HORMONE USE AND HIV ALTER CARDIOVASCULAR BIOMARKER PROFILES IN TRANSGENDER WOMEN

#3472

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Background

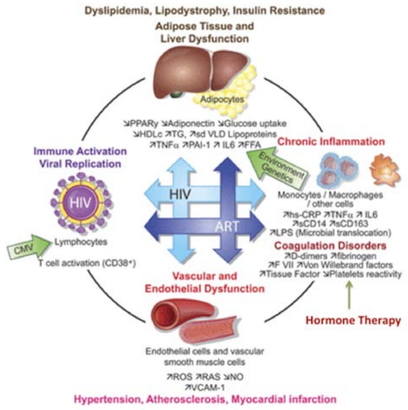


Figure 1. Contributions of HIV and FHT to metabolic and inflammatory disease. Adapted from Hemkens and Bucher. Eur Heart J. 2014.

- Transgender women (TW) are disproportionally affected by HIV and have a high prevalence of modifiable cardiovascular disease (CVD) risk factors.[1,2]
- Feminizing hormonal therapy (FHT) and HIV potentially alter CVD risk in TW.[3]
- We assessed serum biomarkers of CVD risk and inflammation among TW by HIV serostatus and FHT use, compared to cis-gender male (CM) controls.

Methods

Population:

- TW from community-based organizations and clinics in Los Angeles, California and Houston, Texas
- TW were frequency-matched to Multicenter AIDS Cohort Study CM on age, race, substance use and antiretroviral therapy (ART) type.
- All participants with HIV were on ART.
- For regression analyses, TW with HIV (n=51) had HIV-1 RNA<50 copies/mL.

Analysis:

- Serum biomarker profiles were assessed via ELISA.
- Wilcoxon rank sum and Fisher's exact tests compared group differences.
- Multivariable linear regression analyses assessed factors associated with natural log-transformed biomarker concentrations after adjusting for HIV serostatus, gender, age, race/ethnicity, body mass index (BMI), and smoking.

Results

Table 1: Baseline Characteristics

	CM, HIV- (N=40)	CM, HIV+ (N=40)	TW, HIV- (N=47)	TW, HIV+* (N=75)
Age	43 (35, 52)	48 (43, 54)	40 (32, 48)	43 (37, 52)
Black race	13%	23%	13%	27%
Hispanic ethnicity	65%	60%	64%	57%
Overweight/obese	58%	67%	30%	24%
Smoking history (former or current)	80%	86%	50%	48%
Recreational drug use	28%	48%	23%	41%
Alcohol use				
<14 drinks/week	73%	78%	37%	45%
>=14 drinks/week	5%	3%	11%	8%
Hypertension	40%	39%	17%	33%
Diabetes mellitus	13%	19%	15%	13%
ART regimen				
NNRTI-based		43%		24%
PI-based		45%		20%
INSTI-based		13%		49%
CD4+ T lymphocyte count (cells/µL)		650 (466,846)		580 (391,841)
CD4+ T lymphocyte nadir <200 (cells/µL)		48%		54%
Detectable HIV-1 RNA		0%		32%
Any AIDS diagnosis		8%		36%
Feminizing Hormonal Therapy			66%	68%

Frequency or median (interquartile range) presented. *When restricting to TW with suppressed HIV-1 RNA, age and smoking and alcohol use frequency more closely resembled CM. TW=transgender women, CM=cis-gender men, NNRTI= non-nucleoside reverse transcriptase inhibitors, PI=protease inhibitors, INTI=integrase strand transfer inhibitors

