Arterial spin-labeling MR imaging in moyamoya disease compared with clinical and other MR imaging findings

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Purpose

Moyamoya disease (MMD) is a progressive intracranial vascular stenoocclusive disease of unknown etiology which was first reported in 1957 by Takeuchi et al [1]. MMD is characterized by progressive occlusion of distal part of internal carotid artery (ICA) as well as proximal part of middle (MCA) and anterior cerebral arteries (ACA) which are main branches within the circle of Willis [2]. Conventional angiography is a standard method to evaluate the blood vessels and provide the useful information for treatment. However, after the guideline for the diagnosis and treatment of MMD was published in 1997, magnetic resonance imaging (MRI) and three-dimensional time-of-flight MR angiography (MRA) has been well accepted as a noninvasive diagnostic modality [3-8].

On the other hand, brain perfusion studies cannot be performed frequently in the clinical practice. The reasons include facilities, costs, and invasiveness. Although nuclear medicine imaging examinations like positron emission tomography (PET) or single-photon emission CT (SPECT) imaging are the gold standard for estimating brain perfusion [9-12], they need special equipments and expensive examination agents. There have been comparatively new methods of dynamic susceptibility contrast MRI (DSC-MRI) and dynamic helical CT for performing brain perfusion studies [13, 14]. However, these have disadvantages including the administration of the contrast material and the procedural difficulties such as a bolus injection technique, especially for children.

Arterial spin-labeling (ASL) is a non-invasive imaging technique to acquire the blood flow information on MRI [15]. ASL-MRI is expected to be helpful for evaluating the blood flow changes in MMD if feasible [16]. However, the clinical relevance of ASL-MRI for MMD has not been evaluated yet. Our purpose in this study is to reveal the clinical relevance of ASL-MRI for MMD by comparing with clinical manifestations and other MRI findings.

Methods and Materials

The current retrospective research was approved by our institutional review board (No.20-39).

Patients

From June 2008 to June 2009, 73 MMD patients (male, 24; female, 49; age range and average (years), 7-71 and 30.4, respectively) were enrolled in this study. The patients were diagnosed according to MRI and MRA Guidelines for the diagnosis of MMD proposed by the Research Committee on the Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare, Japan [5] (Figure 1). They presented initially with transient ischemic attack (TIA) (n=48), hemorrhage (n=7),
cerebral infarction (n=11), headache (n=2), epilepsy (n=1), unknown symptom (n=1), or no symptoms (n =3). The age range and average at onset (years) were 1-60 and 19.6, respectively. Of these 73 patients, 49 underwent revascularization surgery on either (n=20) or both sides (n=29).

**MR imaging**

ASL-MRI as well as other MR imagings were performed as a component of routine clinical brain MR examination on a clinical 3.0-Tesla MR imaging unit (MAGNETOM Trio, A Tim System, Siemens AG, Erlangen, Germany) with a 12-channel head coil.

1) **ASL-MRI**

The ASL-MRI images were obtained using the second version of a system for the quantitative imaging of perfusion with thin-slice Ti1 periodic saturation (Q2TIPS), a pulsed ASL-MRI method that enables the acquisition of multiple sections (Figure 2) [18].

Voxel-wise calculation and subsequent mapping of the ASL-MRI images (ASL-MRI map) were performed according to the following equation for quantitative CBF, as proposed by Wang et al. [19]:

\[ f = \frac{\# \times \#M}{(2\# \times M0 \times TI1 \times \exp(-TI2/T1a))} \]  ------ (1)

where \( f \) is the regional cerebral blood flow, \( \# \) is the brain/blood partition coefficient of water, \( \#M \) is the difference of the longitudinal magnetization between the unlabeled and labeled images in the region of interest (ROI), \( \# \) is the inversion efficiency, \( M0 \) is the equilibrium magnetization of the regional brain tissue, and \( T1a \) is the longitudinal relaxation time of blood. In order to clarify the implication of this equation, Q2TIPS were detailed as following.

