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Femoral-gluteal subcutaneous and intermuscular adipose tissues have independent and opposing relationships with CVD risk

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Abstract

—Femoral-gluteal adipose tissue (AT) may be cardioprotective through fatty acids uptake. Femoral-gluteal AT has previously been defined as leg fat measured by dual energy x-ray absorptiometry (DXA); however, subcutaneous adipose tissue (SAT) and intermuscular adipose tissue (IMAT) are inseparable using DXA. This study investigated the independent relationships between femoral-gluteal SAT, femoral-gluteal IMAT, and cardiovascular disease (CVD) risk factors [fasting serum measures of glucose, total cholesterol (TC), high density lipoprotein cholesterol (HDL), triglycerides (TG) and insulin] and whether race differences exist in femoral-gluteal AT distribution. Adult Caucasians (56 men and 104 women), African-Americans (37 men and 76 women), and Asians (11 men and 35 women) had total AT (TAT) including femoral-gluteal AT (upper leg SAT and IMAT) and visceral AT (VAT) by magnetic resonance imaging (MRI). General linear models identified the independent effects of femoral-gluteal SAT and femoral-gluteal IMAT on each risk factor after covarying for TAT, VAT, age, race, sex, and two-way interactions. Femoral-gluteal IMAT and glucose ($P < 0.05$) were positively associated independent of VAT. There were also significant inverse associations between femoral-gluteal SAT and insulin ($P < 0.01$) and TG ($P < 0.05$), although the addition of VAT rendered these effects nonsignificant, possibly due to collinearity. Asian women had less femoral-gluteal SAT and greater VAT than Caucasians and African-Americans ($P < 0.05$) and Asian and African-American men had greater femoral-gluteal IMAT than Caucasians, adjusted for age and TAT ($P < 0.05$ for both). Femoral-gluteal SAT and femoral-gluteal IMAT distribution varies by sex and race, and these two components have independent and opposing relationships with CVD risk factors.

Keywords

leg fat; body composition; health risk

Adipose tissue and its distribution are important determinants or predictors of metabolic and cardiovascular disease risk (20). Whereas the association between intra-abdominal or visceral adipose tissue (VAT) and metabolic abnormalities is well established (6), it is less clear the role played by subcutaneous adipose tissue (SAT) and intermuscular adipose tissue (IMAT) distributions. Greater lower body adiposity (stored in the femoral-gluteal region) measured by dual energy x-ray absorptiometry (DXA) has been shown to exert protective effects against cardiovascular disease in postmenopausal women (38), and increased midhigh girth and subcutaneous fat mass are reported to convey greater protection against ischemic heart disease

(19). Low amounts of leg SAT combined with high whole body IMAT were found to be independent predictors of insulin resistance in obese HIV+ women (1). The femoral-gluteal adipose tissue (AT) depot is postulated to play a role in the uptake of fatty acids from the circulation and to act as a reservoir for excess triglycerides storage in adipose cells (9). Femoral-gluteal AT is a metabolically inert depot with a low blood flow and low rate of fatty acid release (9,37). The rate of lipolysis of femoral-gluteal SAT is lower than that of the trunk SAT (27). Collectively, uptake of free-fatty acids, a lower lipolytic rate, and greater insulin sensitivity of femoral-gluteal adipocytes are the mechanisms postulated to confer cardioprotection.

A limitation of previous studies that used the DXA technique to report on lower body adiposity, specifically leg fat, is that DXA provides a single value for leg fat that includes two anatomically distinct AT depots, namely, IMAT and SAT, which DXA is unable to discriminate. Similarly, the DXA trunk region provides a single value for fat that encompasses trunk SAT and VAT and DXA is unable to separate these two depots. Whole body magnetic resonance imaging (MRI) allows for the quantitative measurement of whole body AT and regional compartments, i.e., VAT, SAT, and IMAT (2,11,35).

