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Plasma lipid concentrations in nondiabetic African American adults: associations with insulin resistance and the metabolic syndrome

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Abstract

Despite higher rates of cardiovascular disease, African Americans have a more favorable lipid profile. The purpose of the study was to examine the association between plasma lipid concentrations and insulin resistance in African Americans and to determine if insulin resistance is present at a lower triglyceride (TG) threshold than is used for metabolic syndrome criteria. Data were examined on 185 nondiabetic African American men (n = 61) and women (n = 124), mean age, 39.8 years. Measurements included blood pressure, anthropometrics, oral glucose tolerance test, and insulin sensitivity (M) by insulin clamp. The relationship between lipids and insulin sensitivity was analyzed by correlation analysis and by comparing TG levels among tertiles of M. Despite relatively low mean (± SD) TG level (87.8 ± 55.2 mg/dL), there were statistically significant correlations of M with TG ($r = -0.23$, $P < .002$), high-density lipoprotein cholesterol (HDL-C; $r = 0.19$, $P < .01$), and TG/HDL-C ratio ($r = -0.23$, $P < .002$). The correlations were strongest in men. Subjects with TG in an intermediate range (110-149 mg/dL) had insulin resistance equivalent to that of the high-TG group (≥150 mg/dL). In African Americans, TG levels below the current metabolic syndrome threshold criterion are associated with insulin resistance.

1. Introduction

Insulin resistance, defined as impaired insulin-mediated glucose uptake, has been identified as a pathogenic factor leading to cardiovascular disease (CVD) and diabetes mellitus (DM) [1-3]. Compared with white populations, African Americans have greater insulin resistance [4-6], which could contribute to a higher prevalence of CVD and DM in this group [7]. A leading theory to explain the mechanism underlying the detrimental effect of insulin resistance on cardiovascular injury is the association of insulin resistance with atherosclerotic dyslipidemia [8]. Insulin resistance, or impaired insulin sensitivity, is difficult to quantify clinically, and the concept of the metabolic syndrome has developed as a strategy to identify individuals with the multiple CVD risk factors that co-segregate with insulin resistance. Despite greater insulin resistance, African Americans have more favorable lipid profiles than whites, including lower triglyceride (TG) and higher high-density lipoprotein cholesterol (HDL-C) concentrations [9-11]. Prior studies in African Americans yielded conflicting results regarding the association of insulin resistance with elevated TG and decreased HDL concentrations [9,10,12-14]. Some reports describe a significant association between measures of insulin resistance and plasma lipid concentrations in African Americans despite more favorable lipid profiles [10]. Others have not detected a relationship of insulin resistance with TG [13], possibly because of higher levels of lipoprotein lipase among African Americans [9].

In an attempt to identify individuals at risk for CVD and DM because of underlying insulin resistance, clinical criteria have been developed for a condition termed the metabolic syndrome, which is a clustering of cardiovascular risk factors linked with underlying insulin resistance [15,16]. According to these definitions, the clinical diagnosis of the metabolic syndrome requires the presence of several cardiovascular risk factors within an individual,

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although no one specific risk factor is required. Although varying definitions of the metabolic syndrome exist, the risk parameters that are consistently included are high TG, low HDL, central obesity, high blood pressure (BP), and elevated plasma glucose [15,17,18]. Epidemiologic studies that apply these clinical criteria to population data have reported a lower prevalence of metabolic syndrome in African Americans compared with whites despite greater adiposity among African Americans [19,20]. Because of lower TG concentrations among African Americans compared with other race groups, African Americans may less frequently meet the metabolic syndrome TG criterion (TG $\geq$150 mg/dL) [20]. However, the same relationship between insulin resistance and TG may exist in African Americans but at a lower TG threshold. The purpose of this study was to determine if there is a significant relationship between plasma lipid concentrations and insulin resistance in African Americans and to examine the use of different TG threshold levels for the detection of underlying insulin resistance in this racial population.