The Q2TIPS system consists of both labeling and image-acquisition sequences. The labeling sequence has several important parameters: a labeling slab position; an imaging slab position; and 3 given timing parameters termed TI1, TI1S and TI2 [18]. The labeling slab is the region in which proximal arterial blood is labeled by an inversion recovery radiofrequency (IR) pulse. The imaging slab is the region in which perfusion imaging data are acquired. Firstly, saturation pulses are performed on the imaging slab in order to reduce the noises. Secondly, IR pulse is performed in order to label the arterial blood (the current elapsed time is assumed as t = 0). Thirdly, the periodic saturation pulse is performed at the distal area of the labeling slab after a given waiting time termed TI1 (t = TI1). Therefore, \{ f x TI1 \} represents the blood volume passing from the labeling slab to the distal part and TI1 is related to the amount of the labeled arterial blood volume. Fourthly, the saturation pulse is stopped after a given time termed TI1S (t = TI1S). Finally, the imaging data acquisition is performed on the imaging slab after a given time termed TI2 (t = TI2) [18-20]. When Ma is defined as the equilibrium magnetization of the arterial
blood, \( \{ f \times T_{I1} \times M_a \times (1 - 2\# \times \exp(-T_{I2}/T_{I1a})) \} \) is given as the total amount of the longitudinal magnetization of the labeled regional arterial blood. The unlabeling imaging acquisition is performed in the same way as the labeling acquisition only without the slice-selection gradient on the labeling slab at \( t=0 \). The total longitudinal magnetization of the unlabeled regional arterial blood amounts to \( \{ f \times T_{I1} \times M_a \} \). Since the perfusion image is calculated from the unlabeling imaging subtracted by the labeling imaging, \#M is calculated as follows [20]:

\[
#M = \{ f \times T_{I1} \times M_a \} - \{ f \times T_{I1} \times M_a \times (1 - 2\exp(-T_{I2}/T_{I1a})) \}
\]

\[
= \{2\# \times M_a \times f \times T_{I1} \times \exp(-T_{I2}/T_{I1a})\} \quad \text{(2)}
\]

\# equals to the ratio of \( M_0 \) to \( M_a \) because the equilibrium magnetization of the tissue is generally proportional to its water content. Therefore, the equation (2) is matched with the equation (1) by inserting \( M_0/# \) instead of \( M_a \). In the present study, the parameters were as follows: \( T_{I1} / T_{I1S} / T_{I2} \) (ms) = 700 / 1800 / 2000; the labeling slab width / the imaging slab width / the gap between the two slabs (mm) = 100 / 114 / 25; \# (g/mL) = 0.9; \# = 0.95; \( T_{Ia} \) (ms) = 1496.19.

The image acquisition in the Q2TIPS system employed an echo-planar imaging (EPI) sequence. The imaging sequence has an important parameter, a flow limit. The flow limit means the cut-off value of flow velocity of eliminating fast-moving spins by crusher gradients. If the flow limit is set to infinity, or no crusher gradients, the perfusion values will be overestimated. On the other hand, if the flow limit is set to 0 cm/s, the gain in flow accuracy will be canceled out by extended echo time (TE) and decreased signal-to-noise ratio (SNR). It was empirically confirmed that the flow distribution were more physiologically reasonable values if the flow limit were set between 1 and 5 cm/s [21]. In our series, a flow limit = 4 cm/s was chosen as a trade-off. The other parameters of the imaging sequence were as followed: repetition time / echo time (ms) = 2500 / 17; field of view (mm) = 256 x 256 x 114; slice thickness / interslice gap (mm) = 6 / 1.2; total slice number = 16; coverage area: whole brain; slice acquisition order: sequential, proximal-to-distal direction; matrix = 64 x 64; voxel size (mm) = 4 x 4 x 6; phase partial Fourier acquisition rate = 7 / 8; total image number = 91 (first image volume acquired without a labeling pulse as an M0 image volume, and 45 pairs of labeled and unlabeled image volumes). The acquisition time of Q2TIPS (minutes: seconds) amounted to 3: 57.

