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Determinants of Black-White Differences in the Risk of Cerebral Infarction: The National Health and Nutrition Examination Survey Epidemiologic Follow-up Study
[Original Investigation]

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Abstract

Objective: To determine whether blacks in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study remained at increased risk for cerebral infarction after adjusting for stroke risk factors and sociodemographic factors.

Methods: A cohort study involving 8203 whites and 1362 blacks who participated in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. During the 13-year follow-up, 538 and 122 cerebral infarctions occurred in whites and blacks, respectively.

Results: The black-white risk for cerebral infarction varied by age ($P=.007$ for race-age interaction). Compared with whites of the same age, blacks aged 35 to 44 years were at significantly increased risk for cerebral infarction (relative risk, 2.62; 95% confidence interval, 1.23 to 5.57), while older blacks, those older than 64 years, were not at increased risk (relative risk, 1.14; 95% confidence interval, 0.90 to 1.46). The relative risk for cerebral infarction decreased to 2.07 (95% confidence interval, 0.97 to 4.42) in younger blacks and 0.82 (95% confidence interval, 0.29 to 2.33) in older blacks after adjustment for age, sex, education, history of heart disease, diabetes, systolic blood pressure, treatment for hypertension, Quetelet index, and serum hemoglobin and magnesium levels.

Conclusions: These results indicate that much of the increased risk for cerebral infarction experienced by blacks can be explained by their higher prevalence of stroke risk factors, especially diabetes, hypertension, and lower educational attainment. Younger blacks, however, may still be at increased risk after adjusting for stroke riskfactors.

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Recent History

Studies in the United States have demonstrated that stroke incidence [1-4] and stroke mortality [5] are higher among blacks than whites. Although this excess stroke risk has frequently been attributed to the higher prevalence of hypertension and diabetes mellitus among blacks, a convincing explanation is lacking because few prospective epidemiologic studies have included a sufficient number of black participants [6]. Analysis of stroke events accrued during the first 10 years of follow-up from the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study (NHEFS) showed that blacks remained at significantly increased risk for stroke after adjustment for age, hypertension, and diabetes mellitus, suggesting that a more complete understanding of the determinants of stroke would be necessary to account for the excess risk experienced by blacks [7]. This previous report was limited in two regards. First, owing to the relatively small number of events among blacks, it was not possible to separate stroke events into cerebral infarction, intracerebral hemorrhage, and subarachnoid hemorrhage. This may be important since the risk factors for stroke vary depending on stroke subtype. Second, there was no adjustment for other factors associated with stroke. The present analysis of 13-year follow-up data from the NHEFS was undertaken to determine whether blacks remained at higher risk for cerebral infarction, the most frequent type of stroke, after adjustment not only for age, hypertension, and diabetes mellitus but also for other stroke risk factors, including sociodemographic factors.

SUBJECTS AND METHODS

The First National Health and Nutrition Examination Survey (NHANES I) was carried out by the National Center for Health Statistics, Hyattsville, Md, from 1971 through 1975 to collect health-related information on a probability sample of the US civilian noninstitutionalized population. To increase the sample size in select subgroups, there was oversampling of the elderly, persons living in poverty areas, and women of childbearing age [8-10].

The NHEFS was jointly initiated by the National Center for Health Statistics, the National Institute on Aging, the National Institute of Neurologic Disorders and Stroke, and other contributing institutes within the National Institutes of Health, Bethesda, Md. The objective of the NHEFS was to follow up the 14407 examinees in NHANES I who were between 25 and 74 years of age at the time of that survey [11]. Data collection for this analysis includes follow-up through 1987 and tracing all NHANES I participants for morbidity and mortality [12]. Only individuals older than 35 years were included in this analysis. Of the 10750 participants who were between 35 and 74 years of age during NHANES I, the following groups were excluded: persons who reported an affirmative response to the question "Has a doctor ever told you that you had a stroke?" (290 persons); persons whose race was other than black or white (105 persons); and persons who lacked follow-up information (938 persons). This resulted in a final study population of 9565 persons (3559 white men, 4644 white women, 551 black men, and 811 black women) Table 1. The percentage of blacks (18%) excluded was twice that of whites (9%).

