Abdominal Obesity and Risk of Ischemic Stroke
The Northern Manhattan Stroke Study

Seung-Han Suk, MD, PhD; Ralph L. Sacco, MS, MD; Bernadette Boden-Albala, DrPH; Jian F. Cheun, MS, MD; John G. Pittman, MS; Mitchell S. Elkind, MS, MD; Myunghee C. Paik, PhD

Background and Purpose—Obesity is well recognized as a risk factor for coronary heart disease and mortality. The relationship between abdominal obesity and ischemic stroke remains less clear. Our aim was to evaluate abdominal obesity as an independent risk factor for ischemic stroke in a multiethnic community.

Methods—A population-based, incident case-control study was conducted July 1993 through June 1997 in northern Manhattan, New York, NY. Cases (n=576) of first ischemic stroke (66% ≥65 years of age; 56% women; 17% whites; 26% blacks; 55% Hispanics) were enrolled and matched by age, sex, and race-ethnicity to stroke-free community controls (n=1142). All subjects were interviewed and examined and had measurements of waist-to-hip ratio (WHR). Odds ratios (ORs) of ischemic stroke were calculated with gender-specific quartiles (GQs) and gender-specific medians of WHR adjusted for stroke risk factors and body mass index (BMI).

Results—Compared with the first quartile, the third and fourth quartiles of WHR had an increased risk of stroke (GQ3: OR, 2.4; 95% CI, 1.5 to 3.9; GQ4: OR, 3.0; 95% CI, 1.8 to 4.8) adjusted for other risk factors and BMI. Those with WHR equal to or greater than the median had an overall OR of 3.0 (95% CI, 2.1 to 4.2) for ischemic stroke even after adjustment for other risk factors and BMI. Increased WHR was associated with a greater risk of stroke in men and women and in all race-ethnic groups. The effect of WHR was stronger among younger persons (test for heterogeneity, $P<0.0002$) (<65 years of age: OR, 4.4; 95%CI, 2.2 to 9.0; ≥65 years of age: OR, 2.2; 95% CI, 1.4 to 3.2). WHR was associated with an increased risk among those with and without large-artery atherosclerotic stroke.

Conclusions—Abdominal obesity is an independent, potent risk factor for ischemic stroke in all race-ethnic groups. It is a stronger risk factor than BMI and has a greater effect among younger persons. Prevention of obesity and weight reduction need greater emphasis in stroke prevention programs. **(*Stroke*. 2003;34:1586-1592.)**

Key Words: body constitution ■ epidemiology ■ obesity ■ risk factors ■ stroke

The prevalence of Americans who are overweight or obese rapidly increased from 47% to 61% between 1980 and 1999.[1] The impact of obesity on public health is a growing concern because obesity is well recognized to be related to many diseases such as type 2 diabetes mellitus, hypertension, dyslipidemia, gall bladder disease, respiratory disease, sleep apnea, and cancer.[2–4] The unfavorable effect of obesity on coronary heart disease[5–7] and all-cause mortality[8–12] is well recognized. In addition, abdominal obesity measured by waist-to-hip ratio (WHR) is related to an increased risk of coronary artery disease.[13,14] The relationship between obesity and ischemic stroke, however, remains less clear.

In the most recent guideline statements for healthcare professionals from the Stroke Council of the American Heart Association, obesity was categorized as a "less well documented or potentially modifiable risk factor."[15] Several studies have shown an association of obesity as defined by body mass index (BMI) with the risk of stroke. The Honolulu Heart Program reported that BMI was associated with increased risk of thromboembolic stroke among nonsmoking men in older middle age.[16] In the Framingham Heart Study, an association between metropolitan relative weight and atherothrombotic stroke was found in women but not in men.[5] The Nurses' Health Study showed that women with increased BMI had an increased risk of ischemic stroke, but not after adjustment for hypertension, diabetes mellitus, and high cholesterol.[17] In contrast, other studies have failed to find an independent relationship between obesity measured by BMI and increased risk of stroke in women[18–20] or men.[21,22] Therefore, the association of obesity with stroke remains controversial. Furthermore, BMI may not be a good indicator of stroke risk.

Few studies have examined the relationship between abdominal obesity defined by WHR and stroke. Swedish

Received November 18, 2002; final revision received January 27, 2003; accepted January 29, 2003.

From the Department of Neurology (S.-H.S., R.L.S., B.B.-A., J.F.C., J.G.P., M.S.E.), Sergievsky Center (R.L.S.), Department of Socio-Medical Science (B.B.-A.), and Department of Biostatistics (J.F.C., M.C.P.), Columbia University College of Physicians and Surgeons and the Mailman School of Public Health, New York, NY; and the Department of Neurology, Wonkwang University College of Medicine, Chonpuk, South Korea (S.-H.S.)

Presented in part at the 27th International Stroke Conference, February 6-9, 2002.

