Race, Visceral Adipose Tissue, Plasma Lipids, and Lipoprotein Lipase Activity in Men and Women

The Health, Risk Factors, Exercise Training, and Genetics (HERITAGE) Family Study


Abstract—Abdominal obesity is associated with numerous metabolic alterations, such as hypertriglyceridemia and low levels of high density lipoprotein (HDL) cholesterol. However, compared with abdominally obese white individuals, abdominally obese black individuals have been characterized by higher plasma HDL cholesterol levels, suggesting that the impact of abdominal fat accumulation on the lipoprotein-lipid profile may differ among ethnic groups. Therefore, we have compared the associations between body fatness, visceral adipose tissue (AT) accumulation, and metabolic risk variables in a sample of 247 white men and 240 white women versus a sample of 93 black men and 143 black women. Although no difference in mean total body fatness was found between the 2 race groups, white men had higher levels of visceral AT than did black men (P<0.001). Despite the fact that black women had a greater body fat content than did white women, black women had levels of visceral AT that were similar to those of white women, suggesting a lower susceptibility to visceral obesity in black women. This lower accumulation of visceral AT in blacks was accompanied by significantly reduced apolipoprotein B concentrations and ratios of total cholesterol to HDL cholesterol as well as higher plasma HDL cholesterol levels (P<0.05) compared with those values in whites. Irrespective of sex, higher postheparin plasma hepatic lipase (HL) and lower lipoprotein lipase (LPL) activities were found in whites, resulting in an HL/LPL ratio that was twice as high in whites as in blacks (P<0.005). Although differences in lipoprotein-lipid levels were noted between whites and blacks, results from multiple regression analyses revealed that after control for morphometric and metabolic variables of the study (body fat mass, visceral AT, LPL, HL, and age), ethnicity had, per se, only a minor contribution to the variance in plasma lipoprotein levels. Thus, our results suggest that the higher plasma HDL cholesterol levels and the generally more cardioprotective plasma lipoprotein profile found in abdominally obese black versus white individuals are explained, at least to a certain extent, by a lower visceral AT deposition and a higher plasma LPL activity in black individuals. (Arterioscler Thromb Vasc Biol. 2000;20:1932-1938.)

Key Words: race • sex • visceral adipose tissue • lipase activities • lipoproteins

Abdominal obesity has been shown to be associated with the features of the insulin resistance–dyslipidemic syndrome, especially among patients characterized by an excess of visceral adipose tissue (AT).1–5 Race differences have been reported in the relationship of body fatness to visceral AT accumulation, with whites being more prone to visceral AT deposition than blacks for any level of total body fat.6–8 We have also previously shown that excess visceral AT accumulation was related to reduced plasma HDL cholesterol levels in obese white subjects.9 Because obese black individuals have been characterized by higher plasma HDL cholesterol levels than obese white individuals,6,7,10 we have tested the hypothesis that the lower accumulation of visceral AT could be responsible for the higher plasma HDL cholesterol levels in blacks than in whites.

In addition, lipase activities measured in postheparin plasma, ie, postheparin lipoprotein lipase (PH-LPL) and postheparin hepatic lipase (PH-HL), have been shown in several studies to be important correlates of plasma HDL cholesterol levels.11–13 However, their contribution to the black-white difference in plasma HDL cholesterol levels is not known. Therefore, we have measured body composition,
visceral AT accumulation, plasma lipoprotein levels, and PH-LPL and PH-HL activities in a sample of 723 subjects (247 white men, 240 white women, 93 black men, and 143 black women). Potential race differences in the interrelationships among these variables were examined.

### Methods

#### Subjects

The Health, Risk Factors, Exercise Training, and Genetics (HERITAGE) Family Study cohort has been previously described. Briefly, the HERITAGE subjects came from families that included the natural mother and father (aged $\leq 65$ years) and at least 3 adult offspring (aged $\geq 17$ years). The present study describes the results of baseline data from 723 subjects studied. Subjects were healthy and sedentary and met a number of inclusion and exclusion criteria. The study protocol had been previously approved by the Institutional Review Board at each of the 4 clinical centers. Informed consent was obtained from each subject.

#### Anthropometric and Body Composition Measurements

Body weight, height, and waist and hip circumferences were measured according to standardized procedures, and the waist-to-hip ratio was calculated. Body density was measured by the hydrostatic weighing technique. The mean of the highest 3 (of 10) measurements was used in the calculation of percent body fat from body density by using the equation of Siri. Fat mass was obtained by multiplying body weight by percent body fat. These measurements have been shown to be highly reproducible, with no difference between clinical centers or drift over time.

