Metabolic Syndrome in African Americans: Implications for Preventing Coronary Heart Disease

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Summary: The metabolic syndrome represents a specific clustering of cardiovascular risk factors in the same individual (abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance, a prothrombotic state, and a proinflammatory state). Almost 50 million American adults (about one in four) have the metabolic syndrome, which puts them at increased risk for the development of diabetes mellitus and cardiovascular disease. African Americans, especially African-American women, have a high prevalence of the metabolic syndrome. This is attributable mainly to the disproportionate occurrence in African Americans of elevated blood pressure, obesity, and diabetes. Management of the metabolic syndrome consists primarily of modification or reversal of the root causes (overweight/obesity and physical inactivity) and therapy to reduce or control the risk factors. Although all components of the metabolic syndrome should be addressed, optimal control of atherogenic dyslipidemia and elevated blood pressure may reduce cardiovascular risk by more than 80%.

Key words: African Americans, cardiovascular disease, metabolic syndrome

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Introduction

Cardiovascular disease (CVD), the leading cause of death in all Americans, is highly prevalent in persons of African ancestry.¹ In fact, African Americans have the highest mortality rate from coronary heart disease (CHD) of any ethnic group, particularly out-of-hospital deaths, and especially at younger ages.^{1–3} Among possible reasons for the excess mortality among African Americans is the higher prevalence and greater degree of clustering of certain coronary risk factors in blacks than in whites (Fig. 1, Table 1).^{4,5} Several of these risk factors—notably obesity, hypertension, and type 2 diabetes mellitus—are also common to the metabolic syndrome.

The metabolic syndrome refers to a clustering of specific cardiovascular risk factors in the same individual.³ Almost 50 million American adults (about one in four) have the metabolic syndrome,⁶ which puts them at increased risk for the development of diabetes mellitus and CVD.⁷ Studies have confirmed that the metabolic syndrome may increase the risk of developing CVD by as much as 4-fold.^{8–13} Presence of the metabolic syndrome also increases morbidity and mortality in patients both with and without clinical evidence of CVD.^{9,12,13} Although the U.S. mortality rate from CVD has been decreasing over the past several decades, the increasing prevalence of obesity and the metabolic syndrome may, at least partially, reverse this trend.

Definition of the Metabolic Syndrome

The American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI) define the metabolic syndrome as a constellation of metabolic risk factors strongly associated with type 2 diabetes—atherogenic dyslipidemia (elevated triglycerides and apolipoprotein B, small low-density lipoprotein [LDL] particles, and low levels of high-density lipoprotein cholesterol [HDL-C]), elevated blood pressure, elevated plasma glucose, a prothrombotic state, and a proinflammatory state.⁸ The AHA/NHLBI identifies two underlying risk factors, or causes, for the metabolic syndrome as abdominal obesity and insulin resistance.⁸

FIG. 1 Risk-factor clustering by race and gender. Adapted from Ref. No. 4 with permission.

According to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), diagnosis of the metabolic syndrome can be made when three or more of five abnormalities are present, as shown in Table 2.^{3,8}

Prevalence of the Metabolic Syndrome in African Americans

Although the age-adjusted prevalence of the metabolic syndrome in all African Americans (21.6%) is similar to that in the overall US population (23.7%),⁶ African-American women have an approximately 57% higher prevalence of the metabolic syndrome than their male counterparts (25.7 vs. 16.4%, respectively) (Fig. 2).⁶ This higher prevalence is attributable mainly to the disproportionate occurrence of elevated blood pressure, type 2 diabetes, and obesity and physical inactivity, two root causes of the metabolic syndrome, in African-American women.⁵

TABLE 1 Cardiovascular risk factors more prevalent in African Americans than in whites

Associated with increased risk
Hypertension
Type 2 diabetes mellitus
Obesity
Cigarette smoking
Physical inactivity
Left ventricular hypertrophy
Associated with decreased risk
Higher levels of high-density lipoprotein cholesterol
Association with coronary heart disease risk unclear
Higher lipoprotein(a)

Source: Ref. No. 2.

TABLE 2 Clinical identification of the metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III^a

Risk factor	Defining level
Abdominal obesity (waist circumference)	
Men	> 102 cm (> 40 in)
Women	> 88 cm (> 35 in)
Triglycerides	≥ 150 mg/dl
HDL cholesterol	
Men	< 40 mg/dl
Women	< 50 mg/dl
Blood pressure	≥ 130/≥ 85 mmHg
Fasting glucose	≥ 100 mg/dl ^b

^a Diagnosis requires presence of 3 or more criteria.

