High-Resolution Magnetic Resonance Wall Imaging Findings of Moyamoya Disease

Sookyung Ryoo, MD; Jihoon Cha, MD; Suk Jae Kim, MD; Jin Wook Choi, MD; Chang-Seok Ki, MD; Keon Ha Kim, MD; Pyoung Jeon, MD; Jong-Soo Kim, MD; Seung-Chyul Hong, MD; Oh Young Bang, MD, PhD

Background and Purpose—Diagnosis of Moyamoya disease (MMD) is based on the characteristic angiographic findings. However, differentiating MMD from intracranial atherosclerotic disease (ICAD) is difficult. We compared vessel wall imaging findings on high-resolution magnetic resonance imaging between MMD and ICAD.

Methods—High-resolution magnetic resonance imaging was performed on 32 patients with angiographically proven MMD and 16 patients with acute infaracts because of ICAD. Bilateral internal carotid arteries and steno-occlusive middle cerebral artery were analyzed for wall enhancement and remodeling.

Results—Enhancement patterns and distribution were different. Most patients with MMD (90.6%) showed concentric enhancement on distal internal carotid arteries and middle cerebral arteries, whereas focal eccentric enhancement was observed on the symptomatic segment in ICAD. MMD was characterized by middle cerebral artery shrinkage; the remodeling index and wall area were lower in MMD than in ICAD (remodeling index, 0.19±0.11 versus 1.00±0.43; wall area, 0.32±0.22 versus 6.00±2.72; P<0.001).

Conclusions—MMD was characterized by concentric enhancement on bilateral distal internal carotid arteries and shrinkage of middle cerebral artery, regardless of symptoms. (Stroke. 2014;45:2457-2460.)

Key Words: angiography ■ magnetic resonance imaging ■ Moyamoya disease

Moyamoya disease (MMD) is a unique cerebrovascular disease characterized by progressive stenosis of the distal internal carotid artery (ICA) and a hazy network of basal collaterals. Differentiation of MMD from intracranial atherosclerotic disease (ICAD) is important for the treatment of patients with intracranial occlusive disease (revascularization surgery for MMD versus aggressive medical treatment for ICAD). However, it is often difficult, especially in Asians, in whom both MMD and ICAD are prevalent.

With the high-resolution magnetic resonance imaging (HR-MRI) techniques, vessel wall imaging findings for different causes of intracranial stenosis have been reported.1-3 However, wall imaging of MMD is seldom reported.1,4 In this study, we compared vessel wall imaging findings for MMD and ICAD on HR-MRI in a large cohort.

Methods

Patients

We prospectively recruited patients ≥18 years with middle cerebral artery (MCA) steno-occlusive disease. Thirty-two patients with digital subtraction angiographically (DSA) proven MMD were enrolled, with 16 patients with acute infarction from ICAD as controls. Diagnosis of MMD was made with current diagnostic criteria,1,6 and patients who had significant stenosis of relevant artery and did not show basal collaterals on DSA or time-of-flight MR angiography were categorized under ICAD. Patients with potential sources of cardioaortic embolism, ≥50% extracranial stenosis, or other stroke mechanisms were excluded. Local institutional review boards approved this study. All patients or patients’ guardians provided informed consent.

MRI Protocols

All patients underwent 3-Tesla MRI. Three-dimensional (3D), time-of-flight MR angiography of intracranial arteries was initially obtained. Black-blood HR-MRI using spatial presaturation technique was performed: (1) axial/sagittal proton-density (repetition time [TR]/echo time [TE]=2150/12.5 ms, echo train length=10, slice thickness=2 mm, flip angle=90°, matrix=280x280, field of view [FOV]=14 cm, number of average=2); (2) axial/sagittal T2-weighted images (TR/TE=2150/100 ms, echo train length=10, slice thickness=2 mm, flip angle=90°, matrix=280x280, FOV=14 cm, number of average=2); (3) sagittal T1 fluid-attenuated inversion recovery pre- and postcontrast (TR/TE=2100/10 ms, inversion time=860 ms, echo train length=6, slice thickness=2 mm, flip angle=90°, matrix=280x280, FOV=14 cm, number of average=2); (4) axial postcontrast 3D T1-weighted volumetric isotropic turbo spin echo acquisition (VISTA; TR/TE=350/20 ms, turbo spin echo factor=25, 0.5 mm isotropic voxel, flip angle=90°, matrix=360x360, FOV=18 cm, number of average=2).
Imaging Analysis

We evaluated vessel walls of MCA at the site of maximal stenosis or just proximal to the occlusion on 3D time-of-flight MR angiography and bilateral distal ICAs immediately after branching ophthalmic arteries. The vessel boundaries were traced manually on T2/proton-density–weighted images. Wall area was estimated as the difference between vessel area and lumen area. Remodeling index was the ratio of vessel area at MCA to the reference vessel. The percentage degree of stenosis was calculated as (1–lumen area of MCA/reference lumen area)×100%. Because most patients with MMD did not have a normal MCA, midbasilar artery served as reference values.