	Men, No. (%)		Women, No. (%)	
	Black (n=488)	White (n=1091)	Black (n=593)	White (n=4095)
Prior strokes	26 (5.3)	113 (10.3)	42 (7.1)	108 (2.1)
Unavailable for follow-up	61 (12.5)	182 (16.7)	100 (16.9)	257 (6.3)
Only vital status ascertained	31 (6.3)	37 (3.4)	41 (6.9)	81 (2.0)
Participants after exclusions	551 (88.2)	3559 (91.6)	811 (91.5)	4644 (91.2)

Table 1. Baseline Participants Aged 35 to 74 Years and Reason for Exclusion by Race and Sex

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PREVALENCE OF CEREBRAL INFARCTION

Cerebral infarction events were determined by hospital record or death certificate diagnosis of one of the following International Statistical Classification of Diseases, Injuries, and Causes of Death, Based on the Recommendations of the Ninth Revision Conference, 1975, Clinical Modification (ICD-9-CM) codes: 433-434, cerebral occlusion, or 436-438, ill-defined stroke. There were 660 cerebral infarctions (280 in white men, 258 in white women, 52 in black men, and 70 in black women) during the follow-up period.

DETERMINATION OF STROKE RISK FACTORS AT BASELINE

Potential risk factors for cerebral infarction included age, sex, race (black vs white), education, systolic blood pressure, treatment for high blood pressure, diabetes, history of heart disease, Quetelet index (weight (in kilograms)/height (in meters, squared)), alcohol intake (milliliters per day), and serum cholesterol, hemoglobin, and magnesium levels. All measures were obtained prospectively during the NHANES I baseline interview. The race of the respondent was determined by observation as "white," "black," or "other." If the appropriate category was unclear, then the respondents were asked to define their race [13]. Diabetes mellitus was determined by patient report or physician coding. A history of heart disease was defined as a history of myocardial infarction, congestive heart failure, or angina, as determined by patient report or physician coding.

Three sitting blood pressure determinations were obtained during the NHANES I physical examination. The mean of the second and third blood pressure determinations was used for this analysis. The NHANES I procedures for blood pressure have been described in detail previously [8]. Participants were also asked whether they were currently taking antihypertensive medication. Persons who responded in the affirmative were defined as treated hypertensives. Using this information, we divided study participants into four mutually exclusive blood pressure groups: persons whose blood pressure was less than 140/90 mm Hg and who reported that they were not taking antihypertensive medication (normotensive); persons whose blood pressure was less than 140/90 mm Hg and who reported that they were taking antihypertensive medication (controlled hypertensives); persons whose blood pressure was 140/90 mm Hg or greater and who reported that they were taking antihypertensive medication (hypertensives receiving medication); and persons whose blood pressure was equal to or exceeded 140/90 mm Hg and who reported that they were not taking antihypertensive medication (hypertensives not receiving medication).

STATISTICAL ANALYSIS

Since the interval of follow-up varied among individuals, Cox proportional hazards analysis was used to estimate the relative risk for cerebral infarction among blacks compared with whites. Ninety-five percent confidence intervals (CIs) were calculated using a Taylor series approximation for the standard error of the relative risk [14].

To assess the association between potential stroke risk factors and cerebral infarction, separate age-adjusted Cox proportional hazards analyses were performed with cerebral infarction as the outcome variable and the potential stroke risk factor and age as the independent variables. Because of the possibility of nonlinear associations between potential stroke risk factors (continuous variables only) and cerebral infarction, a squared term was first entered into the model. If the squared term was not significant (P<.05), a second age-adjusted analysis was undertaken without the squared term. Factors that were found to be significantly associated with cerebral infarction were entered into a Cox proportional hazards model that adjusted for all stroke risk factors (full model).

INTERACTIONS BETWEEN RACE AND STROKE RISK FACTORS

To determine if certain factors were more potent predictors of cerebral infarction among blacks than among whites, an interaction term between race and each cerebral infarction risk factor was entered into a Cox proportional hazards model. This model included age, race, the stroke risk factor, and the race by risk factor interaction term. Interaction terms that were significant or borderline significant (P<.1) were then added to the full model.

RESULTS

The present analysis included 9565 persons (3559 white men, 4644 white women, 551 black men, and 811 black women). There were 660 cerebral infarctions during the follow-up period. An interaction was found between race and age (P=.007). Compared with whites of the same age, younger blacks, those aged 35 to 44 years, had a relative risk of 2.62 (95% CI, 1.23 to 5.57), while older blacks, those older than 64 years, had a relative risk of 1.14 (95% CI, 0.90 to 1.46) Table 2.