#### Computed Tomography

Visceral AT accumulation was assessed by computed tomography with the use of previously described procedures. Briefly, each subject was examined in the supine position with both arms stretched above the head. The scan was performed at the abdominal level (between L4 and L5 vertebrae) by use of an abdominal scout radiograph to standardize the position of the scan to the nearest millimeter. Total AT area was calculated by delineating the abdominal scan with a graph pen and then computing the AT surface with an attenuation range of $-190$ to $-30$ Hounsfield units. The abdominal visceral AT area was measured by drawing a line within the muscle wall surrounding the abdominal cavity. The abdominal subcutaneous AT area was calculated by subtracting the visceral AT area from the total abdominal AT area.

#### Plasma Lipid, Lipoprotein, and Apolipoprotein Measurements

Blood sampling was achieved in subjects after a 12-hour fast. Cholesterol and triglyceride (TG) levels were determined in plasma and in lipoprotein fractions by enzymatic methods with a Technicon RA-500 analyzer (Bayer Corp Inc). Plasma VLDL (density $<1.006$ g/mL) was isolated by ultracentrifugation, and the HDL fraction was obtained after precipitation of LDL in the infranatant (density $>1.006$ g/mL) with heparin and MnCl$_2$. The cholesterol and TG contents of the infranatant fraction were measured before and after the precipitation step. ApoB concentration was measured in plasma by the rocket immunoelectrophoretic method of Laurell, as previously described. The lyophilized serum standards for apolipoprotein measurements were prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control. The cholesterol content of HDL$_2$ and HDL$_3$ subfractions was also determined after further precipitation of HDL$_2$ with dextran sulfate. Reproducibility of all lipid-lipoprotein measurements has been examined and found to be excellent.

#### Postheparin Plasma Lipase Activities

LPL and HL activities were also measured on one occasion in subjects after a 12-hour overnight fast, 10 minutes after an intravenous injection of heparin (60 IU/kg body wt). The postheparin plasma lipase activities (PHLAs) were measured by using a modification of the method of Nilsson-Ehle and Ekman, as previously described. The 2 lipolytic enzyme activities were expressed as nanomoles of oleic acid released per milliliter of plasma per minute. These measures have also been found to be highly reproducible.

#### Statistical Analysis

Values are expressed as mean±SD. Pearson product-moment correlation coefficients were used to quantify the relationships among variables. General linear model analyses were used to test the differences between men and women as well as between sex and race. Multiple regression analyses were also performed to estimate the independent contribution of age, sex, race, total body fat mass, visceral AT, and PH-LPL and PH-HL activities to the variations in fasting plasma TG, HDL cholesterol, and apo B levels and in the ratio of total cholesterol to HDL cholesterol.

### Results

#### Effect of Sex

Physical characteristics of men and women are presented in Table 1. In both ethnic groups, women had a greater percentage of body fat than did men. Regional body fat deposition also differed between the sexes. In whites, women displayed...
lower waist circumference values and levels of visceral AT compared with the values in men, but they were characterized by a greater accumulation of subcutaneous AT compared with the accumulation in men. No sex difference was found in waist girth or in visceral AT accumulation in blacks. However, compared with black men, black women were characterized by increased subcutaneous AT levels.

These differences in adiposity and in AT distribution were accompanied by sex differences in the lipoprotein profile (Table 2). Compared with white women, white men had a less favorable metabolic risk profile, as revealed by increased fasting plasma TG and apoB levels as well as by a higher ratio of total cholesterol to HDL cholesterol. In addition, compared with white women, black men showed increased TG and apoB concentrations as well as a higher ratio of total cholesterol to HDL cholesterol. Compared with black men, black women also showed lower HDL cholesterol concentrations. Furthermore, compared with white women, black women showed increased HDL and lower cholesterol, TG, and apoB levels. Compared with black men, white men showed reduced PH-LPL and higher PH-HL activities, whereas compared with white women, black women were characterized by higher PH-LPL and lower PH-HL activities. These differences resulted in a higher HL-to-LPL ratio in whites compared with blacks.

Figure 1 illustrates the relationships of body fat mass to abdominal visceral and subcutaneous AT accumulation in men and women of both ethnic origins. Irrespective of race, body fat mass was positively correlated with visceral and subcutaneous AT accumulation. However, although the relationship of subcutaneous AT to total body fat mass was similar across race groups, there were differences in the relationships of visceral AT to body fat mass. Indeed, black men and black women had, for a given amount of total body fat mass, less visceral AT than did whites.

