Poor Long-Term Blood Pressure Control After Intracerebral Hemorrhage

Darin B. Zahuranec, MD, MS; Jeffrey J. Wing, MPH; Dorothy F. Edwards, PhD; Ravi S. Menon, MD; Stephen J. Fernandez, MPH; Richard E. Burgess, MD, PhD; Ian A. Sobotka, BS; Laura German, BS; Anna J. Trouth, MD; Nawar M. Shara, PhD; M. Chris Gibbons, MD, MPH; Bernadette Boden-Albala, MPH, DrPH; Chelsea S. Kidwell, MD

Background and Purpose—Hypertension is the most important risk factor associated with intracerebral hemorrhage. We explored racial differences in blood pressure (BP) control after intracerebral hemorrhage and assessed predictors of BP control at presentation, 30 days, and 1 year in a prospective cohort study.

Methods—Subjects with spontaneous intracerebral hemorrhage were identified from the DiffErenCes in the Imaging of Primary Hemorrhage based on Ethnicity or Race (DECIPHER) Project. BP was compared by race at each time point. Multivariable linear regression was used to determine predictors of presenting mean arterial pressure, and longitudinal linear regression was used to assess predictors of mean arterial pressure at follow-up.

Results—A total of 162 patients were included (mean age, 59 years; 53% male; 77% black). Mean arterial pressure at presentation was 9.6 mm Hg higher in blacks than whites despite adjustment for confounders (P=0.065). Fewer than 20% of patients had normal BP (<120/80 mm Hg) at 30 days or 1 year. Although there was no difference at 30 days (P=0.331), blacks were more likely than whites to have Stage I/II hypertension at 1 year (P=0.036). Factors associated with lower mean arterial pressure at follow-up in multivariable analysis were being married at baseline (P=0.032) and living in a facility (versus personal residence) at the time of BP measurement (P=0.023).

Conclusions—Long-term BP control is inadequate in patients after intracerebral hemorrhage, particularly in blacks. Further studies are needed to understand the role of social support and barriers to control to identify optimal approaches to improve BP in this high-risk population. (Stroke. 2012;43:00-00.)

Key Words: hypertension • intracerebral hemorrhage • secondary prevention • racial differences

Hypertension is a critical risk factor for primary intracerebral hemorrhage (ICH) and is the most important modifiable risk factor for prevention of recurrent ICH.1 Minority populations, including blacks, are at increased risk of both hypertension and ICH.2,3 Preliminary clinical trial evidence suggests that blood pressure (BP)-lowering immediately after ICH may be an important treatment target to prevent hematoma expansion, although it has not been proven to be beneficial.4 In the chronic phase, poor BP control has been associated with increased risk of recurrent stroke and cardiovascular events.5

Prior studies based on the National Health and Nutrition Examination Survey (NHANES) have identified that control of BP in stroke survivors is often suboptimal.6,7 These studies used patient self-report to identify stroke; therefore, they did not have information on stroke type, clinical presentation, or time from stroke to BP assessment in these studies. Because the burden of ICH is highest in black and Hispanic/Latino populations compared with other race–ethnic groups,3 long-term BP control after ICH is even more important in these populations.

We performed a longitudinal cohort study of ICH survivors in a multiracial population from the Washington, DC, metro area. The goals of this study were to (1) explore racial differences in BP after ICH; (2) investigate predictors of higher BP at the time of ICH presentation; and (3) identify factors associated with higher BP in the first year after ICH.

Methods

Study Setting, Case Identification, and Eligibility

This study was a part of the DiffErenCes in the Imaging of Primary Hemorrhage based on Ethnicity or Race (DECIPHER) Project.8 DECIPHER is a longitudinal observational cohort study of individ-
uals with ICH designed primarily to investigate racial differences in ICH with a focus on MRI findings, including cerebral microbleeds. Patients with ICH from the Washington, DC, metro area were identified at one of the following hospitals: Washington Hospital Center, Georgetown University Hospital, Suburban Hospital (Bethesda, MD), National Rehabilitation Hospital, and Howard University Hospital. Patients were identified through active surveillance of all patients admitted to a study hospital with brain hemorrhage. Eligibility criteria for DECIPHER included a primary (nontraumatic) ICH within 30 days before enrollment, age ≥18 years, no contraindication to brain MRI, and informed consent signed by the patient or a legally authorized representative. Exclusion criteria were pregnancy, coagulopathy (international normalized ratio >3 at the time of ICH), central nervous system tumor, need for craniotomy or craniectomy, active central nervous system infection or inflammatory process, central nervous system arteriovenous malformation or aneurysm, or central nervous system trauma within 2 weeks. The current study did not focus on MRI findings, although MRI is required for the primary aims of DECIPHER and therefore all patients in the current study had to be able to undergo MRI.