Results

Table 2a: Biomarker Concentrations by Gender in Participants Without HIV

	TW (N=47)	CM (N=40)	P-value
Adiponectin (ng/mL)	3034.7 (1696.8-5015.4)	2723.0 (1307.0-3678.9)	0.344
Human ENRAGE (ng/mL)	9971.1 (8182.2-10796.5)	**2272.5 (877.6-3325.0)**	**<0.001**
LpPLA2 (ng/mL)	243.5 (197.8-289.4)	250.7 (234.7-279.8)	0.268
Oxidized LDL (mg/dL)	52260.8 (38632.2-67630.7)	**34833.5 (29078.1-48335.0)**	**<0.001**
sCD14 (pg/mL)	1687.7 (1296.3-1928.3)	1638.8 (1459.1-1868.6)	0.517
sCD163 (pg/mL)	500.7 (407.5-682.1)	534.1 (407.0-668.1)	0.583
sTNFR I (ng/mL)	1057.5 (920.6-1492.2)	**980.5 (814.0-1120.4)**	**0.037**
sTNFR II (ng/mL)	2698.4 (2242.2-3450.7)	**2220.1 (1971.1-2806.3)**	**0.008**
VCAM-1 (ng/mL)	717.5 (505.4-879.1)	683.4 (509.9-759.4)	0.501
VWF (IU/dL)	1736.4 (1100.6-2308.6)	1957.1 (1481.2-3737.0)	0.057
P-Selectin (ng/mL)	113.9 (91.6-144.6)	**90.0 (73.1-108.1)**	**0.010**
Endothelin-1 (pg/mL)	4.6 (3.0-6.8)	**7.6 (5.3-8.6)**	**0.004**
IL-6 (pg/mL)	4.5 (1.7-9.4)	**1.9 (1.2-4.8)**	**0.048**
IL-8 (pg/mL)	49.6 (31.3-310.5)	**7.1 (3.9-12.8)**	**<0.001**
PAI-1 (ng/mL)	206907.8 (177575.5-252684.4)	**124326.9 (93968.2-146791.6)**	**<0.001**
Insulin (mU/mL)	15.5 (9.4-23.3)	15.0 (9.7-23.1)	0.93

Median and interquartile range presented, TW=transgender women, CM= cis-gender men

Table 2b: Biomarker Concentrations by Gender in Participants with HIV

	TW (N=75)	CM (N=40)	P-value
Adiponectin (ng/mL)	3499.2 (1965.5-5335.0)	2926.0 (1323.3-4454.1)	0.215
Human ENRAGE (ng/mL)	**9498.6 (6875.6-12461.0)**	**912.9 (787.4-2797.4)**	**<0.001**
LpPLA2(ng/mL)	242.6 (208.6-309.4)	220.8 (194.1-254.3)	0.013
Oxidized LDL (mg/dL)	**51166.2 (34108.9-60422.8)**	**37248.1 (31470.8-46385.6)**	**0.007**
sCD14 (pg/mL)	**1878.2 (1524.5-2200.9)**	**2024.0 (1783.6-2353.3)**	**0.026**
sCD163 (pg/mL)	608.1 (384.4-944.0)	727.0 (576.1-843.6)	0.178
sTNFR I (ng/mL)	**1369.0 (1176.0-1604.5)**	**989.4 (787.7-1194.0)**	**<0.001**
sTNFR II (ng/mL)	**3243.1 (2656.9-4344.5)**	**2669.8 (2041.4-3718.3)**	**0.005**
VCAM-1 (ng/mL)	730.0 (576.5-1098.0)	766.9 (613.9-867.4)	0.577
VWF (IU/dL)	**1797.9 (1410.4-2910.9)**	**2719.1 (1916.8-3890.7)**	**0.002**
P-Selectin (ng/mL)	116.0 (91.5-149.4)	97.8 (79.0-129.0)	0.094
Endothelin-1 (pg/mL)	**3.7 (1.9-5.0)**	**5.9 (3.0-7.4)**	**0.005**
IL-6 (pg/mL)	2.5 (1.5-7.7)	3.2 (2.0-7.8)	0.368
IL-8 (pg/mL)	**31.3 (19.7-54.3)**	**10.7 (5.6-17.4)**	**<0.001**
PAI-1 (ng/mL)	**191640.1 (152676.2-260532.7)**	**96152.4 (75255.7-150325.9)**	**<0.001**
Insulin (mU/mL)	19.0 (14.7-30.6)	15.9 (12.4-22.7)	0.29

Median and interquartile range presented, TW=transgender women, CM=cis-gender men

