Impact of Obesity and the Metabolic Syndrome on Risk Factors in African American Stroke Survivors

A Report From the AAASPS

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Background: The rates of obesity and the metabolic syndrome and the impact on traditional vascular risk factors in African American stroke survivors are unknown.

Objective: To describe the relationships between body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters) and hypertension, dyslipidemia, and diabetes mellitus.

Design: We classified 1711 subjects as underweight (BMI, <18.5), normal (BMI, 18.5-24.9), overweight (BMI, 25.0-29.9), or obesity class 1 (BMI, 30.0-34.9), 2 (BMI, 35.0-39.9), or 3 (BMI, >40.0). We compared the proportions with hypertension, dyslipidemia, and diabetes mellitus and control of these factors by clinical history and results of physical examination and laboratory analysis across BMI groups.

Setting: Multicentered clinical trial.

Patients: African American subjects with previous ischemic stroke.

Main Outcome Measures: Rates of obesity and the metabolic syndrome, odds ratios (ORs) of associated vascular risk factors at baseline, and relationship to longitudinal risk factor control.

Results: Overall, 76% were overweight or obese (70% of men and 81% of women). Hypertension, dyslipidemia, and diabetes mellitus were all present in 43.3% of men and 29.1% of women with obesity class 3. The ORs for having the metabolic syndrome were 2.14 (95% confidence interval [CI], 1.52-3.01) for class 1, 1.92 (95% CI, 1.26-2.91) for class 2, and 1.98 (95% CI, 1.27-3.09) for class 3 obesity. In addition, increasing BMI was negatively associated with systolic (P<.001) and diastolic (P<.001) blood pressure and glycemic control (P<.001).

Conclusion: Our analysis of the data from the African American Antiplatelet Stroke Prevention Study supports the association of increasing risk factor profiles with increasing weight in African American stroke survivors.

Arch Neurol. 2005;62:386-390

The coexistence of abdominal obesity, DL, HTN, and insulin resistance is known as the metabolic syndrome.9 The NHANES III reported the age-adjusted prevalence of the metabolic syndrome in the United States to be nearly 24%.10 Little information exists regarding the impact of body mass index (BMI) on the presence and control of vascular risk factors in stroke survivors. Our objective was to describe the rates of obesity and the metabolic syndrome and their relationship to HTN, DL, and diabetes mellitus (DM) in African American stroke survivors.

METHODS

The African American Antiplatelet Stroke Prevention Study (AAASPS) is a multicenter,
double-blind, randomized clinical trial comparing ticlopidine hydrochloride, 250 mg twice a day, with aspirin, 325 mg twice a day, in the prevention of recurrent stroke, myocardial infarction, and vascular death. Patients with cardioembolic stroke and symptomatic carotid artery stenosis requiring endarterectomy were excluded. The AAASPS enrolled 1809 subjects from December 12, 1995, through October 1, 2001. Baseline evaluations were performed a mean of 45 days from the eligibility stroke. Each subject underwent a history, physical examination, and laboratory assays including complete metabolic and lipid profiles.

The BMI was defined as baseline weight in kilograms divided by the square of the height in meters. The BMI results were categorized by the following classification scheme of the National Heart, Lung, and Blood Institute: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), class 1 obesity (30.0–34.9), class 2 obesity (35.0–39.9), and class 3 obesity (>40.0).

Hypertension was defined as a blood pressure of greater than 140/90 mm Hg, use of antihypertensive medication, or a self-reported history of HTN. According to protocol, blood pressure was to be measured in the right arm at heart level with an appropriate-sized cuff after being seated for 5 minutes and at least 30 minutes after the ingestion of caffeine or after smoking. The average of 2 measurements at least 2 minutes apart was recorded, and further measurements were obtained if the initial difference was greater than 5 mm Hg.

Diabetes mellitus was defined as a casual plasma glucose level of greater than 200 mg/dL (>11.1 mmol/L), the use of insulin or oral hypoglycemic agents, or a self-reported history of DM. The glucose value of greater than 200 mg/dL (>11.1 mmol/L) was used in accordance with the American Diabetic Association recommendation for identification of DM in nonfasting plasma specimens.

Dyslipidemia was defined in accordance with the criteria of the Second Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults as a total cholesterol level of greater than 240 mg/dL (>6.2 mmol/L) or a high-density lipoprotein level of less than 35 mg/dL (<0.9 mmol/L), the use of medication to lower lipid levels, or a self-reported history of hypercholesterolemia.

The proportions of subjects with HTN, DM, DL, a combination of any 2, and all 3 vascular risk factors were determined and compared across BMI groups. The metabolic syndrome was defined as the presence of obesity, HTN, DM, and DL.

