Plaque Distribution and Characteristics in Low-Grade Middle Cerebral Artery Stenosis and Its Clinical Relevance: A 3-Dimensional High-Resolution Magnetic Resonance Imaging Study

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Objectives: The significance of atherosclerotic plaques in the parental artery with low-grade stenosis remains undetermined. We used three-dimensional high-resolution magnetic resonance imaging (3D HR-MRI) to investigate plaque distribution and characteristics of low-grade middle cerebral artery (MCA) stenosis and its clinical relevance with stroke events. *Methods:* We retrospectively studied 22 symptomatic patients and 24 asymptomatic patients with low-grade MCA stenosis (<50%). By 3D HR-MRI, each identified plaque was classified as either culprit (plaque on the ipsilateral side of a stroke) or nonculprit (plaques in asymptomatic patients or not within the vascular territory of a stroke). Plaque enhancement grades and distribution were assessed and compared between the groups. The association between plaque enhancement and distribution and ischemic stroke was evaluated. *Results:* We identified 22 culprit plaques and 31 nonculprit plaques. More culprit plaques showed contrast enhancement compared to the nonculprit plaques (95.5% versus 29.0%, $P < .001$). Culprit plaques were more frequently superiorly distributed than the nonculprit plaques (46.9% versus 17.5%, $P < .01$). Contrast enhancement (odds ratio [OR] 17.0, 95% confidence interval [CI] 3.7-77.4) and superior distribution (OR 4.2, 95% CI 1.4-12.1) of a plaque were associated with a recent ischemic stroke, of which single subcortical infarctions accounted for the largest percentage (50%). *Conclusions:* Contrast enhancement and superior distribution may serve as indicators of culprit plaques in low-grade MCA stenosis, and they were significantly related to a recent ischemic stroke. **Key Words:** Atherosclerosis—middle cerebral artery—magnetic resonance imaging—cerebral infarction.

Introduction

Intracranial atherosclerotic disease (ICAD) is a common cause of ischemic stroke, especially in Asian populations.[1] The lumenography-based method has been used to assess the disease for many years. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, which is currently the most widely used system for establishing ischemic stroke etiology, defines large-artery atherosclerosis (LAA) as when the luminal stenosis in the corresponding artery is more than 50%. ICAD with low-grade stenosis (<50%) with the potential to generate downstream embolization was ignored and categorized as cryptogenic stroke.[2]

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Studies have shown that single subcortical infarction (SSI) of less than 20 mm can be attributed to LAA rather than small vessel disease if an atherosclerotic plaque in the parental artery is identified, even when the arterial stenosis is less than 50%.[3,4] This condition is relatively common, especially in Asian populations.[5,6] Several groups of authors modified the TOAST criteria to improve the detection of ICAD and to reduce strokes wrongly assigned to small vessel disease or an undetermined cause in low-grade intracranial artery stenosis, such as the Korean TOAST and Chinese ischemic stroke subclassification.[7,8] Understanding the culprit plaques in the parental artery with low-grade stenosis may facilitate the understanding of stroke etiology and assist in determining optimal treatment strategies.

Traditional modalities including computed tomography angiography, magnetic resonance angiography (MRA), or digital subtraction angiography are limited to identifying the potential pathologies in low-grade ICAD, especially in nonstenotic ICAD when stenosis is less than 30%. High-resolution magnetic resonance imaging (HR-MRI) is effective for identifying plaques, even in low-grade stenotic arteries; previous studies using two-dimensional (2D) HR-MRI have demonstrated that atherosclerotic plaques can be detected in about 42%-60% SSI patients with nonstenotic middle cerebral arteries (MCA).[3,4,9] Three-dimensional (3D) HR-MRI enables large volume coverage and high spatial resolution compared to 2D HR-MRI, and it may not miss small plaques on the vessel walls. However, most of the previous studies only assessed ICAD patients with high-grade MCA stenosis (>50%).[10-12] To the best of our knowledge, the investigation of plaques in low-grade MCA stenosis with 3D HR-MRI is limited, and individual studies have been small.[13,14]

In this study, we used a 3D turbo spin echo technique known as Sampling Perfection with Application Optimized Contrast Using Different Angle Evolutions (SPACE) to assess the distribution and characteristics of atherosclerotic plaques in symptomatic and asymptomatic patients with low-grade MCA stenosis and to investigate its clinical relevance to stoke events.

