Contrast-Enhanced Three-Dimensional Magnetic Resonance Angiography of Atherosclerotic Internal Carotid Stenosis as the Noninvasive Imaging Modality in Revascularization Decision Making

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Background and Purpose—In patients with severe internal carotid artery stenoses, thromboendarterectomy significantly reduces both ischemic stroke and the risk of more ischemic attacks. Digital subtraction angiography (DSA) is the accepted preoperative test to determine whether a high-grade stenosis is present and requires surgical therapy. However, DSA has a procedural risk of stroke between 0.7% and 1%. An accurate, noninvasive imaging protocol with no risk of severe complications would significantly increase the benefit of surgical treatment. The aims of the study were (1) to evaluate the diagnostic accuracy of contrast-enhanced magnetic resonance angiography (CEMRA) in detecting and grading internal carotid artery stenoses and (2) to assess the misclassification rate of vessels suitable for revascularization by CEMRA.

Methods—Ninety-two patients with sonographic evidence of neck vessel stenosis were enrolled in the study. All patients were submitted to CEMRA and DSA. CEMRA images were evaluated for the presence of mild, moderate, or severe stenosis and occlusion.

Results—Sensitivity, specificity, and diagnostic accuracy were 97%, 82%, and 92.5%, respectively. Agreement with DSA was optimal at \( \kappa = 0.87 \). The misclassification rate of CEMRA was 3.1% because of its tendency to overestimate the stenosis.

Conclusions—The high diagnostic accuracy and limited misclassification rate suggest that CEMRA can be considered a powerful tool for the preoperative, noninvasive evaluation of atherosclerotic pathology of carotid arteries. (Stroke. 2003; 34:660-664.)

Key Words: carotid arteries ▪ carotid endarterectomy ▪ comparative study ▪ magnetic resonance angiography

Ischemic stroke is a major healthcare problem, and the social cost of treatment of survivors is extremely high. In high-grade (a)symptomatic internal carotid artery (ICA) stenosis in which the stenosis exceeds 70% of the lumen, the efficacy of thromboendarterectomy has proved itself effective by significantly reducing the risk of more ischemic attacks.\(^1,2\) Recently, the North American Symptomatic Carotid Endarterectomy Trial Collaborators (NASCET) demonstrated surgical benefits for selected patients with stenoses as low as 50%.\(^2\)

Currently, digital subtraction angiography (DSA) is considered the gold standard in detecting and grading carotid stenosis, but the procedural risk of stroke for this method is 0.7% to 1%.\(^3\) Thus, a more accurate imaging protocol with no severe complications would significantly increase the benefit of surgical treatment. For this reason, new and noninvasive diagnostic tools such as spiral CT, enhanced magnetic resonance angiography (MRA), and color Doppler ultrasound were developed. Among these techniques, classic MRA, based on signal properties of moving blood, is frequently used in the assessment of neck vessels. Sensitivity of MRA in detecting carotid stenosis ranges between 75% and 100%; specificity ranges between 59% and 99%.\(^4,5\) The main pitfall of this technique remains the overestimation of high-grade stenosis resulting from intravoxel phase dispersion in cases of turbulent flow.\(^6\) The advent of contrast-enhanced MRA (CEMRA) has dramatically improved the diagnostic accuracy of MRA in many vascular areas.\(^7\) CEMRA technique is based on shortening of blood T1 when a bolus of paramagnetic contrast media is infused.\(^7\) The introduction of high-perf-
mance gradients allowed rapid acquisition in an attempt to image the first passage of paramagnetic contrast media in the arteries. Promising results have been reported by several authors in evaluations of supraortic vessels, especially in cases of carotid pathology also with medium-field MR equipment.

The role of preoperative, noninvasive examinations in surgical decision making is currently debated. At the moment, no studies concerning the use of CEMRA in the revascularization decision making are available. Thus, the aims of this study were (1) to evaluate the diagnostic accuracy of CEMRA in detecting and grading ICA stenoses and (2) to assess the misclassification rate of vessels suitable for revascularization by CEMRA.

Methods

Patients

Ninety-two patients (71 men, 21 women; mean age, 66.5±10 years; range, 45 to 82) with clinical and ultrasound evidence of carotid artery stenosis were enrolled in the study. Forty-five were affected by an acute or subacute nondisabling ischemic stroke; 42 had transient ischemic attack; and 5 were asymptomatic. All patients underwent MRA in addition to conventional angiography with DSA technique, and written consent to diagnostic and eventual therapeutic procedures was given previously.

