Mexican Americans With Atrial Fibrillation Have More Recurrent Strokes Than Do Non-Hispanic Whites

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Background and Purpose—Atrial fibrillation is a common cause of stroke with a known preventive treatment. We compared poststroke recurrence and survival in Mexican Americans (MAs) and non-Hispanic whites (NHWs) with atrial fibrillation in a population-based study.

Methods—Using surveillance methods from the Brain Attack Surveillance in Corpus Christi Project, cases of ischemic stroke/transient ischemic attack with atrial fibrillation were prospectively identified from January 2000 to June 2008. Recurrent stroke and all-cause mortality were compared by ethnicity with survival analysis methods.

Results—A total of 236 patients were available (88 MAs, 148 NHWs). MAs were younger than NHWs, with no ethnic differences in severity of the first stroke or proportion discharged on warfarin. MAs had a higher risk of stroke recurrence than did NHWs (Kaplan-Meier estimates of survival free of stroke recurrence risk at 28 days and 1 year were 0.99 and 0.85 in MAs and 0.98 and 0.96 in NHWs, respectively; \( P=0.01 \), log-rank test), which persisted despite adjustment for age and sex (hazard ratio=2.46; 95% CI, 1.19–5.11). Severity of the recurrent stroke was higher in MAs than in NHWs \( (P=0.02) \). There was no ethnic difference in survival after stroke in unadjusted analysis or after adjusting for demographic and clinical factors (hazard ratio=1.03; 95% CI, 0.63–1.67).

Conclusions—MAs with atrial fibrillation have a higher stroke recurrence risk and more severe recurrences than do NHWs but no difference in all-cause mortality. Aggressive stroke prevention measures focused on MAs are warranted. (Stroke. 2010;41:2132-2136.)

Key Words: prevention ■ stroke care

Atrial fibrillation (AF) is the most common sustained heart rhythm abnormality, affecting >2.2 million adults in the United States.\(^1\) AF is an important risk factor for both incident and recurrent stroke.\(^2\) Cardioembolic stroke, most of which is due to AF, is the most lethal subtype of ischemic stroke\(^3\) and has a higher risk of disability than other stroke subtypes.\(^4\) Strokes due to AF are largely preventable with warfarin therapy, which results in a 64% relative risk reduction.\(^5\) However, the use and effectiveness of warfarin have been suggested to be suboptimal in Hispanics and other minority groups.\(^6,7\)

Mexican Americans (MAs) are the largest subgroup of Hispanic Americans, the largest minority population in the United States.\(^8\) MAs have a higher incidence of stroke than do non-Hispanic whites (NHWs)\(^9\) yet have better poststroke survival.\(^10\) However, little is known about poststroke outcomes in MAs with AF. The objective of this study was to investigate ethnic differences in stroke recurrence and poststroke mortality in a population-based study of individuals with AF and stroke.

Received April 30, 2010; accepted June 2, 2010.

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Stroke is available at http://stroke.ahajournals.org

DOI: 10.1161/STROKEAHA.110.589127

Clinical Sciences
ischemic attack (TIA) carried the same definition as ischemic stroke except that symptoms resolved within 24 hours.9

BASIC methodology included an extended chart abstraction of a randomly selected subset of cases and also included a review of ECG reports. The study population consisted of BASIC patients with ischemic stroke or TIA between January 1, 2000, and June 30, 2008, who underwent extended abstraction and were found to have either a chart history of AF or AF noted on the admission ECG. TIA were included up to July 31, 2007, as BASIC stopped surveillance for TIA after that date. Some patients in the current study were included in prior reports of stroke recurrence13 or poststroke mortality19 from BASIC; however, the majority (160 of 236, 68%) of patients in the current study were not included in these prior articles owing to a longer period of case ascertainment and minor differences in inclusion criteria.

Demographics and Stroke Risk Factors

Stroke risk factors, including coronary artery disease, diabetes, hyperlipidemia, hypertension, previous stroke, smoking, insurance status, and presence of a primary care physician, were obtained from the medical record. National Institutes of Health Stroke Scale (NIHSS) at the time of the index event and at the time of stroke recurrence was abstracted from the medical record.14 Use of warfarin or antiplatelet agents at discharge from the index event and at the time of presentation with recurrent stroke was abstracted from the medical record. Education level was obtained from patient or proxy interview and was treated as a dichotomous variable defined by completion of high school. Ethnicity was determined from the medical record, as we have previously shown 97% agreement between medical record and patient self-report (kappa = 0.94).9

