

Racial-ethnic disparities in acute blood pressure after intracerebral hemorrhage

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ABSTRACT

Objective: To assess race-ethnic differences in acute blood pressure (BP) following intracerebral hemorrhage (ICH) and the contribution to disparities in ICH outcome.

Methods: BPs in the field (emergency medical services [EMS]), emergency department (ED), and at 24 hours were compared and adjusted for group differences between non-Hispanic black (black), non-Hispanic white (white), and Hispanic participants in the Ethnic Racial Variations of Intracerebral Hemorrhage case-control study. Outcome was obtained by modified Rankin Scale (mRS) score at 3 months. We analyzed race-ethnic differences in good outcome ($mRS \leq 2$) and mortality after adjusting for baseline differences and included BP recordings in this model.

Results: Of 2,069 ICH cases enrolled, 30% were white, 37% black, and 33% Hispanic. Black and Hispanic patients had higher EMS and ED systolic and diastolic BPs compared with white patients ($p = 0.0001$). Although attenuated, at 24 hours after admission, black patients had higher systolic and diastolic BPs. After adjusting for baseline differences, significant race/ethnic differences persisted for EMS systolic, ED systolic and diastolic, and 24-hours diastolic BP. Only ED systolic and diastolic BP was associated with poor functional outcome, and no BP predicted mortality. We found no race-ethnic differences in 3-month functional outcome or mortality after adjusting for group differences, including acute BPs.

Conclusions: Although black and Hispanic patients had higher BPs than white patients at presentation, we did not find race-ethnic disparities in 3-month functional outcome or mortality. ED systolic and diastolic BP was associated with poor functional outcome, but not mortality, in this race-ethnically diverse population. *Neurology*® 2016;87:786–791

GLOSSARY

BP = blood pressure; **CI** = confidence interval; **ED** = emergency department; **EMS** = emergency medical services; **ERICH** = Ethnic/Racial Variations of Intracerebral Hemorrhage; **GCS** = Glasgow Coma Scale score; **ICH** = intracerebral hemorrhage; **INTERACT2** = Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial; **mRS** = modified Rankin Scale; **OR** = odds ratio.

Intense and rapid lowering of blood pressure (BP) following acute spontaneous intracerebral hemorrhage (ICH) is increasingly recognized to be safe and may be of clinical benefit.^{1,2} Findings from the Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT2) suggest that systolic BP reductions below a target of 140 mm Hg may improve functional outcome.³ Factors that lead to acute and persistent BP elevations after ICH are not completely understood and may include racial-ethnic disparities. The prevalence and severity of hypertension varies greatly in people of different race and ethnicity, raising the possibility that such differences also exist in acute ICH and contribute to racial-ethnic disparities in outcome. Here, we examine any racial-ethnic differences in the acute BP response to ICH in the NIH-funded Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH; U01-NS069763) study and analyze whether such differences contribute to disparities in outcome.

Supplemental data
at Neurology.org

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METHODS The design and methods of the ERICh study have been published previously.⁴ Briefly, ERICh is an ongoing multicenter prospective case-control study of ICH in non-Hispanic whites (whites), non-Hispanic blacks (blacks), and Hispanics. Participants are recruited from 42 US recruitment sites. Inclusion into the study requires age >18 years, residency within 50 miles of the recruitment center (100 miles for population centers <1 million), white, black, or Hispanic race-ethnicity, and a spontaneous ICH, defined as the sudden onset of severe headache, altered level of consciousness, or focal neurologic deficit associated with a focal collection of blood within the brain parenchyma, seen on neuroimaging or at autopsy, and not attributable to hemorrhagic conversion of a cerebral infarction or other structural vascular anomalies.

All enrolled participants or designated proxies underwent a standardized data collection protocol including a personal interview and medical chart abstraction, with emphasis on medical history and history of present illness. Management of ICH proceeded in accordance with local medical practice and was not protocol prescribed. BP measurements in the dataset included the recordings in the field (emergency medical services [EMS]), first recorded BP on arrival in the emergency department (ED), and the closest BP to 24 hours after hospital admission. We also recorded medications used for treatment of ICH during the ED stay. Outcome at 3 months was assessed by a telephone modified Rankin Scale (mRS). The current analysis is of cases with ICH only and does not include controls, and is restricted to enrollment of ICH patients who presented to an ED between September 2010 and December 2013.

