Incidence Rates of First-Ever Ischemic Stroke Subtypes Among Blacks
A Population-Based Study

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Background and Purpose—The aim of this study was to determine the incidence rates of ischemic stroke subtypes among blacks.

Methods—Hospitalized and autopsied cases of stroke and transient ischemic attack among the 187 000 blacks in the 5-county region of greater Cincinnati/northern Kentucky From January 1, 1993, through June 30, 1993, were identified. Incidence rates were age- and sex-adjusted to the 1990 US population. Subtype classification was performed after extensive review of all available imaging, laboratory data, clinical information, and past medical history. Case-control comparisons of risk factors were made with age-, race-, and sex-matched control subjects.

Results—Annual incidence rates per 100 000 for first-ever ischemic stroke subtypes among blacks were as follows: uncertain cause, 103 (95% confidence interval [CI], 80 to 126); cardioembolic, 56 (95% CI, 40 to 73); small-vessel infarct, 52 (95% CI, 36 to 68); large vessel, 17 (95% CI, 8 to 26); and other causes, 17 (95% CI, 9 to 26). Of the patients diagnosed with an infarct of uncertain cause, 31% underwent echocardiography, 45% underwent carotid ultrasound, and 48% had neither. Compared with age-, race-, and sex- (proportionally) matched control subjects from the greater Cincinnati/northern Kentucky region, the attributable risk of hypertension for all causes of first-ever ischemic stroke is 27% (95% CI, 7 to 43); for diabetes, 21% (95% CI, 11 to 29); and for coronary artery disease, 9% (95% CI, 2 to 16). For small-vessel ischemic stroke, the attributable risk of hypertension is 68% (95% CI, 31 to 85; odds ratio [OR], 5.0), and the attributable risk of diabetes is 30% (95% CI, 10 to 45; OR, 4.4). For cardioembolic stroke, the attributable risk of diabetes is 25% (95% CI, 4 to 41; OR, 3.1).

Conclusions—Stroke of uncertain cause is the most common subtype of ischemic stroke among blacks. Cardioembolic stroke and small-vessel stroke are the most important, identifiable causes of first-ever ischemic stroke among blacks. The incidence rates of cardioembolic and large-vessel stroke are likely underestimated because noninvasive testing of the carotid arteries and echocardiography were not consistently obtained in stroke patients at the 18 regional hospitals. Most small-vessel strokes in blacks can be attributed to hypertension and diabetes. (Stroke. 1999;30:2517-2522.)

Key Words: blacks ■ cardioembolic stroke ■ incidence ■ lacunar infarction ■ risk factors ■ stroke, ischemic

The age- and sex-adjusted incidence rate of first-ever ischemic stroke among blacks in greater Cincinnati/northern Kentucky is 246 per 100 000 as derived from data from the first 6 months of 1993 compared with a rate of 144 per 100 000 among the predominantly white population of Rochester, Minn (data collected from 1985 through 1989; both rates adjusted to the 1990 US population). The Northern Manhattan Stroke Study (NOMASS) reported that the incidence rate of first-ever ischemic stroke for blacks was significantly greater than that among whites. Possible explanations for the increased rate of stroke in blacks include an increased incidence rate of risk factors for stroke, of particular subtypes of stroke (eg, cardioembolism), or of all ischemic stroke subtypes among blacks compared with whites.

The Greater Cincinnati/Northern Kentucky Stroke Study is the largest population-based metropolitan study of temporal trends in stroke incidence rates and outcome within a biracial US population. Our population is similar to that of the United States in terms of age, economic status, and proportion of blacks. In this report, we present the incidence rates of the subtypes of hospitalized or autopsied ischemic stroke among blacks for the first 6 months of 1993 and the prevalence of risk factors for stroke in the black population that are associated with each ischemic stroke subtype.
Methods