2. Methods

2.1. Subjects

The sample for this study was drawn from a cohort enrolled in a previous study of BP, insulin resistance, and cardiovascular risk. The subjects were all self-identified African Americans recruited from urban Philadelphia and were tested between January 2001 and April 2006. Caribbean African Americans were not enrolled. The European admixture of this African American cohort has been previously analyzed and found to be 12.7% to 13.6% [21]. Participant age at the time of examination was 39.8 $\pm$ 3.9 years (mean $\pm$ SD), with an age range of 28 to 51 years. Individuals with known or newly identified DM were excluded from this analysis. At the time of enrollment, all subjects provided written informed consent for a protocol on a consent form approved by the Institutional Review Board of the Thomas Jefferson University. All women were premenopausal at enrollment, and all procedures were conducted in the prefollicular phase of their menstrual cycles.

2.2. Procedures

Enrollment assessment consisted of anthropometric measurements (height, weight, skinfold thickness), BP measurement, fasting blood sample, and an oral glucose tolerance test (OGTT) after a 12-hour fast. Anthropometric measurements were used to calculate body mass index (BMI, kg/m^2), percent body fat, and fat-free mass [22]. Blood pressure was measured by using a mercury column sphygmomanometer with the participant in a seated position after 10 minutes of rest. An average of 2 measurements for systolic BP (SBP) and diastolic BP (DBP) was determined. For the OGTT, an oral 75-g glucose solution (Glucola, Ames Laboratories, Elkhart, IN) was ingested. Blood samples were drawn before glucose load (fasting) and at 30, 60, and 120 minutes after glucose load. All samples were assayed for plasma insulin and glucose concentrations after storage at -80°C.

The euglycemic-hyperinsulinemic clamp procedure was administered to assess insulin-stimulated glucose utilization [23,24]. For the euglycemic clamp procedure, each participant returned to the clinic at 8 AM after a 12-hour fast. The euglycemic clamp procedure was conducted according to methods previously described [25]. In brief, 2 peripheral venous catheters were placed after the subject had rested for at least 20 minutes. Three samples were withdrawn to determine fasting plasma glucose and insulin concentration. Euglycemic hyperinsulinemia was induced with a priming dose and infusion rate of insulin according to the method of Rizza et al [24]. The infused insulin was administered at 1000 mU/mL in normal saline (Novolin R, Eli Lilly, Indianapolis, IN). By this method, euglycemic hyperinsulinemia was maintained at 80 to 120 μU/mL above fasting insulin concentration for 120 minutes. Glucose was infused as 20% dextrose (Abbott Laboratories, Abbott Park, IL) to maintain euglycemia. The glucose infusion rate was adjusted as a function of the plasma glucose concentrations sampled every 10 minutes, according to the negative feedback equation of DeFronzo et al [23]. Insulin-stimulated glucose metabolism, designated as *M* (in milligrams per kilogram per minute), was quantified as the mean glucose infusion rate required to maintain euglycemia during the final 60 minutes (clamp period) of the hyperinsulinemic procedure.

The fasting blood sample from the enrollment assessment was analyzed for serum lipid concentrations (total cholesterol, HDL-C, and TGs) by a lipid research laboratory using standard enzymatic methods and an automated analyzer (Hitachi 704, Boehringer-Mannheim Diagnostics, Indianapolis, IN). HDL was isolated by using a method previously described [26]. The Friedewald equation was used to calculate low-density lipoprotein (LDL) cholesterol [27]. Coefficients of variation for inter- and intra-assay variability for the lipid assays and the above glucose and insulin assays were less than 5%.

2.3. Data analysis

The Adult Treatment Panel III guidelines were used to define metabolic syndrome [28], with the exception that BMI of 30 kg/m^2 or greater was used in place of waist circumference (>102 cm in men, >88 cm in women) [29]. Subjects were considered to have the metabolic syndrome if they met 3 or more of the following criteria: TG, 150 mg/dL or greater; HDL, less than 50 mg/dL for women and less than 40 mg/dL for men; fasting glucose, 100 mg/dL or greater; BP, 130/85 mm Hg or greater; BMI, 30 kg/m^2 or greater. For a more accurate assessment of elevated fasting glucose, subjects met this criterion if they had fasting glucose concentrations of 100 mg/dL or greater both on the morning of the OGTT and on the morning of the euglycemic clamp.

