Activated Monocytes and Myocardial Fibrosis Among Persons Living with HIV in South Africa

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INTRODUCTION

- Antiretroviral therapy (ART)-treated persons living with HIV (PLWH) are at higher risk of heart failure (HF)[1] and related pathologies, such as myocardial fibrosis.[2,3]
- Contemporary data on the pathogenesis of HIV-associated myocardial injury are needed, particularly in global regions with a high prevalence of both HIV and HF, such as South Africa.[4,5]
- Immune activation is both a hallmark of chronic HIV infection[6] and mechanistically involved in the pathology of fibrosis.[7]

STUDY AIM: Estimate myocardial fibrosis via cardiovascular magnetic resonance (CMR) and evaluate associations with HIV-associated inflammatory markers among ART-treated persons living with HIV in South Africa.

STUDY DESIGN AND ENROLLMENT

- Cross-sectional design.
- Participants recruited in Khayelitsha, South Africa (near Cape Town) receiving routine HIV care.
- **Eligibility**: age ≥30 years old, no evidence of prior/known CVD, continuous ART ≥1 year, and viral suppression (i.e., HIV RNA <200 copies/mL) at most recent laboratory.

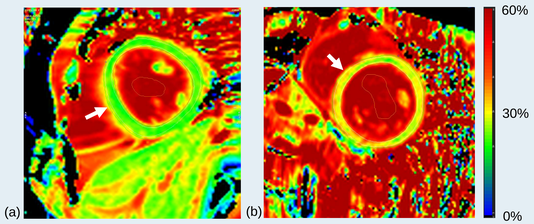
DATA COLLECTION

- **Clinical data:** standard clinic protocols, medical records, and interviews
- **Biomarkers:** flow cytometry on stored PBMCs, immunoassays on stored plasma
- **CMR:** large bore 3T Siemens Skyra MRI scanner and standardized single breath-hold Shortened Modified Look-Locker Inversion Recovery sequence

STATISTICS

- **Primary inputs:** monocyte phenotype (percentage of HLA-DR$^+$ myeloid cells) or protein ($\log_2$-transformed plasma concentration)
- **Response:** extracellular volume (ECV) fraction
- Linear regression adjusted for age, sex, current smoking status, body mass index, and hypertension.
- Analysis conducted using SAS version 9.4 and two-sided type I error of 0.05.

FIGURE 1. Fibrosis maps obtained via CMR from participants with low and high ECV fraction.



Extracellular volume fraction (ECV) maps, short-axis view at cardiac mid-slice. Participant (a) exhibits low average ECV fraction within normal range, and participant (b) exhibits high average ECV fraction with diffuse myocardial fibrosis.

TABLE 1. Participant characteristics (n=69).

Characteristic	Mean (SD) or % (n)
Demographics	
Female sex at birth	71% (49)
Age, years	48 (10)
Black African race	100% (69)
Clinical History	
Current tobacco smoker	30% (21)
Diabetes diagnosis	6% (4)
Hypertension diagnosis	33% (23)
Prior active tuberculosis infection	57% (39)
HIV diagnosis duration, years	9 (6)
HIV suppression duration ≥4 years	36% (25)
Prior AIDS	45% (31)
Clinical Data	
Body mass index, kg/m^2	26.5 (6.7)
Systolic blood pressure, mmHg	132 (18)
Diastolic blood pressure, mmHg	79 (12)
Total cholesterol, mg/dL	175 (30)
High density lipoprotein cholesterol, mg/dL	63 (23)
HIV viral load <200 RNA copies/mL	97% (67)
CD4+ cell count, cells/μL	583 (261)
CD4+ nadir, cells/μL	266 (207)
Myocardial Tissue Characteristics	
Extracellular volume fraction, %	30.9 (5.9)
Native T1, ms	1248 (41)
Late gadolinium enhancement (LGE) presence	74% (49)
LGE presence, diffuse or patchy pattern	19% (13)
Circulating Soluble Proteins	
Interleukin-6 (IL-6), pg/mL	2.50 (2.01)
Tumor necrosis factor receptor-1 (TNFR1), pg/mL	420 (138)
Cluster of differentiation-14 (sCD14), ng/mL	6637 (7736)
Cluster of differentiation-163 (sCD163), ng/mL	798 (273)
Circulating Monocyte Subsets	
Total CD14^{++}CD16$^-$ (classical), %	25.4 (15.4)
Total CD14^{++}CD16$^+$ (intermediate), %	1.89 (2.35)
Total CD14$^+$CD16^{++} (non-classical), %	0.85 (0.90)

HIV-associated activated monocyte phenotypes are positively associated with myocardial fibrosis among ART-treated persons living with HIV in South Africa.

FIGURE 3. Cross-sectional associations between monocyte cell phenotypes and myocardial fibrosis assessed via CMR among ART-treated persons living with HIV in South Africa.

Estimated using multivariable linear regression, adjusting for age, sex, current smoking, body mass index, and hypertension.

The role of monocyte activity in myocardial tissue remodeling and subsequent HF risk among PLWH in the current ART era warrants further investigation.

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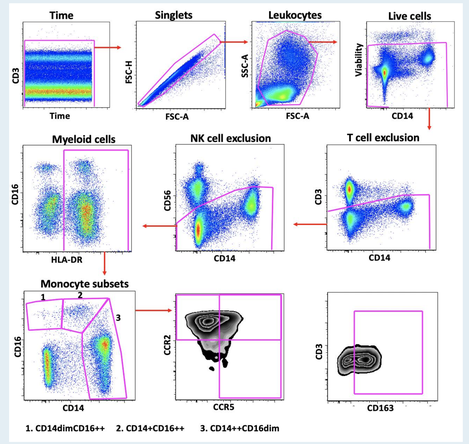
FIGURE 2. Flow cytometry gating strategy.



Gating was defined using fluorescent-minus-one experiments where a particular antibody was omitted from the panel to set the position of the negative gate.

TABLE 2. Cross-sectional associations between soluble plasma proteins and ECV fraction.

Protein	Mean Difference in ECV (95% CI)
IL-6	-0.81 (-1.63 to 0.03)
TNFR1	-0.23 (-1.08 to 0.62)
sCD14	-0.18 (-1.00 to 0.64)
sCD163	0.13 (-0.73 to 0.99)

Mean difference in extracellular volume (ECV) fraction estimated per two-fold increment in plasma protein concentration using multivariable linear regression adjusting for age, sex, current smoking, body mass index, and hypertension.

PRIMARY LIMITATIONS

- Cross-sectional design: temporal ambiguity and no causal inference.
- Possible selection bias due to recruitment strategies.
- Small sample size limits the ability to detect moderate to small effect sizes.

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Conflicts of Interest: None declared.