Data Collection
The method for data collection, case criteria, and calculation of incidence rates has been previously reported. The study consisted of 2 parts. Part 1 focused on all inpatient and autopsied stroke cases among blacks from January 1, 1993, through June 30, 1993; part 2 focused on all inpatient and a representative sample of all out-of-hospital strokes for whites and blacks from July 1, 1993, through June 30, 1994. Methods for monitoring of inpatient and out-of-hospital stroke in part 2 have been previously reported. The present report focuses on the incidence rates of hospitalized or autopsied strokes among black patients in the first 6 months of 1993. The study population was defined as all residents of the greater Cincinnati/northern Kentucky region, which included 2 southern Ohio counties and 3 contiguous northern Kentucky counties that abut the Ohio river. To qualify as an incidence case, a person must have met criteria for 1 of 6 stroke/transient ischemic attack (TIA) subcategories (cerebral ischemia, hemorrhagic stroke, subarachnoid hemorrhage, intracerebral hemorrhage, stroke of uncertain cause, and TIA), lived at a zip code within the 5-county region at the time of stroke onset, and had the onset of stroke between January 1, 1993, and June 30, 1993, for black Americans. The criteria that defined the various diagnostic categories of stroke, including ischemic stroke subtypes, were adapted from the Classification of Cerebrovascular Diseases III, 1989 and from epidemiological studies of stroke in Rochester; they are listed in the Appendix. Strokes were classified as first ever or recurrent on the basis of evidence of prior clinical stroke in the written history and physical examination of the admitting physician, emergency department physician, consulting neurologist, and nurse. Cases of first-ever stroke by history for which imaging studies indicated an additional old “silent” cerebral infarct were classified as a first-ever cerebral infarction for incidence rate calculations.

Grounds for excluding potential cases of stroke were as follows: (1) the patient had no clinical history of stroke, and the only evidence of stroke was a diagnosis on the death certificate without an area of neurological deficit, autopsy, or head CT. All excluded cases and the reasons for exclusion were recorded. Recurrent strokes were classified as per the criteria for first stroke. Cases that met criteria for cerebral infarction were sorted by the operational categories listed in the Appendix. A patient could qualify for 1 or several of the 6 categories of cerebral infarction. For instance, a patient may have had a potential cardiac source of embolism and ≥50% stenosis of an appropriate extracranial carotid artery. In cases that met criteria for >1 category, the study physician made a final judgment about the most likely cause of cerebral infarction. Classification decisions were made by a single neurologist for all cases.

Calculations and Comparison of Incidence Rates
The denominators for incidence rate calculations were based on linear extrapolations of county populations in race, sex, and age subcategories for 1993. The 1990 US census population figures for each of the 5 counties by race, age, and sex were used to calculate the linear function. Incidence rates were calculated for each age, sex, and race category. For comparison with other studies, including the stroke incidence study in Rochester for 1985 through 1989, the incidence rates for all ischemic stroke and for each stroke subtype were adjusted to the 1990 US population. Then, 95% confidence intervals (CIs) for the incidence rates were calculated by use of a Poisson distribution. The 95% CIs for the difference in rates by race, sex, etc, incorporated a pooled estimate of the variance in incidence rates.

Calculation of Attributable Risk
The prevalence of risk factors among blacks in the Cincinnati population was drawn from the Greater Cincinnati/Northern Kentucky Stroke Survey. This telephone survey was designed to ensure that respondents were randomly selected and that the demographic characteristics of the respondents approximately matched the population characteristics of patients with acute stroke within the study population with respect to age, race, and sex. For the survey, the required number of control subjects for each age group was determined by extrapolating the expected number of stroke cases in the greater Cincinnati population for 1993. The age- and sex-specific incidence rates of ischemic stroke in Rochester from 1974 through 1984 were used to generate the expected number of stroke cases for each age group by sex. The racial distributions of stroke incidence were estimated from a prior study of the incidence rates of intracerebral hemorrhage and subarachnoid hemorrhage in greater Cincinnati during 1988. Only those respondents in the telephone survey whose age, race, and sex matched an unfilled demographic category were interviewed. For each subtype, control subjects were then proportionally matched for each age group by race and sex.

