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 FEV1) and increased risk for Chronic Obstructive Pulmonary Disease (COPD).
- There remain major gaps in our understanding of in 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)
  - PRM analysis of inspiratory and expiratory CT images, whether small airways disease even in the cohort by HIV and COPD status
  - 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)

Analysis Plan

- Quantile regression models assessing the association between HIV and % PRM20 among participants with and without COPD
- Models adjusted for Demographics, Smoking (Pack Years), IDU, Lung Function (FEV1), and pneumonia history

Results

Participants:

- 353 total
- 132 w/ COPD
- 240 PLWH
  - Predominantly African American / Male
  - High Prevalence of Smoking
- Figure depicts the unadjusted distribution of PRM20 in the cohort by HIV and COPD status
- Highest burden of PRM20 among PLWH who had COPD

Table 1. Participant Characteristics by HIV and COPD Status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants without COPD</th>
<th>Participants with COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>White (87%), Black (13%)</td>
<td>White (88%), Black (12%)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male (94%), Female (6%)</td>
<td>Male (83%), Female (17%)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>Median: 55 (IQR: 45-66)</td>
<td>Median: 54 (IQR: 44-66)</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>372 (91%)</td>
<td>128 (91%)</td>
</tr>
<tr>
<td>History of Pneumocystis Pneumonia</td>
<td>23 (6.5%)</td>
<td>14 (10.2%)</td>
</tr>
<tr>
<td>CDC Category</td>
<td>CD4+ &gt; 500</td>
<td>CD4+ &lt; 200</td>
</tr>
<tr>
<td>HIV Status</td>
<td>HIV-uninfected (88%)</td>
<td>HIV-infected (12%)</td>
</tr>
</tbody>
</table>

Table 2. Factors Associated with Differences in Functional Small Airways Disease (%PRM20) on CT by COPD Status

HIV & COPD Status

<table>
<thead>
<tr>
<th>HIV Status</th>
<th>COPD Status</th>
<th>N</th>
<th>Median Difference (95% CI)</th>
<th>p-value</th>
<th>Median Difference (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-uninfected</td>
<td>HIV-infected</td>
<td>275</td>
<td>-0.9 [0.1-1.8]</td>
<td>0.10</td>
<td>0.1 [0.7-1.6]</td>
<td>0.10</td>
</tr>
</tbody>
</table>

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