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Measures of Adipose Tissue Redistribution and Atherosclerotic Coronary Plaque in HIV

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Abstract

Objective: People with HIV(PWH) well-treated on antiretroviral therapy remain at increased risk for body composition changes including increased visceral adipose tissue(VAT) and reduced subcutaneous adipose tissue(SAT), as well as increased cardiovascular disease(CVD). The relationship between adipose compartments and coronary disease is not well understood among PWH.

Methods: 148 PWH and 68 uninfected individuals without CVD were well-phenotyped for VAT and SAT via single-slice abdominal computed tomography(CT) at L4. Coronary artery calcium(CAC) score was assessed by non-contrast cardiac CT and coronary plaque composition by coronary CT angiography.

Results: Increased VAT significantly related to increased presence of plaque (OR 1.55 per 100cm^2,P=.008) and CAC>0(OR 1.56 per 100cm^2,P=.006) in the HIV group. In contrast,

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Author Contributions:

Principal contributions of the authors are study conception (SKG, JL), study design (SKG, JL), subject recruitment and implementation of the protocol (KVF, SEL, JL), data acquisition and analysis and database management (MB, KVF, ML, MT, MVZ, SEL, SI, VJT, SS, JL), statistical analysis and interpretation (MB, SS, SKG, JL), drafting of the manuscript (MB, SS), critical revision of the manuscript (MB, SS, SKG, JL), and supervision of the study (SKG, JL).

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increased SAT related to reduced presence of plaque(OR 0.79 per 100cm^2,P=.057) and reduced CAC>0 (OR 0.69 per 100cm^2,P=.007) among PWH. The VAT:SAT ratio showed a strong relationship to overall presence of calcified plaque (OR 3.30,P=.03) and CAC>0(OR 3.57,P<.001) in the HIV group. VAT and waist-to-hip ratio, but not SAT, were strong predictors of plaque in the uninfected group. BMI did not relate in either group.

Conclusions: Fat redistribution phenotyping by simultaneous quantification of VAT and SAT as independent measures, could help identify those PWH at higher risk of CVD.

Keywords

HIV; subcutaneous adipose tissue; visceral adipose tissue; coronary plaque; calcified plaque; calcium score

Introduction

People with HIV (PWH) can present with acquired changes in body composition and are at significantly higher risk of cardiovascular disease (CVD) compared to uninfected individuals[1–4]. Composite risk for CVD in HIV may be inclusive of traditional and non-traditional risk factors[5, 6], such as antiretroviral therapy (ART) use[7, 8], inflammation, and immune activation[9, 10]. Relevant to this, PWH are predisposed to a unique fat redistribution clinically characterized by loss of subcutaneous (peripheral) adipose tissue (SAT) and/or accumulation of visceral adipose tissue (VAT), which may contribute to increased inflammation [11–13]. Relative changes in adipose depots, ranging from the loss of SAT and/or accumulation of VAT, are associated with the development of dyslipidemia[14], insulin resistance[15], and increased markers of inflammation[13], which are key contributors to CVD[11–13, 16–18].

Our group and others have previously assessed coronary calcification and plaque using cardiac computed tomography (CT) and coronary CT angiography (CTA) and have demonstrated PWH have higher prevalence of coronary plaque[19–22] and greater coronary artery calcium (CAC) scores[22] compared to uninfected individuals[23]. Few studies have investigated the relationship of specific adipose compartments to CVD in HIV. Those studies have been largely limited to single sex cohorts[24, 25] and have not evaluated CT assessment of calcium score and CTA in parallel imaging among a combined male and female population, nor in comparison to an uninfected group. In the current study, we sought to assess the relationship of body composition parameters with coronary calcification and plaque indices. We hypothesized measures of abnormal fat redistribution, particularly related to increased VAT and reduced SAT, would be associated with features of atherosclerotic coronary plaque.

