Original Paper

Endovascular Therapy and Ethnic Disparities in Stroke Outcomes

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Keywords

Acute stroke · Cerebral ischemia · Thrombectomy · Ischemic stroke · Cerebrovascular procedures · Quality and outcomes

Abstract

Background and Purpose: Ethnic disparities in stroke are well described, with a higher incidence of disability and increased mortality in Blacks versus Whites. We sought to compare the clinical outcomes between those ethnic groups after stroke endovascular therapy (ET). **Methods:** We performed a retrospective review of the prospectively acquired Grady Endovascular Stroke Outcomes Registry between September 1, 2010 and September 30, 2015. Patients were dichotomized into two groups – Caucasians and African-Americans – and matched for age, pretreatment glucose level, and baseline National Institutes of Health Stroke Scale (NIHSS) score. Baseline characteristics as well as procedural and outcome parameters were compared. **Results:** Out of the 830 patients treated with ET, 308 pairs of patients ($n = 616$) underwent primary analysis. African-Americans were younger ($p < 0.01$), had a higher prevalence of hypertension ($p < 0.01$) and diabetes ($p = 0.04$), and had higher Alberta Stroke Program Early CT Score values ($p = 0.03$) and shorter times to treatment ($p = 0.01$). Blacks more frequently had Medicaid coverage and less private insurance (29.6 vs. 11.4% and 41.5 vs. 60.3%, respectively, $p < 0.01$). The remaining baseline characteristics, including baseline NIHSS score and CT perfusion-derived ischemic core volumes, were well balanced. There were no differences in the overall distribution of 90-day modified Rankin scale scores ($p = 0.28$), rates of successful reperfusion (84.7 vs. 85.7%, $p = 0.91$), good outcomes (49.1 vs. 44%, $p = 0.24$), or parenchymal hematomas (6.5 vs. 6.8%, $p = 1.00$). Blacks had lower 90-day mortality rates (18

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vs. 24.6%, $p = 0.04$) in univariate analysis, which persisted as a nonsignificant trend after adjustment for potential confounders (OR 0.52, 95% CI 0.26–1.03, $p = 0.06$). **Conclusions:** Despite unique baseline characteristics, African-Americans treated with ET for large vessel occlusion strokes have similar outcomes as Caucasians. Greater availability of ET may diminish the ethnic/racial disparities in stroke outcomes.

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Introduction

Disparities in stroke disability and mortality between different ethnic groups are well described, with stroke being twice as common and associated with higher mortality rates in Blacks compared to Whites [1, 2]. This also holds true when it comes to geographic location. Patients residing in the “stroke belt” of the USA have 40% more stroke-related deaths compared to those in the rest of the country [3]. Despite the overall decline in stroke-related deaths for adults suffering a stroke across racial groups, age-adjusted rates remain higher within the African-American community [4]. This might be due to several factors such as access to care, socioeconomic status, social habits, genetics, etc. [1, 5]. Over the past few years, stroke care has progressed tremendously, with proven efficacy of endovascular therapy (ET) and the widening of the scope of its indications. However, this promising therapy has been mostly validated in populations of Caucasian dominance [6–10]. The differences in stroke etiology and outcomes among ethnic groups as well as the fact that racial minorities are projected to constitute more than 40% of the US population by 2050 [5] hasten the need to further evaluate this therapy in other ethnic groups.

Here, we compare the functional outcomes and mortality between Blacks and Whites undergoing stroke ET at a large-volume tertiary care center in the “stroke belt.”

Methods

Patient Selection and Measures of Outcomes

We reviewed our prospectively collected Grady Endovascular Stroke Outcomes Registry between September 1, 2010 and September 30, 2015 to identify patients with large vessel occlusions who underwent intra-arterial therapy with documented ethnic information. Race-ethnicity information was based on self-identification [11]. Patients with incomplete information or identifying as Hispanic, Asian, mixed, or belonging to other ethnicities were excluded. Patients were then categorized into two groups: (1) Caucasian/White and (2) African-American/Black.

