Diabetes Mellitus as a Risk Factor for Stroke Incidence and Mortality in Mexican American Older Adults

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Background. Little is known regarding diabetes mellitus as a risk factor for stroke incidence and death in older Mexican Americans. The authors studied diabetes and other potential risk factors for stroke in a sample of community-dwelling older Mexican Americans.

Methods. A prospective cohort design was used that involved the Hispanic Established Population for the Epidemiologic Study of the Elderly, a longitudinal study using a weighted probability sample of Mexican Americans (aged older than 65 years) living in the southwestern United States. 3050 older Mexican American persons were originally interviewed and tested at baseline and then followed with reassessment at 2, 5, and 7 years. The incidence of stroke and stroke death were studied for the participants during a 7-year follow-up period.

Results. 690 participants were identified at baseline with diabetes. 238 participants experienced a first-time stroke during the follow-up period. 66 died as a result of a stroke. Cox proportional hazard regression analysis revealed an increased hazard ratio (HR) for stroke in persons with diabetes (HR, 1.80; 95% confidence interval [CI], 1.32 to 2.44; p < .0002) when adjusted for age, sex, body mass index, smoking, systolic blood pressure, previous heart attack, and lower extremity function. The stroke mortality rate was also higher (HR, 2.02; 95% CI, 1.04 to 3.93) for persons with diabetes when adjusted for covariates.

Conclusion. Diabetes was associated with an increased incidence of stroke and death in older Mexican Americans, particularly those taking insulin.

STROKE is a major health problem and a primary cause of death and disability in the United States. Approximately 500,000 new or recurrent cases occur each year, with 350,000 patients surviving (1). Stroke is the third leading cause of death in the United States and is exceeded only by heart disease and cancer (1). The stroke mortality rate has steadily decreased since the early 1900s, and now the United States has one of the lowest stroke mortality rates in the world (2). Advances in medical technology, improved therapeutics, and changing demographics have resulted in increased stroke prevalence due to an improved likelihood of stroke survival and a growing elderly population (1,3).

An extensive research literature exists on the risk factors for stroke incidence and death (4–7). Hypertension is the most important risk factor for stroke (6,7). It is also well known that persons with diabetes mellitus are at increased risk for both hypertension and stroke (8–10). Until recently, risk factors for stroke have been identified through epidemiologic studies using predominantly non-Hispanic white cohorts. As a result, racial and ethnic disparities in the stroke incidence and mortality rate remain relatively unexplained (11–13). Increasing attention is being devoted to the potential effect of race and ethnicity on established risk factors for stroke (14–16).

Diabetes is metabolically distinct in older adults (17), and its prevalence is higher in the Hispanic population (11,17). The role of diabetes as a risk factor for stroke in Hispanic older adults is a new area of research (11,18). Sacco and colleagues (19) reported that type 2 diabetes increased stroke risk in black and Caribbean Hispanic persons compared with non-Hispanic white persons. In contrast, coronary artery disease was more important as a stroke risk factor for non-Hispanic white persons compared with black and Caribbean Hispanic persons.

The prevalence of hypertension and diabetes in the Hispanic population is high (16), and information on risk factors, incidence of stroke, and functional outcomes in this population is inadequate (20,21). Previous studies of risk factors in the Hispanic population are limited by the definition of Hispanic ethnicity (19). Members of the Hispanic population may have origins in Mexico, South America, and the Caribbean islands. Evidence exists that risk factors vary across different groups traditionally identified as Hispanic (13,14).

