Ethnic Disparities Trump Other Risk Factors in Determining Delay to Emergency Department Arrival in Acute Ischemic Stroke

James E. Siegler, BS; Amelia K. Boehme, MSPH; Karen C. Albright, DO, MPH; Sheryl Martin-Schild, MD, PhD

Objectives: Historically, Blacks receive treatment for acute ischemic stroke (AIS) less frequently than Whites, even after considering contraindications to treatment and socioeconomic status. Blacks also experience a longer delay between symptom onset and Emergency Department (ED) arrival for unclear reasons. The purpose of our study was to determine if these disparities exist within our biracial patient population and why.

Methods: All patients who presented to our center with AIS between July, 2008 and December 2010 were identified from a prospective registry. The relationship between patient demographics and delay to ED arrival was investigated, excluding patients with unknown time of last seen normal (LSN), race other than Black or White, in-hospital strokes, and patients who bypassed the ED.

Results: Of the 596 patients screened, 368 met inclusion criteria (median age 65 years, 39.8% female, 67.8% Black). Blacks were more likely to have a longer delay from LSN to ED arrival compared to Whites (median delay of 339 min vs 151 min, $P=.0028$). Black race remained an independent predictor for delayed ED arrival even after adjusting for age, sex, stroke severity, and home medication use. The same proportion of Whites and Blacks who presented within the 3-hour window received thrombolytic treatment ($P=.9763$).

Conclusion: Black race appeared to be the driving force in a multivariate analysis evaluating predictors of ED arrival >3 hours after LSN. Despite the increased delay to ED arrival Blacks were just as likely to receive IV tPA as Whites. Improving stroke awareness and symptom recognition may reduce delays in seeking hospitalization. (*Ethn Dis*. 2013;23[1]: 29–34)

Key Words: Ethnic Disparities, Acute Ischemic Stroke, Treatment

From the Stroke Program, Department of Neurology, Tulane University Hospital, New Orleans, LA (JES, SMS); the Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, (KCA, AKB); the Health Services and Outcomes Research Center for Outcome and Effectiveness Research and Education (COERE), University of Alabama at Birmingham (KCA); the Center of Excellence in Comparative Effectiveness Research for Eliminating Disparities (CERED)/Minority Health & Health Disparities Research Center (MHRC), University of Alabama at Birmingham (KCA); and the Department of Neurology, School of Medicine, University of Alabama at Birmingham (KCA).

Address correspondence to Sheryl Martin-Schild, MD, PhD; Stroke Program at Tulane University Hospital; Department of Neurology; 1440 Canal Street, TB-52, Suite 1000; New Orleans, LA 70112-2715; (504) 988-0972; (504) 988-6263 (fax); smartin2@tulane.edu

Introduction

Despite major advances in neurological and cerebrovascular research, stroke remains a leading cause of death and the number one cause of permanent disability in the adult population.[1] Intravenous tissue plasminogen activator (IV tPA) remains the only acute treatment with proven efficacy for patients with acute ischemic stroke (AIS) who present within 3 hours following symptom onset.[2] However, roughly 3%–5% of patients diagnosed with AIS in American hospitals are treated with thrombolytic therapy, depending on the database investigated.[3] This leaves an overwhelming majority of patients untreated due to one or more contraindications or warnings to therapy—most commonly a delay from symptom onset to Emergency Department (ED) arrival.[4,5] Studies have shown that Black patients are significantly less likely than White patients to receive thrombolytic therapy for stroke,[5–8] although this matter is debated.[9] Similar racial disparities have been reported in the treatment of coronary artery disease as well.[10–12] The reasons for the ethnic disparity in treatment rates for AIS are unclear, but implicit bias among physicians,[13] longer delays within the ED,[14] and more frequent contraindications to therapy[5] have been implicated. The purpose of our study was to identify any racial disparities in treatment rates among patients with AIS and to explore the reasons for these disparities.

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Methods

We performed a single-center analysis of patients who presented with AIS between July 2008 and December 2010. A retrospective review was performed on the prospectively collected stroke registry database at Tulane University Hospital. Patients were excluded if they had an unknown time of last seen normal (LSN), were a race other than Black or White or if racial data were missing, experienced an in-hospital stroke, bypassed the ED, or were transferred from an outside facility. Race is a self-reported data element in our clinical registry. Patient demographics, time of LSN and ED arrival, and treatment with IV tPA were collected. Stroke severity was measured using a validated and reliable scoring method, the National Institutes of Health Stroke Scale (NIHSS).[15–17] IV tPA treatment rates were compared between Blacks and Whites for the entire population,