AT and its distribution vary as a function of age, sex, ethnicity, and level of fatness. Age-associated changes in fat distribution include a greater fat accumulation in the abdomen (3), less fat in the extremities (16,36), and an increase in IMAT (11,35). Several reports indicate race differences in fat topography between Caucasian, African-American, and Asian (7,25, 40) adults. Asians have a lower body mass index but higher percent body fat than whites (10, 40) and more VAT compared with whites and African-Americans (7,25), whereas African-American men have less VAT than Caucasian men (11,15). We previously reported a significantly greater increment in the proportion of total AT (TAT) as IMAT in African-Americans compared with whites and Asians, and VAT accumulation was greater than IMAT accumulation in Asians and Caucasians (11). However, whether femoral-gluteal AT varies by race/ethnicity has not been previously reported.

The primary aims of this study were to investigate the independent relationships between femoral-gluteal SAT, femoral-gluteal IMAT, and cardiovascular disease risk factors, and whether race/ethnic differences exist in the distribution of femoral-gluteal AT. A secondary aim was to determine how DXA and MRI values for leg fat and femoral-gluteal SAT, respectively, compare in their relationships to CVD risk factors.

METHODS

Subjects

The study was carried out by evaluating the relationship between femoral-gluteal AT and specific cardiovascular risk factors in healthy subjects. The study sample consisted of 319 healthy men and women (aged ≥ 18 yr) who previously participated in studies at St. Luke's-Roosevelt Hospital's Body Composition Unit between 1996 and 2002. The subjects were Caucasian (56 men and 104 women), African-American (37 men and 76 women), and Asian (11 men and 35 women). Subjects with fasting glucose >126 mg/dl were excluded from this study. Race was self-reported by the subjects, and both parents and grandparents were required to be of the same racial group. All studies were approved by the Institutional Review Board.

Study Procedures

A detailed description of study procedures was previously published for this same cohort (11,41). Subjects fasted overnight for study. Body weight and height were measured with subjects wearing a hospital gown and foam slippers and with the use of a calibrated scale (Weight Tronix, NY) and stadiometer (Holtain Stadiometer, Crosswell, Wales). Body mass

index (BMI) was calculated (kg/m^2) from height and weight. Body composition was determined by DXA and MRI.

DXA—Total body fat and regional fat (arm fat, trunk fat, and leg fat) were measured with a whole body DXA (DPXL, GE Lunar, Madison, WI), and analysis was performed using software version 3.4. With the use of specific anatomic landmarks as previously described (12), regions of the head, trunk, arms, and legs were distinguished (Fig. 1A). Methanol and water bottles with a volume of 8 liters, simulating fat and fat-free soft tissues, respectively, were scanned monthly as soft tissue quality control markers (25,39).

MRI—Total body skeletal muscle and TAT mass, including total SAT, VAT, and IMAT, were measured from whole body multi-slice MRI images by 1.5-T scanner (6X Horizon; General Electric, Milwaukee, WI) as previously described (11). The protocol involved the acquisition of 40 axial images of 10-mm thickness at 40-mm intervals across the whole body. SLICEOMATIC image analysis software (version 4.2; Tomovision, Montreal, Canada) was used to analyze images. MRI volume estimates were converted to mass by using assumed density of 1.04 kg/l for skeletal muscle and 0.92 kg/l for AT (34). The technical errors for four repeated readings by the same observer of MRI-derived SAT, VAT, and IMAT volumes are 1.7%, 2.3%, and 5.9%, respectively. Specific MRI subcompartments for AT were defined as follows (Fig. 1B): 1) lower leg AT from toes to the superior margin of patella; 2) upper leg AT as femoral-gluteal AT from the superior margin of patella to the level of the greater trochanter; 3) trunk AT from the level of the greater trochanter to the level of shoulder; and 4) arm AT from the level of shoulder to finger tips.

DXA fat distribution vs. MRI AT distribution—Trunk, arm, and leg fat values were determined by DXA. Trunk AT, arm AT, upper leg AT (as femoral-gluteal AT), and lower leg AT were determined by MRI. In our analyses, we assumed that DXA-measured trunk AT corresponded to MRI-measured trunk AT (combination of trunk SAT, trunk IMAT, and VAT) and DXA-measured leg fat corresponded to MRI-measured upper and lower leg AT (combination of upper and lower leg SAT and IMAT).

Biochemical Analysis

Subjects had fasted overnight and blood samples were obtained for the biochemical analysis in the morning. Blood samples were analyzed in a commercial laboratory (Corning Clinical Laboratories and Quest Diagnostics, Teterboro, NJ). Fasting glucose, triglycerides (TG), total cholesterol (TC), and high density lipoprotein cholesterol (HDL) were measured by enzymatic methods, and insulin was determined by radioimmunoassay using commercially available kits.

