Diagnosis of Moyamoya Disease With Magnetic Resonance Angiography

Kiyohiro Houkin, MD; Takeshi Aoki, MD; Akihiro Takahashi, MD; Hiroshi Abe, MD

**Background and Purpose** Present criteria for the diagnosis of moyamoya disease emphasize the use of conventional cerebral angiography as an indispensable requirement. However, magnetic resonance angiography (MRA) is fast becoming a reliable diagnostic modality for occlusive cerebrovascular diseases. The purpose of this study is to assess the accuracy of MRA compared with conventional angiography.

**Methods** Thirty-nine patients (23 children and 16 adults) with moyamoya disease confirmed by conventional angiography (78 side views) were examined with MRA (three-dimensional time-of-flight technique with a 256x256 or 256x512 matrix). T1- and T2-weighted MR images were also taken.

**Results** The stenotic or occlusive change at the carotid fork was clearly revealed by MRA, which correlated well with conventional angiography (83% good correlation, 17% overestimation). Apparent moyamoya vessels were clearly shown as a signal void on the MR image and fine unusual vessels on MRA, particularly in children with moyamoya disease (82%). However, small moyamoya vessels were poorly shown on both MR images and MRA, particularly in adults (63%).

**Conclusions** MRA can be an alternative to conventional angiography in typical moyamoya disease cases (the bilateral type of moyamoya disease in children). However, in the early or the end stages of moyamoya disease, diagnosis by means of MRA should be carefully evaluated.

**Key Words** - angiography, magnetic resonance - genetics - moyamoya disease

For the diagnosis of moyamoya disease, the Japanese committee on spontaneous occlusion of the circle of Willis (moyamoya disease), sponsored by the Japanese Ministry of Health and Welfare, requires that conventional angiography be done to reveal the stenotic change of the main arteries or development of moyamoya vessels. Considering the basic pathological change of this disease, this requirement is indispensable. However, conventional angiography is not necessarily safe, particularly in children. Most of the patients with this disease are children, and angiography must be performed at least twice (both preoperatively and postoperatively). Follow-up angiography is not indispensable for treatment, but information obtained by angiography is also important to determine the long-term history of this disease. In addition, as revealed recently, moyamoya disease is a polygenic hereditary disease. Therefore, a screening test for high-risk patients is clinically important.

Magnetic resonance angiography (MRA) is becoming a reliable alternative for diagnosing occlusive cerebrovascular disease. The merit of MRA is its noninvasive nature. In addition, this technique is spreading widely and is becoming a popular routine examination in many major clinical centers. The diagnosis of moyamoya disease by means of MRA should be discussed as a practical possibility, and the limitations of MRA should be precisely evaluated. Recently Yamada et al analyzed 12 cases and investigated the usefulness of MRA in the diagnosis of moyamoya disease. In this report we analyze 39 patients with moyamoya disease and study the effectiveness of MRA with high-resolution options (256x512 matrix, magnetization transfer contrast, and tilted optimized nonexcitation) in the diagnosis of moyamoya disease.

**Subjects and Methods**

**Patients**

From April 1992 to October 1993, 39 patients with idiopathic occlusion of the circle of Willis (moyamoya disease) were examined by MRA. All patients met the requirements of diagnosis as set by the Japanese committee on the idiopathic occlusion of the circle of Willis. The clinical details are summarized in Table 1. All patients underwent both MRA and conventional angiography. Thirty-two patients had both MRA and conventional angiography within 1 month. Thirty-four patients underwent combined revascularization surgery with direct bypass surgery and indirect bypass surgery. Five patients had only indirect bypass surgery. Twenty-four patients (62%) had both preoperative and postoperative examinations; 15 patients (old postoperative cases) had only postoperative MRA. The study group included 23 children (aged ≤15 years) (mean age, 9.4 years; 7 males, 16 females) and 16 patients aged ≥16 years (adult group; mean age, 33.5 years; 4 males, 12 females). In total we investigated 39 cases of moyamoya disease. Eight patients (5 children and 3 adults) showed unilateral atypical findings of moyamoya disease, and the other 31 patients showed bilateral findings. Consequently, 70 abnormal sides (8 sides plus 62 sides) and 8 normal sides were analyzed.

