Racial Variations in Location and Risk of Intracerebral Hemorrhage

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Background and Purpose—Risk factors for intracerebral hemorrhage (ICH) vary by location. Incidence rates of ICH are known to be higher in American blacks than whites, but how rates may differ by hemorrhage location is unknown. We sought to define incidence rates for different ICH locations in a biracial population.

Methods—All hospitalized patients age ≥20 years with spontaneous ICH were identified in the Greater Cincinnati/Northern Kentucky metropolitan area from May 1998 to July 2001 and August 2002 to April 2003. Incidence rates per 100 000 persons were age, sex, and race adjusted as appropriate to the 2000 US population. Risk ratios (RRs) with 95% CIs were calculated from unadjusted incidence rates.

Results—There were 1038 qualifying ICHs. Annual incidence rates per 100 000 persons ≥20 years of age were 48.9 for blacks and 26.6 for whites. Annual incidence rates per 100 000 blacks in lobar, deep cerebral, brain stem, and cerebellar locations were 15.2, 25.7, 5.1, and 2.9, respectively. Annual incidence rates per 100 000 whites in the same locations were 9.4, 13.0, 1.3, and 2.9. The greatest excess risk of ICH in blacks compared with whites was found among young middle-aged (35 to 54 years) persons with brain stem (RR, 9.8; 95% CI, 4.2 to 23.0) and deep cerebral (RR, 4.5; 3.0 to 6.8) hemorrhage.

Conclusions—The excess risk of ICH in American blacks is largely attributable to higher hemorrhage rates in young and middle-aged persons, particularly for deep cerebral and brain stem locations. Hypertension is the predominant risk factor for hemorrhages in these locations. (Stroke. 2005;36:000-000.)

Key Words: epidemiology ■ incidence ■ intracerebral hemorrhage ■ racial differences

Incidence rates for nontraumatic intracerebral hemorrhage (ICH) in the United States are higher for blacks than whites, but how rates may differ by ICH location is unknown. Better knowledge of ICH patterns may help reduce the burden of ICH, particularly among those with the highest rates of disease, because risk factors for ICH are known to vary by location. Hypertension, a potentially modifiable risk factor, is the predominant cause of deep cerebral ICH, whereas amyloid angiopathy, as yet untreatable, is an important cause of lobar ICH. We present the largest population-based study of ICH to date, with the goal of calculating incidence rates for ICH defined by location in a biracial population.

Materials and Methods

The Genetic and Environmental Risk Factors for Hemorrhagic Stroke (GERFHS) study is an ongoing, population-based study of ICH and subarachnoid hemorrhage (SAH) in the Greater Cincinnati/Northern Kentucky (GCNK) region. The methodology of the GERFHS study has been described. All patients ≥18 years of age who reside within a 50-mile radius of the University of Cincinnati and are admitted to 1 of 16 local hospitals with ICH or SAH are enrolled and their charts abstracted by a trained nurse. Study nurses currently maintain active surveillance (“hot pursuit”) at several hospitals that treat most ICH and SAH in the city by reviewing neurosurgery logs and patient rosters several times each week. They also screen primary and secondary International Classification of Diseases, 9th Revision (ICD-9) codes (430 to 432 through October 1999 and 430 to 438.9 thereafter) at all regional hospitals. Study physicians personally review each abstracted file to determine whether or not it qualifies as a case. Among qualifying cases, a subset of patients are interviewed and enrolled in a case-control study that includes genetic analyses. For these patients, radiographic films are reviewed by a study neurologist. Radiographic films are also reviewed for other qualifying patients if location or mechanism of hemorrhage cannot be determined from available reports. The most common reasons patients were not enrolled in the case-control portion of the GERFHS study were early mortality, late contact by study personnel (secondary to retrospective ICD-9 code review), inability to provide consent, and patient refusal to participate in the interview/genetic testing arm.

The present study includes all cases of ICH in persons ≥20 years of age occurring within the 5 metropolitan counties of the GCNK region from May 1998 to July 2001 and August 2002 to April 2003. The dates from August 2001 to July 2002 were not included because...
of an interruption of study funding during that period. Patients ages 18 to 20 were excluded because population denominators are not available for ages 18 and 19, exclusive of ages 15 to 17. Residents of the 5 county GCNK region seek care almost exclusively at 1 of the 16 participating metropolitan hospitals. Patients living within the 50-mile radius required by the GERFHS study but outside of the 5 counties of interest were excluded by zip code of residence. The definition of ICH used has been described. For the present study, exclusion criteria included previous ICH (but not previous ischemic stroke), traumatic ICH, hemorrhagic cerebral infarction, and hemorrhage associated with brain tumor, encephalitis, endarterectomy, and thrombolytic treatment of ischemic stroke. ICH associated with vascular malformations or anticoagulation was included. ICH location was defined as lobar (gray matter or subcortical white matter), deep cerebral (periventricular white matter, caudate, globus pallidus, putamen, internal capsule, thalamus), cerebellar, or brain stem (midbrain, pons, medulla). Cases designated as pure intraventricular hemorrhage after review of all available films were categorized as deep cerebral ICH. To estimate cases of ICH presenting as sudden death, all coroners’ cases in the 5 county GCNK regions from 1998 to 2000 were also screened by trained nurses.

