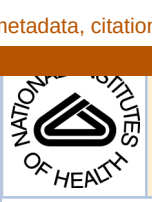

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The Associations of Regional Adipose Tissue with Lipid and Lipoprotein Levels in HIV-infected Men

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Abstract

Background—HIV infection and antiretroviral therapy are associated with dyslipidemia, but the association between regional adipose tissue depots and lipid levels is not defined.

Methods—The association of MRI-measured visceral (VAT) and regional subcutaneous adipose tissue (SAT) volume with fasting lipid parameters was analyzed by multivariable linear regression in 737 HIV-infected and 145 control men from the study of Fat Redistribution and Metabolic Change in HIV Infection (FRAM).

Results—HIV-infected men had higher median triglycerides (TG) (170mg/dl vs. 107mg/dl, p<0.0001), lower high density lipoprotein (HDL-C) (38mg/dl vs. 46mg/dl, p<0.0001) and lower low density lipoprotein (LDL-C) (105mg/dl vs. 125mg/dl, p<0.0001) than controls. After adjustment, greater VAT was associated with higher TG and lower HDL-C in both HIV-infected and control men, while greater leg SAT was associated with lower TG in HIV-infected men with a similar trend in controls. More upper trunk SAT was associated with higher LDL-C and lower HDL-C in controls, while more lower trunk SAT was associated with higher TG in controls. After adjustment, HIV infection remained strongly associated (p<0.0001) with higher TG (+76%, CI: 53, 103), lower LDL-C (−19%, CI: −25,−12), and lower HDL-C (−18%, CI: −22,−12).

Conclusions—HIV-infected men are more likely than controls to have higher TG and lower HDL-C, which promote atherosclerosis, but also lower LDL-C. Less leg SAT and more VAT are important factors associated with high TG and low HDL-C in HIV-infected men. The reduced leg SAT in HIV-infected men with lipoatrophy places them at increased risk for pro-atherogenic dyslipidemia.

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Background

Abnormalities of lipid and lipoprotein levels are prevalent among HIV-infected individuals. HIV infection itself is associated with reductions in HDL cholesterol (HDL-C) and LDL cholesterol (LDL-C), with increases in triglycerides appearing with development of AIDS[1-4]. Therapy with HIV protease inhibitors (PI) is associated with increases in triglycerides, LDL-C and total cholesterol[5-9]. A syndrome of HIV-associated lipodystrophy was described that included peripheral fat wasting and central fat gain, associated with increased triglycerides and cholesterol and decreased HDL-C; this syndrome was initially attributed to treatment with PIs [10]. Subsequent studies demonstrated that PI-induced changes in lipid and lipoprotein levels are seen before any changes in body composition[9,11-13]. Studies linking HIV lipodystrophy to dyslipidemia have mostly used clinical definitions and varied in their inclusion of peripheral fat wasting and central fat gain[10,14-17]. It is now recognized that subcutaneous lipoatrophy is the HIV-specific change and that peripheral lipoatrophy and central lipohypertrophy are not linked in the same syndrome[18-21].

The clinical assessment of lipoatrophy underestimates the changes in HIV compared to direct measurement of adipose tissue volume. Even HIV-infected subjects who do not have the clinical syndrome of lipoatrophy may have significantly less subcutaneous adipose tissue (SAT) in their lower body (legs and lower trunk) than healthy controls [20,21]. The amount of visceral adipose tissue (VAT) is independent of leg SAT in HIV-infected men [20,21].

Given the association of total adipose tissue with dyslipidemia in the general population, a major aim of the study of Fat Redistribution and Metabolic Change in HIV Infection (FRAM) was to define the relationship between regional adipose tissue volume measurements by MRI with fasting triglycerides, directly measured LDL-C and HDL-C in HIV-infected men with comparison to control men while taking into account demographic factors and lifestyle factors such as physical activity. A second goal was to assess the contribution of HIV and HIV-related factors to these metabolic parameters after adjusting for factors known to affect lipids, especially adipose tissue.