**Methods**

The machine used in this study was a Magneton SP (Siemens) with a static magnetic field strength of 1.5 T. As a routine examination, we used the three-dimensional time-of-flight (3D TOF) technique with gradient motion refocusing. The parameters were as follows: repetition time (TR), 36 milliseconds; echo time (TE), 7 milliseconds; flip angle, tilted...
Comparison of Conventional Angiography and MRA

The standard for the staging of stenotic change based on conventional angiography has been established by Suzuki and Takaku.* Briefly, they classified this disease into six stages based on the findings of conventional angiography: (1) stenosis of the intracranial bifurcation of the internal carotid artery, (2) first appearance of moyamoya vessels (dilatation of the intracerebral arteries), (3) increase of moyamoya vessels (disappearing process of the middle and anterior cerebral arteries), (4) finer formation of moyamoya vessels (disappearing process of the posterior cerebral artery), (5) shrinking of moyamoya vessels, and (6) disappearance of moyamoya vessels and dominant appearance of collateral circulation only from the external carotid system.

However, most of the cases (not only in our study but also in most of the studies on moyamoya disease) were in stages 1, 2, 3, and 4. Therefore, three simple stages were used: normal or mild, which indicates a minimal stenotic change of the carotid fork (Suzuki's stage 1); moderate, which indicates obvious stenotic change (Suzuki's stage 2); and severe, which indicates a severe stenosis or nearly complete occlusion of the carotid fork (Suzuki's stage 3 or more). These three stages were also applied to the evaluation of MRA. The evaluation of findings of conventional angiography, MRA, and MRI was blindly done by the same readers in each case.

In general, the \( \chi^2 \) test was performed for statistical analysis. However, in this study all cases were diagnosed by the occlusive change seen by conventional angiography (according to the aforementioned criteria). Consequently, the comparison between conventional angiography and MRA in terms of the diagnosis of occlusive change of the carotid fork was impossible by the \( \chi^2 \) test, which needs a 2 x 2 table. Therefore, this was tested by the 95% confidence limits test.

Results

Evaluation of Occlusive Change of the Carotid Fork

Table 2 summarizes our results. Of 12 cases of mild stenosis diagnosed by conventional angiography, 9 cases (75%) were correctly evaluated by MRA and 3 cases were overestimated. Of 18 cases of moderate stenosis diagnosed by conventional angiography, 8 cases (44%) were evaluated correctly by MRA and 10 cases were overestimated. Of 48 cases of severe stenosis diagnosed by conventional angiography, 48 cases (100%) were evaluated correctly by MRA. Of a total of 78 side views (70 moyamoya, 8 normal [unilateral type]), 65 side views (83%) showed the same extent of stenotic change on both conventional angiography and MRA. Generally, there was a good correlation between MRA and conventional angiography. However, the 95% confidence limits were 0.75 to 0.91, as derived from 0.83+1.96 \( \sqrt{0.83(1-0.83)/78} \) (which did not reach 1 (100% of conventional angiography). This means that statistically MRA is inferior to conventional angiography with regard to occlusive change of the carotid fork.

Fig 1 illustrates a good correlation between MRA and conventional angiography. In this case, the mild stenotic change of the carotid fork revealed on conventional angiography was correctly disclosed on MRA.

There can be two types of poor correlation between conventional angiography and MRA: overestimation and underestimation. In cases of overestimation, MRA shows a stenotic lesion more severely than conventional angiography; in cases of underestimation the opposite occurs. As shown in Table 2, in our series there were no cases of underestimation, but of 78 side views, 13 (17%) showed overestimation on MRA.

Fig 2 illustrates a case of typical overestimation. On conventional angiography, the bilateral middle cerebral arteries were severely stenotic. On MRA, the right middle cerebral artery was severely stenotic, which

Table 2. Evaluation of Steno-Occlusive Change by Magnetic Resonance Angiography Compared With Conventional Angiography

<table>
<thead>
<tr>
<th>MRA</th>
<th>Conventional Angiography</th>
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<td></td>
<td>--</td>
</tr>
<tr>
<td>--</td>
<td>9</td>
</tr>
<tr>
<td>+</td>
<td>3</td>
</tr>
<tr>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Correct</td>
<td>9/12 (75%)</td>
</tr>
<tr>
<td>Overestimation by MRA</td>
<td>3/12 (25%)</td>
</tr>
</tbody>
</table>

MRA indicates magnetic resonance angiography: --, normal or mild stenotic change (Suzuki's stage 1); +, moderate stenotic change (Suzuki's stage 2); and ++, severe stenosis or occlusion (Suzuki's stage 3 or more) (see "Materials and Methods").