Figure 1: Differences in Biomarker Concentrations by Gender and HIV Serostatus

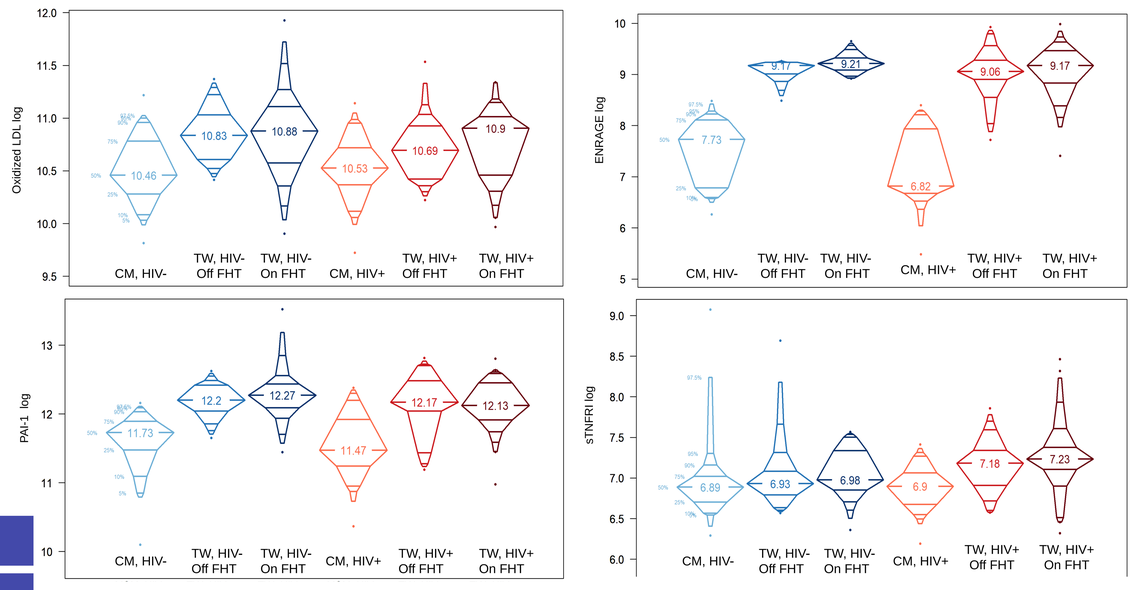


Table 3: Biomarker Concentrations by Gender, FHT Use and HIV Serostatus

	HIV+				HIV-			
	TW on FHT (N=51)	TW not on FHT (N=24)	CM (N=40)	P-value	TW on FHT (N=31)	TW not on FHT (N=16)	CM (N=40)	P-value
ENRAGE (ng/mL)	9642.3 (6834.2-12857.7)	8596.5 (7345.9-10696.7)	912.9 (787.4-2797.4)	<0.001	10021.4 (8182.2-11471.4)	9652.8 (8018.3-10254.8)	2272.5 (877.6-3325.0)	<0.001
LpPLA2 (ng/mL)	235.9 (208.6-304.3)	263.6 (199.5-318.8)	220.8 (194.1-254.3)	0.040	243.5 (195.5-287.4)	241.5 (217.5-305.2)	250.7 (234.7-279.8)	0.499
Oxidized LDL (mg.dL)	54347.4 (34837.7-60737.1)	44096.3 (32866.8-55587.9)	37248.1 (31470.8-46385.6)	0.023	52924.3 (38632.2-67630.7)	50779.3 (39381.7-65883.7)	34833.5 (29078.1-48335.0)	0.004
sTNFRI (ng/mL)	1385.7 (1212.3-1604.5)	1315.2 (992.9-1574.3)	989.4 (787.7-1194.0)	<0.001	1071.4 (941.6-1575.1)	1022.6 (880.6-1197.8)	980.5 (814.0-1120.4)	0.061
sTNFRII (ng/mL)	3225.9 (2634.0-4396.9)	3300.2 (2801.3-4205.0)	2669.8 (2041.4-3718.3)	0.017	2698.4 (2242.2-3921.1)	2842.9 (2318.5-3380.6)	2220.1 (1971.1-2806.3)	0.031
VWF (IU/dL)	1750.7 (1289.6-2644.3)	1901.0 (1599.4-3444.1)	2719.1 (1916.8-3890.7)	0.005	1573.5 (940.5-2186.8)	1970.3 (1343.1-2449.5)	1957.1 (1481.2-3737.0)	0.078
Endothelin-1 (pg/mL)	3.6 (1.3-4.8)	4.1 (2.1-5.2)	5.9 (3.0-7.4)	0.012	4.5 (2.8-6.1)	5.1 (3.0-8.3)	7.6 (5.3-8.6)	0.007
IL-8 (pg/mL)	31.3 (20.6-45.1)	31.3 (16.4-90.4)	10.7 (5.6-17.4)	<0.001	35.4 (31.3-297.0)	89.8 (31.3-355.6)	7.1 (3.9-12.8)	<0.001
PAI-1 (ng/mL)	184436.3 (148166.6-259048.4)	193237.3 (169630.9-267712.5)	96152.4 (75255.7-150325.9)	<0.001	213929.0 (177999.5-254385.6)	198819.6 (165473.8-250659.3)	124326.9 (93968.2-146791.6)	<0.001