Methods

Subjects

The methods of the Study of Fat Redistribution and Metabolic Changes in HIV infection (FRAM), which was conducted between June 2000 and September 2002, have previously been described in detail [20,22]. HIV-infected participants enrolled in FRAM were selected from coded lists of patients seen in 16 HIV or infectious disease clinics or cohorts in the US and were representative of HIV-infected men living in the U.S.[22,23]. Control subjects were recruited for FRAM from two centers of the Coronary Artery Risk Development in Young Adults (CARDIA) study[24,25] that followed participants longitudinally enrolled in the Visceral Fat and Metabolic Rate in Young Adults (VIM) ancillary study of CARDIA. CARDIA participants were originally recruited as a population-based sample of healthy 18- to 30-year old Caucasian and African-American men and women from four cities in 1985-86 for a longitudinal study of cardiovascular risk factors. The VIM ancillary study recruited participants from two of the four CARDIA Centers in 1995-96. VIM enrolled approximately 100 CARDIA participants from each of the race-gender groups with BMI distributed similarly above and below race-gender specific medians of the population-based CARDIA study. Participants in the CARDIA study were stratified for the 2 races and sexes. Institutional Review Boards at all participating sites approved the study protocol and consent process.

Of the 980 men in FRAM, 737 HIV-infected and 145 control men were included in this analysis. Among the HIV-infected men, 72 were excluded due to missing lipid or MRI data and 16 were excluded due to a recent opportunistic infection. Among the control men, 10 were excluded due to missing lipid or MRI data. For comparisons of HIV and control characteristics, 390 (of the 737) HIV-infected men of similar age to control men were included. The results in women will be reported separately.

Study Procedures

Standardized questionnaire instruments were used to assess physical activity, alcohol intake, smoking, illicit drug use, and adequacy of food intake of FRAM participants[25-27]. Food intake was based on self-report from a validated instrument, where subjects were asked whether they had adequate access or resources to get the food needed. Medical history was also assessed. Research associates interviewed HIV-infected participants and reviewed medical charts to determine the dates of use of individual antiretroviral medications.

Blood was drawn following a 12-hour overnight fast and sent to Covance central laboratory (Indianapolis, IN) for determination of total cholesterol (TC), HDL-C, triglycerides and directly measured LDL-C. LDL-C was measured using the LDL-C Plus assay (Roche Diagnostics, Indianapolis, IN). The lower limit of detection of the triglyceride assay is 12 mg/dL (the inter- and intra-assay coefficients of variation were 2.88%-3.25% and 1.09%, respectively). The lower limit of detection of the HDL assay is 10 mg/dL (the inter- and intra-assay coefficients of variation were 5.45%-7.41% and 1.4%, respectively). The lower limit of detection of the LDL-C Plus assay is 3.1 mg/dL (the inter- and intra-assay coefficients of variation were 2.61%-2.68% and 1.7%, respectively). CD4+ T lymphocyte counts were determined by flow cytometry (Becton Dickinson, Franklin Lakes, NJ), and HIV RNA levels determined by the Amplicor HIV-1 MONITOR test (Roche Diagnostics, Branchburg, NJ) with a linear range from 400 - 750,000 copies/mL.

Weight and height were determined using standard methods. Whole body magnetic resonance imaging was performed to quantify body composition using a standard protocol[28] as described previously[20] [22]. MRI scans were segmented using image analysis software (Tomovision Inc., Montreal, Canada). Volume of each tissue for the space between two consecutive slices was calculated via a mathematical algorithm[29]. Using these methods we quantified adipose tissue volume in the following sites: leg, lower trunk (abdomen and back, ending at last slice where liver area is greater than lung area), upper trunk (chest and back), arm, total subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT) and total adipose tissue.

Statistical Methods

For numerical values, data are presented as median values and 95% Confidence Interval (CI), with distribution free confidence intervals constructed for the median[30] and p-values calculated using the Mann-Whitney U test. Fisher's exact test was used for categorical values. We did not adjust for multiple comparisons, because there were many inter-related positive results that reinforced each other by fitting together in a coherent pattern.

