CHRONIC HIV PULMONARY DISEASE (CHPD) IN NEVER SMOKING HIV PATIENTS

Antonella Santoro[1] , Riccardo Scaglioni[2] , Giulia Besutti[2] , Andrea Malagoli[1] , Jonathon Leipsic[3] , Janice Leung[4], Cristina Mussini [1], Stefano Zona [1], Guido Ligabue[2] , Giovanni Guaraldi[1]

1-Infectious Disease Department, Policlinic Hospital, University of Modena and Reggio Emilia, Modena, Italy; 2-Radiology Department, Policlinic Hospital, University of Modena and Reggio Emilia, Modena, Italy; 3-Department of Radiology, University of British Columbia Department of Medicine, Vancouver, Canada, 4-Department of Medicine Respiratory Division, Vancouver, British Columbia, Canada

Corresponding Author: antonella.santoro7@gmail.com

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INTRODUCTION

COPD is the inflammatory response to cigarette smoke, nevertheless never-smokers may also develop COPD as the result of a complex interplay of long-term cumulative exposure to noxious gases and particles, combined with a variety of host factors.

We can assume that HIV and COPD share similar pathogenetic pathways, which are mediated by the increased expression of multiple inflammatory factors.

OBJECTIVE

We hypothesized that the inflammatory milieu associated with chronic HIV infection may play a role in the pathogenesis of a HIV related lung disease.
In order to dissect the contribution of HIV to the impact of smoke risk factor, we selected never-smokers HIV patients. Id est people who neither were smoking at the time of the inclusion in the cohort, nor have been smoking during their life.

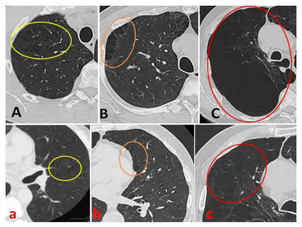
The aim of this study was to characterize structural, functional and clinical lung abnormalities in never smoking HIV patients on antiretroviral therapy, not referred for pulmonary diseases.

METHODS

Observational retrospective cohort of 329 consecutive never smokers HIV+.
Patients were selected among 1920 HIV+ patients attending MHMC from 2006 and 2015 for Coronary Calcium Score screening protocol.

Inclusion criteria:
- ✓**No current smoke**,
- ✓**Pack year =0**
- ✓On HAART

Exclusion criteria:
- ✓No heart or pulmonary acute disease



Morphologic emphysema subtypes in HIV smokers attending MHMC

Morphologic emphysema subtypes in HIV **never smokers** attending MHMC

A:centrilobular **B**:paraseptal **C**:panlobular

METHODS AND RESULTS

Tab 1. Demographic and clinical characteristics of the cohort.

Variable Median(S.D.)/ n(%)	Total 329	Women 86 (26.14%)	Men 243 (73.86%)	P value
Age	49.57 (8.89)	48.3 (8.84)	50.02 (8.88)	0.06
Anthropometry				
BMI	24.64 (3.75)	23.71 (3.93)	24.97 (3.64)	<0.01
Obesity	31 (9.54%)	8 (9.41%)	23 (9.58%)	1
SAT	159.5 (94-232)	213 (143-273)	143 (82-198)	0
VAT	127 (88-178.5)	101 (76-131)	137 (98.5-201)	0
Inflammation Markers				
C-Reactive-Protein	0.92 (9.38)	0.91 (6.31)	0.92 (10.26)	0.98
White blood cells	2825.18 (3168.35)	1302.04 (2683.38)	3358.66 (3157.76)	0
Homocysteine	12.25 (6.6)	10.95 (5.4)	12.72 (6.94)	0.01
Cardiovascular				
Calcium score	0 (0-16)	0 (0-0)	0 (0-35)	<0.01
Calcium score >100	39 (11.8%)	2 (0.6%)	37 (11.2%)	<0.01
Framingham score	3 (1-7)	0 (0-1)	4 (2-8)	<0.01
HIV factors				
MSM	143 (43.47%)	0 (0%)	143 (58.85%)	
Heterosexual	133 (40.43%)	70 (81.4%)	63 (25.93%)	
CD4 cell count	616.63 (242.71)	590.45 (217.37)	626.17 (251.07)	0.2
CD4 Nadir	210 (100-300)	202 (102-287)	216 (100-304)	0.67
Previous PCP	3 (0.91%)	0 (0%)	3 (1.23%)	0.7
Duration of HIV infection	182.75 (76)	196.85 (65.96)	177.95 (78.67)	0.07
Lipodystrophy				
No lipodystrophy	71 (25.54%)	10 (14.29%)	61 (29.33%)	0.05
Peripheral Atrophy	80 (28.78%)	23 (32.86%)	57 (27.4%)	
Central Adiposity	33 (11.87%)	7 (10%)	26 (12.5%)	
Mixed form	94 (33.81%)	30 (42.86%)	64 (30.77%)	
Lung Abnormalities				
Bronchiectasis	51 (15.69%)	5 (5.88%)	46 (19.17%)	
Bronchiolitis	38 (11.59%)	10 (11.63%)	28 (11.57%)	
Emphysema	47 (14.29%)	7 (8.14%)	40 (16.46%)	
Nodules >4mm	33 (10.12%)	4 (4.65%)	29 (12.08%)	