Table 1
Participant characteristics

	Men (n = 61)	Women (n = 124)	Total (N = 185)	P*
Age (y)	39.7 ± 3.9	39.8 ± 3.6	39.8 ± 3.7	.86
Weight (kg)	93.2 ± 23.1	90.6 ± 22.2	91.5 ± 22.5	.47
BMI (kg/m^2)	29.7 ± 6.8[a]	33.4 ± 8.0	32.2 ± 7.8	.002
% Body fat	25.4 ± 7.4[b]	38.4 ± 4.4	34.1 ± 8.3	<.001
SBP (mm Hg)	128.9 ± 15.2	124.0 ± 19.4	125.6 ±18.3	.09
DBP (mm HG)	76.1 ± 11.9	72.6 ± 12.1	73.8 ± 12.1	.07
Fasting insulin (μU/mL)	9.5 ± 8.4	10.9 ± 9.8	10.5 ± 9.4	.02
Fasting glucose (mg/dL)	101.4 ± 9.6	97.9 ± 10.6	99.1 ± 10.4	.03
2-h glucose (mg/dL)	122.5 ± 39.2	128.1 ± 33.3	126.3 ± 34.4	.31
Total cholesterol (mg/dL)	182.0 ± 38.8	184.0 ± 35.4	183.4 ± 36.4	.72
LDL (mg/dL)	117.5 ± 39.8	118.6 ± 32.4	118.2 ± 34.9	.85
HDL-C (mg/dL)	49.4 ± 20.4	49.7 ± 13.6	49.6 ± 16.1	.95
TG (mg/dL)	95.5 ± 72.2	84.0 ± 44.5	87.8 ± 55.2	.25
TG/HDL-C	2.34 ± 2.65	1.86 ± 1.29	2.02 ± 1.86	.19
Metabolic syndrome (%)	18	21	19	

Values are expressed as mean ± SD unless otherwise indicated.
* P values for t test comparing means of men and women.

Mean ± SD of participant characteristics were calculated for men, women, and the total sample. The t test was used to determine whether significant differences existed in mean values between men and women. The Pearson r was used to examine correlations of plasma lipid concentrations and insulin sensitivity (M) with other continuous variables. To further examine the associations with insulin sensitivity, the sample was stratified into tertiles of insulin sensitivity based on total M, with the lower third being most insulin resistant and the upper third being most insulin sensitive. Differences among tertiles were analyzed by 1-way analysis of variance (ANOVA). In addition, we stratified the sample by 3 categories of plasma TG concentration to compare parameters and prevalence of metabolic syndrome in different TG ranges. The mean TG concentration in the most insulin resistant tertile was designated as the upper limit of normal. Thus, the sample was stratified by TG concentrations as normal (<110 mg/dL), intermediate (110-149 mg/dL), and high (≥150 mg/dL). To examine the possibility of using TG of 110 mg/dL or higher as a cut point for risk in African Americans, 1-way ANOVA was used to compare differences in means for continuous variables among TG stratifications. The χ^2 test was used to compare rates of the metabolic syndrome between insulin sensitivity tertiles and in the total population with different TG cut point applications. To correct for simultaneous multiple comparisons, but which were often correlated, we considered $P \leq .01$ to be statistically significant. However, all observed P values are provided. Statistical analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

3. Results

Complete data for this study were available on 185 nondiabetic African American subjects, including 61 men and 124 women. The age of this sample was 39.8 ± 3.7 years (mean ± SD; range, 28−51 years). Table 1 provides the anthropometric, BP, and metabolic characteristics. In this sample, 55% were obese and 38% had high BP. Men and women had comparable mean characteristics, with the exception that, compared with men, women had significantly higher mean BMI and percent body fat. Despite higher BMI, women had TG and HDL concentrations comparable with men. Insulin sensitivity (M) was lower in women compared with men, but the difference was not statistically significant (mean M, 5.46 ± 2.82 in women vs 6.26 ± 2.91 in men; $P = .074$). Overall, 19% of this African American sample met the current criteria for the metabolic syndrome. However, all subjects with type 2 diabetes mellitus, most of whom were previously undetected and found to be diabetic on oral glucose tolerance testing, were excluded from this analysis.

