Emphysema Severity, FEV_1/FVC ratio (to account for differences in COPD status between groups)
- Associations with DLCO by HIV and COPD status (HIV-infected with COPD, HIV-uninfected with COPD, HIV infected with COPD), with HIV-uninfected participants without COPD as the reference group

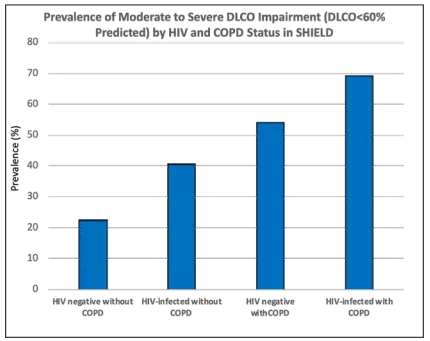
Results

Participants:

- 353 total
- 131 w/ COPD
- 241 PLWH
  - 70% with viremic control (<400 copies/ml)
  - Median CD4 374
- Predominantly African American / Male
- High Prevalence of Smoking

Participant Characteristics	Overall (353)	HIV+ (241)	HIV- (112)
Age (SD)	50.9 (9)	51 (7)	50.8 (10)
Male, n(%)	235 (69)	160 (70)	75 (68)
Black Race, n(%)	300 (89)	201 (90)	99 (88)
Current Smoker, n(%)	271 (80)	176 (77)	95 (86
Smoking, pack-years (SD)	18 (18)	17 (19)	22 (17)
Current IDU, n(%)	93 (27)	58 (24)	35 (31)
Lung Function Characteristics			
COPD, n(%)	131 (39)	60 (26)	71 (65)
FEV_1 % Predicted (SD)	86 (18)	87 (18)	82 (17)
DLCO % Predicted	62 (16)	61 (14)	63 (15)
<60% Predicted, n (%)	156 (46)	109 (48)	47 (42)
HIV Characteristics			
VL (<400 copies/ml), n (%)		169 (70)	
CD4 T-Cell Count [IQR]		375 [247-571]	

- Prevalence of significant DLCO impairment among PLWH with COPD (69.3%) was greater than in HIV-uninfected participants with COPD (54.2%) (P<0.01)
- High Prevalence of significant DLCO Impairment observed among PLWH without COPD

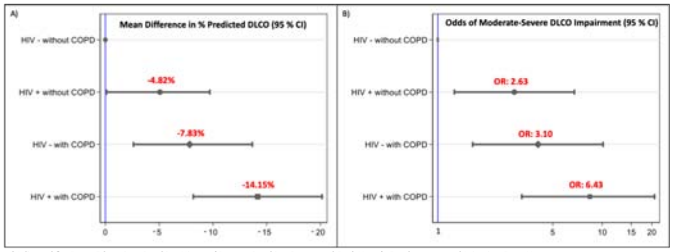


HIV is Independently Associated with Lower DLCO and Greater Odds of Moderate- Severe DLCO Impairment After Adjusting for CT Emphysema and Traditional Risk Factors

Predictors of DLCO Impairment	Mean Difference in % Predicted DLCO			Odds of Moderate-Severe Impairment (<60% Predicted)		
	β	95% CI	P-Value	Odds Ratio	95% CI	P-Value
HIV	**-4.03**	**-7.59 to -0.53**	**0.02**	**1.93**	**1.12-3.32**	**0.01**
Black Race	-8.58	-14.08 to -3.08	<0.01	2.38	0.94-6.04	0.07
Female	-3.12	-6.74 to 0.49	0.09	1.40	0.83-2.38	0.21
Current Smoker	-4.89	-9.43 to -0.34	0.04	2.13	1.06-4.30	0.03
Pack Years of Smoking	-0.04	-0.14 to 0.06	0.39	0.99	0.99-1.02	0.56
Current IDU	1.25	-3.16 to 5.66	0.58	1.05	0.52-2.11	0.88
Pulmonary Characteristics						
FEV_1 / FVC Ratio (per 0.10 increase)	4.72	2.61 to 6.83	<0.01	0.60	0.45-0.88	<0.01
% CT Emphysema (per 1% increase)	-0.42	-1.06 to 0.02	0.20	1.12	1.00-1.26	0.05

*Adjusted for age, sex, race, education, smoking status (current smoking and pack years), IDU, FEV_1/FVC, CT Emphysema

Figure*. The relationship between HIV,COPD status and DLCO impairment A) represents mean difference (95% CI) in DLCO % predicted for differing groups and B) represents odds ratio (OR [95% CI]) of moderate to severe DLCO impairment (<60% predicted) compared to HIV negative participants without COPD. Note panel B is displayed with a log scale.



*Adjusted for Race, Education, Smoking History (Current Smoking Status and Pack Years), Emphysema, and Injection Drug Use

Lower CD4 Count May Also be Associated with Greater DLCO Impairment

Predictors of DLCO	Mean Difference in % Predicted DLCO			Odds of Moderate-Severe Impairment (<60% Predicted)		
	β	95% CI	P-Value	Odds Ratio	95% CI	P-Value
HIV						
CD4 > 350	-2.58	-6.62 to 1.45	0.21	1.66	0.90-3.03	0.09
CD4 ≤ 350	**-6.16**	**-10.5 to -1.86**	**<0.01**	**2.33**	**1.25-4.35**	**<0.01**
Pulmonary Characteristics						
FEV_1/FVC Ratio	4.88	2.74 to 7.02	<0.01	0.62	0.46-0.89	<0.01
% CT Emphysema	-0.42	-1.07 to 0.23	0.20	1.12	1.00-1.26	0.05

*Adjusted for age, sex, race, education, smoking status (current smoking and pack years), IDU, FEV_1/FVC, CT Emphysema

Conclusions

- HIV is independently associated with greater DLCO impairment independent of COPD and emphysema severity
- Our data suggests an additive effect of HIV and COPD on DLCO Impairment
- Individuals with HIV (even without COPD and emphysema) may also experience significant DLCO impairment
- Individuals with poorer immunologic control (lower CD4 count) may face greater DLCO impairment
- Limitations:
  - This primarily male, African-American cohort with a high prevalence of smoking may not be representative of the HIV population as a whole
  - Over selected participants with COPD and lung disease, representing a sicker population
- Multiple strengths with a well characterized high-risk study population, often missed in research studies, with Chest CTs and Full PFTs
- Future efforts should focus on characterizing other contributors to DLCO impairment in HIV (i.e Pulmonary Vascular Disease and Early Interstitial Lung Disease)
- Efforts should also focus on better characterizing DLCO progression over time and targets for intervention to preserve DLCO and lung health among PLWH