Multivariate logistic regression methods were used to estimate ORs by BMI category using those subjects with normal weight as the reference group. Backward elimination techniques were used to assess the influence of covariates such as BMI category, sex, age group (<55 vs ≥55 years), and smoking status (never smoked vs past or current smoker) on the presence of HTN, DM, DL, a combination of any 2, or all 3 risk factors. The criterion for a covariate to remain in the model was P<0.05. With respect to DM, an additional covariate considered in the analyses was presence of DL, as DM could influence the presence of DL. Stability of the resulting estimates is reflected by 95% confidence intervals (CIs). Clinically meaningful interactions were included in all of the models considered. We used χ² analysis to compare proportions in BMI groups by stroke subtype. Longitudinal analysis methods were used to assess the relationship between BMI and blood pressure and levels of cholesterol and glucose over time, taking into account within- and between-subject variability with respect to the time-varying covariates. We performed Cox proportional hazards regression analyses to assess the relationship between BMI and recurrence. For all analyses, statistical significance is defined as P<.05.

**RESULTS**

Of 1809 subjects enrolled in the AAASPS, 1711 had baseline height and weight recorded. The baseline characteristics are shown in Table 1. Overall, 76% of subjects (70% of men and 81% of women) were overweight or obese. Extreme obesity (class 3) was seen in 19.5% of women younger than 55 years and in 7.0% of men in the same age group (Table 2). There were no differences in proportions across BMI categories by stroke subtype.

Presence of DM increased with increasing BMI for both sexes. Although the proportion with HTN was high for all weight categories, a more modest but similar relationship was seen. The proportion with DL increased with increasing BMI for men but was stable across normal and higher weight categories for women. All 3 risk factors were present in 26.1%, 29.4%, and 43.3% of men and 34.7%, 31.3%, and 29.1% of women with obesity classes 1, 2, and 3, respectively (Table 3).

Logistic regression analyses resulted in several covariates being statistically significant. For the presence of DM and HTN, BMI group, age, sex, and smoking status were significant. For the presence of DL and any 2 risk factors, BMI group, age group, and sex were significant. For the presence of all 3 risk factors, BMI group, sex, and smoking status were significant. Interaction analyses showed a significant interaction between sex and age group with respect to the presence of HTN, DL, and any 2 risk factors.

After adjustment for age, sex, and smoking status, referred to those with normal BMI, the OR of having DM across BMI categories increased from 1.74 (95% CI, 1.32–2.29) for overweight to 2.77 (95% CI, 1.84–4.16) for obesity class 3. The OR of having HTN ranged from 1.71 (95% CI, 1.05–2.78) for overweight to 2.79 (95% CI, 1.04–7.48) for obesity class 3. However, only a modest association was seen for DL (overweight OR, 1.41 [95% CI, 1.09–1.83]; obesity class 3 OR, 1.29 [95% CI, 0.87–1.97]).

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**Table 1. Baseline Characteristics of 1711 AAASPS Subjects With Available BMI Data**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>61.3 ± 10.6</td>
</tr>
<tr>
<td>Median (range)</td>
<td>61 (28-89)</td>
</tr>
<tr>
<td>Female</td>
<td>53.4</td>
</tr>
<tr>
<td>History</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>9.2</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>3.6</td>
</tr>
<tr>
<td>Peripheral arterial vascular surgery</td>
<td>1.6</td>
</tr>
<tr>
<td>Current cigarette smoking</td>
<td>38.3</td>
</tr>
<tr>
<td>Regular exercise</td>
<td>37.5</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
</tr>
<tr>
<td>Large-vessel atherothrombotic</td>
<td>19.7</td>
</tr>
<tr>
<td>Small-vessel occlusive</td>
<td>67.5</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>12.8</td>
</tr>
</tbody>
</table>

Abbreviations: AAASPS, African American Antiplatelet Stroke Prevention Study; BMI, body mass index. (Calculated as weight in kilograms divided by the square of height in meters).

*Unless otherwise indicated, data are expressed as percentage of subjects.
The odds of meeting criteria for the metabolic syndrome nearly doubled for all categories of obesity (class 1 OR, 2.14 [95% CI, 1.52-3.01]; class 2 OR, 1.92 [95% CI, 1.26-2.91]; and class 3 OR, 1.98 [95% CI, 1.27-3.09]) (Table 4).

The longitudinal analyses indicated that control of systolic blood pressure ($P < .001$), diastolic blood pressure ($P < .001$), and glucose level ($P < .001$), when measured over time, are negatively associated with increasing BMI. There was no association between increasing BMI and total cholesterol level over time ($P = .65$). Body mass index did not significantly influence recurrence in univariate models adjusting for typical covariates such as hypertension status, sex, age, and study treatment assignment.

### Table 2. Proportions of 1711 Subjects by BMI

<table>
<thead>
<tr>
<th>Sex, Age, y</th>
<th>No. of Subjects</th>
<th>Underweight (≤ 18.5)</th>
<th>Normal (18.5-24.9)</th>
<th>Overweight (25.0-29.9)</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men &lt;55</td>
<td>798</td>
<td>0.8</td>
<td>29.0</td>
<td>40.0</td>
<td>20.2</td>
</tr>
<tr>
<td>≥55</td>
<td>913</td>
<td>1.1</td>
<td>18.2</td>
<td>28.9</td>
<td>25.0</td>
</tr>
<tr>
<td>Women &lt;55</td>
<td>236</td>
<td>0.0</td>
<td>17.4</td>
<td>23.3</td>
<td>22.0</td>
</tr>
<tr>
<td>≥55</td>
<td>677</td>
<td>1.5</td>
<td>18.5</td>
<td>30.9</td>
<td>26.0</td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).