Table 2 provides the correlation coefficients for plasma lipid concentrations with BMI, BP, and metabolic variables. There were significant correlations of both TG and HDL-C with other components of the metabolic syndrome. There

Table 2
Correlations of plasma lipid concentrations with variables

	BMI		SBP		DBP		Fasting glucose		Fasting insulin		Total M	
	r	P	r	P	r	P	r	P	r	P	r	P
Total cholesterol	0.002	.98	−0.08	.28	−0.01	.94	0.07	.36	−0.04	.56	−0.08	.29
LDL	0.03	.69	−0.05	.54	0.04	.63	0.06	.36	−0.02	.81	−0.12	.10
HDL-C	−0.17	.02	−0.15	.05	−0.17	.02	0.15	.04	−0.21	.004	0.19	.01
TG	0.10	.19	0.18	.02	0.19	.01	0.24	<.001	0.17	.02	−0.23	.002
TG/HDL-C	0.11	.13	0.19	.01	0.21	.004	0.23	<.001	0.23	.02	−0.23	.002

Table 3
Characteristics across tertiles of insulin sensitivity (*M*)

	Insulin resistant (lowest *M*), n = 60	Mid sensitivity (mid *M*), n = 63	Insulin sensitive (highest *M*), n = 62	*P* (1-way ANOVA)
Age (y)	39.9 ± 3.1	39.8 ± 4.05	39.6 ± 3.8	.89
% Body fat	38.3 ± 5.6	35.3 ± 6.4	28.9 ± 9.3	<.001
BMI (kg/m^2)	37.6 ± 8.1	31.5 ± 6.2	27.6 ± 5.5	<.001
SBP (mm Hg)	130.8 ± 19.0	123.8 ± 16.7	122.4 ± 18.2	.02
DBP (mm HG)	76.9 ± 11.7	73.6 ± 10.9	70.9 ± 13.1	.02
Fasting insulin (μU/mL)	15.4 ± 12.2	9.3 ± 7.7	6.9 ± 4.8	<.001
Fasting glucose (mg/dL)	100.3 ± 12.3	98.9 ± 9.6	97.9 ± 9.1	.44
2-h glucose (mg/dL)	140.7 ± 37.7	128.3 ± 30.3	110.3 ± 31.5	<.001
Total cholesterol (mg/dL)	185.9 ± 34.4	188.8 ± 38.7	175.4 ± 35.1	.09
LDL (mg/dL)	122.5 ± 33.9	125.1 ± 36.8	107.1 ± 31.6	.01
HDL-C (mg/dL)	43.6 ± 9.6	52.4 ± 18.2	52.5 ± 17.4	.002
TG (mg/dL)	108.5 ± 68.3	79.0 ± 39.7	76.6 ± 49.6	.002
TG/HDL-C	2.81 ± 2.63	1.61 ± 0.87	1.67 ± 1.42	<.001
M (mg kg^{-1} min $^{-1}$)	2.89 ± 0.61	5.26 ± 0.82	8.93 ± 2.27	<.001
I (clamp) (μU/mL)	92.5 ± 29.7	77.7 ± 23.6	67.4 ± 24.3	<.001
Metabolic syndrome, % meeting criteria	35	17	6	<.001

Values are expressed as mean ± SD unless otherwise indicated. *I* (clamp) indicates mean insulin concentration collected during the hyperinsulinemic clamp procedure.

were statistically significant correlations of HDL-C with fasting insulin and *M*. In addition, there were significant correlations of TG with DBP, fasting glucose, and *M*. Neither total cholesterol nor LDL had significant correlations with any of the above variables. Although there were no significant differences between men and women in mean values for TG, HDL-C, and *M*, gender differences were detected when the correlations of TG level with *M* were examined for men and women separately. Among men, the correlation coefficient for TG with *M* increased to $r = 0.38$ ($P = .003$). Among the women, the correlation coefficient for TG with *M* decreased to $r = 0.15$ ($P = .10$), indicating that when all diabetic subjects were excluded, the significant association of TG with *M* was largely driven by the men.

Because insulin resistance is the core abnormality of the metabolic syndrome, the relationships of insulin sensitivity (*M*) with other components of the metabolic syndrome were examined. There were significant correlations of *M* with fasting insulin concentration ($r = -0.30$, $P < .0001$), SBP ($r = -0.20$, $P = .01$), and DBP ($r = -0.20$, $P = .01$). There were also significant correlations of *M* with the anthropometric measures of BMI ($r = -0.53$, $P < .001$) and percent body fat ($r = -0.48$, $P < .001$).

