Comparison of Preperfusion and Postperfusion Magnetic Resonance Angiography in Acute Stroke

Salvador Pedraza, MD; Yolanda Silva, MD; José Méndez, MD; Luis Inaraja, MD, PhD; Joana Vera, MD; Joaquín Serena, MD, PhD; Antoni Dávalos, MD, PhD

Background and Purpose—The multimodal magnetic resonance imaging study in acute stroke includes perfusion-weighted imaging (PWI) after administration of contrast and magnetic resonance angiography (MRA). However, MRA may overestimate the degree of vessel obstruction caused by limitations to detect low flow states. Our aim was to determine the usefulness of a new fast imaging protocol combining classical MRA, PWI, and postperfusion MRA to improve the diagnostic management in acute ischemic stroke.

Methods—We studied 31 patients with a middle cerebral artery (MCA) infarction within the first 12 hours from the onset of symptoms. All patients had an MCA stenosis or occlusion. The study protocol included a preperfusion MRA and a postperfusion MRA. Modified thrombolysis in myocardial infarction (TIMI) classification was used to assess the patency of vessels.

Results—In 17 patients (group A, 55%), preperfusion MRA and postperfusion MRA accorded in the estimation of vascular status, whereas in 14 patients (group B, 45%) postperfusion MRA showed a better vascular flow than preperfusion MRA. The improvement in the depiction of flow was from a complete occlusion (TIMI I) to a partial occlusion (TIMI II) in 9 patients and from TIMI II to normal patency (TIMI III) in 5 patients. Thirty-six percent of the patients with suspected internal carotid artery occlusion in the preperfusion MRA showed flow in the intracranial internal carotid artery in the postperfusion MRA.

Conclusions—Postperfusion contrast-enhanced MRA can demonstrate arterial segments with low flow and avoid overestimation of vascular obstruction. (Stroke. 2004;35:2105-2110.)

Key Words: angiography ■ contrast media ■ magnetic resonance ■ myocardial infarction

The vascular assessment in the acute ischemic stroke can reveal the presence of a vascular occlusion or a normal patency caused by early recanalization of the vessel obstruction. The distinction is important because it has therapeutic and prognostic consequences. It has been reported that patients with complete occlusion of the distal internal carotid artery are unlikely to recanalize with intravenous thrombolytic therapy. In addition, patients with distal occlusion of internal carotid artery have worse prognosis compared with those with proximal middle cerebral artery (MCA) occlusion. The prognosis is especially poor when leptomeningeal collaterals are insufficient. The optimal magnetic resonance imaging (MRI) protocol in acute stroke includes diffusion-weighted imaging (DWI) to detect acute ischemic lesion, fluid attenuation inversion recovery to assess chronic lesions, magnetic resonance angiography (MRA) to detect vascular occlusion, and perfusion-weighted imaging (PWI) to estimate brain perfusion. The time of flight (TOF) is the most common MRA technique. However, TOF overestimates the severity of the arterial stenosis caused by the saturation of slow flow and therefore can produce a false diagnosis of vascular occlusion. This diagnostic uncertainty impedes the correct assessment of the hemodynamic status and falsely predicts a worse prognosis. Previous studies have shown that the use of MRA with contrast is an approach to clarify this uncertainty. The contrast shortens the T1 of blood, decreasing the saturation effects and improving the depiction of small vessels and blood–tissue differentiation, particularly in situations of slow flow. However, there are only a few studies on the value of MRA after contrast administration in the setting of acute stroke.

Our aim was to determine the usefulness of a new and fast imaging protocol combining preperfusion MRA and postperfusion MRA to improve the diagnostic management of acute ischemic stroke.

Materials and Methods

This is a secondary study of patients with acute hemispheric ischemic stroke admitted consecutively within the first 12 hours after
the onset of symptoms between July 2001 and December 2002. The primary aim of this still-ongoing prospective study is to investigate whether the molecular factors associated with early neurological deterioration correlate to the evolution of the DWI, PWI, and MRA abnormalities in the acute phase of territorial infarctions. Clinical exclusion criteria were coma on admission, pure lacunar syndromes, transient ischemic attack, previous cerebral infarction impeding the clinical and neuroradiological evaluation, and chronic severe diseases. For the purpose of this investigation, only patients with an acute MCA infarction associated with a vascular stenosis or occlusion of the MCA in the preperfusion MRA were studied. The ethics committee approved the study and written informed consent was obtained from all the patients or relatives before imaging.

