Ischemic Stroke Subtypes
A Population-Based Study of Incidence Rates Among Blacks and Whites

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Background and Purpose—Blacks have an excess burden of stroke compared with whites; however, data comparing ischemic stroke subtypes among the 2 groups are limited and typically involve relative frequencies. The objective of this study is to compare the incidence rates of ischemic stroke subtypes between blacks and whites within a large, representative, biracial population.

Methods—The Greater Cincinnati/Northern Kentucky Stroke Study is designed to measure incidence rates and trends of all strokes within a well-defined, large, biracial population. Hospitalized cases were ascertained by International Classification of Disease (9th revision; ICD-9) discharge codes. Out-of-hospital events were ascertained by prospective screening of emergency department admission logs, review of coroners’ cases, and monitoring all public health and hospital-based primary care clinics. A sampling scheme was used to ascertain events from nursing homes and all other primary care physician offices. All potential cases underwent detailed chart abstraction and confirmed by physician review. Based on all available clinical, laboratory, and radiographic information, ischemic stroke cases were subtyped into the following categories: cardioembolic, large-vessel, small-vessel, other, and stroke of undetermined cause. Race-specific incidence rates were calculated and compared after adjusting for age and gender, and standardizing to the 1990 US population.

Results—Between July 1, 1993, and June 30, 1994, 1956 first-ever ischemic strokes occurred among blacks and whites in the study population. Small-vessel strokes and strokes of undetermined cause were nearly twice as common among blacks. Large-vessel strokes were 40% more common among blacks than whites, and there was a trend toward cardioembolic strokes being more common among blacks.

Conclusions—The excess burden of ischemic strokes among blacks compared with whites is not uniformly spread across the different subtypes. Large-vessel strokes are more common and cardioembolic stroke are as common among blacks, traditionally thought to be more common among whites. (Stroke. 2004;35:1552-1556.)

Key Words: stroke ■ racial differences ■ incidence ■ epidemiology ■ stroke, ischemic

Blacks have an excess burden of stroke compared with whites; however, incidence data comparing blacks and whites by ischemic stroke subtype are limited. It is not known whether the excess burden of ischemic stroke among blacks is uniformly spread across the different subtypes. The objective of the current study is to examine racial differences in the incidence rates of ischemic stroke subtypes within a large, representative, biracial population demographically similar to the US populations of blacks and whites.

Materials and Methods
The Greater Cincinnati/Northern Kentucky Stroke Study (GCNKS) is designed to measure incidence rates and trends of all stroke within a defined large biracial population whose demographic characteristics reflect the black and white populations of the US as a whole (% black, % below the poverty level, education, and age). The methods for case identification, data collection, and calculation of incidence rates have been previously described in detail. In summary, the study population is defined as all residents of the greater Cincinnati and northern Kentucky region, which include 2 contiguous southwestern Ohio and 3 northern Kentucky counties along the Ohio River. This current report includes all first-ever ischemic strokes occurring between July 1, 1993 and June 30, 1994.

Study nurses screened the medical records of all inpatients with primary or secondary stroke-related ICD-9 discharge diagnoses (430 to 438) from all 19 acute-care hospitals in the study region. The catchment area of these hospitals exceeds the geographic boundaries of the included 5-county study region. A previous study has documented that residents of these counties exclusively seek care at these 19 hospitals rather than seeking care at more distant hospitals.
in the outlying region. The study nurses also reviewed all coroners’ cases in which stroke was listed as the primary or secondary cause of death. Strokes not found by inpatient monitoring or from the coroners’ offices were ascertained by monitoring all visits to 18 of the hospitals’ emergency departments (Cincinnati Children’s Hospital was excluded), 16 public health clinics, and 14 hospital-based outpatient clinics and family practice centers. In addition, a sampling scheme to identify other out-of-hospital events was used. Monitoring was performed in a random sample of 50 of the 878 primary care physicians’ offices and 25 of the 193 nursing homes in the greater Cincinnati metropolitan area. Events found by out-of-hospital monitoring were checked against inpatient records to prevent double counting. The study was approved by the institutional review boards at all participating hospitals.