Standard protocol approvals, registrations, and patient consents. All participants, or their health care proxies, gave written informed consent, and the ERICh study was approved by all local institutional review boards prior to initiating the study.

Statistical methods. Baseline characteristics, BP recordings at EMS, ED, and 24 hours, and ED treatment of ICH between each race/ethnic group were analyzed using χ^2 tests for categorical data and a 1-way analysis of variance for continuous data. Multivariate analyses were performed on continuous outcomes using generalized linear models and adjusted for known risk factors. We then analyzed race-ethnic differences in good outcome defined as a mRS ≤ 2 after adjusting for baseline differences. This was repeated for mortality. In a multivariate regression model, we included systolic and diastolic BP obtained by EMS, ED, and at 24 hours in this model (entered individually) to determine if the effect on mortality and functional outcome (3 months mRS) is mediated by BP. Distribution, conditional normality, and homogenous variance assumptions were checked. No transformations were required for the continuous outcomes. We also examined BP at 24 hours analyzing factors associated with a systolic BP >140 mm Hg. This particular threshold was chosen as this was the BP target in the intense BP treatment group of the INTERACT2 study. We also tested for the presence of interactions of BP levels and race-ethnicity to determine whether there was a differential effect of BP by race-ethnicity. Only available data were analyzed, and missing data were not imputed.

RESULTS Cohort description. Among 2,069 patients, 30% were white, 37% were black, and 33% were Hispanic. White patients (69 ± 14 years) were significantly older than black patients (58 ± 13 years) and Hispanic patients (59 ± 14 years) ($p < 0.0001$),

had a more frequent history of dyslipidemia, and had more lobar hemorrhages (43% vs 25% for black patients and 26% for Hispanic patients; $p < 0.0001$) (table 1). Black patients had a more frequent history of hypertension, reported more substance use, including history of cocaine use and smoking, and had smaller hemorrhage volumes. Hispanic patients were more likely diabetic and had fewer women with ICH (table 1).

Acute elevations in BP. BP recordings by EMS were available in 720, within ED in 2,035, and at 24 hours in 2,018 cases. A total of 904 (44%) were transferred between ED departments, and the original ED records and BPs were not available for review in 13%. The number of recordings available by EMS differed between the racial-ethnic groups, with more BPs obtained in Hispanic patients (40%) than in white patients (31%) and black patients (33%) ($p = 0.002$), but no differences in the number of recordings available for review were noted in the ED or at 24 hours. Black patients and Hispanic patients had significantly higher EMS and ED systolic and diastolic BPs (all p values <0.0001) compared with white patients (table 2). At 24 hours, group differences were attenuated, but black patients continued to have higher systolic and diastolic BPs. After adjusting for baseline group differences, including age, sex, diabetes, dyslipidemia, hypertension history, smoking history, cocaine use, location of ICH (lobar vs subcortical), and hematoma volume, the differences between the race-ethnic groups remained significant for EMS systolic, ED systolic and diastolic, and 24-hour diastolic BP (all p values <0.04). BP differences persisted despite more intense antihypertensive treatment in black patients. In the ED, 75% of black patients, 67% of Hispanic patients, and 56% of white patients received treatment for BP and IV medication use was more frequent in black patients compared with white patients and Hispanic patients (41% vs 27% and 33%, respectively).

Factors associated with systolic BP ≥ 140 mm Hg at 24 hours after admission were a history of hypertension, sex, EMS diastolic, ED systolic, and diastolic BP, and a subcortical hemorrhage location (table e-1 on the *Neurology*[®] Web site at Neurology.org). Hispanic ethnicity and lower ED Glasgow Coma Scale score (GCS) were associated with a systolic BP ≥ 140 mm Hg at 24 hours in a multivariate model including age, sex, race-ethnicity, history of hypertension, location of hematoma (lobar vs subcortical), ED GCS, and ED medications received.