**MRI Protocol**

All patients had a MRI study on admission within the first 12 hours after stroke onset. MR images were obtained on a 1.5-T system (Intera, Philips) with echoplanar capabilities of 25-mTses/m and 300- to 350-μsec rise times. The MRI protocol included DWI, fluid attenuation inversion recovery, preperfusion MRA, PWI with gradient-echo echo-planar technique, and postperfusion MRA sequences. The PWI sequence was obtained with a single-shot spin-echo planar pulse with a diffusion gradient b-value of 0 and 1000 s/mm² along 3 axes. The other parameters were 20 slices, 7-mm slice thickness, 0 gap, 134 ms echo time (TE), 6000 ms repetition time (TR), 67 (epi factor), and 36 seconds of duration. Abnormalities were analyzed in the trace image to avoid anisotropy. The PWI sequence was acquired after administration of 0.2 mL per kilogram of gadolinium DTPA with a bolus technique (5 mL/sec). The parameters were 260, 30 (TR/TE), 12 slices of 10-mm slice thickness, 0 gap, 60 dynamic scans, and 1 minute and 4 seconds of duration. The volume of hypoperfused tissue was measured in the mean transit time map using a threshold of 4 seconds. A secondary analysis was performed using a threshold of 6 seconds.

Preperfusion MRA was performed before PWI and postperfusion MRA was performed immediately after the end of the PWI without the administration of a supplementary dose of contrast. That means that postperfusion MRA was performed 1 minute and 4 seconds after the administration of contrast. While the post-perfusion MRA was being performed, the quality of the PWI maps were checked. Preperfusion and postperfusion MRA were performed using conventional parameters when we did not have any time pressure to administer specific therapies, and when patients were still. We used this high-quality TOF sequence to examine the Circle of Willis and cranial and cervical ICA to rule out the presence of ICA occlusion. The imaging parameters were 18/6/9/20 (TR/TE/flip angle), 230 field of vision, 256×256 matrix, 1 slab with 200 slices, 0.6-mm slice thickness, and tilted optimized nonsaturating excitation pulse. The acquisition time was 6 minutes and 14 seconds. In candidates for thrombolytic therapy and in restless patients, preperfusion and acquisition time was 6 minutes and 14 seconds. In candidates for thrombolytic therapy and in restless patients, preperfusion and acquisition time was 1 minute and 41 seconds. We performed preperfusion and postperfusion MRA using the same location and coverage regarding the MCA territory. In a group of patients first studied with the longer TOF sequence, the faster sequence was subsequently and immediately performed to explore the concordance between the 2 types of TOF sequences in the preperfusion MRA.

After the MRI, a cranial and cervical duplex sonography study was performed. Catheter angiography was not used in this study. A neuroradiologist (S.P.) who was blinded to the clinical and ultrasonographic findings and stroke outcome evaluated the degree of vascular stenosis. Modified thrombolysis in myocardial infarction (TIMI) classification was used to assess the patency of MCA. We considered 3 degrees of vascular status: (1) complete occlusion (TIMI grade I) defined as the absence of opacification of the distal vessels or distal flow; (2) partial occlusion (TIMI grade II) defined as an obstruction with opacification of the distal vessels with delayed or slow-flow signal; and (3) complete recanalization (TIMI grade III). Defined as unimpeded perfusion of the distal vasculature, regardless of whether a residual proximal stenosis or a normal proximal flow was present. To avoid MRA contrast limitations such as venous enhancement and differentiation with collateral circulation, we used a 3-step strategy. First, we performed a modified maximum intensity projection (MIP) of the postperfusion MRA erasing the cavernous sinus, transverse sinus, and nasal mucous. Second, we compared the MIP of the preperfusion MRA with that of the postperfusion MRA. Third, we compared the source of images of preperfusion and postperfusion MRA.

PWI and DWI volumetric analysis were performed with a manual segmentation method. First, the perimeter of the area of abnormal signal intensity was traced on each DWI and PWI map and, subsequently, the volumetric software estimated the total volume using the thickness and the traced area on each slice. The window level and window width were chosen to obtain the best contrast between the lesion and the normal surrounding tissue. Each volume calculation was performed 3 times, and the mean value was taken as definitive. The mismatch volume was defined as the difference between the volumes of diffusion and perfusion abnormalities. We considered the existence of a significant mismatch when this volume was higher than 20% of the volume of the diffusion abnormality.

**Clinical Assessment**

A certified neurologist evaluated stroke severity by using the National Institute of Health Stroke Scale (NIHSS) score on admission. We recorded whether the patient received thrombolytic treatment with recombinant tissue plasminogen activator (rt-PA) before or after the MRI study.

**Statistical Analysis**

Categorical variables are presented in percentages, and continuous variables are presented as mean±SD or median (quartiles), depending on their normal distribution or not. Continuous variables were compared between 2 groups with the Student t test or the Mann–Whitney test as appropriate. Proportions were compared with the Fisher exact test. P<0.05 was established as statistically significant.