Methods

Study Participants

One hundred forty-eight PWH and 68 uninfected individuals were previously enrolled between 2006-2011 and had both cardiac and abdominal CT imaging available as part of a prior investigation. PWH were recruited from local clinics and health centers and by

advertisements in the Boston area. Uninfected individuals were recruited from identical communities. PWH with known HIV infection for at least 5 years and who reported a stable ART regimen for at least 3 months prior to enrollment only were included. Inclusion and exclusion criteria were otherwise similar for both groups as previously described[19, 20]. Individuals were between 18-60 years of age with a body mass index (BMI) between 20-35 kg/m^2 and had no known cardiac disease. Individuals were excluded for any acute infectious illness or anti-inflammatory medication use, as well as for known renal disease or Cr>1.5mg/dL. Informed consent was obtained from all enrolled individuals. This study was approved by the institutional review board of the Partners Human Research Committee. Data relevant to coronary artery disease have been previously reported in this cohort[19, 20], whereas new data on body composition and coronary plaque are the focus of the current investigation.

Body Composition Phenotyping

A measurement of the waist-to-hip ratio (WHR) was taken using the iliac crest and the broadest hip as anatomic reference points. Abdominal VAT and SAT were derived from the level of the L4 pedicle using a cross-sectional CT scan. Scan parameters were standardized for individual images (144 table height, 80 kV, 70 mA, 2 seconds, 10mm slice thickness, 48cm FOV). Fat attenuation coefficients were fixed at −50 to −250 HU. Using commercial software (Vitrak, Merge e/Film), an offline analysis utilizing tracings was performed to evaluate abdominal VAT and SAT areas.

Atherosclerotic Plaque Characteristics

CAC score was assessed by non-contrast cardiac CT. CTA imaging using a 64-slice dual source CT scanner (Siemens Medical Solutions) was performed with a standardized protocol which included assessment of calcified and noncalcified plaque segments as previously described[19, 20].

HIV-specific Parameters

HIV viral load was determined by ultrasensitive RT PCR (Roche COBAS Amplicor) (lower limit of detection, 50 copies/mL). For values below the limit of detection, imputed values just below the limit of detection were used for purposes of data analysis (i.e. viral load 49 copies/mL). CD4 and CD8 T cell counts were assessed by flow cytometry.

Statistical Analysis

Logistic regression was used to evaluate presence of plaque in relation to body composition parameters based on HIV serostatus. Linear regression was applied using Pearson's correlation coefficient to assess continuous relationships between body composition and coronary plaque parameters among HIV and non-HIV groups. Variables that were not normally distributed were log transformed for univariate correlations. Multivariate regression modeling with CAC and total calcified plaque volume as separate dependent variables was performed. VAT:SAT ratio, VAT and SAT were chosen as the independent variables in these models, as these variables captured the most relevant body composition abnormalities among PWH, while controlling for HIV-related parameters. A formal outlier

test was performed via the Tukey Method for VAT:SAT ratio to identify potential outliers, and a level greater than the third quartile plus 1.5*(interquartile range) or lower than the first quartile minus 1.5*(interquartile range) was regarded as an outlier. Statistical significance was defined as $P<0.05$. All analyses were performed using SAS JMP Pro (version 14.0).

Results

Demographics and clinical characteristics

PWH and uninfected individuals were of similar age (47±7 vs. 46±7 years) and demonstrated a similar proportion of race (55% vs. 53% Caucasian) and sex (65% vs. 60% male). The HIV group had a history of HIV infection for 14±6 years, a duration of ART use for 8±5 years, and well-controlled immunological parameters with mean $CD4^+$ cell count 549±293 cells/μl and mean $\log_{10}$ HIV viral load 1.82±0.47 copies/mL. In the HIV group, 95% reported current nucleoside reverse transcriptase inhibitors use, 57% protease inhibitor use, 38% non-nucleoside reverse transcriptase inhibitors use, and 15% integrase strand transfer inhibitor use. (Table 1)

Assessment of body composition of PWH and uninfected individuals showed similar BMI (26.7±4.8 vs. 27.8±4.9 kg/m^2, P=.11), WHR (0.94±0.07 vs. 0.93±0.07, P=.29), and VAT (108 [61, 209] vs. 103 [55, 177] cm^2, P=.45), and significantly different SAT (198 [125, 287] vs. 241 [150, 380]cm^2, P=.02) and VAT:SAT ratio (0.54 [0.30, 1.13] vs. 0.42 [0.23, 0.84], P=.04). While HDL (49 [40, 61] vs. 49 [42, 62]mg/dL, P=.89) and LDL (99 [80, 122] vs. 106 [89, 128]mg/dL, P=.25) were similar between the two groups, the HIV group had higher triglyceride levels (97 [76, 174] vs. 86 [63, 126] mg/dL, P=.003). Glucose did not differ between groups (88 [79,95] vs. 89 [80,96] mg/dL, P=.86, PWH vs. uninfected individuals). (Table 1) A relatively small proportion of the HIV group (14%) were receiving statin therapy.