Outcomes. A good 3-month outcome (mRS ≤ 2) was achieved in 171 (32%) white patients, 242 (38%) black patients, and 220 (37%) Hispanic patients ($p = 0.004$). Mortality at 3 months was 157 (30%)

Table 1 Baseline characteristics

	White	Black	Hispanic	p Value
No. (%) (total = 2,069)	624 (30)	758 (37)	687 (33)	
Age, y, mean \pm SD	69.2 \pm 13.6	57.9 \pm 12.9	59.3 \pm 14.3	<0.0001
Women, n (%)	283 (45.4)	322 (42.5)	259 (37.7)	0.0172
Hypertension history, n (%)	457 (74.2)	642 (85.9)	520 (77.5)	<0.0001
Diabetes history, n (%)	159 (25.5)	207 (27.3)	226 (32.9)	0.0076
Dyslipidemia history, n (%)	346 (56.4)	295 (39.6)	288 (42.7)	<0.0001
Smoker, n (%)				
Current	82 (13.1)	225 (29.7)	103 (15.0)	<0.0001
Former	229 (37.0)	173 (22.8)	191 (27.8)	
Cocaine/crack use, n (%)	10 (1.8)	107 (15.5)	32 (5.1)	<0.0001
GCS at arrival, median	15	14	15	0.4562
ICH location, n (%)				
Supratentorial	534 (88.3)	631 (85.6)	558 (85.5)	0.2637
Infratentorial	71 (11.7)	106 (14.4)	95 (14.6)	
ICH location, n (%)				
Lobar	266 (42.6)	186 (24.5)	178 (25.9)	<0.0001
Nonlobar	358 (57.4)	572 (75.5)	509 (74.1)	
Hematoma volume, mL, mean \pm SD	23.7 \pm 28.7	17.4 \pm 23.8	21.1 \pm 25.4	<0.0001
Intraventricular hemorrhage, n (%)	281 (45.0)	351 (46.3)	300 (43.7)	0.6026

Abbreviations: GCS = Glasgow Coma Scale score; ICH = intracerebral hemorrhage.

in white patients, 135 (21%) in black patients, and 125 (21%) in Hispanic patients ($p = 0.0008$). Tables 3 and 4 show factors independently associated with functional outcome and mortality in a multivariate regression model. Although ED systolic and diastolic

BP were independent predictors of functional outcome, stronger associations with functional outcome were found for age, female sex, and hematoma volume. Interestingly, cocaine use was associated with improved functional outcome. Mortality was independently

Table 2 Blood pressure recordings and treatment early after intracerebral hemorrhage

	White	Black	Hispanic	p Value
EMS BP, mm Hg (total n = 720), mean \pm SD				
Systolic	175.7 \pm 31.9	193.4 \pm 39.4	190.3 \pm 40.1	<0.0001
Diastolic	96.8 \pm 30.2	106.2 \pm 31.9	104.4 \pm 28.7	<0.0001
ED BP, mm Hg (total n = 2,035)				
Systolic	176.4 \pm 35.0	193.1 \pm 37.5	187.5 \pm 38.5	<0.0001
Diastolic	94.3 \pm 23.0	109.9 \pm 25.8	103.3 \pm 25.3	<0.0001
24-hour BP, mm Hg (total n = 2,018)				
Systolic	138.4 \pm 20.9	141.9 \pm 22.9	138.2 \pm 21.7	0.0084
Diastolic	71.1 \pm 15.2	77.9 \pm 15.8	73.5 \pm 15.6	<0.0001
Any ED BP treatment, n (%)	346 (55.8)	560 (74.6)	459 (67.2)	<0.0001
Continuous IV infusion for BP treatment, n (%)	405 (27.0)	618 (41.2)	252 (32.8)	<0.0001
ED visit and stroke onset, n (%)				0.9563
ED visit same day as stroke	486 (78.9)	599 (80.4)	552 (80.5)	
ED visit 1 day after stroke	72 (11.7)	80 (10.7)	73 (10.6)	
ED visit \geq 2 days after stroke	58 (9.4)	66 (8.9)	61 (8.9)	

Abbreviations: BP = blood pressure; ED = emergency department; EMS = emergency medical services.

