Stroke Risk After Transient Ischemic Attack in a Population-Based Setting

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Background and Purpose—Stroke risk after transient ischemic attack (TIA) has not been examined in an ethnically diverse population-based community setting. The purpose of this study was to identify stroke risk among TIA patients in a population-based cerebrovascular disease surveillance project.

Methods—The Brain Attack Surveillance in Corpus Christi (BASIC) Project prospectively ascertains stroke and TIA cases in a geographically isolated Southeast Texas County. The community is approximately half Mexican American and half non-Hispanic white. Cases are validated by board-certified neurologists using source documentation. Cumulative risk for stroke after TIA was determined using Kaplan–Meier estimates. Cox proportional hazards regression was used to test for associations between stroke risk after TIA and demographics, symptoms, risk factors, and history of stroke/TIA.

Results—BASIC identified 612 TIA cases between January 1, 2000, and December 31, 2002; 60.9% were female and 48.0% were Mexican American. Median age was 73.8 years. Stroke risk within 2 days, 7 days, 30 days, 90 days, and 12 months was 1.64%, 1.97%, 3.15%, 4.03%, and 7.27%, respectively. Stroke risk was not influenced by ethnicity, symptoms, or risk factors.

Conclusions—Using a population-based design, we found that early stroke risk after TIA was less than previously reported in this bi-ethnic population of Mexican Americans and non-Hispanic whites. Approximately half of the 90-day stroke risk after TIA occurred within 2 days. (Stroke. 2004;35:1842-1846.)

Key Words: cerebral ischemia, transient stroke population surveillance Hispanic Americans Mexican Americans risk mortality
they are retrained. Retraining has not been necessary. Patients who had a validated diagnosis of TIA between January 1, 2000, and December 31, 2002, were included. TIA was defined by the World Health Organizations criteria as “rapidly developed clinical signs of focal or global disturbance of cerebral function, with no apparent nonvascular cause.”8 To avoid confusing stroke with TIA, symptoms must have been documented to abate within 24 hours. Patients who left the ED with symptoms, without documented resolution within 24 hours, were considered to have stroke rather than TIA. This categorization is consistent with studies that suggest that as many as 60% of TIA resolve within 60 minutes.9 TIA cases were assigned a classification of probable (onset of acute focal neurological deficit and documented exclusion of other possible causes) or possible (onset of acute focal neurological deficit without supportive clinical or laboratory evidence to exclude other possible causes).

Demographics, history, symptoms, risk factors, and neurology consultation were obtained from the chart for all cases. Race/ethnicity was obtained from the chart. This method was previously validated.10 The abstractors’ laptop computer has a randomization algorithm that selects two thirds of patients for interview. The interview cooperation rate was 84%. Interview data were not used for the current analysis. Among those interviewed, the computer also randomly selects two thirds for extended abstraction to collect information regarding discharge medications, brain, vascular, and cardiac imaging, and electrocardiograms.

The primary outcome was cumulative stroke risk after TIA. A secondary outcome was cumulative all-cause mortality risk after TIA.

Mortality cases were identified using active and passive surveillance of in-hospital stroke cases and data obtained from the Texas Department of Health death certificate database. Because Nueces County is not an immigrant community, it is unlikely that residents go to another country to die. Five pieces of data collected from the medical record (first name, last name, social security number, date of birth, and permanent address) were used to link with the Texas Department of Health death database. At least 3 of the 5 items must have been identical to be considered a match. We also have close interaction with the Nueces County medical examiner to identify additional stroke deaths.

**Statistical Analysis**

Cumulative risk for ischemic stroke, intracerebral hemorrhage (ICH), and all stroke types combined after presentation for TIA was determined using Kaplan–Meier product limit estimates. In individuals with multiple TIAs or multiple strokes, the date of the first TIA or stroke captured by BASIC was considered. Individuals were censored at death. The main analysis included probable and possible TIAs. A subanalysis was performed on probable TIAs only. Cumulative risk for all-cause mortality after a TIA was also determined using Kaplan–Meier estimates. Cox proportional hazards regression was used to test the associations between stroke risk and demographic (age, gender, ethnicity), symptoms (motor, sensory, visual, language), risk factors (diabetes, hypertension, atrial fibrillation, smoking, coronary artery disease, high cholesterol), number of risk factors, and history of stroke/TIA. First, univariate analyses were conducted with each variable and the primary outcome. Second, a multivariable model was constructed by including variables that were associated with stroke risk in the univariate analyses at the P<0.20 level. Age was modeled continuously. All other variables were modeled dichotomously. Descriptive statistics were used to analyze discharge medications and the proportion of patients receiving brain, vascular, and cardiac imaging, as well as electrocardiograms, in the random sample of cases for which this information was available.

