CT abnormalities in never-smoking HIV patients

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Purpose

Since the introduction of effective antiretroviral therapy (ART), an increase in morbidity and mortality due to chronic comorbidities such as cardiovascular diseases and chronic obstructive pulmonary disease (COPD) has been observed among HIV infected patients [1-3]. These patients have higher risk of developing COPD and emphysema when compared to uninfected patients, and frequently show these conditions at younger ages [4-7]. The increased risk for COPD is partly attributable to the higher prevalence of smoking and other risk factors such as drug use, and a higher susceptibility to cigarette smoking has been suggested in other studies [5;8]. Besides, a higher prevalence of COPD and emphysematous changes has been registered also after correction for cigarette smoking and in never smoking HIV-infected patients, suggesting an independent role of infection itself in the development of chronic lung disease [5;8].

HIV-infected patients typically experiment an altered distribution of body fat towards an increase in visceral adiposity and ectopic fat e.g. liver steatosis or epicardial adipose tissue [9;10]. In the general population, an association have been demonstrated between visceral fat and COPD, probably in relation to an increase in circulating IL-6 and other adipokines [11;12].

CT is a comprehensive tool which allows to rapidly assess signs of chronic lung disease, mainly emphysematous changes, and to quantify the amount of adipose tissue in different fat compartments.

The aim of this study is to assess the prevalence of CT signs of chronic lung disease in a large cohort of never smoking HIV-infected patients. Risk factors for presence of emphysema have also been investigated particularly focusing on the relationship between CT lung changes and anthropometric measurement of body fat redistribution.
Methods and materials

Patients:

The study included 329 consecutive never smoking HIV-infected patients (mean age 49.6 ± 8.9 years; 73.9% men) who were evaluated for cardiometabolic risk assessment in a tertiary care clinic at the University of Modena and Reggio Emilia, Italy between May 2006 and February 2015. All subjects provided a written consent to participate in the study.

Inclusion criteria for the study were: serologically documented HIV-1 infection, more than 18 years of age, at least 18 months of ART exposure and having undergone at least one thoracic CT scanning for the assessment of Coronary Artery Calcium score (CACs). Never smokers were defined as patients currently non-smoking and with a pack-year history=0.

Clinical data:

On the same day of the CT scan metabolic and HIV-specific variables, and anthropometric measurements such as waist circumference and body mass index (BMI) were collected.

CT examination:

All patients underwent ECG-gated chest CT scan for the evaluation of CACs and 8 CT slices at the level of L4-L5 for the assessment of subcutaneous and visceral adipose tissue (SAT-VAT) [13;14].

The presence of CT signs of chronic lung disease such as emphysema, respiratory bronchiolitis (RB), bronchiectasis, bronchial wall thickening, fibrosis and non-calcified nodules (diameter ≤4 mm), was recorded. Lung emphysema was semi-quantitatively graded, visually assigning a score from 0 to 4 to each lobe based on quartile of lung involvement (total score: 0=absence; 1-4=mild to moderate; >4=severe).

SAT e VAT were calculated in all patients, while the measurement of epicardial adipose tissue (EAT) was obtained in a subset of 153 patients only [15].

Statistical analysis:

Prevalence of CT signs of chronic lung disease and distribution of emphysema severity were calculated.

Patients were grouped based on the presence of emphysematous changes (emphysema score =0 and >1). ANOVA, Kruskal-Wallis and X2 tests were used where appropriate to compare variables among and within groups with correction for multiple testing.
Multivariable logistic regression analysis was performed to identify factors independently associated with the presence of emphysema.

A p-value < 0.05 was considered statistically significant.
Results

Emphysema was found in 52 patients (15.6%, 13 patients with score>4), RB in 39 (11.7%), bronchiectasis in 52 (15.8%) and nodules in 33 (10%). Representative cases of emphysematous changes and other lung abnormalities are depicted in Fig. 1 and Fig. 2.

Results of univariable analysis are shown in Table 1: significant associations were found between the presence of emphysema and: age (p<0.01), BMI (p=0.05), Framingham risk score (p<0.01), CACs (p<0.01), VAT (p<0.01), and EAT (p<0.01). Associations of emphysema with VAT and EAT are further depicted in Fig. 3.

No significant association was found between emphysema and HIV-related factors or inflammatory markers.

In a multivariable model, significant predictors of emphysema were: age (OR=1.098; p=0.01), and EAT (OR=1.015; p=0.03), as reported in Fig. 4.
Fig. 1: Representative cases of different patterns of emphysematous changes, with a predominant centrilobular (A), paraseptal (B) and mixed (C) distribution, and different degrees of parenchymal involvement with respective emphysema scores (D-E).

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Fig. 2: Representative cases of other lung abnormalities seen on CT scan. A: diffuse ill-defined centrilobular nodules suggestive for respiratory bronchiolitis. B: bronchial wall thickening (arrow). C: diffuse cilindric bronchiectasis (arrow). D: spiculated lung nodule in the anterior segment of the right upper lobe.

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Table 1: Univariate analysis: demographic, anthropometric and clinical characteristics with relative p-value of the cohort as a whole and according to presence of emphysematous changes. Data presented as percent, mean ± S.D., or median (IQR). Abbreviations: BMI, body mass index; PCP, pneumocystis carinii pneumonia; S.D., standard deviation.

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**Fig. 3:** Box-plot representing distribution of VAT and EAT according to the presence of emphysematous changes. Abbreviations: VAT, visceral adipose tissue; EAT, epicardial adipose tissue.

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Fig. 4: Independent predictors of presence of emphysema with relative OR, 95% C.I. and p-value. Abbreviations: CAC, Coronary Artery Calcium score; EAT, Epicardial Adipose Tissue; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.

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Conclusion

CT signs of chronic lung disease, especially emphysema, are common in this large cohort of relatively young never-smoking HIV infected patients, most likely representing a chronic subclinical lung injury.

Besides traditional risk factors other than cigarette smoking, such as age, also cardiovascular risk indicators (Framingham risk score and CACs) were associated with the presence of emphysema, confirming the results of previous studies which underlined the link between cardiovascular and lung comorbidities in HIV infected patients [16].

Finally, emphysema was associated with epicardial and visceral adiposity, but not with HIV-related variables, underlying a common pathogenetic mechanism linking lung CT abnormalities and ectopic fat accumulation. The missing link between these two conditions may be represented by adipocyte-specific proinflammatory cytokines or tissue inflammatory agents, that have not been detected in the present study.
References