Assessment of body composition and presence of coronary plaque

Relationship to Presence of Coronary Plaque—In the HIV group, adipose redistribution characterized by increased VAT was significantly related to increased presence of coronary plaque (OR 1.55 per $100cm^2$, 95% CI [1.10, 2.17], P=.008). In contrast, increased SAT tended to be related to reduced presence of coronary plaque (OR 0.79 per $100cm^2$, 95% CI [0.61, 1.01], P=.06). The VAT:SAT ratio showed a strong relationship to overall presence of coronary plaque (OR 3.36, 95% CI [1.51, 7.48], P=.002). Similarly, VAT was significantly related to presence of coronary plaque among uninfected individuals (OR 1.75 per $100cm^2$, 95% CI [1.02, 2.98], P=.03), whereas increased SAT was not related to presence of coronary plaque in the uninfected group. (Table 2)

Relationship to Coronary Plaque Type and Clinically Used Plaque Indices—Among PWH, increased VAT was strongly related to CAC score > 0 (OR 1.56 per $100cm^2$, 95% CI [1.13, 2.16, P=.006]), whereas increased SAT was strongly related in the opposing direction (OR 0.69 per $100cm^2$, 95% CI [0.52, 0.92], P=.007). The VAT:SAT ratio captured the differential contributions of VAT and SAT to CAC among the HIV group and was robustly related to CAC score > 0 (OR 3.57, 95% CI [1.65, 7.70], P<.001). Similarly,

VAT:SAT ratio was most strongly related to the presence of calcified plaque segments, (OR 3.30, 95% CI [1.12, 9.74], P=.03) among PWH. (Table 2)

Among uninfected individuals, VAT was related to CAC score > 0 (OR 1.71 per 100cm^2, 95% CI [1.01, 2.89], P=.04), but neither SAT nor VAT:SAT ratio were related. In addition, WHR (per 0.1 unit) was strongly related to presence of plaque (OR 2.75, 95% CI [1.20, 6.30], P=.01) and CAC score > 0 (OR 3.14, 95% CI [1.30, 7.58], P=.006) among uninfected individuals, but not among PWH. BMI did not relate to presence of plaque or CAC score > 0 in either group. (Table 2)

In this study, we assessed volumetric indices of plaque in addition to analysis by segments and overall CAC score. Similar relationships were seen, with strong associations between VAT and total calcified plaque volume, contrasting with inverse associations between SAT and calcified plaque volume in the HIV group. Among uninfected individuals only VAT, but not SAT, related to calcified plaque volume. In addition, WHR was strongly related to calcified plaque volume among uninfected individuals, but not among PWH. (Table 3)

Independent effects of body composition on CAC score and Total Calcified Plaque Volume among PWH

In adjusted analyses controlling for traditional coronary risk factors (using the Framingham Risk Score, which includes sex, as an aggregate measure) CD4 and viral load, VAT, but not SAT, remained independently related to increased CAC score. Similarly, the VAT:SAT ratio (β=35.884, p=.02) was significantly related to CAC score, independent of traditional CVD risk factors. (Table 4) This relationship between VAT:SAT ratio (β=32.454, p=.03) and CAC score also held additionally controlling for statin use. Similar adjusted analyses revealed that the VAT:SAT ratio (β=29.829, p=.02) was significantly associated to total calcified plaque volume, independent of traditional CVD risk factors. (Table 4) When controlling individually for sex rather than for sex as part of a composite risk score, adjusted analyses confirmed that the VAT:SAT ratio and VAT were independently related to both CAC score and total calcified plaque volume. (Supplemental Table 1a)

Discussion

In the current study, we investigated the association of discrete adipose depots with subclinical atherosclerosis in HIV, using sophisticated radiologic techniques to measure presence of plaque and CAC score. Prior studies show that atherosclerotic plaque and CAC score are increased in PWH vs. uninfected populations [19, 20, 23]. Importantly, no prior studies have related specific adipose depots to the presence of plaque, plaque volume, and its composition in HIV, comparing these relationships to non-HIV. To our knowledge, this is the first study to demonstrate a clear differential association between SAT and VAT using CAC score and CTA among a mixed gender group, comparing HIV and non-HIV groups, with respect to overall plaque and calcified plaque. Whereas increased VAT was related to more plaque, in contrast, more SAT was related to less plaque among the HIV group. Given the opposite associations with these plaque indices, the VAT: SAT ratio was robustly related to plaque parameters among PWH, including presence of plaque, CAC score and calcified plaque volume, but not among uninfected individuals.

