BRIEF REPORT

Racial Differences in Blood Lipids Lead to Underestimation of Cardiovascular Risk in Black Women in a Nested Observational Study

在巢式观察研究中，血脂方面的种族差异导致了对黑人妇女心血管风险的低估。

Las diferencias raciales en los lípidos sanguíneos derivan en la infravaloración del riesgo cardiovascular en mujeres negras en un estudio observacional anidado

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ABSTRACT

Background: During screening for enrollment in a clinical trial, we noticed potential racial disparities in metabolic syndrome variables in women who responded to our study advertisement. We designed a nested observational study to investigate whether metabolic syndrome variables differed between non-Hispanic blacks and non-Hispanic whites.

Methods: The cohort comprised of women who have met the preliminary clinical trial criteria (body mass index [BMI] 25-45, age 20-75 years, and no use of lipid-lowering medications or supplements). These women, including 116 blacks and 138 whites, provided fasting blood samples for analysis of serum lipid profile.

Results: Blacks had lower mean triglycerides (81.1 ± 3.3 mg/dL vs 140.6 ± 5.9 mg/dL; $P < .0001$), total cholesterol (176.1 ± 3.6 mg/dL vs 201.6 ± 3.3 mg/dL; $P < .0001$), and low-density lipoprotein (111.7 ± 3.3 mg/dL vs 128.2 ± 2.9 mg/dL; $P < .001$) and higher mean BMI (37.2 ± 0.5 vs 35.2 ± 0.5; $P < .01$) and diastolic blood pressure (82.4 ± 0.8 mmHg vs 79.4 ± 0.7 mmHg; $P < .01$) than whites. Only 7% of blacks, compared with 41% of whites, had triglycerides ≥150 mg/dL; as a result, fewer black women met metabolic syndrome criteria than white women. Additionally, in women with waist circumference ≥88 cm (N = 215), high-density lipoprotein was higher in blacks than in whites (48.3 ± 1.5 mg/dL vs 44.2 ± 1.3 mg/dL; $P < .05$).

Conclusions: Due to racial differences in blood lipids, current metabolic syndrome criteria may result in underestimation of cardiovascular risk in blacks.

摘要

背景：在甄选临床试验中的注册人员过程中，我们从回应了我们的研究宣传的妇女中，注意到代谢综合症在变量上的潜在种族差异。我们设计了一种巢式观察研究，调查代谢综合征的变量在非西班牙裔黑人与非西班牙裔白人之间是否有所不同。

方法：该人群包括满足了初步临床试验条件的妇女（身体质量指数［BMI］25–45，年龄 20–75 岁，且不使用降脂药物或补品）。这些妇女（包括 116 名黑人和 138 名白人）提供了空腹血样以供进行血清血脂分析。

结果：与白人相比，黑人的甘油三脂平均值偏低（81.1 ± 3.3 mg/dL 对 140.6 ± 5.9 mg/dL；$P < .0001$）、总胆固醇（176.1 ± 3.6 mg/dL 对 201.6 ± 3.3 mg/dL；$P < .0001$）和低密度的脂蛋白（111.7 ± 3.3 mg/dL 对 128.2 ± 2.9 mg/dL；$P < .001$）以及更高的平均 BMI（37.2 ± 0.5 对 35.2 ± 0.5；$P < .01$）和舒张压（82.4 ± 0.8 mmHg 对 79.4 ± 0.7 mmHg；$P < .01$）。与 41% 的白人相比，仅有 7% 的黑人甘油三脂 ≥150 mg/dL；结果显示，与白人相比，黑人妇女达到代谢综合症标准的较少。另外，在腰围 ≥88 cm（N = 215）的妇女当中，黑人的高密度脂蛋白比白人高（48.3 ± 1.5 mg/dL 对 44.2 ± 1.3 mg/dL；$P < .05$）。

结论：由于血脂方面的种族差异，当前的代谢综合症标准可能会导致低估黑人的心血管风险。

SINOPSIS

Fundamentación: Durante la selección para la inscripción en un ensayo clínico, observamos posibles diferencias raciales en las variables del síndrome metabólico en las mujeres que respondieron a nuestro anuncio del estudio. Diseñamos un estudio observacional anidado para investigar si las variables del síndrome metabólico diferían entre las personas no hispanas negras y las blancas.

Métodos: La cohorte se compuso de mujeres que cumplían los criterios preliminares para el ensayo clínico (índice de masa corporal [IMC] de 25 a 45, edad entre 20 y 75 años y que no usen medicamentos o complementos hipolipemiantes). Estas mujeres, incluidas 116 mujeres negras y 138 blancas, proporcionaron muestras de sangre en ayunas para el análisis del perfil de lípidos séricos.