Baseline Data Collection
Prestroke medical comorbidities, education, occupation, health insurance status, marital status, medication use, drug or alcohol use (>2 drinks per day), and smoking were collected from the medical records and through interviews with patients or a proxy (if the patient was unable). Race was determined by self-report; individuals of nonblack or nonwhite race were excluded from the current analysis due to low numbers. Marital status at baseline was dichotomized as married versus not married for analysis. BP medications were reviewed and classified into one of the following categories: β blocker, α blocker, calcium channel blocker, diuretic, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, nitrate, and other.

Initial Glasgow Coma Scale and baseline body mass index were determined based on the medical chart. Admission National Institutes of Health Stroke Scale was abstracted from the first documented examination using a previously validated method. The first BP recorded in the emergency department record was recorded as the baseline BP. Education and occupation were combined to generate the Hollingshead 2-factor index of social position as a measure of socioeconomic status, which was dichotomized as middle to upper (referent, index of social position ≥47) and lower to lower-middle for analysis.

ICH volume was calculated based on initial head CT scan in DICOM format by volumetric analysis using a semiautomated approach using Multi-Image Analysis GUI (MANGO) software. Five cases had only a baseline MRI rather than CT and volume data were converted using a validated method.

Data Collection at 30 Days and 1 Year
Enrolled subjects underwent an in-person evaluation at approximately 30 days and 1 year from the time of initial presentation. The subject’s location was recorded and dichotomized as living in a personal residence versus living in a facility for a diagnosis. The interview consisted of questions about medication use as well as a BP measurement. Trained study staff measured BP with an automated monitor (LifeSource UA-767 Plus, cuff size varied to fit arm circumference) according to a protocol recommended by the American Heart Association. In the initial stages of the project, a single BP measurement was taken, although the study procedures were later changed to include 2 measurements taken at least 2 minutes apart with the average used for analysis. Medication management was left available at either 30 days or 1 year.

Statistical Analysis
Baseline characteristics were summarized for categorical variables as frequencies and percents and for continuous variables as means and SDs or medians and interquartile ranges. BP at follow-up (30 days and 1 year) was reported by race continuously and categorized as normal, prehypertension, Stage I hypertension, or Stage II hypertension based on the Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII). Baseline characteristics and BP were compared by race using t tests, χ² tests, or nonparametric rank sum tests as appropriate.

Multivariable linear regression was used to investigate predictors of higher mean arterial pressure (MAP) at presentation and longitudinal linear regression models were developed (excluding 4 patients discharged to hospice) to investigate BP control at 30 days and 1 year after ICH. Candidate variables for inclusion in the models were preselected based on biological plausibility or expected association with BP. Age (continuous, centered at mean value), race, and sex were used to generate the base models. Covariates were individually added to the base model with a plan to retain variables if they either improved the model fit based on R² (baseline model) or Akaike information criterion (longitudinal model) or if they altered the association of other variables with the outcome. Time was treated as a dummy variable for Year 1 with Day 30 as the reference.

Statistical analysis was done in SAS Version 9.2 (SAS Institute, Cary, NC) This study was approved by the Institutional Review Boards of Georgetown University and all participating institutions. Patients or their legally authorized representatives gave their written informed consent for participation.

Results
The study population consisted of 162 patients who had BP data available at either 30 days (140 patients) or 1 year (103 patients). A total of 806 patients with spontaneous ICH were screened for DECIPHER during the study period with 198 of these enrolled (reasons for nonenrollment included died or discharged before consent: 218; refused: 164; MRI contraindication: 40; other exclusion: 186). Four patients were ineligible for the current study due to nonblack or nonwhite race, and 32 were excluded due to missing BP data at both 30 days and 1 year. There was no significant difference in age, race, sex, or initial National Institutes of Health Stroke Scale comparing those included with those excluded for lack of BP data.