Statistical Analysis

Group data are presented as means $\pm$ SDs. Differences between race groups for descriptive data were determined using an analysis of variance. Mean values for fat or AT compartments were adjusted for age, sex, and total body fat or TAT, and the mean values for total body fat and/or TAT were adjusted for age, height, weight, and sex using general linear regression analysis.

The associations of cardiovascular risk factors (glucose, insulin, total cholesterol, TG, HDL) on leg fat and trunk fat were determined using general linear models (GLM), controlling for confounding variables, including total body fat, age, sex, and two-way interactions. The independent effects of femoral-gluteal AT on each risk factor after covarying for femoral-gluteal IMAT, TAT, age, race, sex, and two-way interactions were analyzed by GLM.

Residuals from the GLM were checked for normality. All analyses were performed with SAS 9.1 for Windows (SAS Institute, Cary, NC).

RESULTS

Baseline Characteristics

The descriptive characteristics for this study cohort have been reported previously (11,41) and are presented in Table 1. Analyses were conducted on 160 Caucasian, 113 African-American, and 46 Asian men and women with mean ages that were not significantly different. Among men, Caucasians (81.92 ± 12.74 kg) weighed more than Asians (72.96 ± 11.58 kg), but BMI did not differ significantly between Caucasians, African-Americans, and Asians. Among women, the African-Americans weighed more and had a higher mean BMI (29.99 ± 5.26) than the Caucasians (24.60 ± 5.02) and Asians (21.73 ± 2.98). Height was lower in Asians for both sexes than in Caucasians and African-Americans.

Race Difference in Regional Fat and AT Subcompartments

The DXA fat results by region are shown in Table 2. Asians had a significantly smaller leg fat mass and greater trunk fat mass after covarying for age, sex, and total body fat compared with Caucasians and African-Americans ($P < 0.05$). There were no significant differences in adjusted arm fat and total body fat mass by race ($P < 0.05$).

The MRI results by AT compartment are shown in Table 3. African-American men had less TAT than Asian men after covarying for age, height, weight, and sex ($P < 0.05$). Asian men and women had significantly smaller total SAT than Caucasian and African-American men and women after adjustment for age, sex, and TAT ($P < 0.05$). There were no significant differences in trunk SAT by race, but total leg SAT and arm SAT were less in Asian men compared with Caucasian and African-American men. Asian women had less femoral-gluteal SAT compared with Caucasian and African-American women. Total IMAT was greater in Asian and African-American men compared with Caucasian men and in African-American women compared with Caucasian and Asian women. Femoral-gluteal IMAT was greater in African-American and Asian men than in Caucasian men, but trunk IMAT was greater only in Asian men. In women, femoral-gluteal IMAT was greater in African-Americans than in Caucasians. VAT mass was greater in Caucasian men compared with African-American men and greater in Asian women compared with Caucasian and African-American women. There were significant race and sex interactions in arm SAT ($P = 0.01$) and trunk IMAT ($P = 0.03$), where Asian men had less arm SAT and more trunk IMAT compared with Asian women, Caucasians, and African-Americans.

Independent Associations Between Leg Fat and Trunk Fat (by DXA) With Cardiovascular Risk Factors

The independent associations between leg fat and cardiovascular risk factors are shown in Table 4. Inverse associations between leg fat adjusted for total fat, age, race, sex, and two-way interactions were found with insulin and TG, whereas leg fat was positively associated with HDLC ($P < 0.05$). No independent associations were found for leg fat with glucose and total cholesterol. The relationships between trunk fat and cardiovascular risk factors are shown in Table 5. Statistically significant independent associations between trunk fat adjusted for total body fat, age, race, sex, and two-way interactions were found with insulin, TG, and HDLC ($P < 0.05$). No independent associations were found for trunk fat with glucose and total cholesterol.