To further examine the relationship of plasma lipid concentrations with insulin sensitivity quantified by the insulin clamp procedure, we divided the sample into tertiles of insulin sensitivity based on *M* value and compared the relevant variables. These data are provided in Table 3. There were no significant differences between the *M* tertile groups in LDL, total cholesterol, fasting glucose, or age. There were significant differences in BMI, fasting insulin, 2-hour glucose, HDL-C, TG, and TG-HDL-C across tertiles. The insulin-resistant (lowest *M*) tertile had the highest percent of subjects who met the criteria for the metabolic syndrome

Table 4
Stratification by TG concentration

	Low TG (<110 mg/dL), n = 143	Intermediate TG (110-149 mg/dL), n = 23	High TG (≥150 mg/dL), n = 19	*P* (1-way ANOVA)
Total *M*	6.09 ± 2.97	4.40 ± 2.28	4.62 ± 1.83	.01
Age (y)	39.9 ± 3.6	38.8 ± 3.0	40.4 ± 4.7	.31
Weight (kg)	89.7 ± 23.0	98.3 ± 21.3	96.3 ± 18.1	.14
% Body fat	33.8 ± 8.6	34.7 ± 7.9	35.3 ± 5.6	.73
BMI (kg/m^2)	28.3 ± 12.8	34.2 ± 6.9	33.6 ± 6. 9	.24
SBP (mm Hg)	124.3 ± 16.5	122.7 ± 14.4	139.4 ± 30.0	.002
DBP (mm HG)	73.1 ± 11.8	71.2 ± 9.5	81.8 ± 14.4	.01
Fasting insulin (μU/mL)	9.2 ± 7.7	11.8 ± 6.6	17.9 ± 17.6	<.001
Fasting glucose (mg/dL)	97.7 ± 9.4	101.9 ± 10.8	105.7 ± 14.1	.002
2-h glucose (mg/dL)	124.4 ± 34.9	129.0 ± 40.5	137.1 ± 31.3	.32
Total cholesterol (mg/dL)	179.1 ± 33.2	194.3 ± 37.2	202.3 ± 50.1	.01
LDL (mg/dL)	116.6 ± 31. 9	122.2 ± 38.6	125.7 ± 50.1	.48
HDL-C (mg/dL)	51.3 ± 16.5	45.4 ± 10.0	41.4 ± 15.7	.02
TG (mg/dL)	66.1 ± 19.4	124.6 ± 12.7	205.9 ± 88.6	<.001
TG/HDL-C	1.40 ± 0.594	2.84 ± 0.591	5.68 ± 3.75	<.001

Values are expressed as mean ± SD.

Table 5
Metabolic syndrome rate with TG criteria greater than 150 and greater than 110 mg/dL

	TG >150 mg/dL	TG >110 mg/dL
Total population (%)	19	25
Insulin sensitivity tertiles		
Insulin resistant (%)	35	52
Intermediate (%)	17	21
Insulin sensitive (%)	6	6

(35%), whereas only 5% of subjects within the insulin-sensitive (highest *M*) tertile met criteria. The mean TG (106.1 ± 68.6 mg/dL) in the most insulin resistant tertile was substantially lower than the threshold metabolic syndrome criterion for hypertriglyceridemia (>150 mg/dL). Across all tertiles of insulin sensitivity, mean TG/HDL-C ratio was less than 3, whereas a ratio greater than 3 is considered to be associated with insulin resistance [14].

We then examined the TG threshold for associations with components of the metabolic syndrome. Cases were classified according to TG concentration. A TG concentration that was below the mean value in the most insulin resistant tertile was classified as normal TG (TG < 110 mg/dL); TG of 150 mg/dL or greater was classified as high TG; and TG value falling between 110 and 149 mg/dL was classified as intermediate TG. Table 4 provides the mean values for the anthropometric, BP, and metabolic variables in each TG group. ANOVA on variables across TG groups showed significant differences in fasting insulin, fasting glucose, SBP, DBP, and total cholesterol. There was also a significant difference in insulin sensitivity (*M*) among TG groups. However, as can be seen in Table 4, the intermediate- and high-TG groups had nearly identical mean values for both *M* and HDL-C. There were no significant differences among TG groups in age, BMI, percent body fat, or LDL.