Mean age was 58.9 years, 53% of the cohort was male, 77% were black, and 85% had a history of hypertension. Baseline demographics, medical history, and clinical characteristics are shown in Table 1 overall and by race. Seven of the included 162 patients died within the first year after ICH, whereas 4 had recurrent ICH and 2 had a subsequent ischemic stroke. Black participants were younger than whites (P<0.001), more likely to be smokers (P=0.014), and less likely to be married at baseline (P=0.005). Blacks were also more likely than whites to have a baseline diagnosis of hypertension (P=0.001) and had higher BP at presentation (P=0.002 for MAP).

The racial difference in MAP at presentation persisted when adjusting for age and sex in a multivariable linear regression model as shown in Table 2. Younger age was also associated with higher MAP at presentation in this model, and age did confound the association between race and baseline MAP (>10% change in parameter estimate, data not shown). Adding the other preselected covariates did not result in a substantial improvement in model fit based on the R² and did
Table 1. Description of the Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N=162)</th>
<th>White (N=37)</th>
<th>Black (N=125)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>58.9 (12.3)</td>
<td>65.3 (12.3)</td>
<td>57.1 (11.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>85 (52.5%)</td>
<td>20 (54.1%)</td>
<td>65 (52.0%)</td>
<td>0.826</td>
</tr>
<tr>
<td>Black race</td>
<td>125 (77.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.9 (14.8–34.7)</td>
<td>26.4 (22.9–33.3)</td>
<td>30.0 (25.7–34.9)</td>
<td>0.05*</td>
</tr>
<tr>
<td>Married</td>
<td>68 (42.0%)</td>
<td>23 (62.2%)</td>
<td>45 (36.0%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Private health insurance</td>
<td>92 (56.8%)</td>
<td>23 (62.2%)</td>
<td>69 (55.2%)</td>
<td>0.453</td>
</tr>
<tr>
<td>Socioeconomic status middle class or greater (4 missing)</td>
<td>95 (60.1%)</td>
<td>28 (77.8%)</td>
<td>67 (54.9%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Current smoker</td>
<td>43 (26.5%)</td>
<td>4 (10.8%)</td>
<td>39 (31.2%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Cocaine use (2 missing)</td>
<td>25 (15.6%)</td>
<td>2 (5.6%)</td>
<td>23 (18.6%)</td>
<td>0.059†</td>
</tr>
<tr>
<td>Hypertension (3 missing)</td>
<td>135 (84.9%)</td>
<td>24 (66.7%)</td>
<td>111 (90.2%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>179.9 (34.8)</td>
<td>160.9 (28.6)</td>
<td>185.5 (34.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>99.8 (23.6)</td>
<td>92.4 (20.6)</td>
<td>102.0 (24.0)</td>
<td>0.029</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>126.5 (25.8)</td>
<td>115.2 (21.6)</td>
<td>129.8 (26.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>National Institutes of Health Stroke Scale</td>
<td>6 (3–13)</td>
<td>6 (3–13)</td>
<td>6 (3–12)</td>
<td>0.590*</td>
</tr>
<tr>
<td>ICH volume, mL (5 missing)</td>
<td>7.5 (3.2–20.2)</td>
<td>11.4 (3.6–29.5)</td>
<td>7.2 (3.1–16.7)</td>
<td>0.212*</td>
</tr>
<tr>
<td>On any antihypertensive medication</td>
<td>88 (55.0%)</td>
<td>14 (37.8%)</td>
<td>74 (60.2%)</td>
<td>0.017</td>
</tr>
<tr>
<td>No. of classes of blood pressure medicine</td>
<td>1.2 (1.4)</td>
<td>0.8 (1.1)</td>
<td>1.3 (1.4)</td>
<td>0.066</td>
</tr>
</tbody>
</table>

Continuous variables presented as mean (SD) or median (interquartile range).
ICH indicates intracerebral hemorrhage.
*Wilcoxon.
†Fisher exact.

not alter the magnitude of the association between race and MAP (eg, <10% change in parameter estimates). Therefore, none of the other covariates met our prespecified criteria for inclusion in the model, although both the demographics-only model and a model with all prespecified covariates are shown in Table 2 to demonstrate the minimal change in the race and age effects when adjusting for other factors. Note that the model β estimates can be interpreted as the average difference in MAP (in mm Hg) for a one-unit change in the predictor variable adjusted for all other model covariates. In other words, black participants had a MAP that was average approximately 9.6 mm Hg higher than whites adjusted for other model covariates.