Study nurses performed a comprehensive medical record abstraction regarding the stroke hospitalization and obtained available neuroimaging studies for all potential stroke cases. Classification of race was recorded as self-reported in the medical administrative records. Classification of risk factors was based on a prestroke assessment. Laboratory values and results of diagnostic tests were also abstracted. All borderline cases were abstracted for physician review to ensure complete case ascertainment.

Study physicians reviewed the case abstraction and relevant neuroimaging (available films and report) to determine whether a potential case met the criteria as an incident case. Criteria for stroke categories and ischemic stroke subtypes were adapted from the Classification of Cerebrovascular Diseases III7 and from epidemiologic studies in Rochester, Minn.8,9 To be included as a case, a subject had to meet the criteria for 1 of 5 categories of stroke (cerebral ischemia, subarachnoid hemorrhage, intracerebral hemorrhage, stroke of uncertain cause, and transient ischemic attack [TIA]).1 must have lived within the 5-county study area by zip code at the time of the incident event, and had the onset of stroke during the study period. All ischemic stroke cases were further subtyped by the study physician based on all available clinical and radiographic information. Subtype categories were the following: cardioembolic, large-vessel, small-vessel, other, and undetermined cause (Appendix). In cases meeting the criteria for >1 cause, the study physician made a final judgment about the most likely cause, except when cases met the criteria for both large-vessel and cardioembolic stroke, which were then classified as large-vessel stroke.

SAS version 8.2 (SAS Institute Inc) was used for data analysis. The numerator for incidence rate calculation was the number of cases confirmed by physician review. For the sampling scheme of primary care physicians’ offices and nursing homes, physician confirmed cases were weighted to estimate the total number of events in the study population. In this manner, cases ascertained in the primary care physicians’ offices and nursing homes sampled were multiplied by 17.56 (878 possible sites/50 sampled) and 7.72 (193 possible sites/25 sampled), respectively. The denominator was the total population for the 5 counties as extrapolated from the 1990 census as reported by the US Census (www.census.gov). Race, age, and sex subcategories for the years 1993 to 1994 were extracted and the mean of the 2 years used for calculation. The at-risk population for 1993 to 1994 included 197 541 blacks and 1 114 092 whites. Incidence rates for first-ever ischemic stroke and subtype-specific stroke were adjusted by age and gender to the 1990 US population. Incidence rates were calculated using the numerators and denominators as defined and confidence intervals (CIs) were estimated using a Poisson distribution. The Student t test or χ² test was used to compare subtype-specific proportions, demographic differences, and stroke risk factors by race as appropriate.

**Results**

From July 1, 1993 to June 30, 1994, a total of 1956 first-ever ischemic strokes occurred among blacks and whites in the greater Cincinnati and northern Kentucky study region. The overall race-specific incidence rates per 100 000 population for first-ever ischemic stroke among blacks was 230 (207 to 253, 95% CI) compared with 134 (128 to 141, 95% CI) for whites with a risk ratio of 1.7 (1.4 to 2.0, 95% CI).

Table 1 shows the race-specific incidence rates by stroke subtype. Small-vessel strokes and strokes of undetermined cause were nearly twice as common among blacks as compared with whites. The incidence rate of large-vessel strokes was 1.4 times more common among blacks as compared with whites. Cardioembolic strokes had a trend toward higher incidence among blacks. Included in Table 1 for comparison are ischemic stroke subtype data from Rochester, Minn, which had a 96% white population at the time the data were collected.

Table 2 lists the demographic characteristics, risk factors, and proportion of each ischemic stroke subtype by race. Of 1956 ischemic strokes, 362 (19%) occurred among blacks. Blacks (68±15 years) with an ischemic stroke were significantly younger than whites (73±14 years; P<0.05). After adjusting for age, blacks had significantly higher rates of hypertension, current smoking, and a trend toward more diabetes, whereas whites had significantly higher rates of hypercholesterolemia, previous TIA, and a trend toward more atrial fibrillation.