Contrast-Enhanced Magnetic Resonance Angiography

CEMRA was performed with a superconductive GE High Speed Horizon 1.5-T system with high-performance gradients (maximum gradient strength, 40 mT/m; slew rate, 150 mT/m ms). CEMRA was obtained with a 3-dimensional (3D) fast spoiled gradient echo acquisition in the oblique coronal plane (repetition time, 5.7; echo time, 1.6 ms; flip angle, 30°; number of excitations, 0.5; matrix size, 192×256; zero filling in slice and frequency direction; bandwidth, 62.5 kHz; thickness, 1.8; partitions, 40; field of view, 24 cm; a dedicated phased-array neurovascular coil). A 30-mL dose of Gd-DTPA was injected intravenously with an MR-compatible (Spectris MEDRAD) power injector at a flow rate of 2 mL/s. Scan delay was automatically calculated by placing a navigator echo in the aortic arch with a smart preparation technique. The CEMRA image data set was transferred to a dedicated workstation (Advantage Window 4.0). The images, which were reformatted with a maximum-intensity projection algorithm and multiplanar volume reconstruction, were evaluated by 2 independent radiologists. A third radiologist evaluated DSA results. The reduction in vessel lumen was measured with the NASCET criteria and classified as mild, moderate, or severe corresponding to <50%, between 50% and 70%, and >70%, respectively. Occlusion was assessed when no lumen was visible. The indication for endarterectomy was based on clinical and radiological criteria as recommended by guidelines for carotid endarterectomy.

An ICA stenosis >70% was considered a surgical indication in symptomatic and asymptomatic patients; in selected symptomatic patients, a surgical approach was proposed in patients with stenosis >50%. The endovascular treatment was performed in patients with a stenosis >70% who could not be submitted to a surgical procedure because of a poor general condition.

The presence of ICA occlusion, severe tandem stenosis of ICA, and associated common carotid artery occlusion or severe stenosis was considered a radiological contraindication to a revascularization. The misclassification rate was determined as the difference between the number of vessels identified for revascularization by DSA and CEMRA normalized to the total number of vessels studied.

Comparison of CEMRA and DSA Results

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEMRA</td>
<td>45</td>
<td>2</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>DSA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>23</td>
<td>33</td>
<td>66</td>
<td>20</td>
</tr>
</tbody>
</table>

Digital Subtraction Angiography

Within 1 month of the CEMRA evaluation, all patients underwent DSA with selective catheterization of carotid arteries with a 5F Headhunter catheter and 100 mL iodinate contrast.

Statistical Analysis

Sensitivity, specificity, positive and negative predictive values, and accuracy of CEMRA for detecting and grading of ICA stenoses were calculated, with DSA considered the gold standard. Agreement between CEMRA and DSA and intraobserver and interobserver variability were calculated by use of Cohen’s k statistic. k Values between 0.4 and 0.8 indicated a moderate agreement; values >0.8 were considered excellent; and a perfect value was 1.

Results

Feasibility and Safety

No minor or major side effects occurred during or after MR examination or after contrast media injection. The quality of CEMRA examinations was good in all examined patients. In 2 cases, CEMRA was repeated for the presence of a ringing artifact. Image quality worsened in 10 patients because of a venous overlapping and in 3 others because of motion artifacts resulting from patient movement; these problems were solved after maximum-intensity projection algorithm reconstruction. All evaluated arteries were completely visualized by CEMRA with a feasibility of 100%.

Diagnostic Accuracy of CEMRA

DSA showed 66 severe stenoses: 33 moderate, 23 mild, and 20 occlusions (4 tandem stenoses of the ICA petrous tract were associated with bifurcation stenosis). Seventy ICA stenotic lesions were graded as severe, 29 as moderate, 21 as mild, and 21 as occlusions by CEMRA. A comparison between CEMRA and DSA results is reported in the Table. Sensitivity, specificity, and accuracy were 97%, 82%, and 92.5%, respectively; positive and negative predictive values were 93% and 92%. There was excellent agreement between the results of CEMRA and DSA for ICA (κ=0.87).

Of the 6 severe stenoses with a string sign on DSA, 5 were detected with CEMRA. Of the 17 ulcerated plaques on DSA, 15 were correctly detected by CEMRA. Intraobserver and interobserver agreement was 0.94 and 0.90.

Misclassification Rate of CEMRA

Forty-eight patients were submitted to revascularization. Within the group of revascularized patients, 44 had radiological indication of revascularization (ICA stenosis of >70%).

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whereas 4 showed stenoses between 50% and 70% but were symptomatic with ulcerated plaque and thus candidates for revascularization. Thirty-three patients were submitted to endarterectomy; 12 were treated with internal carotid stenting and 3 with percutaneous transluminal angioplasty. Within the group of patients revascularized because of a DSA radiological finding, CEMRA recommended revascularization in all but 1 patient who had a subocclusion of ICA that was misinterpreted as an occlusion. In the group of operated patients with symptomatic stenosis of <70%, CEMRA overestimated 1 case of moderate stenosis as severe, giving radiological results leading to revascularization, but there was only a clinical indication. In the group of medically treated patients, CEMRA recommended an unnecessary revascularization in 4 patients in whom moderate stenoses on DSA were overestimated as severe. The misclassification rate of CEMRA was 3.1%. The reasons for misclassification were overestimation of 5 stenoses of <70% and 1 misclassification of a preocclusive ICA as occlusion. Other radiological contraindications to revascularization were not documented. All 4 tandem stenoses of the ICA petrous tract were correctly detected with CEMRA.