These data generated from our current study, using HIV as a model of acquired changes in body composition with lipodystrophic features, may be relevant to the broad range of congenital and acquired lipodystrophies, in which reduced SAT may also have adverse metabolic implications. Information on CVD in other forms of lipodystrophy are limited due to the rare nature of these clinical presentations. Nonetheless, increased CVD risk may be clinically applicable in other forms of lipodystrophy, given that data are available demonstrating an increased prevalence of traditional CVD risk factors, such as dyslipidemia and diabetes, among those with non-HIV associated lipodystrophies[26].

The WHR had consistent associations to coronary plaque presence and CAC score among uninfected individuals, but not among HIV. In lieu of direct adipose measurements requiring advanced radiologic techniques, WHR has been used to provide a clinical surrogate for the assessment of metabolic risk[27]. Our data suggest that the WHR and BMI, clinically obtainable measures, may not be adequate risk predicting measures and are much more limited than VAT and SAT measurements among PWH to assess atherosclerotic disease risk. Previous data have suggested that for a matched BMI, adipose depots are redistributed uniquely among HIV and non-HIV groups[11, 28]. Similarly, adipose tissue biology and redistribution profiles in HIV may be more complex systemically than quantified by circumferential measurements and therefore, inadequately represented by the WHR. Neither BMI nor even WHR truly differentiate VAT and SAT distribution, and thus both may have less utility in this regard among the HIV group, in whom parallel, but divergent changes in various adipose depots are seen. Similarly, there may be clinical utility in measuring VAT and SAT depots, as opposed to BMI or WHR alone, in other forms of lipodystrophy to better gauge metabolic risk.

Fat redistribution may have important implications for traditional calcified plaque burden compared to the less traditional non-calcified plaque. Calcified plaque tends to be stable, hardened, slow-forming, develops chronically over time[23, 29] and represents the overall burden of atherosclerotic disease, and non-calcified atherosclerotic plaque tends to unstable, soft, inflamed, and more prone to rupture[30, 31]. Among PWH, studies have shown overall increases in non-calcified plaque [19, 23], but such data do not minimize the importance of the presence of calcified plaque, which is known to be a marker of atherosclerosis in the general population and more often associated with traditional risk factors. Given the unique changes in adipose biology among PWH, studies are critically needed to determine how body composition abnormalities and shifts in adipose depots independently relate to coronary atherosclerosis in the HIV population.

Although studies in the non-HIV population show that CAC score derived from cardiac CT is a clinical predictive marker of subclinical atherosclerosis and future CVD events[32], the impact of calcified plaque on CVD in PWH remains unclear. No studies to date have examined the role of calcified plaque or CAC score on predicting CVD events in HIV, and this will be addressed for the first time in the ongoing REPRIEVE trial[33].

Our study demonstrated greater VAT accumulation was associated with increased likelihood of coronary plaque presence and correlated with CAC score, regardless of serostatus, in both PWH and uninfected groups. Studies focused on uninfected individuals have demonstrated

that VAT volume is linked to CVD risk, and furthermore that VAT volume and VAT:SAT ratio are associated with increased CVD events. In contrast, SAT may be a less robust predictor of CVD events among uninfected individuals[34], a point further emphasized by data from the uninfected group in the current study. Unique from the uninfected group, we show SAT loss is related to presence of coronary plaque, and calcium specific measures, including CAC score and calcium volume in PWH. These findings likely reflect differences in adipose biology among PWH, who are at increased risk for VAT accumulation and SAT loss, compared to uninfected individuals.