and then between Blacks and Whites presenting within the first 3 hours of known LSN. Rates of exclusion criteria for IV tPA treatment[18] were compared in Blacks and Whites among patients who presented within 3 hours of LSN but were not treated with IV tPA. We also examined the association between presenting symptoms and delay to ED presentation according to the following categories and definitions using the NIHSS score: "gaze deficit" was defined as >0 points on item 2; "visual field deficit" as >0 points on item 3; "weakness" as >1 point on either item 5a, 5b, 6a, or 6b; "sensory deficit" as >0 points on item 8; language disturbance, or "aphasia" as >0 points on item 9; "neglect" as >0 points on item 11 (see Brott et al, 1989, for an explanation of item scoring).[17] Finally, we examined the relationships between time from onset to presentation, dichotomized at 3 hours and as a continuous variable, and discharge disability (using the validated modified Rankin Scale score)[19,20] among all patients and among patients split by race and by treatment with IV tPA.

Continuous variables were compared using Student's t-test or Wilcoxon Rank sum where appropriate. Categorical variables were investigated using Chi-square tests or Fisher's exact test where appropriate. Crude and adjusted logistic regression was used to calculate odds ratios for Blacks presenting within the first 3 hours. Multivariable logistic regression models were created using backwards selection with a cut point of $P=.20$ to establish the best model. All tests were done at the $\alpha=.05$ level (two-sided). This study was approved by the Tulane University institutional review board.

RESULTS

Patient Population

Five-hundred ninety-six consecutive patients diagnosed with AIS were identified from the retrospective review of our prospective database. Among these patients, 168 were excluded because of unknown LSN (median age 62 years, 45.2% female, 64.6% Black) and 72 because they bypassed the ED, experienced an in-hospital stroke, or they were transferred from an outside facility (median age 62 years, 54.2% female, 54.3% Black). These two exclusion criteria groups were not mutually exclusive resulting in 368 eligible patients for this study. Of the 368 included patients (median age 65 years, 39.8% female, 67.8% Black), the odds of a Black patient having a history of stroke was twice the odds of a White patient (OR 2.059, 95% CI=1.292–3.283). Black patients were nearly twice as likely to report having a history of hypertension (OR 1.884, 95% CI=1.142–3.109) and nearly three times as likely to have a history of diabetes (OR 2.870, 95% CI=1.692–4.871). Blacks were more likely to be taking an antihypertensive agent (OR 1.527, 95% CI=0.966–2.412) or a diabetic agent at home (OR 2.282, 95% CI=1.315–3.960) when compared to Whites. Baseline demographics comparing Whites and Blacks are shown in Table 1.

Table 1. Admission demographic information for included patients (*N*=368)

	Blacks	Whites	
	n=249	*n*=119	*P*
Age, median years (IQR)	65 (54.5–77)	64 (55–75)	.9484
Sex, % female	4.6 (101/249)	38.7 (46/119)	.7268
Admission NIHSS, median (IQR)	6 (3–13)	6 (2–14)	.5247
Admission SBP, median mm Hg (IQR)	160 (139–191)	158 (134–182)	.3836
Admission DBP, median mm Hg (IQR)	94 (80–110)	90 (80–104)	.1882
IV tPA received, % patients	31.1 (77/248)	41.2 (49/119)	.0558
Past medical history, % yes			
History of stroke	46.2 (115/249)	29.4 (35/119)	.0022
History of diabetes	39.4 (97/246)	18.5 (22/119)	<.0001
History of hypertension	80.5 (198/246)	68.6 (81/118)	.0124
History of hyperlipidemia	44.9 (110/245)	41.0 (48/117)	.4872
History of coronary artery disease	18.5 (46/249)	20.2 (24/119)	.6985
History of atrial fibrillation	10.2 (25/245)	11.1 (13/117)	.7923
Active smoker	34.8 (86/247)	23.0 (26/113)	.0247
Home medications, % yes			
Anti-platelet agent	44.2 (110/249)	35.3 (41/116)	.1107
Anti-hypertensive agent	25.5 (63/247)	21.0 (25/119)	.3456
Lipid-lowering agent	43.9 (107/244)	33.9 (40/118)	.0707
Diabetic medication[a]	31.6 (77/244)	16.8 (20/119)	.0029
Percentage arriving within 3 hrs, %	36.6 (91/249)	55.4 (66/119)	.0006

IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale score; SBP, systolic blood pressure; DBP, diastolic blood pressure; IV tPA, intravenous tissue plasminogen activator.
[a] Diabetic medication at home includes insulin as well as oral hypoglycemics.

