

# Changes of Lung Function in an Optimally Treated HIV Population: A 4.5 Year Follow Up Study

Ulrik Sloth Kristoffersen<sup>1,2</sup>, Anne-Mette Lebech<sup>3</sup>, Jan Gerstoff<sup>4</sup>, Jann Mortensen<sup>1</sup>, Henrik Gutte<sup>1,2</sup>, Andreas Kjaer<sup>1,2</sup>

<sup>1</sup>Department of Clinical Physiology, Nuclear Medicine & PET, Copenhagen University Hospital, Rigshospitalet, Denmark, <sup>2</sup>Cluster for Molecular Imaging, University of Copenhagen, Denmark

<sup>3</sup>Department of Infectious Diseases, Hvidovre University Hospital, Denmark, <sup>4</sup>Department of Infectious Diseases, Copenhagen University Hospital, Rigshospitalet, Denmark

Ulrik Sloth Kristoffersen, MD  
Department of Clinical Physiology,  
Nuclear Medicine & PET  
Rigshospitalet KF-4011,  
Blegdamsvej 9  
DK-2100 Copenhagen  
P 3545 8460  
F 3532 7546  
E ulriksk@mfi.ku.dk



## Background

Before the introduction of combination antiretroviral therapy (ART), HIV infection was known to be associated with increased pulmonary morbidity. It would be expected that the continuously improving modern ART would reduce this pulmonary morbidity by decreasing viral load and reversing the deficient immune system. However, ART could also be a cause of increased pulmonary morbidity in HIV patients due to drug toxicity, immune reconstitution, or improved overall condition which potentially could unmask previously negligible lung disorders. The aim of the present study was to conduct a prospective follow-up study of lung function in a Western world cohort of HIV patients.

## Methods

A total of 63 HIV patients had a lung function test performed between October 2000 and November 2001. Between July 2005 and March 2007, all patients had their test repeated with a mean follow-up period of 4.5 years (range 3.8 – 5.7). Patients were recruited from the out-patient clinic at the Department of Infectious Diseases, Rigshospitalet, Copenhagen, Denmark. Patient characteristics are summarized in **Table 1** and ART regimes are summarized in **Table 2**. The Danish Ethical Committee approved the study (ref.: KF 01-278/00) and written informed consent was obtained from all participants.

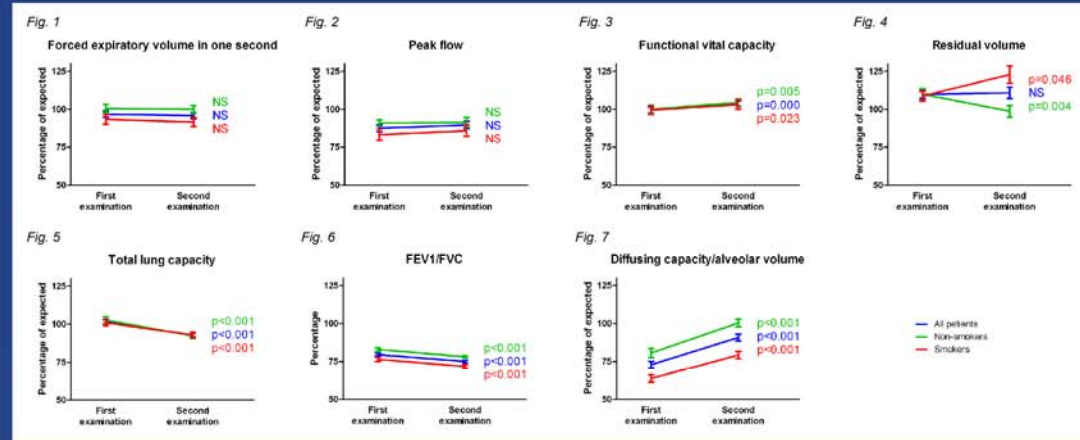
The following lung function parameters were obtained in percentage of the expected value: The forced expired volume in the first second (FEV1%), the functional vital capacity (FVC%), the peak flow (PEF%), the residual volume (RV%), the total lung capacity (TLC%), and the diffusing capacity divided by the alveolar volume (DLCO/VA%). Additionally, the FEV1 as the percentage of the FVC (FEV1%FVC) was calculated.

## Results

At the first examination, 55 of the patients (87%) were already on ART and of these, 47 patients (85%) had HIV loads <100 copies/mL. At the second examination, 61 patients (97%) were on ART and of these, 54 patients (89%) had HIV-loads <100 copies/mL. In the non-smokers, the CD4 cell count increased from 485±42 10<sup>6</sup>/L to 679±62 10<sup>6</sup>/L (p<0.001) and in the smokers, the CD4 cell count increased from 548±48 10<sup>6</sup>/L to 737±67 10<sup>6</sup>/L (p=0.003).