Identification of Recurrent Stroke and Mortality

Recurrent ischemic stroke or intracerebral hemorrhage was determined from BASIC surveillance through June 30, 2008. All-cause mortality through the same date was determined from the medical record for in-hospital mortality or through Texas Department of Health databases or the Social Security Death Index. Through 2005, deaths were identified as previously described,10 with a match on 4 of 5 identifiers (first name, last name, date of birth, Social Security number, and permanent address) needed to confirm a case as deceased. After 2005, the methodology for identifying out-of-hospital deaths changed slightly owing to delays in receiving the Texas Department of Health database and the fact that the Texas Department of Health no longer provided Social Security numbers. The Social Security Death Index then served as the primary method for identifying deaths according to the same matching criteria. After the Social Security Death Index search, patients whose mortality status was unknown were linked to the Texas Department of Health death certificate database by first and last names, date of birth, and permanent address. All 4 items had to be identical to confirm a match, although some manual review was required for special circumstances, such as transposed numbers.

Statistical Analysis

Age was compared by ethnicity with a Student t test, and NIHSS was compared by ethnicity with the Wilcoxon rank-sum test for the index stroke and the first recurrent stroke. Stroke risk factors, demographics, and antithrombotic medications (at discharge from the index event and at time of first recurrent stroke) were compared with χ² tests or Fisher’s exact tests. Stroke recurrence was compared by ethnicity with Kaplan-Meier estimates and the log-rank test, with cases censored at the time of death or at the end of follow-up (June 30, 2008). Multivariable Cox proportional-hazards regression was performed to compare recurrence-free survival by ethnicity. Because we observed a small number of recurrent strokes, our presupposed analysis plan was to adjust for only demographics (age and sex) based on the recommendation to have 10 events per covariate to ensure model validity.15 However, owing to the possibility of strong confounding by diabetes and education, additional exploratory mod-

| Table 1. Demographic Characteristics and Stroke Risk Factors (N=236) |
|-----------------|-----------------|-----------------|-----------------|
|                | NHWs            | MAs             | P Value         |
| n               | 148             | 88              |                 |
| Age, y          | 82 (75, 88)     | 78 (68, 83.5)   | <0.01           |
| Female          | 79 (53%)        | 54 (61%)        | 0.23            |
| Initial NIHSS   | 4 (2, 9)        | 5 (2, 8)        | 0.84            |
| Coronary artery disease | 80 (54%) | 48 (55%)        | 0.94            |
| Ischemic stroke as presenting syndrome | 115 (78%) | 70 (80%) | 0.74 |
| Diabetes mellitus | 39 (26%) | 44 (50%) | <0.01 |
| Hypertension    | 115 (78%)       | 74 (84%)        | 0.23            |
| History of previous stroke or TIA | 51 (34%) | 29 (33%) | 0.81 |
| Current smoking | 17 (12%)        | 7 (8%)          | 0.35            |
| Primary care physician | 143 (97%) | 79 (90%) | 0.03 |
| High school education* | 111 (77%) | 20 (23%) | <0.01 |
| Health insurance coverage† | 144 (99%) | 83 (95%) | 0.20 |

Values are median (IQR) or n (%), as appropriate. *Four cases with missing data. †Three cases with missing data.

els were constructed by adding diabetes and education (together and separately) to the model. Only the first recurrent event was included in the survival analyses, as only 4 patients had >1 recurrent event. Poststroke all-cause mortality through the end of follow-up was compared by ethnicity with Kaplan-Meier estimates and the log-rank test, with cases censored at the end of follow-up. Multivariable Cox proportional-hazards regression was performed to compare survival by ethnicity. Covariates for the mortality model were preselected on the basis of factors that were significantly associated with mortality or that confounded the ethnicity-mortality relation in a prior analysis of poststroke mortality in this population.10 Sex was also preselected to be in the model, based on prior literature showing an association between sex and poststroke survival.16 Final model covariates included age (treated continuously), sex, ethnicity, NIHSS (treated continuously), coronary artery disease, stroke recurrence (modeled as a time-dependent variable), diabetes, and education (dichotomous). Because stroke recurrence risk differed by ethnicity and recurrent stroke could be along the causal pathway between ethnicity and mortality, an additional exploratory analysis was performed by excluding recurrent stroke. Analysis was performed in SAS 9.1.3 (SAS Institute, Cary, NC).

Standard Protocol Approvals, Registrations, and PatientConsents
This study was approved by the institutional review board of the University of Michigan as well as the individual Texas hospitals.

Results
A total of 5681 cases of ischemic stroke or TIA were identified between January 1, 2000, and June 30, 2008. Of these, 1660 were randomly selected for extended chart review including ECG reports, with a total of 236 cases of ischemic stroke/TIA and AF included.