For calculation of incidence rates, the entire population ≥20 years of age at the 5 GCNK counties was considered at risk. Denominator age-, race- and sex-specific populations for each year were obtained from published census estimates. For the first 4 months of 2003, estimates from 2002 were used. Overall incidence rates were age, race, and sex adjusted to the 2000 US population. Risk ratios (RRs) with 95% CIs were calculated for various combinations of ICH location, age, and gender using unadjusted incidence rates. Continuous variables were compared by Student’s t test.

To validate our case ascertainment, we compared cases of ICH ascertained by the GERFHS study with cases of ICH ascertained by another prospective population-based study of all stroke subtypes conducted by our group in the GCNK region during 1999. The institutional review board for each participating hospital system approved the GERFHS study.

Results

During 4 calendar years of case ascertainment, there were 1051 qualifying patients with incident ICH. Among hospitalized patients, 8 cases of ICH in Asian Americans, 1 case in a Hispanic American, 1 case in a person between ages 18 and 20, and 1 case of unknown location were excluded. There were 3 cases of nontraumatic ICH identified at the coroner’s office. The first was a lobar hemorrhage already captured by hospital surveillance. The second and third cases were not captured by hospital surveillance, but because of limited available data, they were also excluded. The remaining 1038 ICHs (823 in whites and 215 in blacks) were included in subsequent analyses.

Annual ICH incidence rates stratified by race and ICH location as well as gender and ICH location are presented in Table 1. The overall age-, race-, and sex-adjusted annual incidence rate was 29.2 per 100 000 persons ≥20 years of age (95% CI, 27.4 to 31.0).

For the current study population, the RR for ICH (using unstandardized rates) in blacks versus whites was 1.6 (95% CI, 1.4 to 1.8), and in men versus women, it was 1.1 (95% CI, 0.9 to 1.2). A comparison of RRs for different ICH locations in blacks versus whites and men versus women is presented in Table 2. The greatest excess risk was seen in blacks (compared with whites) for deep cerebral and brain stem hemorrhages. The RRs for ICH defined by location are further stratified by age for blacks and whites in Table 3. Excess risk for all locations was greatest in young to middle-aged (35 to 54 years) blacks. There was a slight excess of deep cerebral ICH in men compared with women, with the greatest difference also seen in persons ages 35 to 54. Black patients with ICH were significantly younger than white patients (mean age 61.9 years versus 72.1 years; P<0.0001), a relationship that remained significant for each hemorrhage location (data not shown).

Among our ICHs, 35% were lobar, 49% were deep cerebral, 6% were brain stem, and 10% were cerebellar. A comparison of relative proportions of ICH occurring at different locations in our cohort and other population-based studies is presented in Table 4.

When the 1999 GERFHS cases and 1999 epidemiology study databases were compared, 22 cases of ICH missed by the GERFHS study were identified. These cases were reviewed and the reason for the disparity established. In 8 cases, erroneous ICD-9 codes were applied by the original treating physician or administrative personnel. In 3 cases, patients with ICH died in the emergency department and so were not present on screened hospital logs (2 of these patients had ICH in the brain stem or cerebellum). The remaining 10 cases were admitted to a hospital with appropriate ICD-9 codes but were not captured by the GERFHS study.

