# A Population-Based Study of Intracerebral Hemorrhage Survivors' Outcomes

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*Background:* We evaluated 3-month neurologic, functional, cognitive, and quality of life (QOL) outcomes in intracerebral hemorrhage (ICH) overall, and by sex and ethnicity in a population-based study. *Methods:* Spontaneous ICH patients were identified from the Brain Attack Surveillance in Corpus Christi project (November 2008 to December 2013). Outcomes included neurologic (National Institutes of Health Stroke Scale: range 0-42), functional (activities of daily living/instrumental activities of daily living score: range 1-4, higher worse), cognitive (Modified Mini-Mental State Examination [3MSE]: range 0-100), and QOL (short-form stroke-specific QOL scale: range 0-5, higher better). Ethnic and sex differences were assessed with Tobit regression adjusted for age, sex, or ethnicity, and presenting Glasgow coma scale. *Results:* A total of 245 patients completed baseline interviews, with 103 (42%) dying prior to follow-up, leaving 142 eligible for outcome assessment. Three-month follow-up was completed in 100 (neurologic), 107 (functional), 79 (cognitive), and 83 (QOL) participants. Median age was 66 years (interquartile range 58.0-77.0). Cognitive outcomes were worse in Mexican Americans (MA) compared to non-Hispanic whites (NHW) after multivariable adjustment (MA scoring 13.3 3MSE points lower than NHW [95% confidence interval: 5.8, 20.7; $P = .0005$]). There was no difference by sex or ethnicity in neurological, functional, or QOL outcomes, and no sex differences in cognitive outcomes. *Conclusions:* In this population-based study, worse cognitive outcomes were found in MAs compared with NHW. There were no differences between neurologic, functional, and QOL outcomes in ICH survivors based on sex or ethnicity.

**Key Words:** Cerebral hemorrhage—Mexican Americans—patient outcome assessment—activities of daily living—quality of life

**Subject Codes:** Intracranial hemorrhage—cognitive impairment—quality and outcomes—race and ethnicity



## Introduction

Intracerebral hemorrhage (ICH) remains a pervasive public health problem with substantial morbidity. Race-ethnic disparities in ICH presentation and post-ICH mortality are well documented.[1-7] However, there are little data evaluating disparities in patient-centered outcomes, such as functional, neurologic, cognitive, and

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quality of life (QOL) outcomes, following ICH. Mexican Americans (MA) are the largest subgroup of Hispanics, which encompass the largest minority group in the United States.[8] MAs are at increased risk of ICH when compared with non-Hispanic whites (NHW).[9,10] Also, MAs have lower poststroke mortality, experience ICH at a younger age, and are less likely to have a do-not-resuscitate (DNR) order after ICH than NHWs.[1,6,10] Similarly, data addressing ICH outcomes based on sex are limited.[11] Studies, which have addressed sex differences in ICH, have shown variable and contradictory results.[11-13] The objective of this population-based study was to evaluate neurologic, functional, cognitive, and QOL outcomes following ICH and determine if an ethnic or sex disparity exists.

## Materials and Methods

Cases of nontraumatic ICH in Nueces County, Texas between November 2008 and December 2013 were identified through the Brain Attack Surveillance in Corpus Christi (BASIC) Project. BASIC is a population-based surveillance in a community comprised predominantly of 2 ethnicities, MA and NHW. Complete methods of the BASIC project were addressed previously.[14] Nontraumatic ICH cases were identified through screening of daily hospital admission logs as well as evaluation of International Classification of Diseases-9 codes. Potential cases selected through screening were validated by stroke fellowship trained physicians blinded to age and ethnicity. Baseline characteristics, including demographic data (age, sex, education [less than high school/high school or more], health insurance [yes/no], and ethnicity), relevant medical comorbidities (hypertension, atrial fibrillation, diabetes mellitus, history of stroke, and smoking status), pre-ICH cognitive status utilizing the informant questionnaire on cognitive decline in the elderly (IQCODE), pre-ICH disability utilizing the modified Rankin Scale, presenting Glasgow coma scale score (GCS), and DNR status, were obtained through medical records and baseline interviews with the patient or a proxy.[15] The IQCODE has been validated in both English and Spanish and has been shown to have high accuracy and reliability for the assessment of dementia.[16,17] Ethnicity was defined by participant report.