The FEV1/FVC and the DLCO/VA% were both reduced in the smokers compared with the non-smokers, but the remaining lung function parameters showed no differences between the groups at the first examination

Between the two examinations, neither the FEV1%, nor the PEF% changed in either of the two groups (**Figure 1** and **2**). The FVC% increased from 100.1±2.5% to 104.5±2.4% (p=0.005) in the non-smokers and from 99.5±2.9% to 103.1±3.1% (p=0.023) in the smokers (**Figure 3**). The RV% decreased from 109.9±3.8% to 98.8±3.8% (p=0.004) in the non-smokers and increased from 108.8±3.2% to 122.8±5.7% (p=0.046) in the smokers (**Figure 4**). The TLC% decreased from 102.8±2.1% to 92.3±1.7% in the non-smokers (p<0.001) and from 101.0±1.9% to 93.0±1.8% (p<0.001) in the smokers (**Figure 5**). The FEV1%FVC decreased from 83.0±1.0% to 78.3±0.8% (p<0.001) in the non-smokers and from 76.5±1.4% to 71.8±1.2% (p<0.001) in the smokers (**Figure 6**). The DLCO/VA% increased from 80.7±3.1% to 100.4±2.5% (p<0.001) in the non-smokers and from 63.8±2.4% to 79.3±2.4% (p<0.001) in the smokers (**Figure 7**).



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**Table 1.** Patient characteristics at first examination.

	All patients		Non-smokers		Smokers		Smokers vs. Non-smokers P-value
	Mean/(median)	SD/%/(range)	Mean/(median)	SD/%/(range)	Mean/(median)	SD/%/(range)	
Number (N)	63	100%	33	52%	30	48%	
Male (N)	55	87%	27	82%	28	93%	0.2
Age (years)	43.3 ± 9.0		41.6 ± 8.8		45.2 ± 1.6		0.1
Body mass index (kg/m <sup>2</sup> )	23.4 ± 2.7		24.0 ± 2.6		22.6 ± 0.5		0.040
Systolic blood pressure (mm/Hg)	128.8 ± 16.2		133.1 ± 15.7		124.4 ± 2.9		0.037
Diastolic blood pressure (mm/Hg)	80.2 ± 11.7		81.7 ± 9.5		78.7 ± 2.5		0.3
CD4 cell count (10 <sup>6</sup> /L)	520 ± 248		494 ± 235		548 ± 264		0.4
HIV duration (months)	(105)	(12-204)	(108)	(25-202)	(102)	(12-204)	0.8
Patients on ART (N)	56	89%	31	94%	25	83%	0.2
ART duration (months)	(58)	(16-79)	(54)	(16-77)	(59)	(30-79)	0.1
HIV RNA fully suppressed* (N)	47	75%	27	82%	20	67%	0.2
HIV RNA (10 <sup>3</sup> copies/mL)**	(45,500)	(17,900-107,000)	(72,300)	(47,000-72,300)	(33,400)	(17,900-107,000)	0.4

\*) HIV RNA < 100 copies/mL for patients on antiretroviral therapy  
\*\*) for patients not on antiretroviral therapy

**Table 2.** Antiretroviral therapy at follow-up.

Medicament	N	%
Lamivudine	52	83%
Zidovudine	32	51%
Tenofovir	12	19%
Abacavir	28	44%
Didanosine	5	8%
Stavudine	4	6%
Efavirenz	23	37%
Nevirapine	8	13%
Indinavir	4	6%
Saquinavir	10	16%
Lopinavir	10	16%
Ritonavir	30	48%
Nelfinavir	2	3%
Atazanavir	3	5%
Tipranavir	2	3%
<b>Combination</b>	<b>N</b>	<b>%</b>
2 NRTI + 1 NNRTI	20	32%
2 NRTI + 1 or 2 PI	17	27%
3 NRTI + PI	6	10%
NRTI + NNRTI + PI	10	16%
Other combination	8	13%
No ART	2	3%

## Conclusions

In both smoking and non-smoking HIV patients abnormal lung function parameters were present when lung function tests were performed in 2000/2001. On a group basis, both the non-smokers and the smokers had decreased DLCO/VA% and lung function parameters somewhat compatible with signs of early obstructive lung disease. After a mean of 4.5 years of modern HIV management, the DLCO/VA% increased back to normal in the non-smokers and increased in the smokers approximately to the starting point of the non-smokers. Overall, the 4.5 years of modern HIV management seemed to reduce the obstructive component observed at the initial first examination. However remarkably, the elevated RV% which in the non-smokers decreased to a normal level at the second examination, increased further in the smokers. This study suggests that modern HIV management overall is beneficial for the lung status of HIV patients and that some HIV induced changes even seem to be reversed over time when HIV is well-managed. However on a lung level, smoking definitely masks many of the beneficial effects of proper HIV treatment.