Given the prevalence of diabetes in the Hispanic population and the lack of previous research examining stroke in this heterogeneous ethnic group, we studied the effect of diabetes as a risk factor for stroke incidence and death in a large area probability sample of older Mexican American adults. Specifically, we wanted to determine whether diabetes was a risk factor for stroke incidence and death in older Mexican Americans while controlling for age, sex, body mass index (BMI), smoking history (ever smoked), systolic blood pressure, previous heart attack, and lower extremity functional ability.
METHODS

Sample
Data are from the Hispanic Established Population for the Epidemiologic Study of the Elderly (Hispanic-EPESE) (22). The Hispanic-EPESE is an on-going National Institute on Aging–funded community-based study of 3050 older Mexican Americans. Mexican American persons aged 65 years or older were selected using weighted-area probability sampling techniques that involved selection of counties, census tracts, and households. A full description of the rationale, methods, and participant characteristics can be found elsewhere (22). The sample was designed to be representative of approximately 500,000 older Mexican Americans living in 5 southwestern states including Texas, California, Arizona, Colorado, and New Mexico. The current study includes 2357 participants (524 with diabetes and 1833 without diabetes). Follow-up interviews were conducted 2, 5, and 7 years after the baseline assessment. All interviews were conducted in the participants’ homes in either Spanish or English. A description of the interview protocol is available in a previous publication (22) and from the authors.

Diabetes
A history of diabetes was assessed at the baseline interview. Participants were asked whether they had ever had a physician diagnosis of diabetes. A total of 524 (22.2%) participants reported a definite diagnosis of diabetes, 138 (5.9%) reported a borderline diagnosis of diabetes, and 1833 (77.8%) reported no history of diabetes. Participants with a borderline diagnosis of diabetes (n = 138) were not included in the analysis. Participants who reported using any medication during the baseline interview, including taking insulin, were asked to show the medication to the interviewer as a verification check. For the 524 participants reporting a definite diagnosis of diabetes, 458 (87.4%) were taking medication for their diabetes, including 136 (26%) who were using insulin.

Stroke
Stroke was assessed during a 7-year follow-up period. Participants were asked whether they had a physician diagnosis of stroke or had been hospitalized for stroke since the last interview. At the 2-, 5-, and 7-year follow-up assessment interview, 109, 61, and 36 first-time strokes were reported, respectively. If the person was deceased at the time of the follow-up interview, information was collected from the responding family member regarding the cause of death. Vital status was confirmed by a mortality search of the Social Security Administration Death Master File. The validity of self-reported strokes has been established in previous studies (23).

Covariates
Baseline sociodemographics included age and sex. Indicators of baseline health status were smoking history (ever smoked or nonsmoker), BMI (computed as weight in kilograms divided by the square of height in meters), history of previous heart attack (yes or no), systolic blood pressure, and a summary performance measure of lower body function. The summary performance measure is comprised of 3 lower body activities including a timed 4-meter walk, rising from a chair 5 times, and a standing balance task (24,25). Using previously established criteria (26), performance on each lower body activity was classified on a scale ranging from 0 to 4. When summed, the overall performance measure was scored from 0 to 12, where higher scores represented better lower body functioning (24).

Statistical Analyses
We examined demographic variables for all patients using descriptive and univariate statistics for continuous variables and contingency tables (chi-square) for categorical variables. We used chi-square analyses to test for unadjusted differences between diabetic persons (n = 524) and nondiabetic persons (n = 1833) at the baseline assessment interview, and between stroke (n = 206) and no stroke (n = 2151) at the follow-up assessment interviews.

We used Cox proportional hazard models (27) computed with SAS software (SAS Institute, Cary, NC) (28) to estimate the hazard ratios (HR) separately for the incidence of stroke and death during a 7-year period adjusting for relevant covariates. We computed a Cox proportional hazard model to study the relationship between diabetes (definite diabetes versus absent diabetes) at baseline and new-onset stroke (present versus absent) at the 3 follow-up assessment interviews, adjusting for age, sex, smoking status, BMI, systolic blood pressure, history of heart attack, and a summary performance measure of lower body function. Cox proportional hazard models were generated for men and women, adjusting for all covariates and for those persons reporting definite diabetes and the subsample who were using insulin. Sex by diabetes and sex by insulin diabetes interaction terms were created and included in these models. The incidence of stroke death was examined by computing Cox regression models for persons with and without diabetes using the covariates just described.

A modified version of the Bonferroni correction was used to protect against type 1 errors when multiple univariate hypotheses were evaluated (29). When univariate comparisons were made between unequal samples, a t test based on Levene’s test that does not assume equal variances was calculated (29).