The few studies evaluating adipose depots and subclinical atherosclerosis in HIV have been limited to single sex cohorts[24, 25] and our work encompassing both sexes extends these prior data. Palella et al. reported VAT was positively correlated with presence of coronary plaque after adjusting for CVD risk factors and also demonstrated an inverse relationship between SAT and presence of total plaque, studying only men with HIV in the MACS cohort[24]. The WIHS cohort studying only women with HIV reported greater VAT mass was correlated with increased carotid artery stiffness, and conversely, greater SAT mass was associated with a reduced odds of carotid artery lesion prevalence[25]. Guaraldi et al. showed among a mixed sex (although male predominant) study in HIV an association between CAC score and both SAT loss and VAT accumulation, but did not include uninfected individuals[17]. In our study, we had the advantage of obtaining detailed state of the art atherosclerotic measures using both cardiac CT and coronary CTA among both sexes, which is unique from prior studies in HIV, and also included well-matched uninfected controls for a biological comparison.

Notably the relationship between VAT and calcified plaque in HIV remained robust, even controlling for traditional risk factors, including sex, smoking, cholesterol, age, as well as HIV specific parameters of CD4 count and HIV viral load. Additional analyses controlling for sex as an individual variable, similarly demonstrated robust relationships of VAT and VAT:SAT ratio to measures of calcified plaque among PWH. Larger studies powered to study the sex-specific relationship of body composition to atherosclerotic measures are needed to confirm these initial findings in the HIV population and further explore critical gender differences in the relationship of depot-specific fat mass indices to coronary plaque.

Contemporary CVD risk calculators formulated for uninfected individuals do not reliably assess CVD risk in the HIV population and may underpredict CVD risk[35]. In this regard, our data now suggest that adipose redistribution occurring in HIV may contribute to this gap, as measures of specific fat depots affected in HIV relate strongly and differentially to key coronary plaque variables. Thus, changes in body composition may serve as important non-traditional mediators affecting subclinical atherosclerosis in PWH compared to uninfected individuals. Further studies are needed to gauge whether measures of adipose redistribution may inform us about CVD event rates in HIV, as would be predicted by our data, and could be extended to other forms of non-HIV associated lipodystrophy.

Our study has a few limitations, but also a number of advantages including data from men and women, an uninfected control group, and data assessing volumetric indices of coronary plaque. This investigation was cross-sectional in nature, and thus we are unable to confirm

causality between fat redistribution and presence of calcified plaque or CAC score. Nonetheless, these data in a large group of PWH well-phenotyped for specific adipose depots and detailed measures of atherosclerotic plaque begin to inform us that fat redistribution may have critical implications for CVD in HIV. Our study enrolled a diverse group of PWH with a chronic history of HIV infection and ART use who were not selected to specifically have adipose tissue redistribution, and we demonstrated the consistent association between high VAT:SAT ratio and CAC score and presence of calcified plaque. Additional studies are needed in those PWH exposed to more contemporary ART, but nonetheless, many such individuals do experience changes in body composition. This study suggests the important need to consider such changes and for clinicians to have a heightened awareness for subclinical atherosclerosis in relevant PWH, including individuals who have been exposed to older regimens among whom such changes in body composition are especially prevalent. Importantly, further studies will be critical among the increasing population of PWH with obesity in whom VAT and SAT may be increased simultaneously, as to discern the net effects of these changes on subclinical atherosclerotic indices and cardiovascular events[27].

PWH demonstrated a higher risk of subclinical atherosclerosis compared to uninfected individuals, and mechanisms for the pathogenesis of atherosclerotic disease, aside from traditional risk factors, remain unclear in HIV. Fat redistribution and simultaneous quantification of VAT and SAT measures could help identify those PWH at higher risk of CVD, potentially at an earlier subclinical stage, and inform the development inform the development of CVD risk assessment algorithms that include non-traditional risk factors. Clinicians should have a heightened awareness for increased subclinical atherosclerosis in those PWH with either increased visceral adiposity and/or loss of subcutaneous fat, and especially among those who present with both.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is already known about the subject?

- Persons with HIV (PWH) have an increased risk of heart disease compared to uninfected individuals. Traditional cardiovascular disease (CVD) risk factors do not solely account for the increased risk of heart disease.
- Adipose redistribution is prevalent among PWH, and these changes in body composition may be related to the prevalence of cardiometabolic disease in HIV.

What are the new findings in this manuscript?

- Herein, we investigated the association of discrete adipose depots (visceral and subcutaneous adipose tissue [VAT, SAT]) with subclinical atherosclerosis in HIV, using validated state of the art radiologic techniques via CT to measure presence of plaque and coronary artery calcium (CAC) score, in a combined male and female population, including an uninfected comparator group.
- Among PWH, both increased VAT and reduced SAT related to increased presence of plaque and CAC score>0, while among uninfected individuals, VAT, but not SAT, related to increased presence of plaque and CAC score>0.
- By plaque composition, VAT: SAT ratio showed a strong relationship to presence of calcified plaque in the HIV group and did not relate to non-calcified plaque.