To assess the independent associations of body fat depots and other factors with lipids, we performed multivariable regression analysis in separate models for control and HIV-infected subjects. Separate analyses were performed for each of the following lipids: triglycerides, direct LDL-C, and HDL-C. In this first analysis, factors related to HIV infection were initially excluded. The primary predictors were trichotomized amounts of adipose tissue volume from anatomic sites measured by MRI: upper trunk, lower trunk, arm, leg and total SAT, VAT and total fat. Trichotomized versions of the anatomic site measurements were

created using tertile cut offs from the control group of men to facilitate comparison of similar quantities of adipose tissue between control and HIV-infected men.

Demographic predictors unrelated to HIV infection, such as age and ethnicity, were also included. The effect of age was modeled linearly, but with potentially different slopes in the ranges 18 to 40, 40 to 50, and 50+ years old. Other predictors included as candidates in the modeling were level of physical activity (quartiles based on control men), current smoking status, current illicit drug use (marijuana, crack, cocaine, combination use of crack and cocaine), adequate food consumption, and alcohol drinks used in the past year.

Separate multivariable linear regression models for HIV-infected and control men were built using stepwise regression, with p=0.05 for entry and retention, testing for interactions of ethnicity with other factors at each step; age and ethnicity were forced to be included in every model. A fat depot was included in the model if testing showed statistical significance at the 0.05 level. We tested for collinearity among fat depots and found it was not substantial. We performed stepwise regression by evaluating possible models one by one, rather than with an automated stepwise procedure, in order to avoid exclusion of observations that had missing data only on unselected candidate variables. Because of their skewed distribution, the lipids were log-transformed in all linear regression analyses; results were back-transformed to produce estimated percentage effects of each factors. Adjusted geometric mean lipid levels were obtained from the same models using the LSMEANS statement in SAS Proc Mixed for each tertiled level of fat.

Another objective was to compare lipid levels among HIV-infected and control men after adjusting for the common predictors measured in both groups. We used a stepwise multivariable analysis similar to the first one, but with HIV vs. control added as a factor. We tested for interactions of HIV and ethnicity with other factors at each step. For this analysis, age was restricted to 33-45 years old and only data from Caucasians and African-Americans were used to match the demographics of the controls.

In a further stepwise multivariable analysis, we tested whether the addition of factors related to HIV infection affected the association of adipose tissue volumes with the lipids, using the complete HIV-infected cohort. HIV related factors screened in the model were CD4 count, HIV RNA levels, history of AIDS by OI and current antiretroviral therapy in models similar to those previously presented, with current CD4 and HIV RNA forced to be included in the model.

Results

The demographic and clinical characteristics of HIV-infected men of similar age to control men are shown in Table 1, as are the characteristics of all HIV-infected men included in analyses related to HIV factors. Compared to control men in the same age range, HIV-infected men were more likely to smoke and more likely to report inadequate food intake, but less likely to consume alcohol and to exercise. Body mass index (BMI) was lower in HIV-infected than in control men, and HIV-infected men had less visceral adipose tissue and less subcutaneous fat in each regional depot, as well as less total adipose tissue overall. HIV-infected men in the age range of controls were similar to all HIV-infected men with regard to HIV-related characteristics and antiretroviral use (Table 2).

Lipid and Lipoprotein Levels

Compared to controls, HIV-infected men had higher median triglyceride levels (170 mg/dl vs. 107 mg/dl, p<0.001) but lower levels of HDL-C (38 mg/dl vs. 46 mg/dl, p<0.001), LDL-

C (105 vs. 125, p<0.001), and total cholesterol (191 vs. 206, p = 0.003) (Figure 1). Results were similar when stratified by race (data not shown).

The proportion of HIV-infected men with TG >150 mg/dl was higher compared to controls (57% vs. 28%, p<0.001), as was the proportion with TG > 500 mg/dl (9% vs. 2%, p=0.004). The proportion of HIV-infected men with HDL-C < 40 mg/dl was higher compared to controls (54% vs. 27%, p<0.001). In contrast, the proportion of HIV-infected men with LDL-C >130 mg/dl was lower than in controls (26% vs. 45%, p<0.001). HIV-infected men were more likely to be on lipid lowering therapy than were control men (Table 3).

In both HIV-infected and control men, African-American race was associated with similarly lower fasting triglyceride (HIV −22%, Control −23%) and higher HDL cholesterol (HIV +12.5%, Control +12%) levels than Caucasians. There were no statistically significant racial differences in LDL-C seen in either group (data not shown).