^b Revised per the most recent American Diabetes Association definition.

Abbreviations: HDL = high-density lipoprotein, in = inches.

Components of the Metabolic Syndrome in African Americans

Abdominal Obesity

Although obesity is similarly prevalent in African-American and white men, it is twice as common in African-American as in white women.³ From 1988 to 2000, the age-adjusted prevalence of obesity increased by 11.5% in black women compared with 7.2% in white women.¹⁴ In addition, black women saw an average increase in waist circumference of 5.3 vs. 2.4 cm in white women.¹⁵ Obesity and overweight status increase the risk of CHD, hypertension, and type 2 diabetes in African Americans as well as in other racial/ethnic groups.⁷ However, abdominal (central), visceral, or predominantly upper-body distribution of body fat is a stronger risk factor for CVD than is obesity per se.¹⁶

FIG. 2 Age-adjusted prevalence of three or more risk factors for the metabolic syndrome in whites, African Americans, and Mexican Americans. Data from the third National Health and Nutrition Examination Survey, based on criteria of the National Cholesterol Education Program Adult Treatment Panel III; diabetics were included in diagnosis; overall unadjusted prevalence was 21.8%. Source: Ref. No. 6.

Atherogenic Dyslipidemia

The triad of lipid abnormalities referred to as “atherogenic dyslipidemia” consists of elevated triglycerides, decreased HDL-C levels, and a preponderance of small, dense LDL particles.^{3,8} An elevation in LDL cholesterol (LDL-C) is not a part of the metabolic syndrome, although abnormalities in LDL particle size are. In general, African Americans have lower total cholesterol levels than whites and a lower prevalence of hypercholesterolemia, according to population-based studies.² African Americans also have lower levels of triglycerides and small LDL particles than whites, and their LDL particle size is significantly larger and therefore less atherogenic.¹⁷ African-American men have higher levels of HDL-C than white men, although it is not known whether these higher levels protect against CHD.³

Elevated Blood Pressure

In African Americans, hypertension is more common, develops in younger age groups, and is associated with a 3- to 5-times higher cardiovascular mortality rate than in whites.^{2,7} Hypertension is a more potent predictor of CHD in black women than in other racial/gender groups and was associated with a nearly 5-fold increase in CHD risk in African-American women (vs. a 2-fold risk for African-American men) in the Atherosclerosis Risk in Communities study.¹⁸ African Americans appear to experience greater cardiovascular and renal damage at any level of blood pressure than whites, although some investigators have suggested that the higher mortality rates in hypertensive African Americans reflect greater disease severity and more left ventricular hypertrophy.¹⁹

Insulin Resistance/Elevated Plasma Glucose

African Americans are more insulin resistant than whites at a similar extent of adiposity.²⁰ The safest and most effective means for reducing insulin resistance in overweight and obese persons of any ethnicity is weight reduction and increased physical activity. Several available drugs (i.e., the thiazolidinediones and metformin) also appear to reduce insulin resistance. However, it has not yet been demonstrated that these drugs provide an associated decrease in CVD morbidity and mortality in patients with the metabolic syndrome. The benefits of the “insulin sensitizers” for glucose intolerance prior to the onset of frank diabetes, and their possible benefits on cardiovascular risk reduction, are being investigated in ongoing clinical trials.

Proinflammatory State

Levels of the inflammatory marker C-reactive protein (CRP) are increased in persons with the metabolic syndrome, are associated with the individual components of the metabolic syndrome, and add predictive information on cardiovascular risk at all levels of severity of the syndrome.^{3,10} African Americans have higher levels of CRP than whites (median CRP, 3.0 vs. 2.3 mg/l; $p < 0.001$), with African-American women hav-

ing higher levels than white women, black men, or white men (median CRP, 3.5 vs. 3.2, 2.1, and 1.7 mg/l, respectively; $p < 0.001$ for each comparison).²¹ Whether treating normocholesterolemic patients at high cardiovascular risk because of elevated CRP will be beneficial in preventing CVD is yet to be determined in ongoing clinical trials.²²

Prothrombotic State

A prothrombotic state (increased plasminogen activator inhibitor-1 and coagulation factors) may occur more frequently in African Americans, and fibrinogen levels are higher among African Americans than among whites, especially in persons with a family history of CHD or diabetes.^{23,24} In contrast, fibrinolysis may be enhanced in African Americans.²³ Therapies designed to resolve the metabolic abnormalities of the metabolic syndrome are likely to reduce hyperactivity of platelets, decrease the intensity of the prothrombotic state, and normalize the activity of the fibrinolytic system in the blood and vessel walls. Currently, low-dose aspirin is the only routinely recommended antithrombotic therapy for primary prevention of CVD.⁸ Clopidogrel may be beneficial in aspirin-intolerant patients.⁸