### TABLE 1. Annual ICH Incidence Defined by Race, Sex, and Location*

<table>
<thead>
<tr>
<th>Location</th>
<th>All Locations</th>
<th>Lobar</th>
<th>Deep Cerebral</th>
<th>Brain Stem</th>
<th>Cerebellum</th>
</tr>
</thead>
<tbody>
<tr>
<td>All whites</td>
<td>26.6 (24.8–28.5)</td>
<td>9.4 (8.4–10.5)</td>
<td>12.9 (11.6–14.2)</td>
<td>1.3 (0.9–1.7)</td>
<td>2.9 (2.3–3.5)</td>
</tr>
<tr>
<td>All blacks</td>
<td>48.9 (42.3–55.5)</td>
<td>15.2 (11.5–18.9)</td>
<td>25.2 (20.5–30.0)</td>
<td>5.1 (3.0–7.1)</td>
<td>2.9 (1.3–4.5)</td>
</tr>
<tr>
<td>All men</td>
<td>32.2 (29.2–35.2)</td>
<td>9.7 (8.0–11.3)</td>
<td>17.8 (15.6–20.0)</td>
<td>1.8 (1.1–2.4)</td>
<td>3.0 (2.1–4.0)</td>
</tr>
<tr>
<td>All women</td>
<td>26.5 (24.3–28.6)</td>
<td>10.2 (8.8–11.6)</td>
<td>12.0 (10.6–13.5)</td>
<td>1.8 (1.2–2.3)</td>
<td>2.8 (2.1–3.6)</td>
</tr>
</tbody>
</table>

*Annual incidence rates per 100 000 persons ≥20 years of age calculated from the periods May 1998 through July 2001 and August 2002 through April 2003. Age, race, and sex were adjusted to the 2000 US white and black population as appropriate. Parentheses indicate 95% CIs.

### TABLE 2. ICH RRs by Location of Hemorrhage*

<table>
<thead>
<tr>
<th>Location</th>
<th>Lobar</th>
<th>Deep Cerebral</th>
<th>Brain Stem</th>
<th>Cerebellum</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR 95% CI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobar</td>
<td>0.8</td>
<td>0.7–1.0</td>
<td>1.4</td>
<td>1.0–1.8</td>
</tr>
<tr>
<td>Deep</td>
<td>1.3</td>
<td>1.1–1.6</td>
<td>1.7</td>
<td>1.4–2.1</td>
</tr>
<tr>
<td>Brain stem</td>
<td>1.0</td>
<td>0.6–1.6</td>
<td>3.3</td>
<td>2.0–5.5</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0.9</td>
<td>0.6–1.4</td>
<td>0.9</td>
<td>0.5–1.6</td>
</tr>
</tbody>
</table>

*RRs calculated from unadjusted incidence rates. RR >1 indicates greater risk among men vs women and blacks vs whites.
study sampled all local public health departments, several major academic outpatient clinics, and a percentage of area nursing homes and primary care offices to estimate the number of outpatient strokes. There was 1 lobar ICH identified by these screens.

Discussion

Our reported annual ICH incidence rate of 29.2 per 100 000 persons ≥20 years of age in the GCNK region is higher than most previous reports from the United States and Europe, but differences in study design, population denominators, and demographics limit direct comparisons. ICH appears to be more common in Japan than in Western countries, with published rates of 43 to 47 per 100 000 Japanese. Our report highlights the burden of ICH in American blacks. There have been little data previously to explain the excess of ICH in blacks compared with whites. This study demonstrates that the primary excess of ICH in blacks occurs in young and middle-aged persons, particularly for deep cerebral and brain stem locations. The overall rate of lobar ICH was marginally greater in blacks than whites, a difference produced because of excess risk in middle-aged blacks (ages 35 to 54). Rates of lobar ICH in the elderly, in whom amyloid angiopathy becomes a significant cause of hemorrhage, were comparable between races. These findings suggest that the higher rates of ICH in blacks are likely attributable to differences in prevalence and control of hypertension, which, apart from aging, produce the greatest attributable risk for nonlobar ICH.

Hypertension is more prevalent in blacks than whites. Although hypertension was not an independent risk factor for lobar ICH in a previous report of the GERFHS case-control study, risk for lobar ICH was not stratified by age or race. It is possible that in middle-aged persons, among whom amyloid angiopathy is rare, hypertension plays an important role in lobar ICH and varies by race. Treated and untreated hypertension are risk factors for ICH, with untreated hypertension conveying greater risk. In a previous analysis of our ICH patients, blacks were shown to have higher rates of untreated hypertension, although this difference appeared to be a function of insurance status. It is also possible that other, less well-defined risk factors (perhaps genetic) contribute to different rates and patterns of ICH in blacks and whites.

When comparing genders, overall incidence rates were similar in men and women (RR, 1.1). However, men had higher rates of deep cerebral ICH, whereas risk for lobar ICH was marginally greater for women because of higher rates in very old females (data not shown).

Although the documentation of ICH incidence rates defined by location is unique among population-based studies in the United States, smaller population-based studies in Australia, France, Finland, Sweden, and Japan have recorded ICH by location (Table 4). The studies performed in Japan and France, including a total of 437 ICHs, found ICH distributions quite different from those in the GCNK region, with a heavy predominance of deep cerebral hemorrhage. The proportions of brain stem and cerebellar ICH were fairly constant across studies. Whether differences in ICH distribution reflect variations in study methodology, environmental risk factors, or genetics is unclear.

