Intracranial Plaque Characterization in Patients with Acute Ischemic Stroke Using Pre- and Post-Contrast Three-Dimensional Magnetic Resonance Vessel Wall Imaging

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Background: Magnetic resonance vessel wall imaging (VWI) techniques have been developed to assess atherosclerotic plaques in intracranial arteries, which are a cardinal cause of ischemic stroke. However, the clinical roles of plaque-related vulnerability and inflammation remain unclear. Hence, we evaluated plaque characteristics using VWI of the proximal middle cerebral artery (M1) in patients with acute ischemic stroke. *Methods:* We prospectively examined 30 consecutive patients with acute noncardioembolic stroke in the M1 territory using pre-/postcontrast T1-weighted (T1W) three-dimensional (3D) VWI with a 3-Tesla scanner. The contrast ratio (CR) and contrast enhancement of the plaques were measured bilaterally at M1. *Results:* Plaques were identified in the bilateral M1s of all patients, and no substantial stenosis existed. The M1 plaque CRs ipsilateral to the infarct (46.7%-67.9%) were significantly higher than the plaque CRs on the contralateral side (34.3%-69.4%), particularly in patients with lacunar infarcts ($P < .01$). In contrast, the occurrence of plaque enhancement was not different between the ipsilateral (20.0%) and contralateral (16.7%) sides. Further, the CRs in the nonlacunar group were significantly higher than the CRs in the lacunar group ($P < .05$), whereas enhanced plaques tended to be more frequent in the nonlacunar group, but this difference was not significant ($P = .09$). *Conclusions:* T1W 3D-VWI revealed that the signal intensity of M1 plaques was significantly higher in the affected side and in nonlacunar-type infarcts of patients with acute stroke,

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Ethical Standards and Patient Consent: We declare that all human and animal studies have been approved by the institutional ethical committee (H24-156) and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. We declare that all patients gave informed consent prior to inclusion in this study.

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Conflict of interest: The authors declare no conflict of interest associated with this manuscript.

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suggesting that unstable plaques in the M1 can cause stroke events presumably due to atherothrombotic mechanisms. **Key Words:** Vessel wall imaging—MRI—stroke—atherosclerosis.

Introduction

Atherosclerotic plaque, either extracranial or intracranial, is a cardinal cause of ischemic stroke. Besides luminal narrowing, plaque characteristics such as vulnerable composition, inflammation, and neovascularization are considered risk factors for developing ischemic stroke.[1] Plaque characterization of the cervical carotid arteries has been thoroughly investigated using the well-established techniques of magnetic resonance (MR) imaging, ultrasound, or computed tomography.[2,3] However, these modalities have not been able to fully characterize intracranial arterial plaques mainly because of the limitations of spatial resolution and/or accessibility.

Recently, MR vessel wall imaging (VWI) has been applied to directly assess plaques in the intracranial major arteries of stroke patients by using novel techniques such as the high-resolution two-dimensional (2D) fast spin-echo (FSE) method[4-13] and three-dimensional (3D) FSE method.[14] These studies can detect plaques in the proximal middle cerebral artery (MCA) (M1) and vertebrobasilar arteries with/without substantial stenosis. In general, the high signal intensity of cervical carotid plaques on T1W images reflects unstable plaques, which consist of hemorrhagic and/or lipid/necrotic components, as determined from specimens excised by carotid endarterectomy.[3,15] Hence, we can hypothesize that hyperintense intracranial plaques on T1W VWI reflect unstable plaques that can cause stroke events, presumably due to atherothrombotic mechanisms such as branch atheromatous disease and atheroma of the proximal perforating arteries,[16] although pathological validation of the intracranial plaques is generally unattainable. A recent report demonstrated that high signal intensity, which suggests vulnerable plaques on T1-weighted (T1W) VWI, is associated with the artery that is responsible for the stroke event.[14] Other reports showed that strong enhancement, indicating inflammation and/or neovascularization, was observed in the intracranial plaque of the major arteries supplying the stroke territory.[12,13,17,18] However, correlations between the intraplaque imaging characteristics of intracranial arteries and the occurrence and extension of the infarcts have not been fully clarified.

Therefore, we attempted to characterize atherosclerotic plaques of the proximal MCA in terms of vulnerable components and inflammatory changes using a pre- and postcontrast 3D T1W-VWI technique to determine whether unstable plaques in the M1 can cause stroke events in patients with noncardioembolic infarcts in the MCA territories.

Methods

Subjects

The study was performed after obtaining approval from the institutional ethical committee (H24-156) and written informed consent from the patients. From January 2013 to May 2015, we prospectively examined 30 consecutive patients (age range, 45-85 years; median age, 66 years; 15 men and 15 women) with acute ischemic stroke in the proximal MCA territory, ie, the basal ganglia and/or corona radiata, due to noncardioembolic mechanisms. The patient characteristics before hospitalization included hypertension in 22 patients, hyperlipidemia in 11, and diabetes mellitus in 9. None of the patients had other diseases related to the stroke events, such as arterial dissection, artery to artery embolism, vasculitis, moyamoya disease, or hypercoagulation state. As for medications, 9 patients had received antiplatelet agents, 7 received angiotensin-2 receptor blockers, 6 received statin, and 3 received oral hypoglycemic mediations. After hospitalization, all of the patients received standard treatments for ischemic stroke, such as antiplatelet therapy, anticoagulants, neuroprotection, transfusion, and statin therapies, because none of the patients were candidates for thrombolytic therapy or mechanical thrombectomy.

Imaging Protocols

The patients underwent MR examinations using a 3-Tesla scanner with an 8-channel head coil (Discovery MR 750, GE Healthcare, Milwaukee, WI) at 3-27 days after stroke onset (median, 8 days). T1W 3D-VWI was performed before and after intravenous administration of .2 mL/kg gadopentetate dimeglumine (Magnevist, Bayer, Berlin, Germany). The following pulse sequence parameters were used: sagittal flow-sensitized T1W 3D-FSE with variable flip angles; repetition time (TR), 400 ms; echo time (TE), 18.3 ms; echo train length, 24; *b*-value of the flow sensitizing gradients along three axes, 2.2 s/mm^2; field of view (FOV), 25 × 19 cm^2; matrix size, 512 × 512 (after zero-fill interpolation [ZIP]); slice interval, .5 mm (after ZIP); partition, 248; voxel size, .5 × .5 × .5 mm^3; parallel imaging factor, 2; number of excitations, 1; and acquisition time, 3 min 36 s.

Before administering the contrast agent, axial 3D time-of-flight magnetic resonance angiography (MRA) images were obtained with the following parameters: TR, 20 ms; echo time, 3.4 ms; flip angle, 12°; FOV, 24 × 19 cm^2; matrix size, 512 × 320; slice interval, .5 mm (after ZIP); partition, 160; number of excitations, 1. Axial