### *Outcome Measures*

A follow-up interview was performed at approximately 90 days following the ICH. Interviews were conducted in the language preferred by the respondent (English or Spanish). Neurologic status was assessed using the National Institutes of Health Stroke Scale (NIHSS; 0-42) by certified personnel. Functional status was self-assessed by patients (or proxy) according to the difficulty of performing activities of daily living (ADLs) and instrumental activities of daily living (IADLs) by themselves utilizing a Likert scale with responses including 1 (no difficulty), 2 (some difficulty), 3 (a lot of difficulty), and 4 (can only do with help). ADLs included 7 items related to basic function including walking, bathing, dressing, self-feeding, grooming, moving, and toileting. IADLs include 15 items related to daily function (i.e., managing finances, shopping, preparing meals, managing medications, etc.). Responses of the 22 ADL/IADLs were averaged by summing the numerical value of each response and dividing by the total number of responses yielding a score of 1-4.[18] Cognitive function was assessed utilizing the Modified Mini-Mental State Examination (3MSE).[19] 3MSE is a validated and widely accepted screening tool for dementia within the community setting with scores ranging from 0 to 100.[20] The 3MSE has been extensively used to assess cognition in both English and Spanish in Mexican-American populations.[21] A 3MSE score of 80 or below was used as the cut-point for dementia. Cases were excluded from the cognitive outcome assessment if the interview was completed by proxy, or if the patient was unable to correctly answer a brief screening for language dysfunction. QOL assessments began as of July 2010; therefore, the available sample size for this measure is smaller than other assessments. QOL was self-assessed by patients (or proxy) utilizing the 12-item version of the stroke-specific QOL scale (SSQOL). SSQOL is a validated QOL scale that evaluates 12 domains: energy, family roles, language, mobility, mood, personality, self-care, social roles, thinking, upper extremity function, vision, and productivity.[22,23] Scores in each domain range from 1 (total help), 2 (a lot of help), 3 (some help), 4 (a little help), and 5 (no help). The scores of all 12 domains were summed and divided by 12 to obtain an average overall SSQOL score.

### *Statistical Analysis*

Descriptive statistics were calculated for baseline characteristics and outcome measures. Data were calculated for the entire cohort and for ethnicity and sex subgroups. Differences in descriptive characteristics between subgroups were evaluated using chi-square and Krusal-Wallis tests for categorical and continuous variables, respectively. Tobit regression was used to assess unadjusted associations between ethnicity or sex and 90-day outcomes in patients with complete data. Tobit models were then adjusted for age, sex or, ethnicity, and presenting GCS. Tobit models were used to minimize bias in scores constrained to a finite range.[24] Because of the lack of normality of the residuals for the NIHSS model, we used ordinary linear regression with robust standard errors for this outcome only. NIHSS was modeled as natural logarithm of NIHSS plus one due to skewness.

Due to concerns that differential mortality by sex or ethnicity could influence our primary associations of interest (for example, if ethnic differences in use of life-sustaining treatment lead to more deaths among severely affected NHWs), sensitivity analyses were conducted with inverse

probability weighting to account for the probability that an individual was alive at the time of the assessment. Weights were defined by the ratio of model-predicted probabilities as follows: probability of remaining alive at 90 days as predicted by the variables included in the fully adjusted models divided by the probability of remaining alive at 90 days as predicted by these same factors in addition to DNR status (defined as a categorical variable: <24-hour DNR, ≥24-hour DNR, with no DNR as the reference group), ICU admission, length of stay, and NIHSS. Weights ranged from .25 to 5.56. We constructed 95% bootstrap confidence intervals (CIs) for all regression coefficients.

This study was approved by the Institutional Review Boards at the University of Michigan and the participating hospitals. Written informed consent was obtained from the patient or a proxy for participation.

## Results

There were 346 MA and NHW patients with first ICH during the study period (November 2008 to December 2013), with 245 (70.8%) completing the baseline interview. Among these patients, 245 subjects (74.0%) completed the baseline interview. Mortality at 90 days was 42.0% (n = 103), resulting in 142 patients (103 MAs and 39 NHWs) eligible for the outcome interview. Of the 142 patients, 17 (12.0%) refused participation in the outcome interview and 18 (12.7%) could not be located, leaving 107 patients who completed the outcome interview. There were no differences in sex, ethnicity, age, and GCS between the 107 participants completing the outcome interview and the 35 who were alive but did not complete the interview.

Table 1 displays baseline characteristics for patients with outcome data (n = 107) by sex and ethnicity, respectively. MAs had a higher mean BMI, they were more likely to carry a diagnosis of diabetes mellitus, and they were less likely to have completed a high school education than NHWs in this population. Females were more likely to be married and living with their spouse than males. Outcome interview was completed by a proxy in 45 of 107 (42.1%) with no differences in proxy completion by sex ($P = .72$) or ethnicity ($P = .85$).

