Impaired Cardiac Strain and Biomarkers of Immune Activation in HIV

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BACKGROUND

- Chronic HIV infection is associated with an increased risk of cardiovascular disease (CVD) and, specifically, myocardial dysfunction
- Radiological and immunologic markers of subclinical cardiovascular dysfunction are increasingly used to investigate the etiology of this association
- Measures of cardiac strain and cardiac fibrosis by MRI were evaluated with traditional CVD risk factors and biomarkers of immune activation in a cohort of HIV-infected adults without known cardiovascular disease

METHODS

- Prospective cross-sectional study of 95 HIV-infected adults and 30 age, sex, and race-matched health controls, all free of known CVD
- Extracellular volume index was quantified by MRI and used as a measure of myocardial fibrosis
- Regional cardiac strain was derived from grid tagged cine MR images. Greater circumferential strain is more negative (more shortening), while greater radial strain is more positive (more thickening)
- HIV-related and other pertinent history were characterized by review of clinical history
- Fasting laboratories included chemistry, lipid panel, CD4 T cell counts, HIV viral load, biomarkers of inflammation and vascular injury, and immune markers
- Group comparisons were performed using Student's t-tests or chi-square statistics as appropriate. Non-normally distributed variables were log transformed to approximate a normal distribution
- Two sided p-values of p<0.05 were used to determine statistical significance. Values in data tables are presented as mean ± SD unless otherwise indicated.

RESULTS

Table 1: Demographic and clinical characteristics of participants.

	HIV+ (n=95)	Control (n=30)	P-value
Age, years	49 ± 10	46 ± 8	0.17
Sex, n (%)			0.88
Male	70 (74)	22 (73)	
Female	24 (26)	8 (27)	
Race, n (%)			
White	27 (28)	8 (27)	0.80
Black	55 (58)	18 (60)	
Hispanic	9 (10)	4 (13)	
Mixed Race	1 (1)	0 (0)	
Asian	3 (3)	0 (0)	
BMI (kg/m^2)	28.0 ± 5.4	29.8 ± 4.3	0.07
Ever Smoked, n (%)	62 (65)	10 (33)	**0.002**
Smoking Pack-years	11.0 ± 22.3	1.6 ± 3.7	**0.0001**
Diabetes, n (%)	9 (10)	0 (0)	0.09
Hepatitis C, n (%)	18 (19)	0 (0)	**0.01**
Framingham Risk Score (%)	4.5 ± 4.9	3.4 ± 3.2	0.16
Systolic Blood Pressure (mmHg)	127 ± 13	123 ± 13	0.13
Diastolic Blood Pressure (mmHg)	79 ± 9	76 ± 10	0.12
Currently on Lipid Lowering Therapy, n (%)	33 (34.7)	5 (16.7)	0.06

RESULTS

Table 2: Inflammatory biomarkers and MRI measurements of participants.

	HIV+ (n=95)	Control (n=30)	P-value
Inflammation Biomarkers			
D-dimer (ug/mL FEU)	0.32 ± 0.25	0.43 ± 0.31	0.09
CRP (mg/L)	3.6 ± 5.7	3.9 ± 5.3	0.8
Pro-BNP (pg/mL)	57.6 ± 133.7	31.6 ± 32.5	0.09
MCP-1 (pg/mL)	473 ± 249	321 ± 221	**0.003**
LBP (ng/mL)	437 ± 233	410 ± 224	0.6
TIMP-1 (ng/mL)	12.3 ± 61.1	10.1 ± 46.3	**0.03**
Cardiac Strain and Fibrosis MRI			
Systolic Circumferential Strain (%)	-15.8 ± 2.7	-16.4 ± 2.5	0.31
Systolic Radial Strain (%)	21.7 ± 8.6	30.5 ± 14.2	**0.004**
Systolic Radial Strain Rate	99.7 ± 41.0	121.3 ± 49.6	**0.048**
Systolic Epicardial-Endocardial Circumferential Strain (%)	7.0 ± 2.5	8.5 ± 2.8	**0.02**
Myocardial Extracellular Volume Index	0.28 ± 0.04	0.26 ± 0.03	**0.02**
Ejection Fraction (%)	62 ± 6	63 ± 4	0.4

Figure 1: Myocardial Strain and Myocardial Fibrosis Index by Patient Group. * indicated for p-values < 0.05 compared to controls.

