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HIV-Associated COPD is Characterized by Increased Small Airways Dysfunction on CT

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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).
- There remain major gaps in our understanding in of HIV-associated lung disease and features unique to HIV-associated COPD; including HIV's impact on the small airways (the primary site of airflow obstruction).
- Small airways disease is independently associated with respiratory morbidity and occurs prior to emphysema in the lung aging process. However, small airways disease is often undetected on spirometry, and not visualized by traditional CT.
- The development of parametric response mapping (PRM) CT analysis with joint analysis of inspiratory and expiratory CT images, recently made it possible to quantify small airways disease and provide enhanced phenotypic evaluation.

Objectives

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

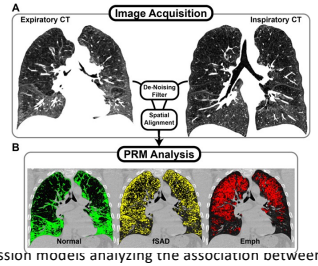
1) Determine whether HIV is associated with an increased burden of functional small airways disease
2) Explore whether novel CT analysis techniques (PRM) can add value in phenotyping HIV-associated COPD

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 and Chest CT Imaging (Inspiratory/Expiratory Images)
- Parametric Response Mapping Analysis applied to describe the quantify percentages of small airways disease(PRM^{fSAD}) and emphysema(PRM^{emph})
- Primary Outcome: % PRM^{fSAD}
- COPD was defined as Post-Bronchodilator FEV_1/FVC ratio <0.70
- Clinical and Laboratory evaluation at the time of Lung Function and CT Included:
  - Lab Measurement: Markers of HIV Status (RNA Levels, nadir $CD4^+$ T-Cell Count)
  - Risk Assessment (Injection Drug Use (IDU), Smoking)

Example: Depicting PRM analysis technique and outcomes



Analysis Plan

- Quantile regression models analyzing the association between HIV and % PRM^{fSAD} among participants with and without COPD
- Models adjusted for Demographics, Smoking (Pack Years), IDU, Lung Function (FEV_1), and pneumonia history

Results

Participants:

- 353 total
- 137 w/ COPD
- 240 PLWH
- Predominantly African American / Male
- High Prevalence of Smoking

Table 1. Participant Characteristics by HIV and COPD Status

	Participants without COPD (216)		Participants with COPD (137)	
	HIV Infected	HIV Un-Infected	HIV Infected	HIV Un-Infected
N	(175)	(41)	(65)	(72)
Demographics				
Age, year	50.0 [45.4-55.3]	50.2 [45.8-55.4]	51.7 [48.5-56.8]	51.5 [46.5-56.8]
Male, n(%)	120 (69)	25 (61)	47 (72)	50 (70)
Race/ethnicity, n(%)				
Black	131 (76)	34 (83)	57 (92)	66 (92)
Smoking Status, n(%)				
Current Smoker	188 (79)	97 (85)	57 (89)	63 (89)
Smoking, pack-years	15.4 [7.3-33.0]	18 [13.5-37.0]	22.8 [13.7-36.0]	24.3 [16.0-36.0]
Recent Injection Drug Use(IDU),n(%)†	27 (15)	13 (31)	16 (25)	26 (36)
HIV Characteristics§				
HIV RNA Detectable, n(%)	63 (36)		20 (30)	
Nadir $CD4^+$ T-cell count (cells/mm^3)	354 [195-485]		344 [231-488]	
History of Pneumocystis Pneumonia, n(%)	7 (4)		2 (3)	
Pulmonary Characteristics				
Lung Function				
FEV_1 Absolute (L)	2.57 [2.08-3.16]	2.51 [1.95-3.06]	1.95 [1.60-2.48]	2.33 [1.82-2.91]
FEV_1 % Predicted	87.1 [72.3-97.0]	81.8 [71.5-93.7]	68.6 [56.6-79.0]	77.7 [63.4-87.9]
PRM CT Characteristics				
PRM^{fSAD}	3.49 [1.06-7.93]	3.31 [1.23-9.25]	14.69 [6.38-22.91]	9.89 [6.29-17.90]
PRM^{emph}	0.05 [0.01-0.26]	0.06 [0.02-0.14]	0.65 [0.19-3.39]	0.38 [0.11-1.36]

*Values presented as median [IQR] unless indicated otherwise
§ Among HIV-infected only

- Figure depicts the unadjusted distribution of PRM^{fSAD} in the cohort by HIV and COPD status
- Highest burden of PRM^{fSAD} among PLWH who had COPD

