Racial Difference in Cerebral Microbleed Burden Among a Patient Population in the Mid-South United States

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Background: Although intracerebral hemorrhage (ICH) is more common among African-Americans, data on the burden of cerebral microbleeds (CMBs) among different races is limited. The purpose of this study is to compare the number, associated factors, and topography of CMBs between African-American and Caucasian populations in the Mid-South United States. *Methods:* Using natural language processing, we extracted all brain MRIs performed during a 2-year period (2012-2013) when the report indicated the presence of CMB. All the extracted MRI studies were evaluated for number and location of CMBs, prior stroke, and deep white matter lesion. Negative binomial regression was used to model for the overdispersed count data. *Results:* A total 167 patients (mean age was 63 ± 15 years, 49% men, 77% African-American, median CMB count: 8) with 1 or more CMBs on their brain MRI were included in this study. There was no significant difference between the 2 groups in terms of CMB locations (P = .086), but there was a significant difference between African-American and Caucasian patients in terms of number of CMBs (16.5 ± 18 versus 6.5 ± 5.5, P < .001). The prevalence of multiple CMBs (CMBs ≥ 5) was similar among African-Americans and Caucasians (72% versus 55%, P = .062). After adjusting for potential confounders, the African-American race was not independently associated with a higher CMB burden (P = .073). *Conclusion:* African-American race was not independently associated with a higher rate of CMB burden when compared to Caucasians after adjusting for potential confounders. We also did not observe a significant racial difference regarding the location and prevalence of multiple CMBs (CMBs ≥ 5).

Key Words: African-American—Caucasian—Epidemiology—Ethnicity—Race—Cerebral small vessel disease—White matter lesion

Introduction

Cerebral microbleeds (CMBs) are small foci of perivascular hemosiderin deposits that can remain in macrophages for years in near normal brain tissue.[1] CMBs are characterized as small, round, hypointense foci, usually 2 mm-5 mm and occasionally up to 10 mm in diameter and are detectable on T2*- gradient recalled echo (T2*-GRE) or susceptibility weighted imaging.[2] CMBs can be seen in approximately 5% of the healthy population with significantly higher prevalence among the elderly population.[3] The prevalence of CMBs can increase up to 70% among patients with cerebrovascular disease.[1,3] The incidence rate of CMBs increases by age and can be as high as 36% among individuals older than 80 years old.[4,5]

Only a few studies have compared the prevalence of CMBs by race or ethnicity. Koch et al[6] reported that

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among 194 patients, the proportion of CMBs related to lacunar infarction was highest in Caribbean blacks (40%), similar in African-Americans and Caribbean Hispanics (25% and 22%), and lowest in non-Hispanic whites (7%). In another study on 87 patients with primary intracerebral hemorrhage, the frequency rate of 1 or more CMBs was 74% among blacks compared with 42% in whites. Likewise, the risk of moderate to severe white matter lesions was much higher among black (69%) versus white (29%) patients with primary diagnosis of intracerebral hemorrhage.[7]

The purpose of this study was to compare the prevalence, burden, and associated factors of CMBs between African-American and Caucasian patients in a tertiary health system in the Mid-South United States.

Methods

Patient Selection

Using natural language processing, we extracted all brain MRIs performed during a 2-year period (2012-2013) when the report indicated the presence of CMB. Our search method included all the possible terms "microbleed(s)," "microh(a)emorrhage(s)," or "petechial h(a)emorrhage(s)" indicating the existence of CMB. The MRIs were obtained for different clinical reasons in either an inpatient or outpatient setting. They were interpreted by the neuroradiology group at the University of Tennessee Health Science Center (UTHSC), Memphis, Tennessee. The neuroradiology team had a uniform approach to reading and dictating the reports. We manually evaluated all the brain MRIs when the report indicated the presence of CMB. All the MRIs were read by our trained junior investigator (N.N.S) and verified by the senior investigator (R.Z). We included adult African-Americans and Caucasians patients with an interpretable T2*- gradient recalled echo (T2*-GRE) and fluid-attenuated inversion recovery (FLAIR). Patients younger than 18-year-old were excluded from the study. The data collection was conducted as part of UTHSC stroke registry previously approved by UTHSC institutional review board.

CMBs were diagnosed and reported as appear in T2*-GRE. Baseline characteristics of patients, including age, race, gender, medical history of hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease, kidney and liver disease, cigarette smoking, body mass index (BMI), the international normalized ratio, and other clinical presentation were obtained.

Imaging Evaluation

All MRI studies included axial diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC), T2 fluid-attenuated inversion recovery (FLAIR), and T2*-weighted gradient echo (GRE) sequences. DWI, ADC, and FLAIR sequences were evaluated for location of the ischemic lesion if any. T2* weighted GRE sequences were evaluated for number and location of CMBs. Patients without FLAIR/T2* weighted imaging or T2* weighted GRE were excluded from the study. All the images were obtained by one of our 2 MRI units (1.5 T and 3 T). To analyze the location of CMBs, we made 2 distinct categories for "strictly lobar microbleeds" (patients who had $\geq$1 CMBs restricted to a lobar location), "deep or infratentorial microbleeds" (patients with $\geq$1 CMBs in a deep or infratentorial location with or without lobar microbleeds).[8] CMBs were defined according to the recent consensus recommendations for MRI studies as round or oval, hypointense lesions with associated blooming on T2*-weighted MRI up to 10 mm in diameter. 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 regarded as calcifications. The Fazekas scale[9] was used to quantify the amount of deep white matter lesions. We did not have any patients with the history of traumatic diffuse axonal injury. We did not count CMBs in stroke bed.

Statistical Analysis

Continuous variables are presented as mean $\pm$ SD (normal distribution) and as median $\pm$ SD (skewed distribution). Statistical comparisons were performed among different groups using the χ^2-test, Fisher's exact test, unpaired *t* test and Mann-Whitney U test as indicated for dichotomous or continuous variables. Negative binomial regression was used to model for the overdispersed count data. Best subset of predictor variables was selected to enter into the model using Akaike information criterion. The algorithm of the response variable was linked to a linear function of nine explanatory variables (both continuous and categorical). We tested for goodness-of-fit of the model with a chi-square test based on the residual deviance and degrees of freedom. The goodness-of-fit test indicates that the negative binomial model fits the data.

Results

A total 167 patients (mean age was 63 $\pm$ 15 years, 49% men, 77% African-American, median CMB count: 8) with 1 or more CMBs on their brain MRI were included in this study. In our cohort, 69% of patients had multiple CMBs (CMBs $\geq$ 5), 57% had severe white matter lesions (large confluent lesions), and 88% had history or imaging evidence of prior stroke. Twenty-one percent of patients in our cohort had 1.5-T MRI. The proportion of patients who underwent 3-T MRI did not differ between African-Americans and Caucasians.

Table 1 includes baseline characteristics of African-American and Caucasian patients. In comparison with Caucasians, African-Americans had a higher rate of hypertension (69% versus 97.8%, $P < .001$). Similarly, African-Americans had a higher prevalence of diabetes