Ethnic Disparity in Thrombolytic Treatment Rates

Among all patients who presented to our center with AIS, 126 (34.3%) were treated with IV tPA (median age 66 years, 45.2% female, 61.1% Black). Although Black patients experienced a significantly greater delay to ED arrival compared to White patients, there was no significant difference in the proportion of Black vs White patients treated with IV tPA (31.1% vs. 41.2%, $P=.0558$). One hundred fifty seven patients arrived at the ED within 3 hours of LSN (42.7% of included patients), with a significantly smaller percentage of Black patients arriving in the 3-hour window when compared to White patients (Table 2). When considering only the patients who arrived at the ED

Table 2. Demographic information and exclusion criteria for IV tPA treatment among patients who arrived to the ED within 3 hours of symptom onset (41.6% of included patients, *n*=153)

	Blacks	Whites	
	n=89	*n*=64	*P*
Age, median (IQR)	66 (56–79)	62 (55–75)	.1470
Admission NIHSS, median (IQR)	8 (4–16)	8 (2–16)	.3840
Percentage of race treated, %	67.4 (60/89)	67.2 (43/64)	.9763
Admission glucose, median mg/dL (IQR)	125 (103–167)	112 (95–134.5)	.0125
Exclusion criteria,[a] % yes			.3829
Minor symptoms[b] or rapid resolution of deficits	28.6 (8/28)	5.9 (1/17)	
Patient refusal	3.6 (1/28)	5.9 (1/17)	
Delayed diagnosis	14.3 (4/28)	17.7 (3/17)	
Stroke in past 3 months	10.7 (3/28)	11.8 (2/17)	
MI in last 3 months	.0 (0/28)	5.9 (1/17)	
History of ICH/SAH	7.1 (2/28)	.0 (0/17)	
Abnormal coagulation studies[c]	10.7 (3/28)	.0 (0/17)	
Platelet count <100,000 cells/mL	3.5 (1/28)	5.9 (1/17)	

IV tPA, intravenous tissue plasminogen activator; ED, emergency department; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale score; MI, myocardial infarction; ICH/SAH, intracerebral hemorrhage/subarachnoid hemorrhage.

[a] Exclusion criteria reflect each patient's primary contraindication to thrombolytic therapy for all patients who presented to the ED and were diagnosed with AIS within the treatment window. Exclusion criteria are consistent with the definitions used in the 2007 AHA guidelines.[18]

[b] Minor symptoms at our institution are defined as baseline NIHSS <5 points in accordance with the 2007 AHA guidelines.[18]

[c] Abnormal coagulation studies are defined as values for international normalized ratio >1.7 or activated partial thromboplastin time >40 in accordance with the 2007 AHA guidelines.[18]

within 3 hours of LSN, there were no statistically significant differences in Blacks and Whites with regard to initial stroke severity or rates of IV tPA treatment exclusion criteria (Table 2).

Ethnic Disparity in ED Delay

Black patients in our population were more likely to have a longer delay from LSN to ED arrival compared to Whites (median delay of 339 min vs. 151 min, *P*=.0028). The crude logistic regression model showed that Black race is an indicator of not arriving to the ED within 3 hours of LSN (OR 2.162, 95% CI=1.387–3.371). As illustrated in Model 6 of Table 3, being Black remained a significant indicator of this outcome even after adjusting for age, sex, baseline stroke severity, insurance status, and diabetic medication use at home (OR 2.108, 95% CI=1.336–3.329). After replacing home diabetic medication in Model 6 (Table 3) with any of the following other home medications, Black race remained a significant independent predictor of a delayed arrival to the ED regardless of which medication was used at home: lipid-lowering agent (OR for Black patients arriving late to ED 2.303, 95% CI=1.459–3.636), anti-hypertensive agent (OR 2.212, 95% CI=1.407–3.478), and anti-platelet agent (OR 2.174, 95% CI=1.377–3.431) (data not shown in table).

Relationship of Initial Stroke Symptoms and ED Delay

There were no significant differences in the proportion of patients presenting with specific stroke symptoms between Blacks and Whites (gaze deficit *P*=.8418, visual field deficit *P*=.8225,

Table 3. Odds ratios, with confidence intervals, for possible predictors of emergency department arrival outside 3-hour treatment window (*N*=368)

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Black race	2.162 (1.387–3.371)	2.155 (1.381–3.362)	2.158 (1.383–3.367)	2.179 (1.392–3.413)	2.210 (1.407–3.469)	2.108 (1.336–3.329)
Age	-	.994 (.981–1.008)	.995 (.981–1.009)	.998 (.984–1.012)	.994 (.978–1.010)	.993 (.978–1.010)
Female	-	-	.931 (.605–1.434)	1.000 (.644–1.551)	.999 (.641–1.555)	.989 (.634–1.544)
Baseline NIHSS	-	-	-	.966 (.938–.995)	.970 (.941–1.000)	.969 (.940–.999)
Insurance status[a]	-	-	-	-	.683 (.357–1.306)	.669 (.349–1.285)
On diabetic medication at home[b]	-	-	-	-	-	1.273 (.773–2.097)

NIHSS, National Institutes of Health Stroke Scale score.

