Diagnostic Accuracy of Magnetic Resonance Angiography for Cerebral Aneurysms in Correlation With 3D–Digital Subtraction Angiographic Images

A Study of 133 Aneurysms

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Background and Purpose—We investigated the sensitivity of 3D–time of flight (3D-TOF) magnetic resonance angiography (MRA) in the detection of cerebral aneurysms with the use of 3D digital subtraction angiography as the gold standard. We also evaluated the effects of location and number of aneurysms (and experience of the reader) on the sensitivity.

Methods—3D-TOF MRA was performed in 82 patients with 133 cerebral aneurysms. Each patient underwent rotational angiography. Three-dimensional reconstructed images were obtained from data of the rotational angiography (as the gold standard). A blind study with 4 readers of different experiences was performed to evaluate the diagnostic accuracy of 3D-TOF MRA for cerebral aneurysms.

Results—One hundred five (79%) of all 133 aneurysms were detected with MRA by a neuroradiologist, 100 (75%) were detected by an experienced neurosurgeon, 84 (63%) were detected by a general radiologist, and 80 (60%) were detected by a resident neuroradiologist. For each reader, the detectability was lower for small aneurysms (<3 mm in maximum diameter) and/or for those located at the internal carotid artery and anterior cerebral artery. False-positive aneurysms were 29 for the neuroradiologist, 19 for the neurosurgeon, 31 for the general radiologist, and 30 for the resident neuroradiologist; most of the aneurysms were at the internal carotid artery. Causes of the false-positive and false-negative results included complex flow in a tortuous artery and susceptibility artifacts.

Conclusions—Although MRA is useful in the diagnosis of cerebral aneurysms, sufficient experience and careful attention are necessary for accurate diagnosis of aneurysms located at the internal carotid and anterior cerebral arteries. (Stroke. 2002;33:1803-1808.)

Key Words angiography, digital subtraction intracranial aneurysm magnetic resonance angiography

Subarachnoid hemorrhage (SAH) caused by ruptured cerebral aneurysm is frequently associated with poor outcome. The only approach that could prevent this outcome is to treat cerebral aneurysms before rupture. Magnetic resonance angiography (MRA) is a noninvasive technique for vascular imaging and is thus widely used to screen for intracranial vascular lesions. Previous studies have suggested that MRA could identify aneurysms measuring >3 mm in size with a high sensitivity of 74% to 98%. However, these studies used conventional digital subtraction angiography (DSA) as the gold standard. Recently, rotational DSA with 3D reconstructed images (3D-DSA) have emerged as a useful technique to visualize intracranial vascular lesions. Compared with the conventional DSA, 3D-DSA can detect intracranial aneurysms with greater levels of sensitivity and accuracy. In the present study, we determined the sensitivity of 3D–time of flight (3D-TOF) MRA in the detection of cerebral aneurysms by using 3D-DSA as the gold standard. We also evaluated the effects of several factors on the sensitivity of 3D-TOF, including location of the aneurysms, number of the aneurysms, and experience of the image reader.

Subjects and Methods

A total of 100 consecutive patients who underwent 3D-TOF MRA and 3D-DSA between January 1999 and December 2000 were enrolled in the present study. They included 64 women and 36 men ranging in age from 36 to 87 years (mean, 61.9 years), 36 with SAH and 64 without SAH. All patients with SAH underwent MRA within 3 days from the initial onset. The presenting clinical features of patients without SAH were ischemic stroke (n=32), headache (n=9), paralysis of oculomotor nerve (n=7), visual disturbances (n=6), intracranial hemorrhage (n=3), and medical checkup of the brain (n=7).
All MRAs were performed with the use of 1.5-T magnetic resonance equipment (VISERT H1, Toshiba) with the following parameters: repetition time 40 ms, echo time 6.8 ms, flip angle 20°, field of view 160 mm, volume thickness 52 mm, matrix 160×256, number of acquisitions 1, and acquisition time 10 minutes 2 seconds. Maximal intensity projection (MIP) reconstructions were performed at the time of imaging. The data were reconstructed around the head-to-foot axis and right-to-left axis. If necessary, target MIP reconstructions were performed.