Table 2. Predictors of Mean Arterial Blood Pressure at Presentation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Demographics Only</th>
<th>Fully Adjusted Model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta (SE)</td>
<td>P Value</td>
</tr>
<tr>
<td>Black race (reference: white)</td>
<td>9.60 (4.72)</td>
<td>0.044</td>
</tr>
<tr>
<td>Age, y (centered at 59)</td>
<td>−0.61 (0.16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>1.80 (3.82)</td>
<td>0.639</td>
</tr>
<tr>
<td>Intercept</td>
<td>118.10 (4.64)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Additionally adjusted for body mass index, private health insurance (reference: all others), hemorrhage volume, current smoking, marital status, cocaine use, and socioeconomic status.

Discussion

We found that BP control was extremely poor at 30 days and 1 year after ICH, particularly in black patients, in this longitudinal cohort study of ICH survivors. Fewer than 20% of the study population had normal BP at follow-up measurements and more than half had BP consistent with Stage I or significantly higher (P=0.029). BP categories by JNC VII criteria at 30 days and 1 year after ICH are shown in the Figure. At each time point, <20% of the overall population had a BP in the normal range. Although there was no significant racial difference at 30 days (P=0.331), blacks were more likely than whites to have BP measurements consistent with Stage I/II hypertension at 1 year (P=0.036). At 30 days, blacks had a higher mean number of classes of antihypertensive medications than whites at 30 days (2.6 versus 1.6; P=0.001). Although this trend continued at 1 year, it was not statistically significant (2.3 versus 1.7; P=0.072).

The longitudinal model predicting MAP at follow-up is shown in Table 4. In contrast to the analysis of MAP at baseline, there was no association of race with MAP at follow-up (β=1.35, P=0.62). The only covariates associated with MAP at follow-up were married status at baseline and living in a personal residence at the time of the follow-up BP measurement. Married individuals had a MAP that was approximately 5 mm Hg lower than nonmarried individuals (β=−5.17, P=0.03). Individuals living in a personal residence at the time of the BP measurement had a MAP that was approximately 5 mm Hg higher than those living in a facility (β=5.47, P=0.02).
Stage II hypertension. Poor control of BP in stroke survivors has been described previously in studies based on NHANES.6,7,15 However, these studies had limitations in that they identified stroke based on self-report, had BP measurements at varying times from their stroke, and were unable to adjust for baseline stroke characteristics such as severity. Although there is some evidence that BP control in stroke survivors may be improving over the last several years,6 our results suggest that efforts to improve BP control after ICH remain critically important in both blacks and whites.

We found that blacks had a higher BP at the time of initial ICH presentation with a MAP that was on average 15 mm Hg higher than whites on unadjusted analysis. Our fully adjusted linear regression model suggested that even when accounting for other factors, blacks had a MAP that was still on average 9.6 mm Hg higher than whites, although this finding was of borderline significance. Elevated BP in the acute phase after ICH is a well-known phenomenon that has been associated with poor outcome16 and hematoma expansion.17 Few studies have specifically investigated racial differences in presenting BP.