Each model designed to adjust for additional possible covariates that may influence emergency department delay.

[a] Insurance status for patients on Medicaid or without insurance.

[b] Diabetic medication at home includes insulin as well as oral hypoglycemics.

Table 4. Delay from "last seen normal" to emergency department according to presenting symptom among patients according to race (*N*=368)

Symptom	Black Patients		White Patients		*P*		
	Not Present	Present	Not Present	Present	P^a	P^b	P^c
Gaze deficit, median delay in min. (range)	454 (18–19170)	207 (27–3090)	174 (10–5801)	80 (20–2077)	**.0188**	.0753	**.0211**
Visual field deficit, median delay in min. (range)	375 (18–19170)	273 (27–7407)	195 (10–5801)	105 (18–2404)	.0741	.1883	**.0467**
Weakness, median delay in min. (range)	500 (18–5865)	300 (25–19170)	213 (10–5801)	123 (15–4750)	.2361	.1150	**.0022**
Sensory deficit, median delay in min. (range)	317 (27–7407)	444 (18–19170)	171 (10–5801)	125 (23–4750)	.4055	.7094	**.0171**
Aphasia, median delay in min. (range)	499 (18–19170)	233 (28–7205)	207 (10–5801)	120 (15–1747)	**.0066**	.1556	**.0425**
Neglect, median delay in min. (range)	350 (18–19170)	272 (30–17351)	176 (10–5801)	96 (23–2404)	.3340	.2097	**.0263**

[a] Delay from last seen normal to emergency department arrival in Black patients with this symptom vs Black patients without this symptom at presentation. (n=249)
[b] Delay from last seen normal to emergency department arrival in White patients with this symptom vs White patients without this symptom at presentation. (n=119)
[c] Delay from last seen normal to emergency department arrival in Black patients vs. White patients with this symptom at presentation.
Values reported as minutes from time last seen normal to emergency department arrival. See text for definitions of each presenting symptom. Statistically significant differences are bolded.

weakness P=.2170, sensory deficit P=.6758, aphasia P=.6376, neglect P=.9655). Weakness was the most common presenting symptom in both Blacks and Whites, with 68.7% of Black patients experiencing weakness compared to 62.2% of White patients. Shorter times from LSN to ED arrival were observed in all patients presenting with weakness (240 vs 342 min., P=.0970) and aphasia (197 vs 346 min., P=.0038) regardless of race. For each and every stroke symptom, Blacks were more likely to arrive at the ED later than Whites with those symptoms (Table 4).

Impact on Outcome

Of the entire sample, we did not find time-to-presentation to be associated with modified Rank in Scale score at discharge. Neither was time-to-presentation associated with outcome when Blacks and Whites were analyzed separately nor when the sample was split by IV tPA treatment (data not shown).

In our predominantly Black patient population, we found that the same proportion of Black and White patients who presented within the 3-hour window for thrombolytic treatment received IV tPA.

DISCUSSION

Ethnic Disparities in Treatment Rates and ED Delay

Contrary to previous studies, we did not find a lower thrombolytic treatment rate for Blacks compared to Whites. We did find, however, that Black patients were less likely to present within the 3-hour treatment window for IV tPA. Among patients who arrived within the 3-hour window, we found no significant differences in the proportion of Black or White patients treated with thrombolysis. Other than delay to ED arrival, we observed no differences in the frequency of other contraindications to IV tPA use for Blacks compared to Whites. This latter finding has been demonstrated in other studies.[5,21]

Previous investigations have shown that delay to hospital arrival for acute stroke is associated with female sex,[22,23] less severe stroke symptoms,[24] and older age.[25] However, we found no differences in delay to ED arrival for any of these variables after adjusting for Black race, as illustrated in Model 6 of Table 3. Our results suggest that Black race is the driving force for ED arrival >3 hours after LSN. Female sex, presenting stroke severity, age, socioeconomic status, and home medication use had no independent effect on delaying ED arrival times among patients seen at our center.