Resultados: Las mujeres negras presentaban valores medios inferiores de triglicéridos (81,1 ffl 3,3 mg/dl frente a 140,6 ffl 5,9 mg/dl; $P < 0{,}0001$), colesterol total (176,1 ffl 3,6 mg/dl frente a 201,6 ffl 3,3 mg/dl; $P < 0{,}0001$), lipoproteínas de baja densidad (111,7 ffl 3,3 mg/dl frente a 128,2 ffl 2,9 mg/dl; $P < 0{,}001$) y valores medios más elevados en el IMC (37,2 ffl 0,5 frente a 35,2 ffl 0,5; $P < 0{,}01$) y la tensión arterial diastólica (82,4 ffl 0,8 mmHg frente a 79,4 ffl 0,7 mmHg; $P < 0{,}01$) en relación con los de las mujeres blancas. Únicamente un 7 % de mujeres negras, en comparación con un 41 % de mujeres blancas, presentó una concentración de triglicéridos igual o superior a 150 mg/dl; como resultado, menos mujeres negras que blancas cumplían los cri-

terios de síndrome metabólico. Además, en mujeres con perímetro de la cintura igual o superior a 88 cm (N = 215), la concentración de lipoproteínas de alta densidad en mujeres negras era superior a la de las mujeres blancas (48,3 ffl 1,5 mg/dl frente 44,2 ffl 1,3 mg/dl; P < 0,05).

Conclusiones: Debido a las diferencias raciales en los lípidos sanguíneos, los criterios actuales de síndrome metabólico pueden resultar en una infravaloración del riesgo cardiovascular en las personas de raza negra.

INTRODUCTION

Metabolic syndrome (MetS) afflicts an estimated 69 million people in the United States, and its incidence worldwide continues to increase.[1,2] MetS is accompanied by a two-fold increased risk of cardiovascular disease (CVD) and a five-fold increased risk of type 2 diabetes.[3] Because MetS represents a cluster of co-occuring metabolic risk factors, differences in its definition exist. For example, the National Cholesterol Education Program Adult Treatment Panel III report (NCEP ATP III) defines MetS as having three or more of the following components: abdominal obesity, assessed by waist circumference (≥88cm for women and ≥102 cm for men); triglycerides ≥150 mg/dL; high-density lipoprotein cholesterol (HDL-C) <50 mg/dL for women and <40 mg/dL for men; elevated blood pressure (BP; ≥130/85 mm Hg); and fasting blood glucose ≥100 mg/dL.[4] On the other hand, the International Diabetes Federation included central obesity (waist circumference ≥80 cm to 88 cm for women and ≥90 cm to 102 cm for men with ethnicity-specific values) as a necessary component for diagnosis, along with any two of the four variables from the lipid, glucose, and BP profile described above.[5] No ethnicity-specific values were provided for any of the other four variables.

To study the efficacy of dietary modification in alleviating MetS in women, we conducted a 12-week clinical trial to investigate whether a phytochemical-rich medical food added to a Mediterranean-style low–glycemic load dietary food plan more effectively impacted MetS variables than the food plan alone. The trial (registered as NCT01010841) was completed and results published.[6] However, during the screening phase for enrollment, we noticed what appeared to be a racial discrepancy in plasma lipids, disproportionately disqualifying blacks from participating in the clinical trial. Therefore, we decided to examine participant data collected during the onsite screening for the clinical trial to confirm whether differences in lipid variables existed between black and white women.

SUBJECTS AND METHODS

A total of 685 women in the metropolitan area of Jacksonville, Florida, responded to our advertisement for a 12-week, randomized, controlled, multicenter study. We interviewed these women over the phone to select those meeting the followin g preliminary criteria: body mass index (BMI) between 25 kg/m² and 45 kg/m², aged 20 to 75 years, and no use of lipid-lowering medications or supplements. Women meeting the initial criteria were invited to attend an onsite screening visit during which they provided fasting blood samples for analysis of lipid profile and glucose levels. Their BMIs were calculated, waist circumferences measured, and vital signs recorded. Method for lipid analysis has been previously published.[6]

Of the 281 volunteers screened on site, 27 self-identified as Asian, Hispanic, mixed race, or unknown and were excluded from the observational analysis. We analyzed the screening data from the remaining 254 women, including 116 non-Hispanic blacks and 138 non-Hispanic whites.