### Table 3. Proportions of Risk Factors for 1711 Subjects by BMI

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Underweight (≤ 18.5)</th>
<th>Normal (18.5-24.9)</th>
<th>Overweight (25.0-29.9)</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>16.7</td>
<td>25.5</td>
<td>38.2</td>
<td>41.0</td>
</tr>
<tr>
<td>HTN</td>
<td>66.7</td>
<td>84.0</td>
<td>85.0</td>
<td>88.8</td>
</tr>
<tr>
<td>DL</td>
<td>33.3</td>
<td>49.4</td>
<td>63.0</td>
<td>65.2</td>
</tr>
<tr>
<td>Any 2 risk factors</td>
<td>16.7</td>
<td>35.1</td>
<td>49.5</td>
<td>46.6</td>
</tr>
<tr>
<td>All 3 risk factors</td>
<td>16.7</td>
<td>14.7</td>
<td>20.4</td>
<td>26.1</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); DL, dyslipidemia; DM, diabetes mellitus; HTN, hypertension.

The rate of obesity in our report of African American stroke survivors enrolled in a clinical trial of stroke prevention is consistent with rates seen in large-scale cross-sectional studies in the United States. Overall, 76% of the AASPS subjects were overweight and 42% of those were classified as obese. These rates in African American subjects are notably higher than in their non-Hispanic white counterparts, ie, 21% in the Behavioral Risk Factor Surveillance Study and 29% in NHANES 1999-2000.

Not surprisingly, AASPS subjects had higher overall rates of vascular risk factors than the general population because they had previous stroke. A metabolic syndrome was seen in 21% of men and 29% of women in the AASPS. Although BMI was not an independent predictor of stroke recurrence, obesity nearly doubled the odds of having a metabolic syndrome compared with the odds of those with normal BMI having DM, HTN, and DL. Furthermore, increasing BMI had a negative association with blood pressure and glycemic control.

Several limitations of our study must be acknowledged. Although use of BMI is a good indicator of total
body fat storage, abdominal adiposity may better correlate with disease. Body mass index may also be less indicative of body fat in men due to increased muscle mass compared with women and in athletes who may have more lean body mass. However, among men it can be reasonably assumed that increasing BMI is associated with increasing adiposity. In addition, the mean age in the AAASPS was 61 years, and only about a third of subjects reported regular exercise, suggesting against confounding by lean body mass due to athleticism. Furthermore, the phenotypic distribution of adipose tissue in African American men and women may be unique compared with that of their counterparts in other racial/ethnic groups, limiting the ability to generalize our data across all groups.

In addition, with respect to the logistic regression analyses, we obtained concordance rates of 58.3% for DM, 64.0% for HTN, 53.0% for DL, 52.0% for the presence of any 2 risk factors, and 56.7% for the presence of all 3 risk factors. These modest concordance rates indicate that although the covariates identified above were significant, a sizable proportion of the likelihood governing the occurrence of these events remains unexplained.

Furthermore, the definition of DL in the metabolic syndrome varies in the literature. The Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults considers elevated triglyceride levels to be a component of the metabolic syndrome, along with decreased high-density lipoprotein levels. However, the AAASPS protocol did not require fasting laboratory specimens and triglyceride levels, which may be more sensitive to temporal dietary influence than total cholesterol or high-density lipoprotein levels. The AAASPS also excluded patients with carotid stenosis requiring endarterectomy, which may have limited our ability to detect a correlation with serum lipid levels. There may also be an acute-phase influence on lipid and glucose levels. However, the mean time from the entry stroke to enrollment was 45 days. Therefore, this effect would not likely have had an adverse impact on our laboratory values. Furthermore, this interval may have had a favorable impact on laboratory values through treatment initiation before hospital discharge, thus obscuring a relationship with increasing BMI.

Our data support the association of increasing risk factor profiles and decreasing risk factor control with increasing weight. This is particularly important in African American stroke survivors, as this group has been shown to have a worse risk factor profile than their non–African American counterparts, putting them at high risk for recurrent stroke. Furthermore, the high morbidity and mortality due to stroke in African Americans should make this an increasing area of public health concern. Clinical investigation of a structured weight loss program to evaluate for improved risk factor control and the reduction of vascular events is warranted.

Accepted for Publication: May 25, 2004.
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Funding/Support: This study was supported in part by grant RO1 NS33430 from the National Institutes of Health/National Institute of Neurological Disorders and Stroke, Bethesda, Md (Dr Gorelick).

References


