PREVALENCE OF SUBCLINICAL MYOCARDIAL ABNORMALITIES IN HIV: THE SMASH STUDY

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BACKGROUND

- PLWH (HIV+) are at increased risk for heart failure compared to the general population.
- Some studies suggest a higher prevalence of myocardial fibrosis.
- The purpose of this study was to evaluate whether PLWH have more subclinical myocardial disease than HIV-uninfected (HIV-) individuals after controlling for multiple potential confounding factors.

METHODS

Participants (n=432)

- Recruited in Baltimore, MD, Washington, DC and Chicago, IL (2015-18) from three NHLBI cohort studies that include HIV+ and at-risk HIV- individuals
- Multicenter AIDS Cohort Study (MACS)
- Women's Interagency HIV Study (WIHS)
- AIDS Linked to the Intravenous Experience Study (ALIVE)
- Age 40-70 years
- eGFR> 45 ml/min/m^2

Cardiac MRI (CMR)

- 1.5 Tesla Siemens Avanto or Aera scanners (Erlangen, Germany) using a standardized protocol.
- Biventricular volumes and mass, left atrial volumes, left ventricular (LV) and left atrial (LA) strain.
- Contrast and T1 mapping for scar patterns and burden, including late gadolinium enhancement (LGE)
- Extracellular volume (iECV) was indexed to LV myocardial volume. This reflects diffuse fibrosis.

Questionnaires

- Detailed assessment of drug and alcohol use
- Additional information harmonized from across the 3 cohort studies.

Statistics

- Multivariable linear and logistic regression analyses.
- Model 1: adjusted for age, sex, race, parent cohort (MACS, WIHS, ALIVE), and education level.
- Model 2: additionally adjusted for cumulative pack-year of smoking, history of or medications used to treat hypertension, diabetes, or dyslipidemia, and cardiovascular disease history, use of heavy alcohol, marijuana, opioids, stimulants, erectile dysfunction drugs, or nitrates in the past 5 years, and body mass index for CMR outcomes not indexed to body surface area.

RESULTS

Table 1: Participant characteristics by HIV serostatus

	% or Median (IQR)		
	HIV-uninfected (N=162)	HIV-infected (N=270)	P-value
Age (years)	55.6 (51.9, 58.8)	54.7 (50.4, 58.4)	0.18
Female sex	27%	31%	0.43
Race: White	25%	21%	0.44
Black	67%	73%	
Hispanic/Other	7%	6%	
Cohort: MACS	44%	44%	0.32
WIHS	16%	21%	
ALIVE	40%	34%	
Education level (<high school)	24)	31%	0.05
Heavy alcohol use (>13 drinks/week)	12%	11%	0.75
Cumulative pk-yr smoking (past 5 yrs)	0.1 (0.0, 2.3)	0.9 (0.0, 2.8)	0.04
Body mass index (kg/m^2)	27.1 (24.1, 31.0)	26.0 (23.1, 30.8)	0.06
Systolic blood pressure (mmHg)	127 (121, 135)	125 (118, 135)	0.08
Hypertensive or taking BP medication	57%	55%	0.69
Diabetic or taking diabetes medication	14%	13%	0.63
Taking lipid-lowering medication	23%	25%	0.75
Known cardiovascular disease	6%	7%	0.54
Recreational substance use (past 5 yrs)			
Marijuana	42%	45%	0.56
Opioids	33%	31%	0.69
Stimulants	36%	41%	0.24
Erectile dysfunction medications	19%	25%	0.25
Nitrates	13%	14%	0.67

Table 2: HIV factors (n= 270)

HIV RNA viral load undetectable, <50 copies/ml	74%
HIV RNA copy number/mL, if detectable	279 (131, 4373)
CD4+ T-cell count (cells/mm^3)	610 (398, 826)
Nadir CD4+ T-cell count (cells/mm^3)	270 (141, 400)
On cART	89%
cART duration (years)	12.3 (4.6, 15.9)
History of clinical AIDS	21%