2) Other MR imaging

Other MR imagings were including MRA and fluid attenuated inversion recovery (FLAIR) imaging. MRA was performed using the following parameters: repetition time (TR) / echo time (TE) (ms) = 22/3.1; flip angle (degree) = 18; field of view (FOV) (mm) = 200*166-180; matrix = 384*320-346; pixel spacing (mm) = 0.5*0.5; slice thickness/interslice gap (mm) = 0.6-1.0/0; number of slices = 102-150; magnetization transfer contrast = no. Maximum-
Intensity projection reconstruction (MIP) images were generated. FLAIR was performed using a fast inversion recovery sequence with parameters as follows: TR/TE/inversion time (TI) (ms) = 9000/63-86/2500; flip angle (degree) = 120-150; FOV = 220*178-213; matrix = 384*312-372; pixel spacing (mm) = 0.6*0.6; slice thickness/interslice gap (mm) = 6.0/1.2; number of slices = 20.

Imaging finding evaluations

1) CBF value of hemisphere measured with a normalized ASL map (ASL-value)

The details on these processing methods have been reported previously [22]. The summation of analysis process was as follows. The ASL map was firstly converted to the analyze format by using the free computer software MRIcro (version 1.40 build 1, Professor Chris Rorden, Georgia Institute of Technology, Atlanta GA, USA, http://www.cabiatl.com/mricro/mricro/index.html). Converted ASL map was normalized, and thereafter smoothed with 8mm of full width at half maximum (FWHM) by using the free computer software package SPM2 (Statistical Parametric Mapping 2, Institute of Neurology, London, http://www.fil.ion.ucl.ac.uk/spm/) running on Matlab (MathWorks Inc., Natick, MA, USA). Masking ROI maps of the bilateral cerebral hemispheres were created using the free add-on software WFU pickatlas (WFU PickAtlas, Joseph Maldjian, MD, Wake Forest University School of Medicine, North Carolina, USA, http://www.fmri.wfubmc.edu/download.htm) running on SPM2. The masking ROI maps were normalized in the same way as for ASL map. The CBF values of ASL map (ASL-value) on bilateral cerebral hemispheres were calculated with the normalized ASL maps and masking ROI maps using ImageJ (Wayne Raqsband, National Institutes of Health, Bethesda, Maryland, USA, http://rsb.info.nih.gov/ij/index.html).

2) MRA grade

Houkin's grading system [23] about MRA on MMD was adopted to evaluate the steno-occlusive severity of intracranial vessels on MRA (Figure 3) [3, 8]. MRA score was determined by the summation of the following internal carotid artery (ICA), middle cerebral artery (MCA), anterior cerebral artery (ACA), and posterior cerebral artery (PCA) scores, which ranged from 0 to 10 (ICA+MCA+ACA+PCA=3+3+2+2). All scores were mainly determined based on MRA MIP images. MRA source images were also used referentially. MRA grading was defined from MRA scores as follows: MRA score from 0 to 1 = MRA grade 1; MRA score from 2 to 4 = MRA grade 2; MRA score from 5 to 7 = MRA grade 3; MRA score from 8 to 10 = MRA grade 4.

3) Moyamoya vessel score

Moyamoya vessels score system was adopted according to the regions where those collateral vessels were seen with any values of window level and window width on
MRA source images [8]. Those regions were the areas of basal ganglia, anterior communicating artery, MCA-ICA tip, PCoA-PCA, and Basilar tip where moyamoya vessels could be seen frequently. Each region occupied one score and the total scores of moyamoya vessels were 5.