Table 1 shows demographic and baseline characteristics of the study population. Compared with NHWs, MAs were younger, less likely to have completed 12 years of education, more likely to be diabetic, and less likely to have a primary care physician. There were no significant ethnic differences in other stroke risk factors as shown in Table 1. There was no
ethnic difference in the proportion of cases discharged on warfarin at the time of their baseline stroke/TIA (MA, 37%; NHW, 40%; P=0.68; 21 cases with missing data) or the proportion discharged on no antiplatelet or anticoagulant medication (MA, 16%; NHW, 19%; P=0.54; 21 cases with missing data).

Thirty-three individuals had at least 1 recurrent event (19 MAs and 14 NHWs) during a median follow-up of 427.5 days (interquartile range [IQR] = 90.5, 1164). All recurrent events were ischemic strokes, with the exception of 1 intracerebral hemorrhage in an MA. Among those with recurrent stroke, no ethnic difference at the time of the recurrence was found in the proportion taking warfarin (MA, 38%, NHW, 36%, P=0.92; 3 cases with missing data) or taking no antiplatelet/anticoagulant medication (MA, 7%; NHW, 19%; P=0.60; 3 cases with missing data). The median NIHSS at the first recurrent event was significantly higher in MAs (median, 10; IQR, 3, 18) than in NHWs (median, 4; IQR, 3, 6; P=0.02). Three MAs and 1 NWH had a second recurrent stroke during the study period, and 1 MA had 3 recurrent strokes during the study period.

MAs had a higher risk of stroke recurrence than did NHWs (P=0.01). Kaplan-Meier estimates of survival free of stroke recurrence at 28 days and 1 year were 0.91 and 0.69 in MAs and 0.82 and 0.65 in NHWs, respectively (Figure 2). There was no difference in survival by ethnicity (P=0.99). Cox proportional-hazards analysis showed no difference in survival by ethnicity in unadjusted analysis (HR=1.00; 95% CI, 0.71 to 1.42) or when adjusted for age, sex, initial NIHSS, coronary artery disease, education, recurrent stroke, and diabetes (HR=1.03; 95% CI, 0.63 to 1.67). Age, initial NIHSS, recurrent stroke, and sex were significantly associated with survival, as shown in Table 2. The exploratory analysis that removed stroke recurrence from the multivariable model also showed no ethnic difference in mortality (1.21; 95% CI, 0.76 to 1.94).

Discussion
This population-based study of stroke/TIA patients with AF found that MAs have more than double the risk of recurrent stroke and a greater severity of recurrent stroke than do NHWs. There was no ethnic difference in poststroke mortal-

![Figure 1. Survival free of stroke recurrence. Kaplan-Meier curve showing survival free of stroke recurrence by ethnicity (P=0.01 log-rank test).](image1)

![Figure 2. All-cause mortality. Kaplan-Meier curve showing survival after stroke by ethnicity (P=0.99, log rank test).](image2)

Table 2. Multivariable Models for Stroke Recurrence and All-Cause Mortality

<table>
<thead>
<tr>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke recurrence (n=236)</td>
<td></td>
</tr>
<tr>
<td>MA*</td>
<td>2.46</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
</tr>
<tr>
<td>Female†</td>
<td>0.94</td>
</tr>
<tr>
<td>All-cause mortality (n=232‡)</td>
<td></td>
</tr>
<tr>
<td>MA*</td>
<td>1.03</td>
</tr>
<tr>
<td>Age</td>
<td>1.06</td>
</tr>
<tr>
<td>Female†</td>
<td>0.60</td>
</tr>
<tr>
<td>NIHSS at index stroke§</td>
<td>1.07</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.19</td>
</tr>
<tr>
<td>High school education</td>
<td>0.99</td>
</tr>
<tr>
<td>Recurrent stroke</td>
<td>3.66</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.03</td>
</tr>
</tbody>
</table>

*Reference was NHW.
†Reference was male.
‡Four cases were excluded from the full model for mortality owing to missing data on education.
§Treated linearly.
ity. A higher risk of recurrence in MAs could be explained by ethnic differences in warfarin use or monitoring, although we found no ethnic differences in the proportion of cases on anticoagulant or antiplatelet medication at discharge or at the time of stroke recurrence. We did not have more detailed data on outpatient use or monitoring of warfarin, which has been shown to be suboptimal in Hispanic Medicare beneficiaries with AF. Therefore, we cannot exclude the possibility that ethnic differences in warfarin management contributed to the observed ethnic differences in stroke recurrence. Therapeutic use of warfarin has been associated with a lower stroke severity. The greater severity of recurrent stroke in MAs could therefore be consistent with less effective control of anticoagulation in this group. Others have also suggested that warfarin may be less efficacious in minority populations than in NHWs.