Median and interquartile range presented, FHT=feminizing hormonal therapy, TW=transgender women, CM=cis-gender men

Table 4: Adjusted Associations for TW (vs CM) and Biomarker Concentrations

	Difference in Log Biomarker (95% CI)	P-value
Adiponectin (ng/mL)	0.06 (-0.20, 0.33)	0.648
ENRAGE (ng/mL)	**1.82 (1.58, 2.06)**	**<0.001**
LpPLA2 (ng/mL)	0.06 (-0.03, 0.15)	0.209
Oxidized LDL (mg/dL)	**0.26 (0.12, 0.39)**	**<0.001**
sCD14 (pg/mL)	**-0.09 (-0.19,-0.00)**	**0.048**
sCD163 (pg/mL)	**-0.27 (-0.47,-0.08)**	**0.007**
sTNFR I (ng/mL)	**0.20 (0.07, 0.34)**	**0.003**
sTNFR II (ng/mL)	**0.17 (0.03, 0.30)**	**0.017**
VCAM-1 (ng/mL)	-0.05 (-0.17, 0.07)	0.425
VWF (IU/dL)	**-0.41 (-0.63,-0.19)**	**<0.001**
P-Selectin (ng/mL)	**0.26 (0.08, 0.45)**	**0.006**
Endothelin-1 (pg/mL)	**-0.35 (-0.64,-0.05)**	**0.021**
IL-6 (pg/mL)	**0.53 (0.12, 0.94)**	**0.012**
IL-8 (pg/mL)	**2.08 (1.49, 2.67)**	**<0.001**
PAI-1 (ng/mL)	**0.67 (0.50, 0.83)**	**<0.001**
Insulin (mU/mL)	-0.01 (-0.41, 0.38)	0.942

Adjusted for HIV status, age, race/ethnicity, BMI, and smoking status.

Summary & Conclusions

- **Compared to matched cis-gender males, transgender women have altered profiles of biomarkers associated with systemic inflammation and CVD that seem to be influenced by both FHT and HIV.**
- **TW had significantly higher ENRAGE, oxidized LDL, sTNFRI, sTNRFII, IL-8 and PAI-1 concentrations, regardless of HIV serostatus.**
- **Stepwise increase of oxidized LDL, ENRAGE, PAI-1, and sTNFRI were seen, with CM < TW not on FHT < TW on FHT.**
- **Clinical outcomes data and mechanistic studies are needed to understand the contributions of FHT and HIV to CVD risk among TW.**

References and Acknowledgements

[1]*Lancet Infect Dis* 2013;13(3):214-22 [2]*Arch Sex Behav*. 2005;34:679-90 [3]*Clin Endocrinol.* 2010; 72(1):1-10

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