There was no difference between blacks and whites with regards to the use of echocardiograms (ECHO), carotid Doppler tests, or conventional cerebral angiograms (Table 2). Less than 5% of patients underwent a conventional cerebral angiogram and only 8% underwent magnetic resonance angiography (MRA). Blacks were more likely to have received an MRA as compared with whites (12% versus 7%; P<0.005). A carotid Doppler was obtained in 58% of patients and an ECHO was
obtained in 51%. Thirty percent of patients received neither a carotid Doppler nor an ECHO. Thirty-nine percent of patients with stroke of undetermined cause did not have either a carotid Doppler or ECHO compared with only 20% of patients with a determined cause of stroke ($P<0.0001$).

The risk factor characteristics for each ischemic stroke subtype are shown in the Figure. Patients with cardioembolic stroke were older when compared with all other subtypes (mean age $76\pm12$ years versus $71\pm15$ years; $P<0.0001$) because of the association with atrial fibrillation, which becomes more prevalent with age. Those with stroke caused by other infrequently identified causes were younger when compared with all other subtypes (mean age $56\pm22$ years versus $72\pm14$ years, $P<0.0001$). Patients with stroke of undetermined cause had lower rates of hypertension than patients with commonly identified causes of stroke ($57\%$ versus $67\%$, $P<0.0005$). Current tobacco smoking was most prevalent in patients with large-vessel stroke compared with all other subtypes ($33\%$ versus $18\%$, $P<0.0001$). Previous TIA occurred in $14\%$ of all stroke patients and was more common in large-vessel stroke compared with all other subtypes ($20\%$ versus $13\%$, $P<0.005$). As expected, atrial fibrillation was most frequently seen in patients with cardioembolic stroke. However, $9\%$ of large-vessel stroke patients and $5\%$ of small-vessel stroke patients had a history of atrial fibrillation.

### Discussion

The $70\%$ greater incidence rate of ischemic strokes among blacks as compared with whites is not uniformly reflected among the different ischemic stroke subtypes. Blacks have nearly twice the rate of both small-vessel strokes and strokes of undetermined cause than whites. The excess burden of small-vessel stroke among blacks is thought to relate to the higher prevalence of hypertension, cigarette smoking, and diabetes among blacks. However, when comparing blacks and whites with small-vessel stroke, there was no significant difference in diabetes ($36\%$ versus $30\%$), whereas hypertension ($80\%$ versus $66\%$; $P<0.05$) and current cigarette smoking ($39\%$ versus $18\%$; $P<0.005$) was more common among blacks even after adjusting for age. The nearly 2-fold increased incidence of stroke of undetermined type among blacks is not caused by a lack of diagnostic testing as compared with whites. As shown in Table 2, there was no statistically significant difference between blacks and whites in the frequency of common diagnostic tests. Furthermore,
there was a trend toward more carotid Doppler tests performed among blacks, and MRA was obtained more frequently among blacks than whites, which relates to a higher proportion of blacks cared for at the single academic hospital in our region where MRA was obtained more frequently than all other hospitals in the study region during the study period.

Petty et al have reported the incidence of ischemic stroke subtypes among residents of Olmstead county (Rochester, Minn) using a similar classification scheme as the GCNKSS. Results of both studies are listed in Table 1 for comparison. The differences between the 2 studies are important to note. First, residents of Rochester during their study period were 96% white, which precludes racial comparisons. Second, ascertainment of outpatient stroke differs with all cases being ascertained in Rochester because of their relatively small population and unique community-wide medical record system. On the contrary, the GCNKSS ascertains outpatient stroke through monitoring methods that also requires using a sampling scheme as described. With sampling, any bias toward an ischemic stroke subtype among outpatient strokes would potentially skew the results of the study toward that subtype because of magnification of the bias. Furthermore, we cannot exclude an underestimate of events. When we exclude out-of-hospital strokes, blacks continue to show higher incidence rates similar to that reported in Table 1, except that the difference in cardioembolic stroke becomes significant with the lower 95% CI of the risk ratio being 1.1.