Correspondence to Ralph L. Sacco, MD, Neurological Institute, 710 W 168th St, New York, NY 10032. E-mail rls1@columbia.edu

***Stroke* is available at http://www.strokeaha.org** **DOI: 10.1161/01.STR.0000075294.98582.2F**

investigators suggested that increased WHR may be a risk factor for stroke in women[19] and men,[20] but these results were limited by small numbers of cases. The Health Professionals Follow-Up Study showed that the highest quintile of WHR was associated with an increased risk of stroke among men but did not ascertain the effect of hypertension, diabetes, and hyperlipidemia on stroke.[22] Therefore, the information about abdominal obesity as a risk factor for ischemic stroke is very limited, and to date, there has been no study in a multiethnic population in which obesity may be more prevalent.

The purpose of this study was to determine whether abdominal obesity is independently associated with an increased risk of ischemic stroke among white, black, and Hispanic subjects living in the same community. We also examined whether the effect of abdominal obesity differed by age, sex, race-ethnicity, and subtype of ischemic stroke.

Methods

Selection of Cases

We conducted a population-based case-control study in the northern Manhattan community. The methods for case detection in the Northern Manhattan Stroke Study (NOMASS) have been described previously.[23] Briefly, 688 incident cases were prospectively enrolled between July 1, 1993, and June 30, 1997, if they were (1) diagnosed as having a first cerebral infarction, fatal or nonfatal; (2) >39 years of age at onset of stroke; and (3) a resident of northern Manhattan for >3 months in a household with telephone. Patients with intracerebral or subarachnoid hemorrhage and transient ischemic attack were excluded from this analysis.

Case surveillance included screening of all admissions, discharges, and head CT scans at the Columbia-Presbyterian Medical Center (CPMC), the only hospital in the community. Cases were also identified through discharge lists from other area hospitals and through a comprehensive community-based surveillance system for nonhospitalized persons with stroke. Stroke patients not admitted to CPMC were invited to come to CPMC for enrollment in the study.

Waist and hip circumferences were not obtained in 112 subjects (16%); therefore, 576 cases were included in this analysis. We had to exclude 112 subjects predominantly because of an inability to obtain waist and hip measures among those who were confined to bed. To detect any systematic bias among these 576 cases, we compared baseline variables available between the studied cases and the rest of the cohort. No significant differences between demographics, risk factors, and BMI in the study sample and the overall NOMASS case population were detected.

Selection of Controls

The methods of control recruitment and enrollment have been described elsewhere.[24] Stroke-free subjects residing in the northern Manhattan community were recruited by random-digit dialing using dual frame sampling to identify both published and unpublished telephone numbers. When a household was contacted, the research objectives were explained. Participants were interviewed briefly to record age, sex, race-ethnicity, and risk factors if they (1) had never been diagnosed with stroke, (2) were ≥39 years of age, and (3) resided in northern Manhattan for >3 months in a household with a telephone. These telephone interviews were performed by Audits and Surveys, Inc (New York, NY). The telephone response rate was 91%.

Telephone interview data from control-eligible subjects were downloaded to the NOMASS computer system and assigned to cells defined by age, sex, and race-ethnicity. Control subjects were randomly selected from cells matched to the accumulating case group by age, sex, and race-ethnicity. Of those who provided answers to the telephone survey, 75% participated in an in-person evaluation. The subjects who participated in the in-person evaluation were similar to the total telephone population in terms of age, demographics, and vascular risk factors. For this analysis, 80% of the cases were matched to 2 controls, and 12% were matched to 1 control; 8% were matched to other case-control strata by age within 5 years, sex, and race-ethnicity.

Index Evaluation of Cases and Controls

Using standard data collection instruments, bilingual research assistants collected data through interview and medical record review of cases and controls. Study physicians performed physical and neurological examinations, and in-person measurements and fasting blood specimens for lipid and glucose measurements were performed as described elsewhere.[25] In-person evaluations of cases and controls were performed at the medical center or at home for those who could not come in person or who had a nonhospitalized stroke. When the study subject was unable to provide answers, a proxy knowledgeable about the patient's history was interviewed. Race-ethnicity, hypertension, diabetes mellitus, any cardiac disease, any physical activity, moderate alcohol use, and smoking status were defined through the use of standard criteria as previously described.[24,25]

From the results of a comprehensive neurovascular evaluation of the patients, cases of ischemic stroke were classified into infarct subtype categories. Subtypes of cerebral infarction were determined after review of all available data by a diagnostic committee as described elsewhere.[26] Infarct subtypes were classified on the basis of a modified National Institute of Neurological Disorders and Stroke data bank criteria as lacunar, extracranial atherosclerosis, intracranial atherosclerosis, cardioembolic, cryptogenic, or infarct resulting from other known causes. Infarcts related to extracranial atherosclerosis required carotid or vertebral artery occlusion or moderate to severe stenosis (>60%) correlating with the territory of infarction. Infarcts related to intracranial atherosclerosis required intracranial large artery stenosis or occlusion (by cerebral angiography, MR angiography, or transcranial Doppler studies) correlating with the territory of infarction. Lacunar infarcts showed brain imaging evidence of a small, deep infarct or a normal repeated brain image, normal or minimal large-artery stenosis, and no source of cardioembolism. Cardioembolic infarcts required documentation of atrial fibrillation or flutter, valvular heart disease, cardiac intraluminal thrombus, cardiomyopathy, recent (<6 months) myocardial infarction, bacterial or marantic endocarditis, atrial myxoma, or pulmonary vein thrombosis. Cryptogenic infarcts did not meet criteria for infarcts of determined cause or may have had inadequate evaluation that makes diagnostic classification difficult. For this analysis, cases were divided into 2 groups: cerebral infarction resulting from large-artery (extracranial or intracranial) atherosclerosis and the combination of the other categories (lacune, cardioembolism, cryptogenic, and other infarction).