RESULTS
The mean age of the participant sample at baseline was 72.6 years (standard deviation [SD], 6.36). The sample included 1388 (58.9%) women and 969 (41.1%) men. Five hundred twenty-four (22.2%) participants reported a definite diagnosis of diabetes at baseline, and 136 (26%) of these were taking insulin. Table 1 contains basic sociodemographic characteristics for persons with and without diabetes who had complete data for all variables included in the analysis at baseline. Persons with diabetes at baseline were younger (t = 3.54, p < .0001), had a greater BMI (t = 5.36, p < .0001), and were more likely to have had a heart attack (t = 3.82, p < .0001).

During the 7-year follow-up period, 206 (8.7%) participants from the original sample reported a first-time stroke.
The bivariate analysis of persons with and without diabetes produced a significant result ($\chi^2 = 10.19$, $p < .001$, $df = 1$), indicating that the proportion of persons with stroke was greater in participants with diabetes. We also conducted a bivariate analysis comparing only those participants with diabetes and taking insulin with participants without diabetes who experienced a stroke ($\chi^2 = 11.78$, $p = .006$, $df = 1$). Similar results were obtained for those with and without diabetes who died of a stroke during the 7-year follow-up period ($\chi^2 = 17.13$, $p < .001$, $df = 1$).

Table 2 and Figure 1 show the results of the Cox proportional hazard analyses for stroke incidence. The interaction term (sex $\times$ diabetes) was not significant (HR $= 1.59$; 95% CI $= 0.86$ to 2.95; $p = .14$). Table 2 includes the

Table 2. Multivariate Analysis Assessing Risk of Stroke by Diabetic Status (Definite Diabetes and Insulin-Dependent Diabetes) Over a 7-Year Follow-Up Period, Adjusting for Relevant Risk Factors

<table>
<thead>
<tr>
<th>Selected Characteristics</th>
<th>N</th>
<th>%</th>
<th>N</th>
<th>%</th>
<th>N</th>
<th>%</th>
<th>p</th>
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<tr>
<td>65–74</td>
<td>1600</td>
<td>67.9</td>
<td>1206</td>
<td>75.4</td>
<td>394</td>
<td>24.6</td>
<td>.0001</td>
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<tr>
<td>75–84</td>
<td>622</td>
<td>26.4</td>
<td>508</td>
<td>81.7</td>
<td>114</td>
<td>18.3</td>
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<td>≥85</td>
<td>135</td>
<td>5.7</td>
<td>119</td>
<td>88.2</td>
<td>16</td>
<td>11.8</td>
<td>.</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Men</td>
<td>969</td>
<td>41.1</td>
<td>758</td>
<td>78.2</td>
<td>211</td>
<td>21.8</td>
<td>.65</td>
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<tr>
<td>Women</td>
<td>1388</td>
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<td>1075</td>
<td>77.5</td>
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<td>1048</td>
<td>76.6</td>
<td>320</td>
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<tr>
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<td>785</td>
<td>79.4</td>
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<td>&lt;22</td>
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<td>10.3</td>
<td>206</td>
<td>85.1</td>
<td>36</td>
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<tr>
<td>22–29.9</td>
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<td>≥30</td>
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<tr>
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<td>91.3</td>
<td>1691</td>
<td>71.7</td>
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<tr>
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<td>142</td>
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<td>64</td>
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<td>1717</td>
<td>78.9</td>
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<td>64.4</td>
<td>64</td>
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<td>≥140 mmHg</td>
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<td>76.9</td>
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<td>337</td>
<td>14.3</td>
<td>227</td>
<td>67.4</td>
<td>110</td>
<td>32.6</td>
<td>.0001</td>
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<td>78.1</td>
<td>208</td>
<td>21.9</td>
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<tr>
<td>10–12</td>
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<td>23.5</td>
<td>460</td>
<td>83.0</td>
<td>94</td>
<td>17.0</td>
<td>.</td>
</tr>
</tbody>
</table>

Notes: All participants were stroke free at the baseline assessment.