The distribution of cases that met the criteria for metabolic syndrome with the 2 different criteria for elevated TG is provided in Table 5. Of the total sample, 23% had TG of 110 mg/dL or greater When the lower TG concentration of 110 mg/dL or greater was applied as the TG criterion for the metabolic syndrome, the rate of metabolic syndrome increased from 19% to 25% in the total sample. The increase in percent of cases of metabolic syndrome occurred in the most insulin resistant tertile with an increase from 35% to 52%. The mid tertile and high tertiles of insulin sensitivity did not show much change in rates of metabolic syndrome after applying the lower TG criterion.

4. Discussion

In this study of nondiabetic, primarily third- and fourth−decade African American adults, plasma TG concentrations were lower and HDL-C concentrations were higher than lipid concentrations described in white populations. These results are comparable to previous reports [19,30,31]. Although the lipid concentrations in this African American sample were more favorable, there were significant correlations of TG, HDL-C, and TG/HDL-C ratio with insulin resistance measured by the insulin clamp procedure. Despite the association between insulin resistance and TG, only 10% of the sample had elevated TGs according to the Adult Treatment Panel III criteria for metabolic syndrome. Subjects with TG concentrations in an intermediate range of 110 to 149 mg/dL had measures of insulin resistance comparable with those of subjects with elevated TG (>150 mg/dL) and were more insulin resistant than those with TG less than 110 mg/dL. A TG threshold of 110 mg/dL or greater increased the detection of the metabolic syndrome in the most insulin resistant *M* tertile, whereas neither the mid nor high tertiles of insulin sensitivity showed a change in prevalence of metabolic syndrome cases when the lower TG threshold was applied.

Plasma lipid concentrations in African Americans of comparable age and adiposity as the subjects in our study were reported by Sumner et al [9,13]. They also reported an apparently favorable lipid profile in African Americans, despite obesity and relative insulin resistance, but a significant relationship between TG and insulin resistance was not detected. In contrast, we detected a significant correlation of insulin resistance with TG, HDL-C, and TG/HDL-C. Our study included a somewhat larger sample size and a larger proportion of women, and we quantified insulin sensitivity by the insulin clamp procedure rather than the insulin-modified, frequently sampled intravenous glucose tolerance test used by Sumner et al. However, when the association of TG with insulin sensitivity was examined in men and women separately, the correlation increased in men and decreased in women, indicating a significant gender effect on the relationship. Because the women in our study were all premenopausal, the gender difference could be due to some salutary effect of endogenous estrogens. Known diabetic subjects were excluded from the analysis. Also excluded from the analysis were subjects, predominately female, in whom diabetes was identified on oral glucose tolerance testing. It is possible that the exclusion of previously undetected diabetic individuals may have amplified the gender differences in the relationship of TG with insulin sensitivity in this relatively young adult African American sample.

Insulin resistance plays a role in cardiovascular and endothelial damage. Because insulin resistance is difficult to quantify clinically, the constellation of associated cardiovascular risk factors designated as the metabolic syndrome serves as a surrogate clinical strategy to optimize detection of insulin resistance as an underlying pathogenic condition [29]. In whites, there is a strong correlation of TG with insulin resistance as measured by the insulin suppression test, supporting the inclusion of a TG threshold in the metabolic syndrome definition [14]. The data from this study found that even at lower TG concentrations, the relationship of TG with insulin resistance is present in African

Americans. This suggests that a TG criterion of 150 mg/dL or greater may be too high to detect underlying insulin resistance in this high-risk ethnic group. These results support lowering the TG cut point to 110 mg/dL or greater, as subjects with TG between 110 and 149 mg/dL were just as insulin resistant as subjects with TG greater than 150 mg/dL.

Although African Americans appear to have more favorable lipid profiles, it is possible that they have a different threshold for the adverse effects of relative dyslipidemia. One pathway of vascular damage is mediated through oxidative stress. Lopes et al [32] investigated the effect of acute hyperlipidemia on oxidative stress in both African Americans and whites. After infusion of Intralipid and heparin, African American and white subjects experienced a comparable rise in plasma TG concentrations. However, F2-isoprostanes, a biomarker of oxidative stress in humans, increased significantly more in African Americans compared with whites. Although the report by Lopes et al is based on a short-term rise in TG, it does suggest that African Americans could have a heightened sensitivity to increases in TG.