Regional Adipose Tissue Volume and Triglycerides, LDL-C and HDL-C

To assess the association of regional adipose tissue depots with lipids, we performed multivariable analysis that included age, ethnicity, and lifestyle factors. Visceral adipose tissue (VAT) was positively associated with triglycerides in both HIV-infected and control men (Figure 2A). Lower trunk SAT was also positively associated with triglycerides in control men, while there may be a weak positive association of lower trunk SAT with triglycerides in HIV-infected men. In contrast, lower amounts of leg SAT were associated with higher triglycerides in HIV-infected men, with a similar trend in control men.

Associations of adipose tissue with LDL-C appeared to be weaker (Figure 2B). The association of arm SAT with LDL-C appeared to be opposite between HIV-infected and control men (p=0.008). Arm SAT was positively associated with LDL-C in HIV-infected men, although there was not a typical dose-response for adipose tissue volume, while arm SAT appeared to be negatively associated with LDL-C in control men. In control men, upper trunk SAT was positively associated with LDL-C, but there was little apparent association of upper trunk SAT with LDL-C in HIV-infected men.

VAT was negatively associated with HDL-C in both HIV-infected and control men (Figure 2C). Upper trunk SAT was also negatively associated with HDL-C in control men. Leg SAT showed little apparent association with HDL-C in HIV-infected or control men after multivariable adjustment.

HIV Infection and Lipids

After adjustment for demographic and HIV-unrelated factors including adipose tissue volume, HIV infection in men remained strongly associated with higher triglycerides, lower LDL-C, and lower HDL-C compared to controls (Table 4). The percent effects after adjustment (Table 4) were similar to the unadjusted effect (Figure 1).

Among HIV-infected men, little change was seen in the associations with adipose tissue depots even after HIV-related factors (e.g., ARV) were included in the multivariable model (data not shown). Among HIV-related factors, higher current CD4+ cell count was associated with higher triglycerides and lower LDL-C, but showed no apparent association with HDL-C (Table 5). A higher HIV viral load was associated with lower LDL-C and HDL-C. Having a diagnosis of AIDS was associated with higher triglycerides even after adjusting for current CD4+ cell count and HIV RNA.

Being on ritonavir was strongly and independently associated with higher triglycerides, while being on abacavir showed a weaker, but statistically significant positive association

with triglycerides. Treatment with nevirapine or efavirenz was associated with higher HDL-C, while indinavir was associated with lower HDL-C. Associations of antiretroviral drugs with LDL-C were weaker, and none reached statistical significance.

Discussion

HIV infection [1-4] and its therapies [5-9,12,31] are known to be associated with dyslipidemia. We now report that HIV infection remains associated with higher triglycerides, lower HDL-C and lower LDL-C than controls in this large study of HIV-infected and control men even after adjustment for adipose tissue volumes directly measured by MRI, as well as after adjustment for demographics and lifestyle factors. In HIV positive men, inclusion of HIV-related factors such as CD4+ count, viral load and antiretroviral drugs had little effect on the association of adipose tissue with lipids.

Most associations of adipose tissue volume with lipids were similar for HIV-infected and control men. For example, more VAT was associated with higher triglycerides and lower HDL-C in both HIV-infected and control men. Less leg SAT was associated with higher triglycerides in HIV-infected men, and also likely in control men.

The leg depot is of particular interest due to the prevalence of HIV-associated lipoatrophy. While clinical HIV-lipodystrophy has been associated with hypertriglyceridemia, past studies have usually pooled lipoatrophy and lipohypertrophy [10,14-17]. Here we show that lower amounts of leg SAT (the fat depot most affected with lipoatrophy in HIV-infected men [20] are independently and negatively associated with hypertriglyceridemia. Studies of familial and acquired lipodystrophy syndromes in HIV-uninfected patients have also shown a link between lipoatrophy and hypertriglyceridemia [32-34]. To facilitate comparison of similar quantities of adipose tissue in HIV-infected and control men, we used tertiles based on cutoffs for control men. A similar quantitative relationship was found for HIV-infected and control men; being in the highest tertile for leg SAT was associated with 29% lower triglyceride levels. Given the prevalence of lipoatrophy in HIV-infected men, more HIV-infected men fall into the ranges of low leg fat, contributing to hypertriglyceridemia.