Among all patients in our population, sudden onset weakness and language difficulty (aphasia) resulted in earlier ED arrival. Compared to White patients, Blacks were more likely to have a delayed presentation to the ED regardless of the type of initial stroke symptom(s). However, among Blacks, a shorter LSN to ED arrival time was associated with gaze deficit or aphasia. Whether this reflects an underlying disparity in recognition of stroke symptoms cannot be determined.

In spite of finding a significant difference in delay to ED arrival among Blacks, we did not find an association between delay to ED arrival and poor functional outcome by discharge. While controlled trials demonstrate that the likelihood of a good outcome with IV tPA compared to patients randomized to placebo goes down over time,[26] we were unable to perform similar analyses, since all eligible patients were treated with IV tPA in our sample. Earlier presentation, however, is associated with an increased likelihood of treatment with IV tPA. Earlier presentation in

patients ineligible for IV tPA has not been demonstrated to improve outcome, though we would like to think that earlier management of stroke would confer a greater chance of recovery.

Limitations

We present the results of a single stroke team from one academic center, as in other studies.[27,28] Our study is retrospective in nature, and therefore we are unable to determine a causal relationship between ethnicities and outcome measures (eg, delay to ED arrival, treatment with IV tPA). In contrast to other studies,[5,9] our center admitted a higher percentage of patients within the IV tPA treatment window. This, in addition to our small sample size, resulted in a small number of patients with non-time related IV tPA exclusion criteria, possibly impairing our ability to adequately compare non-time related exclusion criteria between Blacks and Whites. Our small sample size might also have precluded us from observing any statistically significant differences in outcomes based on delay to ED arrival. Additionally, there may be other factors that influence ED delay, which were not assessed using our registry, such as the location where Black patients reside and its distance from our center as compared to Whites. Although we report a single center's experience, which may lack generalizability, the completeness of our data with regard to documentation of LSN (unless unknown), time of ED arrival, time decision regarding IV tPA was made, and documented exclusion criteria for IV tPA makes our study unique.

Future Directions

The problem persists as to why Black patients may not present to the ED as early in their stroke as White patients, a finding that may be related to the racial disparity in treatment frequency described throughout the literature.[5,7,27,29] One possible explanation is the cost of treatment, as this may discourage patients of lower socioeconomic standing from seeking treatment.[30,31] While insurance status does not equate to socioeconomic standing, our results do not suggest that socioeconomic standing influences delay to ED arrival after controlling for Black race. Another possible explanation for ED delay is the inadequacy of patient education with regard to stroke recognition.[32–34] One study demonstrated that there is an acceptable general knowledge of stroke symptom identification—particularly in underserved populations; however, the authors also found that a large percentage of people fail to act in a timely manner when a stroke actually occurs.[35] Other studies have shown that there is generally poor understanding of stroke symptoms, and a poor response to react appropriately at the onset of a cerebrovascular event by dialing 9-1-1.[33,34] Our results suggest there may be an inherent difference in baseline understanding or recognition of stroke symptoms (increased eagerness in seeking medical attention for symptoms of weakness or aphasia among all patients, and gaze deficit in Black patients alone), but these results cannot be confirmed here.

Even after taking into account the delay to ED arrival, studies have shown that other obstacles exist that can create a disparity in treatment rates between Black and White patients.[6,13,14] One such obstacle may be treatment decision bias among treating physicians. However, as a recent study suggested, if a majority of the patient population is Black, race may not influence the health care provider's treatment decision.[5] In our predominantly Black patient population, we found that the same proportion of Black and White patients who presented within the 3-hour window for thrombolytic treatment received IV tPA. There were no significant differences between Whites or Blacks among other contraindications to therapy once we accounted for delay from LSN to ED arrival. Based on our findings, we believe that the delay to ED arrival among Black patients seen at our center may help to explain previous reports of Blacks not being treated with IV tPA. Given previous evidence of undertreatment in Blacks, we would encourage centers to examine their practice for treatment disparities and to identify individual barriers for equality in their respective regions. Only after we have examined our clinical practice for racial disparities in treatment rates and explored the reasons for such disparities can we be assured that we are providing optimal care to all patients, regardless of race or ethnicity.

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AUTHOR CONTRIBUTIONS

Design and concept of study: Siegler, Martin-Schild
Acquisition of data: Siegler, Martin-Schild
Data analysis and interpretation: Siegler, Boehme, Albright, Martin-Schild
Manuscript draft: Siegler, Boehme, Albright, Martin-Schild
Statistical expertise: Boehme, Albright
Administrative: Siegler, Martin-Schild
Supervision: Siegler, Martin-Schild