4) Ivy score

It is well known that the "ivy sign" on FLAIR images is the result of the slow-flowing engorged pail convexity vessels and thickened arachnoids membrane which can be detected in Moyamoya disease [8, 25-27]. The following modified Yoon's [27] three degrees were adopted for evaluating the ivy sign [8]:

point 0: the absence of ivy sign

point 1: ivy patterns with the same signal intensity as the brain parenchyma were dominantly observed

point 2: high-intense ivy patterns were dominantly observed.

5) CVA lesion

The presence or absence of Cerebrovascular attack (CVA) lesions was evaluated on FLAIR and T2WI.

Imaging Evaluations Method

All images were observed on a computer viewer system (ViewR version1.09.15, Yokogawa Electric Corporation, Tokyo, Japan) with a 54-cm class color LCD monitor (Radioforce R22, EIZO NANAO CORPORATION, Ishikawa, Japan). MR imaging was studied by two observers (MN with 2-year-experience for neuroradiology, TN with 7-year-experience for neuroradiology) in consensus fashion.

Statistical Analysis

The relevance of ASL-values in 146 hemispheres was assessed in relation to 5 clinical factors (age at MR exam, age at onset, sex, family history, and revascularization surgery) and 4 MR imaging factors (MRA grade, Moyamoya vessel score, Ivy score, and CVA lesion). Student's t-tests were performed to estimate the differences in ASL-values between male vs. female, the presence vs. absence of family history, revascularization surgery, and CVA lesion. Spearman's signed-rank tests were performed to estimate the relationships between ASL-values vs. MRA grades, ASL-values vs. Moyamoya vessel scores, and ASL-values vs. Ivy scores. Multiple regression analysis of ASL-values was
performed with the factors which were statistically significant in univariable analyses described above. All analyses were evaluated under the significant level of 0.05.

Images for this section:

Table 1. Guidelines for the diagnosis [5]

1. Diagnostic criteria
   
   (A) Cerebral angiography is indispensable for the diagnosis, and should present at least the following findings:
   1. Stenosis or occlusion at the terminal portion of the internal carotid artery and/or at the proximal portion of the anterior and/or the middle cerebral arteries.
   2. Abnormal vascular networks in the vicinity of the occlusive or stenotic lesions in the arterial phase.
   3. These findings should present bilaterally.
   
   (B) When magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) clearly demonstrate all the below described findings, conventional cerebral angiography is not mandatory.
   1. Stenosis or occlusion at the terminal portion of the internal carotid artery and at the proximal portion of the anterior and middle cerebral arteries on MRA.
   2. An abnormal vascular network in the basal ganglia on MRA.
   3. (1) and (2) are seen bilaterally.
   
   (C) Because the etiology of this disease is unknown, cerebrovascular disease with the following basic diseases or conditions should thus be eliminated:
   
   (D) Instructive pathological findings:
   1. Intimal thickening and the resulting stenosis or occlusion of the lumen are observed in and around the terminal portion of the internal carotid artery usually on both sides. Lipid deposits are occasionally seen in the proliferating intima.
   2. Arteries constituting the circle of Willis such as the anterior and the middle cerebral and the posterior communicating arteries often show stenosis of various degrees or occlusion associated with fibrocellular thickening of the intima, a waving of the internal elastic lamina.
   3. Numerous small vascular channels (perforators and anastomotic branches) are observed around the circle of Willis.
   4. Reticular conglomerates of small vessels are often seen in the pia mater.