Reports on dyslipidemia in whites describe a significant positive correlation between visceral adiposity and TG concentration [33]. Both central obesity and insulin resistance are associated with TG elevation in whites. However, in an earlier report from the Insulin Resistance Atherosclerosis Study (IRAS) [6], the association between insulin resistance and lipoproteins was independent of waist-hip ratio in African American adults. Data from this study detected no relationship between TG and BMI or percent body fat, which is consistent with the IRAS findings. It is possible that the relationship of obesity with insulin resistance is overemphasized, as insulin resistance has been documented in lean individuals [34].

A limitation of our study may be the small sample size in relation to large-scale epidemiologic reports. However, compared with the number of African American subjects in earlier studies of insulin resistance in nondiabetic subjects, the present study had a similar sample size, if not larger. In addition, the subjects were representative of the African American population. Among our subjects, 55% were obese, which is similar to the middle-aged African Americans described by the National Health and Nutrition Examination Survey [35]. Therefore, the results of our study may apply to nondiabetic African Americans aged between 30 and 50 years.

Because there are presently no quantifiable criteria that designate insulin resistance within individuals, the use of the lowest *M* tertile as a stratum of insulin resistance could be considered arbitrary. However, the euglycemic hyperinsulinemic clamp procedure used in the present study to quantify insulin-mediated glucose uptake is considered the gold standard in measuring insulin sensitivity [13]. Moreover, clustering of components of the metabolic syndrome segregated in the lowest *M* tertile, indicating that this designation was reasonable.

Until recently, data on the metabolic syndrome were derived from predominately white populations. Recent observations from various ethnic and racial groups have questioned the validity of applying the same metabolic syndrome criteria to different populations [19,36]. Data from the present study demonstrate that the existing TG threshold of 150 mg/dL or greater may underdetect insulin resistance in African Americans. Reaven [37] has suggested that insulin resistance is the underlying pathology for developing CVD and that the concept of the metabolic syndrome may be misleading. The diagnosis of the metabolic syndrome, although flawed, can be clinically useful to detect patients with probable insulin resistance. Even if the diagnosis of metabolic syndrome is abandoned, African Americans with characteristics of insulin resistance, including high BP, obesity, and prediabetic blood glucose levels, but with seemingly normal TG and HDL may benefit from risk factor reduction. Further studies are needed to evaluate CVD in insulin-resistant African Americans and to determine if lower lipid thresholds contribute to CVD progression.

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References

[1] Meigs JB, Wilson PW, Fox CS, et al. Body mass index, metabolic syndrome and risk of type 2 diabetes or cardiovascular disease. J Clin Endocrinol Metab 2006;91:2906-12.

[2] Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes 1988;37:1595-607.

[3] Morisco C, Lembo G, Trimarco B. Insulin resistance and cardiovascular risk: new insights from molecular and cellular biology. Trends Cardiovasc Med 2006;16:183-8.

[4] Ryan AS, Nicklas BJ, Berman DM. Racial differences in insulin resistance and mid-thigh fat deposition in postmenopausal women. Obes Res 2002;10:336-44.

[5] Arslanian S, Suprasongsin C, Janosky JE. Insulin secretion and sensitivity in black versus white prepubertal healthy children. J Clin Endocrinol Metab 1997;82:1923-7.

[6] Haffner SM, D'Agostino R, Saad MF, et al. Increased insulin resistance and insulin secretion in nondiabetic African-Americans and Hispanics compared with non-Hispanic whites. The Insulin Resistance Atherosclerosis Study. Diabetes 1996;45:742-8.

[7] Forouhi NG, Sattar N. CVD risk factors and ethnicity—a homogeneous relationship? Atheroscler Suppl 2006;7:11-9.

[8] Reaven GM. Compensatory hyperinsulinemia and the development of an atherogenic lipoprotein profile: the price paid to maintain glucose homeostasis in insulin-resistant individuals. Endocrinol Metab Clin North Am 2005;34:49-62.

[9] Sumner AE, Vega GL, Genovese DJ, Finley KB, Bergman RN, Boston RC. Normal triglyceride levels despite insulin resistance in African Americans: role of lipoprotein lipase. Metabolism 2005;54:902-9.