Discussion

A recent meta-analysis identified the need for further clinical evidence to establish the effectiveness of MRA in diagnosing ICA stenosis and in making decisions about revascularization. In this study, CEMRA was evaluated as a highly safe, feasible tool for assessing patients with suspected carotid atherosclerosis, showing high accuracy and agreement with DSA in detecting and grading ICA stenosis (Figure 1). Although CEMRA tends to overestimate stenosis severity, the misclassification rate of stenosed vessels considered radiologically suitable to revascularization was low.

The relative low specificity revealed a trend for CEMRA to overestimate stenosis severity (Figure 2). A main cause of overestimation is the incorrect timing of contrast peak in respect to the central k-space data collection, which is an intrinsic limitation of CEMRA. During CEMRA acquisition, variation in infusion timing is known to affect the relative degree of arterial enhancement. The center of k space (low spatial frequencies) contributes to image contrast, whereas the periphery of k space (high spatial frequencies) contributes to smaller details. Maximum arterial signal intensity with a minimum of artifact occurs when the infusion is timed so that the acquisition of the central portion of k space coincides with the peak arterial gadolinium concentration. In clinical practice, if the center of the k space is not collected during the arterial peak, artifacts can lead to an overestimation of the vessel diameter and ringing widening of the apparent lumen.

The CEMRA technique is based on T1 shortening when a bolus of paramagnetic contrast media is infused. This procedure was initially considered not influenced by inflow effects, but recently, intravoxel dephasing was induced by velocity. In clinical practice, this type of artifact has a limited role, and with the currently applied voxel size, the reduction in voxel volume translates to sharper vessel margins. Signal loss caused by T2* dephasing was noted in a study of subclavian arteries when the subclavian vein was near or immediately under the artery and was demonstrated to be a susceptibility effect of the high concentration of gadolinium. In high-grade ICA stenoses, a theoretical component of T2* dephasing resulting from the high gadolinium concentration can help explain the total signal loss in the
string vessel stenosis. However, despite these technical considerations, CEMRA overestimation was reduced compared with rotational angiography.\textsuperscript{23} The 3D approach and the high number of projections available with CEMRA are comparable to the projections of rotational angiography instead of the 3 classic projections of conventional DSA. In our experience, 2 patients with high-grade stenosis of ICA needed accurate evaluation of the conventional angiogram because the stenosis was not easily identifiable, whereas multiplanar volume reconstruction of an MRA data set allowed easier, more confident detection of the high-grade stenosis (Figure 3). Moreover, CEMRA was effective in detecting preclusive stenoses, which are difficult to recognize with other noninvasive techniques,\textsuperscript{24} and ulcerated plaques. The capability of CEMRA to assess plaque morphology can be useful in identifying complex plaques that have high ischemic potential and a tendency to rupture independently of their size.\textsuperscript{25}

There are doubts about the potential role of CEMRA in clinical decision making.\textsuperscript{26} Recently, Johnstone and Goldstein\textsuperscript{27} showed that the misclassification rate of patients as candidates for revascularization of ICA stenosis was 18\% for MRA, which was reduced to 7.9\% when MRA was used in association with ultrasound. It is important to note that only 1\% of MRA studies was performed with contrast-enhanced technique. In our study, CEMRA was applied in all patients, and the misclassification rate of arteries suitable for revascularization was low. The only misclassification was overestimation of stenosis severity; 1 preclusion was considered occluded, and 5 moderate stenoses were considered severe. However, one of these severe stenoses was revascularized because it was ulcerated and symptomatic. Furthermore, CEMRA was effective in identifying tandem stenosis of the ICA petrous tract, a frequent misclassification by other noninvasive techniques.\textsuperscript{28} This is due to the panoramic imaging capability of CEMRA that can identify stenosis from the common carotid origin to the intracranial ICA segments.\textsuperscript{29}

A limitation of the study was the biased selected population with a high pretest probability of ICA stenosis because CEMRA was used in most patients as a second-level technique to confirm the ultrasound evidence of stenosis. There is general accordace that DSA is not necessary when there is concordance between these noninvasive methods;\textsuperscript{20} thus, patients without noninvasive evidence of ICA stenosis were automatically excluded. Because of the high diffusion of color Doppler ultrasound equipment and the low costs, color Doppler ultrasound remains the method of choice in the first evaluation of carotid stenosis. The misclassification rate of noninvasive techniques combining color Doppler ultrasound and CEMRA results was not evaluated, so further studies are necessary to assess that rate. However, state-of-the-art MRA, ie, with contrast enhancement and 3D reconstruction, has high diagnostic accuracy in the evaluation of atherosclerotic pathology of the ICA with excellent agreement with DSA in grading stenosis severity and thus can be used as a noninvasive diagnostic tool for planning revascularization of stenosed carotid arteries.

References


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