We compared pre- and postcontrast T1 fluid-attenuated inversion recovery images to determine the presence and pattern of enhancement. Enhancement was regarded as concentric if it was circular or uniform. Enhancement was considered eccentric if it was not 360° circumferential or if the thickest part was more than twice the thinnest part where circumferential enhancement was observed. All the measurement was made blinded to clinical information.

Results

Baseline Characteristics

Of 32 patients with MMD, 25 had definite MMD and 7 probable MMD; 9 had acute stroke (within 4 weeks), 17 chronic stroke, and 6 asymptomatic. Female and younger patients were more frequent in MMD, whereas diabetes mellitus and dyslipidemia were more common in patients with ICAD (P<0.05; Table 1).

Changes in Vessel Wall and Luminal Areas

MMD was characterized by MCA shrinkage (Table 1; Figure). Wall area and Remodeling index were smaller in MMD than in ICAD although the degree of stenosis was higher in patients with MMD (P<0.001).

Enhancement of Vessels

Patients with MMD had a distinct pattern and distribution of enhancement (Table 1; Figure). Patients with MMD showed concentric enhancement on distal ICA, regardless of the presence of symptoms (93.3% in symptomatic versus 73.5% in asymptomatic segments). However, in most patients with ICAD, enhancement was observed on symptomatic (68.8% versus 0% in MMD; P<0.001). Many patients with MMD had concentric enhancement, whereas all patients with ICAD except 1 showed eccentric enhancement (P<0.001). Concentric enhancement on bilateral distal ICAs was observed exclusively in patients with MMD (56.3% versus 0%); P<0.001). The pattern and distribution of MCA enhancement was similar to distal ICA in both patients with MMD and patients with ICAD.

Subgroup Analysis of MMD

We performed subgroup analysis to validate our HR-MRI findings for MMD. Two distinct findings, MCA shrinkage and concentric enhancement on distal ICA, were consistent, irrespective of subtype (definite versus probable), angiographic stage (Suzuki grade), or presence of symptoms (acute symptomatic versus chronic symptomatic versus asymptomatic; Table 2).

Receiver Operating Curve Analysis

HR-MRI showed high diagnostic accuracy as DSA. Sensitivity was 90.6% for HR-MRI finding of concentric enhancement of distal ICA or MCA, 93.8% for MRI finding of thinning of stenotic segment, and 84.4% for both findings. Area under the receiver operating curves were 0.89, 0.91, and 0.92, respectively (Figure I in the online-only Data Supplement).
Discussion

The main findings of this study were that MMD was characterized by shrinkage of MCA and concentric enhancement on bilateral distal internal carotid arteries (ICAs; arrowheads). The HR-MRI wall imaging of MMD has been previously reported. Two case series reported no thickening or enhancement in patients with MMD. However, the case number was small, with little data on the presence or acuteness of symptoms or MMD severity. In our study of 32 patients with MMD of various stages, HR-wall MRI consistently showed a small vessel diameter, thin vessel wall, and diffuse concentric

<table>
<thead>
<tr>
<th>MMD Subtype</th>
<th>Definite (n=25)</th>
<th>Probable (n=7)</th>
<th>Suzuki 1–3 (n=16)</th>
<th>Suzuki 4–6 (n=16)</th>
<th>Symptomatic (n=26)</th>
<th>Asymptomatic (n=6)</th>
<th>Acute Symptomatic (n=9)</th>
<th>Chronic Symptomatic (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wall area, mm²</td>
<td>0.32±0.24*</td>
<td>0.35±0.16*</td>
<td>0.35±0.24*</td>
<td>0.30±0.21*</td>
<td>0.34±0.24*</td>
<td>0.28±0.16*</td>
<td>0.34±0.34*</td>
<td>0.33±0.15*</td>
</tr>
<tr>
<td>Remodeling index</td>
<td>0.18±0.09*</td>
<td>0.26±0.16†</td>
<td>0.22±0.12*</td>
<td>0.16±0.09*</td>
<td>0.19±0.10*</td>
<td>0.19±0.15†</td>
<td>0.15±0.08*</td>
<td>0.22±0.11*</td>
</tr>
<tr>
<td>Stenosis degree, %</td>
<td>84.3±9.6‡</td>
<td>81.0±9.7</td>
<td>81.9±10.0‡</td>
<td>85.4±9.1</td>
<td>83.0±10.2‡</td>
<td>85.7±7.2</td>
<td>87.9±5.1†</td>
<td>79.9±11.4</td>
</tr>
</tbody>
</table>

Enhancement on vessels

<table>
<thead>
<tr>
<th></th>
<th>Distal ICAs, n (%)</th>
<th>MCA, n (%)</th>
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</thead>
<tbody>
<tr>
<td>Concentric</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wall area, mm²</td>
<td>41 (87.2)*</td>
<td>6 (12.8)*</td>
</tr>
<tr>
<td>Remodeling index</td>
<td>3 (60.0)</td>
<td>2 (40.0)</td>
</tr>
<tr>
<td>Stenosis degree, %</td>
<td>26 (86.7)*</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Eccentric</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wall area, mm²</td>
<td>18 (81.8)*</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>Remodeling index</td>
<td>9 (90.0)*</td>
<td>7 (15.6)</td>
</tr>
<tr>
<td>Stenosis degree, %</td>
<td>38 (84.4)*</td>
<td>1 (14.3)</td>
</tr>
</tbody>
</table>

IC indicates internal carotid artery; MCA indicates middle cerebral artery; and MMD, Moyamoya disease. All P values were compared with intracranial atherosclerotic disease.

