Abstract #730

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Monocyte and Cellular Activation are Associated with Coronary Atherosclerosis in HIV-infected Participants in the MACS

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Background

- Immune activation is a proposed mechanism for increased cardiac risk in HIV infection. Little is known as to how different types of immune activation contribute to this outcome.

Objective

- To determine whether cellular immune activation is independently associated with different measures of coronary atherosclerosis.

Methods

- Cross-sectional analyses of HIV-uninfected (n=92) and virally suppressed HIV-infected (n=139) men in Los Angeles, in the Multicenter AIDS Cohort Study (MACS).
- Non-contrast cardiac computed tomography (CT) to assess coronary artery calcium (CAC) was performed on all participants and CT angiograms for presence of calcified plaque (CP), mixed plaque (MP), non-calcified plaque (NCP), total plaque (TP) and coronary stenosis (CS) were performed on 81 HIV-uninfected and 115 HIV-infected.
- CD8+ T cell activation (CD38+/HLA-DR+) was assessed by flow cytometry on fresh cells in a single laboratory at a time proximal to the coronary studies.
- Soluble monocyte activation markers, sCD163 and sCD14 were measured by ELISA on the day of the CT.
- Associations between immune activation and presence of atherosclerosis were assessed with logistic regression, adjusting for age, ethnicity and cardiovascular risk factors using multiple imputation for missing data.

Results

- HIV- infected were significantly younger and had higher CD8 T-cell activation, sCD14 and sCD163 levels than uninfected (Table 1 and 2).
- No difference in frequency of atherosclerosis between the HIV-infected and uninfected (Table 3).
- Activation markers did not predict atherosclerosis in HIV-uninfected but did in infected (Table 4), with cellular activation associations mostly seen after adjusting for HIV-related factors (data no shown).

Table 1: Baseline Characteristics

	HIV-uninfected (n=92)	HIV-infected (n=139)
Age, mean years (SD)*	55 (7)	52 (7)
Race/ethnicity (%)		
White	59	52
African American	24	17
Hispanic/other	17	31
CD4 count, median cells/uL (IQR)		
Current	NA	656 (450, 786)
Nadir		265 (129, 383)
Time on antiretrovirals, median years (IQR)	NA	9.7 (7.3, 12.4)

SD, standard deviation; IQR, interquartile range

Table 2: Markers of Activation

Marker	HIV-uninfected (n=92)	HIV-infected (n=139)
Cellular markers, median percent (IQR)		
CD38+/HLA-DR+ CD8+ T cells	2.15 (1.44, 3.36)	3.79 (2.4, 6.52)
Soluble markers, median ng/mL (IQR)		
sCD14*	1243 (1051, 1418)	1582 (1356, 1830)
sCD163*	581 (412, 746)	688 (529, 879)

IQR, interquartile range; *p<0.05 (Kruskal-Wallis or Chi-square test for comparison between HIV-uninfected and infected)

Table 3: Prevalence of Coronary Atherosclerosis

Measure	HIV-uninfected (n=81)	HIV-infected (n=115)
Computerized tomography findings (%)		
CAC*	50	50
CP	43	36
NCP	51	59
MCP	40	37
TP	79	76
CS	12	20

CAC, coronary artery calcium; CP, calcified plaque; NCP, non-calcified plaque; MCP, any mixed calcified plaque; TP, any plaque; CS, >50% coronary stenosis; *For this assessment there are 92 HIV-uninfected and 139 HIV-infected participants

Results (Continued)

Table 4: Odds ratio (95% Confidence Interval) in multivariate analysis† (per 1 SD increase in CD38+/HLA-DR+ , sCD14 and sCD163).

	HIV-infected			HIV-uninfected		
	CD38+/HLA-DR+	sCD14	sCD163	CD38+/HLA-DR+	sCD14	sCD163
CAC	1.62 (1.01, 2.59)	1.10 (0.65, 1.84)	1.96 (1.17,3.27)	0.43 (0.08, 2.27)	1.67 (0.61, 4.62)	1.33 (0.65, 2.71)
CP	1.84 (1.09, 3.10)	1.35 (0.76, 2.40)	1.86 (1.07, 3.25)	1.71 (0.53, 5.57)	2.17 (0.93, 5.07)	2.01 (0.96, 4.23)
NCP	0.88 (0.51, 1.50)	0.89 (0.52, 1.51)	1.13 (0.63, 2.03)	0.95 (0.33, 2.73)	1.14 (0.58, 2.23)	0.70 (0.39, 1.24)
MCP	1.34 (0.84, 2.13)	1.40 (0.82, 2.36)	2.97 (1.53, 5.76)	0.58 (0.11, 3.11)	1.08 (0.42, 2.79)	1.13 (0.54, 2.38)
TP	1.07 (0.64, 1.79)	1.23 (0.68, 2.22)	2.84 (1.25, 6.47)	1.45 (0.37, 5.66)	1.52 (0.53, 4.35)	1.52 (0.53, 4.38)
CS	2.02 (1.00, 4.06)	0.75 (0.39, 1.42)	1.68 (0.80, 3.52)	N/A*	N/A*	N/A*

CAC, coronary artery calcium; CP, calcified plaque; NCP, non-calcified plaque; MCP, any mixed calcified plaque; TP, any plaque; CS, >50% coronary stenosis. †adjusted for gender, ethnicity, CV and HIV factors; *N/A, not applicable because too few events in this population. Yellow shaded boxes represent significant associations.

Summary/Conclusion

- **Virologically suppressed HIV-infected participants have higher levels of cellular and monocyte activation markers than HIV-uninfected participants.**
- **Although not significant, HIV-infected had increased frequency of non-calcified plaque and coronary stenosis than uninfected participants.**
- **In adjusted model, a soluble marker of monocyte activation was associated with multiple types of plaque in HIV-infected but not uninfected participants.**
- **In adjusted model, particularly after including HIV-related factors, a marker of cellular activation was associated with increased risk of select types of plaque and coronary stenosis in HIV-infected but not uninfected participants.**

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