The two groups were matched for age, baseline National Institutes of Health Stroke Scale (NIHSS) score, and pretreatment glucose level [12]. Baseline characteristics and demographics as well as procedural parameters were collected. The primary outcome measure was the overall degree of disability as measured by the modified Rankin scale (mRS) at 90 days. The secondary endpoints included the rates of good outcomes (defined as 90-day mRS scores of 0–2) and successful reperfusion as defined by a modified Thrombolysis in Cerebral Infarction score of 2b–3. The safety endpoints included the rates of any parenchymal hematoma (PH) as per the European Cooperative Acute Stroke Study criteria [13] and 90-day mortality.

Imaging Protocol, CT Perfusion Parameters, and Final Infarct Volume Calculation

All patients underwent an institutional imaging protocol, including noncontrast CT with or without CT angiography and CT perfusion. The imaging acquisition parameters were the same for all patients included in the study. CT perfusion was evaluated with a fully automated software environment (RAPID version 4.5.0; iSchemaView, Menlo Park, CA, USA). The ischemic tissue volume (ischemic core) was defined by a voxel relative cerebral blood flow <30% of that of normal tissues. The total hypoperfused volume was defined by >6 s delay in the time to maximum tissue residue function and a penumbral volume of at-risk tissue defined by the difference between total hypoperfused and ischemic core tissue estimates [14].

Follow-up imaging included noncontrast CT or MRI documenting the final infarct volume within 5 days of treatment. Diffusion-weighted imaging was preferentially utilized if MRI was obtained within the first 72 h of the stroke, and fluid-attenuated inversion recovery was used if MRI was performed between 3 and 5 days. Edema producing sulcal effacement was not excluded. Hemorrhagic transformation was incorporated into the final infarct volume whenever present. Final infarct volumes were measured following export of raw DICOM data to the Fiji release of the ImageJ software platform using a standardized, semiautomated approach (<http://imagej.nih.gov/ij/>) [14].

Matching Methodology

A matching method based on weighted Euclidean distances was used to obtain a pair of subjects considered to be the nearest neighbors in a three-dimensional space of age, baseline NIHSS score, and pretreatment glucose levels, as previously described [12]. The distance between each White-Black pair was computed using the %FIND_NEIGHBORS Macro in SAS[®] University Edition (SAS Institute, Cary, NC, USA). Each Black patient was matched with the nearest White patient (having the smallest Euclidean distance).

After matching, the distribution of Euclidean distances was studied to identify outliers and a threshold was determined as follows: threshold = $Q75 + 1.5 \times (Q75 - Q25)$, where Q25 and Q75 are the 25th and 75th percentile, respectively. Pairs with distances greater than the threshold were considered extreme values at the tail of the distribution and eliminated from further consideration.

Statistical Analysis

The Shapiro-Wilk test was used to assess the normality of the variables. Continuous variables were reported as mean $\pm$ standard deviation if normally distributed or median [interquartile range] if nonparametric. Categorical variables were reported as proportions. Between groups, comparisons for continuous/ordinal variables were made with the Student *t* test, the Mann-Whitney U test, or ANOVA, as appropriate. Categorical variables were compared by the χ^2 test or the Fisher exact test, as appropriate [15]. The overall distribution of 90-day mRS scores was compared between groups (shift in disability levels) using the van Elteren test. Ordinal regression was computed for ORs to assess the association between ethnicity and mRS score. Multivariate logistic regression analyses for predictors of good outcomes, successful reperfusion, any PH, and mortality were performed for variables at the 0.1 level of significance on univariate analysis (stepwise backward LR method). Significance was set at $p < 0.05$ and all *p* values were two-sided.

Statistical analysis was performed using IBM[®] SPSS[®] Statistics 23 (IBM, Armonk, NY, USA) and SAS[®] University Edition. Graphical output was obtained from MATLAB[®] (MathWorks, Natick, MA, USA).