Anthropometric Assessment

Cases and controls had waist and hip circumference measurements (in inches) performed by trained research assistants using flexible measuring tape. These circumferences were measured with participants standing and relaxed without heavy outer garments. Measurements were done supine among those cases who were unable to stand. Waist circumference was measured at the level of the umbilicus, and hip circumference was measured at the level of the bilateral greater trochanters. WHR was defined as waist divided by hip circumference. Height (in inches) and weight (in pounds) were measured with a standard scale. In <5% of subjects, height and weight measurements were obtained from medical record review or self-report. BMI was calculated as weight in kilograms divided by height squared in meters after transformation.

Statistical Analysis

Statistical analyses were performed with SAS software (SAS Institute). Simple and multiple conditional logistic regression models for matched case-control data were used to calculate the odds ratio (OR) and 95% confidence interval (CI) for gender-specific quartiles (GQs) and gender-specific medians of WHR and ischemic stroke. Adjusted

TABLE 1. Distribution of Demographics and Vascular Risk Factors Among Cases and Controls in NOMASS

Characteristics	Cases (n=576), n (%)	Controls (n=1142), n (%)
Age ≥65 y	381 (66)	807 (71)
Women	320 (56)	691 (61)
Race-ethnicity		
Hispanic	322 (55)	517 (46)
Black	150 (26)	359 (31)
White	95 (17)	56 (22)
Other	9 (2)	10 (1)
Hypertension*‖	488 (85)	810 (71)
Diabetes‖	190 (33)	228 (20)
Any cardiac disease‖	227 (39)	296 (26)
Current smoking status	114 (21)	198 (18)
Moderate alcohol use‡‖	115 (20)	337 (30)
No physical activity†‖	325 (66)	347 (30)
Obesity§‖	118 (21)	305 (27)
Education higher than high school‖	177 (31)	559 (49)

*Self-report of a history of hypertension, use of an antihypertensive agent, systolic blood pressure recording ≥140 mm Hg, or diastolic blood pressure recording ≥90 mm Hg based on the average of the 2 blood pressure measures.

†No participation in leisure physical activities within the prior 2 wk.

‡1 drink/mo to ≤2 drinks/d on average over the past year.

§BMI ≥30 kg/m^2.

‖$P<0.01$.

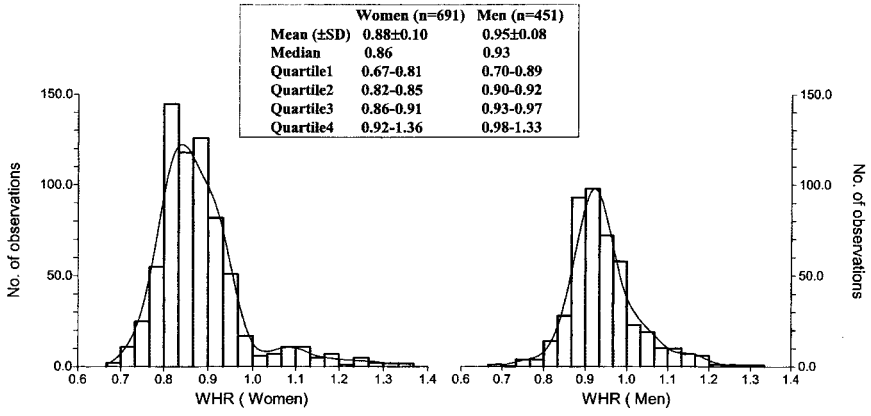
ORs were calculated after adjustment for potential confounding factors (hypertension, diabetes, low-density lipoprotein [LDL] cholesterol, high-density lipoprotein [HDL] cholesterol, any cardiac disease, no physical activity, current smoking, moderate alcohol use, and education level) and BMI. Age, sex, race-ethnicity, and stroke subtype strata were evaluated. Tests for heterogeneity were done to assess statistically significant differences between ORs in the stratified analyses.

Results

A total of 576 ischemic stroke cases and 1142 controls were evaluated in this analysis. Table 1 shows the demographics and distribution of stroke risk factors in cases and controls. Among the cases, 67% were ≥65 years of age; 56% were women; 55% were Hispanic; 26% were black; 17% were white; and 2% were other. The prevalence of obesity, defined by BMI, was slightly greater among controls than cases in our univariate analysis. Among our stroke-free community subjects, waist circumference was highly correlated with BMI ($r=0.58$, $P<0.0001$), whereas WHR was relatively independent of BMI ($r=0.09$, $P<0.0001$).