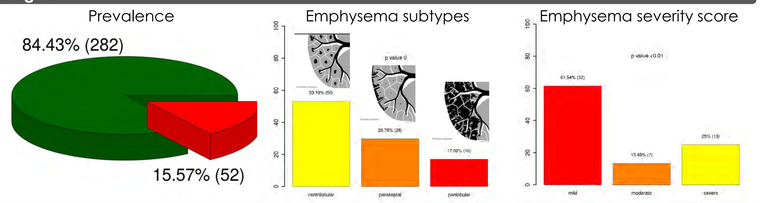
Tab 2. Univariate model for prediction for emphysema.

Variable Median(S.D.)/ n(%)	Total	Emphysema=0 282 N, 85.7%	Emphysema≥1 47 N, 14.3 %	P value
Demographic				
Age	49.57 (8.89)	48.88 (8.59)	53.68 (9.62)	**0**
Male	243 (73.86%)	203 (71.99%)	40 (85.11%)	0.09
BMI	24.64 (3.75)	24.48 (3.69)	25.6 (4.03)	**0.05**
VAT	127 (88-178.5)	124 (86-166)	155 (110.5-221)	**<0.01**
EAT	76.4 (48.-100)	69.7 (47-97)	102 (79.8-131)	**<0.01**
Calcium score	53.04 (244.91)	8.33 (32.95)	68.86 (282.76)	**<0.01**
Framingham	3 (1-7)	0 (0-1)	4 (2-8)	**<0.01**
HIV factors				
CD4 cell count	616 (242)	619 (245)	599.2 (229)	0.91
CD4 Nadir	210 (100-300)	215 (108-300)	176 (79.5-307)	0.37
Months with HIV	182.75 (76)	184.17 (74.69)	174.2 (83.79)	0.38
Previous PCP	3 (0.91%)	3 (1.06%)	0 (0%)	1
Inflammation markers				
CRP	0.92 (9.38)	1.02 (10.13)	0.27 (0.39)	0.19
White Blood Cell	2825 (3168.)	2693.(3127)	3547(3331)	0.07
Homocysteine	12.25 (6.6)	11.92 (6.11)	14.18 (8.76)	0.1
D-dimer	277.23 (211.29)	274.7 (210.11)	291.28 (220.01)	0.74
CD4/CD8 ratio	0.75 (0.55-1.0)	0.76 (0.56-1.04)	0.68 (0.52-0.92)	0.36

1.Structural Changes

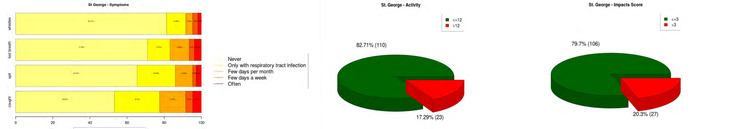
A proportion of these patients the same day of CT were evaluated for respiratory symptoms and lung function as a part of a multidisciplinary assessment offered free of charge at MHMC
Lung Abnormalities (329 observations): CT Images were evaluated for pulmonary findings as defined by the Fleischner Society glossary of terms by 3 radiologists by consensus. Based on a modified method of Kazerooni , semi-quantitative scores were assigned to all scans. A score was assigned to each of 6 lobes (for a maximum score of 24) to describe the burden of lung emphysema manifested as bullae, centrilobular or paraseptal lesions.