The questions asked were identical to those in the Third National Health and Nutrition Examination Survey (NHANES III). Risk factor information was gathered by careful chart review in cases and by direct telephone survey for control subjects. The prevalence of each risk factor was then calculated for cases and control subjects. Definitions of risk factors for cases have been previously reported. The attributable risk and 95% CIs of each risk factor for first-ever ischemic stroke and ischemic stroke subtype disease were calculated by use of the case-control formula for attributable risk as given by Fleiss.

Results

Incidence Rates
We reviewed the records of 1003 black patient encounters at 19 regional hospitals and 5 coroners’ offices from January 1, 1993, through June 30, 1993, that were coded as potential stroke or TIA. Of the 1003 encounters, 270 patients lived outside the study region, did not have their stroke during the time period for the present study, or were miscoded as a stroke. The remaining 733 incidences occurred in blacks who were residents of the study region and had their event during the study period. Of the 733 encounters, 332 blacks had 351 events that led to hospitalization or autopsy and met the criteria for a stroke or TIA during the study period after review of all clinical and imaging data by the study physicians. Of the 332 subjects with a stroke or TIA, 213 had a first-ever stroke or TIA (no previous history of stroke although prior TIA allowed), 92 had a recurrent stroke, and 27 had a recurrent TIA. Of the 213 with a first-ever stroke or TIA, 181 (84%) had a cerebral infarction and 32 had a first-ever TIA.

Of the 181 cases of first-ever cerebral infarction, there were 41 with cardioembolic stroke, 39 with small-vessel stroke, 14 with stroke from other causes, 12 with large-vessel stroke, and 75 with stroke of uncertain cause. The other
TABLE 1. Prevalence Rate of Risk Factors in Blacks With Ischemic Stroke

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>All (n=181)</th>
<th>Small Vessel (n=39)</th>
<th>Large Vessel (n=12)</th>
<th>Cardioembolic (n=41)</th>
<th>Other (n=14)</th>
<th>Uncertain (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>67</td>
<td>85*</td>
<td>67</td>
<td>71</td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td>Diabetes</td>
<td>33</td>
<td>38</td>
<td>42</td>
<td>37</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>25</td>
<td>39*</td>
<td>33</td>
<td>21</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Age &lt;65 y</td>
<td>38</td>
<td>59*</td>
<td>17*</td>
<td>32*</td>
<td>64</td>
<td>29</td>
</tr>
</tbody>
</table>

Percentage with risk factor (n=total number of patients for each subtype).

* P<0.05; P values calculated as prevalence of a risk factor for each subtype compared with all other subtypes of stroke.

Risk Factors

Initial analysis of subtypes were performed by making comparisons in the prevalence of each factor between stroke subtypes (Table 1). Age >65 years was associated with cardioembolic stroke, large-vessel stroke, and stroke of uncertain cause, whereas more small-vessel strokes and strokes of other causes occurred in patients <65 years of age.

A history of hypertension was found in 67% of all ischemic stroke patients and in 85% of patients with small-vessel stroke. Current smoking was reported in the medical records of 25% of patients, and a history of any smoking was present in 42% of ischemic stroke patients. Hypertension (P=0.017) and current smoking (P=0.045) were more common in small-vessel stroke compared with the other stroke subtypes. A history of diabetes was found in 33% of ischemic stroke patients but was not more common in any particular ischemic stroke subtype.

We then compared the presence of risk factors among 181 black cases and 337 control subjects for the Greater Cincinnati/Northern Kentucky Stroke Survey. For each subtype, control subjects were proportionally matched to cases by age and sex for risk factor comparison. The crude attributable risk is the percentage of disease that theoretically could be prevented if the excess amount of the risk factor in patients compared with control subjects was eliminated from the study population.11 Table 2 shows the attributable risk of each risk factor for first-ever ischemic stroke and subtype of ischemic stroke. For example, if the adverse effects of hypertension could be eliminated, then 68% of small-vessel strokes could theoretically be prevented. Only statistically significant risks are listed.

