Factors Associated with Chronic Obstructive Pulmonary Disease in a High Risk HIV-Infected Cohort

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Background:
HIV-infected subjects have been reported to be at higher risk of COPD than their HIV-negative counterparts [1-3], due to increased prevalence and magnitude of exposure hazards (i.e. smoking)[4-6], and possible interactions with HIV-infection [7;8].

Objectives:
To evaluate HIV-related and unrelated factors associated with COPD in a cohort of high risk smoking HIV-infected subjects aged ≥40 years.

Methods:
- Cross sectional prevalence study of COPD diagnosed with spirometry nested in the ANRS EP48 HIV CHEST cohort, a French, multicentre, ongoing prospective study evaluating low dose chest tomography (CT) for early lung cancer diagnosis in HIV-infected subjects (NCT01207986).
- Primary inclusion criteria were age ≥ 40 years, history of smoking within 3 years of at least 20 pack-years, CD4 T-lymphocyte nadir cell count < 350/µl, and actual CD4-T cell count > 100 cells/µl.
- Non inclusion criteria were active cancer or AIDS-classifying diseases, lung infection within 2 months, pregnancy, breastfeeding or contra-indication to thoracic surgery.
- COPD was defined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations (http://www.goldcopd.org)(table 1).
- Primary outcome was the prevalence of COPD.
- Logistic regression models evaluated factors associated with COPD (table 3).
- A subgroup completed lung volume evaluation with plethysmography.

Table 1: Severity classification of Airflow Limitation (based on post-bronchodilator FEV_1), of patients with FEV1/FVC <0.70 (COPD). Forced expiratory volume in one second (FEV_1) ; forced vital capacity (FVC).

GOLD 1 : mild	$FEV_1 \geq 80\%$ predicted
GOLD 2 : moderate	$50\ \% \leq FEV_1 < 80\ \%$ predicted
GOLD 3 : severe	$30\ \% \leq FEV_1 < 50\ \%$ predicted
GOLD 4 : very severe	$FEV_1 < 30\ \%$ predicted

Results:
- Study flow chart is shown in figure 1.
- COPD was diagnosed in 83 subjects (24.9%; CI 95% [20.2 ; 29.5]); 45 (54%) and 34 (41%) were GOLD grade 1 and 2 respectively. In 62 subjects (75%), COPD was unknown before study entry.
- Characteristics of the 334 subjects included are shown in table 2. Univariate and multivariate analysis are shown in table 3.

