Differences in Systemic Oxidative Stress Based on Race and the Metabolic Syndrome: The Morehouse and Emory Team up to Eliminate Health Disparities (META-Health) Study

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Abstract

Background: Classification schema such as metabolic syndrome may underestimate cardiovascular disease (CVD) risk in African Americans, despite a higher burden of CVD in African Americans. Oxidative stress results from an imbalance of prooxidants and antioxidants and leads to endothelial dysfunction that promotes vascular inflammation and atherosclerosis. Aminothiol markers of oxidative stress are associated with CVD risk factors and metabolic syndrome; however, little is known about racial differences in levels of oxidative stress. We sought to investigate whether oxidative stress would be higher in African Americans compared to whites independently of traditional risk factor burden.

Methods: We assessed oxidative stress in a biracial, community-based cohort. In 620 subjects (59% female, 52% African American) in the Morehouse and Emory Team up to Eliminate Health Disparities (META-Health) study, we measured plasma levels of glutathione, an intracellular antioxidant, and its redox potential as a ratio of reduced and oxidized glutathione (E_h glutathione).

Results: African Americans had lower glutathione levels ($P < 0.001$) compared to whites. There was a trend toward more oxidized E_h glutathione ($P = 0.07$) in African Americans; however, this did not reach statistical significance. After adjustment for demographics and CVD risk factors, African-American race remained a significant correlate of lower glutathione levels ($P < 0.001$) and a more oxidized E_h glutathione ($P = 0.04$). After further adjustment for high-sensitivity C-reactive protein (hsCRP), glutathione remained significantly lower in African Americans ($P = 0.001$). African Americans with or without metabolic syndrome had lower glutathione levels compared to whites with or without metabolic syndrome, respectively (both $P \leq 0.001$), and African Americans without metabolic syndrome had a more oxidized E_h glutathione compared to whites without metabolic syndrome ($P = 0.003$).

Conclusions: African Americans have higher levels of oxidative stress than whites, even after adjustment for differences in CVD risk factors and inflammation. Racial differences in oxidative stress may play a key role in understanding observed racial disparities in CVD.

Introduction

ALTHOUGH THERE HAS BEEN an overall decline in cardiovascular disease (CVD) mortality over the past decades, vascular disease and its complications carry

significantly higher morbidity and mortality in African Americans compared with whites.¹ These observations may be partly explained by a higher prevalence of CVD risk factors, such as obesity, hypertension, type 2 diabetes mellitus, and tobacco use among African Americans.^{2,3}

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However, the higher mortality from CVD in African Americans exceeds what would be expected based on a higher prevalence of traditional risk factors alone. Excess inflammation and oxidative stress promote atherosclerotic plaque formation and instability that contribute to CVD risk and mortality.^{4,5} Previous studies have found higher levels of inflammatory biomarkers such as high-sensitivity C-reactive protein (hsCRP) in African Americans, but little is known about racial differences in oxidative stress.⁶

Oxidative stress leads to endothelial dysfunction that promotes vascular inflammation, which in turn promotes further oxidation in a feed-forward fashion. The definition of oxidative stress continues to be refined to account for macromolecular damage from free radical intermediates and disruption of thiol redox circuits, which lead to aberrant redox signaling and control.^{7,8} Quantification of the major intracellular and extracellular aminothiols compounds, such as glutathione and its oxidized counterpart, provide a measure of *in vivo* oxidative stress. Intracellularly, glutathione is a major antioxidant that helps eliminate peroxides and maintain the redox state of ascorbate and (indirectly) vitamin E in their reduced and functional forms.⁹ The oxidized disulfide form of glutathione, GSSG, is formed during the reaction of glutathione peroxidase with hydrogen peroxide or by a direct reaction of glutathione with peroxynitrite and other oxidants. Using the measured glutathione and GSSG concentrations in plasma, the redox potential of the glutathione/GSSG couple (E_h glutathione) can be calculated using the Nernst equation.¹⁰

