Cardiovascular magnetic resonance imaging reveals that Human Immunodeficiency Virus is an independent risk factor for vascular stiffness

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INTRODUCTION

Patients with HIV on combination Antiretroviral Therapy (cART) are at increased risk of cardiovascular (CV) events although the aetiology of this excess risk remains unclear. Reports of premature atherosclerosis and increased vascular stiffness among patients with HIV have generally been attributed to metabolic abnormalities associated with cART and a greater burden of traditional CV risk factors. However, it remains unclear whether HIV infection *per se* is associated with increased CV risk independent of metabolic abnormalities and traditional CV risk factors.

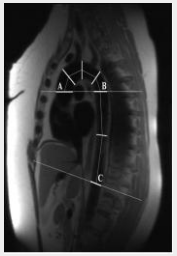
AIM

In this study, aortic pulse wave velocity (PWV), a non-invasive measure of aortic stiffness; predictive of CV morbidity and mortality, was investigated to determine whether HIV *per se* is associated with increased aortic stiffness independent of metabolic abnormalities and traditional CV risk factors.

METHODS

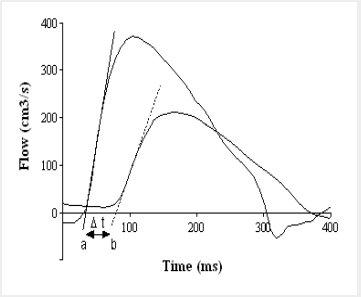
In total, 90 patients with HIV and no history of CV disease were compared to 74 matched controls. Anthropometric data was collected and fasting venous samples were taken for analysis of plasma metabolites. To assess aortic PWV, cardiovascular magnetic resonance imaging was used to measure through-plane flow in the ascending aorta at the at the level of the pulmonary artery and the descending aorta 11 cm below the pulmonary artery .

Figure: 1. Distance Δx is calculated as the total distance between A (ascending aorta) and C (abdominal aorta) using the sum of the distances between the centre points of lines drawn at 45°, 90° and 135° to the scan level.



Aortic PWV (m/s) was determined as Δx/Δt where Δx is the aortic distance between the two imaging levels (Figure 1) and Δt is time delay between the arrival of the foot of the pulse wave between these imaging levels (Figure 2). Bivariate correlations for all subjects were calculated using Pearson correlation coefficients. Significance was assumed at a probability value of $p < 0.05$.

Figure 2. Aortic flow/time curves used to calculate the arrival times of aortic pulse waveform. Δt represents the time (m/s) between the intercepts (b-a) of the tangents to the curve at the half maximal point of flow in the ascending aorta (a) and the abdominal aorta (b).



RESULTS

Patients with HIV and controls were well matched for several traditional CV risk factors (Table 1). Triglycerides were elevated in patients with HIV and HDL was reduced. Smoking was more prevalent among patients with HIV. Total cholesterol and waist to hip ratio was higher in the control group.

Table 1: Characteristics of the study population

	HIV (n = 90)	Controls (n= 74)	P value
Age (years)	45 ± 10	44 ± 10	0.610
SBP (mmHg)	121 ± 17	118 ± 14	0.179
DBP (mmHg)	77 ± 9	75 ± 9	0.226
BMI (kg/m^2)	26 ± 5	27 ± 5	0.243
Waist/hip ratio	0.86 ± 0.07	0.89 ± 0.08	0.005*
Triglycerides (mmol/L)	1.6 ± 1.4	1.0 ± 0.56	<0.001*
Cholesterol (mmol/L)	4.5 ± 1.4	4.9 ± 0.95	0.048
HDL-C (mmol/L)	1.1 ± 0.4	1.4 ± 0.3	<0.001*
Insulin (mmol/L)	7.9 ± 8.3	6.4 ± 5.8	0.218
Glucose (mmol/L)	5.1 ± 1.2	4.9 ± 0.5	0.175
HOMA-IR	2.0 ± 3.1	1.5 ± 1.4	0.164
History of Smoking (%)	37	10	<0.001*
PWV (m/s)	6.5 ± 2.1	5.6 ± 1.2	<0.001*

* $p < 0.05$

Aortic PWV was significantly higher in patients with HIV compared to controls (Table 1). Correlates of aortic PWV are presented (Table 2). Of note, there was no association between class of antiretroviral drug, duration of cART or any plasma metabolite and aortic PWV. Multivariable regression with aortic PWV as the dependent variable and age, SBP, smoking and HIV infection as independent variables revealed that HIV infection (β 0.70, $p = 0.006$), age (β 0.07, $p < 0.001$) and SBP(β 0.02, $p = 0.005$) were all independent predictors of aortic PWV (overall R^2 of the model = 0.32, $p<0.001$).

Table 2: Correlates of aortic PWV in the study population

	Pearson Correlation	P value
Age (years)	0.475	<0.001*
SBP (mmHg)	0.379	<0.001*
DBP (mmHg)	0.364	<0.001*
BMI (kg/m^2)	0.069	0.377
Waist to hip ratio	-0.014	0.862
Triglycerides (mmol/L)	0.083	0.296
Cholesterol (mmol/L)	-0.001	0.991
HDL-C (mmol/L)	-0.118	0.141
Insulin (mmol/L)	0.034	0.673
Glucose (mmol/L)	0.138	0.082
HOMA-IR	0.048	0.544
History of Smoking	0.224	0.004*
Duration of cART(years)	0.201	0.093
Nadir CD4 count (10^6/L)	-0.129	0.296
Current CD4 count (10^6/L)	0.263	0.014*
Viral load (copies/mL)	0.064	0.561
NRTIs	0.112	0.218
NNRTIs	0.05	0.581
PIs	0.060	0.508
HIV infection	0.252	0.001*
Length of HIV infection (years)	0.219	0.006*

* $p < 0.05$

CONCLUSIONS

- HIV is predictive of increased aortic stiffness and this effect is independent of metabolic abnormalities and traditional CV risk factors.
- HIV may be mechanistically associated with increased vascular stiffness which could underlie the pathophysiology of premature vascular disease.