BURDEN OF CORONARY DISEASE IN TRANSGENDER WOMEN WITH AND WITHOUT HIV

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JE Lake[1], H Feng[2], H Miao[2], P Debroy[1], A Dobs[3], S Haberlen[3], L Kingsley[4], J Margolick[3], K McGowan[3], FJ Palella[5], W Post[3], MD Witt[6], S Bhasin[7], M Budoff[6], TT Brown[3]

[1]UTHealth McGovern Medical School, Houston, TX USA; [2]UTHealth School of Public Health Houston, TX USA; [3]Johns Hopkins University, Baltimore, MD, USA; [4]University of Pittsburgh, Pittsburgh, PA, USA; [5]Northwestern University, Chicago, IL, USA; [6]The Lundquist Institute, Torrance, CA, USA; [7]Brigham and Women's Hospital, Boston, MA, USA

Correspondence:
Jordan E. Lake, M.D., M.Sc.
6431 Fannin St., MSB 2.112
Houston, TX 77030
Jordan.E.Lake@uth.tmc.edu

BACKGROUND

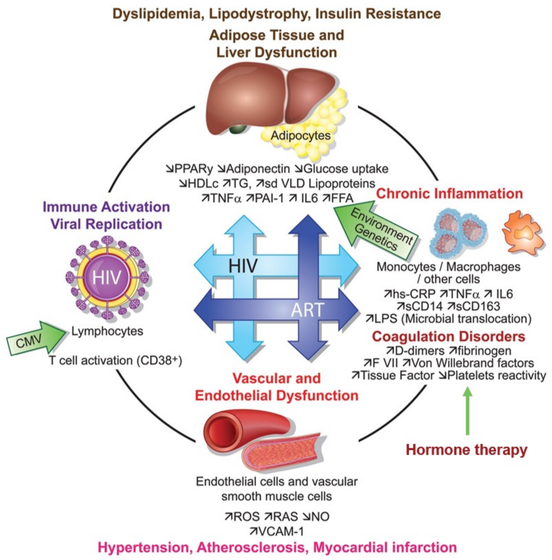


Fig. 1: Contributions of HIV and GAHT to metabolic and inflammatory disease. Adapted from Hemkens and Bucher. *Eur Heart J. 2014*

- Transgender women (TW) are disproportionally affected by HIV and have a high prevalence of modifiable cardiovascular disease (CVD) risk factors.[1,2]
- HIV, antiretroviral therapy (ART), and gender-affirming hormone therapy (GAHT) have each been associated with altered body composition, inflammatory and coagulation pathway abnormalities, and cardiometabolic disturbances.[3-5]
- We compared CVD burden and biomarker profiles between TW and matched cisgender men (CM).

METHODS

Study Population:
- Adult TW on GAHT were recruited from Houston, TX and Baltimore, MD
- Matched control CM were selected from participants in The Multicenter AIDS Cohort Study (MACS) Cardiovascular Sub-studies 2 or 3

Inclusion Criteria:
- Self-identification as a TW with GAHT use ≥ 3 months
- 40-70 years of age
- If living with HIV, on ART with HIV-1 RNA <50 copies/mL at screening

Exclusion Criteria:
- History of coronary artery bypass grafting, heart valve surgery, coronary angioplasty or atrial fibrillation
- Estimated glomerular filtration rate <60 mL/min
- History of contrast nephropathy

Study Design:
- Observational, cross-sectional (2018-2020)
- CM were matched 2:1 to TW on HIV serostatus, age within 5 years, race/ethnicity, BMI category and ART type (latter where possible)

Study Procedures and Analysis:
- Body composition was measured by non-contrast, computed tomography (CT) cardiac imaging and single slice scans of the abdomen at the level of the umbilicus and the mid-thigh
- Sex hormones and inflammatory biomarker concentrations were measured centrally at end of study
- Wilcoxon rank-sum and Pearson χ^2 tests were used to compare continuous and categorical variables, respectively, between groups
- Due to limited number of participants without HIV, results are not stratified by HIV serostatus
- Results in TW are stratified by those with suppressed (TW-S) vs not suppressed (TW-T) total testosterone (<50 mg/ml)