**Results**

From an initial series of 55 patients with acute stroke, 31 had an acute MCA infarction and vascular stenosis or occlusion of the MCA in the preperfusion MRA. Twenty-four patients were excluded because of the absence of contrast administration (n=5), absence of ischemic lesion in the MCA territory (n=4), or absence of vascular stenosis in the MCA (n=15).

Eight patients were studied between 0 to 3 hours, 18 patients between 3 to 6 hours, and 5 patients between 6 to 12 hours after symptoms onset. Table 1 shows the concordance between preperfusion MRA and postperfusion MRA regarding vascular patency. We classified patients in 2 groups: group A (n=17) patients who showed the same vascular patency in MCA in both studies (Figure 1) and group B (n=14) patients who showed a better depiction of flow in
postperfusion MRA than in preperfusion MRA (Figure 2). Group A included 4 patients with unchanged MCA occlusion but with a better depiction of flow in ICA (2 patients) or posterior cerebral artery (PCA) (2 patients) after contrast. Seventeen patients were studied with the shorter MRA technique, 10 in group A and 7 in group B ($P=0.11$). In the group of 10 patients in whom the longer and the shorter preperfusion MRA techniques were sequentially used, we did not find any difference between them on TIMI classification. Postperfusion MRA disclosed prominent venous signal in all patients; however, in 90% of them MIP improved qualitatively the arterial detail over the venous background.

Six patients were treated with intravenous rt-PA before the MRI study, 1 in group A and 5 in group B ($P=0.08$), and 6 patients were treated with intravenous rt-PA after the MRI study, 3 in group A and 3 in group B. One patient was treated with desmoteplase/placebo after the MRI study in group B.

There were no differences in age, sex, time from symptoms onset to MRI, initial NIHSS, PWI lesion volume, and in the frequency of PWI/DWI mismatch between the 2 groups (Table 2). Patients in group B had, however, a nonsignificant lower proportion of MCA occlusion ($P=0.06$) and smaller DWI lesion volume ($P=0.16$). Combined MCA and intracranial ICA occlusion in preperfusion MRA was found in 9 patients (53%) of group A and in 5 patients (36%) of group B ($P=NS$). Duplex sonography showed ICA cervical occlusion in all cases. However, postperfusion MRA showed a normal flow in the intracranial ICA with persistent MCA occlusion in 2 patients of group A and a normal flow in the intracranial ICA and MCA in 3 patients of group B. Consequently, 36% (5/14) of the patients with suspected intracranial ICA occlusion in the preperfusion MRA showed flow in
the postperfusion MRA (Figure 3). In patients without intracranial ICA occlusion in the postperfusion MRA, PWI lesion volume was also comparable between the 2 groups (144 mL [5, 174]) (median [lower quartile, upper quartile]) in group A and 111 mL (85, 147) in group B, \( P = 0.81 \). When the PWI lesion volume was calculated using the threshold of 6 seconds, we obtained similar results.

**Discussion**

This study shows that a new fast combined protocol with postperfusion MRA is useful in the diagnosis of vessel patency in acute ischemic stroke. Nearly half of the patients studied within 12 hours with an MCA stenosis or occlusion in the preperfusion MRA showed a better depiction of MCA flow in the postperfusion MRA. To our knowledge, there are no previous references about the use of MRA after PWI.

We have not found clinical or neuroimaging factors associated with a lack of agreement between preperfusion and postperfusion MRA, except a nonsignificant higher proportion of rt-PA treatment before the MRI study in group B and a lower initial DWI volume in group B. Furthermore, PWI lesion volume was comparable between groups, either in the total number of patients or in the subgroup without true ICA occlusions. Although we have studied a limited number of patients, our findings support the notion that integrated information from preperfusion MRA and PWI is not suitable to rule out or suspect an overestimation of vascular obstruction in patients with low flow.

Postperfusion MRA may have therapeutic consequences.\(^1\)\(^-\)\(^7\) In this study, 36% of patients showing an intracranial ICA occlusion in the preperfusion MRA had an overestimation of vascular obstruction, because the intracranial segment of the ICA was patent in the postperfusion study. After rt-PA treatment, ICA occlusion has a lower proportion of recanalization (31%) compared with MCA occlusion (88%).\(^4\) In this context, the occlusion of the ICA without MCA patency has been proposed as a relative exclusion criteria for thrombolysis in acute ischemic stroke.\(^1\)\(^,\)\(^2\) Following this criteria, preperfusion MRA findings might erroneously prevent the administration of intravenous rt-PA in more than one third of patients with suspected intracranial ICA occlusion, which, in this study, represented 10% of the studied population. Further studies must address the issue of therapeutic implications of postperfusion MRA.