Table 3 Multivariate analysis of predictors of functional outcome at 3 months after intracerebral hemorrhage (ICH) (modified Rankin Scale >2)

	OR	95% CI ^a	p Value
Age	1.28	1.21-1.34	<0.0001
Female sex	1.38	1.07-1.69	0.0126
Lobar hemorrhage	0.29	0.22-0.39	<0.0001
Log hematoma volume	2.61	2.29-2.97	<0.0001
Cocaine use	0.57	0.36-0.91	0.0193
Race-ethnicity			0.1792
Black vs white	1.33	0.96-1.86	0.0886
Hispanic vs white	1.07	0.28-1.48	0.6760
Inclusion of BP individually			
EMS systolic	1.02	0.99-1.05	0.3188
EMS diastolic	0.99	0.95-1.04	0.7744
ED systolic	1.02	1.01-1.04	0.0106
ED diastolic	1.03	1.01-1.06	0.0177
24-hour systolic	1.00	0.97-1.03	0.8643
24-hour diastolic	0.98	0.95-1.02	0.4482

Abbreviations: BP = blood pressure; CI = confidence interval; ED = emergency department; EMS = emergency medical services; OR = odds ratio.

^aOR and CI for age and BP traits represent 5-unit change; full model included age, sex, diabetes, dyslipidemia, history of hypertension, smoker, cocaine use, ICH location (cortical vs subcortical), ICH volume, and race-ethnicity.

associated with age, dyslipidemia history, lobar ICH location (cortical vs subcortical), and hematoma volume. BP and race-ethnicity were not associated mortality.

In an analysis stratified by race-ethnicity, EMS systolic BP was associated with worse functional outcome in white patients (odds ratio [OR] 1.08; 95% confidence interval [CI] 1.01–1.16) and ED diastolic BP in Hispanic patients (OR 1.07; 95% CI 1.01–1.13). No association of BP with mortality was found when analysis was stratified by race-ethnicity.

DISCUSSION Observational studies have suggested an association between elevated BP during the first 24 hours after ICH and stroke outcome.⁵ This finding has been replicated in several different race-ethnicity groups, but there have been no direct racial-ethnic comparisons of acute BP differences as reported in our study. We demonstrated significant BP differences among the 3 racial-ethnic groups at different time points during the first 24 hours after ICH. These differences were more pronounced in the acute setting (EMS and ED) and less so when examined at 24 hours. We found an association of ED systolic and diastolic BP elevation on functional outcome but not mortality. We did not find race-ethnic disparities in mortality or functional outcome after adjusting for baseline differences.

In contrast to previous studies examining the relationship between acute BP and ICH outcome, we were able to assess long-term functional outcome and not just mortality. Our results support previous findings that acute BP elevations are a predictor of poor outcome after ICH, and extend those findings to long-term outcomes. In a study of Chinese stroke

Table 4 Multivariate analysis of predictors of 3-month mortality after intracerebral hemorrhage (ICH)

	OR	95% CI ^a	p Value
Age	1.35	1.28-1.44	<0.0001
Female sex	1.00	0.74-1.35	0.9846
Hypercholesterolemia	0.63	0.46-0.87	0.0051
Lobar location	0.40	0.28-0.57	<0.0001
Log hematoma volume	2.66	2.27-3.11	<0.0001
Race-ethnicity			0.8725
Black vs white	1.10	0.76-1.60	0.6173
Hispanic vs white	1.03	0.71-1.48	0.8927
Inclusion of BP individually			
EMS systolic	1.00	0.97-1.04	0.7802
EMS diastolic	1.00	0.96-1.04	0.9501
ED systolic	1.00	0.98-1.03	0.6398
ED diastolic	1.00	0.97-1.03	0.9492
24-hour systolic	0.99	0.95-1.02	0.3844
24-hour diastolic	0.99	0.94-1.04	0.6188

Abbreviations: BP = blood pressure; CI = confidence interval; ED = emergency department; EMS = emergency medical services; OR = odds ratio.