2. Diagnosis
   
   In reference to 1 mentioned above, the diagnostic criteria are classified as follows: Autopsy cases not undergoing cerebral angiography should be investigated separately while referring to (D).
   1. Definite case: One which fulfills either (A) or (B) and (C). In children, however, a case which fulfills (A) (1) and (2) or (B) (1) and (2) on one side and with remarkable stenosis at the terminal portion of the internal carotid artery on the opposite side is also
   2. Probable case: One which fulfills (A) (1) and (2) or (B) (1) and (2) and (C) (unilateral involvement)

Fig. 1: Guidelines for the diagnosis [5]
Fig. 2: Schematic illustration of the Q2TIPS sequence chart, which was modified from that of Luh and associates [18]. The gray and white bars on each line indicate the targeting field of the slab selection gradient. The white bar of gradient is alternately applied for labeling and control states. In-plane presaturation pulses on imaging slab followed by the sech inversion labeling pulse on labeling slab were applied. Periodic saturation pulses applied from TI1 to TI1S consist of a train of 90° excitation pulses, each followed by a crusher gradient. 16 imaging slices of echo planar imaging (EPI) acquisition are applied at TI2.
<table>
<thead>
<tr>
<th>Artery</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ICA</strong></td>
<td>Normal</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Stenosis of C1 (small caliber of C1 compared to M1)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Discontinuity of C1 signal (C2-M2 and C2-A2 discontinuity)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Invisible (C2-M2, C2-A2 and PCoA discontinuity)</td>
<td>3</td>
</tr>
<tr>
<td><strong>MCA</strong></td>
<td>Normal</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Stenosis of M1 (small caliber of the proximal part compared to distal part)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Discontinuity of M1 signal (C2-M2 and A2-M2 discontinuity)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Invisible (invisible M2 branches)</td>
<td>3</td>
</tr>
<tr>
<td><strong>ACA</strong></td>
<td>Normal A2 and its distal</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>A2 and its distal signal decrease or loss (less signal intensity of A2 compared to AFA)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Invisible (invisible A2)</td>
<td>2</td>
</tr>
<tr>
<td><strong>PCA</strong></td>
<td>Normal P2 and its distal</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>P2 and its distal signal decrease or loss (P2 discontinuity)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Invisible (invisible PCoA)</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>0 — 10</td>
</tr>
</tbody>
</table>


**Note 2:** MRA grade 1 = MRA score 0-1, MRA grade 2 = MRA score 2-4, MRA grade 3 = MRA score 5-7, MRA grade 4 = MRA score 8-10

**Fig. 3:** Summary of the MRA score [24]
Results

ASL-MRI perfusion map and the other MR imagings are shown for a patient with MMD on Figure 1.

Table 2 showed the results of the relevance of ASL-values with clinical and MR imaging factors.

Negative relationship of ASL-values vs. MRA grades reached the significant level, which might mean that ASL-values in MMD were adversely affected by the intracranial stenoocclusive change assessed by MRA grading system.

ASL-values were negatively related with ages at MR exam with the significant level as well. It might suggest that the aging was one of the regressive factors for ASL-values.

ASL-values in the absence of CVA lesion were significantly higher than those in the opposite. This result might make sense because CVA lesion was a consequence of the cerebrovascular events and had the low cerebral perfusion distribution.

We also observed that ASL-values in the presence of family history were significantly higher than those in the opposite, which did not have reasonable accounts so far.

Of those significant positive 4 factors, MRA grade (p<0.05) and CVA lesion (p<0.01) revealed the significant effective factors in multiple regression analysis of ASL-values, which might suggest that those were main 2 factors strongly affecting ASL-values on MMD.

On the other hand, no statistical significances were observed in age at onset, sex, revascularization surgery, Moyamoya vessel score, or Ivy score.