$n = 2357$ includes 1833 nondiabetics and 524 diabetics; 142 nondiabetics and 64 diabetics reported a stroke.

$**n = 1969$ includes 1833 nondiabetics and 136 insulin-dependent diabetics; 142 nondiabetics and 22 insulin-dependent diabetics reported a stroke.

HR = hazard ratio; CI = confidence interval.
Figure 1. Hazard ratios and 95% confidence intervals for males and females with diabetes ($n = 206$) and with insulin-dependent diabetes ($n = 164$). Analyses were adjusted for age, body mass index, smoking, systolic blood pressure, previous heart attack, and lower extremity function.

proportional hazard results adjusted for age, sex, BMI, smoking history (ever smoked), systolic blood pressure, previous heart attack, and summary lower extremity performance measure. Table 2 includes results for the same Cox proportional hazard models for persons taking insulin. The results reveal an increased hazard ratio for stroke in persons taking insulin ($HR = 2.58; 95\% CI = 1.61$ to $4.15; p < .0001$) after adjusting for age, sex, BMI, smoking history (ever smoked), systolic blood pressure, previous heart attack, and lower extremity function.

Figure 1 shows the hazard ratios and confidence intervals associated with the incidence of stroke for persons with diabetes and those taking insulin separated by sex. The hazard ratios are statistically significant for women in both diabetic conditions.

Table 3 includes the hazard ratios for stroke death for persons with diabetes and those who were insulin-dependent. The results indicate a significant increase in mortality risk for persons with diabetes who experience a stroke ($HR = 1.99; 95\% CI = 1.12$ to $3.51$) adjusted for age, sex, smoking history (ever smoked), BMI, systolic blood pressure, previous heart attack, and lower extremity function.

**DISCUSSION**

Hypertension is the most important risk factor for stroke (1). In addition, diabetic patients are at an increased risk for hypertension and stroke (1, 5, 8). Although many studies have identified diabetes mellitus as an independent risk factor for stroke, there is inconsistency in the research literature (8, 9). In a review article on diabetes and the risk for stroke, Chuckwuma and Tuomilehto (30) identified several issues requiring additional research. One was the effect of diabetes in different racial and ethnic groups. Several recent studies evaluating risk factors for stroke in the Hispanic population used data from the Northern Manhattan Stroke Study (15, 19). This study includes detailed information on medical history and stroke outcome for a well-defined sample. Results from the Northern Manhattan Stroke Study indicate a twofold increase in the incidence of stroke associated with diabetes for Hispanic persons versus non-Hispanic white persons (19). The Hispanic cohort in the Northern Manhattan Stroke Study, however, is predominately of Caribbean origin. In a related study, Valderrama-Gama and colleagues (31) examined chronic disease (including cerebrovascular disease and diabetes) in 1001 older adults in Madrid, Spain. They reported that cerebrovascular disease, depression, and diabetes were the conditions most closely related to disability.

Rodriguez-Saldana and others examined cardiovascular risk factors, functional and cognitive impairment, anxiety/depression, and mortality rates in a sample of older adults in Mexico City (18). They found a lower prevalence of diabetes (15.1%) than reported for persons of Mexican origin living in the United States. The mortality rate was greater for persons with diabetes, and these persons had more coronary artery disease than did persons without diabetes. These investigations suggest a complex relationship among stroke, diabetes, depression, and cognitive impairment. Although the relationship among these variables has been examined in the non-Hispanic white population, there is little research on the interaction of these factors in older Mexican Americans (16, 18). This area requires further investigation.