The Figure shows the frequency distribution, mean, median, and quartiles of WHR in male and female controls. The mean and median WHRs were greater for men than for women. Therefore, we categorized WHR into GQ and medians. In a simple model unadjusted for stroke risk factors, the ORs for ischemic stroke of WHR GQ2, GQ3, and GQ4 compared with GQ1 were 1.3 (95% CI, 0.9 to 2.0), 3.4 (95% CI, 2.4 to 4.9), and 5.1 (95% CI, 3.6 to 7.4), respectively. In multivariate analysis matched for age, sex, and race-ethnicity and adjusted for stroke risk factors, WHR GQ3 (adjusted OR, 2.3; 95% CI, 1.5 to 3.6) and GQ4 (adjusted OR, 2.6; 95% CI, 1.6 to 4.1) were associated with an increased risk for ischemic stroke (Table 2). In a subsequent multivariate analysis matched for age, sex, and race-ethnicity and adjusted for stroke risk factors except HDL, LDL, and physical inactivity, WHR GQ3 (adjusted OR, 2.7; 95% CI, 1.8 to 4.1) and GQ4 (adjusted OR, 3.7; 95% CI, 2.4 to 9.8) were more strongly associated with an increased risk of ischemic stroke. In analyses adjusted for BMI and stroke risk factors, GQ3 and GQ4 still had statistically significant ORs of 2.4 (95% CI, 1.5 to 3.9) and 3.0 (95% CI, 1.8 to 4.8) for ischemic stroke, respectively.

Because GQ2 was not associated with an increased risk and both GQ3 and GQ4 exerted a similar increased risk of ischemic stroke, further analyses were done using the gender-specific medians of WHR (men, 0.93; women, 0.86). Compared with those with WHR less than the gender-specific median, those with WHR greater than or equal to gender-specific medians had an increased ischemic stroke risk (unadjusted OR, 3.7; 95% CI, 2.8 to 4.8). After adjustment for stroke risk factors, the association was attenuated (adjusted OR, 2.8; 95% CI, 2.0 to 4.0). After further adjustment for BMI, the association did not change (adjusted OR, 3.0; 95% CI, 2.1 to 4.2) (Table 2). No interactions were observed between WHR and hypertension or diabetes. No significant association was observed between stroke and waist circumference as a continuous variables or using gender-specific cut



Frequency distribution of WHR for female and male community controls: NOMASS.

TABLE 2. Association of Ischemic Stroke With GQs and Gender-Specific Medians of WHR in NOMASS

	Unadjusted*		Adjusted for Risk Factors†		Adjusted for Risk Factors† and BMI	
	OR	95% CI	OR	95% CI	OR	95% CI
GQ1	1.0	...	1.0	...	1.0	...
GQ2	1.3	0.9–2.0	0.8	0.4–1.3	0.8	0.5–1.4
GQ3	3.4	2.4–4.9	2.3	1.4–3.6	2.4	1.5–3.9
GQ4	5.1	3.6–7.4	2.6	1.6–4.1	3.0	1.8–4.8
Dichotomous‡	3.7	2.8–4.8	2.8	2.0–4.0	3.0	2.1–4.2

*Matched by age, sex, and race-ethnicity.

†Matched by age, sex, and race-ethnicity and adjusted for hypertension, diabetes mellitus, any cardiac disease, current smoking status, no physical activity, moderate alcohol drinking, level of LDL cholesterol, level of HDL cholesterol, and education.

‡Dichomotous analyses were performed using the gender-specific medians of WHR as the cut point in conditional logistic regression models. Gender-specific medians of WHR: men ≥0.93, women ≥0.86.

points based on National Heart, Lung and Blood Institute guidelines (women, >35 in; men, >40 in).[4]

When the effect of WHR on ischemic stroke was stratified by sex, men with WHR ≥0.93 and women with WHR ≥0.86 had significantly increased risks of ischemic stroke in simple and multivariate models (Table 3). In analyses adjusted for risk factors and BMI, the risk among men (OR, 3.8; 95% CI, 1.8 to 5.0) was greater ($z=2.9$, $P<0.0038$) than that among women (OR, 2.5; 95% CI, 1.6 to 4.0). The influence of WHR on risk of ischemic stroke also differed by age (Table 3). The OR among those <65 years of age (OR, 4.4; 95% CI, 2.2 to 9.0) was greater ($z=4.1$, $P<0.0002$) than among those ≥65 years of age (OR, 2.2; 95% CI, 1.4 to 3.2) in dichotomous analysis adjusted for risk factors and BMI.

In analyses stratified by race-ethnicity, WHR was associated with an increased risk of ischemic stroke among non-Hispanic whites, Hispanics, and non-Hispanic blacks after adjustment for stroke risk factors and BMI (Table 3). The point estimates of the OR among whites and Hispanics appeared slightly greater than that among blacks, but the difference was not statistically significant, and the impact of WHR on ischemic stroke was similar among the 3 race-ethnic groups.