	No. of Persons	No. of Strokes	Risk per 100	RR†	95% CI‡
Age group, y					
35-44					
White	2192	21	0.96	1.00	Referent
Black	385	10	2.60	2.63	1.29-5.37
45-54					
White	1783	57	3.20	1.00	Referent
Black	279	18	6.45	2.11	1.23-3.58
55-64					
White	1438	55	3.83	1.00	Referent
Black	195	16	8.21	2.10	1.29-3.64
65+					
White	2782	405	14.51	1.00	Referent
Black	520	78	15.01	1.14	0.90-1.45
Sex					
Women					
White	4644	258	5.56	1.00	Referent
Black	811	70	8.63	1.72	1.32-2.24
Men					
White	3559	280	7.87	1.00	Referent
Black	520	82	9.44	1.19	0.89-1.59
History of heart disease					
No					
White	7549	439	5.82	1.00	Referent
Black	1281	113	8.99	1.59	1.30-1.95
Yes					
White	654	86	13.14	1.00	Referent
Black	101	8	8.91	0.68	0.34-1.34

†First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1987.
‡RR indicates relative risk, adjusted for age.
§95% confidence interval.

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Table 2. Black-White Risk for Cerebral Infarction Stratified by Age, Sex, and History of Heart Disease

Black women were 70% more likely than white women to suffer a cerebral infarction, while black men were only 16% more likely than white men to suffer such an event (P=.07 for race-sex interaction) [Table 2](#). Among those without a history of heart disease, blacks were more likely than whites to suffer a cerebral infarction. In contrast, among those with a history of heart disease, blacks were less likely to suffer a cerebral infarction than were whites (P=.012 for race-history of heart disease interaction) [Table 2](#).

STROKE RISK FACTORS

Analyses using a squared term to check for nonlinear associations between possible stroke risk factors and cerebral infarction revealed significant effects for serum hemoglobin level and Quetelet index [Table 3](#). These relationships were primarily J shaped and U shaped, with subjects in the second and third quartile having a lower relative risk than those in the lowest and highest quartiles.

	RR†	95% CI‡	P§	RR†	95% CI‡	P§
Age						
18-24	1.00			1.00		
25-34	1.00			1.00		
35-44	1.00			1.00		
45-54	1.00			1.00		
55-64	1.00			1.00		
65-74	1.00			1.00		
75+	1.00			1.00		
Sex						
Male	1.00			1.00		
Female	1.00			1.00		
Education						
<High school	1.00			1.00		
High school	1.00			1.00		
Some college	1.00			1.00		
College graduate	1.00			1.00		
Postgraduate	1.00			1.00		
Marital status						
Married	1.00			1.00		
Single	1.00			1.00		
Divorced	1.00			1.00		
Widowed	1.00			1.00		
Smoking						
Never	1.00			1.00		
Former	1.00			1.00		
Current	1.00			1.00		
Alcohol						
None	1.00			1.00		
Light	1.00			1.00		
Heavy	1.00			1.00		
Hypertension						
None	1.00			1.00		
Medication	1.00			1.00		
Not medication	1.00			1.00		
Diabetes						
None	1.00			1.00		
Medication	1.00			1.00		
Not medication	1.00			1.00		
Heart disease						
None	1.00			1.00		
Medication	1.00			1.00		
Not medication	1.00			1.00		
Stroke						
None	1.00			1.00		
Medication	1.00			1.00		
Not medication	1.00			1.00		

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Table 3. Age-Adjusted Cox Proportional Hazards Analysis Results for Cerebral Infarction

Factors that did not have a significant squared term in the age-adjusted analysis were entered into a second age-adjusted analysis without the squared term [Table 3](#). In these analyses, the following additional factors were found to be associated with cerebral infarction: increasing age, male sex, decreasing education, diabetes, a history of heart disease, and decreasing serum magnesium levels.

All three hypertensive groups (controlled hypertensives, hypertensives receiving medication, and hypertensives not receiving medication) were at increased risk for cerebral infarction compared with normotensive persons [Table 3](#). Controlled hypertensives and hypertensives receiving medication were almost 2.5 times more likely to suffer an infarction than were normotensive persons.

PREVALENCE OF STROKE RISK FACTORS

The races differed significantly in terms of the prevalence of all cerebral infarction risk factors except for age and a history of heart disease [Table 4](#). Blacks tended to have fewer years of education, lower serum hemoglobin and magnesium levels, and a higher prevalence of diabetes. Blacks were less likely to be normotensive and substantially more likely to be hypertensive and receiving medication. Each of these factors placed blacks at an increased risk for cerebral infarction.