RESULTS

Table 1: Baseline Characteristics

	CM (N=60)	TW-T (N=21)	TW-S (N=10)	*P*-Value CM vs TW-S
Age	54 (48, 56)	53 (43, 59)	51 (46, 57)	0.37
Black race	48%	43%	70%	0.35
Hispanic ethnicity	22%	33%	0%	0.23
BMI (kg/m²)	29 (25, 33)	28 (25-32)	34 (27, 39)	0.20
Current smoker	27%	43%	20%	0.66
Hypertension	46%	33%	22%	0.18
Fasting glucose (mg/dL)	98 (92, 106)	92 (87, 94)	98 (90, 106)	0.98
HOMA-IR	1.9 (1.5, 3.4)	1.7 (1.2, 3.1)	2.6 (1.1, 2.9)	0.70
Total cholesterol (mg/dL)	182 (156, 203)	170 (157, 219)	178 (156, 205)	0.74
HDL cholesterol (mg/dL)	45 (37, 55)	46 (39, 58)	51 (47, 60)	0.06
LDL Cholesterol (mg/dL)	112 (91, 128)	103 (91, 140)	104 (95, 117)	0.58
Triglycerides (mg/dL)	125 (78, 163)	121 (73, 147)	92 (85, 117)	0.21
Lipid-lowering agent use				
Statins	15%	43%	20%	
Fibrates	3%	10%	10%	
Other	7%*	0%	0%	
% living with HIV	73%	84%	63%	0.52
INSTI-based ART	33%	57%	40%	0.68
CD4+ T-cell count (cells/μL)	726 (579, 1051)	813 (732, 920)	772 (600, 1076)	0.88
Estradiol (pg/ml)	22 (18, 29)	75 (31, 120)	96 (63, 308)	<0.001
Total testosterone (ng/dl)	440 (347, 570)	532 (310, 764)	13 (11, 16)	<0.001
Free testosterone (ng/dl)	13 (10, 16)	13 (7, 18)	0.6 (0.5, 0.6)	<0.001
SHBG (nmol/l)	33 (29, 46)	69 (38, 91)	77 (65, 146)	<0.001

Frequency or median (interquartile range) presented; CM=cisgender men, TW-T=Transgender women with total testosterone >/=50ng/ml, TW-S=Transgender women with total testosterone <50ng/ml, BMI=Body mass index, INSTI=Integrase strand transfer inhibitor, ART=Antiretroviral therapy
* Ezetimibe (N=1), Niacin (N=1), Omega-3 Fatty Acid (N=2)

Table 2. Body Composition

	CM (N=60)	TW-T (N=21)	TW-S (N=10)	P-value CM vs TW-S
Abdominal subcutaneous fat (cm²)	**279 (153, 413)**	**281 (252, 420)**	**450 (316, 578)**	**0.04**
Abdominal visceral fat (cm²)	154 (106, 207)	131 (87, 199)	161 (114, 190)	0.9
Thigh muscle fat (cm²)	**7 (4, 10)**	**15 (12, 18)**	**27 (15, 34)**	**<0.001**
Thigh subcutaneous fat (cm²)	45 (27, 80)	50 (35, 59)	78 (44, 108)	0.2
Epicardial fat (cm²)	70 (44, 96)	59 (44, 69)	59 (52, 73)	0.5
Intrathoracic fat (cm²)	**141 (83, 214)**	**77 (64, 87)**	**90 (55, 112)**	**0.04**
Thoracic peri-aortic fat (cm²)	**20 (11, 32.4)**	**7 (6, 10)**	**8 (6, 19)**	**0.04**
Liver-spleen attenuation ratio	1.2 (1.1, 1.3)	1.3 (1.3, 1.3)	1.3 (1.2, 1.6)	0.4
Moderate-to-severe hepatic steatosis (Liver-spleen ratio <1.0)	9%	8%	0%	0.4

Median (interquartile range) or frequency presented; CM=cisgender men, TW-T=Transgender women with total testosterone >/=50ng/ml, TW-S=Transgender women with total testosterone <50ng/ml

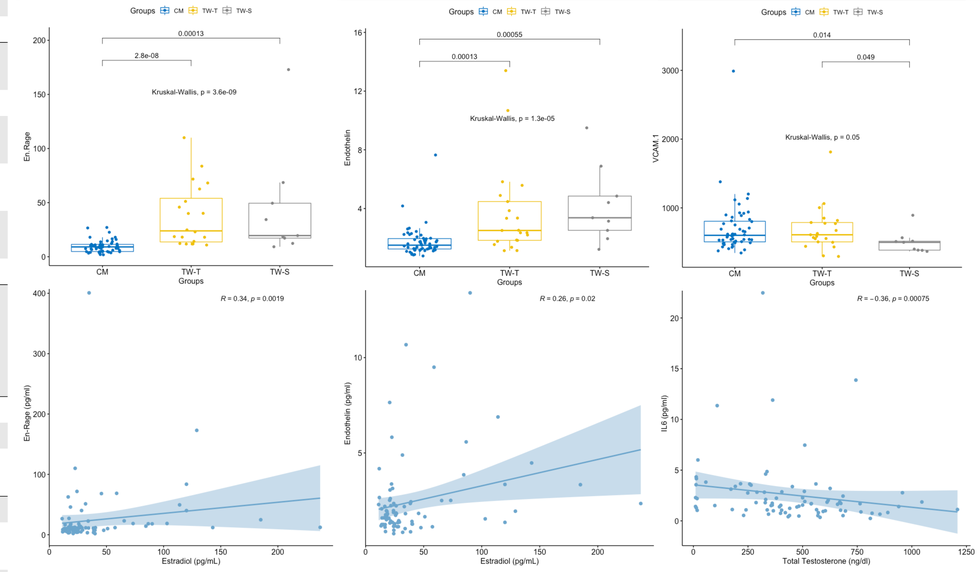
- **Correlations between sex hormone concentrations and fat quantity unremarkable**
- **Testosterone correlated more consistently (and negatively) with abdominal, visceral and thigh fat outcomes (and estradiol levels overall lower than expected)**