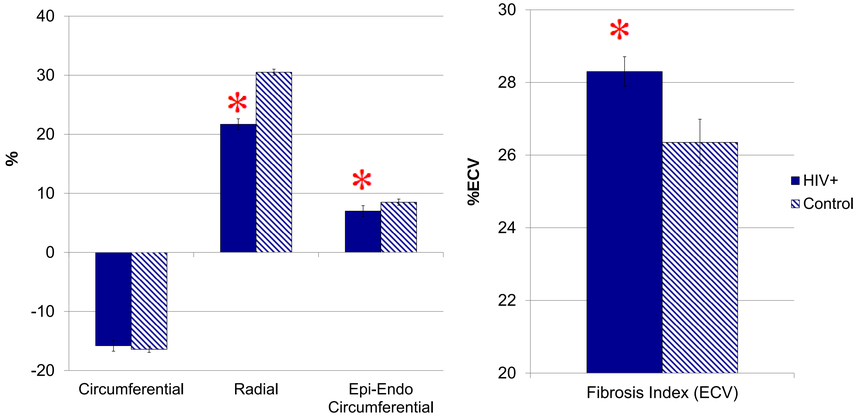

Table 3: Clinical characteristics of the HIV+ group.

	HIV+ (n=95)
Duration HIV diagnosis, years	14 ± 8
Current ARV use, n (%)	88 (93)
Duration of ARV use, years	9 ± 6
Current CD4 T-cells, cells/μL	615 ± 276
Nadir CD4 T-cells, cells/μL	235± 182
Undetectable HIV viral load (M50 copies/mL), n (%)	80 (84.2)

Figure 2: Correlations of Inflammatory Biomarkers with Radial Strain in HIV.

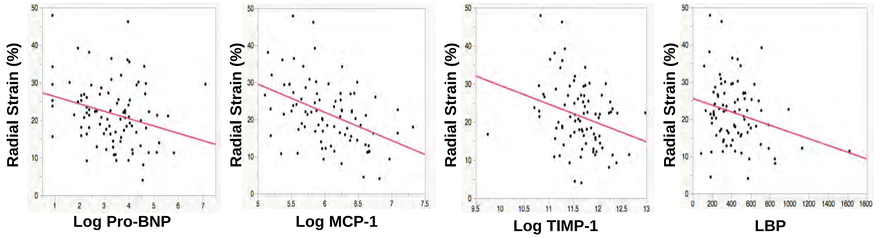

Table 4: Correlates of Subclinical Radial Strain Impairment.

	Correlation Coefficient	P-value	Multivariate Model	
			Estimate	P-value
HIV Status	--	**0.0083**	2.29	**0.04**
Age (years)	0.05	0.62	0.12	0.24
Smoking pack-years	0.20	**0.03**	-0.04	0.41
logMCP-1 (pg/mL)	0.49	**<0.0001**	-8.22	**0.0002**
logPro-BNP (pg/mL)	0.07	0.48	-0.11	0.89
logTIMP-1 (ng/mL)	0.32	**0.0007**	0.41	0.86
LBP (ng/mL)	0.10	**0.027**	-0.005	0.21

The multivariate model s a multivariate regression analysis including HIV status, age, smoking pack-years, logMCP-1, logPro-BNP, logTIMP-1, and lipopolysaccharide binding protein (LBP).

CONCLUSIONS

- Strain indices, a marker of systolic dysfunction, were decreased in HIV-infected subjects
- Diffuse myocardial fibrosis, a potential early marker of LV impairment, is increased in asymptomatic HIV compared to controls
- Subclinical impairment in cardiac strain tracks with markers of chronic inflammation and chronic immune activation, which may serve as targets for future therapeutic strategies to optimize long-term cardiovascular health in persons living with HIV