Dilated Virchow–Robin Spaces in First-Ever Lacunar Stroke Patients: Topography and Clinical Correlations

Hongyan Yang, MD,* Rui Shen, MD,† Zhi Jin, MD,* Junwen Li, MD,* Ying Wu, MD,* Yu Xu, MD,‡ Ting Hua, MD,‡ Xueyuan Liu, MD,* and Jing Huang, MD*

Background and Purpose: Dilated Virchow–Robin spaces (dVRSs) were regarded as a phenotype of cerebral small-vessel disease (SVD). However, the clinical correlations of dVRS were still unclear. In this study, we aimed to investigate the topography and clinical correlations of dVRS in first-ever lacunar stroke patients. *Methods:* Patients with first-ever lacunar stroke were recruited and had magnetic resonance scans to identify the presence and degree of dVRS in the basal ganglia (BG-dVRS), dVRS in the central semiovale (CSO-dVRS), leukoaraiosis, and silent brain infarction (SBI). The neurological deficits after stroke onset and functional outcome after 1 year were evaluated using National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale, respectively. Clinical and radiological features were compared between patients with high and low degrees of dVRS, and between patients with favorable and unfavorable outcomes. Logistic regression models were constructed to identify the risk factors of unfavorable outcome. *Results:* The NIHSS scores were not statistically different between patients with high and low degrees of dVRS. More patients with high degrees of BG-dVRS had unfavorable outcomes than those with low degrees of BG-dVRS. Logistic regression showed that the degrees of BG-dVRS, leukoaraiosis, and SBIs were not independent risk factors for the unfavorable outcome, whereas the total burden of SVD was an independent risk factor for the unfavorable outcome. *Conclusion:* The degrees of either BG-dVRS or CSO-dVRS were not associated with the severity of first lacunar stroke. BG-dVRS was related to the unfavorable 1-year outcome. This association might be based on the total severity of SVD. **Key Words:** Dilated Virchow–Robin spaces—leukoaraiosis—silent brain infarctions—lacunar stroke.

From the *Department of Neurology, Shanghai Tenth People's Hospital of Tongji University, Shanghai, China; †Department of Neurosurgery, Shanghai Tenth People's Hospital of Tongji University, Shanghai, China; and ‡Department of Radiology, Shanghai Tenth People's Hospital of Tongji University, Shanghai, China.

Received May 15, 2015; revision received September 7, 2015; accepted September 28, 2015.

Both Hongyan Yang and Rui Shen contributed equally to this paper.

This study was supported by grants from the National Natural Science Foundation of China (Nos. 81000492, 30971029, and 81171163).

Address correspondence to Xueyuan Liu, MD, Department of Neurology, Shanghai Tenth People's Hospital of Tongji University, Middle Yanchang Rd. 301#, Zhabei District, Shanghai, China; or Jing Huang, MD, Department of Neurology, Shanghai Tenth People's Hospital of Tongji University, Middle Yanchang Rd. 301#, Zhabei District, Shanghai, China. E-mail: huangjing.neurology@gmail.com; xylshtj@yahoo.com.cn.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2015.09.034

Introduction

Virchow–Robin spaces are the perivascular spaces surrounding the penetrating arteries and arterioles in the brain. Physiologically, these spaces may play a role in interstitial fluid drainage. When dilated, they become detectable by magnetic resonance imaging (MRI), especially in the basal ganglia (BG) and central semiovale (CSO).[1] Accumulating evidence suggests that dilated Virchow–Robin space (dVRS) in the basal ganglia (BG-dVRS) and dVRS in the central semiovale (CSO-dVRS), respectively, are associated with hypertensive arteriopathy and cerebral amyloid angiopathy, both of which are common pathological changes of small-vessel disease (SVD).[2-6] Now dVRSs are widely regarded as a marker of SVD.[1,7,8]

dVRSs are similar with other phenotypes of SVD including leukoaraiosis, silent brain infarctions (SBIs), and microbleeds in various aspects. For example, they are all age-related changes, with hypertension as the common vascular risk factor, and are associated with a higher prevalence of cognitive dysfunction.[1,9,10] Leukoaraiosis might be the most distinguished phenotype of SVD and has been studied for years among healthy community and patients of stroke. The severity of leukoaraiosis is associated with the prevalence, severity, and functional outcome of lacunar stroke.[11-13] Similarly to leukoaraiosis, dVRSs are also more frequently detected among patients of lacunar stroke. However, it is still unclear whether dVRSs of different regions are associated with the severity and outcome of lacunar stroke.