When ischemic stroke was stratified by stroke subtype, there was an unfavorable effect of high WHR on all stroke subtypes in simple and multivariate analyses (Table 4). The association in an unadjusted model was greater in those with large-artery atherosclerotic subtype compared with the other subtypes. After adjustment for risk factors and BMI, the association appeared to be similar for those with and those without large-artery atherosclerotic stroke subtypes.

Discussion

Our data show a significant and independent association between ischemic stroke and abdominal obesity as defined by

TABLE 3. Association of Ischemic Stroke With WHR Greater Than the Gender-Specific Medians Stratified by Sex, Age, and Race-Ethnicity in NOMASS

	Unadjusted*		Adjusted for Risk Factors†		Adjusted for Risk Factors† and BMI	
Variable	OR	95% CI	OR	95% CI	OR	95% CI
Sex						
Women	3.3	2.4–4.5	2.6	1.7–4.2	2.5	1.6–4.0
Men	4.3	2.8–6.7	3.2	1.9–5.5	3.8	1.8–5.0
Age, y						
<65	5.7	3.4–9.6	4.4	2.3–8.9	4.4	2.2–9.0
≥65	2.8	2.1–3.8	2.1	1.4–3.1	2.2	1.4–3.2
Race-ethnicity						
White	4.0	2.1–7.5	3.3	1.3–8.2	3.3	1.3–8.6
Hispanic	3.6	2.5–5.2	3.0	1.9–4.7	3.4	2.1–5.4
Black	3.3	2.1–5.4	2.5	1.3–4.8	2.4	1.3–4.7

Gender-specific medians of WHR: men ≥0.93, women ≥0.86.

*Matched by age, sex, and race-ethnicity.

†Matched by age, sex, and race-ethnicity and adjusted for hypertension, diabetes mellitus, any cardiac disease, current smoking status, no physical activity, moderate alcohol drinking, level of LDL cholesterol, level of HDL cholesterol, and education.

TABLE 4. Association of Ischemic Stroke With WHR Greater Than the Gender-Specific Medians Stratified by Stroke Subtype

	Large-Artery Atherosclerotic Infarct Subtype			
	Yes*		No†	
	OR	95% CI	OR	95% CI
Unadjusted‡	5.4	2.7–10.9	3.4	2.6–4.5
Adjusted for risk factors§	3.0	1.2–7.3	2.7	1.9–4.0
Adjusted for risk factors§ and BMI	3.2	1.3–8.1	2.9	2.0–4.2

Gender-specific medians of Waist-Hip Ratio: men ≥0.93, women ≥0.86.

*91 cases, 179 controls.

†485 cases, 963 controls. Combined category of cardioembolic, lacunar, cryptogenic, and other determined cause.

‡Matched by age, sex and race-ethnicity.

§Matched by age, sex, and race-ethnicity and adjusted for hypertension, diabetes mellitus, any cardiac disease, current smoking status, no physical activity, moderate alcohol drinking, level of LDL cholesterol, level of HDL cholesterol, and education.

an elevated WHR. Vague[27] first suggested that atherosclerotic risk was higher in those with abdominal obesity compared with lower-body obesity. Other investigators also have reported that abdominal fat distribution is highly related to an increased prevalence of cardiovascular risk factors.[18,28–31] The measurement of waist circumference alone is a simple indicator of abdominal obesity but has not been found to be a good predictor of stroke in this and other studies.[13,19,22] The effect of WHR was apparent after controlling for BMI. In our study population, BMI was not significantly associated with ischemic stroke. In fact, BMI had a slight inverse association with ischemic stroke. This finding has been noted by others.[22] In some studies, current smoking[32] and heavy alcohol drinking[33] may lead to a reduced BMI and an increase in the risk of stroke and therefore confound the association between BMI and stroke. Moreover, weight or BMI can decrease with age because of a loss of lean body mass[22,34,35] and a measurement of WHR may be a more useful method to assess abdominal fat accumulation and a better predictor of an increased risk for stroke than BMI or waist circumference. Because WHR is a more difficult measure to standardize in the clinic compared with BMI and to measure in large persons, it has been used less extensively in practice. Despite these limitations, the value of WHR argues for adding this measurement to vascular risk assessments.

Abdominal obesity may increase the risk of ischemic stroke through conventional vascular risk factors, but our study demonstrated an effect independent of these mechanisms. Other mechanisms such as insulin resistance or the metabolic syndrome could also help account for the effects of abdominal obesity. Some studies have shown that uncomplicated abdominal obesity is related not only to endothelial dysfunction, an early marker of atherosclerotic disease,[36] but also to hemorheologic disorders associated with blood flow disturbances and atherogenesis such as blood hyperviscosity, hyperfibrinogenemia, reduced red cell deformability, and erythrocyte aggregability,[37] as well as platelet activation through enhanced lipid peroxidation and inflammation.[38] The finding of a significant effect of WHR for those with and without large-artery atherosclerotic stroke, even when controlling for stroke risk factors, also supports the existence of other nonatherosclerotic mechanisms. As shown in Table 4, the OR for atherosclerotic stroke decreased substantially after controlling for other stroke risk factors, whereas the OR for those without large-artery atherosclerotic stroke did not. This implies that there is less confounding of the association of abdominal obesity among those without large-artery atherosclerotic stroke by conventional risk factors and a possible effect through other mechanisms.