The higher burden of recurrent stroke in MAs could also be explained by a greater frequency of noncardioembolic recurrent strokes in MAs than in NHWs. Indeed, MAs were more likely than NHWs to have diabetes, which is an important risk factor for small-vessel disease and is a risk factor for stroke in AF. However, it is unlikely that the excess small-vessel disease in MAs is responsible for the ethnic difference in recurrence, as adjustment for diabetes in exploratory analyses did not alter the higher risk of recurrent stroke in MAs. We did not formally classify the recurrent stroke subtype in the current work, as a diagnosis of small-artery occlusion requires that cardioembolic sources be absent, and therefore, no cases in this study would have been classified as small-vessel disease, because all had AF.

Access to care or socioeconomic factors also may have contributed to the higher risk of recurrence in MAs. However, the Corpus Christi population is nonimmigrant, with the majority of MA stroke patients in this community having been born in the United States. There was no ethnic difference in health insurance coverage in this community, although MAs were less likely than NHWs to have a primary care physician (97% vs 90%, \( P=0.03 \)). Although this difference in the presence of a primary care physician was statistically significant, the absolute difference may have been too small to be clinically important. MAs were significantly less likely than NHWs to have completed high school, and adjusting for high school education in the multivariable model attenuated the relation between ethnicity and risk of recurrence, although this exploratory analysis should be interpreted with caution owing to the small sample. Lack of a high school education has been associated with stroke in both MAs and NHWs in this population. Lower educational levels might directly contribute to difficulty in following directions for warfarin monitoring and the associated dietary restrictions, or it could be a marker for lower socioeconomic status.

Despite the higher risk of stroke recurrence, there was no ethnic difference in poststroke mortality. This is somewhat surprising, particularly given that recurrent stroke itself was a potent predictor of mortality and that MAs had more recurrent strokes that were more severe than NHWs. The exploratory analysis that removed recurrent stroke from the multivariable mortality model resulted in an increase in the HR for risk of death in MAs (from 1.03 to 1.21), but it remained nonsignificant. We have previously shown a higher risk of stroke recurrence and a lower risk of death in MAs compared with NHWs when all ischemic strokes in this community were examined. Better than expected mortality in Hispanics has been seen in other diseases and has been termed the “Hispanic paradox.” We did not demonstrate lower mortality in MAs than in NHWs in this study. However, the finding of similar mortality by ethnicity despite a higher recurrence risk in MAs may still be reflective of a broader protective effect of Hispanic ethnicity against mortality. Ethnic differences in social support networks or do-not-resuscitate orders may also play a role, and this requires further study.

Use of warfarin at the time of discharge or at the first recurrent event was 40% or less in both ethnic groups. We cannot comment on the appropriateness of this treatment pattern because we were unable to systematically assess for contraindications to warfarin and did not track outpatient medications or time spent in the range of therapeutic anticoagulation. Therefore, it is possible that patients not prescribed warfarin at discharge had contraindications to treatment or had anticoagulation initiated at a subsequent outpatient visit. However, contraindications to warfarin are unlikely to be the sole reason for the low proportion of patients treated with warfarin. A study of Medicare patients hospitalized with AF, which was able to assess for contraindications, still found that only two thirds of ideal candidates were prescribed warfarin. Therefore, the finding of a relatively low proportion of AF patients treated with warfarin is not unique to this community.

This work has limitations. This was a retrospective review of prospectively collected data. Some potentially important factors such as warfarin contraindications were not systematically assessed. We were unable use a stroke risk stratification scheme for AF, such as the CHADS score, owing to a lack of data on recent congestive heart failure exacerbation. However, all patients in this study were at high risk of recurrent stroke and were potential candidates for warfarin, given their presentation with stroke or TIA. The small sample and the low number of recurrent events limited our ability to adjust for confounders in the recurrence analysis. However, the strength of the association between ethnicity and stroke recurrence despite the small sample suggests that this is an important association that deserves further study.

In conclusion, MAs with AF and stroke/TIA have a higher risk of stroke recurrence and greater severity of recurrent stroke, yet there are no differences in poststroke survival when compared with NHWs. Aggressive stroke prevention measures are warranted in this population, and further study is needed to investigate reasons for the higher risk of recurrence and severity in MAs.

Sources of Funding

This study was supported by the National Institutes of Health (NINDS R01 NS38916). Dr Simpson received a travel fellowship award from the American Neurological Association to present the data in this manuscript. Dr Skolari received research support from the American Academy of Neurology Clinical Research Training Fellowship.
Disclosures

None.

References


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Stroke. published online September 9, 2010;
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

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/early/2010/09/09/STROKEAHA.110.589127.citation

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