Magnetic resonance angiography (top) and conventional angiography (bottom) in a 10-year-old boy. Magnetic resonance angiography (top left, basal view; top right, anteroposterior view) shows severe stenosis of the right middle cerebral artery (MCA) and occlusion of the left MCA. Well-developed moyamoya vessels are clearly revealed. Conventional angiography (bottom left, right carotid; bottom right, left carotid) reveals severe stenosis of the right MCA and nearly complete occlusion of the left MCA. Well-developed basal moyamoya vessels are shown.

Correlated well with conventional angiography. However, the left middle cerebral artery was shown as almost occluded on MRA (overestimation).

Table 3 illustrates the difference between children and adults in the evaluation of steno-occlusive change. Overestimation was higher in adults than in children (22% versus 13%, respectively) in our study. However, there was no statistically significant difference between children and adults ($P = .3033$ by $\chi^2$).

**Evaluation of Moyamoya Vessels**

Small moyamoya vessels are not always opacified even in conventional angiography. As shown by Suzuki and Takaku4 and Suzuki and Kodama,5 in stages 1 and 2 the moyamoya vessels are not obvious. Table 4 summarizes the evaluation of moyamoya vessels by MRA, MRI, and conventional angiography. In our series (39 patients, 78 side views), moyamoya vessels were observed on conventional angiography in 70 side views (89%). Moyamoya vessels were observed in 38 of 46 side views (82%) in cases of childhood moyamoya disease. There was no statistically significant difference between MRA and conventional angiography in the evaluation of moyamoya vessels ($P = .0079$ by $\chi^2$). The evaluation of moyamoya vessels by means of MRA was significantly better in children than in adults ($P = .0454$ by $\chi^2$). Fig 1 illustrates a case of good visualization of moyamoya vessels.

Routine MRI was useful for the detection of moyamoya vessels. Fig 3 shows a typical MR image, in which moyamoya vessels are revealed clearly. Well-developed basal moyamoya vessels were shown as a small signal void on the axial T1 image and the coronal image (30/78 side views [38%]). However, in cases in which the moyamoya vessels were poorly developed, these signal voids were not easily seen on routine MRI. Therefore, regarding visualization of the moyamoya vessels, routine MRA was inferior to MRA in both children and adults ($P < .0001$ and $P = .0244$, respectively, by $\chi^2$).

**Discussion**

The diagnosis of moyamoya disease is particularly controversial in Japan, where its worldwide distribution shows an extraordinarily high rate of occurrence. Recently Goto and Yonekawa18 reported that of 4063 officially reported cases worldwide, 3000 cases (74%) were from Japan. In addition to this geographic feature, this disease has a specific age distribution, predomi-
nantly involving children.3-5 The Japanese government supports medical expenditures for patients with moyamoya disease by setting up special budgets and funding a research committee (the research committee on spontaneous occlusion of the circle of Willis of the Ministry of Health and Welfare). Accurate diagnosis of moyamoya disease is, therefore, important from the viewpoint of reasonable application of this budget and benefit for true patients. On the other hand, from the viewpoint of the parents (in the case of children), less invasive diagnostic methods than conventional angiography are both expected and appreciated.

The requirements for the diagnosis of moyamoya disease are (1) bilateral steno-occlusive change of the carotid fork and (2) development of moyamoya vessels (dilatated perforating arteries) and anastomosis via the external carotid artery system.1-3 These two pathological changes are not independent of each other, ie, moyamoya vessels are the collateral circulation (abnormally dilatated perforators of the basal ganglia) developed secondary to the stenotic change of the carotid fork.1-5 In other words, detection of the moyamoya vessels is the most important factor in the diagnosis of this disease and differential diagnosis. However, in the very early stage (stage 1) and advanced stages (stages 4, 5, and 6), these moyamoya vessels are difficult to detect even with conventional angiography.1-4

Table 3. Evaluation of Steno-Occlusive Change by Magnetic Resonance Angiography Compared With Conventional Angiography In Children and Adults

<table>
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<tr>
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<th>Children (≤15 y)</th>
<th>Adults (≥16 y)</th>
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<tr>
<td>Good correlation</td>
<td>40/46 (87%)*</td>
<td>25/32 (78%)*</td>
</tr>
<tr>
<td>Overestimation</td>
<td>6/46 (13%)</td>
<td>7/32 (22%)</td>
</tr>
<tr>
<td>Underestimation</td>
<td>0/42 (0%)</td>
<td>0/32 (0%)</td>
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P = .3033 (NS) by $x^2$ (a vs b).