VAT is positively associated with triglyceride levels in both HIV-infected and Control men. We have shown previously that VAT and leg SAT are not inversely linked in HIV infection [20,21], but that there are men with lipoatrophy who have high amounts of VAT [20]. Thus HIV-infected men with both low leg SAT and increased VAT have two independent risk factors for high triglycerides.

HIV-related factors also contribute to hypertriglyceridemia. The association between a diagnosis of AIDS and higher triglycerides has previously been observed in men in the pre-HAART era [2] and was found again here.

While more VAT is associated with lower HDL-C levels, the associations of leg SAT with HDL-C were very small and did not approach statistical significance. After controlling for HIV-related factors in the multivariable model, including ARV, little change was seen in the association with adipose tissue depots. Higher HIV viral load was also associated with lower HDL-C levels, consistent with the lower levels of HDL-C seen before the introduction of effective combination antiretroviral therapy[2,35].

LDL-C levels do not strongly correlate with obesity or visceral adiposity in the general population. Therefore, it is not surprising that we found only a weak relationship of VAT with LDL-C. The associations with upper trunk and arm SAT found here are novel, but these depots are not traditionally measured. We have also found that upper trunk SAT is independently associated with insulin resistance in both HIV-infected and control

subjects[36]. The significance of these associations needs further exploration. The associations of CD4+ counts and HIV viral load are consistent with the previously described effect of HIV on lowering LDL [2,3].

It is important to note that the median triglyceride and LDL-C levels in our cohort of men between 33 and 45 years of age remained in the normal ranges. More HIV-infected than control men were on lipid lowering agents. Sensitivity analyses excluding those on lipid-lowering therapy or controlling for those on lipid-lowering therapy showed little change in the relationships of adipose tissue depots and HIV infection status to lipids. However, 12% of HIV-infected men and 22% of Control men still had LDL-C levels above standard cutoffs where behavioral or lipid-lowering therapy should be considered (LDL-C ≥160). Despite this, only 27% of HIV-infected men and 3% of control men with LDL-C ≥160 were on lipid lowering therapy. The higher prevalence of smoking in HIV-participants offers another area in which cardiovascular risk reduction could be done.

A strength of our study is its size and direct measurements of regional adipose tissue volume, which allowed for multivariable analysis of associations of depots and HIV related factors with lipid levels. A limitation of our study is the cross-sectional design. Hence the study risks confounding of ARV effects by other factors, such as prior outcomes (participants may have been removed form a drug because of a metabolic effect, thus decreasing or even reversing the association). Nevertheless, similar to other studies, we found that being on ritonavir was associated with higher triglycerides[5,6,12,31] and being on nevirapine or efavirenz was associated with higher HDL-C[37-39]. While use of older antiretroviral drug regimens has declined greatly in industrialized nations, lipoatrophy persists after discontinuation of the responsible ARV drugs. Furthermore, similar drug regimens associated with lipoatrophy are still frequently used in the developing world. The associations of adipose tissue with lipids and lipoproteins in this analysis were independent of and not influenced by current ARV, hence can be extrapolated to current patients with HIV-associated lipoatrophy or visceral obesity. Finally, the cross-sectional design also limits the ability to make causal inferences regarding changes in HIV disease status. However, the ability to adjust for regional adipose tissue depot volumes provides important information on the link between those depots and HIV effects. The associations of regional fat distributions with lipid levels in HIV infection, while similar to findings in the general population, will require further validation in other cohorts.

In summary, HIV-infected men have higher triglycerides, lower HDL-C, and lower LDL-C than control men that are independent of amounts of adipose tissue. Less leg SAT and more VAT are important risk factors for adverse lipid profiles in men. Because leg fat is the fat depot most affected in HIV associated lipoatrophy, HIV-infected men may be at particular risk for hypertriglyceridemia as low leg fat adds to the effects of more VAT, ritonavir and HIV infection itself. Increased VAT also is associated with lower HDL. These data define the effects of body fat, HIV infection, and antiretroviral therapy that should help health care providers and patients understand the metabolic complications of HIV infection and its therapies.