The detrimental effect of adiposity on plasma lipoprotein levels is shown in Figure 2. Increased adiposity, expressed as either total body fat or visceral AT accumulation, was associated with a decrease in HDL cholesterol concentrations in all subgroups of subjects. Furthermore, in the whole cohort, visceral AT also showed significant positive correlations with TG ($r=0.52$, $P<0.0001$) and apoB ($r=0.55$, $P<0.0001$) levels as well as with the ratio of total cholesterol to HDL cholesterol ($r=0.56$, $P<0.0001$). These relationships were also noted with total body fat mass, although associations were of lower magnitude ($r=0.36$) than with visceral AT accumulation.

### Effect of Race

When race-related differences in body fatness and AT distribution in men were examined (Table 1), we found that compared with black men, white men were characterized by an increased visceral AT deposition, despite the fact that both groups had similar body mass index and body fat mass values. In women, race was mostly associated with differences in overall adiposity indices: compared with white women, black women were characterized by increased body weight, body mass index, percentage of body fat, and fat mass. This elevated adiposity in black women also resulted in an increased waist girth and higher levels of subcutaneous AT compared with the values in white women. Thus, black women were more obese than white women. However, the 2 groups of women had similar levels of visceral AT despite the higher overall adiposity of black women, suggesting that white women were more prone to visceral AT deposition than were black women.

When the plasma lipoprotein profile was compared between the 2 ethnic groups (Table 2), we found that black men and women were generally characterized by a more favorable profile than were white men and women. Indeed, compared with black men, white men showed increased TG and apoB concentrations as well as a higher ratio of total cholesterol to HDL cholesterol. Compared with black men, white men also showed lower HDL cholesterol concentrations. Furthermore, compared with white women, black women had lower cholesterol, TG, and apoB levels. Compared with black men, white men showed reduced PH-LPL and higher PH-HL activities, whereas compared with white women, black women were characterized by higher PH-LPL and lower PH-HL activities. These differences resulted in a higher HL-to-LPL ratio in whites compared with blacks.

### TABLE 2. Metabolic Characteristics of the Subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Men</th>
<th>Women</th>
<th>Race Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Values</td>
<td>SD</td>
<td>Values</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>247</td>
<td>240</td>
<td>93</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.54±1.00</td>
<td>4.42±0.89</td>
<td>NS</td>
</tr>
<tr>
<td>TGs, mmol/L</td>
<td>1.54±0.89</td>
<td>1.19±0.59</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.06±0.85</td>
<td>2.92±0.77</td>
<td>0.0525</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>0.93±0.20</td>
<td>1.14±0.26</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL₃ cholesterol, mmol/L</td>
<td>0.27±0.12</td>
<td>0.43±0.19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL₄ cholesterol, mmol/L</td>
<td>0.67±0.12</td>
<td>0.71±0.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Apo B, g/L</td>
<td>0.90±0.25</td>
<td>0.81±0.22</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total/HDL cholesterol</td>
<td>5.11±1.62</td>
<td>4.04±1.14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL₃ cholesterol/HDL₄ cholesterol</td>
<td>0.40±0.16</td>
<td>0.62±0.29</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PH-LPL, nmol · mL⁻¹ · min⁻¹</td>
<td>49.6±26.6</td>
<td>63.1±32.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PH-HL, nmol · mL⁻¹ · min⁻¹</td>
<td>244.0±62.4</td>
<td>174.1±62.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PH-HL/PH-LPL</td>
<td>8.55±12.96</td>
<td>4.45±6.75</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are mean±SD.
We have also examined the potential associations between visceral AT accumulation and PH-LPL as well as PH-HL activity (Figure 3). In women, we found that visceral AT accumulation was positively associated with PH-HL activity regardless of ethnicity. As opposed to what was found in women, visceral AT accumulation was not correlated with PH-HL in either black or white men. In all groups, visceral AT was not correlated with PH-LPL activity.

Finally, we have also attempted to quantify the independent contributions of age, sex, race, body fat mass, visceral AT accumulation, and PHLA to the variance of TG, apoB, HDL cholesterol, and the ratio of total cholesterol to HDL cholesterol (Table 3). PH-LPL activity was the best predictor of fasting HDL cholesterol concentrations. On the other hand, visceral AT accumulation was by far the best correlate of the variations in TG, apoB, and the ratio of total cholesterol to HDL cholesterol. The important finding of these analyses was that after control for body fatness, visceral AT accumulation, and PH-LPL activity, ethnicity, per se, had a trivial contribution to the variance of metabolic risk variables. Indeed, after control for the morphometric and metabolic variables examined in the present study, race explained only 1.6% and 0.5% of the variance in fasting plasma TG and apoB concentrations, respectively.