Oxidative stress is a common denominator in many aspects of cardiovascular pathogenesis, causing inactivation of nitric oxide that results in endothelial dysfunction, activation of matrix metalloproteinases, and oxidation of lipid particles that generate fatty streaks and atherosclerotic plaques.¹¹ Lower levels of glutathione, as a measure of increased oxidative stress, are associated with coronary artery disease (CAD) and its risk factors, including age, type 2 diabetes, cigarette smoking, and metabolic syndrome.^{12–14} Studies of plasma redox as a biomarker of oxidative stress show that E_h glutathione is increasingly oxidized in association with age, smoking, endothelial dysfunction, and subclinical vascular disease, such as increased carotid intima media thickness.^{12,13} Previous analyses have also indicated that oxidative stress may have proinflammatory effects. Studies of oxidative stress markers such as free oxygen radicals, oxidized low-density lipoprotein (LDL), and urinary F_2 isoprostanes have shown a positive correlation with hsCRP.^{15–17}

Metabolic syndrome, characterized by a cluster of CVD risk factors, including insulin resistance, hypertension, dyslipidemia, and visceral adiposity, has been associated with increased oxidative stress.^{18–20} Compared to whites, African Americans have higher insulin resistance, higher high-density lipoprotein cholesterol (HDL-C) levels, and lower triglyceride levels.^{21,22} Because of this, there has been controversy regarding whether the components of metabolic syndrome carry a similar CVD risk in African Americans and whites. The lower prevalence of dyslipidemia among African Americans, in particular because it accounts for two of the five components of metabolic syndrome, places African Americans at increased risk for underrecognition of this disease state. We hypothesized that oxidative stress, as measured by glutathione, GSSG, and/or E_h glutathione, would be higher in African Americans than in whites independently of traditional CVD risk factor burden and higher

levels of inflammation measured by hsCRP. In addition, classification according to absence or presence of metabolic syndrome would not account for racial differences in levels of oxidative stress.

Methods

Subjects

The Morehouse and Emory Team up to Eliminate Health Disparities (META-Health) Study was a two-stage cross-sectional study of both traditional and psychosocial risk factors for CVD and metabolic syndrome. The first stage was a random digit dialing survey of African-American and white ($N=3,391$) residents of metropolitan Atlanta, ages 30–65 years. The second stage included a subset of participants ($n=753$) from the first stage who agreed to come to either Emory or Morehouse Schools of Medicine for a detailed study visit. For this analysis, we excluded participants for missing data on biomarkers of oxidative stress ($n=41$), or for missing data on components of metabolic syndrome, or medical and smoking history ($n=92$). Compared to those who were included in the analysis, there was a lower percentage of females (50% vs. 59%), but a similar number of African Americans (52% vs. 53%) in the 133 participants who were excluded. History of diabetes and hypertension were defined by participant self-report or use of antidiabetic or antihypertensive medications. Smoking history, obtained using standardized questionnaires, was defined as current or never/former (no cigarettes within the past 30 days). Level of education and annual income were defined by participant self-report. Height and weight were measured, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Participants with three or more of the following were defined as having metabolic syndrome: (1) Waist circumference ≥ 102 cm in men or ≥ 88 cm in women, (2) triglycerides ≥ 150 mg/dL, (3) HDL-C < 40 mg/dL in men or < 50 mg/dL in women, (4) blood pressure $\geq 130/85$ mmHg or use of medication for hypertension, and (5) fasting plasma glucose ≥ 100 mg/dL.²³ Pregnant women and subjects with acute illnesses were excluded. The study was approved by the Emory University and Morehouse School of Medicine Institutional Review Committees. Informed consent was obtained from all participants.

Blood tests

Participants were instructed to fast for 12 h before the study visit. Venous blood was collected in sodium heparin tubes, and the following plasma measurements were made. Serum levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), HDL-C, triglycerides, and glucose were measured by spectrophotometry. HsCRP was measured by immunonephelometry (Siemens/Dade Behring).

Detailed procedures for measurements of blood glutathione, GSSG, and E_h glutathione have been described previously.²⁴ For sample collection, 1.35 mL of blood was immediately transferred to a microcentrifuge tube containing 0.15 mL of a preservative solution consisting of 0.5 mol L-serine/L, 9.3 mmol bathophenanthroline disulfonate sodium salt (BPDS)/L, 0.165 mol γ -glutamylglutamate/L, 0.4 mol boric acid/L, 0.1 mol sodium borate/L, 0.144 mol sodium iodoacetate/L, and 2.5 mg sodium heparin/mL to reduce autooxidation. The samples were centrifuged, and the