Results

Inclusion/Exclusion

Of the 830 patients treated over the study period, 49 were excluded because they were identified as belonging to other ethnicities (Hispanic [$n = 21$], Asian [$n = 17$], and others [$n = 11$]). Of the remaining 781 patients, 440 (56%) were categorized as Caucasian/White and 341 (44%) as African-America/Black.

The two groups of patients were matched for age, baseline glucose levels, and baseline NIHSS score. Patients with missing information regarding these three parameters ($n = 20$) were excluded and did not undergo the matching process. After matching, 332 pairs of White-Black patients were generated, of which 24 had an Euclidean distance higher than the preset threshold and 308 underwent primary analysis (Fig. 1).

Baseline Characteristics

African-Americans were younger (61.51 ± 13.98 vs. 64.68 ± 12.75 years, $p < 0.01$), had higher rates of hypertension (81.2 vs. 68.5%, $p < 0.01$) and diabetes (28.9 vs. 21.8%, $p = 0.04$), and had higher baseline Alberta Stroke Program Early CT Score values (8 [7–9] vs. 7 [6–8], $p = 0.03$) and shorter times from last known normal to groin puncture (300 [236–530] vs. 391

Fig. 1. Distribution of individual subjects after matching based on their baseline National Institutes of Health Stroke Scale (NIHSS) score, age, and glucose level.

[248–461] min, $p = 0.01$) compared to Whites. Blacks were less often transferred from an outside hospital (40.3 vs. 83.4%, $p < 0.01$) (Table 1).

Insurance coverage was different between both ethnic groups ($p < 0.01$), with Blacks having more Medicaid and less private coverage (29.6 vs. 11.4% and 41.5 vs. 60.3%, respectively, $p < 0.01$).

Efficacy and Safety Outcomes

Univariate Analysis. The mRS score distribution (OR 1.16, 95% CI 0.86–1.54, $p = 0.28$) and the rates of good outcomes (49.1 vs. 44%, $p = 0.15$) at 90 days were similar across the two groups. African-American patients had lower 90-day mortality rates (18 vs. 24.6%, $p = 0.04$) compared to Caucasians (Table 2; Fig. 2). There were no statistically significant differences in the rates of successful reperfusion (modified Thrombolysis in Cerebral Infarction score 2b–3, 84.7 vs. 87.7%, $p = 1.00$) or PH (6.5 vs. 6.8%, $p = 1.00$). The final infarct volumes were 42.06 [10.96–61.59] vs. 35.43 [23.13–72.47] cm³, $p = 0.05$. Sensitivity analysis looking at outcome differences according to sex showed that there were no differences in 90-day good outcomes or mortality in the male group between Blacks and Whites (53.3 vs. 44.8%, $p = 0.13$, and 21.3 vs. 26.4%, $p = 0.03$, respectively). In the female group, 90-day good outcomes were comparable (44.4 vs. 43.5%, $p = 0.89$), while African-American women had lower mortality rates (13.5 vs. 22.9%, $p = 0.049$).

Multivariate Analysis. After adjusting for confounders, there was a nonsignificant trend for lower 90-day mortality in Blacks compared to Whites (adjusted OR 0.52, 95% CI 0.26–1.03, $p = 0.06$). There was no significant association between ethnicity and 90-day good outcomes, successful reperfusion, or PH. The predictors of 90-day mortality, good outcome, successful reperfusion, and PH are summarized in Table 3.