Images for this section:
Fig. 1: A 10-year-old girl with MMD with post-bilateral revascularization operation state. 3D-TOF-MRA bottom-to-top-view MIP image showed poor visualization of distal ICA to proximal MCA and ACA bilaterally (a; arrows). Right and left MRA grades were 3 and 4, respectively. T1WI showed flow voids at bilateral thalami (b; arrows) and small CVA lesion at left caudate head (arrowhead). FLAIR showed ivy sign, that is, punctate or tortuous high signal intensities along sulci (c; arrowheads). Bilateral ivy sign scores were 2 in both sides. Colored ASL perfusion imaging fused with M0 image showed high perfusion at deep gray matter (d; arrows) and low perfusion at surface side of cerebrum (d; arrowheads), which suggested increased blood flow thorough moya vessels and decreased blood flow thorough circle of Willis.
### Table 3. Analyses of the relevance of ASL-values with clinical and MR imaging factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number of hemisphere</th>
<th>ASL value {mean±SD}</th>
<th>p value (rs*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(mL/100g/min)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>(male) 48</td>
<td>20.3±9.7</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>(female) 98</td>
<td>23.5±10.2</td>
<td></td>
</tr>
<tr>
<td>Age at MR exam</td>
<td>146</td>
<td>22.5±10.1</td>
<td>p&lt;0.05 (rs=-0.17)</td>
</tr>
<tr>
<td>Age at onset</td>
<td>146</td>
<td>22.5±10.1</td>
<td>n.s. (rs=-0.10)</td>
</tr>
<tr>
<td>Family history</td>
<td>(yes) 28</td>
<td>28±9.3</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>(no) 118</td>
<td>21.2±9.8</td>
<td></td>
</tr>
<tr>
<td>Revascularization surgery</td>
<td>(yes) 78</td>
<td>22.7±9.4</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>(no) 68</td>
<td>22.2±10.9</td>
<td></td>
</tr>
<tr>
<td>MRA grade</td>
<td>(1) 1</td>
<td>20</td>
<td>p&lt;0.01 (rs=-0.11)</td>
</tr>
<tr>
<td></td>
<td>(2) 69</td>
<td>25.4±10.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3) 71</td>
<td>20±9.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(4) 5</td>
<td>18±9.9</td>
<td></td>
</tr>
<tr>
<td>Moyamoya vessel score</td>
<td>(0),(1) 0</td>
<td>—</td>
<td>n.s. (rs=0.09)</td>
</tr>
<tr>
<td></td>
<td>(2) 2</td>
<td>10.6±4.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3) 4</td>
<td>33.3±2.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(4) 38</td>
<td>23.6±9.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(5) 102</td>
<td>21.9±10.2</td>
<td></td>
</tr>
<tr>
<td>Ivy score</td>
<td>(0) 14</td>
<td>25.7±9.7</td>
<td>n.s. (rs=0.03)</td>
</tr>
<tr>
<td></td>
<td>(1) 39</td>
<td>23.1±9.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2) 93</td>
<td>21.7±10.3</td>
<td></td>
</tr>
<tr>
<td>CVA lesion</td>
<td>(yes) 108</td>
<td>20.4±9.4</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>(no) 38</td>
<td>28.4±9.6</td>
<td></td>
</tr>
</tbody>
</table>

*rs: correlation coefficient by Spearman's signed-rank test
**SD: standard deviation
**Fig. 2:** Analyses of the relevance of ASL-values with clinical and MR imaging factors
Conclusion

Discussion

In the previous study of ASL-MRI in moyamoya disease compared with SPECT imaging, the authors reported that CBF values measured on ASL-MRI were correlated with those on N-isopropyl-4-{123I}iodoamphetamine (123I-IMP) both with and without acetazolamide [28]. This result might suggest that ASL-MRI could show not only obvious but also potential dangerous zones for ischemia. Therefore, ASL-MRI might detect the hemispheric side where the medical treatment was seriously required. On the other hand, the relationships between ASL-MRI and various states or conditions of MMD were not precisely estimated up to the present.

In the current study, we revealed several results which were important to comprehend the characteristics of ASL-MRI on MMD.

MRA grade revealed one of the significant effective factors in both the univariate analysis and the multiple regression analysis of ASL-values. MRA grade can express the severity of intracranial arterial stenoocclusions was proved to be significantly consistent with Suzuki’s stages [8]. In addition, Hoshi et al investigated that the regional relative blood flow ratios both with and without acetazolamide decreased in proportion to the angiographic grades classified according to Suzuki’s stages. Together with these previous findings, our result could be anticipated.