Table 4. Distribution of Selected Risk Factors for Cerebral Infarction According to Race

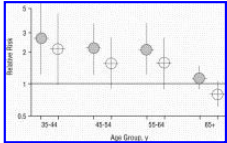
Risk Factor	White	Black	PT
Sample size, No.	8003	1362	
Mean age, y	55.19	55.54	.850
Sex, % men	43.13	40.40	.043
Mean education level, y	13.30	9.22	<.001
Blood pressure treatment group, %			
Normotensive	47.13	30.32	
Controlled hypertensive	1.00	3.67	
Hypertensive receiving medication	9.16	16.08	<.001
Hypertensive not receiving medication	42.07	49.93	
Diabetes, %	5.47	9.00	<.001
History of heart disease, %	7.97	7.42	.480
Quetelet index, %			
<22.8	25.41	22.54	
22.8-25.4	25.98	19.10	
25.5-28.5	25.41	22.47	<.001
>28.5	23.21	25.89	
Hemoglobin level, % g/L			
<135	23.24	42.73	
135-144	23.15	25.40	
145-155	24.70	19.75	<.001
>155	28.92	12.11	
Mean magnesium level, mmol/L (mg/dL)	0.70 (1.70)	0.62 (1.45)	<.001

*First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1987.
†One-way analysis of variance tests are used to compare means, and χ^2 tests are used to compare dichotomous variables. P values are two-sided.
‡One test for definition of blood pressure groups.
§Reported values are based on means, rounded.

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RESULTS OF MULTIVARIATE ANALYSIS

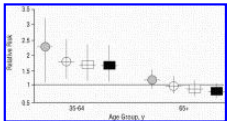
After adjustment for age, sex, education, blood pressure treatment group, systolic blood pressure, diabetes, a history of heart disease, Quetelet index, and serum hemoglobin and magnesium levels, compared with whites of the same age, blacks aged 35 to 44 years had a relative risk of 2.07 (95% CI, 0.97 to 4.42) [Figure 1](#). In contrast, older blacks, those older than 64 years, had a relative risk of 0.82 (95 CI, 0.29 to 2.33) after adjustment for the same factors [Figure 1](#).



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Figure 1. Black-white relative risk for cerebral infarction stratified by age, First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1987. Whites are the referent group. Full model is adjusted for age, sex, education, blood pressure treatment group, systolic blood pressure, diabetes, a history of heart disease, Quetelet index, and serum hemoglobin and magnesium levels. Open circle indicates full model; shaded circle, age adjusted

To determine the role of individual stroke risk factors in reducing the magnitude of the increased stroke risk experienced by blacks, we sequentially added risk factors to the Cox proportional hazards model. After adjustment for age and sex, for persons aged 35 to 64 years, the black-white risk for cerebral infarction was 2.27 (95% CI, 1.16 to 3.19) [Figure 2](#); the further adjustment for diabetes mellitus, blood pressure treatment group, and systolic blood pressure lowered the black-white risk to 1.80 (95% CI, 1.27 to 2.54); and the addition of education further reduced the risk to 1.70 (95% CI, 1.20 to 2.40). There was little change in the black-white risk after adjustment for the remaining factors (history of heart disease, Quetelet index, and serum hemoglobin and magnesium levels).



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Figure 2. Black-white relative risk for cerebral infarction stratified at age 65 years, First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1987. Whites are the referent group. Full model is adjusted for age, sex, education, blood pressure treatment group, systolic blood pressure, diabetes, a history of heart disease, Quetelet index, and serum hemoglobin and magnesium levels. Shaded circle indicates sex and age adjusted; open circle, sex, age, diabetes, and hypertension; open square, sex, age, diabetes, hypertension, and education; and solid square, full model

COMMENT

We found a strong interaction between race and age when we examined black-white differences in the risk of cerebral infarction. Compared with whites of the same age, younger blacks were at higher risk (relative risk=2.07) than older blacks (relative risk=0.82). The Evans County Study also reported an interaction between race and age similar to the results presented herein [\[2\]](#). This observation is particularly important because the use of age adjustment heavily weights the summary relative risk toward the contribution of the older age groups in which stroke is more frequent. This tends to obscure the larger black-white differences seen in the younger age groups. An analysis of years of disability or years of life lost may reflect the excess stroke burden experienced by blacks better than age-adjusted incidence rates.