Previous studies performed in subacute stroke and not using PWI have shown the usefulness of contrast administration to improve the depiction of intracranial vessels.\(^10\) Yano et al found that MRA with contrast improved the detection of distal MCA branches in 61% of the patients, and that 30% of the branches of MCA became visible only after contrast.\(^11\) Other reports have shown that after the administration of contrast, the depiction of flow in MRA changes from apparent occlusion to normal pattern in 17% of patients and in 7% of vessels.\(^5\)\(^,\)\(^13\) The present study further demonstrates the usefulness of a new acute imaging protocol, performing MRA after PWI without the administration of a supplementary dose of contrast. The proposed protocol does not increase the cost or the length of the study, because the standard dose of contrast is used and the postperfusion MRA is performed while the qualities of the perfusion maps are checked.

MRA in acute stroke should follow 2 essential requirements. First, postperfusion MRA must be performed immediately after PWI because of the short half-life of gadolinium DTPA (10 minutes).\(^11\) Second, in acute stroke, MRA sequence must be short and fast to not delay the treatment and management of the patient. Several authors have proposed some strategies to improve the sensitivity of the postperfusion MRA technique, such as the infusion of higher doses of contrast, different flip angle, different TR,\(^11\)\(^,\)\(^16\) and different tilt of the slab.\(^13\) However, the present findings show that MRA after PWI with a standard dose of contrast, using the same parameters as in the classical MRA, is more helpful

**Table 2. Clinical and MRI Findings in the 2 Groups at Baseline**

<table>
<thead>
<tr>
<th></th>
<th>Group A (n=17)</th>
<th>Group B (n=14)</th>
<th>( P )</th>
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<tbody>
<tr>
<td>Age</td>
<td>67.6±12 0.7</td>
<td>67.2±12.0</td>
<td>0.924</td>
</tr>
<tr>
<td>Sex, male</td>
<td>47%</td>
<td>57%</td>
<td>0.72</td>
</tr>
<tr>
<td>Time from symptom onset</td>
<td>240 (186, 310)</td>
<td>238 (165, 344)</td>
<td>0.95</td>
</tr>
<tr>
<td>Initial NIHSS score</td>
<td>17 (10, 20)</td>
<td>15 (7, 19)</td>
<td>0.40</td>
</tr>
<tr>
<td>Initial volume in DWI, mL</td>
<td>22.5 (124)</td>
<td>8 (6, 25)</td>
<td>0.16</td>
</tr>
<tr>
<td>Initial volume in PWI, mL</td>
<td>164 (23, 180)</td>
<td>100 (33, 135)</td>
<td>0.26</td>
</tr>
<tr>
<td>PWI/DWI mismatch</td>
<td>10 (59%)</td>
<td>8 (57%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Thrombolysis before MRI</td>
<td>1 (7.7%)</td>
<td>5 (35.7%)</td>
<td>0.08</td>
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**MCA Occlusion**

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
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</thead>
<tbody>
<tr>
<td>Preperfusion MRA</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>Postperfusion MRA</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>

**MCA Stenosis**

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
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</thead>
<tbody>
<tr>
<td>Preperfusion MRA</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Postperfusion MRA</td>
<td>1</td>
<td>9</td>
</tr>
</tbody>
</table>

**ICA Occlusion**

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preperfusion MRA</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Postperfusion MRA</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>
show the patency of distal vessels not seen in the preperfusion study.

The present study has other limitations. First, we used 2 different types of TOF sequences depending on the collaboration of the patient at the acute setting and on the time pressure. However, the comparison of both techniques sequentially performed in a small group of patients did not show differences in the estimation of TIMI degree, so we think this fact did not influence our findings. Second, we cannot completely rule out an overestimation of false MCA occlusions in this series because of the more frequent use of intravenous thrombolysis before MRA in group B. Although the time between preperfusion and postperfusion MRA was too short to suspect a recanalization between the 2 examinations, we cannot rule out in some patients with overestimated MCA occlusions in the preperfusion MRA that the better flow in the postperfusion MRA could be related to the rt-PA treatment. A further point of interest is that postperfusion MRA results cannot be fully translated into meaningful information on blood supply of the tissue, because PWI lesion volume was comparable in patients with and without overestimation of ICA and/or MCA obstructions. This finding indicates that most overestimated obstructions reflect an extremely low flow (in many instances caused by ICA proximal occlusions) insufficient to provide a significantly better tissue perfusion status in comparison with true arterial obstructions.

The data presented show that precontrast MRA overestimates the degree of vascular obstruction. Postperfusion contrast-enhanced MRA can demonstrate arterial segments with low flow and avoid overestimation of vascular occlusion. Although this information may be crucial for patients eligible for reperfusion therapies, a PWI study is necessary to obtain comprehensive information on tissue perfusion.

Acknowledgments

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References


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