Table 1. Baseline characteristics as well as imaging and procedural parameters

	Caucasians (n = 308)	African-Americans (n = 308)	p value
Age, years ¹	64.68±12.75	61.51±13.98	<0.01
Glucose, mg/dL ¹	117 [103–125]	123 [104–133]	0.12
Baseline NIHSS score ¹	18.04±5.42	18.59±6.34	0.62
Male sex	173 (56.2%)	163 (52.9%)	0.47
Hypertension	211 (68.5%)	250 (81.2%)	<0.01
Dyslipidemia	111 (36%)	125 (40.6%)	0.28
Atrial fibrillation	100 (29.9%)	100 (29.9%)	0.54
Diabetes	67 (21.8%)	89 (28.9%)	0.04
Smoking	69 (22.4%)	60 (19.5%)	0.43
Health insurance			<0.01
Uninsured	32 (10.4%)	32 (10.6%)	
Medicaid	35 (11.4%)	89 (29.6%)	
Medicare	53 (17.3%)	53 (17.6%)	
Private	185 (60.3%)	125 (41.5%)	
Veterans Affairs	2 (0.7%)	2 (0.7%)	
Transfers	257 (83.4%)	124 (40.3%)	<0.01
Low-density lipoprotein, mg/dL	91.23±39.09	93.18±41.20	0.93
International normalized ratio	1 [1–1.1]	1 [1–1.1]	0.56
Systolic blood pressure, mm Hg	138.88±28.18	154.18±39.57	0.74
Occlusion site			
Anterior cerebral artery	1 (0.3%)	4 (1.3%)	0.37
Middle cerebral artery M1	128 (41.6%)	137 (44.5%)	0.52
Middle cerebral artery M2	39 (12.7%)	51 (16.6%)	0.21
Middle cerebral artery M3	6 (1.9%)	5 (1.6%)	1.00
ICA terminus	41 (13.3%)	53 (17.2%)	0.22
Extracranial ICA	7 (2.3%)	8 (2.6%)	1.00
Vertebrobasilar	32 (10.4%)	27 (8.8%)	0.50
Tandem occlusion	54 (17.5%)	23 (7.5%)	<0.01
ASPECTS	7 [6–8]	8 [7–9]	0.03
CT perfusion	137 (44.5%)	119 (38.6%)	0.17
rCBF <30%, cm ³	31 [6.7–44.9]	26.9 [5.9–40.3]	0.26
T _{max} >6 s, cm ³	161.7 [118.2–214.4]	163.1 [113–265.6]	0.44
Intravenous tPA	137 (44.8%)	137 (44.8%)	1.00
Procedural parameters			
LKN puncture	391 [248–461]	300 [236–530]	0.01
Procedural length	70 [48–105.5]	73 [51–112]	0.23
Monitored anesthesia care	183 (59.6%)	175 (57.2%)	0.57
Stent retriever	207 (67.2%)	184 (59.7%)	0.07
Stroke etiology			0.34
Cardioembolism	145 (47.1%)	145 (47.1%)	
Large vessel atherosclerosis	54 (17.5%)	47 (15.3%)	
ICAD	23 (7.5%)	26 (8.4%)	
Undetermined	74 (24%)	86 (27.9%)	
Other	12 (3.9%)	4 (1.3%)	

Data are presented as mean ± standard deviation, median [interquartile range], or n (%). ASPECTS, Alberta Stroke Program Early CT Score; ICA, internal carotid artery; ICAD, intracranial atherosclerotic disease; INR, international normalized ratio; LDL, low-density lipoprotein; LKN, last known normal; NIHSS, National Institutes of Health Stroke Scale; rCBF, relative cerebral blood flow; T_{max}, time to maximum tissue residue function; tPA, tissue plasminogen activator. ¹The two groups were matched for these variables.