Independent Associations of Femoral-Gluteal SAT, Femoral-Gluteal IMAT, and VAT (by MRI) With Cardiovascular Risk Factors

The relationships between femoral-gluteal SAT and femoral-gluteal IMAT and cardiovascular risk factors were assessed (Table 6) and the significance of covariates (including skeletal muscle, VAT, TAT, height, age, race, sex, and TAT-by-race) were tested. Statistically significant inverse associations were found between femoral-gluteal SAT and insulin ($P < 0.01$) and TG ($P < 0.05$, Fig. 2A), but with VAT as a covariate in the model, these effects were no longer statistically significant. The nonsignificance of femoral-gluteal SAT in this model is likely a consequence of a relatively high degree of collinearity between SAT and VAT. Correlations between these two variables after partialling out covariates used in the model ranged between -0.60 and -0.83 in all race/sex groups (except for the small Asian male subgroup where they were uncorrelated). A positive association between femoral-gluteal IMAT and glucose ($P < 0.05$, Fig. 2B) was found that was independent of VAT.

The independent association between VAT and cardiovascular risk factors are shown in Table 7. VAT adjusted for trunk IMAT and SAT, TAT, age, sex, and two-way interactions was positively associated with insulin and TG ($P < 0.01$) and inversely associated with HDLC ($P < 0.05$). No independent associations were found for VAT with glucose and TC.

DISCUSSION

In this study of healthy Caucasian, African-American, and Asian adults, a significant association was found between femoral-gluteal SAT and levels of insulin and TG, but with VAT as a covariate in the model, these effects were no longer statistically significant. Femoral-gluteal IMAT was significantly associated with glucose level, independent of VAT. VAT was positively associated with insulin and TG and inversely associated with HDLC that was independent of trunk IMAT and SAT. Racial differences in regional fat were found such that Asian women had less femoral-gluteal SAT and African-American and Asian men had greater femoral-gluteal IMAT after adjusting for age, sex, and TAT.

Regional Fat Distribution Effects on CVD Risk Factor and Metabolism

The differential effects of upper body vs. lower body fat distribution on diabetes and cardiovascular disease are well recognized. Many studies have shown that an abdominal fat distribution is positively associated with increased risk of cardiometabolic disease and type 2 diabetes (5,24). Waist circumference, which is a surrogate measure of abdominal fat distribution, is independently and positively associated with increased risk of diabetes, dyslipidemia, and hypertension, whereas hip circumference is negatively associated with these same risk factors (30,32). A smaller hip circumference is associated with increased metabolic risk, myocardial infarction, and mortality (29,33,42). Greater fat in the legs measured by DXA was positively associated with hip circumference in the Hoorn study (31) (age 60- to 87-yr-old men and women) and DXA leg fat was found to be protective in relation to lower glucose levels. In the current study, insulin and TG were inversely related to femoral-gluteal SAT but with VAT as a covariate in the model, these effects were no longer statistically significant. The latter suggests that the metabolic protective effects of femoral-gluteal SAT in this cohort are overshadowed by the amount of VAT present as VAT is a stronger determinant of insulin and TG than femoral-gluteal SAT. There may also be a problem of collinearity between VAT and femoral-gluteal SAT measures as their partial correlation was high. A larger sample, or one with more independent variation in these two variables, is required to confirm their independent effects. Moreover, the lack of a stronger influence of femoral-gluteal SAT could in part be influenced by the narrow spread in the CVD risk factor values, values that fell primarily within the range of “normal” combined with few elderly persons.

Mechanisms thought to be involved in the protectiveness of femoral-gluteal fat in relation to insulin resistance and CVD risk include the hypothesis that excess energy intake results in expansion of the adipocytes within the subcutaneous depot. When the functionally normal capacity of these adipocytes has been exceeded (4,26), excess energy is then stored in ectopic fat storage depots, including nonadipose tissues such as liver, muscle, and pancreatic beta-cells, where the latter is accompanied by insulin resistance and dysfunction of the pancreatic cells.

Femoral-gluteal fat may act as a metabolic sink for circulating nonesterified fatty acid (9,32). Isolated adipocytes in the femoral region are relatively insensitive to lipolytic stimuli (27) and the femoral fat depot has a relatively high lipoprotein lipase activity (28). Greater differences in lipolytic sensitivity between femoral-gluteal fat and abdominal subcutaneous fat has been demonstrated in more women than men (18). It is also possible that regional differences exist in the secretion of adipokines between abdominal SAT and femoral-gluteal SAT (32).