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APPENDIX

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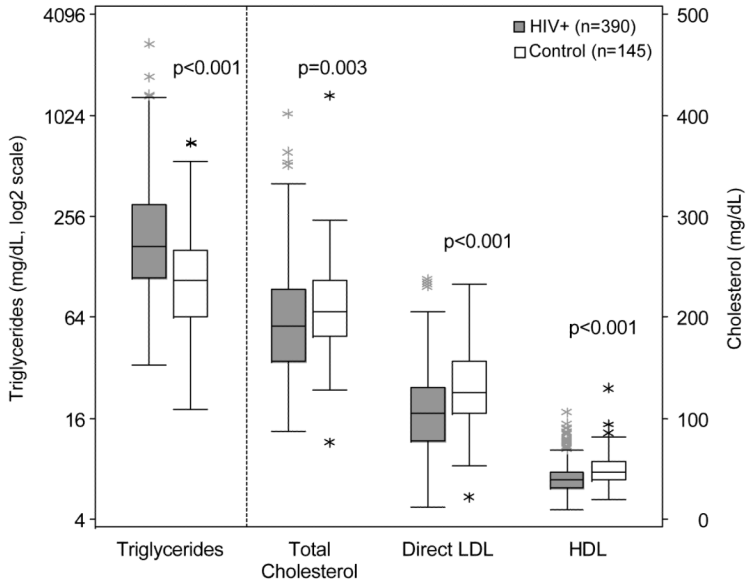

Figure 1.

Lipid and lipoprotein levels stratified by HIV-status.

Levels are in mg/dL. Closed boxes: HIV+. Open boxes: Control. The data are from the HIV-infected and Control men in the age range of 33-45. Median is indicated by black center line, and the IQR (first and third quartiles) are the edges of the box. Whiskers denote Q1 – 1. 5× IQR and Q3 + 1.5 × IQR. Asterisks denote outliers beyond 1.5 × the IQR.

Figure 2 A (Triglycerides): Multivariable association of regional adipose tissue with lipid and lipoprotein levels in HIV-infected and Control men (not age restricted)

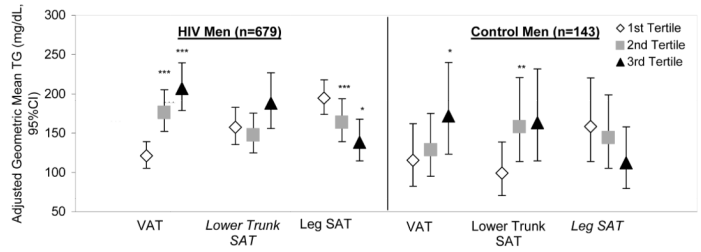

Figure 2B (LDL Cholesterol):

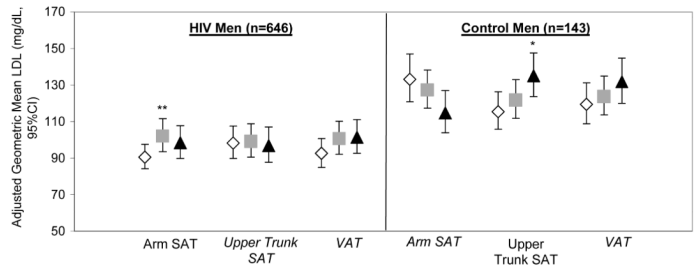

Figure 2C (HDL Cholesterol):

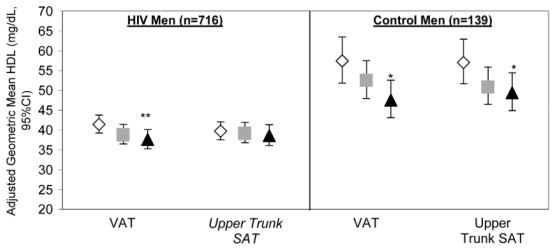

Figure 2.

Multivariable association of regional adipose tissue with lipid and lipoprotein levels in HIV-infected and Control men (not age restricted).

A. Triglycerides. B. LDL Cholesterol. C. HDL Cholesterol.

Levels are in mg/dL.