Table 2. Outcomes

	Caucasians (n = 308)	African-Americans (n = 308)	p value
Reperfusion			
mTICI 2b–3	264 (85.7%)	261 (84.7%)	0.91
mTICI 3	119 (38.6%)	115 (37.3%)	0.87
Any PH	21 (6.8%)	20 (6.5%)	1
Final infarct volume, cm ³	35.43 [23.13–72.47]	42.06 [10.96–61.59]	0.05
90-day mRS score	(n = 293)	(n = 283)	
0	16 (5.5%)	22 (7.8%)	
1	62 (21.2%)	48 (17%)	
2	51 (17.4%)	69 (24.4%)	
3	44 (15%)	31 (11%)	
4	28 (9.6%)	39 (13.8%)	
5	20 (6.8%)	23 (8.1%)	
6	72 (24.6%)	251 (18%)	
0–2	129 (44%)	139 (49.1%)	0.24
Mortality	72 (24.6%)	251 (18%)	0.04

Data are presented as *n* (%) or median [interquartile range]. mRS, modified Rankin scale; mTICI, modified Thrombolysis in Cerebral Infarction; PH, parenchymal hematoma.

Fig. 2. Functional outcome at 90 days according to the score on the modified Rankin scale (mRS).

Discussion

Our data from a large biracial population suggest that there are no clinical or procedural outcomes disparities between Whites and Blacks undergoing ET for large vessel occlusion acute stroke. Specifically, we demonstrated a similar distribution of 90-day mRS scores with comparable rates of successful reperfusion, good outcomes, and PH. Notably, we did not observe any mortality increase in Blacks versus Whites as previously reported in other large cohort studies. This suggest that aggressive stroke intervention might attenuate some of the mortality disparities in stroke. Our results remained stable after adjustment for potential confounders in multivariate analysis.

Blacks are historically known to have a higher stroke incidence and mortality compared to Whites [1, 2, 4]. This might be explained by several factors, including the higher prevalence

Table 3. Predictors of 90-day mortality, good outcome (mRS score 0–2), successful reperfusion (mTICI 2b–3), and PH

	OR	95% CI	p value
90-day mortality			
Age	1.05	1.02–1.08	0.02
Glucose	1.01	1.00–1.02	0.006
Baseline NIHSS score	1.20	1.11–1.29	<0.001
Ethnicity (Black)	0.52	0.26–1.03	0.06
International normalized ratio	2.53	1.06–6.05	0.03
ASPECTS	0.78	0.63–0.97	0.02
Monitored anesthesia care	0.33	0.16–0.68	0.002
mTICI 2b–3	0.22	0.10–0.48	<0.001
Any PH	5.51	1.84–16.46	0.002
90-day mRS score 0–2			
Age	0.96	0.94–0.98	<0.001
Glucose	0.99	0.98–0.99	0.03
Baseline NIHSS score	0.90	0.86–0.95	<0.001
International normalized ratio	0.51	0.24–1.11	0.09
ASPECTS	1.59	1.32–1.90	<0.001
Procedure length	0.99	0.98–0.99	0.01
Monitored anesthesia care	2.31	1.36–3.92	0.002
mTICI 2b–3	4.22	1.88–9.49	<0.001
Any PH	0.20	0.05–0.80	0.02
mTICI 2b–3			
Smoking	1.99	1.01–3.92	0.045
Monitored anesthesia care	1.72	1.06–2.78	0.03
Stent retriever	2.05	1.26–3.32	0.004
Any PH			
Baseline NIHSS score	1.11	1.03–1.19	0.006

ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; PH, parenchymal hematoma.

of vascular risk factors such as hypertension, diabetes, smoking, or excessive alcohol use among this patient population [1]. In the Northern Manhattan Stroke Study, hypertension and diabetes were more prevalent among the Black and Hispanic groups, while atrial fibrillation was more common in Whites [11]. Our analysis confirms historic data, with Blacks having strokes at a younger age as well as a higher prevalence of hypertension and diabetes. Interestingly, stroke etiologies were comparable between groups, in contrast to previous studies showing that Whites had more cardioembolic strokes while Blacks tended to have more lacunar or small vessel infarcts [16]. This finding is likely related to a selection bias since this is primarily an ET cohort, but it could also have been introduced during the matching process.