IMAT was first described (14) from a single mid-thigh slice where a negative association was found between IMAT and insulin sensitivity in lean and obese glucose-tolerant subjects and obese subjects with diabetes mellitus. Higher IMAT was significantly associated with the metabolic syndrome in normal weight and overweight, but not in obese men and in women (13). In more African-American than Caucasian nondiabetic women, higher IMAT was found to be an independent predictor of lower insulin sensitivity (2), and we recently reported a strong independent association of IMAT with fasting glucose, independent of VAT in healthy adults (41), and with insulin resistance in HIV+ women (1). The exact mechanisms of IMAT effect on glucose and lipid metabolism are unknown. IMAT is in close proximity to skeletal muscle, which could influence skeletal muscle glucose uptake/metabolism. Other suggested possible mechanisms relate to IMAT influence on insulin levels by impairing muscle blood flow (13) or enhancing rates of lipolysis within skeletal muscle (23).

VAT being an independent risk factor for metabolic and cardiovascular disorders (21,22) was supported by VAT's positive association with insulin and TG and inverse association with HDLC.

Race Differences in AT Subcompartments

Differences in the trunk-to-leg-length ratio (8) may contribute in part to the observed racial differences in fat distribution, where Asians had a significantly smaller leg and greater trunk fat mass compared with Caucasians and African-Americans. To our knowledge there has been no previous study including Asians that investigated race differences in subcutaneous fat. Asians were found to have significantly less total SAT and leg SAT compared with Caucasians and African-Americans after adjustment for age, sex, and TAT, whereas trunk SAT mass was not significantly different between race groups.

Study Limitations

All subcompartments of body fat are potentially influenced by dietary intake, levels of physical activity and/or inactivity, and exercise, for which no independent measures were acquired. Diet composition in particular has a direct influence on serum lipids, insulin, and glucose levels; however, cardiovascular risk factor measures were all acquired after a 12-h overnight fast. This study used a convenience sample of urban dwelling healthy adults and cannot be considered representative of the general adult population. The presence of unreported and undiagnosed medical conditions that could affect body composition cannot be ruled out. Race group was determined by self-report, which is reported to be a suitable proxy for genetic ancestry, especially when assessing disease risk (17), but does not take into account degrees of admixture. The Asian sample size was significantly smaller than the Caucasian and African-American

sample, and it is possible, given the significant differences in BMI among the race groups, that the variables in our models do not adequately take into account the differences in BMI.

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Fig. 1. Body regions measured by dual energy X-ray absorptiometry (A) and whole body magnetic resonance imaging (B).

Fig. 2. Adjusted triglycerides (TG) after adjustment for femoral-gluteal inter-muscular adipose tissue (IMAT), total adipose tissue (TAT), age, race, sex and 2-way interactions as a function of femoral-gluteal subcutaneous adipose tissue (SAT; A) and adjusted glucose after adjustment for femoral-gluteal (FG) SAT, TAT, age, race, sex, and 2-way interactions as a function of FG IMAT (B).

Table 1
Descriptive data

	Caucasians	African-Americans	Asians
<i>n</i>			
Men	56	37	11
Women	104	76	35
Age, yr			
Men	44.86±16.93	45.32±18.33	45.09±26.11
Women	43.86±16.43	45.21±16.56	48.71±19.97
Weight, kg			
Men	81.92±12.74*	79.94±11.79*†	72.96±11.58†
Women	65.66±13.81†	77.42±15.58*	54.61±9.07‡
Height, cm			
Men	178.40±7.06*	176.75±7.65*	168.86±10.31†
Women	163.39±7.04*	163.23±7.28*	158.34±6.14†
BMI, kg/m ²			
Men	25.75±3.93	25.57±3.26	25.33±2.26
Women	24.60±5.02†	29.00±5.26*	21.73±2.98‡

All values are means ± SD. BMI, body mass index. Means not bearing the same superscript are significantly different at $P < 0.05$ by Duncan's multiple test.