Small-vessel strokes are more common among blacks, as demonstrated in several studies. This racial difference is confirmed in the current study as well, with blacks having nearly twice the incidence of small-vessel stroke than whites. Blacks have a greater incidence of hypertension, diabetes, and smoking compared with whites, which may in part explain the established racial difference. Even within the greater Cincinnati and northern Kentucky population, blacks with stroke have a higher prevalence of these risk factors, although diabetes was similar between the 2 racial groups among those with small vessel strokes. These risk factors among blacks are a target for intervention in the primary prevention of stroke to reduce the racial disparity and burden of stroke among blacks.

A number of studies have suggested that blacks have less cardioembolic stroke than whites. However, these studies are limited by referral bias and nonpopulation-based study design limiting comparisons of subtype incidence rates, which provide a better comparison of the burden of disease among a population. For instance, when proportions are used to compare blacks and whites in the GCNKSS, whites have a higher proportion of cardioembolic stroke and large-vessel stroke (Table 2). However, when comparing the incidence rates to understand the burden of disease between the 2 races, blacks have higher rates of large-vessel stroke and a trend toward more cardioembolic stroke (Table 2). Examining the proportions of subtypes within a racial group may provide practical application in terms of prioritizing testing strategy for an individual patient. However, race is not a strong enough predictor of ischemic stroke subtyping to make it a useful variable in everyday practice.

Data on large-vessel stroke between blacks and whites have been further complicated by location of disease (intra-cranial versus extracranial). Earlier studies found a greater frequency of intracranial atherosclerosis among blacks and greater frequency of extracranial disease among whites. More recent studies have had conflicting results. Witky et al found a greater proportion of extracranial carotid lesions among whites than blacks, but no difference for intracranial lesions. On the contrary, Sacco et al observed in a tri-ethnic population no difference in the proportion of extracranial stenosis among stroke patients, but blacks and Hispanics had a higher frequency of intracranial stenosis compared with whites. Limitations of these studies include proportional comparisons rather than incidence rates, referral bias, and nonpopulation-based case ascertainment. We found a significantly increased incidence of large-vessel stroke among blacks compared with whites in our study with a risk ratio of 1.4 (95% CI, 1.2 to 1.5). The majority of our large-vessel subtypes were diagnosed based on carotid ultrasonography of the extracranial vessels. Because <5% of hospitalized stroke patients in the current study underwent contrast angiography and only 8% underwent MRA, the incidence rate for large-vessel stroke among blacks in our population may be falsely low, further underscoring the difference between blacks and whites.

Limitations of the study include use of a sampling scheme to measure out-of-hospital stroke cases as noted. With this large population of 1.3 million, >800 primary care physician offices, and almost 200 nursing homes, it would be an enormous task to monitor all of those sites. Including cases that are ascertained out-of-hospital is important to get an accurate estimate of the true incidence rate. Furthermore, if there are racial differences in access to hospitalization, then the inclusion of out-of-hospital cases would reduce ascertainment bias. Another potential limitation would be a systemic racial bias by study physicians to include more black events as cases or exclude white events as noncases. However, based on our quality-assurance assessment, black events were no more likely to be included than white events, and white events were no more likely to be excluded during physician case review. The difference in rates of ischemic stroke subtypes between blacks and whites is not completely understood, but likely relates to differences in traditional risk factors, genetic differences, and socioeconomic status. Our study is limited by insufficient data on socioeconomic status and lack of genetic material to explore these stroke risk factors and the complex interaction they may have with more traditional stroke risk factors. This will be the subject of ongoing work in the GCNKSS. Finally, the current study is limited by its nature as an observational epidemiologic study. There was no uniformity of test use within the population of patients, and it is possible that some tests were obtained after hospitalization in an outpatient setting. In fact, 30% of cases did not receive either a carotid Doppler or an ECHO during hospitalization. However, testing does not guarantee identification of the stroke cause. In fact, 61% of stroke cases of undetermined cause had either a carotid Doppler or an ECHO.