We found an increased risk for stroke in older Mexican Americans with self-reported diabetes compared with stroke rates in participants without diabetes. The hazard ratio for Mexican Americans taking insulin was 2.58 (95\% CI = 1.61 to 4.15; $p < .0001$) after controlling for factors normally associated with increased risk for stroke. These factors included age, sex, BMI, history of smoking, systolic blood pressure, history of heart attack, and lower extremity mobility and balance functions. The risk for death from stroke was also significantly greater for persons with diabetes than for those without diabetes ($HR = 1.99; 95\% CI = 1.12$ to $3.51$). The mortality risk appeared to increase with the severity of diabetes, as evidenced by a hazard ratio of 5.48 (95\% CI = 2.08 to 14.41) for persons with diabetes who were taking insulin. When the analysis was conducted separately for men and women, the risk for death was significantly greater for women with diabetes ($HR = 2.06; 95\% CI = 1.40$ to $3.04$) than for women without diabetes. The hazard ratio for men was 1.37, but this was not significant (95\% CI = 0.83 to 2.28). The effect of sex on the stroke mortality rate in Mexican Americans with (and without) diabetes is an area that requires further investigation.

Data from the National Center for Health Statistics for 1989 through 1991 suggested that stroke mortality rates were similar in Hispanic and non-Hispanic white persons aged 46 to 64 years. At ages 65 and older, Hispanic persons had stroke mortality rates that were substantially lower than those for non-Hispanic white persons (15). The data from this and a small number of other studies have led to speculation that ethnic differences in stroke mortality rates may be due, in part, to lower blood pressure in Hispanic than in non-Hispanic persons (15, 32) or perhaps to genetic differences (8). The findings from the current investigation...
suggest that any advantage of lower blood pressure in the general Hispanic population is lost in persons with diabetes, and, in fact, diabetes may be a more significant risk factor for stroke incidence and death in Mexican Americans than in non-Hispanic white persons.

We consider these findings preliminary but believe they strongly suggest the need for additional research on diabetes as a risk factor for stroke in the Mexican-American population. The importance of our findings is based on the following strengths of the current investigation. We collected longitudinal information from a large, well-defined sample representative of, at baseline, 500,000 Mexican Americans in the southwestern United States (22). The reliability and consistency of the data collection procedures in the Hispanic-EPESE investigation are well established (22). Our sample included Mexican Americans, whereas most previous studies of racial–ethnic epidemiology for stroke have included multiple Hispanic subgroups, or in the case of the Northern Manhattan Stroke Study, focused on Hispanics from the Caribbean islands. The Hispanic-EPESE sample represents a population (Mexican American) that is known to have a high rate of diabetes and related complications (13,22) but has not been comprehensively studied. Relatively little is known regarding health disparities and risk factors associated with stroke in this population (12,15,32).

The limitations of the investigation include the fact that several key variables were reported by the participants themselves. Previous researchers have reported good validity for self-reported diabetes and stroke confirmed by physician diagnosis (23,33,34). Persons in this community-dwelling sample should have good recall of a major health event associated with hospitalization, such as a stroke. Receiving a diagnosis of diabetes, however, is less dramatic. As noted previously, if a participant reported using insulin or other medications, the interviewer asked to see those medications. Thus, the study interviewers verified the diabetes diagnosis for persons taking insulin or other diabetic medications. Many of the participants with diabetes at baseline (87.4%) reported taking some type of diabetic medication. Those participants identified as not having diabetes probably included some persons with undiagnosed diabetes. This misclassification would tend to weaken any association between diabetes and stroke. We also excluded 138 participants who were classified in the interview as having “borderline” diabetes. These persons were either not able to produce diabetic medication or were unclear in providing evidence of a definite physician diagnosis of diabetes.

Insulin use can be considered a marker for disease severity in persons with diabetes. The duration of diabetes is also a potential marker for disease severity and a risk factor for stroke in this population. We did not have consistent information on the duration of diabetes for the participants in the Hispanic-EPESE sample, nor did we have any measure of glycemic control for the participants.

This study is part of a series of investigations evaluating risk factors for disability and chronic diseases in Hispanic older adults (21,35–39). This particular investigation highlights the need for a more aggressive focus on identifying risk factors associated with stroke in the Hispanic population. Our findings suggest that diabetes may be a more significant risk factor in older Mexican Americans than in other ethnic or racial groups (e.g., non-Hispanic white persons). Research is needed concerning how diabetes and its complications contribute to increased risk for stroke in all populations. The results of this research must be incorporated into diabetes education and prevention programs, particularly those aimed at the Mexican American population.

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