Testing

The number of evaluations performed by subtype are shown in Table 3. Only 31% of patients with an uncertain cause of infarction had echocardiograms, and 45% had carotid ultrasound. One patient (1.3%) had a cerebral angiogram, and 9 patients (12%) had a magnetic resonance angiogram. Of 181
patients with first-ever ischemic stroke, cerebral angiogram was performed in 9 patients (5%), and magnetic resonance angiogram was performed in 17 (9%). An ECG was documented during hospitalization in 90% of patients with first-ever ischemic stroke, and there was no statistically significant difference in frequency of ECG by stroke subtype.

Extent of testing was not significantly different if a neurologist was involved with the case. Carotid ultrasound was performed 52% of the time when a neurologist was involved and 58% of the time when a neurologist was not (P=0.483). Echocardiogram was performed 46% of the time when a neurologist was involved and 44% of the time when a neurologist was not (P=0.780). Both carotid ultrasound and echocardiogram were performed 31% of the time when a neurologist was involved and 38% of the time when a neurologist was not (P=0.368). Neither a carotid or echocardiogram was performed 33% of the time when a neurologist was involved and 36% of the time when a neurologist was not (P=0.651).

**Discussion**

**Incidence Rates**

Stroke of uncertain cause occurred more frequently in the black population of greater Cincinnati/northern Kentucky than any other stroke subtype. Approximately 40% of patients in our study were categorized as uncertain cause of stroke, which is similar to that reported in the Stroke Data Bank study. In that study, only 23% of patients had both a carotid ultrasound and an echocardiogram, and 43% of patients did not have either study. Similarly, two thirds of our patients diagnosed with uncertain cause of infarction did not have an echocardiogram during hospitalization. Patients categorized thusly may have had a potential cardioembolic source that was not included in the strict criteria for that subtype (eg, mitral valve prolapse, aortic valve disease) or not detected because of a lack of testing.

We found that cardioembolism and small-vessel ischemic stroke are the most important, identifiable causes of ischemic stroke among blacks in our study. The incidence rate of small-vessel ischemic stroke among blacks was 52 per 100 000, which is twice the rate of 25 per 100 000 in the white population of Rochester (Table 4). The incidence rate of cardioembolism in blacks from greater Cincinnati/northern Kentucky (56 per 100 000) was significantly greater than the rate of 40 per 100 000 for the predominately white population of Rochester. The incidence rate of large-vessel atherothrombotic disease among blacks in greater Cincinnati/northern Kentucky (17 per 100 000) was significantly less than the rate of 27 per 100 000 among whites in Rochester, although the number of black patients with large-vessel stroke was small. The incidence rate of other causes of ischemic stroke among greater Cincinnati blacks (17 per 100 000) was 4 times that in the Rochester population (4 per 100 000). The incidence rate of ischemic stroke of uncertain type among blacks in greater Cincinnati/northern Kentucky (103 per 100 000) was double that in the Rochester population (52 per 100 000).

There have been several reports that blacks are at a higher risk for intracranial atherosclerosis compared with whites. Caplan et al reported that 85% of patients with middle cerebral atherosclerosis were black. Gorelick et al reported that blacks had more lesions and a higher degree of stenosis of the middle cerebral artery and the supraclinoid internal carotid artery compared with whites. It is possible that the low rate of large-vessel ischemic stroke in our patient population is due to a lack of diagnostic testing. In our study, of the black patients diagnosed with stroke of uncertain cause, only 45% had a carotid ultrasound and only 15% had a cerebral angiogram or intracranial magnetic resonance angiogram. Practical considerations of how diagnostic studies might (or might not) change the management of a stroke patient likely influenced the frequency and type of tests performed by physicians at regional hospitals.

To make valid comparisons of stroke incidence rates across ≥2 populations, incidence rates should be adjusted to a standardized population, and the definitions for stroke and stroke subtype should be similar. Reports that compare the relative proportions of ischemic stroke subtypes in 2 populations are misleading. For example, small-vessel stroke subtype accounted for only 22% of ischemic stroke patients in blacks in greater Cincinnati/northern Kentucky and 17% among whites in Rochester, suggesting a relatively similar importance as a stroke subtype for whites and blacks. Yet the age- and sex-adjusted rate for small-vessel strokes for blacks was double the rate of small-vessel stroke among whites in Rochester.