The reasons for the race-age interaction are not clear. Since blacks tend to develop hypertension at a younger age than whites [\[15\]](#), the target organ effects of hypertension may manifest themselves at a younger age in blacks than in whites, explaining the increased risk in younger blacks. The higher prevalence of stroke risk factors in blacks may also result in blacks suffering stroke events and dying at a younger age, and, consequently, surviving older blacks (those older than 65 years) may be "healthier" than their white counterparts, lowering their risk of stroke. In addition, the black-white "crossover" in stroke risk occurs at approximately age 65 years, the age when many Americans become eligible for Medicare. It is possible that Medicare eligibility may eliminate some of the racial barriers in access to medical care, lowering the risk of stroke in blacks.

Black women were 70% more likely than white women to suffer a cerebral infarction, while black men were only slightly more likely than white men to suffer an infarction. This finding is consistent with coronary heart disease mortality results from the Charleston Heart Study, which reported that black women had higher coronary heart disease mortality rates compared with white women, while black men had similar mortality rates compared with white men [\[16\]](#).

The interaction between race and a history of heart disease should be viewed with caution since only nine strokes occurred among blacks with a history of heart disease. If blacks are less likely than whites to be diagnosed as having heart disease because of a perception that heart disease is rare in blacks [17-19] or because of differential access to medical care, many blacks with heart disease may be misclassified as not having heart disease. This misclassification may lead to an overestimation of the black-white risk for cerebral infarction among persons without heart disease and an underestimation of the risk among persons with heart disease.

Persons who were hypertensive were at increased risk for cerebral infarction when compared with normotensive persons. Persons receiving antihypertensive medication, regardless of control status, were almost 2.5 times more likely to suffer a cerebral infarction. This finding may be secondary to treated hypertensives having had years of uncontrolled hypertension. In fact, among persons with a blood pressure greater than 140/90 mm Hg, persons who were receiving medication had a mean blood pressure of 164/94 mm Hg, while persons who reported not taking medication had a mean blood pressure of 152/92 mm Hg. Since hypertensives receiving medication have more severe hypertension when compared with hypertensives not receiving medication, it is not surprising that treated hypertensives also have a higher stroke risk. In any event, treatment and control of hypertension do not reduce the risk of stroke to that of persons who never develop hypertension [20], underscoring the extreme importance of the primary prevention of stroke risk factors.

As expected, the higher prevalence of diabetes and hypertension among blacks contributed to their excess stroke risk. The adjustment for diabetes, blood pressure treatment group, and systolic blood pressure reduced the black-white relative risk among younger persons from 2.27 to 1.80. Education was also an important covariate, further reducing the risk for cerebral infarction from 1.80 to 1.70, suggesting that unmeasured factors associated with low educational attainment or socioeconomic status were partly responsible for the higher stroke risk experienced by younger blacks. These unmeasured factors could include other health-related habits or access to and utilization of preventive services.

The present analysis has a number of limitations. First, stroke risk factor data were limited to information collected during the NHANES I baseline interview. Change in risk factor status during the 13-year follow-up was not considered. Second, the analysis is likely to underestimate the contribution of factors with measurement error such as blood pressure [21] and cholesterol level [22]. Because of this underestimation, we may overestimate the magnitude of the adjusted black-white difference in stroke risk. Third, the data on stroke ascertainment were limited to diagnoses abstracted from hospital admissions and death certificates. Blacks were more likely than whites to have been unavailable for follow-up Table 1. If persons unavailable for follow-up had a higher rate of stroke than those who were available for follow-up, we may have underestimated the black-white difference in stroke risk. Finally, in the NHANES I baseline survey, information on cigarette smoking was obtained on only a fraction of the survey respondents. For this reason, we did not include smoking status as a covariate in our analysis. However, we have performed the analysis adjusting for smoking status using imputed data for persons who were not asked about cigarette smoking. This analysis did not substantially change the risk estimates presented in this report.

Despite these limitations, to our knowledge this study is the first to report the determinants of black-white differences for the risk of cerebral infarction in a prospective study of a population derived from a national probability sample. Our findings suggest that currently known risk factors and socioeconomic status account for a substantial amount of the racial difference in the incidence of cerebral infarction and, hence, that public health measures targeted at risk factor reduction and the elimination of racial differences in socioeconomic status should be given a high priority.

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Blacks; Cerebral Infarction; Cerebrovascular Disorders; Diabetes Mellitus; Educational Status; Hypertension; Nutrition; Whites

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