*P<0.001, †P<0.01, ‡P<0.05.
enhancement. Our MRI findings are consistent with recent advances in the understanding of the pathogenesis of MMD and ICAD (Figure II in the online-only Data Supplement). There is increasing evidence that MMD is primarily a proliferative disease of the intima. Intimal hyperplasia from proliferation of smooth muscle cells or endothelium can cause stenosis. Therefore, diffuse concentric enhancement within vessels could represent hyperpliferation of the vessel wall components, whereas focal eccentric enhancement in patients with ICAD could represent focal atherosclerotic plaque.

Second, in contrast to proliferative changes of the intima, MMD was also characterized by thinned media. Caspase-dependent apoptosis and overproduction of matrix metalloproteinase have been implicated as contributory mechanisms in the associated degradation or remodeling of the arterial wall.

Therefore, diffuse and severe thinning of the wall area in our patients with MMD with could represent media shrinkage, which was not observed in our patients with ICAD. Our data indicated that HR-wall MRI could be an imaging biomarker specific to MMD. The frequency of characteristic HR-wall MRI findings did not differ by MMD stage (Suzuki grade) or subtype (definite versus probable), or the presence or acuteness of symptoms (acute symptomatic versus remote symptomatic versus asymptomatic). In contrast, none of our patients with ICAD showed characteristic HR-wall MRI findings of both diffuse concentric enhancement and shrinkage on the affected segment. Our receiver operating characteristic curves showed that HR-MRI findings had a diagnostic accuracy for DSA-proven MMD, which raises the possibility of noninvasive diagnosis of MMD (Figure I in the online-only Data Supplement).

Our study has limitations. First, patients with steno-occlusive disease other than MMD could have been included in the MMD group because no biomarkers or imaging tools are specific for MMD. However, all MMD cases were confirmed by DSA. Second, additional studies with histological confirmation are needed. Finally, the wall enhancement observed in our patients may have been because of luminal (and not wall) enhancement coming from slow-moving blood adjacent to the wall of the vessel (pseudoe enhancing or slow flow artifact). Additional studies using true double-inversion recovery sequences are needed. However, in patients with MMD, enhancement was often observed on the nonstenosed segment, either asymptomatic side or nonstenosed distal ICA, on time-of-flight-MR angiography. On the contrary, enhancement was rarely observed on the asymptomatic stenosed segment in patients with ICAD.

In conclusion, MMD was characterized by concentric enhancement on bilateral distal ICAs and shrinkage of MCA. These findings were consistent regardless of clinicoradiological characteristics. These distinct radiological findings could help explain the pathogenesis of MMD and differentiate MMD from ICAD.

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Disclosures
None.

References
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Supplemental figure I. ROC analysis
Participants were 32 MMD and 16 ICAD patients. Diagnostic accuracy of HR-MRI findings as (a) concentric enhancement of distal ICA and/or MCA, (b) thinning of stenotic segment (RI < 0.4), or (c) both were evaluated. Receiver operating characteristic (ROC) curves were used to compare discrimination power of conventional angiographic MMD criteria and HR-MRI criteria.

Criteria using HR-MRI showed high diagnostic accuracy as digital subtraction angiography. Sensitivity was 90.6% for HR-MRI finding of concentric enhancement of distal ICA and/or MCA, 93.8% for MRI finding of thinning of stenotic segment, and 84.4% for both findings. Area under the ROC curves (AUC) were 0.89, 0.91, and 0.92, respectively.
**Supplemental figure II.** Histological characteristics of MMD and ICAD

### Histological characteristics

**MMD**

#### Intimal layer
- Hyperproliferation of the vessel wall components
- Active angiogenesis
- Stratification of internal elastic lamina
- Matrix accumulation

**Medial layer**
- Degeneration of smooth muscle (shrinkage)

#### Medial thinness

**ICAD**

#### Intimal layer
- Atheroma (lower portion)
- Subintima hemorrhage (arrowhead)

**Medial layer**
- Increase in collagenous fibers which replace muscle elements, producing heavy bands of collagen fibers

**Medial thickening**

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<table>
<thead>
<tr>
<th>Intimal &amp; medial thickness of MMD vs. control</th>
<th>MMD (n=35)</th>
<th>Control (n=6)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intimal, MCA</td>
<td>16.4 ± 9.7</td>
<td>8.0 ± 4.7</td>
<td>0.0041</td>
</tr>
<tr>
<td>Medial, MCA</td>
<td>23.0 ± 7.7</td>
<td>61.8 ± 30.4</td>
<td>0.0009</td>
</tr>
</tbody>
</table>

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