STATISTICAL ANALYSIS

Lipid profiles, BMI, waist circumference, BP, and fasting glucose were compared between whites and blacks by using two-sided unpaired t-tests. Racial distribution for triglycerides ≥150 mg/dL was analyzed by a chi-square test. Triglycerides were analyzed adjusting for potential confounders (BMI, waist circumference, and BP) by using a general linear model; none of these variables had a significant influence on triglycerides levels in either blacks or whites (data not shown). Data were analyzed using SAS (software version 9.1, SAS Institute Inc, Cary, North Carolina), with the type I error set at a nominal 5%. The numerical data are reported as means ffl standard error (SE), and the dichotomous data are reported as percentage based on sample size of each race.

Table 1 Cardiometabolic and Body Composition Variables of Onsite Screening Participants

	Blacks		Whites		
	N	Mean ± SE	N	Mean ± SE	*P* value
Age (y)	116	41.2 ± 0.9	138	46.6 ± 0.8	<.01
BMI (kg/m²)	116	37.2 ± 0.5	138	35.2 ± 0.5	<.01
Systolic BP (mmHg)	116	127.3 ± 1.3	138	124.8 ± 1.2	NS
Diastolic BP (mmHg)	116	82.4 ± 0.8	138	79.4 ± 0.7	<.01
WC (cm)	100	110.5 ± 1.2	122	108.1 ± 1.2	NS
TC (mg/dL)	116	176.1 ± 3.6	138	201.6 ± 3.3	<.0001
TG (mg/dL)	116	81.1 ± 3.3	138	140.6 ± 5.9	<.0001
HDL (mg/dL)	116	48.2 ± 1.4	138	45.3 ± 1.2	NS
LDL (mg/dL)	116	111.7 ± 3.3	138	128.2 ± 2.9	<.001
Glucose (mg/dL)	116	95.6 ± 1.9	138	97.7 ± 1.5	NS
TC/HDL	116	3.9 ± 0.1	138	4.9 ± 0.2	<.0001
TG/HDL	116	1.9 ± 0.1	138	3.8 ± 0.2	<.0001

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, not significant; SE, standard error; TC, total cholesterol; TG, triglycerides; WC, waist circumference.

RESULTS

Racial Differences in Lipid Profiles

The mean triglycerides level of blacks was significantly lower than that of whites ($P < .0001$, Table 1). Triglycerides ≥150 mg/dL is the threshold for diagnosis of MetS;[7] only 7% of blacks vs 41% of whites had triglycerides ≥150 mg/dL ($P < .0001$). Compared with whites, blacks also exhibited lower mean total cholesterol levels ($P < .0001$) and LDL levels ($P < .001$). HDL levels trended higher in blacks than in whites ($P > .05$). However, blacks had significantly higher BMI ($P < .01$) and diastolic BP ($P < .01$) than whites. No significant differences were found in systolic BP, waist circumference, or fasting glucose levels between the two groups.

Blacks Exhibited Lower Total Cholesterol:High-density Lipoprotein and Triglycerides:High-density Lipoprotein Ratios

The ratios of total cholesterol to HDL (TC:HDL) and of triglycerides to HDL (TG:HDL) are emerging biomarkers for assessing risk for heart disease; a lower ratio equates to lower risk.[8-10] Both the TC:HDL and TG:HDL ratios in blacks were significantly lower than those of whites ($P < .0001$, Table 1).

Few Black Women Met Criteria for the Lipid Triad

Grundy suggested that the combination of elevated triglycerides, increased small LDL particles, and low HDL represent increased cardiovascular risk.[11] A variation of the lipid triad definition posited by Bestehorn uses values from a standard lipid profile and includes the following factors[12]: triglycerides ≥200 mg/dL, HDL <35 mg/dL, TC:HDL >5. In our study, <1% of blacks met these latter criteria for the lipid triad, and approximately 10% of whites met these criteria.

Subanalysis of Women With Waist Circumference ≥88 cm

Some individuals may have a high BMI without central obesity. We conducted a subanalysis in those with waist circumference ≥88 cm (n = 215), which included 84% of the blacks and 86% of the whites. Results were similar to those seen in the whole cohort with respect to significantly lower mean triglycerides, total cholesterol, and LDL, and significantly higher BMI and diastolic BP in black women (Table 2). However, HDL levels were significantly higher in the blacks than in whites ($P < .05$).

