## Racial Difference in Cerebral Microbleed Burden among Ischemic Stroke Patients

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> Background and Aims: Data on the epidemiology of cerebral microbleeds (CMBs) among patients with ischemic stroke are limited. This study compared the number, associated factors, and topography of CMBs between African American and Caucasian ischemic stroke patients in the Mid-South United States. Method: We evaluated consecutive ischemic stroke patients admitted to our tertiary stroke center, University of Tennessee Health Science Center, Memphis, Tennessee, in a two-year period. We analyzed T2\*-weighted magnetic resonance images for the number, location, and topography of CMBs, as well as patients' demographic and clinical information. Results: Among 760 ischemic stroke patients who were included (mean age was  $62.1 \pm 13.9$  years, 51.4% men), 450 (59.2%) were African American. In comparison with Caucasians, African Americans were about five years younger (P = .000) and had a higher rate of hypertension (80.9% vs. 74.5%, P = .036). Similarly, African Americans had a higher prevalence of diabetes mellitus (P = .001). There was no significant difference between African-Americans and Caucasians in terms of CMBs presence and location. African Americans had a higher number of CMBs in comparison with Caucasians, but the difference was not significant. African Americans were more likely to have CMBs  $\geq$ 5 (*P* = .047). Although African American stroke patients had a higher rate of large confluent white matter lesions, there was no significant racial difference regarding the rate and severity of deep white matter lesions. Conclusion: We did not observe any differences between African American and Caucasian patients with ischemic stroke patients regarding the presence, number, and location of CMBs. However, our results suggested that the prevalence of multiple CMBs (CMBs  $\geq$ 5) might be higher among African American stroke patients. Key Words: Cerebral microbleeds-ischemic stroke-epidemiology-ethnicity-cerebral small vessel disease.

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#### Introduction

Cerebral microbleeds (CMBs), also known as microhemorrhages, are punctuated hypointense, round to ovoid lesions of <10 mm in diameter in T2\* Gradient-Recall Echo (GRE) and Susceptibility-Weighted (SWI) Magnetic Resonance Imaging sequences.<sup>1,2</sup> Histopathological studies have shown remnants of previous bleeding in the form of hemosiderin-laden macrophages, ferritin, or deoxyhemoglobin,<sup>3-6</sup> as well as intact erythrocytes,<sup>6</sup> at the site of CMBs. Accordingly, CMBs are assumed to be an indicator of cerebral microangiopathy with an advanced risk of vascular vulnerability, ischemia, and hemorrhage.<sup>7-10</sup>

Although CMBs can be detected in neuroimaging of healthy individuals, they are more frequent among patients with cerebrovascular diseases.4,5,11,12 Various cerebrovascular pathologies are associated with CMBs. Hypertensive arteriopathy and cerebral amyloid angiopathy are the most common histopathological patterns resulting in CMBs.8 Cumulative analysis of populationbased studies with a total of 8267 healthy participants reported a prevalence of 4.5% CMBs (3.9% multiple CMBs).5 Whereas, the prevalence of CMBs in stroke patients is reported to be 17% to 71% depending on the type of stroke and study population.<sup>4,13-16</sup> The presence of CMBs is also associated with an increased risk of future stroke in healthy subjects<sup>17</sup> or patients with transient ischemic attacks.18,19 Similarly, the prevalence of CMBs in patients with recurrent stroke is higher than other stroke patients.<sup>18,20</sup>

Studies suggest that racial differences exist in the frequency and topography of CMBs among stroke patients.<sup>21,22</sup> It has been shown that among patients who experienced a primary ICH, prevalence and number of CMBs were higher in the black than in the white population.<sup>21</sup> In addition, black patients had a higher distribution of CMBs in subcortical, deep, and infratentorial structures.<sup>21</sup> There are also racial differences in the prevalence of CMBs and both deep and periventricular white matter lesions among patients with a lacunar infarct.<sup>22</sup> Likewise, the risk of moderate to severe white matter lesions is much greater in blacks versus white patients with primary ICH.<sup>21</sup>

The purpose of this study was to compare the prevalence, number, topography, associated factors, and topography of CMBs between African American and Caucasian ischemic stroke patients in a tertiary stroke center in the Mid-South United States. We also compared the amount of deep white matter lesions (DWML) between African American and Caucasian patients.

### Methods

We evaluated consecutive ischemic stroke patients who were admitted to our tertiary stroke center, University of Tennessee Health Science Center, Memphis, Tennessee,

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in a 2-year period (2013-2014). MRIs are routinely considered for all patients in our center. We excluded patients who could not have a brain MRI or patients without an interpretable brain MRI. We excluded patients who received intravenous tissue plasminogen activator (IVtPA). We also excluded Hispanic and patients with other ethnicities.

Baseline characteristics of patients included age, gender, race, history of hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, epilepsy or prior stroke, smoking habits and clinical laboratory findings were recorded. National Institutes of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS) at discharge were obtained per institutional protocol. This study was part of the University of Tennessee Stroke Registry, which had received Institutional Review Board (IRB) approval.

#### Imaging Evaluation

All MRI studies included axial diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC), T2 fluid-attenuated inversion recovery (FLAIR), T2\*weighted gradient-echo (GRE), and T1-weighted sequences. The majority of patients in our cohort had 3-T MRI (71%). We used DWI, ADC, and FLAIR sequences to evaluate the location of ischemic lesions. Number and location of CMBs were examined by T2\*-weighted GRE sequences. We analyzed the location of CMBs according to two distinct categories: "strictly lobar microbleeds" (patients who had ≥1 CMBs restricted to a lobar location) and "deep or infratentorial microbleeds" (patients with ≥1 CMBs in a deep or infratentorial location with or without lobar microbleeds).23 CMBs were defined per recent consensus recommendations for MRI studies as up to 10 mm in diameter, round, or oval shaped, hypointense lesions with associated blooming on T2\*weighted MRI. Hypointense lesions within the subarachnoid space were regarded as pial blood vessels. Hypointense lesions in the areas of symmetric hypointensity of the globus pallidus were considered as calcifications. The Fazekas scale<sup>24</sup> was used to quantify the amount of deep white matter lesions (DWML)-T2 hyperintense lesions usually attributed to chronic small vessel ischemia.

#### Statistical Analysis

The baseline data was presented as mean ± standard deviation, median (interquartile range), or number (percent). The distribution and normality of each parameter were studied through the Kolmogorov-Smirnov test. The difference between each subgroup was studied by the Chi-square, Fisher exact test, unpaired t-Test, Mann Whitney U-test, or analysis of variance (ANOVA). To reduce the effect of confounders and study the main effect of each

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