### *Neurological Outcomes*

Complete NIHSS data were available for 100 of 107 (93%) patients (53 males, 47 females, 30 NHWs, and 70 MAs). Median NIHSS was 2 (interquartile range [IQR] 1-6) for the entire cohort, 2 (IQR 1-6) for males, 2 (IQR 1-7) for females, 1 (IQR 1-6) for NHWs, and 2.5 (IQR 1-6) for MAs. In unadjusted and adjusted models, no differences were found between sex and ethnic groups (Table 2).

### *Functional Outcomes*

Complete ADL/IADL data were available for 107 of 107 (100%) patients (57 males, 47 females, 32 NHWs, and 75 MAs). Median ADL/IADL was 2.8 (IQR 1.8-3.5) for the entire cohort, 2.6 (IQR 1.6-3.5) for males, 2.9 (IQR 1.8-3.6) for females, 2.7 (IQR 1.3-3.6) for NHWs, and 2.8 (IQR 1.9-3.5) for MAs. In other words, the majority of patients tended to report a score of at least 2 (indicating "some difficulty") across the ADL and IADL items. In unadjusted and adjusted models, no differences were found between sex and ethnic groups (Table 2).

### *Cognitive Outcomes*

Complete 3MSE data were available for 79 of 107 (74%) patients (42 males, 37 females, 24 NHWs, and 55 MAs). Cognitive outcome interviews were done in Spanish in 5 of 79 cases (6%). Among the 28 cases with missing cognitive outcomes, 21 failed the language screen (15 MAs [71%)]and 6 NHWs [29%]). The other 7 cases were excluded from cognitive outcomes because they were completed by proxy interviews (5 MAs and 2 NHWs). Median 3MSE was 88 (IQR 76-95) for the entire cohort, 91 (IQR 78-94) for males, 84 (IQR 75-96) for females, 93.5 (IQR 80.5-97) for NHWs, and 84 (IQR 75-93) for MAs. Details of cognitive outcomes by sex and ethnicity are shown in Table 2. In unadjusted and adjusted models, no differences were found between sex groups. In unadjusted models, MAs had a 3MSE score that was 8.96 (95% CI: 1.40, 16.52) points lower than NHWs ($P = .020$). After adjustment for age, ethnicity, and GCS, the ethnic association became stronger with MAs having on average 13.38 (95% CI: 5.96, 20.79) 3MSE points lower than NHWs ($P = .0004$). A greater proportion of MAs (41.8%) met the criteria for poststroke dementia (score of 80 points or lower) than NHWs (25.0%).

### *QOL Outcomes*

Because QOL assessments began as of July 2010, a smaller number of participants were eligible for QOL assessment (n = 84). Of these patients, 1(1.2%) did not complete the QOL assessment, leaving 83 patients with QOL data (44 males, 39 females, 26 NHWs, and 57 MAs). Median SSQOL was 2.9 (IQR 2.1-3.9) for the entire cohort, 2.8 (IQR 2.1-3.9) for males, 2.9 (IQR 2.0-3.9) for females, 3.0 (IQR 2.3-4.1) for NHWs, and 2.8 (IQR 2.0-3.7) for MAs. In unadjusted and adjusted models, no differences were found between sex and ethnic groups (Table 2).

### *Sensitivity Analysis*

After using weights to account for differential poststroke mortality by sex and ethnicity, there were no meaningful changes in the associations between sex or ethnicity and the outcome measures. The ethnic difference in cognition remained, with MAs having a 9.5 (95% CI: 4.4, 16.9)