Therapeutic Approach to Metabolic Syndrome in African Americans

The cornerstones of therapy for the metabolic syndrome are weight reduction and increased physical activity, both of which can improve all components of the syndrome. Drug treatment is often necessary for the further improvement of blood pressure, lipids, and glucose, and thereby decreases the risk of CVD. While control of lipids and elevated blood pressure to normal levels may prevent up to 50% of CHD events, control to optimal levels may decrease CHD events by 80% or more.²⁴ Thus, African Americans with the metabolic syndrome, and those at high risk for the syndrome, should be targeted for intensive risk-reduction measures.

The NCEP ATP III guidelines state that LDL-C should be the primary target of lipid-modifying therapy in individuals with the metabolic syndrome. Intensive statin treatment is recommended for high-risk patients.²⁵ Very-high-risk patients—those with the metabolic syndrome or diabetes plus established CVD—are candidates for an optional LDL-C goal of < 70 mg/dl. Individuals at moderately high risk (e.g., metabolic syndrome without CVD) are candidates for the LDL-C goal of < 100 mg/dl.²⁵ When triglyceride levels are > 200 mg/dl, the ATP III guidelines recommend that very-low-density lipoprotein cholesterol be targeted by lowering non-HDL-C to 30 mg/dl higher than the LDL-C goal.³ The non-HDL-C goal can be achieved by intensifying the statin therapy chosen to reduce LDL-C.³ In high-risk patients with the metabolic syndrome, further modification of elevated triglycerides or low HDL-C can be achieved by combination therapy with a statin plus a fibrate or niacin, although the risk of developing myositis may be increased with these combinations.³

Although African Americans were notably absent from many of the large clinical outcome trials of lipid-lowering ther-

apy, the magnitude of LDL-C reduction with statins appears to be similar in blacks and whites.² Furthermore, in the lipid-lowering component of the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT), which enrolled 3,491 (38%) African Americans, statin therapy more effectively lowered the risk of CHD death and nonfatal myocardial infarction in blacks than in non-blacks (relative risk, 0.73 vs. 1.02; $p = 0.03$); the 27% relative reduction in CHD events among blacks treated with pravastatin compared with usual care was statistically significant.²⁶ The major contributor to this isolated positive outcome was that African-American hypertensive patients in the community were less likely to be treated with lipid-lowering drugs than their white counterparts. In the African American Rosuvastatin Investigation of Efficacy and Safety (ARIES) trial,²⁷ the first prospective, randomized, controlled trial comparing intensive lipid-lowering therapy in African Americans, aggressive statin treatment was effective and well tolerated. After 6 weeks of therapy, rosuvastatin 10 and 20 mg lowered LDL-C by 37 and 46%, respectively, compared with 32 and 39% reductions with atorvastatin 10 and 20 mg, and more rosuvastatin-treated patients (66 and 79%) than atorvastatin-treated patients (58 and 62%) achieved their NCEP ATP III LDL-C goal.

Conclusion

The metabolic syndrome is highly prevalent in the United States, currently affecting approximately one in four adults, and its prevalence is increasing. African Americans—especially African-American women—appear to be particularly predisposed to development of the syndrome. Patients with the metabolic syndrome are at high risk for the development of diabetes and accelerated CVD. Obesity, particularly abdominal obesity, is strongly related to the syndrome, and the rising epidemic of obesity in the United States is cause for particular concern. Since the root causes of the metabolic syndrome are reversible and the individual components modifiable, recognition of the metabolic syndrome in African Americans provides an opportunity for intensive risk reduction in this high-risk group of patients.