All angiographic procedures were performed by using a DSA unit (Advantx LCN Plus, GE Medical Systems). Three-dimensional DSA images were produced by a Workstation (Advantage Workstation 3.1, GE Medical Systems) with the use of data from rotational angiographies. Rotational angiography was performed with a 200° rotation of the C arm in 5 seconds. The matrix size of each frame was 512×512 pixels. Fifteen to 25 mL of the contrast medium (iohexol, 300 mg/dL) was injected at a rate of 3 to 5 mL/s via a catheter positioned at the cervical portion of the carotid arteries and/or vertebral arteries. Both mask data and contrast data were automatically transferred to the workstation. Three-dimensional subtraction images were automatically produced on the workstation by a 3D-reconstruction algorithm based on the algebraic reconstruction technique. Reconstructed images, including MIP and shaded surface display were produced from the data. Minimum density threshold processing was automatically performed at the same levels. The maximum diameters of each aneurysm were calculated on the workstation.

Randomized MRA images were blindly interpreted by 4 readers who had different levels of experience: a neurosurgeon (NS, 20 years of experience), a neuroradiologist (NR, 12 years of experience), a general radiologist (GR, 11 years of experience), and a resident neuroradiologist (RR, 4 years of experience). On the first interpretation, all readers were blinded to clinical information. They rein-terpreted the same cases again 12 months later after being provided with clinical information and CT. Two other neuroradiologists retrospectively compared the MRA findings with those of 3D-DSA. First, they discussed and interpreted 3D-DSA and excluded patients without aneurysms. Then they assessed the sensitivity of detection of the cerebral aneurysms and recorded differences in the sensitivity due to reader experience, location and size of the aneurysms, and the presence or absence of SAH and differences in the first and second interpretations. Furthermore, in definitely detected aneurysms, they assessed the correlation between MRA and 3D-DSA findings with regard to the following parameters: maximum diameter, neck size, shape, relationship of the aneurysm and neighboring branches (involved or not), and the presence or absence of blebs. Causes of false-negative were also investigated. These differences in sensitivity due to each factor were subjected to statistical analysis. Differences based on readers and locations were tested by the Scheffe test. The Mann-Whitney test was used for analysis of differences in the detectability according to size, amount (single or multiple), and existence of SAH. The Wilcoxon signed rank test was used for analysis of differences in the detectability according to the first and second interpretations. The statistical level of significance was set at P<0.05.

Results

As the gold standard, 3D-DSA demonstrated 133 aneurysms in 82 patients included in the present study. Therefore, we excluded 18 patients in whom the aneurysms could not be detected by 3D-DSA. Cerebral aneurysm in 1 patient with SAH could not be detected by 3D-DSA. The aneurysms were located in the internal carotid artery (ICA, n=49), middle cerebral artery (MCA, n=35), anterior communicating artery (AcoA, n=25), anterior cerebral artery (ACA, n=14), basilar artery (BA, n=7), vertebral artery (n=1), posterior cerebral artery (n=1), and posterior inferior cerebellar artery (n=1). Thirty-five aneurysms were ruptured, and 98 were unruptured. The mean size of all aneurysms was 5.2 mm (range 0.5 to 25 mm), whereas that of ruptured aneurysms was 5.8 mm (range 1.5 to 17.6 mm). Of 35 ruptured aneurysms, 10 were <3 mm, 22 were 3 to 10 mm, and 3 were >10 mm in maximum diameter. On the other hand, the size of intact aneurysms ranged from 0.5 to 25.0 mm (mean 5.1 mm). Of 98 unruptured aneurysms, 30 were <3 mm, 61 were 3 to 10 mm, and 7 were >10 mm in maximum diameter.

The sensitivities of MRA in detection of cerebral aneurysms are demonstrated in Figures 1 to 6. The sensitivity in
Detection of aneurysms was 79% for NR, 75% for NS, 63% for GR, and 60% for RR (Figure 1). The difference in sensitivity between NR and GR was significant \( (P<0.05) \), as was the difference between NR and RR \( (P<0.05) \). With regard to aneurysm location, the sensitivity of all readers was lower in identifying aneurysms located at ICA (47% to 71%) and ACA (14% to 50%) than at other locations (Figure 2). Significant differences in sensitivity were noted between detecting ACA and MCA aneurysms by NS, GR, and RR \( (P<0.05, P<0.05, \text{ and } P<0.05, \text{ respectively}) \), ACA and posterior circulation by NS \( (P<0.05) \), ACA and ACoA by RR \( (P<0.001) \), and ICA and ACoA by RR \( (P<0.05) \). The sensitivity of all readers (38% to 55%) was significantly lower for small aneurysms (ie, those \( <3 \text{ mm in maximum diameter} \) than for large aneurysms (68% to 89%) (Figure 3, \( P=0.0001 \) for NS, NR, and GR and \( P<0.01 \) for RR). The sensitivity in detecting 10 ruptured small aneurysms \( (3 \text{ mm in maximum diameter}) \) was 60% for each reader. The sensitivity in detecting multiple aneurysms (51% to 73%) was significantly lower than that in detecting single aneurysms (77% to 90%) (Figure 4, \( P<0.05 \) for NS, \( P<0.05 \) for NR, \( P<0.05 \) for GR, and \( P<0.001 \) for RR). Sensitivity was lower in the detection of aneurysms with SAH (54% to 79%) than in the detection of aneurysms without SAH (65% to 79%) (Figure 5), albeit statistically insignificant \( (P=0.29 \text{ for NS, } P=0.98 \text{ for NR, } P=0.13 \text{ for GR, and } P=0.24 \text{ for RR}) \). Eighteen false-positive aneurysms were encountered by NS, 29 were encountered by NR, 31 were encountered by GR, and 30 were encountered by RR. The majority of false-positive aneurysms were located in the ICA.