Our study has several limitations. The comprehensive epidemiologic study of all stroke subtypes performed in the GCNK region in 1999 documented 22 ICHs missed by the GERFHS study, mostly because of ICD coding errors and

### Table 3. Age-Specific RRs for ICH Locations, Black vs White*

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Lobar</th>
<th>Deep Cerebral</th>
<th>Brain Stem</th>
<th>Cerebellum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>20–34</td>
<td>2.1</td>
<td>0.5–9.3</td>
<td>2.1</td>
<td>0.5–9.3</td>
</tr>
<tr>
<td>35–54</td>
<td>3.7</td>
<td>2.1–6.7</td>
<td>4.5</td>
<td>3.0–6.8</td>
</tr>
<tr>
<td>55–74</td>
<td>1.7</td>
<td>1.1–2.7</td>
<td>2.3</td>
<td>1.7–3.3</td>
</tr>
<tr>
<td>75–84</td>
<td>1.2</td>
<td>0.7–2.0</td>
<td>1.1</td>
<td>0.7–1.8</td>
</tr>
<tr>
<td>≥85</td>
<td>1.0</td>
<td>0.4–2.2</td>
<td>0.9</td>
<td>0.4–1.9</td>
</tr>
<tr>
<td>All</td>
<td>1.4</td>
<td>1.0–1.8</td>
<td>1.7</td>
<td>1.4–2.1</td>
</tr>
</tbody>
</table>

*RR calculated from unadjusted incidence rates. RR > 1 indicates greater risk among blacks.

### Table 4. Proportional Distribution of ICH by Location

<table>
<thead>
<tr>
<th>Location</th>
<th>Total ICH</th>
<th>Lobar (%)</th>
<th>Deep Cerebral (%)</th>
<th>Brain Stem (%)</th>
<th>Cerebellum (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater Cincinnati</td>
<td>1038</td>
<td>359 (35)</td>
<td>512 (49)</td>
<td>65 (6)</td>
<td>102 (10)</td>
</tr>
<tr>
<td>Izumo City, Japan</td>
<td>350</td>
<td>53 (15)</td>
<td>242 (69)</td>
<td>30 (9)</td>
<td>25 (7)</td>
</tr>
<tr>
<td>Southern Sweden</td>
<td>341</td>
<td>176 (52)</td>
<td>121 (36)</td>
<td>15 (4)</td>
<td>29 (9)</td>
</tr>
<tr>
<td>Jyvaskyla region, Finland</td>
<td>158†</td>
<td>53 (34)</td>
<td>77 (49)</td>
<td>11 (7)</td>
<td>17 (11)</td>
</tr>
<tr>
<td>Dijon, France</td>
<td>87</td>
<td>16 (18)</td>
<td>58 (67)</td>
<td>5 (6)</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Perth, Australia</td>
<td>60*</td>
<td>19 (40)</td>
<td>31 (52)</td>
<td>4 (7)</td>
<td>6 (10)</td>
</tr>
</tbody>
</table>

*Includes 13 ‘massive cortical’ hemorrhages, here included in the deep group.
†Includes 9 intraventricular hemorrhages, here included in the deep group.
oversight of properly coded, hospitalized cases. On the basis of this comparison, the incidence rates published here may underestimate true rates by 5% to 10%. Three cases of ICH were missed in 1999 because patients died in the emergency department. Two of these cases were posterior fossa (brain stem or cerebellum) ICH; if such hemorrhages are more likely to result in rapid death than supratentorial ICH, they may have been disproportionately missed. Our review of coroners’ cases and the 1999 epidemiologic data suggests that any such effect should be small and not significantly affect the balance of ICH subtypes in our study. Our study did not account for nonhospitalized patients with ICH, but unlike ischemic stroke, these cases are very rare. In the present report, we could not statistically analyze the contribution of risk factors such as hypertension to the occurrence of ICH when stratified by race and location because of limitations of our study design (eg, lack of population controls, with data obtained in a similar fashion to cases). Attempting to better define these relationships will be an important area of future investigation.

We report incidence rates for ICH defined by location in the largest population-based study of ICH to date. The high ICH burden in American blacks is largely explained by an excess of hemorrhages in young and middle-aged persons, particularly for deep cerebral and brain stem locations. The most plausible explanation for this difference is variation in the prevalence and treatment of hypertension, although other risk factors may contribute. Overall ICH rates are similar in men and women, with a slight predominance of deep cerebral ICH in men and lobar ICH in women.

Acknowledgments
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References
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