Open: 1st Tertile (lowest amount of fat)

Light grey: 2nd Tertile

Dark grey: 3rd tertile (highest amount of fat)

Asterisks denote comparison with first tertile: *** p<.001, ** p <.01, * p < .05 Analyses also control for demographic and lifestyle factors and include all HIV-infected men.

Italicized depots did not reach statistical significance and were not included in the model, but are shown to facilitate comparison. Abbreviations: VAT = visceral adipose tissue; SAT = subcutaneous adipose tissue.

Table 1

Demographic and Clinical Characteristics of HIV-infected and Control Men

		Age-Restricted (33-45 years)*			All
		Control	HIV	P-value	HIV
n		145	390		737
Age (y)	Median (IQR)	40.0 (38.0-43.0)	40.0 (37.0-43.0)	0.64	43.0 (38.0-49.0)
Race	Caucasian	55%	57%	0.053**	56%
	African-American	45%	31%		32%
	Hispanic	0	11%		9%
	Other	0	1.5%		2%
Physical Activity***	1st Quartile	26%	43%	0.001	49%
	2nd Quartile	26%	17%		20%
	3rd Quartile	25%	22%		17%
	4th Quartile	23%	17%		15%
Inadequate Food		12%	22%	0.010	20%
Current Smoker		21%	45%	<.0001	41%
Alcohol	None	15%	24%	0.013	25%
	<1/week	24%	30%		28%
	1-7/week	37%	31%		31%
	>7/week	24%	15%		17%
BMI (kg/m^2)	Median (IQR)	26.9 (24.6-29.8)	24.3 (22.3-26.6)	<.0001	24.3 (22.1-26.6)
VAT (L)	Median (IQR)	2.0 (1.1-3.0)	1.6 (0.68-2.7)	0.006	1.7 (0.75-3.0)
Leg SAT (L)	Median (IQR)	4.5 (3.7-5.7)	2.9 (2.0-4.2)	<.0001	2.8 (2.0-4.0)
Lower Trunk SAT (L)	Median (IQR)	5.6 (4.1-7.4)	3.4 (2.0-5.3)	<.0001	3.3 (2.1-5.1)
Upper Trunk SAT (L)	Median (IQR)	3.0 (2.3-4.16)	2.5 (1.7-3.5)	<.0001	2.5 (1.7-3.6)
Arm SAT (L)	Median (IQR)	1.1 (0.89-1.4)	0.97 (0.78-1.4)	0.018	0.97 (0.79-1.3)
Total Adipose Tissue (L)	Median (IQR)	17.0 (12.9-21.5)	11.9 (8.7-17.3)	<.0001	11.9 (8.8-17.1)

P-value from Mann-Whitney test or Fisher's Exact Test. Excluding all participants with recent opportunistic infections

*HIV-infected participants are those restricted to the age range of controls.

**: Race comparison is proportion of Caucasians vs. African-Americans

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***: First quartile of physical activity is least active, and fourth quartile is most active.

Note: Adipose tissue measures are height-normalized and back-transformed

Abbreviations: IQR = interquartile range; IDU = illicit drug use; MSM = men having sex with men.