At the second interpretation performed with clinical information made available, sensitivity in the detection of aneurysms was 79% for NR, 81% for NS, 67% for GR, and 74% for RR (Figure 6). The sensitivity significantly improved in RR \( (P<0.05) \) compared with the initial interpretation. In NS and GR, the sensitivity slightly improved, although it was statistically insignificant \( (P=0.059 \text{ for NS, } P=0.25 \text{ for GR}) \).

Diameters of the neck and dome measured on MRA were significantly correlated with the diameters calculated on 3D-DSA. The correlation coefficients of neck diameter and dome diameter, respectively, were 0.764 and 0.863 for NR and 0.764 and 0.886 for NS. The coincidence ratios of shape, relationship of the aneurysm and neighboring branches, and the presence or absence of blebs were 78% (73 of 93), 85% (79 of 93), and 77% (72 of 93) for NR and 74% (63 of 85), 55% (47 of 85), and 70% (59 of 85) for NS, respectively.

In retrospective analysis, 71% of the false-negative aneurysms were detectable. The causes of false-negative interpretations are listed in the Table. Thirty-one of 67 false-negative aneurysms were simply overlooked. Ten were caused by inhomogeneous signal intensity due to atherosclerotic changes or turbulent flow. Nine were not visible because of the small size, 6 were not distinguishable from a branch artery, and 5 were due to an overlapping of artery and aneurysm. The main factors that contributed to false-positive interpretations included tortuous origin of the branch, infundibular widening of the posterior communicating artery, and large and/or tortuous ACoA.

**Discussion**

The high sensitivity of MRA in the detection of cerebral aneurysms has already been reported.\(^7\)-\(^{15}\) MRA is ideal for screening cerebral aneurysms because the procedure is non-invasive and the patient is not exposed to radiation. The majority of previous studies used 3D-TOF MRA.\(^7\)-\(^{11}\) Ikawa et al\(^15\) reported that 3D-TOF MRA had a sensitivity higher than that of phase-contrast MRA (92.6% versus 70.4%, respectively). In a recent prospective study involving 23 aneurysms, however, contrast-enhanced MRA showed a sensitivity higher than that for 3D-TOF MRA (100% versus 96%,...
respectively). In the latter study, only 1 aneurysm was not detected by 3D-TOF MRA, which was of poor quality because of patient movement artifact. Furthermore, differences in diagnostic confidence in the presence of an aneurysm were not significant between contrast-enhanced MRA and 3D-TOF MRA. Other groups have reported that contrast-enhanced MRA of giant aneurysms is better than 3D-TOF MRA because such aneurysms have slow flow and are partially thrombosed. Because such aneurysms are not frequent and are detected only in cross-sectional images and because the cost of the examination is high, we used 3D-TOF MRA without contrast medium material in the present study. Previous studies have reported sensitivities of MRA in the detection of aneurysms ranging from 74% to as high as 98%. These reports have suggested that MRA allows the identification of the majority of cerebral aneurysms measuring ≥3 mm in size. The sensitivity in the present study was 60% to 79%, which is lower than the percentages reported in previous studies. Conventional DSA was used as the gold standard in previous studies. Small aneurysms can be overlooked on conventional DSA because of overlapping cerebral arteries. Recently, 3D-DSA has emerged as a useful technique for visualizing intracranial vascular lesions. Compared with the conventional DSA, 3D-DSA can detect intracranial aneurysms with greater levels of sensitivity and accuracy because it allows the examiner to observe cerebral arteries from any projection. The high detectability of cerebral aneurysms on 3D-DSA should affect the sensitivity reported in the present study. In clinical practice, however, a diagnostic study is usually observed by a single reader, whereas in some reports, the sensitivity in the detection of cerebral aneurysms was the result of examination by ≥2 readers, which could have resulted in a positive bias toward MRA.