Table 2
Fat compartments (by DXA) in men and women by race group

	Caucasians		African-Americans		Asians	
	Men	Women	Men	Women	Men	Women
ARFAT	1.97±0.41	1.89±0.44	1.98±0.33	2.08±0.59	1.94±0.19	1.95±0.26
LEFAT	7.99±1.06*	8.39±1.17*	8.56±0.93*	8.13±1.61*	7.30±0.63†	7.30±0.87†
TRFAT	10.40±1.12*†	10.09±1.07†	9.82±0.90†	10.15±1.43†	10.96±0.63*	10.94±0.87*
TOFAT	20.97±4.85	21.63±5.64	20.83±3.84	19.92±10.63	23.64±2.38	22.76±6.73

All values are means ± SD in kg. Fat compartment [ARFAT (arm fat), LEFAT (leg fat), and TRFAT (trunk fat)] is adjusted for age, sex, and total fat (TOFAT). TOFAT is adjusted for age, height, weight, and sex. DXA, dual x-ray absorptiometry. Means not bearing the same superscript are significantly different at $P < 0.05$ by Duncan's multiple test.

Table 3
Adipose tissue depots (by MRI) in men and women by race group

	Caucasians		African-Americans		Asians	
	Men	Women	Men	Women	Men	Women
LLSAT	1.93±0.33*	1.99±0.43*	1.98±0.36*	1.85±0.44*	1.62±0.36†	1.84±0.32*
ULSAT	6.20±0.84*††	6.47±1.13*†	6.69±0.79*	6.52±1.65*†	5.94±0.49††	5.60±0.78†
TRSAT	9.68±0.73	9.61±1.23	9.62±0.69	9.82±1.63	10.23±0.32	9.82±0.93
ARSAT	2.96±0.40*	2.83±0.45*	2.82±0.38*	2.87±0.60*	2.47±0.40†	2.92±0.62*
TOSAT	20.68±1.23*	20.81±0.74*	21.03±1.15*	20.97±0.95*	20.19±0.93†	20.10±0.76†
LLIMAT	0.04±0.03†	0.05±0.03†	0.09±0.04*	0.08±0.05*†	0.07±0.03†	0.05±0.02c
ULIMAT	0.41±0.15†	0.41±0.15†	0.50±0.16*	0.51±0.22*	0.51±0.11*	0.46±0.14*†
TRIMAT	0.37±0.14†	0.40±0.23†	0.43±0.17†	0.43±0.25†	0.59±0.06*	0.41±0.19†
ARIMAT	0.06±0.03†	0.05±0.03†	0.07±0.03*†	0.07±0.04*†	0.08±0.03*	0.07±0.10*†
TOIMAT	0.87±0.29†	0.91±0.37††	1.08±0.35*†	1.09±0.47*†	1.25±0.17*	0.99±0.35††
VAT	1.93±1.15†	1.77±0.61††	1.39±0.98†	1.43±0.73†	2.05±0.87*†	2.39±0.66*
TAT	23.72±3.94*†	23.62±3.34*†	22.66±3.57†	23.08±4.09†	25.07±2.88*	23.98±2.92*†

All values are means ± SD in kg. Adipose tissue depot [LLSAT (lower leg subcutaneous adipose tissue), ULSAT (upper leg subcutaneous adipose tissue), TRSAT (trunk subcutaneous adipose tissue), ARSAT (arm subcutaneous adipose tissue), TOSAT (total subcutaneous adipose tissue), LLIMAT (lower leg intermuscular adipose tissue), ULIMAT (upper leg intermuscular adipose tissue), TRIMAT (trunk intermuscular adipose tissue), ARIMAT (arm intermuscular adipose tissue), TOIMAT (total intermuscular adipose tissue), VAT (visceral adipose tissue)] is adjusted for age, sex, and TAT (total adipose tissue). TAT is adjusted for age, height, weight, and sex. Means not bearing the same superscript are significantly different at $P < 0.05$ by Duncan's multiple test.