Therefore, although blacks have a higher rate of ischemic stroke than whites, the increase does not reflect a uniform increase in all subtypes of ischemic stroke. Uncertain causes of stroke, small-vessel stroke, cardioembolic stroke, and other causes of stroke are more common in blacks in greater Cincinnati/northern Kentucky, and large-vessel stroke is more common in whites in Rochester. When the data concerning stroke in the white and black population of the greater Cincinnati/northern Kentucky region are completed for the following study year, we will be able to confirm whether these racial differences in the incidence rate of stroke subtypes persist when compared in the same study population. In addition, small or minor strokes may be missed in hospital or autopsy-based studies. For the subsequent year, we will have estimates of outpatient strokes for both whites and blacks.
**Risk Factors**

One explanation for some of the differences in stroke incidence rates between blacks and whites is a higher prevalence of several important stroke risk factors among blacks. Smoking, hypertension, and diabetes have been found to be increased in blacks compared with whites. NHANES III (1988 to 1991) reported a rate of hypertension of 32% in blacks compared with 24% in whites.\(^{10}\) NOMASS reported that the rate of hypertension was more prevalent in blacks with stroke compared with whites with stroke (76% versus 63%) and that the rate of current smoking in blacks with stroke was 31% versus 18% for whites with stroke.\(^3\) The Current Population Study (CPS, 1993), which is a continuous monthly survey conducted by the Bureau of the Census that examines self-reported rates of smoking among Americans, found that the national rate of current smoking for blacks was 31% compared with 26% for whites.\(^{17}\) NHANES III reported that the rate of diabetes in the black population was 6.9% compared with 5.0% in whites.\(^{18}\) In a population-based study, Brancati et al\(^{19}\) reported that the prevalence rate of diabetes was 10.3% for blacks compared with 4.6% for whites. After adjustments for differences in age, socioeconomic status, and obesity, blacks remained more than twice as likely to have diabetes compared with whites (odds ratio, 2.35; \(P = 0.0003\)), suggesting that race is an independent risk factor for the development of diabetes.

The prevalence of these known stroke risk factors changes with age. Although we expected all subtypes of stroke to increase with age, we discovered that 59% of small-vessel strokes occurred in patients \(<65\) years of age \((P = 0.016)\). In comparison, 32%, 17%, and 29% of cardioembolic, large-vessel, and undetermined stroke, respectively, occurred in patients \(<65\) years of age.

The rates of hypertension and current smoking were found to be significantly increased in patients with small-vessel stroke compared with other stroke subtypes. It is known that the rate of current smoking declines with age.\(^{20}\) Because small-vessel stroke tends to occur in younger patients (see above), we suspect that the increased prevalence of current smoking in patients with small-vessel stroke is due primarily to the younger age of these patients.

The same argument cannot be used for the increased rate of hypertension in patients with small-vessel stroke. Unlike the decline in the rate of smoking with advancing age, hypertension has been found to increase in prevalence with age.\(^{21}\) Despite the predominately young age of patients that had small-vessel infarction, the rate of hypertension was still found to be significantly increased in patients with small-vessel ischemic infarction compared with other stroke subtypes. In our study, 85% of patients with small-vessel ischemic infarction had hypertension. According to the attributable risk, if hypertension in the black population were eliminated, 68% of small-vessel ischemic strokes and 27% of all ischemic strokes in blacks could be prevented.

Diabetes was found to be a risk factor for stroke in several studies (the Framingham study,\(^{22}\) Honolulu Heart Program,\(^{23}\) Copenhagen Stroke Study\(^{24}\) and Rochester study\(^{25}\)). As measured by attributable risk, elimination of the effects of diabetes could have prevented 30% of small-vessel strokes, 25% of cardioembolic strokes, and 21% of all ischemic strokes in the black population in our study.