supernatant frozen at -80°C , which showed no significant loss for up to 1 year. Analyses by high-performance liquid chromatography were performed after dansyl derivitization on a 3-aminopropyl column with fluorescence detection to quantify glutathione and GSSG concentrations in plasma.²⁵ Issues of sample collection, stability, analysis, and standardization have been extensively studied, and the method has been used in several clinical studies.¹² On the basis of glutathione and GSSG concentrations, E_h glutathione was calculated using the Nernst equation ($E_h = E_o + (RT/nF)\ln([GSSG]/[GSH])^2$). E_h glutathione was expressed in mV, with higher (less negative) values being indicative of higher levels of oxidative stress. The coefficients of variation were 5% for glutathione and 9.7% for GSSG, and the standard deviation (SD) for week-to-week variation among individuals for glutathione redox potential was 3.22 mV.

Statistical analysis

Continuous variables were tested for normality using the Kolmogorov-Smirnov criterion. Study variables are expressed as means $\pm$ SD for normally distributed continuous variables, median and interquartile range for nonnormally distributed continuous variables, or frequencies and percentages for categorical variables. Because glutathione, hsCRP, and GSSG were highly skewed, they were natural log transformed for any parametric analysis. Chi-squared tests were used to compare categorical variables, whereas unpaired *t*-tests or Wilcoxon rank sum tests were used to compare continuous variables between the two racial groups.

Simple linear regression was performed for variable selection and data reduction. First, multivariable linear regression models were fit to ascertain whether African-American race was a correlate of hsCRP levels, after adjusting for traditional CVD risk factors, presence of metabolic

syndrome, and glutathione. Second, two-step multivariable linear regression models were fit to ascertain whether African-American race was a correlate of levels of oxidative stress independently of traditional CVD risk factors and hsCRP. We intentionally adjusted for all CVD risk factors despite some collinearity because of baseline differences in risk factor burden between African Americans and whites. However, this method did not adversely influence the results. Model 1 adjusted for race, age, gender, smoking status, waist circumference, blood pressure, triglycerides, LDL-C, HDL-C, glucose, and presence of metabolic syndrome. Model 2 adjusted Model 1 further for hsCRP. To display the magnitude of the difference in glutathione levels with each adjustment, percentage change in glutathione was computed using the formula $[1 - (\exp^{\beta})] \times 100\%$.

Secondary analyses were performed to evaluate racial differences in levels of oxidative stress by metabolic syndrome criteria. Racial differences in levels of glutathione and E_h glutathione were evaluated using unpaired *t*-tests or Wilcoxon rank sum tests, respectively, according to presence or absence of metabolic syndrome. All tests of statistical significance were two-tailed, and *P* values < 0.05 were considered significant. Statistical analyses were performed with the Statistical Analysis System, version 9.1 (SAS Institute Inc, Cary, NC).

Results

Subject characteristics

Demographic and clinical characteristics of the 620 subjects are presented in Table 1. The sample was 59% female and 52% African American, and the mean age was 50 ± 9 years. Compared to whites, African Americans were younger and more likely to have a history of hypertension, type 2

TABLE 1. SUBJECT CHARACTERISTICS BY RACE

	African American n = 322	White n = 298	P
Age, years	48.7 $\pm$ 8.8	51.8 $\pm$ 9.2	<0.001
Female, %	55.9%	61.4%	0.2
History of hypertension, %	46.6%	32.2%	<0.001
History of diabetes, %	14.6%	5.5%	<0.001
Current smoking, %	28.3%	12.8%	<0.001
Education			<0.001
Less than high school	30.2%	9.3%	
Some college	35.5%	22.1%	
College graduate	34.3%	68.5%	
Income (\$K/year)	12.5 (10.0, 22.5)	12.5 (10.0, 37.5)	0.048
Metabolic syndrome, %	21.1%	26.5%	0.1
BMI (kg/m^2)	31.5 $\pm$ 7.7	28.1 $\pm$ 6.4	<0.001
Waist circumference (cm)	100.8 $\pm$ 17.2	95.8 $\pm$ 16.5	<0.001
SBP (mmHg)	124.7 $\pm$ 19.9	119.1 $\pm$ 17.0	<0.001
DBP (mmHg)	80.4 $\pm$ 11.9	76.3 $\pm$ 10.9	<0.001
LDL-C (mg/dL)	119.3 $\pm$ 35.5	118.5 $\pm$ 33.6	0.7
HDL-C (mg/dL)	58.7 $\pm$ 15.9	59.2 $\pm$ 18.8	0.7
Triglycerides (mg/dL)	100.0 $\pm$ 44.8	132.9 $\pm$ 82.8	<0.001
Glucose (mg/dL)	94.4 $\pm$ 29.1	92.9 $\pm$ 23.3	0.4
hsCRP (mg/L)	2.1 (0.8–5.5)	1.4 (0.7–3.4)	<0.001
Glutathione (μM)	1.4 (1.0–1.8)	1.6 (1.2–2.0)	<0.001
E_h glutathione (mV)	–134.4 $\pm$ 14.1	–136.3 $\pm$ 11.5	0.07