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Table 2

HIV-related Characteristics of HIV-infected Men

		HIV-infected Men			
		All		Age-Restricted (33-45 years)*	
n		737		390	
HIV Risk Factors	Heterosexual	10%		10%	
	IDU	17%		14%	
	MSM	67%		70%	
	Other	7%		5%	
Duration HIV (y)	Median (IQR)	8.0 (5.0-12.0)		8.0 (5.2-12.0)	
HIV RNA (1000/mL)	Median (IQR)	0.4 (0.4-13.2)		0.4 (0.4-9.4)	
CD4 (cells/uL)	Median (IQR)	339 (219-520)		358 (230-517)	
Current ARV Use and Duration (years):		%	Median (IQR)	%	Median (IQR)
	HAART	80%	3.0 (1.6-4.4)	82%	2.9 (1.7-4.4)
	NRTI	87%	4.1 (2.3-5.6)	88%	4.0 (2.3-5.4)
	NNRTI	41%	1.5 (0.8-2.2)	39%	1.5 (0.8-2.1)
	PI	57%	3.1 (1.6-4.4)	60%	3.0 (1.8-4.4)
	Lamivudine	63%	3.1 (1.5-4.5)	62%	3.0 (1.6-4.4)
	Stavudine	44%	3.0 (1.4-4.2)	43%	2.9 (1.4-4.1)
	Abacavir	20%	1.2 (0.6-2.1)	22%	1.1 (0.6-2.0)
	Didanosine	17%	1.8 (0.7-2.9)	18%	1.9 (0.7-2.9)
	Zalcitabine	1%	2.9 (1.3-4.5)	1%	3.3 (1.7-5.0)
	Zidovudine	31%	2.7 (1.2-4.3)	33%	2.6 (1.3-4.1)
	Ritonavir	29%	1.1 (0.5-2.4)	33%	1.3 (0.6-2.5)
	Indinavir	18%	3.1 (1.8-4.5)	16%	3.1 (1.8-4.5)
	Nelfinavir	17%	2.5 (1.6-3.7)	16%	2.7 (2.0-3.5)
	Lopinavir	12%	0.5 (0.2-0.8)	13%	0.5 (0.1-0.9)
	Saquinavir	10%	2.5 (1.6-3.7)	13%	2.5 (1.5-3.6)
	Amprenavir	6%	1.0 (0.5-1.4)	7%	1.0 (0.2-1.4)
	Efavirenz	28%	1.4 (0.7-2.1)	25%	1.5 (0.7-2.1)
	Nevirapine	12%	1.6 (0.8-2.4)	13%	1.2 (0.7-2.0)

		HIV-infected Men			
		All		Age–Restricted (33–45 years)*	
Ritonavir Dose	Delavirdine	1%	1.2 (0.4-2.1)	1%	1.7 (0.3-3.3)
	>400 mg/day	7%		9%	
	≤400 mg/day	23%		24%	
	None	70%		67%	

Excluding all participants with recent opportunistic infections

*HIV-infected participants were restricted to those in the age range of controls.

Abbreviations: IQR = interquartile range.

Table 3

Proportion of HIV-infected and control men on lipid lowering therapy

	HIV+	Control	P-value
Any lipid lowering therapy	13.8%	1.4%	**<.0001**
Statin	8.9%	0.7%	**0.0003**
Fibrate	6.8%	0.0%	**0.0004**
Other Hypolipidemic	0.0%	0.7%	0.27

Note: analysis is age-restricted and OI-excluded.

Table 4

Multivariable association of HIV infection with lipid and lipoprotein levels.*

	HIV vs. Control		
	% Effect	**95% CI**	**p-value**
Triglycerides	76	(53,103)	**<.0001**
LDL-C	−19	(−25,−12)	**<.0001**
HDL-C	−18	(−22,−12)	**<.0001**

* multivariable, linear regression of combined HIV and Control populations controlling for demographics, lifestyle factors, and regional adipose tissue volume.

Note: analysis is age-restricted and OI-excluded.

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Table 5

Multivariable, linear regression analysis of HIV-related factors associated with lipid and lipoprotein levels in HIV+ Men*

	Triglycerides n=665			LDL n=637			HDL n=705		
	% Effect	**95% CI**	**p-value**	**% Effect**	**95% CI**	**p-value**	**% Effect**	**95% CI**	**p-value**
Current CD4+ cell count (log2)	8	(2,15)	**0.014**	6	(3,10)	**0.001**	1	(−1,4)	0.24
Current HIV Viral Load (log10)	0	(−6,7)	>0.99	−5	(−9,−1)	**0.015**	−7	(−9,−4)	**<.0001**
AIDS Defining Illness by OI/CD4	24	(8,42)	**0.002**						
Currently on: Ritonavir	52	(34,73)	**<.0001**						
Currently on: Abacavir	16	(1,33)	**0.040**						
Currently on: Nevirapine							21	(12,30)	**<.0001**
Currently on: Efavirenz							10	(4,16)	**0.001**
Currently on: Indinavir							−7	(−13,−1)	**0.025**

*NOT age-restricted

Note: Model also controls for demographic and lifestyle factors, and regional adipose tissue volumes

N differs for the different lipid and lipoprotein levels due to missing fasting lipid data