Discussion

Effect of Sex

Sex differences in body fatness and in regional AT distribution are well documented. Compared with men, women are generally characterized by a greater body fat content. Furthermore, women also show a preferential accumulation of AT in the gluteofemoral region, whereas men are more prone to abdominal fat deposition, particularly in the abdominal cavity, a condition that has been described as visceral obesity.2,3,9,30–32 In the present study, compared with men, women were characterized by an increased body fat content. White men also showed a higher visceral AT accumulation than did white women. Despite the fact that black women had more total body fat than did their male counterparts, no sex difference in the absolute amount of visceral AT was found in this ethnic group, suggesting, as in whites, that black women were less prone to visceral AT deposition than were men. These observations confirm our previous results in white subjects.32

As expected, compared with men, women showed a more favorable metabolic risk profile. Previous studies had reported sex differences in fasting plasma lipoprotein-lipid concentrations, including lower TG and higher HDL cholesterol levels in women than in men.33,34 In the present study, compared with white women, white men were characterized by higher plasma TG and apoB concentrations as well as lower HDL cholesterol levels. These differences were also noted in blacks. However, results of our multivariate analyses revealed that with the exception of plasma HDL cholesterol levels, which were characterized by a significant sex effect,
differences in the plasma lipid profile between men and women were largely explained by differences in visceral AT and PH-LPL activity. In addition to the variation in lipoprotein-lipid levels between men and women, a significant sex difference in PHLA was also found, a finding that is concordant with several,\textsuperscript{35–38} but not all,\textsuperscript{39,40} previous reports.

In the present study, lower PH-HL activity was found in women compared with men. However, higher PH-LPL activity in women was noted only in whites.

**Effect of Race**

Race differences have been reported in body composition and AT distribution. At any level of total body fat, compared with black subjects, white subjects have been shown to be characterized by a greater visceral AT accumulation.\textsuperscript{6–8} Results of regression analyses conducted in the present study are concordant with these earlier findings. For any level of total body fat, compared with blacks, whites were characterized by a higher accumulation of visceral AT, supporting the notion that whites are more prone to visceral obesity than are blacks. In contrast, we found no race difference in the relationship of subcutaneous fat to total body fat mass. Thus, the present study supports the view that the cross-sectional area of abdominal subcutaneous fat measured by computed tomography at L4-L5 is a good predictor of total body fat content\textsuperscript{32} and that there does not appear to be major ethnic differences in such a relationship. This issue will have to be examined in other ethnic groups, such as Hispanic and Asian populations.

The main objective of the present study was to verify whether differences in body composition and AT distribution as well as in the activity of enzymes relevant to lipoprotein metabolism could explain the generally more favorable lipoprotein profile found in black than in white individuals. Indeed, compared with white individuals, black individuals have been characterized by lower fasting TG as well as higher HDL cholesterol concentrations.\textsuperscript{6,7,10} Such differences were also found in the present study, inasmuch as white subjects had higher fasting TG and apoB levels than did black subjects. This race-related difference was observed along with the expected sex difference in plasma lipoprotein levels, with women having a more favorable profile than men.

In both sexes, blacks showed a significantly higher PH-LPL activity than did whites. Compared with white individuals, black individuals also showed reduced PH-HL activity, and such ethnic differences were found in both sexes, a finding that is concordant with previous observations.\textsuperscript{41} Such a difference in PHLA is of importance because it may contribute to the more favorable plasma lipoprotein-lipid profile of black individuals compared with white individuals. Thus, the present study found a stepwise increase in TG and apoB levels as well as in the ratio of total cholesterol to HDL.
cholesterol as follows for the various groups: black women (lowest values), white women, black men, and then white men (highest values); this stepwise increase appeared to parallel the gradient in visceral AT and the HL-to-LPL ratio among these 4 groups. Results from our multivariate analyses also revealed that visceral AT was the critical correlate of plasma TG, apoB, and the ratio of total cholesterol to HDL cholesterol in the present study. Thus, our results suggest that the more favorable metabolic risk profile found in blacks than in whites could be due to the fact that white subjects are more prone to visceral AT accumulation than are black subjects. Furthermore, the higher plasma HDL cholesterol levels found in blacks than in whites appear to be explained, at least to a significant extent, by the higher PH-LPL activity in blacks. This effect of ethnicity on PH-LPL activity is concordant with recent findings.42

In summary, results of the present study indicate that the more favorable lipoprotein profile generally found in abdominally obese black individuals could be explained, at least to a significant extent, by their lower visceral AT accumulation and by their higher PH-LPL activity compared with those values in abdominally obese white individuals.

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