Values shown are mean $\pm$ standard deviation (SD), *n* (%), or median (interquartile range).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; E_h glutathione, oxidized glutathione.

diabetes, and be current smokers. African Americans were less likely to be college graduates, and they had lower annual incomes. African Americans also had a higher BMI, waist circumference, and blood pressure, but lower triglyceride levels than whites.

Relationship between race, traditional CVD risk factors, and hsCRP

In univariate analyses, African Americans had higher levels of hsCRP than whites (Table 1). After multivariable adjustment for age, gender, waist circumference, systolic blood pressure (SBP), lipids, glucose, and glutathione, African-American race ($\beta=0.099$, $P=0.02$) and lower glutathione levels ($\beta=-0.111$, $P=0.005$) remained significantly associated with higher hsCRP levels.

Relationship between race, traditional CVD risk factors, hsCRP, and aminothiol markers of oxidative stress

African Americans had lower levels of glutathione than whites, and there was a trend toward a more oxidized E_h glutathione in African Americans (Table 1). To evaluate the association of race and systemic oxidative stress, we conducted linear regression adjusting for demographic variables and traditional CVD risk factors (Model 1), then further adjusting for inflammation (Model 2) given the significant association of race and glutathione with hsCRP levels. After multivariable adjustment for demographic variables and CVD risk factors in Model 1, African-American race remained a significant correlate of higher levels of oxidative stress, accounting for 14% lower levels of glutathione and 2.2 mV more oxidized levels of E_h glutathione in African Americans than in whites. After further adjustment for hsCRP in Model 2, African-American race remained significantly associated with lower levels of glutathione (Table 2); however, the association with a more oxidized E_h glutathione was eliminated (Table 3).

Relationship between traditional CVD risk factors, hsCRP, and aminothiol markers of oxidative stress

There were significant univariate relationships between certain risk factors and glutathione (Table 2) and E_h glutathione (Table 3). Waist circumference, SBP, and triglycerides were associated with both lower levels of glutathione and a more oxidized E_h glutathione, whereas female gender and HDL-C were associated with higher levels of glutathione and less oxidized E_h glutathione. In addition, age, current smoking, glucose, and hsCRP were associated with lower levels of glutathione. After multivariable adjustment for demographic variables and CVD risk factors in Model 2, age and waist circumference remained significantly associated with lower levels of glutathione, whereas HDL-C remained significantly associated with less oxidized E_h Glutathione. None of the risk factors, including race, were predictors of GSSG on multivariable analysis (data not shown).

Effect of metabolic syndrome and race on aminothiol markers of oxidative stress

In the total population, 24% of subjects met criteria for metabolic syndrome, and the results did not differ by race (Table 1). In univariate analyses, presence of the metabolic syndrome was associated with lower levels of glutathione [1.3 (1.0 – 1.7) vs. 1.5 (1.2 – 2.0) $\mu\text{mol/L}$, $P<0.001$] and a more oxidized E_h glutathione (-132.7 ± 13.1 vs. -136.1 ± 12.8 mV, $P=0.005$). As shown in Fig. 1, African Americans with and without metabolic syndrome had lower levels of glutathione compared to whites with and without metabolic syndrome, respectively (both $P\leq0.001$), and African Americans without metabolic syndrome had a more oxidized E_h glutathione compared to whites without metabolic syndrome ($P=0.003$).