The project was approved by the Universities Institutional Review Boards and by each Nueces County hospital.

**Results**

There were 14,212 cases screened by abstractors between January 1, 2000, and December 31, 2002. Of these cases, 2955 met screening criteria and were reviewed by a neurologist for validation. There were 2550 validated cases of cerebrovascular disease during the study time period, with 751 being TIAs. When a patient had >1 TIA, all TIAs that occurred after the first were excluded (n=45), leaving 706 independent TIA cases. Thirty-six cases in those of black race and 3 in those with unknown race/ethnicity were excluded because of small sample size, leaving 667 cases. Fifty-five cases were out-of-hospital cases, leaving 612 cases for the final analysis. A random sample of 171 of the 612 had data regarding discharge medications, brain, vascular, and cardiac imaging, and electrocardiograms.

Table 1 displays demographic and baseline characteristics of the 612 TIA cases. Sixty-one percent were female and 48.0% were Mexican American. Median age was 73.8 years (mean, 72.3; SD, 12.1). One third of patients had a history of stroke or TIA. Twenty-four percent had >2 risk factors. Of the 612 TIA cases, 569 (93.0%) were seen in the ED and 43 (7.0%) were direct admissions to the hospital. Of those seen in the ED (n=569), 64.0% were subsequently admitted.

Of the 55 patients with out-of-hospital TIA cases, 3 (5.5%) had a stroke and 2 (3.6%) died within the study period. Of the 612 patients with ED or direct admission TIA cases, 44 (7.2%) had a stroke within the study period. Forty-one (93.2%) cases were ischemic and 3 (6.8%) were ICH. There were no subarachnoid hemorrhages after TIA. At 2 days, 7 days, 30 days, 90 days, and 12 months, cumulative risk for...
stroke (ischemic or ICH) was 1.64%, 1.97%, 3.15%, 4.03%, and 7.27%, respectively (Table 2). Cumulative risk for ischemic stroke after TIA for the same time points was 1.64%, 1.98%, 3.17%, 4.05%, and 6.62%, respectively (Table 2). Cumulative risk for ICH after TIA was 0.74% at 12 months. The Figure displays cumulative stroke-free survival for the study period. Of the 612 TIAs, 362 were classified as probable TIAs. Among these cases, cumulative risk for ischemic stroke was 1.95% (95% CI, 0.93 to 4.04) at 2 days, 2.51% (95% CI, 1.31 to 4.77) at 7 days, 4.25% (95% CI, 2.58 to 6.95) at 30 days, 5.81% (95% CI, 3.78 to 8.86) at 90 days, and 8.93% (95% CI, 6.22 to 12.74) at 12 months.

Ethnicity was not associated with stroke risk (Table 3). Language symptoms predicted stroke after TIA in univariate analysis (RR, 1.88; 95% CI, 1.03 to 3.45) but was not significant in the multivariable model. Motor symptoms was a borderline significant predictor of stroke risk in univariate analysis (RR, 2.07; 95% CI, 0.99 to 4.30) but also did not reach significance in the multivariable model.

Cumulative all-cause mortality risk after TIA at 7 days, 30 days, 90 days, and 12 months was 0.33%, 1.34%, 3.93%, and 9.77%, respectively (Table 2). The Figure displays cumulative survival after TIA for the 36-month time period.

Table 4 displays the percentages of patients discharged with antiplatelet and anticoagulant therapies and the proportions of patients receiving diagnostic tests assessing TIA cause from a random sample of the TIA patients (n = 171). Nearly 19% of TIA patients did not have documentation regarding specific discharge medications, and 5% had no documentation of head imaging. Ninety-five (55.6%) of the TIA patients underwent carotid ultrasound. Of these 95 patients, 9.5% had carotid stenosis >70% of 1 internal carotid artery. Neurology consultations were performed in 37.6% of the 612 TIA patients.

**Discussion**

There is a lack of recent data on short-term risk of stroke after TIA, especially from prospective population-based studies with large sample size. BASIC is a prospective population-based study of stroke and TIA in an ethnically diverse community and uses rigorous case ascertainment procedures.