The control population used for calculation of attributable risk was drawn from the Greater Cincinnati/Northern Kentucky Stroke Survey. The methods of collecting data were different for cases (chart review) and control subjects (direct telephone interview). This can be a source of potential bias. For example, we would expect that the reported rate of smoking would be higher in a survey or interview than in a chart review. Thus, it is probable that we may have underestimated the attributable risk of smoking and other risk factors because of this bias.

A population-based case-control study can be used to calculate attributable risk,\(^{26}\) which is the proportion of cases that can be attributed to the risk factor.\(^{11}\) This differs from relative risk or odds ratio in that the prevalence of the risk factor in the population is taken into consideration. A risk factor may be highly associated with stroke and thereby have a high relative risk or odds ratio and yet be so rare that the overall burden to society is minimal. In contrast, a risk factor that has a modest association with stroke by relative risk or odds ratio calculation may be highly prevalent in the population and thereby have greater impact on the incidence of stroke. For example, in our study, hypertension has an odds ratio of 1.7 for first-ever ischemic stroke in blacks (Table 2) compared with diabetes, which has an odds ratio of 2.7. Yet hypertension is more prevalent than diabetes in the black population and therefore has a greater attributable risk for first-ever ischemic stroke.

A limitation of the attributable risk is that it does not take into account the complex interactions that 1 risk factor might have on other risk factors. For example, the proportion of small-vessel strokes attributable to diabetes may be due in part to the increased risk of hypertension in diabetics. Therefore, the attributable risks of hypertension (68%) and diabetes (30%) cannot be summed into an overall risk of hypertension and diabetes (98% total).

Whisnant\(^{27}\) reported the results of a computer-intensive model for estimating attributable risk in a multivariate model for the risk factors of ischemic stroke. Multivariate modeling of attributable risk had not been possible previously because of difficulty in determining the standard error of risk factor prevalence estimates in the population.\(^{28}\) To the best of our knowledge, Whisnant’s report is the only multivariate estimate of attributable risk reported for stroke. This proposed approach is the basis for the multivariate model that we are examining to account for the independent influence of each risk factor for each subtype in future analyses.

**Appendix**

**Subtypes of Categories of Ischemic Stroke**

**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 ECG; thrombus in the atrium or ventricle or on the aortic or mitral valve identified by echocardiography or coronary angiography; left ventricular aneurysm 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 also are included.

**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, anterior, and/or posterior cerebral, vertebral, or basilar arteries by angiography or magnetic resonance angiography in ≥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.

**Small-Vessel Stroke**

Either condition 1, 2, or 3 is true. In condition 1, brain images show a deep infarct 1.5 cm in its maximal diameter that is appropriate to a clinical classic lacunar syndrome. In condition 2, brain images show no lesion to explain the clinical syndrome, and the clinical presentation is one (including the following) usually associated with a small deep infarct. Pure motor hemiparesis is hemiparesis or hemiplegia involving the face, 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 has 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 is hemiparesis with ipsilateral ataxia. Paresis is more commonly crural. Dysarthria/clumsy hand syndrome is dysarthria with a clumsy hand. Facial weakness is possible. Hemiballismus, hemiathetosis, or hemidystonia must be another cause. Ataxia-hemiparesis is hemiparesis with ipsilateral ataxia. Paresis is more commonly crural. Dysarthria/clumsy hand syndrome is dysarthria with a clumsy hand. Facial weakness is possible. Hemiballismus, hemiathetosis, or hemidystonia must be acute onset. In sensorimotor stroke, there are weakness and sensory loss involving the face, arm, and leg equally without other neurological findings. In condition 3, 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 1 of the classic syndromes for lacunar stroke.

**Other Cause**

This category included cerebral infarction caused by another clearly identified cause of stroke (eg, traumatic arterial dissection, post–coronary bypass graft surgery, post–carotid endarterectomy, acquired immune deficiency syndrome, and cocaine use).

**Ischemic Stroke of Uncertain Cause**

This category included 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 of the above criteria.

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**References**

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