ASSOCIATION OF IP-10 AND FAT ATTENUATION INDEX IN PWH AND CONTROLS WITHOUT CVD

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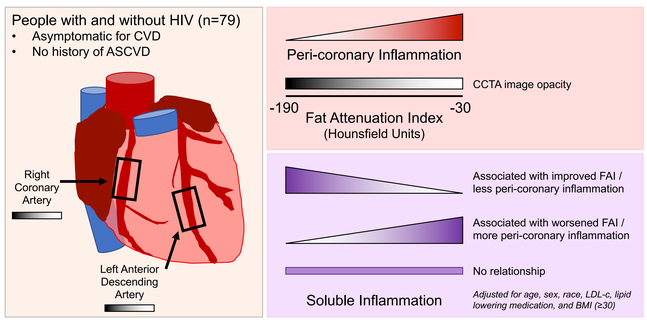
BACKGROUND

Despite antiretroviral therapy (ART) that controls viremia, chronic inflammation is a driver of elevated cardiovascular disease (CVD) risk in people living with HIV infection (PWH). Fat attenuation index (FAI) is a measure of peri-coronary inflammation by coronary computed tomography angiography (CCTA) that independently predicts CVD risk in HIV-uninfected persons and may be an important noninvasive biomarker of asymptomatic CVD in PWH. *Whether FAI is associated with soluble chemokines or other inflammatory mediators is unknown.*

METHODS

- Cross-sectional study: PWH (n=58) and controls (n=21) *without prior CVD* underwent CCTA and had FAI measurements of the right coronary artery (RCA) and the left anterior descending artery (LAD).
- Associations of white blood cell (WBC) count, high sensitivity C-reactive protein (hs-CRP), CCL2, IP-10/CXCL10, CX3CL1/fractalkine, IL-6, CD14, CD163, RANTES/CCL5, TNFR-I, and TNFR-II with FAI values were assessed as tertiles and continuous variables (not shown) in multivariable regression models
- Models were adjusted for age, sex, race, LDL-c levels, BMI ≥30, and use of lipid-lowering medication.

Research Design Schematic



Abbreviations:

ART, antiretroviral therapy; ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; CCTA, coronary computed tomography angiography; FAI, fat attenuation index; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; IP-10, IFN-γ-induced protein 10; LAD, left anterior descending artery; RCA, right coronary artery; PWH, people living with HIV infection; T1, first tertile; T2, second tertile; T3, third tertile; TNFR, tumor necrosis factor receptor; WBC, white blood cell count.

Table 1. Characteristics of Study Population

	People with HIV, N=58 (73.4%)	People without HIV, N=21 (26.6%)	P value
Sociodemographic factors			
Sex at Birth, n (%)			
Female	27 (46.6%)	13 (57.1%)	0.406*
Age at enrollment (years), Mean±SD	51.57±9.37	52.85±4.95	0.441#
Race, n (%)			
Black/African American	47 (82.5%)	12 (60.0%)	0.064**
White	10 (17.5%)	8 (40.0%)	
Clinical Indicators			
Duration of HIV Diagnosis, years, Mean±SD	17.85±9.31	-	
ART Duration, years, Median (Q1, Q3)	6.00 (2.00,8.00)	-	
CD4 cell count/mm^3, Median (Q1, Q3)	682.00 (539.50,1022.50)	-	
Hepatitis B infected, n (%)	5 (8.6%)	0 (0%)	0.320**
Hepatitis B and C infected, n (%)	0 (0%)	0 (0%)	-
Family History CVD, n(%)	19 (32.8%)	11 (55.0%)	0.078*
Baseline ASCVD Risk Score, Median (Q1, Q3)	0.05 (0.02, 0.09)	0.05 (0.04, 0.12)	0.679¥
BMI, Mean±SD	27.16±6.10	33.24±9.73	**0.013**#
RCA Mean FAI,ŧ Mean±SD	-85.80±1.14	-84.91±1.39	**0.007**#
LAD Mean FAI, Mean±SD	-86.11±1.00	-84.95±1.22	**<0.001**#

Bolded values represent statistically significant results.
* *P* value using Chi Square test.
** *P* value using Fisher's Exact test.
# *P* value using Independent t test.
¥ *P* value using Mann-Whitney U test.
Ŧ 6 missing observations: 5 in HIV-infected and 1 in HIV-uninfected

Table 2. Comparisons of WBC and Plasma Marker Concentrations in People with and without HIV

	People with HIV, N=58 (73.4%)	People without HIV, N=21 (26.6%)	*P value
WBC	5.4 (4.4,6.5)	6.1 (5.4,6.7)	0.141
hs-CRP##	2.3 (0.6,4.3)	2.1 (1.0,4.6)	0.745
CCL2#	237.5 (195.5,288.0)	208.0 (159.0,252.0)	0.070
IP-10#	196.0 (145.0,280.5)	158.0 (127.5,213.5)	0.129
CX3CL1#	1000.5 (863.5,1419.5)	997.0 (843.5,1077.5)	0.213
IL-6#	3.6 (2.3,6.0)	2.5 (1.6,6.7)	0.494
CD14	4513463.0 (1874536.3,7259317.5)	5626056.0 (4166930.5,6432032.0)	0.594
CD163	708727.5 (527188.3,1067248.5)	577807.0 (429962.5,668157.5)	**0.010**
CCL5	110068.5 (75159.0,155138.5)	112320.0 (78256.5,143552.0)	0.885
TNFR-I	1641.5 (1262.0,1951.0)	1937.0 (1443.0,2100.0)	0.087
TNFR-II	3389.5 (2959.5,4486.3)	3833.0 (2965.0,4358.5)	0.484