Another factor that could explain historic disparities in stroke outcomes between ethnic groups is that minorities have less access to medical care [1, 5]. In fact, Kumar et al. [5] demonstrated that Blacks were less likely to be treated with thrombolysis (adjusted OR 0.84, 95% CI 0.76–0.92, $p < 0.001$) and intra-arterial therapy (OR 0.73, 95% CI 0.58–0.91, $p = 0.01$). The authors hypothesized that this could be due to delays in symptoms recognition and presentation outside the treatment window, a higher prevalence of contraindications in African-Americans, or a systematic bias in healthcare delivery. Similarly, a recent analysis of the Get With The Guidelines-Stroke data revealed that emergency medical services transport differed by race/ethnicity, with minorities less likely to use them [17]. Moreover, Kissela et al. [1] found that Blacks were more likely to have Medicaid coverage compared to Whites, which

may have contributed to the inequalities in access to treatment. This held true in our analysis, with African-Americans having twice as high Medicaid coverage and less private insurance compared to Caucasians. However, a recent analysis of 279 patients from the Reasons for Geographic and Racial Differences in Stroke cohort showed that underutilization of healthcare after stroke did not explain the poorer long-term outcomes in African-Americans [18], and thus the answer regarding the precise causes of these differences remains elusive.

Clinical trials performed in 2015 have proved the superiority of ET over intravenous recombinant tissue plasminogen activator in the treatment of large vessel occlusion acute ischemic stroke [6–10], with growing potential and expanding indications including mild strokes [19], large core infarcts [20], distal occlusions (including middle cerebral artery M2 [21] and beyond [22]), as well as patients presenting late in the therapeutic window with the recent positive results of the DAWN trial [23]. However, the current evidence for ET has predominantly been obtained from populations of Caucasian dominance. In fact, African-Americans represented only 11.2% of the interventional arm in SWIFT PRIME [6] and presumably an even lower proportion of the recruited patients in the other trials. The differences in stroke etiology and outcomes among ethnic groups and the fact that racial minorities are projected to constitute more than 40% of the US population by 2050 [5] hasten the need to better understand these discrepancies and further evaluate ET in other populations.

Our matched cohort shows that African-Americans equally benefit from ET, with almost half of the patients achieving good outcomes at 90 days and a trend towards lower mortality rates. Blacks had shorter times to treatment, which is explained by the fact that they were more likely to present directly to the emergency department (compared to Whites, who were more commonly transferred) due to the location of our facility within the city and the population demographic it primarily serves. Another intriguing finding is that African-Americans tended to have larger final infarct volumes despite having a younger age, similar infarct burden on presentation, and similar reperfusion rates, which may be explained by worse collateral recruitment and differences in stroke risk factors/pathogenesis [24]. Also, as mentioned above, other factors such as underutilization of poststroke rehabilitation services [25] and secondary stroke prevention medications given insurance status could explain our outcomes.

Our study has several limitations mostly inherent to its retrospective design. As ET was considered our standard of care for the entire duration of the study, we did not have a medically treated control population that would have allowed us to measure treatment effects per ethnic group. Moreover, we did not automatically record those who did not qualify for ET to be able to measure treatment frequency. Additionally, our results might have been different had we used a different study design or matching variables. Our analysis was also limited to a biracial cohort and by having insurance coverage as the sole measure of socioeconomic status.

Conclusions

Despite unique baseline characteristics, African-Americans treated with ET for large vessel occlusion strokes have similar outcomes as Caucasians. Greater availability of ET may diminish the ethnic/racial disparities in stroke outcomes.

Statement of Ethics

This study was approved by the Emory University institutional review board.

Disclosure Statement

M. Bouslama, L.C. Rebello, D.C. Haussen, J.A. Grossberg, A.M. Anderson, S.R. Belagaje, N.A. Bianchi, and M.R. Frankel have no disclosures. R.G. Nogueira: Stryker Neurovascular (TREVO 2 trial principal investigator, DAWN trial principal investigator), Covidien (SWIFT and SWIFT PRIME Steering Committee, STAR Trial Core Lab), and Penumbra (3-D Separator Trial Executive Committee).

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