In summary, in this large population-based study comparing the incidence of ischemic stroke subtypes among blacks and whites, the nearly 2-fold increase risk of ischemic stroke among blacks is not uniformly distributed across all ischemic stroke subtypes. Blacks have nearly twice the incidence of
small-vessel stroke and stroke of undetermined cause when compared with whites. Furthermore, large-vessel stroke is 1.4-times more common and cardioembolic stroke trends toward a higher incidence rate among blacks. This finding underscores the importance of large-vessel and cardioembolic stroke among blacks, traditionally thought to be a more frequent ischemic stroke subtype among whites. Further research of risk factors and genetic differences is needed to better-understand what underlies these differences and the racial disparity by ischemic stroke subtype.

Appendix

Subtypes of Ischemic Stroke

A. Cardioembolic (Rochester Criteria)*

This category includes myocardial infarction within 6 weeks of stroke onset; acute congestive heart failure, mitral stenosis confirmed by clinical examination, echocardiography, or autopsy; artificial heart valve; atrial fibrillation or atrial flutter on electrocardiography; thrombus in the atrium, ventricle, or on the aortic or mitral valve identified by echocardiography or coronary angiography; and sick sinus syndrome identified by monitoring of cardiac rhythm. Patients with an akinetic or hypokinetic wall segment by echocardiogram are also included.

B. Large Vessel Stroke

This category required occlusion or 50% stenosis of the internal carotid artery by carotid ultrasound/duplex studies or 50% stenosis of the carotid, middle, and anterior or posterior cerebral, vertebral, or basilar arteries by angiography or magnetic resonance angiography in at least 1 plane that is in a vascular distribution consistent with stroke symptoms. Distinction between resolving embolism and primary disease of the intracranial vessel was made by the neuroradiologist.

C. Small Vessel Stroke (Condition A, B, or C is true.)

Condition A: Brain images show a deep infarct 1.5 cm in its maximal diameter that is appropriate to a clinical classical lacunar syndrome.

Condition B: Brain images show no lesion to explain the clinical syndrome, and the clinical presentation is one (including the follow- ing) classically associated with a small deep infarct: pure motor stroke: hemiparesis or hemiplegia involving the face, arm, and leg equally or arm and leg equally without other neurological findings. Although mild sensory symptoms can be present, there is no sensory loss on examination that is related to the infarct pure sensory stroke: isolated sensory loss or disturbance involving the entire hemiface and hemibody or the hemibody alone; there may be incidental motor weakness from another cause ataxia-hemiparesis: hemiparesis with ipsilateral ataxia; paresis is more commonly cranial dysarthria/clumsy hand syndrome: dysarthria with a clumsy hand; facial weakness is possible hemiballismus, hemiathetosis, or hemihyposthesia: must be acute onset sensorimotor stroke: weakness and sensory loss involving face, arm, and leg equally without other neurological findings

Condition C: CT scan shows a deep infarct of 1.5 cm in its maximal diameter that is appropriate to the clinical syndrome, but the syndrome is not one of the classical syndromes for lacunar stroke.

D. Other Cause

Cerebral infarction that is caused by another clearly identified cause of stroke (eg, traumatic arterial dissection, postcoronary bypass graft surgery, postcarotid endarterectomy, acquired immune deficiency syndrome (AIDS), cocaine use, etc).

E. Ischemic Stroke of Undetermined Cause

Relatively rapid onset of a major focal neurological deficit that persists >24 hours or is fatal and cannot be attributed to another cause. This category is used when a patient does not meet any other criteria.

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References


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