Bolded value represents statistically significant result. All concentrations are pg/ml.
* *P* value using Mann-Whitney U test.
# N=75 (4 missing observations)
N=77 (2 missing observations)

Table 3. Adjusted Associations between Tertiles of Soluble Markers of Inflammation and FAI

		RCA Mean FAI		LAD Mean FAI	
	Ref:T1	*Beta Coefficient (95% Confidence Interval)	*P* value	Beta Coefficient (95% Confidence Interval)	*P* value
IP-10#	T2	-0.75 (-1.55,0.04)	0.063	-0.32 (-1.03,0.38)	0.360
	T3	0.26 (-0.50,1.01)	0.498	0.66 (0.01,1.31)	**0.047**
CD14	T2	0.28 (-0.53,1.09)	0.492	0.81 (0.11,1.52)	**0.025**
	T3	0.32 (-0.54,1.18)	0.453	0.57 (-0.16,1.30)	0.122

Bolded values represent statistically significant values.
* Regression β coefficients adjusted for age, sex, race, LDL-c level, use of lipid lowering medication and BMI≥30 and T1 as reference category.
# N=76 (4 missing observations)

Each β coefficient corresponding to T2 represents an association between RCA or LAD peri-coronary inflammation (assessed by FAI values) and soluble marker for study participants in the second tertile (T2) of marker values in reference to the first tertile (T1) of marker values. A similar interpretation applies to the β coefficient corresponding to T3.

Table 4. Comparisons of Adjusted Associations of Tertiles of Soluble Markers of Inflammation and FAI in People with and without HIV

		WBC	IP-10#	CCL5	TNFR-I	TNFR-II
RCA Mean FAI	T2*Serostatus	2.84 (0.79,4.90) ***0.008***	1.66 (0.02,3.30) ***0.047***	-0.61 (-2.56,1.35) *0.537*	2.01 (0.06,3.95) ***0.043***	0.42 (-1.75,2.60) *0.697*
	T3*Serostatus	1.74 (-0.53,4.01) *0.129*	2.03 (0.37,3.69) ***0.018***	0.36 (-1.40,2.13) *0.681*	1.61 (-0.26,3.47) *0.089*	0.55 (-1.12,2.22) *0.510*
LAD Mean FAI	T2*Serostatus	-0.43 (-2.43,1.58) *0.670*	-1.11 (-2.55,0.32) *0.126*	-2.12 (-3.63,-0.61) ***0.007***	0.24 (-1.56,2.04) *0.790*	-0.42 (-2.26,1.42) *0.649*
	T3*Serostatus	-0.760 (-2.97,1.45) *0.493*	0.23 (-1.26,1.72) *0.759*	-0.16 (-1.52,1.20) *0.813*	1.21 (-0.46,2.88) *0.153*	1.40 (0.03,2.78) ***0.045***

* Data presented as β coefficient (95% Confidence Interval) *P value*. Regression Coefficients adjusted for age, sex, race, LDL-c level, use of lipid lowering medication and BMI≥30 and T1 as reference category.
# N=75 (4 missing observations)

A positive interaction between T2 and serostatus (T2*serostatus) indicates that compared to the seronegative group, the HIV seropositive group has more peri-coronary inflammation (as assessed by worsened mean FAI change) when going from those in the T2 marker group to those in the T1 marker group. A negative interaction indicates the opposite. A similar interpretation applies to the interaction between T3 and serostatus.

Table 5. Comparisons Adjusted Associations of Tertiles of Soluble Markers of Inflammation Adjusted for Each Other and FAI in People with and without HIV

		*Beta Coefficient (95% Confidence Interval)	*P* value
RCA Mean FAI	IP-10 T2*Serostatus	2.55 (0.33,4.76)	**0.026**
	IP-10 T3*Serostatus	3.14 (1.31,4.98)	**0.002**
	CD14 T3*Serostatus	2.57 (0.67, 4.48)	**0.010**
	CD163 T2*Serostatus	2.09 (0.60,3.60)	**0.008**
	TNFR-I T3*TNFR-II T2	4.57 (1.89,7.24)	**0.002**
LAD Mean FAI	CD14 T3*Serostatus	1.41 (0.29,2.55)	**0.015**
	CCL5 T2*Serostatus	-1.66 (-2.81,-0.50)	**0.006**
	IL-6 T3*hs-CRP T3*Serostatus	1.54 (0.39, 2.71)	**0.010**

Only statistically significant results are shown.

* Regression Coefficients adjusted for age, sex, race, LDL-c level, use of lipid lowering medication and BMI≥30 and T1 as reference category.

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CONCLUSIONS

Several inflammatory factors including plasma IP-10 levels were associated with both RCA and LAD FAI when measured as tertiles or continuous variables (not shown) and may be important *systemic indicators of peri-coronary inflammation* among people without history of CVD. These findings are consistent with elevated levels of IP-10 seen in PWH and the known links of IP-10 to atherosclerosis in HIV-uninfected individuals. The associations with IP-10 and other inflammatory markers suggest that FAI may be a promising noninvasive biomarker to assess asymptomatic CVD in people with and without HIV.

Note: Errors in Tables 4 and 5 were identified in the originally presented poster. This corrected version was uploaded on 2/23/2022.