High Prevalence of Cerebral Microbleeds in Inner City Young Stroke Patients

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Background: Data on cerebral microbleeds (CMBs) in younger populations are lacking, particularly in young stroke patients. We sought to characterize CMBs in an inner city cohort of young adults with stroke. *Methods:* CMB presence, count, and topography were assessed on magnetic resonance imaging (MRI) scans of 104 young stroke patients (≤49 years) presenting to Boston Medical Center between January 2006 and February 2010. Subsequent MRIs were assessed for the occurrence of new microbleeds in 29 patients. We performed cross-sectional analysis comparing baseline characteristics between patients with and without microbleeds, and between predefined microbleed burden and topography categories. We performed additional analysis to assess the determinants of new microbleeds on repeat MRI. *Results:* Microbleeds were present in 17% of the sample. Male sex (odds ratio [OR] 5.7, 95% confidence interval [CI] 1.0-32.6, $P = .049$), hypertension (OR 6.2, 95% CI 1.2-32, $P = .03$), moderate–severe white matter hyperintensities on MRI (OR 5.8, 95% CI 1.6-29.0, $P = .01$), and intracerebral hemorrhage (ICH; OR 5.0, 95% CI 1.2-20, $P = .03$) were over-represented in patients with microbleeds. Patients who developed new microbleeds on repeat MRI (14%) had higher microbleed counts on baseline MRI (50% versus 0% ≥ 3 CMBs, $P = .02$), history of illicit drug use (75% versus 24%, $P = .08$), positive serum toxicology for cocaine (67% versus 13%, $P = .11$), ICH as their presenting stroke subtype (50% versus 8%, $P = .08$), and over-representation of moderate–severe white matter hyperintensities (75% versus 20%, $P = .05$). *Conclusions:* Results from this inner city cohort suggest that microbleeds are prevalent in young stroke patients and are largely associated with modifiable risk factors. **Key Words:** Young—stroke—cerebral microbleeds—small-vessel disease.

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Introduction

Cerebral microbleeds (CMBs) are neuroimaging markers of cerebral small-vessel disease (CSVD), most notably in the form of hypertensive arteriopathy and cerebral amyloid angiopathy (CAA),[1] and are evolving as a promising prognostic marker for future stroke,[2] mortality,[3,4] and hemorrhagic complications from antithrombotic[5,6] and thrombolytic therapies.[7,8] However, data on CMBs in younger populations are currently lacking, particularly in young stroke patients. Better characterization of CMBs within this population is important to better delineate the burden and natural history of CMB-related disease and to isolate potential modifiable risk factors that may be unique to this younger age group.

Inner city populations within the United States may be particularly at risk due to poor compliance with prescribed therapies and over-representation of ethnic minorities who are prone to hypertensive disease. Accordingly, we sought to characterize CMBs in a young cohort that we hypothesized to be particularly at risk for early CSVD.

Methods

Study Design

The present study is both a retrospective cross-sectional analysis of consecutive cases of stroke in young patients (15-49 years of age) captured in the Boston Medical Center (BMC) Young Stroke Database and a longitudinal analysis of a subset of patients who underwent repeat magnetic resonance imaging (MRI) at BMC during their clinical follow-up. Approval for the study was obtained from the BMC Institutional Review Board.

Study Population and Data Collection

Consecutive patients aged 15-49 years admitted to BMC with stroke (ischemic or hemorrhagic) between January 2006 and February 2010 were reviewed (n = 145). Excluded were patients with secondary causes of intracerebral hemorrhage (ICH, n = 6), patient readmissions (n = 8), and cases without MRI or interpretable T2*-weighted gradient echo MRI sequence (n = 27). Hospital admission records were reviewed for demographic information, vascular risk factors, and admission weight and blood pressure measurements, as well as serology measurements of interest (serum creatinine, HBA1c, and cocaine toxicology). Hypertension was defined as either history of hypertension, antihypertensive medication use at presentation, or antihypertensive medication use at discharge. Diabetes mellitus was defined according to history, treatment with glucose lowering agents, or HBA1c greater than 6.5% on admission. Dyslipidemia, coronary artery disease, smoking, and illicit drug use were determined according to the patient's self-reported history and/or medical documentation. Ischemic stroke subtype was determined as per Trial of Org 10172 in Acute Stroke Treatment criteria and confirmed on MRI.[9]

Imaging and Measurements

Structural MRI was performed at 1.5-T field strength using Philips Achieva system (Philips Healthcare, Eindhoven, Netherlands). All participants had axial T2-weighted, axial T2*-weighted gradient echo (GRE) (5-mm slice thickness, repetition time/echo time: 1200/23 milliseconds) and axial FLAIR scans. T2*-weighted GRE images were systematically assessed for the presence, number, and topography of CMBs by 1 rater (A.S.) as per published criteria.[10] Patients with at least 1 CMB were categorized as having either 1-2 CMBs or 3 or more CMBs. This threshold was prespecified to optimize statistical power according to the distribution of the CMB number in our sample. CMB topography was categorized as strictly lobar, strictly deep, or mixed. White matter hyperintensities (WMHs) were rated as per the Age-Related White Matter Changes (ARWMC) scale[11] by a separate rater (L.C.). Moderate–severe WMH was defined as a cumulative score of 5 or higher on the ARWMC scale.[12] In a sample of 20 MRIs, intrarater agreement was 95% (Cohen $\kappa = .90$) for CMB presence, 95% (Cohen $\kappa = .91$) for CMB burden category, 85% (Cohen $\kappa = .75$) for CMB topography, and 90% (Cohen $\kappa = .73$) for presence of moderate–severe WMH.

Hospital records were reviewed for subsequent clinical MRIs that had been ordered as per the discretion of the treating physician following discharge from hospital for the purpose of documenting new CMBs. New CMBs were rated using a side-by-side comparison of the baseline MRI and follow-up MRI. In cases with multiple follow-up MRIs, the most recent one was utilized. All MRI analyses were performed without knowledge of patient baseline and clinical characteristics.

Statistical Analysis

Primary analysis compared patient characteristics between patients with CMBs and those without. Categorical variables were analyzed by Pearson's χ^2 or Fisher's exact test, and continuous variables by the 2-sample *t*-test (for normal distributions, presented as mean and standard deviation) or the Mann–Whitney *U*-test (for non-normal distributions, presented as median and interquartile range). In an attempt to avoid overfitting the regression model, variables associated with CMB presence ($P \leq .10$) were individually inserted into bivariate regression analyses predetermined to control for hypertension. All variables that were associated with the presence of CMBs independent of hypertension ($P < .05$) were then inserted into a backward regression analysis. A similar analysis was performed to characterize the determinants of new CMBs in a subset with subsequent MRI. This subset, however, was too small to allow for meaningful multivariable regression analysis.