How might these results change the direction of research or the focus of clinical practice?

- Characterization of the VAT and SAT depots, beyond other body composition measures, could help identify those PWH at higher risk of CVD, potentially at an earlier subclinical stage, and help inform the development of non-traditional risk factors to guide CVD prediction algorithms.
- Importantly these findings, using HIV as a model of adipose redistribution, may have broader implications for people with congenital and acquired lipodystrophies or individuals with disproportionate VAT in excess with regards to CVD risk.

Table 1.

Baseline Demographic and Clinical Characteristics

	PWH (n=148)	Uninfected Individuals (n=68)	P Value
Demographics			
Age (years)	47±7	46±7	.21
Race (%)			.43
Caucasian	55	53	
African American	37	35	
Male Sex (%)	65	60	.52
HIV-Related Parameters			
$CD4^+$ T cell count (cells/μl)	549±293	*	--
$CD4^+$ T cell nadir (cells/μl)	189±155	*	--
$CD8^+$ T cell count (cells/μl)	918±489	*	--
Log HIV RNA Viral Load (copies/mL)	1.82±0.47	*	--
Undetectable HIV Viral Load (%)	86%	N/A	--
Duration HIV (years)	14±6	N/A	--
Duration ART use (years)	8±5	N/A	--
Current PI use (%)	57	N/A	--
Current NRTI use (%)	95	N/A	--
Current NNRTI use (%)	38	N/A	--
Current INSTI use (%)	15	N/A	--
Body Composition and Metabolic Parameters			
Iliac crest (cm)	97±14	98±15	.80
BMI (kg/m^2)	26.7±4.8	27.8±4.9	.11
Waist to Hip Ratio	0.94±0.07	0.93±0.07	.29
SAT (cm^2)	198 [125, 287]	241 [150, 380]	.02
VAT (cm^2)	108 [61, 209]	103 [55, 177]	.45
VAT to SAT Ratio	0.54 [0.30, 1.13]	0.42 [0.23, 0.84]	.04
HDL (mg/dL)	49 [40, 61]	49 [42, 62]	.89
LDL (m/dL)	99 [80, 122]	106 [89, 128]	.25
Triglycerides (mg/dL)	97 [76,174]	86 [63, 126]	.003
Glucose (mg/dL)	88 [79, 95]	89 [80,96]	.86
Comorbidities			
Current Tobacco use (%)	44	40	.60
Current Diabetes (%)	11	7	.41
Framingham estimate of 10-yr CHD risk (%)	3[1,6]	2[1,5]	.06

Data reported as mean ± standard deviation, percentage, or median [interquartile range].

*Not performed

Abbreviations: PWH, Persons with HIV; N/A, not applicable; ART, antiretroviral therapy; PI, protease inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitors; NNRTI, non-nucleoside reverse transcriptase inhibitors; INSTI, integrase inhibitors; BMI, body mass index; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CHD, coronary heart disease

Table 2.