Table 2 shows univariate model for predictors for emphysema (any grade of severity)



2.Clinical Abnormalities

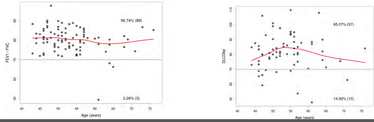
Respiratory Symptoms (92 observations): St. George's Respiratory Questionnaire (SGRQ) is a disease-specific instrument, designed to measure impact on overall health, daily life, and perceived well-being in patients with obstructive airways disease. Means (95% confidence intervals) for SGRQ scores in normal subjects with no history of respiratory disease was 12(C.I. 9-15) for Symptoms Score; 9(C.I. 7-12) for Activity Score and 2(C.I. 1-3) for Impact score. Impairment in each category was defined with a score value above than 95% confidence intervals.



3.Functional Abnormalities

Lung function (97 observations): Spirometry was introduced in 2012 as a routine screening for functional lung abnormalities, including total lung capacity (measurement of residual volume, and pulmonary diffusion capacity (DLCO). Spirometry were performed by a Jaeger Flow Screen spirometer and a Jaeger Master Screen plethysmography cabin 1-2, according to the ATS/ERS recommendation

- ✓ Prevalence of COPD was 3%
- ✓ Constant distribution of FEV1/FVC across different ages
- ✓ Significant reduction of DLCO across age groups.



Additional lung CT abnormalities

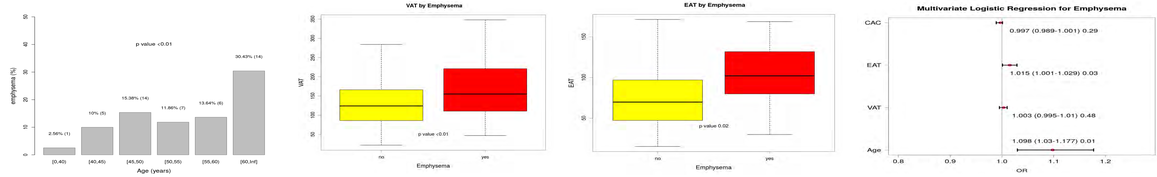
Respiratory bronchiolitis: 39 (12%) Bronchial wall thikening: 131 (39%)



Bronchiectasis: 52 (16 %) Nodules ≥ 4mm : 33 (10%)



Univariate and Multivariate analysis



DISCUSSION

The identified pattern of CHRONIC HIV PULMONARY DISEASE (CHPD) is a complex interaction of structural, functional and clinical lung derangements.
1. Structural changes, Emphysema in particular are function of age and EAT after correction for CAC:
- in the context of the aging epidemic affecting HIV, the prevalence of this condition may increase in years to come.
- EAT is a source of bioactive molecules associated with cardio-metabolic inflammatory state. Clinically, EAT and its changes can be objectively measured and monitored by imaging techniques, and this makes its assessment an appealing tool in the stratification of the cardio-metabolic risk and presumably turn to be a marker of lung disease in HIV

2. Respiratory symptoms are prevalent in never smokers HIV patients. Respiratory symptoms are not specific for COPD and we cannot exclude other concomitant chronic disease conditions including congestive heart disease or pulmonary hypertension. These symptoms were not the reason for CT scanning or medical visit and most of the cases patients considered them as persistent in the course of HIV infection. These symptoms appear to contribute to quality of life and activity of daily living
3. Functional lung impairments are characterized by reduction of carbon monoxide diffusing capacity but only in few cases with pulmonary obstruction diagnostic for COPD.

Time was associated with DLCO reduction, but not FEV1/FVC impairment, suggesting a difference in the pathogenesis of this condition to what expected in tobacco induces COPD.

The lack of recognition and under-diagnosis of CHPD among never smokers, is the result of little knowledge on this condition and poor understanding and appreciation of risk factors other than smoking.

The natural history of CHPD needs to be investigated in prospective studies. Improving understanding of risk factors other than smoking will allow to identify high-risk individuals who require closer disease monitoring and potential future treatment interventions.