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**Table 2. Risk of Stroke or Mortality After TIA**

<table>
<thead>
<tr>
<th>All Strokes*</th>
<th>95% CI</th>
<th>Ischemic Stroke</th>
<th>95% CI</th>
<th>ICH</th>
<th>95% CI</th>
<th>Mortality</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Day</td>
<td>1.64</td>
<td>0.88–3.02</td>
<td>1.64</td>
<td>0.89–3.03</td>
<td>0.00</td>
<td>—</td>
<td>0.00</td>
</tr>
<tr>
<td>7-Day</td>
<td>1.97</td>
<td>1.12–3.44</td>
<td>1.98</td>
<td>1.13–3.45</td>
<td>0.00</td>
<td>—</td>
<td>0.33</td>
</tr>
<tr>
<td>30-Day</td>
<td>3.15</td>
<td>2.02–4.90</td>
<td>3.17</td>
<td>2.03–4.92</td>
<td>0.00</td>
<td>—</td>
<td>1.34</td>
</tr>
<tr>
<td>90-Day</td>
<td>4.03</td>
<td>2.72–5.96</td>
<td>4.05</td>
<td>2.73–5.99</td>
<td>0.00</td>
<td>—</td>
<td>3.93</td>
</tr>
<tr>
<td>12-Month</td>
<td>7.27</td>
<td>5.35–9.86</td>
<td>6.62</td>
<td>4.81–9.10</td>
<td>0.74</td>
<td>0.24–2.29</td>
<td>9.77</td>
</tr>
</tbody>
</table>

BASIC January 1, 2000, to December 31, 2002 (N=612).

*Ischemic stroke and intracerebral hemorrhage (ICH).

**Table 3. Univariate and Multivariable Associations of Risk Factors for Stroke After TIA**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.00 (0.98–1.03)</td>
<td>1.00 (0.98–1.03)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.00</td>
<td>1.00 (0.55–1.84)</td>
</tr>
<tr>
<td>Female</td>
<td>1.00</td>
<td>1.00 (0.55–1.84)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHW</td>
<td>1.00</td>
<td>1.00 (0.55–1.84)</td>
</tr>
<tr>
<td>MA</td>
<td>0.85</td>
<td>0.85 (0.47–1.54)</td>
</tr>
<tr>
<td>TIA Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor</td>
<td>2.07 (0.99–4.30)</td>
<td>1.90 (0.91–3.97)</td>
</tr>
<tr>
<td>Sensory</td>
<td>0.65 (0.35–1.23)</td>
<td>0.66 (0.35–1.26)</td>
</tr>
<tr>
<td>Visual</td>
<td>0.22 (0.03–1.61)</td>
<td>0.26 (0.04–1.92)</td>
</tr>
<tr>
<td>Language</td>
<td>1.88 (1.03–3.45)</td>
<td>1.67 (0.90–3.10)</td>
</tr>
<tr>
<td>Risk Factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.90 (0.94–3.86)</td>
<td>1.83 (0.89–3.74)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.49 (0.81–2.74)</td>
<td>1.42 (0.76–2.62)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.53 (0.65–3.61)</td>
<td>1.52 (0.65–3.61)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.14 (0.61–2.13)</td>
<td>1.13 (0.60–2.12)</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>0.70 (0.30–1.66)</td>
<td>0.69 (0.30–1.66)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.43 (0.75–2.72)</td>
<td>1.42 (0.76–2.62)</td>
</tr>
<tr>
<td>≥2 Risk factors</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;2 Risk factors</td>
<td>1.17 (0.61–2.28)</td>
<td>1.17 (0.61–2.28)</td>
</tr>
<tr>
<td>History of stroke/TIA</td>
<td>1.06 (0.57–1.95)</td>
<td>1.06 (0.57–1.95)</td>
</tr>
</tbody>
</table>

BASIC January 1, 2000, to December 31, 2002 (N=612).

*Adjusted for TIA symptoms, hypertension, and diabetes.

1.0 indicates referent; RR, relative risk; NHW, nonHispanic white; MA, Mexican American.
to acquire all strokes and TIAs that present for medical attention. Data has been collected for 3 years, resulting in a large sample size from which to quantify stroke risk after TIA. Results from our study show a lower risk of stroke than previously published studies, which used data from population-based studies1,2,11 and data from an HMO population.3 Differing case ascertainment methods may partially explain differences in results.