References

1. American Heart Association: *Heart Disease and Stroke Statistics—2005 Update*. Dallas, Texas: American Heart Association, 2005
2. Clark LT, Ferdinand KC, Flack JM, Gavin JR III, Hall WD, et al.: Coronary heart disease in African Americans. *Heart Dis* 2001;3:97–108
3. The Expert Panel: 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): Final report. *Circulation* 2002;106:3146–3421
4. Hutchinson RG, Watson RL, Davis CE, Barnes R, Brown S, et al.: Racial differences in risk factors for atherosclerosis: The ARIC Study. *Angiology* 1997;48:279–290
5. Hall WD, Clark LT, Wenger NK, Wright JT Jr, Kumanyika SK, et al.: The metabolic syndrome in African Americans: A review. *Ethn Dis* 2003;13:414–428
6. Ford ES, Giles WH, Dietz WH: Prevalence of the metabolic syndrome among US adults: Findings from the Third National Health and Nutritional Examination Survey. *J Am Med Assoc* 2002;287:356–359
7. Smith SC Jr, Clark LT, Cooper RS, Daniels SR, Kumanyika SK, et al.: Discovering the full spectrum of cardiovascular disease: Minority Health Summit 2003: Report of the Obesity, Metabolic Syndrome, and Hypertension Writing Group. *Circulation* 2005;111:e134–e139
8. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, et al.: Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112:2735–2752
9. Lakka H-M, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, et al.: The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *J Am Med Assoc* 2002;288:2709–2716
10. Ridker PM, Buring JE, Cook NR, Rifai N: C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: An 8-year follow-up of 14,719 initially healthy American women. *Circulation* 2003;107:391–397
11. Hunt KJ, Resendez RG, Williams K, Haffner SM, Stern MP: National Cholesterol Education Program versus World Health Organization metabolic syndrome in relation to all-cause and cardiovascular mortality in the San Antonio Heart Study. *Circulation* 2004;110:1251–1257
12. Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, et al.: Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001;24:683–689
13. Flegal KM, Carroll MD, Ogden CL, Johnson CL: Prevalence and trends in obesity among US adults, 1999–2000. *J Am Med Assoc* 2002;288:1723–1727
14. Okosun IS, Choi ST, Boltri JM, Parish DC, Chandra KMD, et al.: Trends of abdominal adiposity in white, black, and Mexican-American adults, 1988 to 2000. *Obes Res* 2003;11:1010–1017
15. Despres JP: The insulin resistance–dyslipidemic syndrome of visceral obesity: Effect on patients' risk. *Obes Res* 1998;6(suppl 1):8S–17S
16. Haffner SM, D'Agostino R Jr, Goff D, Howard B, Festa A, et al.: LDL size in African Americans, Hispanics, and non-Hispanic whites: The Insulin Resistance Atherosclerosis Study. *Arterioscler Thromb Vasc Biol* 1999;19:2234–2240
17. Jones DW, Chambless LE, Folsom AR, Heiss G, Hutchinson RG, et al.: Risk factors for coronary heart disease in African Americans: The Atherosclerosis Risk in Communities Study, 1987–1997. *Arch Intern Med* 2002;162:2565–2571
18. Liao Y, Cooper RS, McGee DL, Mensah GA, Ghali JK: The relative effects of left ventricular hypertrophy, coronary artery disease, and ventricular dysfunction on survival among black adults. *J Am Med Assoc* 1995;273:1592–1597
19. Haffner SM, D'Agostino R Jr, Saad MF, Rewers M, Mykkanen L, 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;45:742–748
20. Khera A, McGuire DK, Murphy SA, Stanek HG, Das SR, et al.: Race and gender differences in C-reactive protein levels. *J Am Coll Cardiol* 2005;46:464–469
21. Ridker PM: Rosuvastatin in the primary prevention of cardiovascular disease among patients with low levels of low-density lipoprotein cholesterol and elevated high-sensitivity C-reactive protein: Rationale and design of the JUPITER trial. *Circulation* 2003;108:2292–2297
22. Folsom AR, Qamhieh HT, Flack JM, Hilner JE, Liu K, et al.: Plasma fibrinogen: Levels and correlates in young adults: The Coronary Artery Risk Development in Young Adults (CARDIA) study. *Am J Epidemiol* 1993;138:1023–1036
23. Wong ND, Pio JR, Franklin SS, L'Italien GJ, Kamath TV, et al.: Preventing coronary events by optimal control of blood pressure and lipids in patients with the metabolic syndrome. *Am J Cardiol* 2003;91:1421–1426
24. Grundy SM, Cleeman JI, Bairey Merz CN, Brewer HB Jr, Clark LT, et al.: Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004;110:227–239
25. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group: Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs. usual care: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). *J Am Med Assoc* 2002;288:2998–3007
26. Ferdinand KC, Clark LT, Watson KE, Neal RC, Brown CD, et al.: for the ARIES Study Group: Comparison of efficacy and safety of rosuvastatin versus atorvastatin in African-American patients in a six-week trial. *Am J Cardiol* 2006;97:229–235