Risk Factors of Cerebral Microbleeds in Strictly Deep or Lobar Brain Regions Differed

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Background: T2*-weighted gradient echo magnetic resonance imaging is sensitive in detecting cerebral microbleeds (MBs), but there are few reports on the risk factors of MBs in different brain regions. Therefore, we aimed to investigate whether the risk factors associated with the presence of MBs in strictly deep or lobar brain regions were different. *Methods:* This study consisted of 696 consecutive acute ischemic stroke patients from 6 hospitals in the Chinese IntraCranial AtheroSclerosis Study. We evaluated the number and location of MBs, severity of lacune and leukoaraiosis (LA), and etiologic subtype of ischemic stroke. Multivariable logistic regression was used to analyze risk factors of MBs in different brain regions. *Results:* Among 696 acute ischemic stroke patients, 162 patients (23.3%) had MBs. Of them, 62 patients had strictly deep brain MBs, 49 patients had strictly lobar MBs. There was a significant correlation between the number of MBs, the number of lacune, and the severity of LA ($P < .0001$). In multivariable logistic regression analysis, both strictly deep and strictly lobar brain, MBs were significantly associated with history of cerebral hemorrhage ($P = .037$ and $P = .026$, respectively), presence of lacune ($P = .004$ and $P = .032$, respectively), and severe LA ($P = .002$ and $P = .008$, respectively). However, MBs in strictly deep regions were significantly associated with higher mean arterial pressure ($P = .030$), and those in strictly lobar brain regions were significantly associated with older age ($P = .023$). *Conclusions:* The risk factors of MBs in strictly deep or lobar regions differ modestly, which may be related to heterogeneous vascular pathologic changes. **Key Words:** Microbleeds—risk factors—cerebral small vessel diseases—magnetic resonance imaging.

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Introduction

Cerebral microbleeds (MBs) are visualized as small round or oval lesions of signal void with associated blooming seen on T2*-weighted gradient echo (GRE) magnetic resonance imaging (MRI).[1] Histopathologic studies have confirmed that these hypointense lesions correspond histopathologically to deposits of hemosiderin that remains in macrophages after previous bleeding,[2,3] and that MBs often coexists with arteriolosclerosis or amyloid angiopathy indicating an underlying small vessel pathology.[3,4] Some studies have found a high prevalence of MBs in patients with indicators of small vessel disease such as lacune and severe leukoaraiosis (LA), suggesting that an association exists between MBs and small vessel disease[5,6] Furthermore, the pathologic findings of MBs depend on the regions of the brain.[3] Lobar MBs are considered to be caused by cerebral amyloid angiopathy (CAA), whereas MBs in deep brain regions may be resulted from hypertension and arteriolosclerosis.[5] However, few studies have investigated the risk factors of MBs in different brain regions. The aim of our study was to explore whether the risk factors associated with the presence of MBs in lobar or deep brain regions were different.

Methods

Study Population

The study population arose from the Chinese Intra-Cranial AtheroSclerosis Study, and consisted of 696 consecutive inpatients in 6 hospitals with a final diagnosis of ischemic stroke from October 2007 to June 2009. Ischemic stroke was classified using the Stop Stroke Study Trial of Org 10172 in Acute Stroke Treatment classification criteria. The inclusion criteria included onset of symptoms within 7 days, and age between 18 and 80 years. Exclusion criteria included patients who were clinically unstable (ie, they required close monitoring or were moribund), were disabled before admission (modified Rankin scale >2), and/or unable to comply with MRI examination. We also excluded patients with cardioembolic risk factors (eg, atrial fibrillation, valvular heart disease, postcardiac valve replacement, and so forth) to rule out stroke due to cardioembolism. Patients who suffered ischemic stroke because of undetermined causes or other causes were also excluded. This study was approved by the Ethics Committee of Beijing Tian Tan Hospital and 5 other participating hospitals. All patients or their legal representatives provided written informed consent.

We evaluated clinical and radiological data including age, sex, vascular risk factors, MBs, lacune, LA, and etiologic subtype of ischemic stroke and analyzed the relationship between these factors and the presence of MBs in different brain regions.

MRI Analysis

All 696 ischemic stroke patients underwent cranial MRI on a 3.0-T magnetic resonance scanner. The imaging protocols consisted of T1-weighted imaging (repetition time [TR]/echo time [TE], 1200/11 ms), T2-weighted imaging (TR/TE, 4500/84 ms), T2*-weighted GRE imaging (TR/TE, 613/20 ms), fluid attenuated inversion recovery (FLAIR; TR/TE, 7000/94 ms; inversion time, 2500 ms), diffusion-weighted imaging (TR/TE, 3000/75 ms), and 3-dimensional time-of-flight magnetic resonance angiography (TR/TE, 20-25/3.3-3.9 ms; flip angle = 15°-20°; slice thickness = .65-1.0 mm). All above sequences except magnetic resonance angiography had 5-mm slice thickness and 1.5-mm interslice gap.

MBs were defined as small (generally 2-5 mm in diameter, but up to 10 mm), homogeneous, round or oval lesions of low signal with associated blooming seen on T2*-weighted GRE MRI according to the Standards for Reporting Vascular changes on Neuroimaging consensus.[7] This definition of MBs excludes symmetric lesions in the globus pallidus and lesions in the subarachnoid space, which are likely to represent calcification and adjacent pial blood vessels, respectively. The number of MBs were evaluated and recorded. The locations of MBs were categorized into lobar (cortical gray or subcortical white matter; cerebellum) and deep (deep gray matter of basal ganglia, thalamus; the white matter of the corpus callosum, internal, external, and extreme capsule; brainstem) region, in accordance with the Microbleed Anatomical Rating Scale[8] (Fig 1).

Lacune were defined as round or ovoid, subcortical, fluid-filled cavity (signal similar to cerebrospinal fluid on all sequences) of between 3 mm and 15 mm in diameter according to the Standards for Reporting Vascular changes on Neuroimaging consensus.[7] Lacune were differentiated from dilated Virchow-Robin Spaces by their typical wedge shape and surrounding hyperintensity on FLAIR.[9] The number of lacune in all sections of the brain was classified into 3 grades in accordance with Lee et al[10]: grade 0 (no lacune present); grade 1 (total number of lacune, 1-3); and grade 2 (total number of lacune ≥4).

LA was defined as hyperintense lesion on FLAIR and T2-weighted imaging, which was usually not seen on T1-weighted imaging or showed faint hypointensity.[7] We rated LA using the scoring system presented by Fazekas et al.[11] Diffusion-weighted imaging was used to differentiate acute ischemic stroke lesions from LA.[12] Scores in periventricular white matter hyperintensities and deep white matter hyperintensities were evaluated separately and summed together as Fazekas score. Severity of LA was classified based on Fazekas score (Fazekas score <3 and Fazekas score ≥3).

Two radiologists without knowledge of the patients' clinical profiles independently evaluated MRI data.