We hypothesized that dVRS might play a role in lacunar stroke similarly to leukoaraiosis. To test this hypothesis, we recruited a cohort of patients with lacunar stroke and made a detailed study about the topography and degree of dVRS, and their association with the severity and outcome of stroke.

Subjects and Methods

General Information

This was a prospective study based on the patients attending the department of Neurology of Shanghai Tenth People's Hospital, which is one of the medical centers for stroke in Shanghai. The patients were enrolled during August 2011 and July 2013 if they met the following criteria: (1) single acute lacunar infarction in the thalamus, gangliocapsular regions, corona radiate, and pons identified by MRI, with a diameter less than 1.5 cm on diffusion-weighted images (DWIs); (2) no stenosis greater than 30% on corresponding parent arteries of the infarctions including middle cerebral artery and basilar artery identified by computed tomography angiography; and (3) no history of stroke. Patients undergoing thrombolytic therapy, with potential cardioembolic source including atrial fibrillation and atrial fluctuation, or severe illness of other systems including uncontrolled heart failure, acute myocardial infarction, severe respiratory failure, uremia, or cancer were excluded.

After admission to the hospital, the neurological deficits were evaluated by the designated neurologists according to the National Institutes of Health Stroke Scale (NIHSS). During hospitalization, the patients were treated according to the Chinese Guideline for Diagnosis and Management of Acute Ischemic Stroke (2010). One year after the stroke onset, the functional outcome was evaluated by the same neurologists with the modified Rankin Scale (mRS) by telephone or face-to-face interview. Patients with an mRS score of 2 or higher were identified to have unfavorable functional outcome.

All procedures were approved by the Ethics Committee of the Shanghai Tenth People's Hospital and carried out after the written consent of the patients and their family members.

Magnetic Resonance (MR) Protocol and Image Reviewing

MR scan was performed with A 1.5-T MR scanner (Philips, Amsterdam, The Netherlands) and a 3.0-T MR scanner (Siemens, Munich, Germany). Axial T1-weighted images (repetition time/echo time [TR/TE] = 101/1.92 for the 1.5-T scanner and 2000/9 for the 3.0-T scanner), fluid-attenuated inversion recovery images (TR/TE = 6000/110 for the 1.5-T scanner and 8500/94 for the 3.0-T scanner), DWI (TR/TE = 3393/86 for the 1.5-T scanner and 6000/94 for the 3.0-T scanner), and sagittal T2-weighted images (TR/TE = 1940/120 for the 1.5-T scanner and 4540/96 for the 3.0-T scanner) were obtained with 16 layers.

After the MR images were obtained, the diameter of the acute infarction was measured on DWI. The presence, locations, and degrees of dVRS, leukoaraiosis, and SBIs were recorded. According to the recent consensus criteria, dVRSs were defined as small, sharp delineated cavitations with signals equal or similar to that of CSF, diameters less than 3 mm, following the course of perforating or medullary arteries.[10] The degrees of dVRS in BG and CSO, respectively, were rated. The details of the rating scores were as follows: for BG-dVRS, 0 = 0-5 dVRS, 1 = 6-10 dVRS, 2 = more than 10 but still numberable, and 3 = innumerable dVRS with cribriform change of BG; for CSO-dVRS, 0 = 0-10 dVRS in the total CSO region, 1 = more than 10 in the total CSO region but less than 10 in the slices containing the greatest number of dVRS, 2 = 10-20 dVRS in the slices containing the greatest number of dVRS, and 3 = more than 20 dVRS in the slices containing the greatest number of dVRS.[4,10] The degrees of dVRS were dichotomized into high score (degrees 2 and 3) and low score (degrees 0 and 1), respectively, for BG and CSO-dVRS.

Leukoaraiosis was defined as the scattered or confluent hyperintensities in the periventricular or deep region of the brain in the fluid-attenuated inversion recovery of MRI,[14] and was rated from degree 0 to 3 according to Fazekas' scale, in which degree 0 was defined as no hyperintensities in both periventricular and deep regions,