Discussion

In a biracial, community-based population from metropolitan Atlanta, we found that African Americans had significantly lower levels of plasma glutathione and a more

TABLE 2. LINEAR REGRESSION OF DEMOGRAPHICS AND CARDIOVASCULAR DISEASE RISK FACTORS WITH LOG GLUTATHIONE

	Multivariable linear regression					
	Univariate linear regression		Model 1		Model 2	
	R	P	Beta	P	Beta	P
African-American race	-0.161	<0.001	-0.156	<0.001	-0.150	0.001
Age, years	-0.138	0.001	-0.120	0.004	-0.102	0.02
Female gender	0.083	0.04	-0.016	0.7	-0.004	0.9
Current smoking	-0.088	0.03	-0.055	0.2	-0.030	0.5
Waist circumference, cm	-0.303	<0.001	-0.204	<0.001	-0.177	<0.001
SBP, mmHg	-0.162	<0.001	-0.011	0.8	-0.019	0.7
Triglycerides, mg/dL	-0.155	<0.001	-0.088	0.07	-0.092	0.06
LDL-C, mg/dL	-0.070	0.09	-0.032	0.4	-0.033	0.4
HDL-C, mg/dL	0.196	<0.001	0.075	0.1	0.068	0.2
Glucose, mg/dL	-0.138	0.001	-0.064	0.1	-0.065	0.2
hsCRP, mg/L	-0.146	<0.001	—	—	-0.055	0.2
R ²	—	—	0.154	<0.001	0.144	<0.001

Model 1, adjusted for race, age, gender, smoking status, waist circumference, SBP, triglycerides, LDL-C, HDL-C, glucose, and presence of metabolic syndrome. Model 2, Model 1 further adjusted for hsCRP.

SBP, systolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; SBP, systolic blood pressure.

TABLE 3. LINEAR REGRESSION OF DEMOGRAPHICS AND CARDIOVASCULAR DISEASE RISK FACTORS WITH E_H GLUTATHIONE

	<i>Multivariable linear regression</i>					
	<i>Univariate linear regression</i>		<i>Model 1</i>		<i>Model 2</i>	
	R	P	Beta	P	Beta	P
African-American race	0.072	0.07	0.092	0.04	0.074	0.1
Age, years	0.063	0.1	0.061	0.2	0.040	0.4
Female gender	−0.116	0.004	−0.046	0.4	−0.051	0.4
Current smoking	0.047	0.2	0.002	0.96	−0.004	0.9
Waist circumference, cm	0.174	<0.001	0.085	0.06	0.079	0.1
SBP, mmHg	0.095	0.02	0.007	0.9	0.020	0.6
Triglycerides, mg/dL	0.109	0.007	0.075	0.1	0.078	0.1
LDL-C, mg/dL	0.016	0.7	−0.004	0.9	−0.005	0.9
HDL-C, mg/dL	−0.195	<0.001	−0.122	0.01	−0.122	0.02
Glucose, mg/dL	0.050	0.2	−0.002	0.96	0.003	0.9
hsCRP, mg/L	0.068	0.1	—	—	0.022	0.6
R ²	—	—	0.069	<0.001	0.069	<0.001

Model 1, adjusted for race, age, gender, smoking status, waist circumference, SBP, triglycerides, LDL-C, HDL-C, glucose, and presence of metabolic syndrome. Model 2, Model 1 further adjusted for hsCRP.

E_H glutathione, oxidized glutathione; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; SBP, systolic blood pressure.

oxidized E_H glutathione compared with whites, even after adjustment for traditional CVD risk factors and inflammation. Furthermore, the prevalence of metabolic syndrome was similar in African Americans and whites, but did not account for differences in levels of oxidative stress. Thus, even among participants who would traditionally be considered at lower risk because they did not meet criteria for metabolic syndrome, African Americans had lower levels of glutathione and a more oxidized E_H glutathione. Classification according to conventional risk scores may therefore underestimate racial disparities in CVD risk that could potentially be related to the observed differences in oxidative stress.

Previously, nonthiol markers have been measured in studies examining racial differences in oxidative stress. Among various lipid-based measures of oxidative stress, African-American race was associated with increased levels of lipid hydroperoxides in diabetics, oxidized LDL-C, and plasma isoprostanes after lipid infusion, although no baseline differences were observed.^{26–28} However, there are few other studies that have examined racial differences in aminothiol markers of oxidative stress. In selected small populations, plasma levels of glutathione were lower in healthy African-American adults compared to whites.²⁹ Thus, ours is the largest population-based study to examine racial differences in aminothiol markers of oxidative stress to date.