Table 4. Evaluation of Moyamoya Vessels

<table>
<thead>
<tr>
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<th>Children (≤15 y)</th>
<th>Adults (≥16 y)</th>
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<tbody>
<tr>
<td>MRA</td>
<td>38/46 (83%)*</td>
<td>20/32 (63%)*</td>
</tr>
<tr>
<td>MRI</td>
<td>19/46 (41%)c</td>
<td>11/32 (34%)d</td>
</tr>
<tr>
<td>CA</td>
<td>41/46 (89%)*</td>
<td>29/32 (91%)*</td>
</tr>
</tbody>
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MRA indicates magnetic resonance angiography; MRI, magnetic resonance imaging; and CA, conventional angiography.

MRA children vs adults: $P = .0454$ (a vs b); MRA vs MRI: children, $P < .0001$; adults, $P = .0244$ (a vs c; b vs d); MRA vs CA: children, $P = $NS; adults, $P = .0079$ (a vs e; b vs f).
Many reports emphasize the usefulness of MRI and MRA in the diagnosis of moyamoya disease. Most are case reports that emphasize the dilated moyamoya vessels on MRI and MRA. Yamasaki et al analyzed 12 patients and concluded that 3D time-of-flight (TOF) MRA may have some value in following disease progression. As they demonstrated, more than 80% of suspected moyamoya disease patients can be diagnosed correctly by means of MRA. We also reported the usefulness of MRI in the diagnosis of moyamoya disease in children; some of the children in this study were included in that report. However, in our analysis of 39 patients it was shown that diagnosis of adult moyamoya disease by means of MRA is not always reliable because of poor visualization of moyamoya vessels, although typical moyamoya disease seen in children can be accurately diagnosed by MRA.

In cases of adult moyamoya disease, the stage is generally advanced compared with moyamoya disease in children. Therefore, the moyamoya vessels in adults are less apparent than in children. In addition, the image quality in older patients is inferior to that in younger patients, probably due to artherosclerotic change and turbulent flow, which induce overestimation of the steno-occlusive change. However, in cases of typical moyamoya disease, especially in cases of the bilateral type in children, MRA could disclose the steno-occlusive change of the carotid fork and typical moyamoya vessels, which are the indispensable requirements of diagnosis. As revealed in our study, the steno-occlusive changes of the carotid fork and basal moyamoya vessels were disclosed in most of the cases in children. Therefore, in typical clinical cases (namely, frequent transient ischemic attacks in children), MRA should be the first choice for examination. Other invasive examination techniques, such as conventional catheter angiography, are not necessary and should be avoided if these two findings are revealed on MRA.

MRA is still in its developing stage, and the study of this modality has technical limitations. More specifically, other techniques such as phase-contrast MRA, two-dimensional MRA, higher-resolution MRA, and other magnetic field strength machines (0.5-, 1.0-, and 2.0-T machines) have to be studied in regard to the diagnosis of moyamoya disease. For example, phase-contrast MRA can detect moyamoya vessels more clearly than TOF MRA if the velocity-encoding gradient is properly set.

Another important aspect of this disease is its hereditary tendency. As shown by Fukuyama et al and Yonekawa and Ogata, there is extensive evidence that this disease has a tendency for multifactorial inheritance. Therefore, screening tests for those in the high-risk group, ie, those who have a blood relative who is a moyamoya patient, are clinically important for preventing ischemic and hemorrhagic strokes. From this perspective, conventional angiography is too invasive for use as a screening test for asymptomatic high-risk groups, but MRA is an ideal modality, as shown in our study. In addition, the natural and postoperative courses of this disease are still controversial. First, do the ischemic groups mainly seen in children in fact become the hemorrhagic stroke groups mainly seen in adults? Second, can surgical treatments such as extracranial-intracranial bypass surgery, which is performed to prevent ischemic attacks in children, prevent hemorrhagic strokes by reducing moyamoya vessels? Noninvasive angiography is indispensable as a long-term follow-up to study these important issues. MRA is an ideal modality from this point of view.

MRA is not the perfect diagnostic procedure for moyamoya disease. However, if it is used correctly and evaluated accurately, taking into consideration its limitations, most cases of moyamoya disease can be diagnosed correctly. As a screening test for high-risk groups and long-term follow-up angiographic study, MRA is an ideal examination.

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References


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