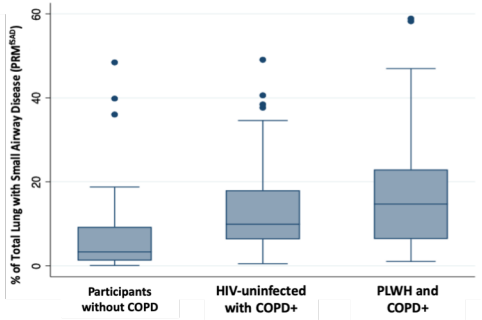


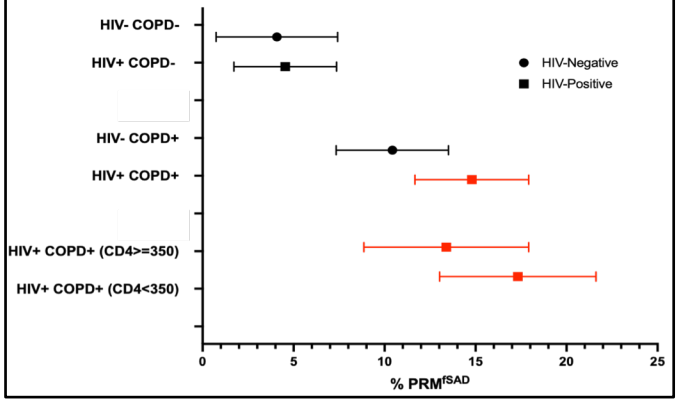
Table 2. Factors Associated with Differences in Functional Small Airways Disease (PRM^{fSAD}) on CT by COPD Status*

	Participants without COPD		Participants with COPD	
	Median Difference (95% CI) % PRM^{fSAD}	p-value	Median Difference (95% CI) % PRM^{fSAD}	p-value
HIV & COPD Status				
HIV Status				
HIV-uninfected			Reference	
Persons Living with HIV	0.45 (-2.12 to 3.03)	0.73	**4.37 (1.82 to 6.91)**	**0.001**
HIV by nadir CD4+ Count				
HIV-positive CD4 >350, COPD	-0.08 (-2.66 to 3.92)	0.96	2.57 (-1.19 to 6.34)	0.195
HIV-positive CD4 < 350, COPD	0.62 (-2.66 to 3.92)	0.72	**6.49 (2.98 to 10.01)**	**<0.001**
Demographics & Lung Function				
Age (per 10 years)	1.89 (0.96 to 2.84)	**<0.001**	3.77 (0.86 to 6.69)	**0.012**
Black Race	-0.07 (-2.11 to 1.98)	0.95	-4.64 (-13.34 to 4.04)	0.29
FEV_1, per (1000ml decrease)	-1.02 (-1.95 to -0.11)	**0.028**	2.35 (-0.87 to 5.57)	0.151

*Adjusted for age, sex, race, smoking pack-years, active IDU, recent pneumonia, and current FEV_1

In addition to PRM^{fSAD} there was also Increased emphysema among PLWH with COPD compared to HIV-negative COPD (median difference 0.32%; 95% CI 0.10-0.55%), though still low emphysema burden overall

Figure. Depicts median estimates (95% CI) of functional small airways disease (PRM^{fSAD}) by HIV and COPD status after adjustment for confounders (demographics, pack-years, FEV_1, IDU, respiratory infections). Items in red are for participants with HIV and COPD



HIV-Associated COPD is linked to Greater Small Airways Dysfunction on CT. Most Significant in those with low nadir $CD4^+$ T-Cell Counts

Conclusions

- HIV-associated COPD is linked to greater small airways dysfunction, independent of lung function and traditional risk factors
- Our data suggests that novel CT analysis techniques like PRM add value in phenotyping HIV-associated COPD beyond traditional lung function data alone
- Individuals with HIV and COPD may experience significant small airways disease even with relatively preserved lung function and minimal emphysema
- Individuals with poorer immunologic control (lower $CD4^+$ count) may face greater disease burden
- Accelerated lung aging may also be a mechanism behind the greater burden of small airways disease in HIV-associated COPD
- Limitations:
  - This primarily male, African-American cohort with a high prevalence of smoking may not be representative of the HIV population as a whole
- Multiple strengths with a well characterized high-risk study population, often missed in research studies, with in-depth lung function and CT data
- Future efforts should focus on characterizing the drivers of and longitudinal impact of small airways dysfunction in HIV-associated COPD