**Table 1.** *Baseline characteristics overall and by sex or ethnicity (n = 107)*

| | Overall % or median (Q1, Q3) | Female (n = 50)% or median (Q1, Q3) | Male (n = 57) % or median (Q1, Q3) | NHW (n = 32) % or median (Q1, Q3) | MA (n = 75) % or median (Q1, Q3) |
|---|---|---|---|---|---|
| Age (years) | 68.0 (58.0, 78.0) | 70.0 (60.0, 81.0) | 66.0 (58.0, 71.0) | 70.0 (62.5, 80.0) | 66.0 (57.0, 75.0) |
| Ethnicity (% MA) or sex (% female)*,† | 70.1 | 60.0 | 78.9 | 62.5 | 40.0 |
| Marital status | | | | | |
| Married/living together* | 55.1 | 44.0 | 64.9 | 53.1 | 56.0 |
| Single | 9.4 | 10.0 | 8.8 | 3.1 | 12.0 |
| Widow | 18.7 | 30.0 | 8.8 | 21.9 | 17.3 |
| Divorced/separated | 16.8 | 16.0 | 17.5 | 21.9 | 14.7 |
| Education† | | | | | |
| Less than high school | 22.4 | 24.0 | 21.1 | 0 | 32.0 |
| High school | 35.5 | 40.0 | 31.6 | 28.1 | 38.7 |
| Vocational/some college | 25.2 | 20.0 | 29.8 | 34.4 | 21.3 |
| College or more | 16.8 | 16.0 | 17.5 | 37.5 | 8.0 |
| Pre-ICH mRS | | | | | |
| 0-1 | 43.9 | 42.0 | 45.6 | 50.0 | 41.3 |
| 2-3 | 46.7 | 48.0 | 45.6 | 40.6 | 49.3 |
| 4+ | 9.4 | 10.0 | 8.8 | 9.4 | 9.3 |
| Health insurance (% uninsured) | 12.2 | 16.0 | 8.8 | 9.4 | 13.3 |
| Atrial fibrillation (%) | 3.7 | 6.0 | 1.8 | 6.3 | 2.7 |
| CAD (%) | 15.9 | 20.0 | 12.3 | 18.8 | 14.7 |
| Diabetes mellitus (%)† | 33.6 | 28.0 | 38.6 | 12.5 | 42.7 |
| Hypertension | 85.1 | 78.0 | 91.2 | 75.0 | 89.3 |
| History of stroke | 19.6 | 20.0 | 19.3 | 15.6 | 21.3 |
| Current/former smoker | 29.0 | 26.0 | 31.6 | 31.3 | 28.0 |
| GCS score | 15.0 (14.0, 15.0) | 15.0 (13.0, 15.0) | 15.0 (14.0, 15.0) | 14.0 (12.5, 15.0) | 15.0 (14.0, 15.0) |
| Pre-ICH IQCODE | 3.1 (3.0, 3.3) | 3.1 (3.0, 3.3) | 3.0 (3.0, 3.3) | 3.0 (3.0, 3.3) | 3.1 (3.0, 3.3) |
| BMI† | 28.4 (24.7, 32.0) | 27.6 (22.5, 31.1) | 29.1 (25.7, 33.4) | 24.9 (21.7, 29.7) | 29.1 (26.3, 32.2) |
| DNR | 9.9 | 7.0 | 12.5 | 14.3 | 7.9 |

Abbreviations: BMI, body mass index; CAD, Coronary Artery Disease; DNR, do not resuscitate; GCS, Glasgow coma scale score; ICH, intracerebral hemorrhage; IQCODE, informant questionnaire on cognitive decline in the elderly; mRS, modified Rankin Scale; NHW, non-Hispanic whites.

*Denotes a difference by sex ($P < .05$).

†Denotes a difference by ethnicity ($P < .05$).

**Table 2.** *Three-month outcomes*

| Outcome measure | Female median (Q1, Q3) | Male median (Q1, Q3) | Difference in mean (females compared to males) (95% confidence interval) | | MA median (Q1, Q3) | NHW median (Q1, Q3) | Difference between mean (MA compared to NHW) (95% confidence interval) | |
|---|---|---|---|---|---|---|---|---|
| | | | Unadjusted | Adjusted† | | | Unadjusted | Adjusted† |
| NIHSS, n = 100 | 2.0 (1.0, 7.0) | 2.0 (1.0, 6.0) | −7%‡ (−48%, 40%) | −14%†(−41%, 26%) | 2.5 (1.0, 6.0) | 1.0 (1.0, 6.0) | 31%‡ (−15%, 102%) | 36%‡ (−10%, 104%) |
| ADL/IADL, n = 107 | 2.9 (1.8, 3.6) | 2.6 (1.6, 3.5) | .15 (−.21, .49) | .10 (−.24, .45) | 2.8 (1.9, 3.5) | 2.7 (1.3, 3.6) | .14 (−.25, .53) | .26 (−.11, .64) |
| 3MSE, n = 79 | 84.0 (75.0, 96.0) | 91.0 (78.0, 94.0) | −1.69 (−8.86,5.46) | −1.79 (−8.54, 4.95) | 84.0 (75.0, 93.0) | 93.5 (80.5, 97.0) | −8.96* (−16.52, −1.4) | −13.38* (−20.79, −5.96) |
| SS-QOL, n = 83 | 2.9 (2.0, 3.9) | 2.8 (2.1, 3.9) | −.06 (−.55, .43) | −.09 (−.58, .40) | 2.8 (2.0, 3.7) | 3.0 (2.3, 4.1) | −.23 (−.75, .29) | −.37 (−.89, .16) |

Abbreviations: ADL/IADL, activities of daily living/instrumental activities of daily living; MA, Mexican Americans; 3MSE, Modified Mini-Mental State Examination; NHW, non-Hispanic whites; NIHSS, National Institutes of Health Stroke Scale; SS-QOL, stroke-specific quality of life.

