Monocyte Activation and Cardiac-MRI-Derived Vascular Dysfunction among Women with HIV

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Background

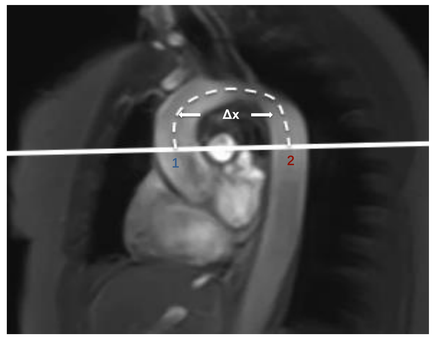
Women with HIV (WHIV) on ART face an increased risk of cardiovascular disease (CVD). Aortic vascular dysfunction, reflected by increased aortic pulse wave velocity (aPWV), presages, predicts, and promotes adverse CVD outcomes and is highly influenced by the local inflammatory milieu. Cognizant of sex-specific patterns of HIV-associated immune dysregulation, we compared aPWV among asymptomatic ART-treated women with HIV vs. women without HIV. We hypothesized that WHIV would evidence vascular dysfunction in association with monocyte activation.

Methods

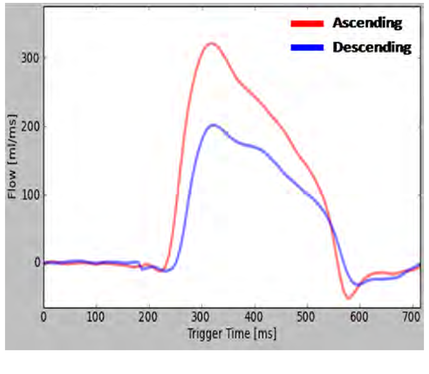
In this prospectively recruited cross-sectional study, 20 asymptomatic WHIV on ART and 14 women without HIV completed cardiovascular magnetic resonance imaging as well as immune and metabolic phenotyping procedures. Aortic vascular function was quantified by measuring the aortic pulse wave velocity (**Figure 1**).

Figure 1. Assessment of aortic arch pulse wave velocity

A



B



$$aPWV = \frac{\Delta x}{\Delta t}$$

Δx = aortic path along midline in vessel lumen (dashed white line in Figure 1A)

Δt = transit time (distance between systolic up-stroke in ascending and descending aorta flow curves in Figure 1B)

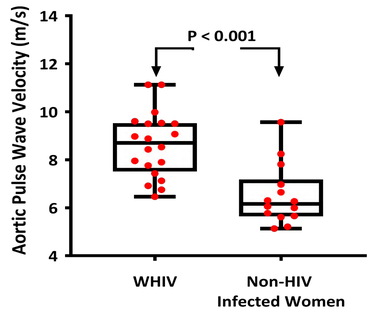
Results

Table 1. Baseline Demographics

	WHIV (n=20)	Non-HIV-infected Women (n=14)	P-value
Age (years)	52 ± 4	53 ± 6	0.61
BMI (kg/m^2)	32 ± 7	32 ± 7	0.73
HTN (%)	25 (5/20)	29 (4/14)	0.82
Current smoking (%)	50 (10/20)	29 (4/14)	0.21
Total Cholesterol (mg/dL)	200 ± 41	203 ± 28	0.80
LDL Cholesterol (mg/dL)	113 ± 33	109 ± 26	0.69
Duration of HIV (years)	19 ± 8	--	--
HIV Viral Load (copies/mL)	19 (19, 19)	--	--
CD4 + T cell count (cells/mm^3)	773 (526, 1202)	--	--

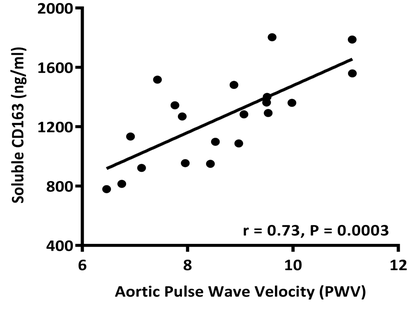
Aortic pulse wave velocity (aPWV) was significantly higher among WHIV vs. women without HIV (8.6 ± 1.3 m/s vs. 6.5 ± 1.3 m/s, P<0.0001; **Figure 2**).

Figure 2. Aortic pulse wave velocity among women with vs. without HIV



Soluble CD163 (sCD163) was higher among WHIV vs. women without HIV (1260 ± 293 ng/mL vs. 938 ± 308 ng/mL; P=0.005) and related directly to aPWV (r = 0.73, P = 0.0003; **Figure 3**). Among the whole group and among WHIV, aPWV related to extracellular volume – a measure of myocardial fibrosis (whole group: r=0.54, P=0.001; WHIV: r=0.47, P=0.04).

Figure 3. Relationship between aortic pulse wave velocity and monocyte activation



Results Continued

Both HIV status and sCD163 levels independently predicted aPWV, even after controlling for age, BMI, cigarette smoking status, and systolic blood pressure (R^2=0.63, P=0.0002; **Table 2**). Among WHIV, sCD163 levels independently predicted aPWV after controlling for duration of HIV, CD4+ T cell count, and HIV viral load (R^2=0.62, P=0.007; **Table 3**).

Table 2. Multivariable Regression Modeling for aPWV (whole group)

Covariate	β-estimate	β-SE	P-value
HIV status [Negative]	-0.69	0.29	0.02
sCD163 (ng/mL)	0.002	0.0009	0.01
Age (years)	0.03	0.05	0.61
BMI (kg/m^2)	-0.03	0.03	0.26
Systolic Blood Pressure (mmHg)	-0.009	0.01	0.47
Current Smoker [No]	0.32	0.23	0.17

Overall model: R^2 = 0.63, P=0.0002

Table 3. Multivariable Regression Modeling for aPWV (WHIV)

Covariate	β-estimate	β-SE	P-value
CD4+ T cell count (cells/mm^3)	-0.0009	0.0006	0.17
sCD163 (ng/ml)	0.004	0.0008	0.0005
HIV viral load (copies/ml)	0.002	0.004	0.68
Duration since HIV diagnosis (years)	-0.03	0.03	0.39

Overall model R^2 = 0.62, P=0.007

Conclusions

Asymptomatic ART-treated WHIV demonstrated increased aPWV. Among WHIV, aPWV related to heightened monocyte activation as well as to downstream cardiac pathology (myocardial fibrosis). Additional studies are needed to identify targeted immune-modulatory therapies which slow the progression from vascular dysfunction to incident cardiac disease in this at-risk population.

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Disclosures

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