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The association of adipose tissue area with subclinical coronary atherosclerosis progression in men with and without HIV

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Cardiovascular disease (CVD) is a major cause of mortality in people with HIV (PWH) in the US. In the general population, subclinical coronary atherosclerosis is associated with CVD events [1]. Thus, risks associated with subclinical coronary atherosclerosis in PWH are of clinical interest.

PWH may experience lipoatrophy and/or visceral and abdominal lipoaccumulation [2]. The associations between adipose tissue (AT) and subclinical CVD in PWH have been assessed in cross-sectional studies [3,4], but data addressing the relationship between AT and the progression of coronary artery stenosis over time among PWH are scarce. Here, we examined the associations between visceral AT (VAT), subcutaneous AT (SAT) and progression of coronary artery stenosis in the Multicenter AIDS Cohort Study (MACS).

The MACS is a prospective cohort study of men who have sex with men recruited at 4 centers in the US. This study included MACS Cardiovascular Ancillary Study participants who underwent baseline coronary CT angiogram (CCTA) in 2010–13 and again in 2015–17. Inclusion criteria were ages 40–70 years, weight <300 pounds, and no history of cardiac surgery or percutaneous coronary intervention at the baseline CCTA [5]. All participants signed informed consent, and the study was approved by Institutional Review Boards at each site.

The outcome was stenosis progression, as defined by an increase by ≥ 2 stenosis severity categories from baseline to follow-up CCTA within a coronary artery segment. Stenosis

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categories were as follows: 0%, 1–29%, 30–49%, 50–69%, and ≥ 70%. Segments with baseline stenosis ≥50% were excluded from the analyses. The three primary baseline exposure variables were VAT, abdominal SAT, and thigh SAT and were measured using noncontrast CT images at the L4-L5 vertebral level and 15 cm above the patellar apex. Abdominal SAT was calculated as follows: total abdominal fat - intra-abdominal fat. Thigh SAT represented the sum of the area of the pixels between −150 and −50 Hounsfield units [3]. AT variables were continuous and winsorized, which assigned outliers the value of the 95th percentile.

Generalized estimating equations with log link, Poisson family, and exchangeable working correlation matrix, to account for clustering within individuals, were used to assess the associations of AT with stenosis progression, accounting for time between CCTA measurements. The AT independent variables were evaluated in separate regressions, and we used a serial adjustment strategy to control for confounding. The minimally adjusted model included age, race, and study center. The first fully adjusted model included age, race, study center, high density lipoprotein cholesterol, total cholesterol, and fasting glucose levels, lipid lowering medication use, systolic blood pressure, antihypertensive medication use, diabetes, and smoking pack years. The second fully adjusted model included the aforementioned variables and body mass index (BMI). An interaction term between HIV serostatus and the AT variable was included in each fully adjusted model involving the total population to assess differences in associations of the AT measurements with stenosis progression by HIV serostatus.

There were 294 men with HIV (MWH) and 216 men without HIV (MWoH) included. MWH were younger (median age 51 vs 56 years, P<0.001) and more likely to be African-American (34% vs 23%, P<0.001) than MWoH. VAT was not significantly different between MWH and MWoH (median area 148.16 vs 136.57 cm^2). MWH had lower median abdominal SAT area (177.61 vs 228.80 cm^2, P<0.001) and lower median thigh SAT area (26.41 vs 46.49 cm^2, P<0.001) than MWoH. The number of observations of stenosis progression was 113 in MWH and was 60 in MWoH (P=0.036).

In minimally adjusted models involving the total population, greater VAT was associated with stenosis progression. In minimally adjusted analyses stratified by HIV serostatus, greater VAT was associated with stenosis progression in MWoH, but this was not observed in fully adjusted models. In MWH, VAT and stenosis progression were not statistically significantly associated in the minimally adjusted model (Table 1).

Neither abdominal nor thigh SAT was associated with stenosis progression. Interaction terms between HIV serostatus and AT variables were not statistically significant.

This longitudinal study demonstrates relationships between baseline AT measurements and coronary artery stenosis progression among MWH. We found that neither VAT nor SAT was associated with stenosis progression in MWH in adjusted analyses. One limitation to this study is that the duration of follow-up may not have been sufficiently long enough to detect more stenosis progression in this cohort of relatively healthy men.

Future directions include determining whether VAT in PWH, compared to PWoH, is more strongly related to CVD events. Such work would improve the understanding of the mechanisms behind the high risk of CVD in PWH.

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Table 1:

The associations of adipose tissue with the development of segment-level coronary artery stenosis progression

	Univariate IRR (95% CI); P value	Minimally adjusted IRR (95% CI); (P value)	Fully adjusted IRR (95% CI); (P value)
VAT in the total population	1.41 (1.16–1.71); p<0.001	1.24 (1.00–1.52); p=0.046	1.10 (0.83–1.45); p=0.52
VAT in men with HIV	1.35 (1.05–1.73); p<0.05	1.11 (0.84–1.46); p=0.48	0.93 (0.65–1.33); p=0.70
VAT in men without HIV	1.52 (1.13–2.05); p<0.01	1.41 (1.02–1.94) (P<0.05)	1.48 (0.93–2.36); p=0.10
Abdominal SAT in the total population	0.98 (0.81–1.20); p=0.88	1.01 (0.82–1.25); p=0.90	0.96 (0.70–1.33); p=0.81
Abdominal SAT in men with HIV	0.91 (0.71–1.17); p=0.47	0.94 (0.72–1.23); p=0.66	0.94 (0.64–1.39); p=0.75
Abdominal SAT in men without HIV	1.24 (0.89–1.72); p=0.20	1.20 (0.85–1.69); p=0.31	1.29 (0.67–2.50); p=0.45
Thigh SAT in the total population	0.83 (0.67–1.02); p=0.08	0.93 (0.74–1.18); p=0.62	0.94 (0.70–1.26); p=0.69
Thigh SAT in men with HIV	0.78 (0.59–1.04); p=0.10	0.93 (0.69–1.25); p=0.62	0.94 (0.64–1.39); p=0.82
Thigh SAT in men without HIV	1.01 (0.69–1.48); p=0.96	0.98 (0.66–1.46); p=0.93	0.82 (0.45–1.51); p=0.53

IRR = incidence rate ratio; CI = confidence interval; NS = not significant; VAT = visceral adipose tissue; SAT = subcutaneous adipose tissue

*Minimally adjusted models included: age, race, and study center.

**Fully adjusted models included the following covariates in addition to the minimally adjusted models: high density lipoprotein cholesterol, total cholesterol, use of lipid lowering medication, systolic blood pressure, use of antihypertensive medication, fasting glucose, diabetes, smoking pack years, body mass index (BMI), and an interaction term between HIV serostatus and adipose tissue. Results of the fully adjusted models that included the aforementioned variables, excluding BMI, are not shown here.

***Separate models were created for the total study population, men with HIV, and men without HIV.