Association of Inflammatory Markers With Cardiac Indices in the MACS

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Background

- People living with HIV (HIV+) are at increased risk of heart failure even after adjustment for demographics and cardiovascular risk factors.
- Among HIV+ without symptoms of heart failure, diastolic dysfunction has been reported to be highly prevalent.
- It is unclear if chronic systemic inflammation may explain changes in cardiac structure and function.

Purpose

- To determine prospective association of inflammatory markers with subclinical myocardial changes on echocardiogram

Methods

Study Design:
- The Multicenter AIDS Cohort Study (MACS) is a prospective observational cohort with both HIV+ and HIV-uninfected (HIV-) MSM.

Study Sites: Baltimore/DC, Pittsburgh, Chicago, Los Angeles

Study Participants:
- **PLWH:** 384 HIV+ men
- **HIV–:** 254 HIV- men

with echocardiograms and inflammatory markers

Assessment:
- **Echocardiogram:** 2-dimensional echocardiogram with tissue Doppler collected in 2018/2019
- **Inflammatory markers:** IL-6, TNF-alpha, hsCRP, D-dimer on frozen specimens collected between 2008-2010

Statistical Analysis:
- Multivariate linear regression

Results

Table 1: Characteristics of study participants

	HIV Negative (254)	HIV positive (384)	p-value
	mean(SD)	mean(SD)	
Age (years)	60(12)	55(11)	<0.001
Race			
Black (%)	22.0	32.6	
White (%)	68.8	47.7%	<0.001
Other (%)	9.4	19.6%	
Systolic BP (mmHg)	131(17)	128(15)	0.002
Diastolic BP (mmHg)	77(11)	78(10)	0.04
BMI (kg/m^2)	27.5(5.4)	27.2(5.0)	0.38

Table 2#:Association of serological inflammatory markers with parameters of cardiac structure and function

	Ejection fraction (%)	LV mass index (g/m^2)	LA volume index (mL/m^2)	Mitral valve E/e' ratio	Mitral valve E/A ratio	Mitral inflow velocity E (m/s)	Mitral annular e' velocity (cm/s)
HIV serostatus † (a)	0.85	3.25	0.92	0.17	**0.07****	0.40	-0.17
IL-6‡ (b)	-0.76	0.10	**2.14****	-0.09	0.00	-4.07	-0.40
TNF-alpha‡ (b)	-0.80	0.46	0.10	0.45	0.03	1.65	-0.19
hsCRP‡ (b)	-0.18	-0.11	1.27	0.05	0.04	2.52	0.23
D-Dimer Quintiles ⚤(b):							
1st	-	-	-	-	-	-	-
2nd	-0.44	0.87	1.11	0.29	-0.01	-0.61	-0.42
3rd	-0.36	1.27	**2.14****	-0.05	-0.04	-1.92	-0.24
4th	0.32	-4.38	**2.16****	0.21	0.06	0.41	-0.19
5th	-1.23	2.94	**2.51****	0.61	0.05	0.79	-0.51

****** p<0.01, ** p<0.05***

Multivariable **adjusted regression coefficients describing change in mean cardiac parameters** (with their appropriate units)

† comparing HIV+ to HIV-; ‡ comparing lowest quintile of inflammatory marker to highest quintile of inflammatory marker**,** other quintiles non-significant and not shown in table; ⚤ comparing each d-dimer quintile to lowest quintile; LA, denotes left atrial; LV denotes left ventricular.

a: Adjusted for age, race, body mass index (BMI), MACS site, and year of MACS enrollment (before/after 2001), hyperlipidemia, systolic and diastolic blood pressure, diabetes.

b: Adjusted for HIV status in addition to risk factors in **a**

Results

- Left atrial volume index was progressively associated with increasing D-dimer quintiles and highest vs lowest IL-6 quintile, independent of HIV serostatus.
- There were no associations between inflammatory markers and echo-derived parameters of diastolic function including transmitral flow velocity (E), mitral annular velocity (e') and E/e' ratio.

Limitations and Strengths

Limitations:
- Inflammatory markers were collected years prior to echocardiogram
- Cross-sectional echocardiogram data limits the evaluation of progression of cardiac structure abnormalities with time

Strengths:
- Comparison groups were similar demographically and in risk factor for HIV infection.

Conclusions

- Larger LA size was associated with markers of heightened systemic inflammation
- Since left atrial dilation predicts future risk of atrial fibrillation and stroke, those with higher inflammation may be at a greater risk of atrial fibrillation and stroke
- Further investigation is needed to evaluate whether systemic inflammation mediates increased atrial arrhythmic risk among both HIV+ and HIV- people

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