Screening for cases in BASIC is accomplished by searching admission and ED logs for validated symptoms or diagnostic terms for cerebrovascular patients.6 Those patients with an admitting diagnosis/symptom suggestive of stroke are selected for case review and validation. The 2 UK study populations differ from our population with respect to ethnic composition, we did not find that ethnicity influences stroke risk. It was recently shown that TIA is more common in Mexican Americans compared with non-Hispanic whites at younger ages (45 to 59 years; RR, 1.96; 95% CI, 1.3 to 2.9), but not at older ages.10 Both populations were similar to our population in terms of other factors, including age, gender, and history of stroke; thus, potential differences in outcome would likely not be attributed to these factors.

Our stroke risks were also lower than that of an analysis based on HMO patients presenting to the ED.3 This study used the ED physician’s primary diagnosis to ascertain TIAs cases. This study population may be biased toward more severe TIAs because of instructions to HMO members concerning ED use12 and financial deterrents to seeking ED medical care, such as copayments.11 This point is supported by the sample’s mean symptom duration of 207 minutes. Longer TIA duration is associated with higher stroke risk.3 We did not record symptom duration; therefore, we could not evaluate whether this impacted our results. Because our definition of TIA excluded patients with persistent symptoms at ED discharge, this may have excluded some patients with longer TIAs and therefore higher stroke risk. The Johnston study’s population was similar to our population with respect to demographics and medical history.

Although we found lower risk of stroke than recent studies, we found that almost half of strokes that occur within 90 days happen within the first 2 days, suggesting that there are TIA patients who are at high immediate risk for a recurrent cerebrovascular event. This finding supports the need for urgent evaluation of TIA patients. Identifying risk factors for this subgroup is essential, because these patients may benefit from immediate intervention strategies. In our data, potential predictors of stroke after TIA were the presence of language or motor symptoms.

Although studies have investigated mortality risk after stroke, few studies have quantified mortality risk after TIA. A recent study using Medicare administrative claims data reported mortality risk to be 1.6% at 1 month. This study population was limited to Medicare recipients aged 65 years or older (median 78 years) with fee-for-service medical coverage.14 In the current analysis, all-cause mortality risk was similar at 1.3% at 1 month.
Despite guidelines regarding use of stroke prophylactic agents, nearly 19% of TIA patients did not have documentation of being discharged with an antithrombotic drug. This estimate is consistent with previous estimates.\textsuperscript{15} Guidelines for diagnostic evaluation were also not always followed. Fourteen percent of TIA patients did not have an electrocardiogram performed, and 5% had no brain imaging performed.

There are limitations to this study that warrant discussion. It is possible we did not capture all TIAs and strokes presenting to medical attention. However, the surveillance methods used in this study offer the highest sensitivity for case capture relative to other methods.\textsuperscript{5} We used rigorous quality-control procedures to ensure that abstractors did not miss cases, including a 2-month training period in which abstractors had to demonstrate 97% agreement with study neurologists for case verification.

Our study population largely consisted of patients presenting to an ED; therefore, our case ascertainment relies on the ability of ED physicians to recognize and document signs and symptoms of TIA. Although they were not trained in eliciting TIA symptoms before the study, we have demonstrated that physicians practicing in the EDs in this community have a high sensitivity for stroke/TIA diagnosis.\textsuperscript{16} Because of our case ascertainment methods, we excluded patients who had a stroke but never presented for medical attention for an initial TIA. We also excluded patients who did not have a stroke and did not present for medical attention for a TIA, so it is not possible to determine the direction of ascertainment bias. In our study community, we have estimated that out-of-hospital TIAs account for 14% of TIAs reported to medical attention; therefore, the majority of patients visit the ED directly for TIA, limiting ascertainment bias.\textsuperscript{10}

Some cases considered “possible” TIAs may not have been true TIAs, perhaps contributing to our lower estimates of subsequent stroke risk. However, results from an analysis of “probable” TIA cases differed little from the overall results, suggesting that the inclusion of “possible” TIAs did not dilute our estimates.

Our study population consists of a large proportion of Mexican Americans providing the first estimates of early stroke risk from an ethnically diverse study population; however, our results may have limited generalizability to populations with different race/ethnic structures.

Acknowledgments
This study was funded by the National Institutes of Health (RO1 NS38916).

References
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Stroke. 2004;35:1842-1846; originally published online June 10, 2004;
doi: 10.1161/01.STR.0000134416.89389.9d
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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World Wide Web at:
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