Some authors have shown that sensitivity improved with combined readings of MIP and source images. In clinical practice, however, routine use of the source images may be difficult in some institutions because of the necessary time and cost.

In the present study, aneurysms of the ICA and ACA were difficult to detect with the use of MRA. Because of signal loss due to the saturation effect, detection of aneurysms in the distal ACA located at the margin of the slab may be difficult. Moreover, aneurysms of the ACA were often small. Flow signal loss at the siphon of the ICA is well known. In addition to flow signal loss, overlap of the artery and aneurysm, atherosclerotic changes in the parent artery, and turbulent flow will make detection of aneurysms at the ICA very difficult (Figure 7). On the other hand, aneurysms of the MCA and BA were easily detected. The relatively simple structure of the MCA and BA bifurcation is well evident on MRA.

The size of the aneurysms is one of the important factors affecting sensitivity. Aprile reported that the sensitivity of detecting aneurysms <3 mm in size (25%) was lower than that of aneurysms >3 mm (92%). In the present study, the sensitivity of detection of aneurysms >3 mm in size was 68% to 89%, and that of aneurysms ≤3 mm in size was only 38% to 55%. In agreement with previous reports, the results of the present study support the notion that the 3-mm size is a practical cutoff level for the detection of aneurysms. In this regard, several studies have reported that these small aneurysms are at less risk of rupture (0.05% to 0.7%). In our cases, 10 (25%) of 40 aneurysms, which were <3 mm in size, were ruptured. Detectability of these small ruptured aneurysms was 60% by each reader. Because of the lower sensitivity for small aneurysms, it is probably risky to use only MRA in patients with SAH (Figure 8).

### Causes of False-Negative Cases (n=67)

<table>
<thead>
<tr>
<th>Causes</th>
<th>n</th>
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<tbody>
<tr>
<td>Overlooked</td>
<td>31</td>
</tr>
<tr>
<td>Not visible (too small)</td>
<td>9</td>
</tr>
<tr>
<td>Atherosclerotic changes</td>
<td>7</td>
</tr>
<tr>
<td>Not distinguishable from branch</td>
<td>6</td>
</tr>
<tr>
<td>Overlapping of artery</td>
<td>5</td>
</tr>
<tr>
<td>Turbulent flow</td>
<td>3</td>
</tr>
<tr>
<td>Others</td>
<td>6</td>
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</table>
In patients with multiple cerebral aneurysms, the observers tended to be more watchful for large aneurysms, while overlooking coexistent smaller aneurysms, which were frequently <3 mm in size. One should be careful in examining MRA and search for >1 aneurysm because of the high frequency of multiple cerebral aneurysms.

A number of investigators have indicated that there is little or no difficulty in the identification of aneurysms irrespective of the presence of SAH.\textsuperscript{12,24} In the present study, the sensitivity of detecting aneurysms with SAH (54\% to 79\%) was slightly lower than that of detecting aneurysms without SAH (65\% to 79\%). In our retrospective analysis, we found no difficulty due to the signal intensity of the SAH and parenchymal hematoma in the detection of cerebral aneurysms with SAH. Therefore, the low sensitivity of detection of aneurysms with SAH may be due to motion artifact based on the often poor clinical condition of these patients.

With regard to interreader differences, the sensitivities of NR and experienced NS were higher than those of the others. This suggests that the experience of the observer is also an important factor in improving the sensitivity in the detection of cerebral aneurysms. In the second interpretation performed after providing relevant clinical information, sensitivity in the detection of aneurysms was significantly improved for RR (\(P<0.05\)). We believe that the improvement of detectability by RR depended not only on the availability of the clinical information but also on the improved experience of RR in diagnostic neuroradiology.

The morphological risk factors of rupture of cerebral aneurysms include size of the dome and location and presence of the bleb. Regarding the size of aneurysm (neck and dome), both MRA findings and 3D-DSA findings correlated well; however, detectability of the bleb was relatively lower (70\% to 77\%). Therefore, we believe that it is difficult to assess the angioarchitecture of aneurysms and predict the risk of aneurysm by MRA only.

We used MIP images in the present study. Recent developments in computed technology have included the availabil-
ity of 3D-reconstructed images of MRA within a relatively short time. These 3D magnetic resonance images will contribute to improvement in the detection of cerebral aneurysms. In conclusion, although MRA is a useful tool for the diagnosis of cerebral aneurysms, we consider that the actual sensitivity in the detection of cerebral aneurysms is lower than that described in previous reports. In this regard, experience and careful attention are important factors that could improve sensitivity and accurate detection of single and multiple cerebral aneurysms, especially those located at the ICA and ACA.

References
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