Materials and Methods

Subjects

This study was approved by our institutional review board. Between May 2016 and June 2017, all of the patients with MCA atherosclerotic plaque on HR-MRI in our single institutional database were retrospectively reviewed. A plaque was identified as focal wall thickening when it was evident on both the short axis and long axis of the vessel compared with the nearby vessel wall. The inclusion criteria were as follows: (1) low-grade MCA atherosclerotic stenosis (<50%) calculated on 3D SPACE; (2) absence of significant ipsilateral internal carotid stenosis (≥30%) assessed by ultrasound; (3) 1 or more atherosclerotic risk-factors, including hypertension, diabetes mellitus, hypercholesterolemia, and current cigarette smoking; and (4) the image quality was good enough for evaluation. The exclusion criteria included: (1) nonatherosclerotic vasculopathies, such as vasculitis, dissection, or moyamoya disease; and (2) high-risk factors for cardioembolism, such as atrial fibrillation, valvular heart disease, dilated cardiomyopathy, and infective endocarditis.

Symptomatic patients were defined as who suffered from an ischemic stroke or a transient ischemic attack (TIA) in the distribution of MCA within the most recent 2 weeks according to diffusion-weighted imaging or clinical manifestation and neurological examination. Asymptomatic patients were defined as those with no history of cerebrovascular events or if an ischemic stroke occurred in a vascular territory outside the affected MCA.

Hypertension was defined as blood pressure higher than 140/90 mm Hg or patients receiving antihypertension medicine. Hyperlipidemia was defined as a cholesterol level higher than 200 mg/dl or low-density lipoprotein at 130 mg/dl or higher. Diabetes mellitus was defined as fasting blood sugar at 7.0 mmol/l or higher, or 2-hour post prandial blood sugar at 11.1 mmol/l or higher, or patients receiving medications for diabetes mellitus.

High-Resolution MRI Protocol

The examination was performed with a 3.0 Tesla (T) MR system (Siemens Skyra; Erlangen, Germany) equipped with a 20-channel head-neck coil. 3D time-of-flight MRA was performed using the following parameters: repetition time/echo time (TR/TE), 22/3.6 ms; flip angle, 18°; field of view, 210 × 190 mm; and acquired resolution, .55 × .55 × .55 mm. A 3D black blood sequence was performed using T1-weighted SPACE sequence before and after contrast administration. 3D SPACE can cover the entire range of MCA and is more time-efficient compared with conventional 2D techniques. In T1 weighted SPACE, blood nulling is caused by flow-induced spin dephasing and blood signal would be attenuated by more than 75% for intracranial blood flow velocity exceeding 5 cm/s. Major segments of MCAs would be dephased with no need for increased TE or blood suppression pulse. The short TR in T1-weighted SPACE attenuates cerebrospinal fluid signal and improves delineation of vessel wall of MCAs surrounded by cerebrospinal fluid.[15] The detailed parameters were as follows: TR/TE, 900/4.2 ms; field of view, 240 × 216 mm; turbo-spin factor, 43 echoes; echo spacing, 4.2 ms; acquired resolution, .75 × .75 × .75 mm; reconstruction resolution, .40 × .40 × .75 mm; and acquisition time, 7 minutes. Contrast-enhanced 3D SPACE was started with an approximately 5-minute delay time after administration of .10 mmol/kg contrast agent (gadodiamide, GE Healthcare, Ireland).