[10] Howard BV, Mayer-Davis EJ, Goff D, et al. Relationships between insulin resistance and lipoproteins in nondiabetic African Americans, Hispanics, and non-Hispanic whites: the Insulin Resistance Atherosclerosis Study. Metabolism 1998;47:1174-9.

[11] Hall WD, Clark LT, Wenger NK, et al. The metabolic syndrome in African Americans: a review. Ethn Dis 2003;13:414-28.
[12] Bacha F, Saad R, Gungor N, Janosky J, Arslanian SA. Obesity, regional fat distribution, and syndrome X in obese black versus white adolescents: race differential in diabetogenic and atherogenic risk factors. J Clin Endocrinol Metab 2003;88:2534-40.
[13] Sumner AE, Finley KB, Genovese DJ, Criqui MH, Boston RC. Fasting triglyceride and the triglyceride-HDL cholesterol ratio are not markers of insulin resistance in African Americans. Arch Intern Med 2005;165:1395-400.
[14] McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann Intern Med 2003;139:802-9.
[15] Executive summary of the third report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.
[16] Guidelines Subcommittee. 1999 World Health Organization-International Society of Hypertension guidelines for the management of hypertension. J Hypertens 1999;17:151-83.
[17] Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539-53.
[18] Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the International Diabetes Federation. Diabet Med 2006;23:469-80.
[19] Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. Arch Intern Med 2003;163:427-36.
[20] Cheung BM, Ong KL, Man YB, Wong LY, Lau CP, Lam KS. Prevalence of the metabolic syndrome in the United States National Health and Nutrition Examination Survey 1999-2002 according to different defining criteria. J Clin Hypertens (Greenwich) 2006;8:562-70.
[21] Parra EJ, Marcini A, Akey J, et al. Estimating African American admixture proportions by use of population-specific alleles. Am J Hum Genet 1998;63:1839-51.
[22] Womersley J. A comparison of the skinfold method with extent of 'overweight' and various weight-height relationships in the assessment of obesity. Br J Nutr 1977;38:271-84.
[23] DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol 1979;237:E214-23.
[24] Rizza RA, Mandarino LJ, Gerich JE. Dose-response characteristics for effects of insulin on production and utilization of glucose in man. Am J Physiol 1981;240:E630-9.
[25] Falkner B, Kushner H, Tulenko T, Sumner AE, Marsh JB. Insulin sensitivity, lipids, and blood pressure in young American blacks. Arterioscler Thromb Vasc Biol 1995;15:1798-804.
[26] Bachorik PS, Walker RE, Virgil DG. High-density-lipoprotein cholesterol in heparin-$MnCl_2$ supernates determined with the Dow enzymic method after precipitation of Mn^{2+} with HCO_3. Clin Chem 1984;30:839-42.
[27] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
[28] Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005;112:2735-52.
[29] Reaven GM. The metabolic syndrome: is this diagnosis necessary? Am J Clin Nutr 2006;83:1237-47.
[30] McNeill AM, Rosamond WD, Girman CJ, et al. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the Atherosclerosis Risk in Communities Study. Diabetes Care 2005;28:385-90.
[31] Liao Y, Kwon S, Shaughnessy S, et al. Critical evaluation of Adult Treatment Panel III criteria in identifying insulin resistance with dyslipidemia. Diabetes Care 2004;27:978-83.
[32] Lopes HF, Morrow JD, Stojiljkovic MP, Goodfriend TL, Egan BM. Acute hyperlipidemia increases oxidative stress more in African Americans than in white Americans. Am J Hypertens 2003;16:331-6.
[33] Despres JP, Allard C, Tremblay A, Talbot J, Bouchard C. Evidence for a regional component of body fatness in the association with serum lipids in men and women. Metabolism 1985;34:967-73.
[34] Meigs JB, Wilson PW, Fox CS, et al. Body mass index, metabolic syndrome, and risk of type 2 diabetes or cardiovascular disease. J Clin Endocrinol Metab 2006;91:2906-12.
[35] Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006;295:1549-55.
[36] Lteif AA, Han K, Mather KJ. Obesity, insulin resistance, and the metabolic syndrome: determinants of endothelial dysfunction in whites and blacks. Circulation 2005;112:32-8.
[37] Reaven G. The metabolic syndrome or the insulin resistance syndrome? Different names, different concepts, and different goals. Endocrinol Metab Clin North Am 2004;33:283-303.