The strength of the independent association between abdominal obesity and ischemic stroke in our study was as great as that observed for definite hypertension and diabetes mellitus in other reports.[39] In some cohort studies, WHR was no longer an independent risk factor for stroke after adjustment for hypertension and blood lipid levels or diabetes, but the number of events in these studies was small.[19,21] These studies also failed to differentiate between infarction and hemorrhage as separate outcomes.[18,19,21] The effect of obesity on hemorrhagic stroke may differ from that of ischemic stroke.[17] In our study, the significant effect of WHR on ischemic stroke was present in models with and without adjustment for blood lipid levels.

Our study demonstrated an effect of abdominal obesity in both younger and older subjects, but the influence of WHR on ischemic stroke may be greater among those <65 years of age. Age differences in the contribution of obesity to the risk of cardiovascular disease have been noted in the Framingham Heart Study using the metropolitan relative weight.[5] That study suggested that older subjects may have been a selective group in the prospective cohort because they remained resistant to the influence of obesity during their earlier life. Weight control needs further emphasis at all ages, but messages may need to be targeted to younger individuals for obesity control in stroke prevention campaigns.

The distribution of WHR differed by sex, with greater values in men, in our study and in other studies.[29,40] It is not clear, however, whether the impact of abdominal obesity on ischemic stroke is different by sex. In other studies, the risk of stroke was 2.3 times greater in the highest quintile of WHR (≥0.98) for men[22] and 1.6 times greater in the highest tertile of WHR (>0.87) for women.[18] Our results showed that men with increased WHR appeared to have a statistically greater risk for ischemic stroke than women. However, it may be difficult to compare directly the impact of WHR between men and women because of the use of sex-specific cut points in this analysis. Of note, when BMI was added to our model as a confounding factor, the OR between WHR and ischemic stroke decreased among women, whereas it increased among men. This could suggest that the relationship between ischemic stroke, abdominal obesity, and BMI may differ by sex because of differences in the operation of other vascular risk factors.

Several limitations of our study design deserve discussion. Our study was a case-control rather than prospective cohort study. The population-based approach of this case-control design, however, and the matching by age, sex, and race-ethnicity help to minimize the potential biases often associated with case-control studies. Some control selection bias

could have existed, with overweight or obese persons more likely to agree to participate in the study. This selection bias, however, would have biased our effect estimates to the null value. The distribution of WHR in our control subjects was similar to other study populations, implying that control selection bias was less likely. The cut point of quintile 5 of WHR in the Health Professional Follow-Up Study was 0.98, the same as quartile 4 for WHR among men in our study.[22] The quartiles of WHR among women in our study were slightly greater than those of the Nurses' Health Study, which was a younger cohort.[13] In addition, the median value of WHR chosen as a sex-specific cut point was comparable to reference values described in the literature (WHR, 0.92 in men and 0.82 in women) as criteria for abnormal regional fat distribution.[35]

Our anthropometric measurements were performed after the stroke and may not accurately reflect the premorbid status of obesity because weight and waist and hip circumferences could be changed by inadequate nutritional intake after acute stroke. By design, however, we made special efforts to collect anthropometric data within 72 hours after stroke, and it is unlikely that significant changes in waist or hip measurements would have occurred in that time. Measurement error may also have occurred because WHR was measured in the supine position in some cases who were unable to stand. In a pilot study, waist circumferences measured when supine were slightly smaller than when measured standing, whereas hip circumferences did not differ by position measured. Therefore, measurement errors in WHR because some cases could not stand would have led to an underestimation of the OR.

Our study has important public health implications, particularly for minority groups. Blacks and Hispanics have a greater stroke incidence and mortality.[41,42] The prevalence of obesity was 26.9% among blacks in 1998, the highest prevalence among race-ethnic subgroups studied. In addition, the prevalence of obesity among Hispanics, one of the fastest growing minority groups in this country, increased from 1991 to 1998 by 80% (11.6% to 20.8%).[43] NOMASS has provided specific information not only on the incidence of stroke among whites, blacks, and Hispanics but also on significant modifiable risk factors that are pertinent to each of these race-ethnic groups. With this analysis, we have demonstrated that increased WHR is independently associated with an increased risk of ischemic stroke among older whites, Hispanics, and blacks. This study corroborates other studies among younger blacks that abdominal obesity independently contributes to vascular risk factor elevations[29,30] and provides new data on the importance of abdominal obesity among Caribbean Hispanics. Weight reduction may favorably alter cardiovascular risk factors such as blood pressure, blood sugar level, and serum lipid level, which are known to be more prevalent among minority populations.[39,44] Therefore, better behavioral modification programs and treatment of abdominal obesity[45] are greatly needed, particularly among minority populations, and could be effective in reducing stroke risk.