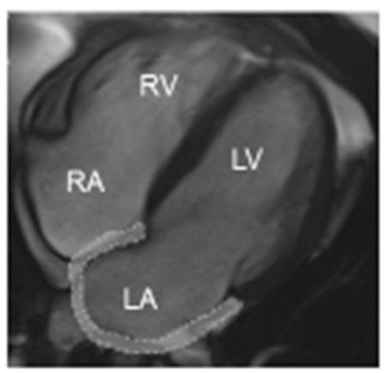

Figure 1: Sample cardiac MRI with left atrial borders.

Table 3: Association between HIV serostatus and mean differences in selected left ventricular (LV) cardiac MR variables (HIV+ vs. HIV-)

		Model 1		Model 2	
	N	Mean difference (95% CI)	P-value	Mean difference (95% CI)	P-value
LV Ejection Fraction (EF) (%)	432	-1.03 (-2.40, 0.34)	0.14	-0.62 (-1.96, 0.71)	0.36
LV Mass, indexed (g/m^2)	432	1.32 (-0.68, 3.31)	0.20	0.98 (-0.96, 2.92)	0.32
LV End-diastolic volume (EDV), indexed (ml/m^2)	432	2.89 (-0.27, 6.06)	0.07	2.87 (-0.23, 5.98)	0.07
LV End-systolic volume (ESV), indexed (ml/m^2)	432	1.62 (-0.06, 3.30)	0.06	1.44 (-0.19, 3.06)	0.08
Global circumferential systolic strain (%)	418	0.55 (-0.30, 1.40)	0.20	0.40 (-0.43, 1.24)	0.34
Peak filling rate (ml/second)	432	-2.17 (-23.54, 19.19)	0.84	2.67 (-18.97, 24.31)	0.81
Native T1 times (msec)	404	-3.55 (-14.09, 6.99)	0.51	-3.43 (-14.17, 7.30)	0.53
Extracelluar volume (ECV) (%)	333	**0.94 (0.08, 1.80)**	**0.03**	0.83 (-0.03, 1.69)	0.06
Indexed ECV	333	**1.03 (0.29, 1.78)**	**0.01**	**0.99 (0.25, 1.73)**	**0.01**

No associations seen with right ventricular indices.

Table 4: Associations between HIV serostatus and left atrial volume indices (LAVI) (HIV+ vs. HIV-)

		Model 1		Model 2	
	N	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
LAVI (min), mL/m^2	420	1.33* [0.23,2.43]	0.02	1.34* [0.24,2.44]	0.02
LAVI (max), mL/m^2	425	2.21* [0.28,4.13]	0.02	2.32* [0.39,4.25]	0.02
LAVI (preA), mL/m^2	420	1.87* [0.28,3.46]	0.02	1.93* [0.33,3.52]	0.02

- No difference in prevalence of focal myocardial scar in unadjusted (32% in HIV- and 37% in HIV+) or adjusted models.
- Low median scar extents, predominantly non-ischemic.
- Ejection Fraction (EF) < 40% prevalence low (0% HIV- and 1% HIV+).
- No difference in EF by HIV serostatus.
- Left atrial volumes were higher in HIV+ than HIV- individuals.
- There were no associations between LA volumes and HIV RNA viral load or CD4 cell counts.
- Indexed extracellular volume was higher in HIV+ than HIV- individuals.

Strengths

- Contemporary cohort of well-treated PLWH
- HIV uninfected group with similar risk behaviors
- Detailed adjustment for potential confounding factors
- Relatively large sample size

CONCLUSIONS

- **Among a comparable group of HIV- and HIV+ individuals, prevalent ventricular systolic dysfunction was rare.**
- **HIV+ serostatus was independently associated with greater diffuse nonischemic fibrosis and larger left atrial phasic volumes, but not focal myocardial scar.**
- **This possibly reflects diastolic dysfunction and could lead to a predisposition to atrial arrhythmias.**

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