When examining BP at follow-up, we found that blacks were somewhat more likely than whites to have elevated BP at 1 year (combined Stage I/II hypertension and higher diastolic BP). However, there was no racial difference seen in BP at 30 days, and race was not associated with MAP at follow-up in our final multivariable model. Due to the relatively small number of white participants at 1 year, we did not have sufficient power to systematically investigate which

Table 3. Unadjusted Blood Pressure at Follow-Up by Race

<table>
<thead>
<tr>
<th></th>
<th>Day 30</th>
<th></th>
<th></th>
<th>Year 1</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Black (N=109)</td>
<td>White (N=31)</td>
<td>P Value</td>
<td>Black (N=82)</td>
<td>White (N=21)</td>
<td>P Value</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>137.7 (19.1)</td>
<td>132.7 (18.1)</td>
<td>0.196</td>
<td>142.5 (27.1)</td>
<td>132.5 (24.4)</td>
<td>0.126</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>81.7 (14.8)</td>
<td>78.3 (13.1)</td>
<td>0.246</td>
<td>87.2 (18.3)</td>
<td>79.7 (12.0)</td>
<td>0.029</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>100.4 (14.2)</td>
<td>96.4 (12.1)</td>
<td>0.162</td>
<td>105.6 (19.9)</td>
<td>97.3 (14.5)</td>
<td>0.076</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure.
specific factors may have explained the racial difference in BP seen on unadjusted analysis. However, a post hoc exploratory analysis identified that both age and marital status acted as confounders of the relationship between race and MAP (>10% reduction in the parameter estimate for race when adding age or marital status to the model). Future studies with larger samples should be performed to allow a more detailed understanding of what factors explain the racial difference in BP post-ICH and to verify whether this racial difference becomes larger over time. In particular, it would be important to understand whether inadequate control is caused by poor medication adherence, poor access to health care, more treatment-resistant hypertension in blacks, failure to prescribe or adjust medications by healthcare providers, or a combination of these.

Our results suggest that future efforts to improve BP control after ICH may wish to target social and environmental factors in addition to traditional medical factors. Marital status at baseline may be a surrogate marker for social support, which we did not directly measure in this study. It is possible that individuals with stroke-related physical, emotional, or cognitive problems may need the assistance of a dedicated social support network to assist with attending regular physician appointments, medication adherence, and maintaining lifestyle modifications, which can help BP control.21,22 Furthermore, being married may represent a set of specific social support dimensions not able to be performed by other networks.21 Our finding of higher BP among those living in a personal residence at the time of follow-up could be due to individuals in an institution receiving more frequent BP monitoring or more consistent medication administration than those living in a personal residence. However, other unmeasured factors could account for these observed differences as well, and these factors should be assessed in larger studies of BP control after stroke to confirm these findings and better understand reasons for these associations.

Few studies have investigated predictors of long-term BP specifically in the ICH population. Studies of BP control in the general population based on NHANES data have had conflicting results on the association with marital status, with some,22 but not all studies suggesting an association.2 Health insurance status and disability have been associated with BP control, although we did not find insurance or disability (as measured by initial stroke severity) to be associated with MAP in our models. Some of the differences between our study and NHANES data that may account for these different findings include the study population (ICH survivors versus general population sample) and the precise definition of the outcome variables (continuous versus categorical analysis of BP).

This study has limitations. The requirement that participants in DECIPHER be able to undergo MRI and complete study assessments may have skewed our population toward milder ICH cases. However, optimal BP control after ICH is important for all ICH survivors regardless of severity, and therefore this limitation would not diminish the importance of our findings. Furthermore, if there is a healthy participant bias in this study population, we might expect that BP control in nonparticipants would be even worse. We did not have data on some potentially important covariates such as medication adherence, regular access to a primary care physician, or detailed assessment of social support and environmental factors.

Summary

In conclusion, we identified suboptimal BP control at 30 days and 1 year after ICH in this predominantly black population. Black participants had higher BP than whites acutely and were more likely to have Stage I/II hypertension than whites at 1 year. Urgent efforts are needed to better understand the factors leading to poor long-term BP control and identify optimal approaches to improve BP management after ICH in both blacks and whites.

Sources of Funding

This work was supported by Award Number U54NS057405 from the National Institute of Neurological Disorders and Stroke (NINDS) and National Institute on Minority Health and Health Disparities (NIMHD; U54NS057405). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NINDS, the NIMHD, or the National Institutes of Health. Dr Zahren is supported by grant K23AG038731 from the National Institute on Aging.

Disclosures

None.

References

Poor Long-Term Blood Pressure Control After Intracerebral Hemorrhage

Stroke. published online August 16, 2012;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
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/2012/08/16/STROKEAHA.112.663047

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/