Acknowledgments

This work was supported by a grant from the National Institute of Neurological Disorders and Stroke (RO1 NS 29993). Dr Suk is a recipient of the Soongsan Fellowship from Wonkwang University (Korea). We would like to thank all the staff of NOMASS for their efforts.

References

1. National Center for Health Statistics. Prevalence of overweight and obesity among adults: United States, 1999. Available at: http://www.cdc.gov/nchs/products/pubs/pubd/hestats/obese/obse99table2.htm. Accessed December 6, 2001.
2. Burton BT, Foster WR, Hirsch J, Van Itallie TB. Health implications of obesity: an NIH consensus development conference. *Int J Obes*. 1985;9:155–169.
3. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA*. 1999;282:1523–1529.
4. National Heart, Lung, and Blood Institute. *The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. Available at: http://www.nhlbi.nih.gov/guidelines/obesity/practgde.htm Accessed February 2, 2002.
5. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation*. 1983;67:968–977.
6. Fraser GE, Strahan TM, Sabate J, Beeson WL, Kissinger D. Effects of traditional coronary risk factors on rates of incident coronary events in low-risk population. *Circulation*. 1992;86:406–413.
7. Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, Hennekens CH. Weight, weight change, and coronary heart disease in women. *JAMA*. 1995;273:461–465.
8. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med*. 1999;341:1097–1105.
9. Lee J-M, Manson JE, Hennekens CH, Paffenbarger RS Jr. Body weight and mortality. *JAMA*. 1993;270:2823–2828.
10. Lindsted KD, Singh PN. Body mass and 26-year risk of mortality among women who never smoked: findings from the Adventist Mortality Study. *Am J Epidemiol*. 1997;146:1–11.
11. Singh PN, Lindsted KD. Body mass and 26-year risk of mortality from specific diseases among women who never smoked. *Epidemiology*. 1998;9:246–254.
12. Schule H, Cullen P, Assmann G. Obesity, mortality and cardiovascular diseases in the Munster Heart Study (PROCAM). *Atherosclerosis*. 1999;144:199–209.
13. Prineas RJ, Folsom AR, Kaye SA. Central adiposity and increased risk of coronary disease mortality in older women. *Ann Epidemiol*. 1993;3:35–41.
14. Rimm EB, Stampfer MJ, Giovannucci E, Ascherio A, Spiegelman D, Colditz GA, Willett WC. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. *Am J Epidemiol*. 1995;141:1117–1127.
15. Goldstein LB, Adams R, Becker K, Furberg CD, Gorelick PB, Hademones G, Hill M, Howard F, Howard VJ, Jacobs B, et al. AHA Scientific Statement: primary prevention stroke: a statement for healthcare professionals from the Stroke Council of the American Heart Association. *Stroke*. 2001;32:280–299.
16. Abott RD, Behrens GR, Sharp DS, Rodriguez BL, Burchifiel CM, Ross W, Yano K, Curb JD. Body mass index and thromboembolic stroke in nonsmoking men in older middle age: the Honolulu Heart Program. *Stroke*. 1994;25:2370–2376.
17. Rexrode KM, Hennekens CH, Willette WC, Colditz GA, Stamper MJ, Rich-Edwards JW, Speizer FE, Manson JE. A prospective study of body mass index, weight change, and risk of stroke in women. *JAMA*. 1997;227:1539–1545.
18. Folsom AR, Prineas RJ, Kaye SA, Munger RG. Incidence of hypertension and stroke in relation to body fat distribution and other risk factors in older women. *Stroke*. 1990;21:701–706.
19. Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjostrom L. distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenburg, Sweden. *BMJ*. 1984;289:1257–1261.
20. Lindenstrom E, Boysen G, Nyboe J. Lifestyle factors and the risk of cerebrovascular disease in women: the Copenhagen City Stroke Study. *Stroke*. 1993;24:1468–1472.

21. Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 years follow up of participants in the study of men born in 1913. *BMJ*. 1984;288:1401–1404.
22. Walker SP, Rimm EB, Ascherio A, Kawachi I, Stampfer MJ, Willett WC. Body size and fat distribution as predictors of stroke among US men. *Am J Epidemiol*. 1996;144:1143–1150.
23. Sacco RL, Boden-Albala B, Gan R, Chen X, Kargman DE, Shea S, Paik MC, Hauser WA, for the Northern Manhattan Stroke Study Collaborators. Stroke incidence among white, black and Hispanic residents of an urban community: the Northern Manhattan Stroke Study. *Am J Epidemiol*. 1998;147:259–268.
24. Sacco RL, Elkind M, Boden-Albala B, Lin I-F, Kargman DE, Hauser WA, Shea S, Paik MC. The protective effect of moderate alcohol consumption on ischemic stroke. *JAMA*. 1999;281:53–60.
25. Sacco RL, Roberts JK, Boden-Albala, Gu Q, Lin I-F, kargman DE, Berglund L, Hauser WA, Shea S, Paik MC. Race-ethnicity and determinants of carotid atherosclerosis in a multi-ethnic population. *Stroke*. 1997;28:929–935.
26. Gan R, Sacco RL, Kargman DE, Roberts JK, Boden-Albala B, Gu Q. Testing the validity of lacunar hypothesis: the Northern Manhattan Stroke Study experience. *Neurology*. 1997;48:1204–1211.
27. Vague J. The degree of masculine differentiation of obesities: a factor determining predisposition to diabetes, atherosclerosis, gout, and uric calculous disease. *Am J Clin Nutr*. 1956;4:20–34.
28. Blair D, Habicht J-P, Sims EAH, Sylwester D, Abraham S. Evidence for an increased risk for hypertension with centrally located body fat and the effect of race and sex on this risk. *Am J Epidemiol*. 1984;19:526–540.
29. Folsum AR, Burke GL, Ballew C, et al. Relation of body fatness and its distribution to cardiovascular risk factors in young blacks and whites: the role of insulin. *Am J Epidemiol*. 1989;130:911–924.
30. Gillum RF. The association of body fat distribution with hypertension, hypertensive heart disease, coronary heart disease, diabetes and cardiovascular risk factors in men and women aged 18–79 years. *J Chronic Dis*. 1987;40:421–428.
31. Daniels SR, Morrison JA, Sprecher DL, Khoury P, Kimball TR. Association of body fat distribution and cardiovascular risk factors in children and adolescents. *Circulation*. 1999;99:541–545.
32. Sempos CT, Durazo-Arvizu R, McGee D, Cooper RS, Prewitt TE. The influence of cigarette smoking on the association between body weight and mortality: the Framingham Heart Study Revised. *Ann Epidemiol*. 1998;8:289–300.
33. Chyou P-H, Burchfiel CM, Yano K, Sharp DS, Rodriguez BL, Curb JD, Nomura AM. Obesity, alcohol consumption, smoking, and mortality. *Ann Epidemiol*. 1997;7:311–317.
34. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960–1994. *Int J Obes Relat Metab Disord*. 1998;22:39–47.
35. Crepaldi G, Belfiore F, Bosello O, Caviezel F, Contaldo F, Enzi G, Melchionda N. Special report: Italian Consensus Conference: overweight, obesity and health. *Int J Obes*. 1991;15:781–790.
36. Arcaro G, Zamboni M, Rossi L, et al. Body fat distribution predicts the degree of endothelial dysfunction in uncomplicated obesity. *Int J Obes*. 1999;23:936–942.
37. Solerte SB, Fioravanti M, Pezza N, et al. Hyperviscosity and microproteinuria in central obesity: relevance to cardiovascular risk. *Int J Obes*. 1997;21:417–423.
38. Davi G, Guagnano MT, Ciabattoni G, et al. Platelet activation in obese women: role of inflammation and oxidant stress. *JAMA*. 2002;288:2008–2014.
39. Sacco RL, Boden-Albala B, Abel G, Lin I-F, Elkind M, Hauser WA, Paik MC, Shea S. Race-ethnic disparities in the impact of stroke risk factors: the Northern Manhattan Stroke Study. *Stroke*. 2001;32:1725–1731.
40. Molarius A, Seidell JC, Sans S, Tuomilehto J, Kuulasmaa K. Waist and hip circumferences, and waist-hip ratio in 19 populations of the WHO MONICA Project. *Int J Obes*. 1999;23:116–125.
41. Kittner S, White LR, Losonczy KG, Wolf PA, Hebel R. Black-white differences in stroke incidence in a national sample: the contribution of hypertension and diabetes mellitus. *JAMA*. 1990;264:1267–1270.
42. Howard G, Anderson R, Sorlie P, Andrew V, Backlund E, Burke GL. Ethnic differences in stroke mortality between non-Hispanic whites, Hispanic whites, and blacks. *Stroke*. 1994;25:2120–2125.
43. Mokdad AH, Serdula MK, Dietz WH, Bowman BA, Marks JS, Koplan JP. The spread of the obesity epidemic in the United States, 1991–1998. *JAMA*. 1999;282:1519–1522.
44. Alexander JK. Obesity and coronary heart disease. *Am J Med Sci*. 2001;321:215–224.
45. Despres J-P, Lemieux I, Prud'homme D. Treatment of obesity: need to focus on high risk abdominally obese patients. *BMJ*. 2001;322:716–720.

Abdominal Obesity and Risk of Ischemic Stroke: The Northern Manhattan Stroke Study

Seung-Han Suk, Ralph L. Sacco, Bernadette Boden-Albala, Jian F. Cheun, John G. Pittman, Mitchell S. Elkind and Myunghee C. Paik

Stroke. 2003;34:1586-1592; originally published online May 29, 2003;
doi: 10.1161/01.STR.0000075294.98582.2F
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628