The relationship between markers of inflammation and oxidative stress is also of considerable interest in regard to racial disparities in CVD. Isoprostanes and lipid hydroperoxides correlate with hsCRP levels, providing support for the interconnection between inflammation and oxidative stress in the pathogenesis of atherosclerosis.^{30,31} Although modifiable risk factors such as obesity and type 2 diabetes are major determinants of hsCRP levels, nonmodifiable risk factors such as African-American race and female gender have also been associated with elevated hsCRP levels.^{6,32} We have confirmed these findings in our cohort. In multivariable models, we also found that glutathione was an independent correlate of hsCRP levels, whereas CRP was not a predictor

of glutathione levels. Thus, our data suggest that oxidative stress may contribute to increases in inflammation, and that both of these atherogenic pathways are influenced by race and gender.

Our previous studies in selected smaller cohorts have demonstrated increased levels of aminothiol markers of oxidative stress in subjects with CVD risk factors.^{12,13,33,34} In this community-based cross-sectional study, we have confirmed this association, because we observed lower levels of glutathione and a more oxidized E_H glutathione in the presence of risk factors and with metabolic syndrome. More importantly, we have also demonstrated that African Americans have higher oxidative stress, even after adjusting for racial differences in individual risk factor burden.

Recent animal studies have confirmed a link between intracellular levels of aminothiol markers of oxidative stress and progression of atherosclerosis. In apolipoprotein E-deficient (apo E^{−/−}) mice exposed to metabolic stress, a significant inverse correlation was found between macrophage glutathione content and cell-mediated oxidation of LDL. In addition, supplementation with a specific inhibitor of glutathione synthesis resulted in a 59% increase in atherosclerotic lesion size.³⁵ Although these authors examined intracellular glutathione content and not plasma levels of glutathione, previous data indicate that release of glutathione from the intracellular to the extracellular space occurs as a function of intracellular tissue concentrations.³⁶ These authors identified a novel aminothiol-dependent mechanism associated with the development of atherosclerotic lesions and may be related to previous data from our group associating markers of oxidative stress with carotid intima media thickness.³³

Although our study has uniquely examined the relationship between race and aminothiol markers of oxidative stress, there are some limitations to our analysis. First, our data are cross-sectional and thus causality between racial differences in oxidative stress and disparities in CVD outcomes cannot be addressed specifically. Second, we did not measure other markers of oxidative stress such as

FIG. 1. (A) Box plot of glutathione levels by race and absence or presence of metabolic syndrome. The band near the middle of the box is the median, whereas the top and bottom of the box are the upper and lower quartiles, respectively. The circles represent outliers. (**) $P \leq 0.001$. (B) Box plot of oxidized glutathione (E_h glutathione) levels by race and absence or presence of metabolic syndrome. The band near the middle of the box is the mean, whereas the top and bottom of the box are ± 1 standard deviation, respectively. The circles represent outliers. (*) $P = 0.02$; (**) $P = 0.003$.

isoprostanes or lipid hydroperoxides. However, racial differences in these markers of oxidative stress have been previously reported.^{26,28} Furthermore, because biologic systems generate more nonradical oxidants than free radicals, it is imperative to consider redox systems biology, because the amino thiols are a critical component of oxidative stress that is distinct from free radical-mediated macromolecular damage. Finally, levels of glutathione may be affected by vegetable intake in the diet; however, we did not incorporate this information into our analysis.²⁹

In conclusion, African Americans had higher levels of amino thiol markers of systemic oxidative stress that were independent of traditional risk factor burden and inflammation. Furthermore, this racial disparity in oxidative burden was observed even in subjects who did not meet criteria for conventional risk assessment tools, like metabolic syndrome. The implications of our findings are that increased oxidative stress may contribute to observed racial disparities in CVD, because it is clear that traditional risk factors do not fully account for the observed differences. Estimation of oxidative stress with amino thiol markers may contribute to risk assessment, particularly in African Americans in whom traditional risk scores appear to underestimate their risk for future CVD events. Further studies are needed to confirm our findings in similar populations.

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Author Disclosure Statement

The authors have no financial conflicts of interest to disclose.

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