Table 2 Subanalysis of Clinical Data From Participants With Waist Circumference ≥88 cm

	Blacks		Whites		
	N	Mean ± SE	N	Mean ± SE	*P* value
BMI (kg/m2)	97	37.3 ± 0.5	118	35.1 ± 0.5	<.01
Systolic BP (mmHg)	97	127.6 ± 1.4	118	125.1 ± 1.3	NS
Diastolic BP (mmHg)	97	82.6 ± 0.8	118	79.3 ± 8.4	<.01
WC (cm)	97	111.3 ± 1.1	118	109.1 ± 1.1	NS
TC (mg/dL)	97	176.0 ± 4.1	118	203.4 ± 3.5	<.0001
TG (mg/dL)	97	80.3 ± 3.5	118	147.0 ± 6.6	<.0001
HDL (mg/dL)	97	48.3 ± 1.5	118	44.2 ± 1.3	<.05
LDL (mg/dL)	97	111.7 ± 3.7	118	129.7 ± 3.0	<.001
Glucose (mg/dL)	97	96.0 ± 2.0	118	98.3 ± 1.7	NS
TC/HDL	97	3.9 ± 0.1	118	5.1 ± 0.2	<.0001
TG/HDL	97	1.8 ± 0.1	118	4.0 ± 0.3	<.0001

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, not significant; SE, standard error; TC, total cholesterol; TG, triglycerides; WC, waist circumference.

DISCUSSION

In this nested observational study, we found racial differences in lipid variables in women who were screened for a clinical trial. Black women had significantly lower levels in triglycerides, total cholesterol, and LDL but had significantly higher BMI and diastolic BP than white women. Many of these lipid variables are components of clinical guidelines that are supposed to help healthcare practitioners identify high-risk individuals. Therefore, racial differences in these variables appear to negatively impact the effectiveness of some clinical guidelines for a certain racial group, contributing to significant public health consequence.

For example, lower mean levels of triglycerides in black men and women contribute to fewer diagnoses of MetS among the black population.[13] Yet stroke, myocardial infarction, and type 2 diabetes are more frequent in the black population compared with the white population in the United States. This suggests that the standard definition of MetS is inappropriate for predicting CVD risk in the black population, and the risk goes unnoticed until disease progression has occurred. Similarly, based on Bestehorn's definition of lipid triad,[12] we observed a deceptively low CVD risk profile in black compared with white women due to racial disparities in lipid variables. Others have indicated that TC:HDL and TG:HDL ratios are useful indicators of CVD risk in overweight individuals.[8,10] However, discrepancies in both ratios between whites and blacks suggest that they are not reliable indicators of CVD risk for all populations.

Differences in enzyme activities or in lipoprotein biology may explain racial disparities in triglycerides and HDL levels. Indeed, one genotype analysis in a large cohort of black and white women indicated that genetic polymorphisms in the cholesteryl ester transfer protein gene, lipoprotein lipase gene, or hepatic lipase gene correlate with HDL levels,[14] and another study reported higher lipoprotein lipase mRNA levels in the subcutaneous fat of the obese blacks than of the obese whites.[15] Age, education, social economic status, dietary pattern, and other environmental factors also differ widely by ethnicity[16] and are likely contributors to the observed disparities.

Our observational study was based on a small cohort screened for a clinical trial; comprehensive data, including diet diaries, had not been collected at the screening visit. Therefore, we were not able to address whether racial differences in dietary patterns and other lifestyle factors might confound our observation. Nevertheless, a recent study based on the National Health and Nutrition Examination Surveys 1999-2006 data showed that the racial discrepancies in the MetS persisted even after adjusting for social economic status, education, physical activity, and diet quality.[17] We also acknowledge that there are additional limitations in this nested observational study. The cohort is not a result of random sampling, and there may be selection bias. It may not represent the general population, and the findings cannot be extrapolated to both genders and other ethnic groups.

This is not the first report on racial differences in blood lipids in a MetS study cohort; similar findings have been published in the past few years.[13,17-19] However, we are alarmed by the lack of awareness of this issue among numerous physicians and healthcare practitioners with whom we have had personal communications. As the incidence of type 2 diabetes and heart disease continues to rise, we are faced with the dual challenge of not only managing the burden of disease but also slowing the onset of disease through preventive measures. Without guidelines that can accurately identify at-risk individuals, healthcare strategies cannot be efficiently implemented. Through this brief report (and supported evidence cited in this report), we hope to renew the awareness among the medical community and *Global Advances in Health and Medicine* readers on the issue of underdiagnosis of CVD risk in blacks. We believe it is imperative to develop ethnicity-specific guidelines for MetS criteria, TC:HDL, TG:HDL, lipid triad, and even thresholds used to define hypertriglyceridemia.

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