Table 4
Independent associations of leg fat (by DXA) with CVD risk factors

	LEFAT	TOFAT	Age	Race	Sex	TOFAT*Race	Intercept	r ²	SE
Glucose	-0.61±0.43	0.48±0.17	0.18±0.03 [‡]	AA: 1.22±2.57 [*] As: 15.94±5.40 Ca: 0	M: 1.69±1.40 W: 0	AA: -0.16 ±0.10 [*] As: -0.83±0.27 Ca: 0	73.22±2.20 [‡]	0.22	8.77
Insulin	-1.06±0.35 [‡]	0.59±0.14 [‡]	-0.03±0.03	AA: 0.71±2.28 As: 3.23±3.67 Ca: 0	M: -1.49±1.08 W: 0	AA: 0.03±0.09 As: -0.16±0.17 Ca: 0	6.16±1.82 [‡]	0.29	4.74
Chol	-1.51±1.89	1.91±0.75	0.85±0.14 [‡]	AA: 13.08±11.18 As: 7.65±24.60 Ca: 0	M: -3.55±6.13 W: 0	AA: -0.76±0.44 As: -0.40±1.20 Ca: 0	132.12±9.58 [‡]	0.24	38.05
TG	-8.42±1.79 [‡]	4.41±0.73 [‡]	0.32±0.14 [*]	AA: -3.17±10.68 As: 14.84±22.30 Ca: 0	M: 7.54±5.83 W: 0	AA: -0.36±0.42 As: -0.56±1.12 Ca: 0	44.07±9.15 [‡]	0.24	36.12
HDL	1.52±0.63 [*]	-0.95±0.25 [‡]	0.19±0.05 [‡]	AA: -1.08±3.73 As: -7.26±8.21 Ca: 0	M: -8.52±2.02 [‡] W: 0	AA: 0.07±0.14 As: 0.13±0.40 Ca: 0	55.04±3.16 [‡]	0.21	12.37

Values are regression coefficients ± SE. TOFAT*Race, interaction variable between total fat and race; Chol, cholesterol; TG, triglyceride; HDL, HDL cholesterol; AA, African-American; As, Asian; Ca, Caucasian; M, man; W, woman; CVD, cardiovascular disease. LEFAT adjusted for TOFAT, age, race, sex, and 2-way interactions

*[‡] Significantly different at: * $P < 0.05$; [‡] $P < 0.01$; [‡] $P < 0.001$.

Table 5
Independent associations of trunk fat (by DXA) with CVD risk factors

	TRFAT	TOFAT	Age	Race	Sex	TOFAT*Race	Intercept	r ²	SE
Glucose	0.58±0.47	-0.03±0.24	0.18±0.03 [‡]	AA: 1.11 ±2.57* As: 15.81 ±5.42 Ca: 0	M: 1.80±1.41 W: 0	AA: -0.17±0.10 [‡] As: -0.81±0.27 Ca: 0	72.99±2.17 [‡]	0.22	8.78
Insulin	0.83±0.38*	-0.21±0.20	-0.02±0.03	AA: 0.33 ±2.31 As: 2.98 ±3.76 Ca: 0	M: -1.19±1.11 W: 0	AA: 0.04±0.09 As: -0.13±0.17 Ca: 0	5.65±1.83 [‡]	0.27	4.81
Chol	1.30±2.03	0.71±1.06	0.85±0.14 [‡]	AA: 12.79 ±11.18 As: 7.39 ±24.68 Ca: 0	M: -3.11±6.15 W: 0	AA: -0.74±0.44 As: ±0.58±1.22 Ca: 0	134.41±9.48 [‡]	0.23	38.07
TG	11.06±1.90 [‡]	-4.17±0.99 [‡]	0.30±0.13*	AA: -4.31 ±10.43 As: 9.10 ±21.87 Ca: 0	M: 4.71±5.47 W: 0	AA: -0.23±0.41 As: ±0.17±1.10 Ca: 0	45.03±8.87 [‡]	0.28	35.33
HDL	-1.94±0.67 [‡]	0.57±0.35*	0.19±0.05 [‡]	AA: -0.89 ±3.70 As: -6.22 ±8.19 Ca: 0	M: -7.99±2.02 [‡] W: 0	AA: 0.04±0.14 As: 0.06±0.40 Ca: 0	54.95±3.10 [‡]	0.22	12.31

Values are regression coefficients ± SE. TRFAT adjusted for TOFAT, age, race, sex, and 2-way interactions

*†‡ Significantly different at: * $P < 0.05$; † $P < 0.01$; ‡ $P < 0.001$.