Overall prevalence of hepatic steatosis was low, but 0% TW-S had CT-defined steatosis, which was unexpected.

Table 3. Inflammatory Biomarkers

	CM (N=60)	TW-T (N=21)	TW-S (N=10)	*P*-value CM vs TW-S
EN-RAGE (pg/ml)	**9.1 (4.8, 11.4)**	**24.8 (16.1, 59.7)**	**19.5 (17.2, 49.5)**	**<0.001**
Endothelin-1 (pg/ml)	**1.5 (1.2, 2.0)**	**2.5 (1.8, 4.7)**	**3.4 (2.5, 4.9)**	**<0.001**
VCAM-1 (ng/ml)	**601 (506, 806)**	**586 (502, 774)**	**499 (386, 516)**	**0.01**
Interleukin-6 (pg/ml)	1.6 (0.9, 2.8)	1.6 (1.1, 2.8)	2.3 (1.4, 4.2)	0.09

Frequency presented; CM=cisgender men, TW-T=Transgender women with total testosterone >/=50ng/ml, TW-S=Transgender women with total testosterone <50ng/ml, EN-RAGE=Extracellular newly-identified receptor for advanced glycation end products, VCAM=Vascular cell adhesion molecule

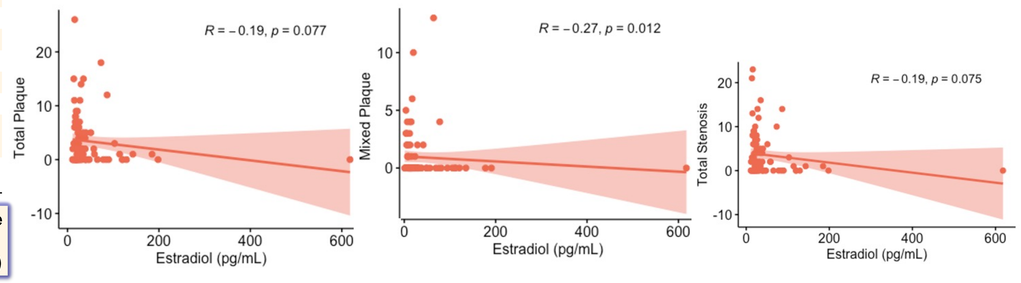


- **Higher estradiol concentrations correlated with higher EN-RAGE and Endothelin-1 concentrations**
- **Lower testosterone concentrations correlated with higher IL-6 concentrations**

Table 4. Cardiac Outcomes

	CM (N=60)	TW-T (N=21)	TW-S (N=10)	*P*-value CM vs TW-S
Any plaque	68%	58%	44%	0.16
Non-calcified plaque	**47%**	**43%**	**0%**	**0.008**
Mixed plaque	35%	11%	22%	0.45
Calcified plaque	45%	42%	44%	0.98
Any stenosis >50%	20%	16%	0%	0.14

Frequency presented; CM=cisgender men, TW-T=Transgender women with total testosterone >/=50ng/ml, TW-S=Transgender women with total testosterone <50ng/ml



Estradiol but not testosterone concentrations correlated with mixed plaque and total plaque and total stenosis

SUMMARY & CONCLUSIONS

- **In older TW with suppressed total testosterone on GAHT, no non-calcified coronary plaque or advanced stenosis was observed, while CM and TW with detectable testosterone had equivalent subclinical CVD burden**
- **Observations occurred independent of HIV serostatus and despite similar traditional CVD risk factor profiles to CM and more obesity among TW with suppressed testosterone.**
- **Longitudinal studies to understand relationships between GAHT and CVD risk in TW are needed.**

References and Acknowledgements

[1]CDC. 2019-2020 [2]Am J Public Health 2019; 109(1): e1-e8 [3]Lancet Infect Dis 2013; 13(11): 964-75 [4]Eur J Endocrinol 2018; 178(2): 163-71 [5]PLoS One 2022; 17(3): e0261312

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