Relationship between body composition and presence of plaque

	Presence of Plaque		Presence of Calcified Segments		Presence of Non-Calcified Segments		CAC Score > 0	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
PWH								
BMI (kg/m^2)	1.00 (0.94, 1.07)	.91	1.01 (0.90, 1.13)	.84	1.03 (0.96, 1.10)	.47	0.98 (0.92, 1.05)	.62
WHR (per 0.1 unit)	1.62 (0.95, 2.78)	.07	1.25 (0.49, 3.17)	.64	1.73 (0.99, 3.02)	.05	1.33 (0.77, 2.30)	.30
SAT (per 100 cm^2)	0.79 (0.61, 1.01)	.06	0.86 (0.56, 1.32)	.46	0.91 (0.71, 1.17)	.46	0.69 (0.52, 0.92)	.007
VAT (per 100 cm^2)	1.55 (1.10, 2.17)	.008	1.51 (0.97, 2.34)	.07	1.35 (0.98, 1.85)	.06	1.56 (1.13, 2.16)	.006
VAT to SAT ratio[a]	3.36 (1.51, 7.48)	.002	3.30 (1.12, 9.74)	.03	1.68 (0.81, 3.49)	.16	3.57 (1.65, 7.70)	<.001
Uninfected Individuals								
BMI (kg/m^2)	1.08 (0.97, 1.19)	.16	1.10 (0.97, 1.25)	.14	0.99 (0.87, 1.12)	.85	1.09 (0.98, 1.22)	.10
WHR (per 0.1 unit)	2.75 (1.20, 6.30)	.01	2.18 (0.85, 5.58)	.09	2.50 (0.95, 6.62)	.05	3.14 (1.30, 7.58)	.006
SAT (per 100 cm^2)	1.15 (0.84, 1.58)	.39	1.28 (0.87, 1.86)	.21	0.93 (0.63, 1.37)	.72	1.19 (0.86, 1.64)	.30
VAT (per 100 cm^2)	1.75 (1.02, 2.98)	.03	1.51 (0.86, 2.64)	.15	1.15 (0.66, 2.00)	.62	1.71 (1.01, 2.89)	.04
VAT to SAT ratio[b]	3.68 (0.87, 15.59)	.07	1.55 (0.29, 8.39)	.61	3.23 (0.64, 16.14)	.15	3.01 (0.70, 12.87)	.14

OR reported as per 1 unit, unless otherwise noted

Abbreviations: CAC, coronary artery calcium; OR, odds ratio; PWH, persons with HIV; BMI, body mass index; WHR, waist to hip ratio; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.

[a] 9 outliers excluded for change as per Tukey Method, P value obtained based on appropriate statistical test

[b] 1 outlier excluded for change as per Tukey Method, P value obtained based on appropriate statistical test

Table 3.

Correlations of body composition with calcium-related parameters of plaque

	CAC Score		Total Calcified Plaque Volume	
	r	P Value	r	P Value
PWH				
BMI (kg/m^2)	−0.06	.49	−0.06	.47
WHR	0.01	.91	0.02	.83
SAT (cm^2)	−0.21	.01	−0.19	.02
VAT (cm^2)	0.18	.03	0.19	.03
VAT to SAT ratio[a]	0.24	.004	0.25	.004
Uninfected Individuals				
BMI (kg/m^2)	0.19	.12	0.19	.13
WHR	0.34	.007	0.35	.006
SAT (cm^2)	0.11	.36	0.11	.39
VAT (cm^2)	0.29	.02	0.30	.01
VAT to SAT ratio[b]	0.23	.06	0.24	.05

r assessed by Pearson's correlation.

Abbreviations: CAC, coronary artery calcium; PWH, persons with HIV; BMI, body mass index; WHR, waist to hip ratio; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.

[a] 9 outliers excluded for change as per Tukey Method, P value obtained based on appropriate statistical test

[b] 1 outlier excluded for change as per Tukey Method, P value obtained based on appropriate statistical test

Table 4.

Models to assess impact of body composition on calcified plaque indices among persons with HIV

	CAC score		Total Calcified Plaque Volume	
	β estimate	**P Value**	**β estimate**	**P Value**
	Model 1 (r^2=0.19, P<.0001)		**Model 1** (r^2=0.21, P<.0001)	
VAT to SAT ratio[a]	35.884	.02	29.829	.02
Framingham estimate of 10-yr CHD risk (%)	3.429	.01	3.179	.007
CD4 T cell count (cells/μl)	−0.003	.90	−0.001	.94
HIV VL (copies/mL)	0.011	.11	.009	.14
	Model 2 (r^2=0.18, P=.0001)		**Model 2** (r^2=0.19, P=.0001)	
VAT (cm^2)	0.139	.04	0.116	.04
Framingham estimate of 10-yr CHD risk (%)	4.497	.002	4.030	.001
CD4 T cell count (cells/μl)	−0.011	.61	−0.010	.58
HIV VL (copies/mL)	0.012	.12	0.009	.16
	Model 3 (r^2=0.16, P=.0005)		**Model 3** (r^2=0.17, P=.0003)	
SAT (cm^2)	−0.066	.19	−0.060	.17
Framingham estimate of 10-yr CHD risk (%)	5.135	.0002	4.556	.0001
CD4 T cell count (cells/μl)	−0.001	.97	−0.001	.96
HIV VL (copies/mL)	0.001	.20	0.008	.25

Abbreviations: CAC, coronary artery calcium; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; VL, viral load.

[a]9 outliers excluded for change as per Tukey Method