For all other outcomes, the comparison represents the absolute difference.

*Denotes $P < .05$ when compared to reference group.

†Adjusted for age, sex, or ethnicity, and GCS.

‡Because of the log transformation model of the NIHSS outcome, the comparison represents the percentage difference in NIHSS by group.

points lower 3MSE score compared with NHWs, after accounting for mortality differences.

## Discussion

In this population-based study, we identified a disparity for worse cognitive outcomes in MAs compared with NHWs with over 40% of MA meeting criteria for post-ICH dementia. There has been limited work on post-ICH cognitive outcomes among MAs, as one of the largest existing studies of post-ICH cognition had a low proportion of Hispanics.[25] The ethnic disparity in cognition widened after adjusting for age, sex, and initial severity, and was not accounted for by differential mortality by ethnicity. Several other factors may contribute to this disparity, and we cannot rule out the possibility of residual confounding, particularly as the small sample size limited our ability to adjust for potential confounders.

Prestroke education level is an important predictor of poststroke cognition,[25,26] and MAs in our population were less likely than NHWs to have education beyond high school, potentially predisposing them to worse cognitive outcomes that may be due to prestroke, rather than post-stroke factors. However, MAs were more likely to be excluded from the cognitive assessments due to more severe language dysfunction than NHWs, if anything this suggests that our data may underestimate the true ethnic disparity in cognitive functions. Hematoma size or lobar location are unlikely to contribute to the ethnic disparity in cognition, as we have previously found that MAs are more likely than NHW to have small, nonlobar hemorrhages.[1] Pre-existing cognitive impairment is also an unlikely contributor as MAs and NHWs had similar pre-ICH cognition scores (IQCODE).[27] Other potentially important confounders of the cognitive outcomes may include ethnic differences in prevalence of diabetes, depressive symptoms, or socioeconomic disadvantage.[28-32] Overall, the net effect of all of these potential confounders is difficult to estimate in ICH. However, in our prior work, investigating ethnic differences in ischemic stroke outcomes, we found that worse cognitive outcomes among MAs persisted despite adjustment for multiple additional factors including education, comorbid illness, and insurance.[33]

Importantly, there were no differences between neurologic, functional, and QOL outcomes in ICH survivors based on sex or ethnicity. Previous studies have addressed disparities in post-ICH mortality and basic assessments of neurologic disability (i.e., modified Rankin Scale), but little information exists on the more detailed outcome measures reported here.[34-36] Furthermore, the population-based nature of our study improves the generalizability of its results to a wider proportion of health care institutions, beyond just academic and tertiary medical centers.

Interestingly, we found no disparity between sex groups in any of our outcome measures. This finding is contrary to our prior studies of ischemic stroke, which

identified sex disparities in poststroke QOL, as well as functional and neurologic outcomes.[18,32,33] Our findings are corroborated by recent studies, which reported no sex-related difference in long-term functional outcomes or adjusted poor outcomes following ICH.[12,13] One population-based study from China identified worse functional outcomes in females 3 months after ICH, this difference did not persist at 6 and 12 months.[37] While the reasons for the differences in outcomes by sex among hemorrhagic and ischemic stroke are unknown, these findings underscore the inherent differences in the poststroke course of survivors of ischemic and hemorrhagic stroke.

Our study has several important limitations. First, due to the small sample size we were limited in our ability to adjust for many confounders, including psychosocial factors such as education. Second, our finding of an ethnic disparity in cognitive outcome was dependent on performance on the 3MSE test. Scores on the Mini-Mental State Exam and its variants have been shown to be susceptible to cultural, language, socioeconomic, educational, and other noncognitive factors.[38-41] Third, our study is susceptible to selection bias in the population of patients agreeing to 3-month outcome assessments. While those lost to follow-up may contribute to an overall favorable outcome profile in this study, we are reassured that there was no difference in demographics or ICH severity between those completing the outcome interview and those alive but not completing the interview. Finally, because our study focused on a single community in Texas and a small number of NHWs were included, its results may not be generalizable to the entire United States.

## Conclusion

MAs experienced worse cognitive outcomes following ICH than NHWs. Our findings highlight the need for continued research to identify factors contributing to ethnic disparities in ICH outcomes, particularly in larger samples that can adjust for a multitude of potential confounders. Further studies may identify medical, psychosocial, and socioeconomic factors that contribute to ethnic cognitive outcome disparities, allowing for targeted interventions in ICH survivors.

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## Competing Interests

The authors have no conflicts of interest to disclose.

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