Figure 1 : flow chart

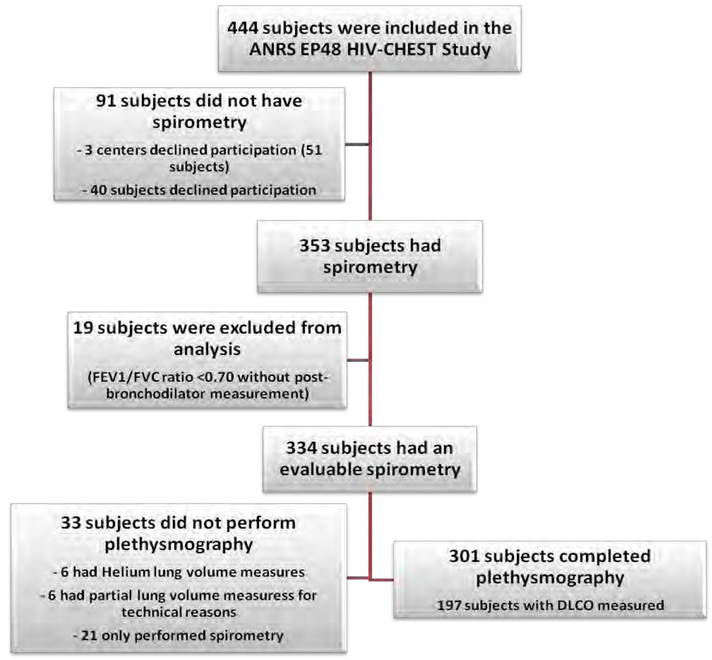


Table 2: Patients' characteristics

Characteristics	Total	COPD	No COPD
numbers	334	83 (24.9)%	251 (75.1%)
Age in years, median (IQR)	50 (46-53)	52 (48-56)	49 (46-53)
Women, n (%)	58 (17%)	13 (16%)	45 (18%)
Lean (BMI<18.5), n (%)	35 (10%)	14 (17%)	21 (8%)
Smoking in pack-years, median (IQR)	30 (25-39)	34 (26-40)	30 (25-37)
History of cannabis consumption, n (%)	116 (35%)	35 (42%)	81 (32%)
History of IDU	84 (25%)	28 (34%)	56 (22%)
CD4 count, median cells/µl (IQR)	574 (396-764)	500 (345-708)	597 (427-784)
Nadir CD4 count, median cells/µl (IQR)	178 (76-261)	162 (71-238)	182 (83-270)
Nadir CD4 <200 cells/µl, %	190 (57%)	49 (59%)	141 (56%)
History of AIDS defining-complication	95 (28%)	29 (35%)	66 (26%)
ART duration (years), median (IQR)	14 (7-16)	13 (7-16)	14 (7-16)
Last Viral load < 50 copies/ml	294 (88%)	73 (88%)	221 (88%)
HCV infection	95 (28%)	30 (36%)	65 (26%)
Pneumocystis/bacterial pneumonia history	30 (9%)	11 (13%)	19 (8%)
FEV1, % of normal (IQR)	94 (82-105)	76 (63-84)	98 (91-107)
FEV1/FVC	0.75 (0.68-0.80)	0.61 (0.54-0.66)	0.77 (0.73-0.81)
TLC % of normal, median (IQR) (n=304)	107 (97-117)	114 (104-126)	105 (96-112)
RV,% of normal (IQR) (n=301)	119 (100-147)	152 (110-176)	114 (99-133)
RV/TLC, % of normal (IQR) (n=301)	104 (92-117)	120 (101-139)	104 (92-117)
DLCO, % of normal median (IQR) (n=197)	71 (62-85)	61 (52-74)	68 (59-83)

BMI: Body Mass Index ; IDU: Intravenous Drug User ; ART: Antiretroviral Therapy; TLC: total lung capacity ; FEV1: Forced expiratory volume in 1 second ; RV: Residual Volume ; DLCO: diffusing lung capacity for carbon monoxide, as corrected for Hemoglobin ; FVC: Forced Vital Capacity.

Table 3: Univariate and multivariate analysis of factors associated with COPD (n = 334).

	Univariate analysis		Multivariate analysis	
Variable	OR [CI95%]	p	OR [CI95%]	p
Sex (woman)	0.85 [0.43 ; 1.67]	0.64		
Age (per 10 years increase)	**2.17 [1.44 ; 3.29]**	**<0.001**	**2.34 [1.48 ; 3.70]**	**<0.001**
Smoking (per 5 pack-years increase)	1.11 [1.00 ; 1.22]	0.046	1.06 [0.95 ; 1.18]	0.30
History of cannabis use (yes/no)	1.53 [0.92 ; 2.55]	0.10	1.69 [0.96 ; 2.99]	0.071
BMI < 18.5 kg/m²	2.22 [1.07 ; 4.60]	0.032	2.05 [0.94 ; 4.46]	0.071
History lung infection/pneumocystis	1.87 [0.85 ; 4.10]	0.16	2.07 [0.90 ; 4.80]	0.089
ART duration	1.01 [0.97 ; 1.05]	0.70		
HCV co-infection	1.62 [0.95 ; 2.75]	0.066	1.45 [0.81 ; 2.62]	0.21
Nadir CD4 T cells < 200/µl	1.12 [0.68 ; 1.86]	0.65		
CD4 cells (per 100/µl increase)	**0.89 [0.81 ; 0.98]**	**0.024**	**0.90 [0.81 ; 0.99]**	**0.039**
HIV viral load <50 copies/ml	0.99 [0.46 ; 2.13]	0.98		

Body Mass Index (BMI) ; Antiretroviral Therapy (ART)

Discussion:
- Prevalence of COPD was high and underdiagnosed, similarly to what is published in the general population [9-12].
- All included subjects were heavy smokers and age was a confounding factor explaining lack of association between smoking and COPD.
- Plethysmography objectified hyperinflation compatible with emphysema.
- Main study limitations were: cross sectional analysis; no quality of life questionnaires; no use of the recently published European mutli-ethnic spirometric reference values FEV1 and FVC values (13); lack of detail on cannabis intoxication.

Conclusion:
- High prevalence of COPD in smoking HIV-subjects ≥ 40 years advocates screening/early diagnosis strategies as recommended by GOLD.
- Cannabis and its potential association with COPD should be further explored.
- Tobacco and cannabis smoking cessation should be highly prioritized in HIV-infected subjects.
- Higher CD4 counts could be protective of COPD, and pleads for early and universal antiretroviral treatment.

(1) Crothers et al. Chest, 2006 (2) Crothers et al. Am J Respir Crit Care Med 2010. (3) Madeddu et al.Infection 2012 (4) Roux et al. Bulletin épidémiologique hebdomadaire 2013. (5) Tesoriero et al. AIDS Behav 2010 (6) Mimiaga et al. Am J Public Health 2013. (7) Morris A et al. J Clin Microbiol 2009. (8) Drummond et al. Thorax 2012. (9) Buist et al. Int J Tuberc Lung Dis 2008 (10) Hill et al.CMAJ 2010 (11) Bednarek et al. Thorax 2008 (12) Soriano Eur Respir J 2010 (13) . Quanjer. et al. Eur Respir J 2012.

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