^aOR and CI for age and BP traits represent 5-unit change; full model included age, sex, diabetes, dyslipidemia, history of hypertension, smoker, cocaine use, ICH location (cortical vs subcortical), ICH volume, and race-ethnicity.

patients, systolic BP >140 mm Hg and elevated diastolic BP on admission were associated with greater in-hospital mortality and discharge disability in 1,760 participants with acute hemorrhagic stroke.⁶ A J-shaped response for admission systolic BP and 30-day mortality was found among 1,097 Japanese patients with brain hemorrhage after adjusting for ICH volume.⁷ In a Finnish population with ICH (n = 425), mean arterial BP during the first 24 hours after stroke onset was one of the 2 most significant predictors of 28-day mortality after adjustment for multiple baseline variables.⁸ While most studies have shown an independent relationship between BP and outcome, this has not consistently been the case.^{9,10}

Of note is that lobar hemorrhages occurred more frequently in white patients and deep hemorrhages more frequently in black patients. The pathophysiology and role of hypertension between lobar and deep ICH may be different. Lobar hemorrhages are likely to be cerebral amyloid related, occurring in older participants, and deep hemorrhages more hypertensive in nature, in younger participants. However, even after adjusting for baseline variables, we found no differences in functional outcome or mortality among the 3 race-ethnic groups. A triethnic comparison of ICH mortality, between 1980 and 1985 in Texas, showed a significant interaction between age and race-ethnicity, with an increased risk of dying in young (<75 years) black and Hispanic (Mexican origin) participants compared with white patients.¹¹ No significant differences in mortality were noted between black and white participants in the Greater Cincinnati/Northern Kentucky Stroke Study and the South London Stroke Register following ICH.^{12,13}

Given any potential differences in race-ethnic ICH outcome and acute BP elevations, we hypothesized that some of the race-ethnic disparities in outcomes may be mediated by BP. While we found that ED systolic and diastolic BP was associated with poor functional outcome, we did not find any race-ethnic disparities in outcome after adjusting for baseline group differences including BP. Overall, the effect of ED BP on outcome was much weaker than other factors known to affect stroke outcome in general, such as age, hematoma size, and volume (table 3). It is possible that a more pronounced effect of acute BP on racial-ethnic outcome could have been mitigated by recent changes in BP management practices and more intense acute BP reductions. We showed race-ethnic differences in the acute management of BP, with black patients receiving more intense BP treatment, with a higher use of continuous IV infusions. This could have mitigated any effect of BP on race-ethnic outcome differences. Our population was also drawn from centers experienced in the care of minorities, which may have further reduced

such potential disparities in outcomes. In fact, approximately 40% of participants were transferred to a more experienced center. We were not able to analyze presenting ED BP in 13% of transferred cases.

The strength of our study includes a large sample size, which provided similar power between racial/ethnic groups, and the inclusion of functional outcome in addition to mortality. As a limitation, we report that BP recordings were not obtained at standardized time points and BP treatment was not by specific protocol. On the other hand, this makes our findings more generalizable. While the overall study population was large, with over 2,000 participants enrolled, BP readings by EMS were less frequently available but were nearly identical to ED BPs and their lack does not affect the principal finding that presentation BP may be higher among minority populations.

We report significantly higher BPs during the first 24 hours after acute ICH in black patients and Hispanic patients compared with white patients. We found an association between acute BP in the ED and poor 3-month functional outcome but not mortality. We did not find any race-ethnic differences in outcome after adjusting for baseline group differences, including BP.

AUTHOR CONTRIBUTIONS

Sebastian Koch: study concept, design, acquisition of data, analysis and interpretation, manuscript writing and revisions, contribution to intellectual content. Mitchell S.V. Elkind: acquisition of data, analysis and interpretation, manuscript revisions, contribution to intellectual content. Fernando D. Testai: acquisition of data, analysis and interpretation, manuscript revisions, contribution to intellectual content. W. Mark Brown: acquisition of data, analysis and interpretation. Sharyl Martini: acquisition of data, analysis and interpretation, manuscript revisions, contribution to intellectual content. Kevin N. Sheth: acquisition of data, analysis and interpretation, manuscript revisions, contribution to intellectual content. Ji Y. Chong: analysis and interpretation, manuscript revisions, contribution to intellectual content. Jennifer Osborne: acquisition of data, analysis and interpretation, manuscript writing and revisions, contribution to intellectual content. Charles J. Moomaw: acquisition of data, analysis and interpretation, manuscript writing and revisions, contribution to intellectual content. Carl D. Langefeld: acquisition of data, analysis and interpretation, manuscript revisions, contribution to intellectual content. Ralph L. Sacco: analysis and interpretation, manuscript revisions, contribution to intellectual content. Daniel Woo: acquisition of data, analysis and interpretation, manuscript revisions, contribution to intellectual content.

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