CVA lesion also showed the other of the significant effective factors associated with ASL-values. The presence of CVA lesion causes from irreversible cerebrovascular attacks and results in overt low CBF areas. Therefore, our result may also indicate that ASL-MRI reflected the manifest ischemic areas.

Negative relations between ASL-values vs. ages at MR exam reached the significant level in the univariate analysis. Occlusive arterial lesions progress, not only in symptomatic but also asymptomatic MMD patients. Kuroda and colleagues revealed that occlusive arterial lesions advanced in 15 of 63 patients (23.8% per patient) during the follow-up period [31]. Our result may follow the age-related progression of intracranial arterial stenoocclusions. On the other hand, no statistical significances were observed in ages at onset. This fact might suggest that the disease progression rate varies between individuals although most previous reports have emphasized the temporal advancement of MMD.

ASL-values in the presence of family history were significantly higher than each of opposites. While there might be some assumptions that MMD patients with family history could be found treated properly in early stage due to the profound awareness about the disease, further investigation would be needed for this result because no other reports investigated the state of the brain perfusion in MMD patients with familial history so far.
It was reported that the female patients were at higher risk for the disease progression of adult MMD than male patients [31]. No statistical significance was observed in sex in our study, which might be partly because both adult and juvenile patients were included for evaluation.

The hemisphere with revascularization surgery had no significant difference compared with those without. This might confirm that revascularization surgery can support the blood supply to the ischemic hemisphere as much as the hemisphere which was not needed for surgical management.

Moyamoya vessel scores presented the extent of the basal moyamoya vessels (BMV) development and had no relationship with ASL-values in our study. In the previous investigation, the moyamoya vessels proliferation suggests insufficient CBF in both pediatric and adult MMD patients [32, 33]. Kuwabara et al. reported a significant reduction in regional CBF in pediatric moyamoya patients with BMV [32]. Piao et al. demonstrated that had the extensive BMV hemispheres exhibited a significantly lower CBF than in diminished BMV hemispheres in the unoperated adult patients without large CVA lesion or intracranial hemorrhage [33]. We included both pre- and postoperative patients in the present study, which might make indistinct results. Further research should be performed in order to confirm the correlation between ASL-MRI and BMV.

The "ivy sign" suggests the leptomeningeal high signal intensity seen on FLAIR images in a patient with moyamoya disease [25, 26, 34, 35]. This finding resembled ivy creeping on stones, was referred to as the "ivy sign". Ivy sign is thought as the slow and stagnant flow in engorged pial vessels via leptomeningeal anastomosis although the mechanism of leptomeningeal enhancement and high intensity is complex and unclear. Recent reports pointed out that the ivy sign indicated decreased cerebral vascular reserve (CVR) in Moyamoya disease [8, 34], which suggested that ivy sign could show potential dangerous zones for ischemia. Thus, some relationship between Ivy sign and ASL-MRI was expected because ASL-MRI could reflect the potential ischemic area as mentioned above. However, no significant relationship was observed between ivy sign and ASL-values in our study. Ivy sign can be partly explained by differences in the development of collateral pathway [35]. The extent of collaterals can vary according to ages or revascularization surgery.

In summary, although our survey aimed the comprehensive investigation between ASL-MRI and the clinical epidemiology and other MR imaging findings in order to know the relevance of ASL-MRI in the present state of MMD, some results were questionable compared with the previous studies which enrolled and investigated specific MMD patients based on the surveying purposes of their own. Stratification analyses would be needed in order to clarify those questions as well as the further latent pathology of MMD in association with ASL-MRI.

Conclusion
Hemispheric CBF measured by ASL-MRI were affected adversely by the intracranial stenoocclusive change estimated by MR angiography, the presence of CVA lesion, and age at MR exam, and positively by the presence of family history on MMD. These results may indicate that the perfusion imaging by ASL has a valuable utility for the clinical evaluation in MMD.

References


**Personal Information**