Table 6
Independent associations of upper leg SAT and upper IMAT (by MRD) with CVD risk factors

	ULSAT	ULIMAT	TAT	Age	Race	Sex	TAT*Race	Intercept	r ²	SE
Glucose	-0.16±0.47	8.66±3.35*	0.20±0.16	0.17±0.03 [‡]	AA: 1.38 ±0.96* As: 22.50 ±8.31 Ca: 0	M: 1.84±1.38 W: 0	AA: -0.15 ±0.11* As: -1.09 ±0.42 Ca: 0	71.53±2.42 [‡]	0.23	9.08
Insulin	-1.07±0.36 [‡]	-1.21±2.88	0.50±0.11 [‡]	-0.04±0.03	AA: 0.13 ±2.30 As: 0.06 ±5.39 Ca: 0	M: -1.09±1.03 W: 0	AA: 0.05 ±0.08 As: 0.02 ±0.26 Ca: 0	6.12±1.92 [‡]	0.31	4.63
Chol	-0.02±1.95	16.12±13.85	1.24±0.56	0.75±0.15 [‡]	AA: 18.08 ±19.31 As: 19.31 ±36.51 Ca: 0	M: -0.87±5.72 W: 0	AA: -0.94 ±0.45 As: -0.97 ±1.81 Ca: 0	127.04±10.04 [‡]	0.23	37.35
TG	-3.88±1.95*	14.82±13.88	2.11±0.66 [‡]	0.29±0.14*	AA: 2.16 ±12.34 As: ±30.68 ±34.17 Ca: 0	M: 13.52±5.74* W: 0	AA: -0.54 ±0.46 As: 2.23 ±1.72 Ca: 0	35.47±10.13 [‡]	0.19	37.26
HDL	0.85±0.72	-0.23±5.10	-0.57±0.24 [‡]	0.21±0.05 [‡]	AA: 1.87 ±4.52 As: 28.23 ±12.60 Ca: 0	M: -9.83±2.10 [‡] W: 0	AA: -0.05 ±0.17 As: -1.58 ±0.63 Ca: 0	55.92±3.70 [‡]	0.19	13.75

Values are regression coefficients ± SE.

*†‡ Significantly different at: * $P < 0.05$; † $P < 0.01$; ‡ $P < 0.001$.

Table 7
Independent associations of VAT (by MRI) with CVD risk factors

	VAT	TRIMAT and TRSAT	TAT	Age	Race	Sex	TAT*Race	Intercept	r ²	SE
Glucose	0.67±0.66	-1.10±0.43	0.25±0.24	0.17±0.04 [‡]	AA: -0.42±2.87 [*] As: 21.93±8.09 Ca: 0	M: 1.81±1.54 W: 0	AA: -0.05 ±0.11 [*] As: -1.06 ±0.41 Ca: 0	72.56±2.69 [‡]	0.22	8.83
Insulin	1.47±0.52 [‡]	0.65±0.35	-0.26±0.20	-0.07±0.04	AA: 0.03±2.29 As: -0.04±5.35 Ca: 0	M: -1.55±1.17 W: 0	AA: 0.07 ±0.08 As: 0.04 ±0.26 Ca: 0	8.28±2.21 [‡]	0.32	4.60
Cholesterol	-0.56±2.84	0.07±1.83	1.48±1.04	0.81±0.16 [‡]	AA: 17.01±12.30 As: 20.75±36.63 Ca: 0	M: 0.40±6.60 W: 0	AA: -0.84 ±0.45 As: -0.99 ±1.82 Ca: 0	124.82±11.50 [‡]	0.22	37.46
HDL	9.49±2.84 [‡]	1.63±1.81	-0.36±1.03	0.17±0.15	AA: -0.63±12.21 As: -31.39±33.85 Ca: 0	M: 6.33±6.54 W: 0	AA: -0.26 ±0.45 As: 2.20 ±1.71 Ca: 0	48.90±11.36 [‡]	0.21	36.89
LDL	-1.99±0.98 [*]	-0.06±0.63	-0.18±0.36	0.27±0.05 [‡]	AA: -1.92±4.28 [*] As: 28.51±11.72 Ca: 0	M: -7.35±2.29 [‡] W: 0	AA: 0.03 ±0.16 [*] As: -1.57 ±0.59 Ca: 0	52.45±3.96 [‡]	0.22	12.77

Values are regression coefficients ± SE. VAT, visceral adipose tissue.

* $P < 0.05$; † $P < 0.01$; ‡ $P < 0.001$.